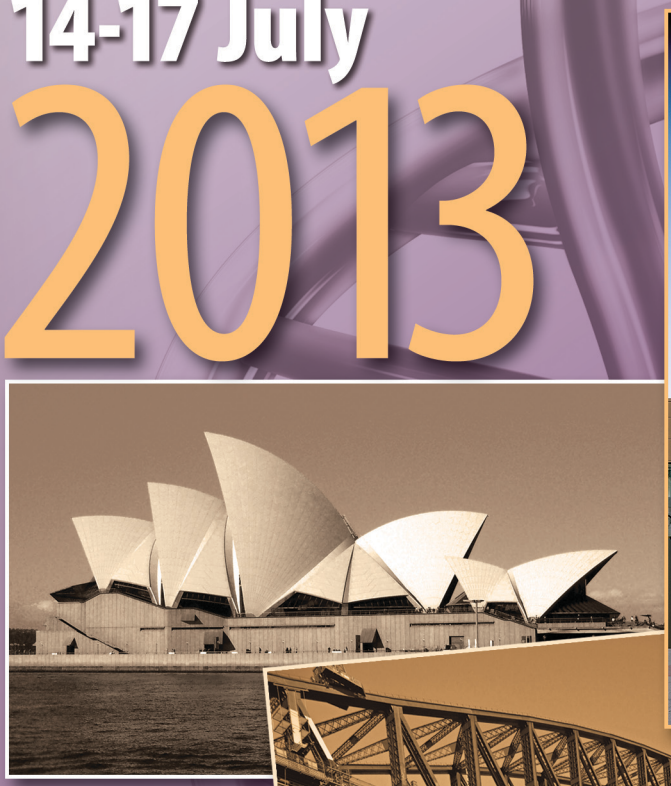
GSA
Genetics Society of AustralAsia Inc.

Annual Conference Sydney

Genetics in the Harbour City

14-17 July

2013



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Mathematics of Planet Earth 2013 AUSTRALIA

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Contents

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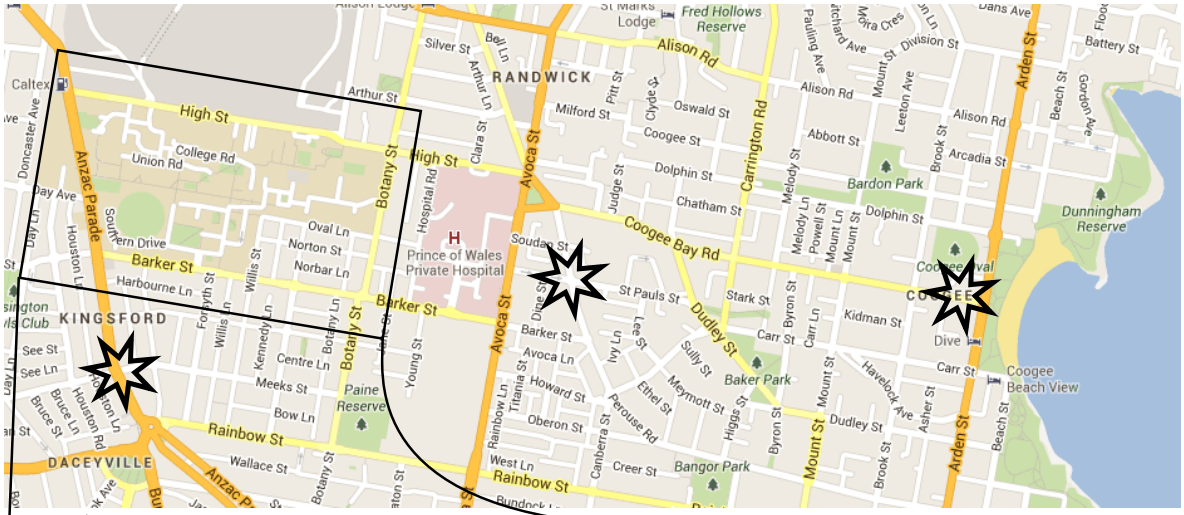
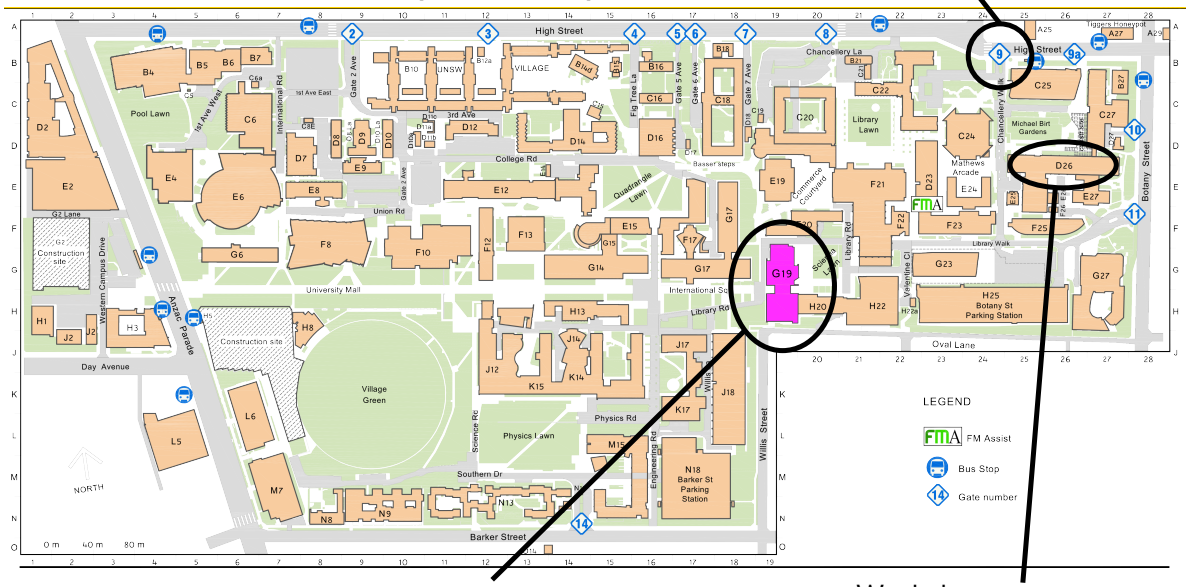


UNSW Campus map



The main conference venue is the John Niland Scientia Building (G19) at the Kensington Campus of the University of NSW. Maps of the campus showing the location of the Scientia Building are available at http://www.facilities.unsw.edu.au/getting-uni/campus-maps. The building is located near the centre of the campus and is within easy walking distance of public transport on Anzac Parade.

All of the conference presentations and poster sessions will be held in various rooms in the Scientia Building. Plenary sessions will be held in Leighton Hall, and other sessions will be held in the Tyree Room or the Galleries. The precise location of each session is detailed in the conference program. The welcome reception and all lunches will be in the main foyer of the Scientia Building. Poster sessions will be held in the Galleries.

The BEAST and GenAIEx workshops on Sunday July 14 will be held in computer labs G08 and G11 on the ground floor of the Biological Sciences Building (D26), located in the upper campus area near Gate 11 Botany Street.

Sunday July 14 2013			
Start	End	Session 1	Session 2
9:00 AM	3:30 PM	**BEAST Workshop** Simon Ho Room G08, Biological Sciences building (D26)	**GenAlEx Workshop** Rod Peakall Room G11, Biological Sciences building (D26)
2:00 PM	6:00 PM	Registration desk open	
4:00 PM	6:00 PM	**Plenary 1 - Leighton Hall - Chair: Mark Tanaka**	
		Michael Turelli (4-5pm) Wolbachia population biology: spread in natural Drosophila simulans populations/ possible dengue control	
		Hugo Bellen (5-6pm) Major Sperm Protein in Amyotrophic Lateral Sclerosis	
6:00 PM	8:00 PM	Mixer (Scientia)	

Monday July 15 2013

Start	End				
8:00 AM	10:00 AM	**Plenary 2 - Leighton Hall - Chair: Neil Youngson**			
		Roger Reddel (8-9am) Too little or too much: telomere maintenance in short telomere syndromes and cancer			
		Anne Ferguson-Smith (9-10am) Intergenerational epigenetic inheritance in a mouse model of undernutrition			
10:00 AM	10:30 AM	Coffee			
		Session 1 - Leighton Hall		Session 2 - Tyree Room	
10:30 AM	12:30 PM	**Symposia 1a - Epigenetics 1 - Chair: Luke Hesson**		**Symposia 1b - Alan Wilton - Chair: Bill Sherwin**	
		Jeff Mann	Histone H3.3 - germ & somatic cells	John Sved	Alan's Drosophila days
		Frank Grützner	Platypus dosage compensation	Rosanne Taylor	Canine Genetics
		Claudia Rodriguez Delgado	Paternal XCI - marsupials	Sheila Van Holst Pellekaan	Genes health and well-being
		Marnie Blewitt	PRC2 - Heamatopoietc stem cells	Stephen Lillioja	Looking for Diabetes Genes
		Sarah Harten	Mouse Rlf mutants	Shaun Brennecke	The Genetics of Preeclampsia
		Shafagh Waters	Methylation - dosage compensation	Kylie Cairns	The history of dogs
		Hardip Patel	Snake dosage compensation	Remembering Alan Wilton	
12:30 PM	1:30 PM	Lunch and posters (Galleries)			
1:30 PM	3:30 PM	**Symposia 2a - Sex determination - Chair: Paul Waters**		**Symposia 2b - Computational & Mathematical Genetics - Chair: Steven Hamblin**	
		Andrew Sinclair	Disorders of sex	Jan Engelstaedter	Adaptation in bacteria
		Deborah Toledo Flores	Platypus NOR heteromorphism	Yue Wu	Drug resistance
		Clare Holleley	ID of sex specific sequence	Ben Kaehler	Genetic Distance
		Dagmar Wilhelm	Mouse ovary decvelopment	Miles Davenport	Estimating HIV recombination rates
		Stefan Bagheri-Fam	ATRX - PML nuclear bodies	Simon Ho	Relaxed-clock models
		Camilla Whittington	Male pregnancy in seahorses and pipefish	Chris Pardy	BCMI - associations in genomic data
		Denis O'Meally	Cold XX male skinks	Andrew Francis	Genetic pathways in bacteria
3:30 PM	4:00 PM	Coffee			
4:00 PM	6:00 PM	**Symposia 3a - Human Genetics - Chair: Greg Peters**		**Symposia 3b - Des Cooper - Chair: Kathy Belov**	
		Alan Cooper	Human disease and pathogen genomes	Kathy Belov	A tribute to Professor Des Cooper
		Christoffer Nellåker	*Face space* - Rare genetic disorders	Jennifer Graves	Sex Determination & Chromosomes
		Andrew Collins	Biases in antibody gene recombination	Jenny Donald	Des Cooper & genetics education
		Marie Kidd	Immunoglobulin variable region	Charles Daugherty	Des Cooper & New Zealand Science
		Marina Carpinelli	Canavan disease - Mouse model	Neil Gemmell	Immunocontraception
		Saira Yousoof	Knockdown of eye disease genes	Rob Miller	Immune regulation - marsupials
		Diako Ebrahimi	Evolution of human retroelements	Janine Deakin	Tammar wallaby 1080 tolerance
		Hamutal Mazrier	Dogs susceptible to atopic dermatitis	Cathy Herbert	Marsupial population management

Tuesday July 16 2013

Start	End						
8:00 AM	10:00 AM	**Plenary 3 - Leighton Hall - Chair: Sven Delaney**					
		Howard Jacobs (8-9am) Phenotypic suppressors of mitochondrial dysfunction in Drosophila					
		Pierre Taberlet (9-10am) Next generation sequencing in ecology					
10:00 AM	10:30 AM	Coffee					
		Session 1 - Leighton Hall		Session 2 - Tyree Room		Session 3 - Galleries	
10:30 AM	12:30 PM	**Symposia 4a - Phylogenetics - Chair: Peter Weston**		**Symposia 4b - Genomic conflict & cooperation - Chair: Paul Fisher**			
		Leo Joseph	Genomics & collections-based science	Jus St. John	Expression patterns in differentiating ES cells		
		Nathalie Nagalingum	Ferns of Australia - Diversity hotspots	Paul Fisher	Complexities in mitochondrial signalling		
		Marcel Cardillo	Patterns of *Banksia* diversification	Neil Gemmell	Trojan Female's - a new biocontrol tool		
		Sebastian Duchene	Calibration & reliability of molecular clocks	William D. Warren	Generation of synthetic mitochondria		
		Steven Cooper	Phylogeography of subterranean diving beetles	Nathan Lo	Essential amino acid synthesis pathways		
		Martyna Molak	Detecting historical population crashes	Ryan Catchpole	Bacterial Translation Initiation - fMet		
		Peter Weston	Molecular phylogeny of the subtribe Hakeinae	Chelsie Rohrscheib	Bacterial symbionts alter neurological function		
12:30 PM	1:30 PM	Lunch, posters (Galleries) and GSA Exec Metting (Room 129, Samules building #F25)					
1:30 PM	3:30 PM	**Symposia 5a - Popluation and Ecological Genetics - Chair: Don Colgan**		**Symposia 5b - Symbiosis - Chair: Carolina Correa**			
		Rod Peakall	Detecting sex-biased dispersal and inbreeding risk	Michael Turelli	Biology of wRi Wolbachia infections		
		Lee Rollins	Genetic diversity and successful introduction	Markus Riegler	Host switch frequency of an insect bacterium		
		Aaron Adamack	Population structure in Australian foxes	Heng Lin Yeap	Monitoring *Wolbachia*-infection		
		Stephen Sarre	Genetic structure in feral possums in New Zealand	Peter Kriesner	Recent rapid spread of *Wolbachia*		
		Mette Lillie	MHC class I in the Australian cane toad	Sandie Degnan	Two kingdoms are better than one		
		Cornelia Gessner	Cryptic female choice in Chinook salmon	Åsa Pérez-Bercoff	Virulence in Scedosporium fungi		
		Darrell Kemp	Colour-based signalling - genetic quality	Lauren Forbes Beadle	Immune function - MACPF protein Torso-like		
3:30 PM	4:00 PM	Coffee					
4:00 PM	5:30 PM	**Symposia 6a - Epigenetics 2 - Chair: Neil Youngson**		**Symposia 6b - Landscape and Conservation Genetics - Chair: Bill Ballard**		**Symposia 6c - Science Communication & Education - Chair: Joanne Lind**	
				Bernd Gruber	Landscape features - population structure		
		Sue Clark	Deregulation of the Cancer Genome	Quintin Lau	MHC class II diversity of koala populations	Sham Nair	Enhancing deep learning - molecular biology
		Luke Hesson	Nucleosomes at the MLH1 promoter	Katrina Morris	Low MHC diversity in the Tasmanian devil	Chee Kai Chan	Peer assessment - third year genetics
		Treve Menheniott	Inflammation and Epigenetics in Cancer	Jane Younger	Ice-dependent animals in a warming climate	Sven Delaney	Live simulations of threshold concepts
		Halina Leung	Novel epigenetic oncogene	Rohan Mellick	Responses of rainforest trees to climate change	Steven Hamblin	Social media
		Catriona Millen	Bovine transcriptomes - allele specific expression	Jonathan Davis	Complex traits & Genome Wide Association Studies	Joanne Lind	YouTube as an educational resource
5:30 PM	7:00 PM	Make way to Circular Quay					
7:00 PM	10:30 PM	Dinner cruise					

Wednesday July 17 2013

Start	End						
8:00 AM	10:00 AM	**Plenary 4 - Leighton Hall - Chair: Paul Waters** Phillip Batterham (8-9pm) Insecticides, pest control and evolution – a systems approach John Mattick (9-10) The human genome as the zip file extraordinaire					
10:00 AM	10:30 AM	Coffee					
		Session 1 - Leighton Hall		Session 2 - Tyree Room		Session 3 - Galleries	
10:30 AM	12:30 PM	**Symposia 7a - Ecological Evolutionary Genomics - Chair: Maurizio Rossetto**		**Symposia 7b - Developmental & Cell Genetics - Chair: Stephen Palmer**		**Symposia 7c - insect Molecular Biology - Chair: Bill Ballard**	
		Pierre Taberlet	Mapping biodiversity via DNA metabarcoding	Sean Millard	Neuron-specific alternative splicing	Stephen Gregory	Targeting Chromosomal Instability
		Marlien Van der Merwe	Phylogeographic dynamics of rainforest flora	Stephen Palmer	Epigenetic regulator in williams-beuren syndrome	Rosemary Manhire-Heath	Downregulation of Frazzled in *Drosophila*
		Carla Sgro	Microevolution under climate change	Irina Voineagu	Autism Spectrum Disorders	Christopher Richards	Highly conserved zinc transporters
		Richard Newcomb	Multi-phyla metagenomics	Sebastian Judd-Mole	Voltage gated chloride channel proteins	Frances Goudie	Heterozygosity at key genes in clonal honey bees
		Paul Rymer	Resilience and adaptive capacity to climate change	Oliver Griffith	Evolution of placental functions in reptiles	John La Marca	Identification and characterisation of *jam*
		Belinda Wright	Genotyping assay for the Tasmanian devil	Joshua Ho	Developmental gene regulation	Trent Perry	Flies and resistance
		Susan Rutherford	Adaptation to climate in a species of *Eucalyptus*	Michelle Henstridge	Torso Receptor Tyrosine Kinase activation	Victoria Twort	The New Zealand Giant Weta Genome
12:30 PM	1:30 PM	Lunch, GSA AGM (Tyree Room)					
1:30 PM	3:30 PM	**Symposia 8a - Genomics - Chair: Irina Voineagu**		**Symposia 8b - Phylogenomics - Chair: Stuart Gilchrist**		**Symposia 8c - Environmental Genetics - Chair: Janine Deakin**	
		Arthur Georges	Draft genome of Australia's Bearded Dragon	Gavin Huttley	Sequence, Assemble, Annotate, Align…	Emily Remnant	Interspecific mating between bees?
		Shih-Feng Tsai	Herbal fungal genome - De novo assembly	Julien Soubrier	Bison paleogenomics	Adam Cardilini	Genetically identifying dispersers
		Marina Telonis-Scott	Transcriptome complexity in Drosophila	Beata Ujvari	The evolution of a contagious cancer	Katherine Shaw	Olfactory receptor variant in *Drosophila*
		Sterling Sawaya	Tandem repeats in human promoters	David Duchene	Accounting for density dependent cladogenesis	Jessie McKenna	Lizards uterine angiogenesis during live birth
		Mike Gardner	Microsatellites and genome size	Elizabeth Ross	Quantitative traits - metagenome	Jian Cui	Toll-like receptors genes in Tasmanian devil
		Zhiliang Chen	Black field cricket - De novo transcriptome assembly	Yicheng Zhu	Influence of sequence neighborhood on mutation	Liz Jones	Defensin peptides in Tasmanian devil
		Emma Carroll	Plankton to Pooh: Plankton community & whale diet	Stuart Gilchrist	Comparing closely related fruit flies	Anna MacDonald	Species from faeces
3:30 PM	4:00 PM	Coffee					
4:00 PM	6:00 PM	**Plenary 5 - Leighton Hall - Chair: Alex Andrianopoulos** Kathy Belov - Can we save the Tasmanian devil from extinction? Camilla Whittington - Evolution of venom: gene discovery in the platypus Jenny Donald - Awards Close					

Program Overview

Sunday, July 14

9:00 - 3:30 p.m.	Workshops
2:00 - 6:00 p.m.	Registration desk open
4:00 - 6:00 p.m.	Plenary 1
6:00 - 8:00 p.m.	Mixer

Monday, July 15

8:00 - 10:00 a.m.	Plenary 2
10:00 - 10:30 a.m.	Coffee break
10:30 - 12:30 p.m.	Concurrent sessions:
	1A: Epigenetics 1
	1B: Alan Wilton memorial
12:30 - 1:30 p.m.	Lunch and posters
1:30 -3:30 p.m.	Concurrent sessions:
	2A: Sex determination
	2B: Computational and mathematical genetics
3:30 - 4:00 p.m.	Coffee break
4:00 - 6:00 p.m.	Concurrent sessions:
	3A: Human genetics
	3B: Des Cooper memorial

Tuesdsay, July 16

8:00 - 10:00 a.m.	Plenary 3
10:00 - 10:30 a.m.	Coffee break
10:30 - 12:30 p.m.	Concurrent sessions:
	4A: Phylogenetics
	4B: Genomic conflict and cooperation
12:30 - 1:30 p.m.	Lunch, posters, and GSA Executive meeting
1:30 -3:30 p.m.	Concurrent sessions:
	5A: Population and ecological genetics
	5B: Symbiosis
3:30 - 4:00 p.m.	Coffee break
4:00 - 6:00 p.m.	Concurrent sessions:
	6A: Epigenetics 2
	6B: Landscape and conservation genetics
	6C: Science communication and education
5:30 - 7:00 p.m.	Make way to Circular Quay
7:00 - 10:30 p.m.	Dinner cruise

Wednesday, July 17

8:00 - 10:00 a.m.	Plenary 4
10:00 - 10:30 a.m.	Coffee break
10:30 - 12:30 p.m.	Concurrent sessions:
	7A: Ecological evolutionary genomics
	7B: Developmental and cell genetics
	7C: Insect molecular biology
12:30 - 1:30 p.m.	Lunch, posters, and GSA AGM
1:30 -3:30 p.m.	Concurrent sessions:
	8A: Genomics
	8B: Phylogenomics
	8C: Environmental genetics
3:30 - 4:00 p.m.	Coffee break
4:00 - 6:00 p.m.	Plenary 5 and awards

Program - Oral Presentations

Sunday, July 14

Plenary 1

Location: Leighton Hall
Chair: Mark Tanaka

04:00 - 05:00	Wolbachia *population biology: from understanding spread in natural* Drosophila simulans *populations to possible dengue control* Michael Turelli
05:00 - 06:00	*Major Sperm Protein in Amyotrophic Lateral Sclerosis: growth cone guidance and muscle mitochondria* Hugo Bellen
06:00 - 08:00	MIXER

Monday, July 15

Plenary 2

Location: Leighton Hall
Chair: Neil Youngson

08:00 - 09:00	*Too little or too much: telomere maintenance in short telomere syndromes and cancer* Roger Reddel
09:00 - 10:00	*Intergenerational epigenetic inheritance in a mouse model of undernutrition.* Anne Ferguson-Smith
10:00 - 10:30	COFFEE BREAK

Session 1A: Epigenetics

Location: Leighton Hall
Chair: Luke Hesson

10:30 - 11:00	*Functions of the histone variant H3.3 in germ and somatic cell development* Jeffrey R. Mann - 1A.1
11:00 - 11:15	*Vive la différence: dosage compensation in monotreme mammals* Frank Grützner - 1A.2
11:15 - 11:30	*Is the paternally derived X chromosome always silenced during marsupial X-inactivation?* Claudia L. Rodriguez Delgado - 1A.3
11:30 - 11:45	*Function of PRC2 accessory factors in haematopoietic stem cells.* Marnie E. Blewitt - 1A.4
11:45 - 12:00	*An ENU mutagenesis screen identifies the first mouse mutants of a novel epigenetic modifier, Rearranged L-Myc Fusion (Rlf).* Sarah K. Harten - 1A.5
12:00 - 12:15	*Evidence for differential DNA methylation on the sex chromosomes of non-eutherian amniote vertebrates* Shafagh A Waters - 1A.6
12:15 - 12:30	*Sex chromosome dosage compensation in tiger snakes* Hardip R Patel - 1A.7

Session 1B: Alan Wilton memorial

Location: Tyree Room
Chair: Bill Sherwin

10:30 - 11:00	*Alan Wilton in his Drosophila days* John Sved - 1B.1
11:00 - 11:15	*Alan Wilton's Canine Genetics work continues* Rosanne Taylor - 1B.2
11:15 - 11:30	*Western NSW families, genes, health and well-being - unfinished business.* Sheila van Holst Pellekaan - 1B.3
11:30 - 11:45	*Looking for Diabetes Genes* Stephen Lillioja - 1B.4
11:45 - 12:00	*The Genetics of Preeclampsia* S P Brennecke - 1B.5
12:00 - 12:15	*New insights on the history of dogs (*Canis lupus familiaris*) in Oceania based on whole mitochondrial genome and autosomal data* Kylie M. Cairns - 1B.6
12:15 - 12:30	*Remembering Alan Wilton* Special talk
12:30 - 01:30	LUNCH AND POSTERS

Session 2A: Sex deteremination

Location: Leighton Hall
Chair: Paul Waters

01:30 - 02:00	*Disorders of Sex Development - gene discovery and diagnosis* Professor Andrew Sinclair - 2A.1
02:00 - 02:15	*Investigating segregation bias and sex-specific NOR heteromorphism in platypus* Deborah Fernanda Toledo Flores - 2A.2
02:15 - 02:30	*Subtractive genomics and the identification of sex specific sequence and genes* Clare Holleley - 2A.3
02:30 - 02:45	*New insights into mouse ovary development* Dagmar Wilhelm - 2A.4

02:45 - 03:00	*ATRX is required for PML nuclear body function in Sertoli cells* Stefan Bagheri-Fam - 2A.5
03:00 - 03:15	*Genomics and evolution of male pregnancy in seahorses and pipefish* Camilla M. Whittington - 2A.6
03:15 - 03:30	*Cool temperatures produce more males in alpine nests of the XY skink,* Bassiana duperreyi Denis O'Meally - 2A.7

Session 2B: Computational and mathematical genetics

Location: Tyree Room
Chair: Steven Hamblin

01:30 - 02:00	*Does natural transformation accelerate adaptation in bacteria?* Jan Engelstaedter - 2B.1
02:00 - 02:15	*Epidemiological control of drug resistance and compensatory mutation under resistance testing and second-line therapy* Yue Wu - 2B.2
02:15 - 02:30	*Genetic Distance for a Non-Stationary Homogeneous Markov Substitution Process* Ben Kaehler - 2B.3
02:30 - 02:45	*Estimating HIV recombination rates in vitro and in vivo* MP Davenport - 2B.4
02:45 - 03:00	*Choosing the number of relaxed-clock models in molecular phylogenetic analysis* Simon Ho - 2B.5
03:00 - 03:15	*Using bias corrected mutual information (BCMI) to discover novel associations in genomic data* Christopher Pardy - 2B.6
03:15 - 03:30	*The acquisition of genetic pathways in bacteria.* Andrew R Francis - 2B.7
03:30 - 04:00	COFFEE BREAK

Session 3A: Human genetics

Location: Leighton Hall
Chair: Greg Peters

04:00 - 04:15	*Using ancient dental calculus to trace the impacts of diet, and the evolution of human disease and pathogen genomes* Alan Cooper - 3A.1
04:15 - 04:30	Face space *separates rare genetic disorders.* Christoffer Nellåker - 3A.2
04:30 - 04:45	*Biases in antibody gene recombination shape the lymphocyte repertoire* Andrew M. Collins - 3A.3
04:45 - 05:00	*Functional gene haplotypes for the immunoglobulin variable region loci* Marie Kidd - 3A.4
05:00 - 05:15	*A new mouse model of Canavan disease displays hearing loss* Marina R Carpinelli - 3A.5
05:15 - 05:30	*Morpholino-mediated knockdown in the zebrafish of eye disease genes identified by next-generation sequencing* Saira Yousoof - 3A.6
05:30 - 05:45	*Evolution and inactivation of human retroelements by editing enzymes* Diako Ebrahimi - 3A.7
05:45 - 06:00	*Identification of a clade of dog breeds susceptible to atopic dermatitis with a unique immunophenotypic profile* Hamutal Mazrier - 3A.8

Session 3B: Des Cooper memorial

Location: Tyree Room
Chair: Kathy Belov

04:00 - 04:15	*A tribute to Professor Des Cooper* Katherine Belov - 3B.1
04:15 - 04:30	*Kangaroo gene mapping and sequencing; insights into mammalian sex chromosomes* Professor Jennifer Graves - 3B.2
04:30 - 04:45	*Des Cooper's impact on human genetics education* Jenny Donald - 3B.3
04:45 - 05:00	*Des Cooper's Contributions to New Zealand Science* Charles Daugherty - 3B.4

05:00 - 05:15 *Immunocontraception: ecological and immunogenetic issues*
Neil J. Gemmell - 3B.5

05:15 - 05:30 *Immune regulation at the fetal maternal interface in marsupials*
Rob Miller - 3B.6

05:30 - 05:45 *The tammar wallaby as a model species for determing the genetic basis behind tolerance to 1080*
Janine Deakin - 3B.7

05:45 - 06:00 *The intersection of reproductive and genetic approaches to marsupial population management: Why is it important for conservation?*
Catherine Herbert - 3B.8

Tuesday, July 16

Plenary 3

Location: Leighton Hall
Chair: Sven Delaney

08:00 - 09:00	*Phenotypic suppressors of mitochondrial dysfunction in* Drosophila Howy Jacobs
09:00 - 10:00	*Next generation sequencing in ecology* Pierre Taberlet
10:00 - 10:30	COFFEE BREAK

Session 4A: Phylogenetics

Location: Leighton Hall
Chair: Peter Weston

10:30 - 11:00	*Genomics and Australo-Papuan collections-based science: thoughts on where we are headed* Leo Joseph - 4A.1
11:00 - 11:15	*Phylogenetic indices for identifying diversity hotspots: an example using the ferns of Australia* Nathalie Nagalingum - 4A.2
11:15 - 11:30	*Evolution of a hotspot genus: geographic patterns of diversification in* Banksia Marcel Cardillo - 4A.3
11:30 - 11:45	*Calibration placement and the reliability of molecular clocks* Sebastian Duchene - 4A.4
11:45 - 12:00	*Speciation underground versus colonisation from the surface: phylogeography of subterranean diving beetles from the Western Australian arid zone.* Steven J. B. Cooper - 4A.5
12:00 - 12:15	*A skyline view through the neck of a bottle: Detecting historical population crashes using DNA sequences* Martyna Molak - 4A.6
12:15 - 12:30	*Molecular phylogeny of the subtribe Hakeinae (Green Plants: Proteaceae tribe Embothrieae) and its implications* Peter H. Weston - 4A.7

Session 4B: Genomic conflict and cooperation

Location: Tyree Room
Chair: Paul Fisher

10:30 - 11:00	*Mitochondrial DNA Haplotypes Define Gene Expression Patterns in Pluripotent and Differentiating Embryonic Stem Cells* Jus St. John - 4B.1
11:00 - 11:15	*New complexities in mitochondrial signalling revealed in the* Dictyostelium *model.* Paul R. Fisher - 4B.2
11:15 - 11:30	*Trojan Female's - a new biocontrol tool* Neil J. Gemmell - 4B.3
11:30 - 11:45	*The Matrix Reloaded: Progress toward the generation of synthetic mitochondria.* William D Warren - 4B.4
11:45 - 12:00	*Maintenance of essential amino acid synthesis pathways in the* Blattabacterium *symbiont of a wood-feeding cockroach* Nathan Lo - 4B.5
12:00 - 12:15	*Evolution of the Unnecessary: How did fMet Become Central in Bacterial Translation Initiation?* Ryan J. Catchpole - 4B.6
12:15 - 12:30	*Mind bending bacteria: Common bacterial symbionts alter neurological function and behaviour in* Drosophila melanogaster*.* Chelsie E. Rohrscheib - 4B.7
12:30 - 01:30	LUNCH AND POSTERS

Session 5A: Population and ecological genetics

Location: Leighton Hall
Chair: Don Colgan

01:30 - 02:00	*Genetic tools for detecting sex-biased dispersal and inbreeding risk* Rod Peakall - 5A.1
02:00 - 02:15	*High genetic diversity is not essential for successful introduction* Lee A. Rollins - 5A.2

02:15 - 02:30 *Identifying population structure in Australian foxes (*Vulpes vulpes*)*
Aaron T Adamack - 5A.3

02:30 - 02:45 *Landscape level microsatellite DNA analysis reveals substantial cryptic genetic structure in feral possums in New Zealand*
Stephen D. Sarre - 5A.4

02:45 - 03:00 *Characterisation of Major Histocompatibility Complex class I in the Australian cane toad,* Rhinella marina
Mette Lillie - 5A.5

03:00 - 03:15 *The genetic basis of cryptic female choice in Chinook salmon (*Oncorhynchus tshawytscha*)*
Cornelia Gessner - 5A.6

03:15 - 03:30 *Genic capture and the evolution of colour-based signalling of genetic quality*
Darrell Kemp - 5A.7

Session 5B: Symbiosis

Location: Tyree Room
Chair: Carolina Correa

01:30 - 02:00 *Comparative biology of wRi* Wolbachia *infections in* Drosophila simulans*,* D. suzukii *and* D. subpulchrella
Michael Turelli - 5B.1

02:00 - 02:15 *What do we know about host switch frequency of a common maternally inherited insect bacterium?*
Markus Riegler - 5B.2

02:15 - 02:30 *A molecular method for monitoring* Wolbachia*-infection in the release of* Wolbachia*-infected* Aedes aegypti
Heng Lin Yeap - 5B.3

02:30 - 02:45 *Recent rapid spread of* Wolbachia *variants in east Australian* Drosophila simulans
Peter Kriesner - 5B.4

02:45 - 03:00 *Two kingdoms are better than one: genome-scale signatures of bacteria and sponges working together to engineer marine ecosystems*
Sandie M Degnan - 5B.5

03:00 - 03:15 *Understanding the causes of virulence in Scedosporium fungi*
Åsa Pérez-Bercoff - 5B.6

03:15 - 03:30 *Investigating the immune function of the* Drosophila melanogaster *MACPF protein Torso-like*
L. J. Forbes Beadle - 5B.7

03:30 - 04:00 COFFEE BREAK

Session 6A: Epigenetics 2

Location: Leighton Hall
Chair: Neil Youngson

04:00 - 04:30 *Regional Deregulation of the Cancer Genome involves Epigenetic Remodeling and a Change in Replication Timing*
Clark SJ - 6A.1

04:30 - 04:45 *Reassembly of nucleosomes at the MLH1 promoter initiates resilencing following decitabine exposure*
Luke B. Hesson - 6A.2

04:45 - 05:00 *Linking Inflammation and Epigenetics in Cancer*
Trevelyan R. Menheniott - 6A.3

05:00 - 05:15 *Defining the tumourigenic function of a novel epigenetic oncogene required for the development of acute myeloid leukaemic stem cells*
Halina H. L. Leung - 6A.4

05:15 - 05:30 *RNA-Seq of Bovine Blood and Liver Transcriptomes Reveals Allele Specific Expression*
Catriona A. Millen - 6A.5

Session 6B: Landscape and conservation genetics

Location: Tyree Room
Chair: Bill Ballard

04:00 - 04:15 *LandPopGenReport - a landscape genetics tool to analyse the effects of landscape features on population structure using genetic data*
Bernd Gruber - 6B.1

04:15 - 04:30 *MHC class II diversity of koala (*Phascolarctos cinereus*) populations across their range*
Quintin Lau - 6B.2

04:30 - 04:45 *Low MHC diversity in the Tasmanian devil pre-dates European settlement*
Katrina Morris - 6B.3

04:45 - 05:00	*Emperor Penguins and Weddell Seals: ice-dependent animals in a warming climate* Jane Younger - 6B.4
05:00 - 05:15	*Predicting demographic responses of rainforest trees to climate change* Dr Rohan Mellick - 6B.5
05:15 - 05:30	*Ecological and evolutionary limits to species distributions in* Eurema *butterflies* Jonathan Davis - 6B.6

Session 6C: Science communication and education

Location: Galleries
Chair: Joanne Lind

04:00 - 04:30	*Enhancing deep learning in an introductory molecular biology course* Sham Nair - 6C.1
04:30 - 04:45	*Effectiveness of using Peer Assessment in assessing Graduate Capabilities in a third year Genetics Subject* Chee-Kai Chan - 6C.2
04:45 - 05:00	*Evaluation of live simulations for the teaching of threshold concepts in first year genetics* Sven Delaney - 6C.3
05:00 - 05:15	*My student is on Twitter: should I be worried?* Steven Hamblin - 6C.4
05:15 - 05:30	*YouTube as an educational resource for visual and kinesthetic learners: A study of DNA replication* Joanne M Lind - 6C.5

Wednesday, July 17

Plenary 4

Location: Leighton Hall
Chair: Paul Waters

08:00 - 09:00	*Insecticides, pest control and evolution - a systems approach* Philip Batterham
09:00 - 10:00	*The human genome as the zip file extraordinaire* John S. Mattick
10:00 - 10:30	COFFEE BREAK

Session 7A: Ecological evolutionary genetics

Location: Leighton Hall
Chair: Maurizio Rossetto

10:30 - 11:00	*Mapping biodiversity via DNA metabarcoding* Pierre Taberlet - 7A.1
11:00 - 11:15	*Using next generation sequencing to explore phylogeographic dynamics of rainforest flora* Marlien van der Merwe - 7A.2
11:15 - 11:30	*Microevolution under climate change* Carla Sgro - 7A.3
11:30 - 11:45	*Multi-phyla metagenomics along an altitudinal gradient on a small temperate island* Richard Newcomb - 7A.4
11:45 - 12:00	*Resilience and adaptive capacity to climate change: an experimental transcriptomics approach* Paul Rymer - 7A.5
12:00 - 12:15	*Using next generation sequencing to develop a genotyping assay for the Tasmanian devil.* Belinda Wright - 7A.6
12:15 - 12:30	*Adaptation to climate in a widespread species of* Eucalyptus *identified through a genome wide scan and phenotypic assessment* Margaret Byrne - 7A.7

Session 7B: Developmental and cell genetics

Location: Tyree Room
Chair: Stephen Plamer

10:30 - 11:00	*Neuron-specific alternative splicing as a mechanism to increase the diversity of brain wiring proteins* S. Sean Millard - 7B.1
11:00 - 11:15	*The role of a novel epigenetic regulation in a craniofacial and neurological features of Williams-Beuren syndrome* S.J. Palmer - 7B.2
11:15 - 11:30	*Functional Genomic Studies of Autism Spectrum Disorders* Irina Voineagu - 7B.3
11:30 - 11:45	*Functional Characterisation of Voltage Gated Chloride Channel Proteins in* Drosophila Sebastian Judd-Mole - 7B.4
11:45 - 12:00	*Gene expression and the evolution of placental functions in reptiles* Oliver W. Griffith - 7B.5
12:00 - 12:15	*Systems analysis of developmental gene regulation* Joshua W. K. Ho - 7B.6
12:15 - 12:30	*Localised control of Torso Receptor Tyrosine Kinase activation in* Drosophila *terminal patterning* M.A. Henstridge - 7B.7

Session 7C: Insect molecular biology

Location: Galleries
Chair: Bill Ballard

10:30 - 11:00	*Targeting Chromosomal Instability* Stephen Gregory - 7C.1
11:00 - 11:15	*Netrin-dependent downregulation of the DCC orthologue, Frazzled, is required for the dissociation of the peripodial epithelium in* Drosophila Rosemary Manhire-Heath - 7C.2
11:15 - 11:30	*Highly conserved zinc transporters performing divergent and specific functional roles in Drosophila melanogaster* Christopher Richards - 7C.3

11:30 - 11:45	*Selection maintains heterozygosity at key genes in a clonal population of honey bees (*Apis mellifera capensis*).* Frances Goudie - 7C.4
11:45 - 12:00	*Identification and characterisation of* jam packed *(*jam*), a novel regulator of stem cell development in the* Drosophila *testis.* John E. La Marca - 7C.5
12:00 - 12:15	*Flies and resistance: A versatile system for studying receptor biology.* Trent Perry - 7C.6
12:15 - 12:30	*Draft Sequencing and assembly of the New Zealand Giant Weta Genome* Victoria G Twort - 7C.7
12:30 - 01:30	LUNCH

Session 8A: Genomics

Location: Leighton Hall
Chair: Irina Voineagu

01:30 - 02:00	*A draft annotated genome sequence for Australia's Bearded Dragon* Arthur Georges - 8A.1
02:00 - 02:15	De novo *Assembly of an Herbal Fungal Genome Using PacBio Long Reads* Shih-Feng Tsai - 8A.2
02:15 - 02:30	*Exon Expression Analysis Reveals New Levels of Transcriptome Complexity at Upper Thermal Limits and Recovery in Natural* Drosophila Marina Telonis-Scott - 8A.3
02:30 - 02:45	*Microsatellite Tandem Repeats Are Abundant in Human Promoters and Are Associated with Regulatory Elements* Sterling Sawaya - 8A.4
02:45 - 03:00	*Microsatellites and genome size* Mike Gardner - 8A.5
03:00 - 03:15	*A* de novo *transcriptome assembly of the black field cricket (*Teleogryllus commodus*)* Zhiliang Chen - 8A.6
03:15 - 03:30	*Plankton to Pooh: Metagenetic approach to investigating plankton community composition and whale diet* Emma L Carroll - 8A.7

Session 8B: Phylogenomics

Location: Tyree Room
Chair: Stuart Gilchrist

01:30 - 02:00	*Sequence, Assemble, Annotate, Align … Species Tree?* Gavin A Huttley - 8B.1
02:00 - 02:15	*Bison paleogenomics: revealing ancient and modern species and populations* Julien Soubrier - 8B.2
02:15 - 02:30	*The evolution of a contagious cancer, the Tasmanian Devil Facial Tumour Disease.* Beata Ujvari - 8B.3
02:30 - 02:45	*Accounting for density dependent cladogenesis clarifies comparisons of diversification rates* David Duchene - 8B.4
02:45 - 03:00	*Predicting Quantitative Traits from the Metagenome: Applications for Greenhouse Gas Mitigation* Elizabeth Ross - 8B.5
03:00 - 03:15	*Quantifying the influence of sequence neighborhood on mutation* Yicheng Zhu - 8B.6
03:15 - 03:30	*Comparing closely related fruit flies: just how close is close?* Stuart Gilchrist - 8B.7

Session 8C: Environmental genetics

Location: Galleries
Chair: Paul Waters

01:30 - 02:00	*Interspecific mating between* Apis cerana *and* A. mellifera*: Does it happen and what does it mean for Australian bees?* Emily Remnant - 8C.1
02:00 - 02:15	*Genetically identifying dispersers: how many loci are enough?* Adam P.A. Cardilini - 8C.2
02:15 - 02:30	*Functional characterisation of a naturally occurring olfactory receptor variant in* Drosophila melanogaster Katherine H Shaw - 8C.3

02:30 - 02:45	*Using lizards to investigate the genetic mechanisms controlling uterine angiogenesis during live birth: consequences for cancer* **Jessie A. McKenna** - 8C.4
02:45 - 03:00	*Characterisation of the toll-like receptors genes in the Tasmanian devil,* Sarcophilus harrisii **Jian Cui** - 8C.5
03:00 - 03:15	*Novel Defensin Peptides of the Tasmanian Devil (*Sarcophilus harrisii*)* **Jones, Elizabeth** - 8C.6
03:15 - 03:30	*Species from faeces: metabarcoding to detect vertebrate prey from predator scats* **Anna J MacDonald** - 8C.7
03:30 - 04:00	**COFFEE BREAK**

Plenary 5

Location: Leighton Hall
Chair: President of the GSA

04:00 - 05:00	*Can we save the Tasmanian devil from extinction?* **Katherine Belov**
05:00 - 05:30	*Evolution of venom: gene discovery in the platypus* **Camilla M. Whittington**

Program - Posters

Monday

1 *Phylogeography within the Australian arid zone. Plio-Pleistocene diversification and genetic structure in the skink Tiliqua rugosa revealed by mitochondrial and nuclear DNA*
Talat H. Ansari

3 *The powerhouse of our body*
J.O. Ballard

5 *Detest the pest: Understanding Spinosad -* Drosophila *interactions*
Joseph Byrne

7 *GTF2IRD1 is an epigenetic regulator of gene expression important in developmental facial skin patterning*
Cesar P. Canales

9 *BloodChIP: An Atlas of Genome-wide Transcription Factor Binding Profiles in Human Haematopoietic Stem/Progenitor Cells*
Diego Chacon

11 *Developing a genetic test for haemophilia A in Australian Kelpies*
Tracy Chew

13 *Genomic conflict and the uniparental inheritance of mitochondria*
Joshua Christie

15 *Comparative genomics of* Campylobacter concisus *isolates reveals genetic diversity and provides insights into disease association*
Nandan P. Deshpande

17 Wolbachia *modulates* Hira *gene expression in* Drosophila melanogaster
Heather A. Flores

19 *The role of Nanog in Germline Development and Spermatogenesis*
Terri-Ann Harris

21 *Identification of genes encoding proteins that interact with the Drosophila MACPF protein Torso-like*
Alex R. Johns

23 *DNA methylation to exon 2 of DNA polymerase gamma A suppresses mitochondrial DNA copy number in fast replicating cells*
William Lee

Tuesday

Plenaries

Wolbachia population biology: from understanding spread in natural *Drosophila simulans* populations to possible dengue control

Michael Turelli[1]

[1] *University of California, Davis*

Wolbachia are maternally inherited endosymbiotic bacteria that live inside the cells of invertebrate hosts. They often spread through populations by manipulating host reproduction. Their most common reproductive manipulation is ``cytoplasmic incompatibility'' (CI), increased embryo mortality when infected males mate with uninfected females. CI produces a frequency-dependent fitness advantage for *Wolbachia* genomes, which are effectively maternally inherited organelles whose evolutionary fate is tied to that of their hosts. If *Wolbachia* impose fitness costs or are imperfectly transmitted, their frequency dynamics can become ``bistable,'' with frequencies tending to increase only above a threshold frequency. Ary Hoffmann and I have studied a CI-causing *Wolbachia* (called wRi) in California populations of *Drosophila simulans* since 1984, using a combination of field and laboratory studies and simple mathematical models to understand frequency dynamics in time and space and coevolution. The wRi-*D. simulans* system provides a paradigm for the rapid spread and evolution of CI-causing infections in nature. We have recently documented the sequential spread of two *Wolbachia* variants, wAu and wRi, in Australian *D. simulans*, with wRi displacing wAu over the past decade. Our new data suggest re-evaluation of the dynamics of wRi in California *D. simulans*. Ironically, our initial, probably incorrect, interpretation of wRi spatial dynamics as bistable provides the correct mathematical framework for understanding how *Wolbachia* can be introduced into novel hosts to control disease transmission. I will describe a Gates-funded project, headed by Scott O'Neill, to control dengue fever by exploiting the fact that some Wolbachia suppress various microbes in their hosts. I will summarize mathematical results predicting: (1) the effort needed to initiate spatial spread of these infections, (2) the conditions sufficient to halt their spread, and (3) rate of spatial spread in uniform habitats. These predictions are now being tested in *Aedes aegypti* field trials in and around Cairns.

Major Sperm Protein in Amyotrophic Lateral Sclerosis: growth cone guidance and muscle mitochondria

Hugo Bellen[1]

[1] *Department of molecular and human genetics, Program in Developmental Biology, Baylor College of Medicine, and HHMI*

Amyotrophic Lateral Sclerosis (ALS) is a lethal, late onset neurodegenerative disease that affects the upper and lower motor neurons. The pathogenesis of the disease is poorly understood and about 15 genes are known to cause ALS, including ALS8, a familial form of ALS that is caused by a mutation in Vamp associated protein B (VAPB). We study the role of this protein in fruit flies and worms to better understand the molecular mechanisms that cause the disease. VAP coordinates some of the functions of the ER, including lipid synthesis and quality control of proteins. The aminoterminal end of VAP, the MSP domain, is also cleaved and secreted. It functions as hormone and binds to growth cone guidance receptors that are expressed on the muscle surface. Binding of VAP to these receptors controls Ca++ homeostasis as well as mitochondrial dynamics in the muscles. We are currently testing the role of MSP in mice and have recently determined the MSP levels in humans.

Too little or too much: telomere maintenance in short telomere syndromes and cancer

Roger Reddel[1]

[1] *Children's Medical Research Institute, Westmead, NSW 2145*

Telomere shortening is a normal accompaniment of the proliferation of normal human somatic cells. This eventually results in permanent withdrawal from the cell division cycle (i.e., cellular senescence) and sets an upper limit on cellular proliferative capacity. In tissues that are highly proliferative, such as bone marrow and gut epithelium, telomere shortening is partially counteracted by a telomere lengthening mechanism (TLM), primarily the enzyme telomerase which reverse transcribes new telomeric sequence. If the TLM is inadequate, the excessive telomere shortening that ensues results in a short telomere syndrome which may be manifest by its effects on a wide variety of organ systems, with the most common causes of lethality being bone marrow failure and pulmonary fibrosis. In severe cases, there may also be developmental defects. Characteristic changes in skin, nails and mucous membranes may be diagnostic. Known genetic causes of short telomere syndromes include mutations in any of the genes that encode the RNA or protein subunits of telomerase, proteins required for its biogenesis, a protein required for its trafficking to telomeres, a protein involved in processing telomere ends, and a telomere-binding protein. Approximately 40% of cases do not yet have a known genetic defect.

In contrast, upregulated TLM activity is a feature of almost all cancers. This completely counteracts the normal telomere shortening process and therefore bypasses the senescence barrier and permits unlimited proliferation. In approximately 85% of cancers the upregulated TLM is telomerase and Alternative Lengthening of Telomeres (ALT) mechanism is upregulated in most of the remainder, especially in sarcomas. How this occurs is incompletely understood, but it has recently been found that activation of telomerase is commonly associated with a mutation (usually somatic, but sometimes germline) in the promoter for the gene encoding its reverse transcriptase subunit, TERT. Activation of ALT is frequently associated with somatic mutations in the ATRX gene. The almost universal occurrence of excessive TLM activity in cancer suggests that telomerase and ALT may be ideal targets for the development of broad-spectrum cancer therapeutics.

Intergenerational epigenetic inheritance in a mouse model of undernutrition.

Anne Ferguson-Smith[1]

[1] *Department of Physiology, Development and Neuroscience. University of Cambridge*

Environmental factors during early life can have an impact on later metabolic health of the individual and future progeny. Using a mouse model of maternal caloric restriction during pregnancy affecting the metabolic physiology of two generations, including via paternal inheritance, we will explore two questions: (i) Are imprinted genes more or less susceptible to environmental compromise and hence may be `developmental programming genes' and (ii) is paternal experience of in utero undernutrition an epigenetically inherited memory transmitted to offspring via his sperm methylome?

Phenotypic suppressors of mitochondrial dysfunction in *Drosophila*

Howy Jacobs[1]

[1] *Institute of Biomedical Technology, University of Tampere; Ttampere University Hospital; Molecular Neurology Research Program, University of Helsinki , Finland*

The core metabolic functions of mitochondria require co-operative interactions between genes in nuclear and mitochondrial DNA, each contributing subunits to the oxidative phosphorylation (OXPHOS) system. Because these two genomes are replicated and transmitted differently, they co-evolve in a manner which could be considered inherently antagonistic, leading sometimes to maladaptive outcomes. In an attempt to understand better the ways in which the nuclear and mitochondrial genomes interact, we have been studying a Drosophila mutant (tko25t) which carries a point mutation in the X-chromosomal gene for mitoribosomal protein S12. tko25t homozygotes or hemizygous males have decreased mitochondrial translational capacity, which results in OXPHOS insufficiency and chronic oxidative stress. This produces an organismal phenotype of bang-sensitivity, delayed larval development and male reproductive impairment, mirroring some features of mitochondrial disease in humans. We have identified three ways in which the mutant phenotype can be partially suppressed. First, we isolated and characterized genetic suppressors, which mapped either in nuclear DNA or in mtDNA. Second, we were able to phenocopy suppression, by making targeted manipulations of nuclear gene activity affecting mitochondrial biogenesis. Third, we were able to effect an environmental suppression by altering the diet of the developing mutant flies.

Next generation sequencing in ecology

Pierre Taberlet[1]

[1] *Laboratoire d'Ecologie Alpine, Universitè Joseph Fourier, Grenoble, France*

The recent improvements in sequencing technologies have a dramatic impact in ecology. My talk will be mainly based on two recent special issues of Molecular Ecology, dealing with ``genotyping by sequencing'' and with ``environmental DNA''. After a brief review of the power of next generation sequencers, I will first present a few recent studies using next generation sequencing for assessing the genetic polymorphism at the genome level, either for population genomics or for genome-wide association. The different methods for simplifying the genome will also be presented (RAD sequencing versus capture). The second part of the talk will focus on environmental DNA and on a new approach called ``DNA metabarcoding''. It corresponds to high-throughput and simultaneous taxa identification based on a very short but informative DNA fragment. DNA fragments of less than 100 bp allow the use of degraded DNA from environmental samples. Environmental DNA extracted from soil allow to assess the diversity of plants and animals in different environments, from Arctic to tropical ecosystems. The same approach can also be used to reconstruct past plant communities, using either permafrost samples or lake sediment cores. These results open unprecedented opportunities for large scale DNA-based biodiversity studies across a range of taxonomic groups using standardised metabarcoding approaches.

Insecticides, pest control and evolution - a systems approach

Philip Batterham[1]

[1] *Department of Genetics, Bio21 Institute, University of Melbourne, Parkville, Victoria*

Chemical insecticides have been deployed as key weapons in the control of insect pests of agriculture, domestic pets and human health. The rapid evolution of resistance to many insecticides has lead to increases in control costs, production losses and the spread of insect vectored disease. The many resistance genes identified have been shown to encode either the protein targets to which insecticides bind or enzymes capable of metabolizing the insecticide. The capacity to observe the adaptation process as it happens has made insecticide resistance a paradigm for the study of natural selection. However, in spite of the convergence of these basic and applied research agendas, throughout its long history insecticide resistance research has used a narrow range of approaches that have failed to fully exploit the value of the system. In terms of the basic research agenda, there has been an ongoing debate on whether adaptation involves a few genetic variants of major effect, or many genetic variants of small effect. While the insecticide resistance literature provides excellent examples of both, researchers have focused on the identification and molecular characterization of genes of major effect. The opportunity to identify the `many genes of small effect' has not been pursued due to the technological challenges it has posed. Therefore the opportunity to understand the molecular basis of polygenic adaptation has to date not been seized. In terms of the applied agenda, there is a need to understand the biology of the interaction between insecticides and the insects they are used to control.

We have instituted a systems approach to study of neonicotinoid insecticide resistance in Drosophila melanogaster larvae. These insecticides target nicotinic acetylcholine receptors (nAChRs). Resistant mutants indicate that the target is formed by the interface of the α1 and α2 nAChR subunits. This hypothesis has now been supported by structural modeling docking neonicotinoids, including imidacloprid, into the α1/α2 interface. A major technological advance in mass spectroscopy has allowed the metabolism on imidacloprid to be followed in vivo. Four imidacloprid metabolites previously associated with Drosophila Cyp6g1 expression in tobacco cell culture, have now been identified in vivo. Interestingly these metabolites, which have all been shown to be toxic in insects, were found to be excreted by D.melanogaster larvae. Given that metabolism is often assumed to equate with detoxification, this observation is significant. Several other imidacloprid metabolites have now been identified. We have sequenced the transcriptome for several sections of the midgut of Drosophila larvae, creating the potential to track metabolism within the midgut identifying the genes responsible. Genome Wide Association Studies and RNAi, examining both metabolism and resistance, will allow many genes responsible for the way in which insects respond to be insecticides to be discovered. This approach will improve our understanding of polygenic adaptation and provide options for the more intelligent control of insect pests.

The human genome as the zip file extraordinaire

John S. Mattick[1]

[1] *Garvan Institute of Medical Research and University of New South Wales*

High throughput analyses have shown that the vast majority of the human genome is dynamically transcribed to produce a previously hidden universe of different classes of small and large, overlapping and interlacing intronic, intergenic and antisense non-protein-coding RNAs. The transcriptome is in fact far more complex than the genome, which is best viewed as a zip file that is unpacked in highly cell-specific patterns during development. These RNAs fulfill a wide range of regulatory functions, with miRNAs and related species being best (although not well) understood. The functions of the large/long noncoding RNAs (lncRNAs) are varied and include central roles in the formation of various differentiation-specific subnuclear organelles. However, recent evidence suggests that the major function of lncRNAs is to guide chromatin-modifying complexes to their sites of action, to specify the architectural trajectories of development. Not surprisingly, it is also emerging that variations in the sequence or expression of these RNAs not only underpin phenotypic differences between individuals and species, but also play significant roles in the etiology of complex diseases. Moreover, the emerging transcriptomic, epigenomic and nuclear structural data point to an extraordinary precision of the 4-dimensional organisation and expression of the genome that far exceeds current understanding.

Can we save the Tasmanian devil from extinction?

Katherine Belov[1]

[1] *Faculty of Veterinary Science, The University of Sydney, NSW, Australia*

The Tasmanian devil, Australia's largest remaining marsupial carnivore, faces extinction in the wild due to the emergence of a new infectious disease. Devil Facial Tumour Disease (DFTD) is a contagious cancer that is spread as an allograft during biting. Devils have low genetic diversity at the Major Histocompatibility Complex (MHC). We originally proposed that devils were essentially immunological clones, and that cancer cells were able to pass between unrelated animals without triggering an immune response due to this lack of MHC diversity. The discovery of MHC-disparate animals in northwestern Tasmania raised hopes that some of these animals may be able to mount an immune response against DFTD. Indeed, the frequency of disease in these populations remains low. However, we have recently shown that the tumour is able to evade the immune response in MHC disparate animals through the down regulation of cell surface MHC. I will discuss the use of genomics and transcriptomics to help us to understand the disease, its evolutionary trajectory and the role of genomics in the quest to save the species from extinction in the wild and in Australia's largest captive insurance program.

Evolution of venom: gene discovery in the platypus

Camilla M. Whittington[1,2], Anthony Papenfuss[3], Christopher Moran[2], Wesley C. Warren[4], and Katherine Belov[2]

[1] *School of Biological Sciences, University of Sydney, Sydney, Australia*
[2] *Faculty of Veterinary Science, University of Sydney, Sydney, Australia*
[3] *Bioinformatics division, The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia*
[4] *The Genome Institute at Washington University, St Louis, USA*

Male platypuses possess spurs used to deliver a complex mixture of venom peptides into the victim. Our knowledge of platypus venom is incomplete. Early proteomic work identified five peptide toxins, with unknown function; further analyses were hampered due to the limited availability of venom. However, the platypus genome now offers an unprecedented opportunity for genomics-based venom studies. Our transcriptomic studies of the platypus venom gland have used next-generation sequencing platforms as well as candidate gene expression studies. We have identified a broad array of novel putative venom toxin genes and their possible functions, paving the way for pharmacological studies, some of which may ultimately yield novel drugs. This work has also provided insights into mechanisms of toxin evolution. We have observed similarities in venom development across many species, including recruitment of toxins from the same protein families; gene duplication and neofunctionalisation; and recruitment of non-toxins to venom. The discovery of the convergent evolution of toxins in widely divergent species, now including the platypus, indicates that there are certain peptide motifs that are preferentially selected during the evolution of venom. The current advances in genomic techniques represent an exciting opportunity to identify features of venom evolution across the kingdom Animalia.

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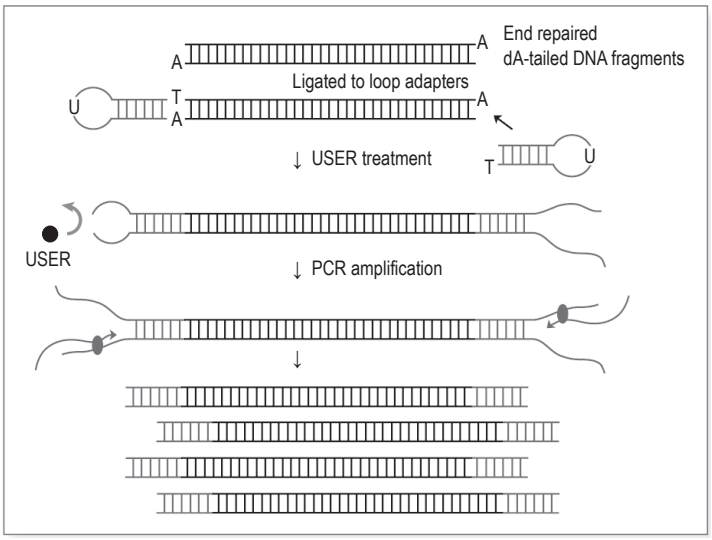

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Oral Presentations

1A.1: Functions of the histone variant H3.3 in germ and somatic cell development

Michelle C-W. Tang[1,2], Shelley A. Jacobs[2], Steve Binos[3], Ben Ong[2], Lee H. Wong[4], and *Jeffrey R. Mann*[2]

[1] *Department of Zoology, The University of Melbourne, Vic. 3010*
[2] *Murdoch Childrens Research Institute, The Royal Children's Hospital, Parkville, Victoria 3052*
[3] *Biosciences Research Division, Department of Primary Industries, Bundoora, Victoria 3083*
[4] *Department of Biochemistry and Molecular Biology, Monash University, Victoria 3800*

Histones package DNA into nucleosomes, the basic unit of chromatin. They also serve fundamental roles as epigenetic modifiers. Post-translational modifications (PTMs) to specific residues in the nucleosome-extrinsic N-terminal tails can act as waypoints in the establishment of higher order chromatin structure. A classic example is the requirement of H3 lysine 9 trimethylation for the establishment of constitutive heterochromatin in fission yeast and in mammals. Probably the most important histone in epigenetic modification is H3. This histone has three isoforms: canonical H3.1 and H3.2 are replication-coupled (RC), while the H3.3 variant is replication-independent (RI), being incorporated into chromatin at any cell cycle stage. This RI property of H3.3 led us to think that it could play an important role in driving the genome-wide dynamic epigenetic changes observed in the mammalian germ line. These changes occur when germ cells are non-dividing. To investigate this possibility, we devised a versatile `conditional allelic replacement' strategy for each of the two genes encoding H3.3 (H3f3a and H3f3b). Here we describe the effects of conditionally replacing each of H3f3a and H3f3b with a fluorescent reporter, producing null mutations. Constitutively mutant mice have severe deficits in growth and fertility, and are revealing non-redundant roles of H3f3a and H3f3b in regulating spermatogenesis. Ultimately, our system will allow for the conditional introduction of single amino acid substitutions in H3.3 at desired germ cell stages. This will allow us to determine the functional significance of particular PTMs in driving epigenetic change in the germ line.

1A.2: Vive la différence: dosage compensation in monotreme mammals

Tasman Daish[1], Anamaria Necsulea[2], Magali Soumillon[2], Angélica Liechti[2], Henrik Kaessmann[2], and *Frank Grützner*[1]

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The evolution of heteromorphic sex chromosomes resulted in a gene dosage imbalance between males and females as well as between sex chromosomes and autosomes in the heterogametic sex. Different mechanisms have evolved to restore balance between expression levels in different species such as X chromosome inactivation (XCI) in therian female somatic cells. Long-non coding RNAs (lncRNAs) play important roles regulating genes in cis and in trans. In eutherian mammals the Xist lncRNA mediates X inactivation in female somatic cells. Only recently an evoluntionarily unrelated lncRNA termed Rsx has been discovered in marsupials and has been proposed to function in a similar way as the eutherian Xist transcript (Grant et al. 2012). Montremes are the most basal mammalian lineage and feature a complex sex chromosome system which is homologous to bird sex chromosomes. So far global XCI has not been observed on any of the five X chromosomes in platypus (Deakin et al. 2008, Rens et al. 2010, Julien et al. 2012) however changes in transcriptional levels indicative of dosage compensation on some chromosomal regions. Deep sequencing of non-coding RNAs in male and female monotreme somatic tissues has revealed sex-biased expression of a number of ncRNAs. Particularly interesting is an X-linked lncRNA (Psx) with extremely female biased expression. We are currently investigating in detail the expression of Psx and the surrounding region to investigate further if Psx is involved in dosage compensation in monotreme mammals.

1A.3: Is the paternally derived X chromosome always silenced during marsupial X-inactivation?

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Marsupials and eutherian mammals have a genetic sex determination system, where females have two copies of the X chromosome and males bear a single X chromosome and a tiny, gene-poor Y chromosome. It has been proposed that genes (or a subset of) on the single X chromosome in males were transcriptionally up-regulated to balance their expression with autosomal genes. However, upregulation of both X chromosomes in females would have resulted in X-linked genes overexpression. In turn, one of the two X chromosomes is transcriptionally repressed in the somatic cells of females via a process known as X chromosome inactivation (XCI). In eutherian mammals, one X is randomly chosen for inactivation, where both paternally and maternally derived X chromosome have an equal chance of inactivation. Decades-long evidence suggests that in marsupials the X chosen for silencing is not random, but that they preferentially inactivate the paternal X chromosome. In this study we use RNA-Seq data from a tammar wallaby family to determine whether marsupial XCI is in fact paternally imprinted, and to what extent.

1A.4: Function of PRC2 accessory factors in haematopoietic stem cells.

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We are interested in epigenetic control in haematopoietic stem cells (HSCs). Our focus is on Polycomb Repressive Complex 2 (PRC2), that has been studied extensively in ES cells, where it represses key developmental regulators. In addition to the core PRC2 members (Ezh1/2, Suz12 and Eed), accessory factors appear to modulate PRC2 activity and target its binding. We have previously shown that reduction in the levels of core PRC2 members results in enhanced HSC repopulating capacity, but the role of PRC2 accessory factors in HSCs has not been described.

Using shRNA knockdown, we examined the function of six PRC2 accessory factors in HSCs by testing the capacity of transduced murine foetal liver cells to competitively reconstitute irradiated recipients. Depletion of the enzymatically inactive histone methyltransferase Jarid2 enhanced contribution to all blood cell lineages compared to cells containing control constructs, similar to the phenotype observed upon depletion of core PRC2 components. Our data suggest that the enhanced activity of Jarid2 depleted cells is due to an increase in HSC number post Jarid2 knockdown, but that this role for Jarid2 is restricted to foetal HSCs. Foetal HSCs are dependent on Ezh2-PRC2 rather than Ezh1-PRC2, so our data suggest Jarid2 is the accessory factor required in Ezh2-containing PRC2 complexes. Interestingly, mutations have been identified in PRC2 core components in haematopoietic malignancy, and recently mutations and deletions in JARID2 have also been reported.

1A.5: An ENU mutagenesis screen identifies the first mouse mutants of a novel epigenetic modifier, Rearranged L-Myc Fusion (Rlf).

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An ENU mutagenesis screen to identify novel epigenetic modifiers was established in mice carrying a variegating GFP transgene that is highly sensitive to epigenetic silencing. Exome sequencing aided in rapid identification of the causative mutations in ~40 lines. Here we report three independent lines with mutations in Rlf, a novel epigenetic modifier. Rlf mutants display a reduced percentage of GFP expressing cells and increased methylation at the transgene compared to wild-types. Furthermore haploinsufficiency for Rlf shifted the coat colour of mice carrying the epigenetically sensitive Agouti viable yellow allele towards pseudoagouti. These findings suggest that Rlf is a modifier of epigenetic state. Rlf homozygous mutants weigh less than wild-types, and show postnatal lethality. Initial histology suggests the presence of a heart defect. Analysis of RNA-Seq data, comparing RNA from wild-type and Rlf mutant fetal livers, showed differential expression of genes involved in metabolism. Our studies also suggest that Rlf may be involved in regulation of genes lacking CpG islands. Genome-wide bisulphite sequencing studies are underway to examine the role of Rlf in the control of methylation both within and outside of CpG islands. The functional effects of non-CpG island methylation, both on gene expression and development are also being investigated.

1A.6: Evidence for differential DNA methylation on the sex chromosomes of non-eutherian amniote vertebrates

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In eutherian and marsupial mammals, with an XY male/ XX female sex chromosome system, genes (or a subset of dosage sensitive genes) on the single X in males are hypothesized to be upregulated to restore transcriptional parity with the autosomes. Hyper-transcription from the two Xs in females would result in functional tetrasomy, so a mechanism has evolved to transcriptionally silence one X in the somatic cells of females - called X chromosome inactivation. As a result, average transcriptional output from the X chromosome is almost equal between the sexes in eutherian and marsupial mammals. In contrast, dosage compensation in chicken (with a ZW female: ZZ male sex chromosome system) and platypus (males have 5 Xs and 5 Ys: females 5 pairs of Xs) of Z/X genes appears less efficient, where average Z/X transcriptional output is higher in the homogametic sex than in the heterogametic sex.

DNA methylation (particularly at CpG-islands) is well studied in the eutherian X inactivation system, and is accepted to be a late and stabilizing step in maintaining transcriptional silence of the X. Although, there is now evidence for transcriptional silencing of sex chromosomes in the homogametic sex in marsupials, monotreme and birds, there are limited detailed data on DNA methylation of sex chromosomes in these linages. Using reduced representation bisulfite sequencing, we analysed CpG dinucleotide methylation to generate male-to-female differential methylation profiles for non-eutherian representative vertebrates (gray short-tailed opossum, platypus and chicken). In all three linages, each with independently evolved dosage compensation systems, we observed DNA methylation differences on the promoters of X/Z genes between sexes.

1A.7: Sex chromosome dosage compensation in tiger snakes

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Differentiated sex chromosomes are common in many animals. In species with male heterogamety (XY male/ XX female), such as mammals and many lizards, males have differentiated sex chromosomes. In species with female heterogamety (ZZ male/ ZW female), such as snakes and birds, females have differentiated sex chromosomes. In many snakes the W chromosome is heterochromatic, rich in repetitive sequences and contains few active genes. This leads to a dosage imbalance between the genes on Z chromosomes and autosomes, and between the ZZ males and ZW females. To date, no studies have explicitly examined the dosage compensation status of sex chromosomes genes in snakes. Here, we use RNA-seq to show that ratio of gene expression from the single Z chromosome in a female Eastern tiger snake, *Notechis scuttatus* (Serpentes: *Elapidae*), is ~0.81 compared to autosomes: contrary to the expectation of ~0.5 ratio. The expression of Z linked genes in males, with two Z chromosomes, is ~1.6 times higher than in females. This evidence suggests an incomplete dosage compensation mechanism in snakes achieved by up-regulation of Z genes in females.

1B.1: Alan Wilton in his Drosophila days

John Sved[1]

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Alan and I worked together over a period of many years on Drosophila fitness experiments. These were all based around a technique (BET) of following balancer chromosomes in population cages to measure inbreeding depression. Alan was not around when this technique was developed, but he played a critical role thereafter in all aspects of its application.

Most of Alan's effort during his PhD and afterwards went into a series of experiments to investigate whether there are sufficient deleterious recessive genes to cause the high amounts of inbreeding depression revealed by the BET. These are long-term population cage experiments, still yet to give a definitive answer.

The BET suffers from the disadvantage that almost 40% of the genome is simultaneously made homozygous. Others had done experiments to find what happened when two chromosomes were made homozygous (almost lethality). We were more interested in going in the opposite direction, to see what happens when only part of the chromosome is homozygous. Initially it seemed unlikely that one could make part of a chromosome homozygous in a population cage, but we found a way of doing this. I will describe the sorry saga of this experiment.

1B.2: Alan Wilton's Canine Genetics work continues

Rosanne Taylor[1], Annie Pan[1], Claire Wade[1], and Peter Williamson[1]

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Alan Wilton's contributions to identifying the genetic mechanisms and to control of inherited disease in dogs have been extensive. Through a two-decade long partnership with Australian Border Collie breeders Alan was successful in identifying and developing tests for Ceroid Lipofuscinosis and Trapped Neutrophil Syndrome (TNS) in Border Collies. TNS, an animal model of Cohen syndrome, causes neonatal loss with ``fading'' puppies and has a high rate of carriers around the world. Border Collie Ceroid Lipofuscinosis (CL), an animal model of Battens disease, causes progressive neurological dysfunction with ataxia and dementia from 12-18 months of age. It was a significant challenge for Border Collie breeders to manage until Alan's team identified a single base substitution in CLN5 gene which leads to formation of a truncated protein. The tests developed have enabled breeders to make substantial progress towards eradication of these diseases and are continued at the Faculty of Veterinary Science by Associate Professor Peter Williamson. Alan's work with the Working Kelpie breeders on Cerebellar Ataxia is being continued by PhD candidate Annie Pan, focused on better defining the clinical and pathological featues of this condition. It appears likely that a more complex genetic basis may underlie this syndrome, with the results of genetic and pathological studies presented elsewhere in this meeting. We are proud to be continuing Alan's legacy of genetic testing and research and appreciate the support and encouragement of dog breeders.

1B.3: Western NSW families, genes, health and well-being - unfinished business.

Sheila van Holst Pellekaan[1]

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Genetic research with Aboriginal Australians from the Darling River region of western New South Wales has proceeded for twenty years. For historical reasons, there is great sensitivity and some resistance to studies directed at the interface between biological and social science. Initial consultation respected these views and has continued with extensive ongoing personal contact. Initially, studies were focused on mtDNA exploring ancestry and resulted in the identification of ancient mt haplogroups that have contributed to the understanding of global human dispersal. The research direction was expanded to explore candidate nuclear loci including several with a health related focus. While some achievements are evident, the process of acquiring ethical approval for genetic research with Aboriginal Australians has become more complex. Two pieces of collaborative research were prevented and delays have halted the full scale development of the research we envisaged. The reasons for resistance to research is understandable, but has resulted in the current situation where very few Indigenous Australians are included in epidemiological genetic studies. An overview of achievements and delays experienced will demonstrate the value of Alan Wilton's collegial and intellectual support.

1B.4: Looking for Diabetes Genes

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In mid 1990's there was great hope that genetic linkage studies would identify the apparent certain genetic components of type 2 diabetes (T2D). Roughly 50 studies eventually published linkage results for T2D or related quantitative traits. Alan and I, with others, decided to also attempt a linkage study. We selected gestational diabetes (GDM) as the model for T2D. The physiology of GDM is similar to T2D, a high proportion of women with GDM develop T2D, both conditions are familial, pregnant women are the only population in Australia systematically examined for glucose tolerance, and at the young age of onset fewer other illness will be contributing to disease. In all we recruited about 200 sib-pairs from about 180 families, and 45% of parents also provided a blood sample. This is probably the only family based collection of gestational diabetes samples worldwide. To focus our potential genetic testing for T2D we reviewed and plotted all linkage results for the disease to identify ``hot spots'' (published 2009). Genome wide association studies also have been disappointing. While our collection has supported a number of graduate level projects we never obtained the resources for a full study and the samples remain available for future studies.

1B.5: The Genetics of Preeclampsia

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Preeclampsia is the most common serious medical disorder of human pregnancy. Worldwide, it is a major cause of maternal and perinatal morbidity and mortality. Clinically, it is a multi-system disorder classically characterised by pregnancy induced hypertension and proteinuria, but its many effects can also include dysfunctions of the maternal neurological, haematological, hepatic and vascular systems and of the fetoplacental unit. There exists a significant maternal genetic predisposition to the development of preeclampsia, but the genetics of this disorder are complex. Pioneering work by Australian researchers including Prof Des Cooper and Dr Alan Wilton on the genetic basis of preeclampsia has evolved into a worldwide endeavour using increasingly sophisticated genomic and bioinformatics methodologies. Clarification of the genetic architecture of preeclampsia is a major goal of contemporary obstetrics. It would provide an aetiological basis to the pathophysiology of the disorder and offer improved options for its prediction, prognosis and clinical management.

1B.6: New insights on the history of dogs (*Canis lupus familiaris*) in Oceania based on whole mitochondrial genome and autosomal data

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The question of how and when dingoes reached Oceania poses a fascinating question for scientists with interest in the historical movements of humans and dogs. The dingo holds a unique position as top terrestrial predator of Australia and exists in a wild undomesticated state. In the first geographical survey of genetic diversity using both whole mitochondrial genomes and autosomal loci in the dingo, we analysed 16,428 bp from the mtDNA and 8,540 bp from 13 autosomal loci in 25 individuals from five separate populations. Phylogenetic and biogeographic analyses support the hypothesis that there are two distinct mitochondrial clades, one of which occurs in the northwest and the other in the southeast of the continent. Autosomal data is congruent with a hypothesis of two dingo immigrations into Australia. Selection was detected at several autosomal loci indicating that on-going positive selection may be shaping modern dingo population genetics. We employed mitochondrial data to estimate the divergence of the dingo clades as at least 25,473 years BP. Together these data suggest dingoes immigrated to Australia twice and were plausibly present upon the oceanic continent of Sahul prior to the closing of the land bridges between Papua New Guinea and Australia 6,500-8,000 years BP.

2A.1: Disorders of Sex Development - gene discovery and diagnosis

Professor Andrew Sinclair[1], Stefan White[1], and Stefanie Eggers[1]

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One of the most fundamental influences on our lives is our sex. If the sex of a baby is not clear it can create many intractable issues, particularly in terms of medical management. Disorders of Sex Development (DSDs) are congenital conditions in which development of gonadal or anatomical sex is atypical. The cause is most often a breakdown of the complex network of gene regulation responsible for proper development of testes or ovaries. For most DSD patients the etiology is unknown and they cannot be given an accurate diagnosis. We aim to identify the underlying changes in gonad genes of DSD patients in an effort to provide an accurate diagnosis as well as gaining insights into gonad development.

We used whole genome microarrays to detect changes in copy number in DSD patients. This identified a potential novel testis specific regulatory region in SOX9. We also showed that deletions and duplications affecting the regulatory sequences of SOX3 can cause it to be ectopically expressed in the developing gonad, allowing it to drive testis development in the absence of SRY in patients with 46,XX testicular DSD. We also identified mutations in the novel gene, MAP3K1 in patients with 46,XY DSD; implicating a new signal transduction pathway. In addition, we have used Massively Parallel Sequencing (MPS) in two different ways to analyse DSD patients. Firstly, we developed a rapid targeted MPS approach allowing in depth analysis of up to 800 known and potential gonad genes in DSD patients. Secondly, we used whole exome capture and MPS on families, trios and single DSD cases.

This work demonstrates the tremendous power of whole genome approaches, especially when combing MPS data with linkage analysis of a large family. Whole genome analysis provides a rapid approach to identification of the disease-causing mutations and molecular diagnosis in patients with DSD as well as providing insights into gonad development and sex differentiation.

2A.2: Investigating segregation bias and sex-specific NOR heteromorphism in platypus

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Monotremes (platypus and echidna) feature a complex sex chromosome system, which shares extensive homology to the ZW bird sex chromosome system and no homology to the therian XY sex chromosomes. Genes of the therian X are mostly on platypus chromosome 6, which also bears a large heteromorphic nucleolus-organizing region (NOR). In the present study we investigated if the NOR heteromorphism is distributed equally between males and females, if it is related to differential DNA methylation and if it is segregated randomly at male meiosis. First we measured the length of both chromosome 6 homologues in each sex and performed clustering analysis to investigate the presence of two distinct lengths of chromosome 6. This approach has shown that females are predominately heteromorphic for chromosome 6. Next we treated platypus cultured fibroblasts with DNA demethylating 5-Aza-2'-deoxycytidine to determine the impact of DNA methylation on the chromosome 6 heteromorphism in both sexes. This shows that DNA methylation does not entirely explain the difference in NOR size. To determine if the longer or shorter version observed in males segregates preferentially with X or Y chromosomes we have also analyzed the length of chromosome 6 on platypus sperm using Fluorescence In Situ Hybridization. Interestingly, this shows that two different lengths of chromosome 6 NOR are still discernable in sperm. Co-localisation with X and Y chromosomes shows preferential segregation of the shorter version of chromosome 6 with the X chromosomes. Together this provides some evidence of a non-random segregation of chromosome 6 homologs in platypus. Study of chromosome 6 may shed light in the understanding of sex chromosome evolution.

2A.3: Subtractive genomics and the identification of sex specific sequence and genes

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Sex chromosomes contain genes with a transformative power over the developing embryo. By triggering the sex determination cascade, these genes set a trajectory towards the male or female phenotype. Sex chromosomes are enriched for fertility and reproduction related genes, suggesting that sex chromosome diversification is intimately coupled with speciation events. Despite the important functional role of sex chromosomes at both a phenotypic and evolutionary scale, heterogametic sex chromosomes remain the most enigmatic and poorly characterized regions of any genome (the Y chromosome of XX/XY systems and the W chromosome of ZZ/ZW systems). Current sequencing technologies have facilitated the production of large quantities of genomic data, however the accurate assembly of sex chromosomes remains elusive due to the presence of large palindromic regions of high sequence identity (>99%) and a extensive landscape of repetitive DNA. Efforts to disentangle sex chromosome assemblies have been further challenged by high degrees X-Y and Z-W homology. Here we have implemented a novel genome subtraction pipeline to isolate and identify of sex specific sequence in the Bearded Dragon (*Pogona vitticeps*), a species with an unusual thermosensitive ZW micro-sex chromosome system of sex determination. Our reference-free K-mer based genome subtraction and conservative denovo assembly has identified putative W-chromosome sequence by extracting regions present in the female genome (ZW) that are absent in the companion male genome (ZZ). The sex-specificity of all putative W chromosome fragments was validated in a panel of 20 unrelated males and 20 unrelated females using PCR. We have interrogated the sex specific sequence using gene prediction algorithms, to annotate known genes and infer the presence of novel coding regions. The validated back-bone of sex-specific sequence was mapped back to the fully assembled female genome to provide a whole genomic context and identify other sex-linked genes. Subtractive genomics empowers us to identify novel sex-determining genes and pathways in the largely unexplored reptile clade. Additionally our model reptile *P. vitticeps*, offers insights into the thermosensitivity of sex-determination genes and the evolution of alternate modes of temperature dependent sex-determination.

2A.4: New insights into mouse ovary development

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In contrast to the developing testis, molecular pathways driving fetal ovarian development have been difficult to characterise. To date no single master regulator of ovarian development has been identified that would be considered the female equivalent of Sry. Using a genomic approach we identified a number of novel protein-coding as well as non-coding genes that were detectable at higher levels in the ovary compared to testis during early mouse gonad development. We were able to cluster these ovarian genes into different temporal expression categories. Of note, the expression of two genes were detected in XX but not XY germ cells before the onset of sex-specific germ cell differentiation marked by entry into meiosis in an ovary and mitotic arrest in a testis. We also defined distinct spatial expression domains of somatic cell genes in the developing ovary and identified the first two markers to differentiate between different somatic cell precursors in the early ovary. Our data expands the set of markers of early mouse ovary differentiation and identifies a classification of early ovarian genes, thus providing additional avenues with which to dissect this process.

2A.5: ATRX is required for PML nuclear body function in Sertoli cells

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The *ATR-X* (alpha thalassemia, mental retardation, X-linked) syndrome is a severe developmental disorder affecting males caused by mutations in the chromatin remodelling gene *ATRX*. 80% of mutations cause genital abnormalities which include hypospadias and ambiguous genitalia. These patients have poorly formed testes containing only a few scattered seminiferous tubules. Previously, we generated a mouse model with *Atrx* specifically inactivated in the Sertoli cells of the testis (*ScAtrxKO*). *ScAtrxKO* mice developed small testes due to prolonged G2/M phase and apoptosis of proliferating Sertoli cells during fetal life. Here, we investigate further the mechanisms underlying these defects in ATRX-deficient Sertoli cells. We show that in control testes ATRX co-localizes with GATA4 and the heterochromatin protein HP1 in a single PML nuclear body (PML-NB) in Sertoli cells. The presence of HP1 indicated that this PML-NB is associated with chromatin. Intriguingly, in *ScAtrxKO mice*, the size of the PML-NB was increased and HP1 expression was reduced or lost. In addition, these PML-NBs were frequently associated with γH2AX, a marker of double strand breaks. Our data support a model in which loss of ATRX in PML-NBs leads to a failure in heterochromatin formation with subsequent chromosome instability and associated chromosome breaks.

2A.6: Genomics and evolution of male pregnancy in seahorses and pipefish

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Male syngnathids (seahorses and pipefish) have specialised brooding structures (pouches) that provide protection, aeration, and possibly osmoregulation and nutrient provisioning to developing embryos. These structures differ widely across the lineage, offering an unprecedented opportunity to study the evolution of reproductive complexity in these viviparous fish. However, despite the novelty of this trait and the utility of this system for evolutionary research, the physiological changes occurring during syngnathid pregnancy are largely unknown. In order to understand the basic biology underlying male pregnancy, we have used transcriptomic technologies (RNAseq) to sequence genes expressed in pouch tissue at key gestational stages across several species. We have identified a number of candidate genes putatively involved in pregnancy in this group, including genes functioning in tissue remodelling and nutrient transfer. Some of these have homology to genes of known reproductive function in mammals, viviparous reptiles, and other live-bearing fish. Our work suggests a common genetic basis for components of the reproductive machinery in divergent evolutionary lineages, and sheds light on the processes and functions within the syngnathid brood pouch.

2A.7: Cool temperatures produce more males in alpine nests of the XY skink, *Bassiana duperreyi*

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The three-lined skink, *Bassiana duperreyi*, has its sex determined by XX/XY sex chromosomes, but the underlying genotype can be reversed by temperature. The species is wide spread in south-eastern Australia, and this broad distribution provides a unique opportunity to examine geographic variation as a possible component of the evolution of thermosensitive sex determination in reptiles. We have previously developed sex linked DNA markers for B. duperreyi and have used these to identify the frequency of sex reversal in this species along an elevational gradient in the Snowy Mountains of NSW. We show for the first time, that naturally occurring nests in alpine regions produce a greater proportion of phenotypic males (74% male, 26% female) despite both XX and XY genotypes being present in equal proportions. In all nests, males' genotypes were concordant with their phenotypic sex at hatching. In alpine nests, 41% of genotypic females developed as males, and one adult male possessed an XX (female) genotype. No other discordant adults were found in either alpine or lowland regions (n=85), suggesting that sex reversal has enormous fitness costs. Concurrently, we are characterising the genomic differences between males and females using advanced molecular cytogenetics and next-generation sequencing. Our ongoing study will explore the options these lizards have for responding to a changing climate by using elevation as a surrogate for temporal climate change.

2B.1: Does natural transformation accelerate adaptation in bacteria?

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Many bacteria undergo recombination through natural transformation, the uptake and genomic incorporation of free DNA from the environment. Mirroring the difficulties of explaining the evolution of sex in eukaryotes, the adaptive significance of natural transformation remains elusive. We present two mathematical models for the impact of natural transformation on the rate of adaptation to a new environment. We show that when DNA is released upon death of bacterial cells and then persists for some time in the environment, transformation may strongly impede adaptation because predominantly old, non-beneficial alleles will be taken up. Nevertheless, transformation can accelerate adaptation through the Fisher-Muller effect when multiple loci and finite populations are assumed. Moreover, when there is fluctuating selection, transformation may be favoured because it allows the bacteria to revert to an earlier, better-adapted genotypic state.

2B.2: Epidemiological control of drug resistance and compensatory mutation under resistance testing and second-line therapy

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The fitness cost of antibiotic resistance without treatment raises the possibility that prudent use of drugs may slow or reverse the rise of resistance. Unfortunately, compensatory mutations that lower this cost may lead to entrenched resistance. Here, we develop a mathematical model of resistance evolution and compensatory mutation to determine when reversion to sensitivity occurs, and how disease control might be facilitated by a second-line therapy. For treatment with a single type of antibiotic, sensitive bacteria reach fixation only under treatment rates so low that hardly any cases are treated. We model a scenario in which sensitivity can be accurately assessed so that an alternative treatment is administered for resistant cases. Before the rise of resistance to the second drug, disease eradication is possible if resistance testing and second-line treatment are conducted at a high enough rate. But if the compensated resistance is strong against both drugs, resistant-compensated bacteria predominate for most of the parameter space. Under such conditions we derive threshold treatment and testing rates separating fixation of resistant-compensated strains from disease eradication. This boundary is sensitive to the underlying basic reproductive number of the pathogen, but less sensitive to fitness parameters of resistance and compensation.

2B.3: Genetic Distance for a Non-Stationary Homogeneous Markov Substitution Process

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Measurement of the genetic distance between biological sequences is of fundamental importance to the field of molecular evolution. It pertains to questions of rates of evolution, phylogenetic inference, and the existence of a molecular clock. Many definitions have been proposed.

Under the class of continuous time substitution models, the distance is commonly defined as the expected number of substitutions at any site in the sequence. We overcome issues of mathematical and computational tractability to eschew almost ubiquitous assumptions of stationarity and time-reversibility and extend the measurement of the expected number of substitutions to general time-homogeneous Markov models.

We fit the general model to samples from across the tree of life to compare distances so obtained with those from standard models and empirical pairwise methods. We discover that existing methods, including those explicitly designed to address non-stationarity, systematically overestimate genetic distances and departures from the molecular clock. The magnitude of the distance bias is proportional to divergence from stationarity.

2B.4: Estimating HIV recombination rates in vitro and in vivo

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The ability of HIV to evade immunity and develop drug resistance depends on HIV reverse transcriptase inducing a high rate of mutation and recombination. We have developed a mathematical framework that integrates factors such as the variable proportion of heterozygous virions, and the number of `unobserved' recombinations to accurately estimate the recombination rate of HIV. Using a system of synonymous marker mutations in HIV-1 gag and pol of pDRNL(AD8) to identify recombination in a single round of infection of PBL, combined with a high-throughput sequencing, we directly estimate the viral recombination and mutation rates. From >7 million nt we observed 4801 recombination events and 859 substitution mutations (≈1.51 and 0.12 events per 1000 nt respectively). We find ≈20% of total substitution mutations are associated with a recombination event. However, it is unclear whether these events are mechanistically linked (for example recombination induces mutation), or whether these events occur independently. We have recently extended this work using publically available data derived from single genome sequencing of HIV soon after transmission in natural infection. We estimate recombination rates in these sequences and show that the `per replicative cycle' recombination rate is very similar in vitro and in vivo.

2B.5: Choosing the number of relaxed-clock models in molecular phylogenetic analysis

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Estimating evolutionary timescales is a common aim of molecular phylogenetic analysis. This can be done using methods based on the molecular clock, which postulates a constancy of evolutionary rates among lineages. Most data sets, however, exhibit significant levels of rate variation among lineages. This can be caused by differences in population size, mutation rate, or the strength of natural selection. Relaxed molecular clocks allow the phylogenetic estimation of evolutionary timescales even when rates vary among branches.

In analyses of large and informative data sets, it is often appropriate to use multiple relaxed-clock models to accommodate differing patterns of rate variation among genes. In most cases, however, there is no clear rationale for preferring one clock scheme over another. If the evolutionary process is modelled with an inadequate number of relaxed clocks, the resulting estimates of rates and timescales might be misled. On the other hand, increasing the number of relaxed-clock models carries the risk of model overparameterization. We present an objective method for selecting the number of relaxed clocks for analyses of multigene data sets.

2B.6: Using bias corrected mutual information (BCMI) to discover novel associations in genomic data

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Large and high-dimensional datasets are increasingly common in genomics. There is a need for exploratory approaches that can identify novel, possibly complex nonlinear, associations in these data which often contain different types of variables (say, continuous and categorical). As it is infeasible to directly inspect plots of all pairs of variables a single measure that can identify a wide class of associations can be of great use. We propose the use of a bias corrected mutual information measure (BCMI) which can be applied to all kinds of variables measured while being comparatively quick and easy to calculate. The use of BCMI provides a novel exploratory approach that can be applied in a wide variety of settings. These association scores can also be used as a basis for clustering and network construction. We demonstrate our approach using genomic data from a mouse model of obesity that contains clinical measurements, microarray gene expression levels (continuous variables) and single nucleotide polymorphisms (SNPs) (categorical variables). We compare our approach with the recently proposed maximal information coefficient (MIC), in particular we show BCMI to have equal or better power than MIC for several common functional relationships.

2B.7: The acquisition of genetic pathways in bacteria.

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Horizontal gene transfer (HGT), in which a strand of DNA from another cell is incorporated into a host, is believed to explain the ability of bacteria to rapidly acquire new genetic traits. In some examples, such as multi-gene drug resistance, this feature can have a significant impact on humans. In this talk I will present a combinatorial model of pathway acquisition that incorporates HGT, the fitness cost of carrying partial pathways, the fitness benefit of carrying the full pathway, and exposure to a beneficial environment. We use this model to study how pathways are acquired, and to explain the observed presence of partial pathways.

3A.1: Using ancient dental calculus to trace the impacts of diet, and the evolution of human disease and pathogen genomes

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Links between the human microbiome and health have become increasingly apparent, but the lack of a fossil record of human bacteria means we know little about how these communities were shaped over time. Skeletal morphologies suggest that the adoption of farming (~10,000 yBP) and the introduction of industrially processed carbohydrates (~1,800 AD) had a major impact on the oral microbiome, and human health. We have found that bacterial DNA survives in ancient dental calculus, or calcified dental plaque, on skeletons from around the world, providing a means to analyse the evolution of the human microbiome through time. We have examined a temporal transect in Europe, from Mesolithic hunter-gatherers, to the first farmers (around 8kyr ago) and on to the metal ages, through the Medieval Period and Industrial Revolution. We can see major changes in pathogenic-associated bacteria that appear to relate to the introduction of large amounts of carbohydrate in the Neolithic (farming) Era, and again at the Industrial Revolution when sugar and processed flour became widely available. The results confirm that dental calculus provides a new record of human health, as well as cultural change and movement, and provide a unique means to examine the genomic evolution of a range of pathogens. We have also examined the evolutionary origins of the human microbiome by comparing it with Neandertal dental calculus, to clarify the extent of co-evolutionary relationships and potential role in human health.

3A.2: *Face space* separates rare genetic disorders.

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One in 17 individuals (400 million) worldwide has a rare genetic disorder, but most fail to receive a genetic diagnosis. Identifying rare syndromes is often serendipitous, depending on expert clinicians recognising characteristic dysmorphisms, frequently cranium or facial features, in multiple individuals.

We collected a database of ordinary photos, uncontrolled for variations in image quality or type, of 1,585 people with one of 12 syndromes (22q11, Angelman, Apert, Cornelia de Lange, Down, Fragile X, Marfan, PACS1, Progeria, Sotos, Treacher-Collins, Williams). We used an algorithmic pipeline to automatically annotate images as the basis for machine learning to create a ``*face space*'' - a generalisable model for human dysmorphic facial variation within which patients sharing a specific dysmorphic disease or syndrome cluster. For four of the syndromes not used in training, the search space for similar patients is reduced by 95.6%. Using *face space* it is possible to provide a quantitative assessment of similarity to known genetic syndromes and objectively identify similarities in facial features in individuals with unknown genetic disorders.

Face space will assist in determining when whole genome sequencing is required for diagnosis, and by the overlay of `*genotype space*' should increase the power to identify novel causative genetic variants.

3A.3: Biases in antibody gene recombination shape the lymphocyte repertoire

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We have used deep sequencing data, from a single individual, to generate empirically-derived probability distributions associated with the independent processes that contribute to the diversity of the antibody gene repertoire. This has allowed us to create large, simulated repertoires of sequences, defining the `shape' and composition of an individual's repertoire, and to cross-validate simulations against datasets from individuals with similar genotype.

Analysis suggests the process of recombination of V, D and J genes has evolved to bias the antibody repertoire towards a relatively small pool of high frequency heavy chain (IGH) sequences. Remarkably, around 5% of possible IGH are carried by 95% of naïve B cells, and these IGH are shared with other individuals. Other low frequency sequences provide extremely diverse IGH that are unique to an individual. In an individual, high frequency IGH are each carried by about a million naïve lymphocytes, while many other IGH are each carried by just a single lymphocyte. A core antibody repertoire appears to be genetically hard-wired, ensuring that each individual possesses a repertoire of functionally important IGH at high copy number. This `shaping' of the repertoire has important implications for the ontogeny of immune responsiveness, and for the kinetics of immune reactivity.

3A.4: Functional gene haplotypes for the immunoglobulin variable region loci

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The variable region of an antibody is encoded by 7 sets of highly similar genes, interspersed between numerous repetitive elements. However, the application of high-throughput sequencing to V(D)J rearrangements allows the inference of phased haplotypes if commonly rearranged genes are heterozygous, as V(D)J recombination is an intrachromosomal event. We have assembled 424 immunoglobulin variable region haplotypes. Deletion polymorphisms were observed involving both multiple IGHV and IGHD genes, and duplications where two sequences previously recognised as allelic variants of a single gene were found to lie on the same chromosome. Phase information has implications for the potential combinatorial diversity of the antibody repertoire. Estimates of the size of the primary human repertoire generally assume that functional genes of the same type (V, D or J) are equally likely to be present in any rearrangement. However, our data show that the frequencies with which different IGHD genes partner with each IGHJ gene are subject to strong, though complex, positional biases. When separately analyzing rearrangements of each chromosome, we see that individuals carrying IGHD gene deletion polymorphisms show a predictable overutilization of other genes. Incorporating these biases into models of repertoire development is essential if we are to understand individual variation in immunocompetence.

3A.5: A new mouse model of Canavan disease displays hearing loss

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Canavan disease is a leukodystrophy caused by mutations in the *ASPA* gene, encoding aspartoacylase. In this disease degeneration of myelin causes progressive mental retardation, motor deficit and death during childhood or teenage years. A novel mouse model of this disease arose during an ethylnitrosourea mutagenesis screen for deaf mice. This mutant mouse, named *Deaf14*, carries a c.516T>A mutation in *Aspa*, that is predicted to cause a p.Y172X protein truncation. Unlike wild-type mice, *Deaf14* mice do not startle in response to loud noise. Their auditory brainstem response thresholds are normal, but peak III is abnormally small. This suggests that the cochlea is functioning normally but auditory signals are unable to propagate through the brain. *Deaf14* brains are extensively vacuolated by early adulthood. At this age, *Deaf14* mice show normal levels of anxiety in the light-dark test and memory in the y maze test. However, they fall off a rotarod faster than wild-type mice and have travel less distance in a locomotor test. This mild ataxia progresses with age. The *Deaf14* mouse has a milder phenotype than other *Aspa* mutants, possibly because of its BALB/c genetic background.

3A.6: Morpholino-mediated knockdown in the zebrafish of eye disease genes identified by next-generation sequencing

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Developmental failure of the anterior eye structures including the lens, cornea, and iris can cause anterior segment dysgenesis (ASD), cataract, microphthalmia and/or glaucoma. Vision may be at risk with reduced corneal transparency or high tension glaucoma. The underlying genetic causes remain elusive in many cases. We have identified a novel candidate disease gene from a balanced translocation patient with severe ocular anterior segment dysgenesis, microphthalmia and cataract. Additional pathogenic variants in this gene have been identified in our ASD/cataract patient cohort by exome sequencing. We used zebrafish to test the candidate gene function in eye development. The spatial expression of the zebrafish ortholog was studied in eye development by in situ hybridisation, and transcript distribution was predominantly restricted to the lens. We designed splice-blocking Morpholino Antisense Oligos (MOs), and these were injected into fertilised zebrafish eggs. Abnormal transcripts in the MO-injected embryos were confirmed by expression analysis. The morphants had small eyes (microphthalmia) and irregularly shaped lenses, with adhesion between the cornea and the lens. These features were consistent with those seen in patients with abnormality of this gene. Our findings highlight the value of the zebrafish as a useful model for investigation of novel disease variants in eye disease.

3A.7: Evolution and inactivation of human retroelements by editing enzymes

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The human and primate genomes encode a family of genes known as APOBEC3. The products of these genes in particular APOBEC3G and APOBEC3F inhibit viral infection. These proteins have been shown to inhibit HIV, HBV as well as a range of endogenous retroelements through mutation and/or mutation-independent mechanisms. In the former mechanism, one or more APOBEC3 molecules are trafficked into a nascent virion and then target the HIV RNA for mutagenesis in a newly infected cell. These enzymes induce context dependent G(guanine)-to-A(adenine) mutations in the positive strand of viral genomes by deaminating C(cytosine) to U(uracil) in the negative strand of viral RNA. APOBEC3G preferentially mutates G within GG; while the other members of this family including APOBEC3F target G within GA. We developed a bioinformatics approach to find the footprints of inactivation and/or evolution by these enzymes on the genomes of HIV and endogenous retroelements ERV, SINE and LINE. Analysis of a large number of sequences from these elements identified individual ERV-K and ERV-1 elements with footprint of GG-to-AG or GA-to-AA changes on their genome. A slight GA-to-AA change was also present in the genome of the entire population of these retroelement families that might suggest an evolutionary pressure by APOBEC3F. The genomes of SINE and LINE elements did not have a G-to-A footprint to suggest a role for APOBEC3 in inactivation or evolution of these sequences. In the case of HIV the footprints were only found on so called ``hypermutated" sequences. The general HIV sequences did not contain signatures of context dependent G-to-A changes.

3A.8: Identification of a clade of dog breeds susceptible to atopic dermatitis with a unique immunophenotypic profile

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Canine breed structure provides a powerful model to analyse complex phenotypes, such as atopic dermatitis (AD). Canine AD has similar clinical signs and pathological features as human AD, and has been increasing in prevalence. Disease pathogenesis involves immune dysregulation and skin barrier impairment, which are linked to both environmental and genetic effects. While many studies report highly represented dog breeds, most have not analysed relative risk (RR). Genetically isolated populations, such as Australian dogs, have the potential to identify candidate genes, but first clarification of breeds with increased RR in this population is required. Records of dogs with confirmed AD (Sydney, n=290; Camden n=456), attending two Sydney University clinics (>23,000 dogs; 2001-2009) were reviewed, and breed prevalence was calculated. Sixteen breeds with RR≥1.5 were identified. Comparison of highly represented breeds from canine AD prevalence studies (1971-2010) with established canine breed haplotype structure suggests a common genetic origin for many susceptible breeds. One clade of dog breeds was identified that is highly represented amongst AD patients worldwide, and with increased RR in Australia. Unique cytokine profiles were found in Staffordshire bullterriers, a breed from this clade. Functional genomics studies in breeds within this over-represented clade may improve understanding of AD pathogenesis.

3B.1: A tribute to Professor Des Cooper

Katherine Belov[1]

[1] *University of Sydney*

This symposium commemorates the research of Professor Des Cooper. Des earned a Bachelor of Science degree (with Honours) at the University of Adelaide, followed by a PhD in the field of sheep genetics under the supervision of Dr Jean Mayo. After the completion of his PhD, Des commenced a CSIRO Overseas Postdoctoral Fellowship at the Agricultural University of Sweden and a postdoctoral fellowship at the University of Wisconsin before returning to Australia in 1968 to take a lectureship at La Trobe University. During his time at La Trobe, Des began work on his long-held view that marsupial and eutherian mammals constitute independent experiments in mammal evolution and could therefore shed light on gene function and evolution, particularly with respect to the sex chromosomes. This line of inquiry would shape Des's academic pursuits for the rest of his career. In 1973, Des moved to Sydney to take up a lectureship in the School of Biological Sciences at Macquarie University. He was promoted to Associate Professor within a year and became Chair of Genetics within a decade. Des stayed at Macquarie for 32 years, and played a pivotal role in teaching, research and administrative management. In 2005, he moved to the School of Biological, Earth and Environmental Sciences at the University of New South Wales where he continued his active research and developed the Masters in Conservation Biology degree, jointly taught with Victoria University in Wellington, New Zealand. In this symposium, speakers will cover Des' achievements in human genetics and marsupial genetics research, including development of the tammar wallaby as a model organism for genetic research, X-inactivation and sex differentiation in marsupials, and sexual development in intersex marsupials, marsupial immunology and population management and fertility control in marsupials. We will also pay tribute the amazing role Des played as a mentor to Australia's geneticists.

3B.2: Kangaroo gene mapping and sequencing; insights into mammalian sex chromosomes

Professor Jennifer Graves[1]

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The deep divergence of marsupials and eutherian mammals 160 million years ago provides genetic variation to explore the evolution of DNA sequence, gene arrangement and regulation of gene expression in mammals. The pioneering work of Professor Desmond W. Cooper in establishing sex linkage of enzyme markers and demonstrating that they are expressed only from the maternal X chromosome set the stage for many contributions to our understanding of mammalian sex chromosome organization, activity and evolution. Emerging techniques in cytogenetics and molecular biology have been adapted to characterize the sex chromosomes of kangaroos and other marsupials. In particular, genetic and genomic work over four decades has shown that marsupial sex chromosomes differ significantly from the eutherian XY chromosome pair in their size, gene content and activity. These differences can be exploited to deduce how mammalian sex chromosomes, sex determination and epigenetic silencing evolved.

3B.3: Des Cooper's impact on human genetics education

Jenny Donald[1]

[1] *Macquarie University*

This talk will look at Des Cooper's contributions in human genetics, and his impact on human genetics education, particularly through Macquarie University.

3B.4: Des Cooper's Contributions to New Zealand Science

Charles Daugherty[1]

[1]*Assistant Vice-Chancellor (Research), Victoria University of Wellington, Wellington, New Zealand*

Presented by Charles Daugherty, Assistant Vice-Chancellor (Research) and Professor of Ecology, Victoria University of Wellington, P.O. Box 600, Wellington, New Zealand

New Zealand was a second home to Des Cooper, and he often stated that he would be happy to live there. Despite never realising this ambition, Des contributed significantly to university research and post-graduate teaching in New Zealand. In 2002, Des initiated development of a jointly taught, one year Master of Conservation Biology programme between Macquarie University and Victoria University of Wellington, designed to compare and contrast the very different conservation problems and approaches taken in Australia versus New Zealand. Over the past decade, well over one hundred students from around the world have completed this truly international degree. Additionally, Des supported development of a New Zealand Centre of Research Excellence - the Allan Wilson Centre for Molecular Ecology and Evolution, a consortium of five universities and Crown Research Institutes. From 2008 - 2012, Des contributed strongly to strategic development of the Centre, served on the Governance Board, and participated in Annual Meetings with great enthusiasm. The graduates of the master's programme and the Allan Wilson Centre are significant legacies of Des' work in New Zealand.

3B.5: Immunocontraception: ecological and immunogenetic issues

Neil J. Gemmell[1]

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Australia and New Zealand share a common problem; following the arrival of Europeans they both experienced the deliberate and accidental introduction of a variety of mammalian species that have wreaked havoc on the indigenous flora and fauna. Beginning about 30 years ago both nations sought to use the latest genetic approaches to establish fertility control for a variety of mammalian species. New Zealand's efforts focused on the brush-tail possum; a species protected in Australia, but one of the most damaging pest species in the New Zealand context. Using recombinant technologies immunocontraception agents were established and significant progress made to establish vectors for the transmission of this immunocontraceptive. The creation of a dispersive, potentially self-perpetuating, marsupial immunocontraceptive raised obvious concerns about the prospect that New Zealand's attempts to control its brush-tail possum population might present a hazard to Australian species should this vector become established in Australia. A lasting memory of mine was the strength of character and conviction that Des Cooper showed when confronted with this possibility. Des advocated against the use of this technology when the consequences were so potentially dire. Here I review some of that debate and Des' role in re-shaping thinking on immuocontraception control strategies.

3B.6: Immune regulation at the fetal maternal interface in marsupials

Rob Miller[1] and Victoria Hansen[1]

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The mechanisms maintaining maternal immune tolerance to allogeneic fetal tissues during pregnancy represent important innovations in the evolution of viviparity in vertebrates. This is particularly true in the mammals with invasive and sustained contact between placental membranes and maternal circulation. Whether or not the maternal immune system is ``aware" of the fetus in marsupials has been a subject of debate. The short gestation times and lack of sustained, invasive placentae in marsupials have lead some investigators to conclude that regulation of the maternal immune response is unnecessary. Indeed, in 1988 Van Oorschot and Cooper demonstrated a lack of antibodies against paternal alloantigens in pregnant tammar wallabies, consistent with a lack of immune recognition of pregnancy. To investigate this further, an Illumina based transcriptome analysis of endometrial immune gene expression during pregnancy was performed using the opossum, *Monodelphis domestica*. As in eutherians, pro-inflammatory cytokines such as IL-1, IL-6, and IL-17 are down-regulated late in gestation in the opossum. However, unlike eutherians this is not due to decidual prolactin, which is not produced in marsupials. Overall the results support active regulation to inhibit inflammatory responses during pregnancy in the opossum, consistent with there being potential harm to embryos due to maternal immune mechanisms. This regulation appears to be one of the fundamental innovations that may have permitted the evolution of viviparity in therian mammals.

3B.7: The tammar wallaby as a model species for determing the genetic basis behind tolerance to 1080

Janine Deakin[1,2]

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[2] *Research School of Biology, The Australian National University, Canberra, Australia*

Prof Des Cooper advocated the use of the tammar wallaby as a model species for marsupial genetics research. He recognised the value of the genetic variation identified between geographically isolated subspecies, which led to the establishment of a pedigreed colony of crosses between Kangaroo Island (South Australia) and Western Australian tammar wallabies. One phenotypic difference between the two subspecies is there difference in susceptibility to the commonly used vertebrate pesticide sodium fluoroacetate (1080). Tammar wallabies from Western Australia are tolerant to 1080 whereas those on Kangaroo Island are not. The availability of genetic and genomic information, combined with this distinct difference in 1080 tolerance between subspecies, makes the tammar wallaby an ideal species in which to study the genetic basis behind 1080 resistance. An examination of the aconitase gene *ACO2*, a candidate gene for 1080 tolerance since this poison inhibits the action of the mitochondrial aconitase enzyme it encodes, has failed to uncover the genetic basis of 1080 tolerance. Future studies will need to take a genome-wide approach using the genetic resources developed by Prof Cooper during his career.

3B.8: The intersection of reproductive and genetic approaches to marsupial population management: Why is it important for conservation?

Catherine Herbert[1]

[1] *Faculty of Veterinary Science, The University of Sydney, NSW, 2006*

Professor Des Cooper left a lifelong impression on me. I initially completed a PhD within his laboratory at Macquarie University. At the time, I was the only student completing a research project that was comprised almost entirely of reproductive biology experiments, in an otherwise molecular genetics lab. Needless to say, I was the black sheep of the lab! However, as I stepped outside my comfort zone, Des instilled in me the importance of incorporating a multidisciplinary approach to research within biological sciences. He also demonstrated that there was a role for genetics in everything we did (much to my dismay at the time!), something that I now appreciate more and more as my research career progresses. Today I will give one example of how reproductive and genetic technologies can be used in a complimentary fashion to manage conservation-dependent marsupial species. The current management regimes for many of our threatened and vulnerable marsupial species, where animals are often confined to enclosed management systems (be they small intensive or large extensive systems), raises two important management issues. The first relates to the management of genetic diversity within these populations. It has long been recognized that we need to maintain as much genetic diversity as possible within these isolated populations to safeguard the future evolutionary potential of these populations. A frequently overlooked management problem, however, is the management of ``overabundance'' within these enclosed systems. When conservation-dependent species are no longer exposed to the threatening processes affecting their survival in the wild, population growth and subsequent overcrowding often becomes an issue. But how should this be managed? In this presentation I will suggest a new approach to this increasing dilemma, which involves the use of intensive genotyping of individuals within these populations, and selective use of reversible fertility control agents, which were initially developed to manage overabundant wildlife populations. As technologies for genetic typing become cheaper, there are unique opportunities to selectively manage the reproductive output of animals in captive breeding programs to maximize the retention of genetic diversity by selectively contracepting individuals with genotypes that are over-represented within the population. This will facilitate a more effective use of the limited ``space'' within captive breeding programs, and help to minimize the discrepancy between the actual population size and the effective population size.

4A.1: Genomics and Australo-Papuan collections-based science: thoughts on where we are headed

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Collections-based research is poised at another exciting transition, which has arisen because of the avenues of research that are made possible on museum and herbarium specimens by the tools of genomics. Phylogenetics benefits from the analytical power of more loci. Ever larger numbers of loci and our ability to choose different kinds of loci stands to strengthen phylogenetic frameworks, notwithstanding the challenges of handling such volumes of data, and the biological inferences they generate. Traditional museum collections are profoundly large repositories of dormant genetic data lying dormant. Now, this treasure trove of taxonomic, spatial and temporal data is within reach, and can complement cryofrozen material. This will revolutionize sampling applied to trenchant problems of species-level systematics, landscape genetics and its temporal span, or indeed on the inclusion in phylogenetic analyses of extinct species, which are only available in collections. A new window is opening on selection in natural populations and prediction of responses of populations to environmental change. Notably, this may call for some changes in the way specimens are collected, and collections have responded to this before. Ecogenomics can enhance rapid environmental assessment as well as monitoring of environmental impacts; it can measure taxonomic diversity from species to phyla within and between soil or water samples. Evolutionary Rescue is a nascent field developing in parallel with genomics tools. It emphasizes a shift to a perspective on evolutionary dynamics that focuses on short time-scales, genetic variants of large effects and absolute rather than relative fitness. An emerging key area in Evolutionary Rescue is the genetic and genomic mechanisms of adaptation to climate change. Collections-based research stands to offer much to this whether from existing collections and the sample sizes they offer, the temporal range that collections have to offer and as repositories of new kinds of specimens.

4A.2: Phylogenetic indices for identifying diversity hotspots: an example using the ferns of Australia

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Diversity is traditionally measured as the number of taxa (typically species but sometimes genera) that occur in a region of interest, and therefore, is a geographic-based index. As an alternative to taxonomic diversity, there are measures that incorporate phylogeny as well as geography. These phylogenetic measures can be calculated for diversity and endemism, and are advantageous because the phylogeny takes into account the relationships among taxa and their evolutionary history. Geographic-only measures use species and genera, but in phylogeny-based measures, the unit is the branch length of a terminal taxon. Using a species as a terminal does not provide substantially more branch length than a genus, and thus, phylogenetic measures are not particularly sensitive to the taxonomic level chosen for analysis. Similarly taxonomic changes to species or genus names do not affect the results. Here we examine phylogenetic patterns of diversity and endemism for the ferns of Australia. Our dataset includes a three-marker phylogeny of almost 90 genera, and their associated distribution records are derived from over 60,000 herbarium collections across the continent. We show that the inclusion of phylogenetic indices can identify new areas that standard metrics do not. Identifying regions with high phylogenetic diversity and endemism can complement current conservation efforts.

4A.3: Evolution of a hotspot genus: geographic patterns of diversification in *Banksia*

Marcel Cardillo[1] and Renae Pratt[1]

[1] *Research School of Biology, Australian National University*

Australia's southwest corner is one of the world's Mediterranean-climate hotspots of angiosperm diversity. The evolutionary and ecological processes underlying the remarkable diversity of these regions are poorly known, but many hypotheses suggest that angiosperm diversification has been more rapid within hotspots compared to elsewhere. Using a new molecular phylogeny of *Banksia*, we find little evidence that diversification rates have been higher in the southwest hotspot compared to the rest of Australia, despite 10-fold higher *Banksia* species richness in the southwest. On the other hand, we find substantial variation in diversification rates between bioclimatic zones within the southwest. Our findings are inconsistent with the view that Mediterranean hotspots are necessarily underpinned by rapid radiations. We suggest that steady accumulation of species at unexceptional rates, but over long periods of time, may also have contributed substantially to the great diversity of these regions.

4A.4: Calibration placement and the reliability of molecular clocks

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The molecular clock is a powerful phylogenetic tool for estimating evolutionary timescales. Many studies rely on these estimates, in fields ranging from phylogeography to molecular epidemiology. One of the most successful applications of the molecular clock is modelling the spread of infectious disease, such as HIV and influenza viruses in human populations.

In order to provide estimates of absolute timescales, molecular clocks need to be calibrated. A common method is to incorporate temporal information from fossils or biogeographic events, which can be used to fix the ages of one or more nodes in the phylogeny. The ages of other nodes can then be estimated by extrapolation.

The placement and number of calibrations can affect phylogenetic estimates of evolutionary timescales. However, actual evolutionary timescales are rarely known, which makes it difficult to compare the performance of different calibration strategies. We addressed this problem by conducting an extensive simulation study.

We found that the most accurate and precise molecular clock estimates are obtained with multiple calibrations or single calibrations at the root of the tree. Our results will provide a useful guide for future studies of evolutionary timescales using molecular clocks.

4A.5: Speciation underground versus colonisation from the surface: phylogeography of subterranean diving beetles from the Western Australian arid zone.

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Isolated calcrete (carbonate) aquifers in the arid zone of Western Australia contain diverse assemblages of subterranean aquatic (stygobiontic) and terrestrial (troglobiontic) invertebrate species, including the world's most diverse assemblage of dytiscid diving beetles. In this presentation we will summarise our research on the evolutionary mechanisms that have generated this extraordinary diversity of beetle species, and consider the evidence that species may have diversified underground. Broad-scale phylogeographic studies of the beetles provided strong evidence that the majority of beetle species evolved from surface ancestors that independently colonised the calcretes, a process driven by ongoing aridity on the Australian continent since the late Miocene. However, there were at least 11 calcretes where sister species pairs or triplets were found, and simulation studies of their evolution provided evidence that a majority of these sister species evolved underground from stygobiontic ancestors. We further investigated the hypothesis that micro-allopatric speciation processes (fragmentation and isolation by distance) occur within calcretes using comparative phylogeographic studies of beetles and amphipod crustaceans from two calcrete aquifers. Phylogenetic and haplotype network analyses of mtDNA sequence data revealed significant population structuring in one of the calcretes (Laverton) and for one species of amphipod in the second calcrete (Sturt Meadows), where there was also evidence for isolation by distance over very small spatial scales in multiple species. These findings suggest that micro-allopatric evolutionary processes within calcretes may be a significant diversifying force, although only a relatively small proportion of stygobiontic beetle species are likely to have resulted from in situ speciation in this system.

4A.6: A skyline view through the neck of a bottle: Detecting historical population crashes using DNA sequences

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Population sizes of living organisms often change over time, due to factors such as climatic changes or anthropogenic pressure. By applying Bayesian skyline methods to DNA sequence data, we can infer past population sizes, as well as the timing and severity of their drops and rises. Such information can be further used to test hypotheses about and the impact of climatic shifts or the appearance of predators or competitors and to evaluate conservation issues.

However, there have been a few instances when historical population drops were not able to be detected using these methods. For example, Bayesian skyline analysis did not find any decrease in population size in the bowhead whale, which was hunted almost to extinction from the 16th to early 20th centuries.

We used real and simulated DNA data sets to detect circumstances in which Bayesian skyline methods are unable to detect historical population crashes. This can occur, for example, when the data set is not sufficiently informative. We provide guidelines for the design and interpretation of Bayesian demographic estimates based on genetic data.

4A.7: Molecular phylogeny of the subtribe Hakeinae (Green Plants: Proteaceae tribe Embothrieae) and its implications

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The phylogeny of the subtribe Hakeinae (Green Plants: Proteaceae tribe Embothrieae) was reconstructed by analysing an alignment of DNA sequences for four chloroplast loci and one nuclear gene. These were sampled from 149 of the 510 known species of Hakeinae plus 9 outgroup genera. The two Bayesian phylogenetic programs that were used to analyse the data, MrBayes and BEAST, produced cladistically identical results. The tree derived using BEAST is a chronogram, which we calibrated using fossil pollen grains of outgroup taxa as age constraints. The tree produced from the full data set strongly supported many putative clades, including the Hakeinae, *Hakea*, and the position of *Opisthiolepis* as sister to the rest of the Hakeinae. However, *Hakea* and *Finschia* are deeply nested within *Grevillea*, rendering the latter paraphyletic and necessitating taxonomic change. A combination of traits was used to infer whether species are pollinated by insects or birds. When inferred pollinators were mapped on the tree using the ancestral state reconstruction package in Mesquite, the Hakeinae were unequivocally resolved as ancestrally insect-pollinated. Bird pollination has evolved independently at least six times in the Hakeinae over the past 25 million years. Secondary reversals to insect pollination have occurred at least eleven times.

4B.1: Mitochondrial DNA Haplotypes Define Gene Expression Patterns in Pluripotent and Differentiating Embryonic Stem Cells

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In mammals, mitochondrial DNA (mtDNA) encodes 13 subunits of the electron transfer chain, which generates the vast majority of cellular energy through oxidative phosphorylation. It also encodes 22 tRNAs and 2 rRNAs. MtDNA haplotypes are associated with various phenotypes, such as increased or decreased susceptibility to disease, environmental adaptations and ageing. Using a mouse embryonic stem cell model, where each line possessed the same Mus musculus chromosomes but harboured one of Mus musculus, Mus spretus and Mus terricolor mtDNA haplotypes, we observed mtDNA haplotype-specific expression of genes involved in pluripotency and differentiation and their potential to produce spontaneously beating cardiomyocytes. The differences in gene expression patterns and cardiomyocyte production were independent of ATP content, oxygen consumption and respiratory capacity, which were considered to be the primary roles of mtDNA. However, there was differential regulation of the master regulators of cardiomyocyte differentiation. Our more recent data show that mtDNA haploytpes significantly influence genome-wide patterns of DNA methylation in pluripotent and differentiating cells and, specifically, DNA methylation of exon 2 of the nuclear-encoded mtDNA-specific replication factor, PolgA, which regulates mtDNA copy number in a cell-specific manner. We propose that mtDNA haplotypes play a pivotal role in cell fate.

4B.2: New complexities in mitochondrial signalling revealed in the *Dictyostelium* model.

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Mitochondria whose respiratory oxidative phosphorylation is collectively compromised or insufficient can signal this to the cell in a variety of ways, including elevated production of reactive oxygen species (ROS), decreased capacity to buffer cytosolic Ca2+ signals and decreased ratios of ATP to AMP and ADP. In each case, the respiratory deficiency can result from defects in any or all of the mitochondrial respiratory complexes and should cause the same downstream outcomes, including activation of cellular stress-sensing protein kinases. AMPK is one such kinase that is activated by a variety of stress signals, including ROS, Ca2+ and AMP/ADP. Using the *Dictyostelium* mitochondrial disease model, we discovered that chronic AMPK activation and the resulting signalling dysregulation causes diverse cytopathological outcomes, some of which are caused by AMPK-mediated inhibition of TOR Complex I. These disease phenotypes were the same, regardless of the underlying genetic cause, provided that the genetic defect coordinately affects multiple respiratory complexes. Unexpectedly different phenotypic patterns were observed to result from isolated (specific) deficiencies in Complex II (succinate dehydrogenase knock down) or Complex I (knockout of two different Complex I assembly factors, MidA/C2orf56/PRO1853 and Ndufaf5). In these isolated respiratory complex deficiencies, the phenotypes include both AMPK-dependent and AMPK-independent cytopathologies. These distinctive disease phenotypes suggest different patterns of dysregulation of intracellular signalling and novel stress kinase-independent pathways of communication between specific mitochondrial respiratory complexes and the rest of the cell.

4B.3: Trojan Female's - a new biocontrol tool

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Pests cause or carry disease, damage or consume food crops and other resources, and drive global environmental change. Conventional pest management usually involves lethal control, but is costly, can be inefficient, and often raises ethical issues. Consequently, pest management via control of reproductive output is increasingly considered an optimal solution. One of the most successful such 'fertility control' strategies developed to date is the sterile male technique (SMT), in which large numbers of sterile males are released into a population each generation. However, this approach is time-consuming, labour-intensive and costly. We use mathematical models to test a new twist on the SMT, utilising maternally inherited mitochondrial (mtDNA) mutations that affect male, but not female reproductive fitness. `Trojan Females' carrying such mutations, and their female descendants, produce `sterile-male'-equivalents under natural conditions over multiple generations. We find that the TFT has the potential to be a novel humane approach for vertebrate pest control. Single large releases and relatively few small repeat releases of Trojan Females both provided effective and persistent control within relatively few generations. Although greatest efficacy was predicted for high turnover species, the additive nature of multiple releases made the TFT applicable to the full range of life histories modelled.

4B.4: The Matrix Reloaded: Progress toward the generation of synthetic mitochondria.

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Mitochondria comprise the simplest genetic system known; two rRNAs and 22 tRNA genes are used to generate only 13 proteins. Unlike the nuclear genome, the genomes of animal mitochondria cannot be readily altered or purposely manipulated *in vivo*. The ability to replace the natural mitochondrial genome with an *in vitro* generated synthetic genome promises to revolutionise our understanding of how the nucleus and mitochondria cooperate to generate energy. In addition, a robust system to deliver genetic material to mitochondria would provide synthetic biologists a unique experimental system for *in vivo* testing of synthetic genetic polymers (e.g. xeno-nucleic acids) for their capacity to sustain and support life. Many attempts to transfect DNA into animal cell mitochondria have been made with few successes. Most reports to date claiming success have subsequently proved to lack utility and/or reproducibility. Using the *Drosophila* system, we are currently developing a simple system to deliver customised DNA molecules into the mitochondria of living animal cells that takes advantage of the ancient endosymbiotic nature of mitochondria. Progress in the development of this technology will be presented.

4B.5: Maintenance of essential amino acid synthesis pathways in the *Blattabacterium* symbiont of a wood-feeding cockroach

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In addition to harbouring intestinal symbionts, some animal species also possess intracellular symbiotic microbes. The relative contributions of gut-resident and intracellular symbionts to host metabolism, and how they co-evolve, are not well understood. Cockroaches and the termite *Mastotermes darwiniensis* present a unique opportunity to examine the evolution of spatially separated symbionts, as they harbour gut symbionts and the intracellular symbiont *Blattabacterium cuenoti*. The genomes of *B. cuenoti* from *M. darwiniensis* and the social wood-feeding cockroach *Cryptocercus punctulatus* are each missing most of the pathways for the synthesis of essential amino acids found in the genomes of relatives from non-wood-feeding hosts. Hypotheses to explain this pathway degradation include: 1) feeding on microbes present in rotting wood by ancestral hosts; 2) the evolution of high-fidelity transfer of gut microbes via social behaviour. To test these hypotheses, we sequenced the *B. cuenoti* genome of a third wood-feeding species, the phylogenetically distant and non-social *Panesthia angustipennis*. We show that host wood-feeding does not necessarily lead to degradation of essential amino acid pathways in *B. cuenoti*, and argue that ancestral high-fidelity transfer of gut microbes best explains their loss in strains from *M. darwiniensis* and *C. punctulatus*.

4B.6: Evolution of the Unnecessary: How did fMet Become Central in Bacterial Translation Initiation?

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All bacteria initiate translation using formylated methionine, yet directly after translation, the formyl-group is removed. This addition and removal appears futile, yet every sequenced bacterial genome encodes the formylating and deformylating enzymes. Puzzlingly, the process is absent from Archaea and Eukaryotes, and moreover, bacterial mutants lacking these enzymes are viable, albeit with diminished growth rate. We created an *E.coli* strain devoid of formylase and deformylase activity. This strain was then cultured for 1400 generations whereupon it reached wild-type growth rate, demonstrating that formylation is dispensible. This raises the question: if formylation is unnecessary, how did it emerge and why has it persisted? Our results show that the formylation-deformylation cycle could have evolved as a toxin-antitoxin pair (TA) with post-segregational killing activity (PSK). We measured PSK and within-host competition between formylase-deformylase encoding plasmids and TA-free plasmids in our evolved strain. We report several lines of evidence consistent with the formylation-cycle having evolved from a plasmid-borne TA: 1) formyl-methionine on proteins is cytotoxic without deformylation, 2) deformylation relieves formyl-methionine cytotoxicity, 3) the loss of plasmids encoding formylase and deformylase results in cessation of growth - a standard PSK phenotype. Together, these results suggest a novel mechanism for the evolution of formylation and deformylation.

4B.7: Mind bending bacteria: Common bacterial symbionts alter neurological function and behaviour in *Drosophila melanogaster*.

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The long held dogma of behavioural research is that behaviour is determined by a complex interplay between genetics and the environment. Consequently, most research has focused on identifying genetic, biomolecular, or environmental factors that alter organism behaviour; symbionts were largely ignored or at best seen as biological oddities that influenced animal behaviour at very specific stages of life. Recent mounting evidence has demonstrated that symbionts can manipulate their host's nervous system in ways that benefit transmission. *Drosophila* are normally infected with two types of bacterial symbionts, the natural flora that resides in the gut and a common intercellular symbiont of insects called *Wolbachia*. Both symbionts have recently shown to alter simple behaviours. Altered gut bacteria changes anxiety like behaviour in mice and mate preference in *Drosophila*. *Wolbachia* are able to reduce olfactory induced locomotion; however the impact these symbionts have on more complex *Drosophila* behaviours and the underlining mechanisms by which these behaviours are modified is unclear.

Three common *Wolbachia* strains that establish low (*w*CS, *w*MelCS) or extreme (*w*MelPop) bacterial densities in adult fly brains were compared to *Wolbachia* free counterparts in male *Drosophila*, reared at 24°C, at three different time point (2, 5, and 8 days in age). Several common *Drosophila* behaviours controlled by the neurotransmitter dopamine will be examined: optomotor response, male aggression, arousal, locomotion, sleep and circadian rhythm, and learning and memory. Additionally, qPCR will be used to estimate changes in expression of several genes within the dopamine biosynthesis pathway, and two dopamine receptors. HPLC will be used to establish total brain dopamine levels. Furthermore, confocal imagaing will be used to identify if *Wolbachia* colocalises to dopaminergic neurons and if the general neuronal anatomy has been affected.

Current results have demonstrated that *Wolbachia* alters optomotor response in adult *Drosophila* infected with *w*CS and *w*MelPop across all ages tested. Male aggression was decreased only in *w*MelPop infected flies. Changes in behaviour correlated with alterations to 2 dopamine biosynthesis pathway genes were, the greatest impact was a decrease in the rate limiting enzyme, Tyrosine Hydroxyase, in flies infected with *w*MelPop.

Our work demonstrates for the first time that *Wolbachia* can influence the biosynthesis of neurotransmitters and consequently complex behaviours related to dopamine in *Drosophila*. The ability of *Wolbachia* to manipulate *Drosophila* behaviour provides an opportunity to understand how this bacteria influences the nervous system on a molecular and cellular level, to explore the general neurological mechanisms that control behaviour, potentially lead to new drug targets for neurological and behavioural disorders, and act as a warning for researchers that use *Drosophila* as a model organisms for behavioural neuroscience. Additionally, studying how gut bacteria influences behaviour will provide new information on how the flora helps to regulate the nervous system, and may link alterations to gut flora to neurological disorders related to dopamine. Overall, this work will help to establish that symbionts play as big of a role in the nervous system as genetics and environmental factors.

5A.1: Genetic tools for detecting sex-biased dispersal and inbreeding risk

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The fine-scale genetic analysis of genotypes in space has largely been overlooked as a potentially powerful tool for improving our understanding of dispersal. We have recently combined spatially explicit computer simulation and nuclear multilocus spatial autocorrelation analysis to investigate how sex-biased dispersal influences the patterns of fine-scale genetic structure. Simulations indicate that with adequate sample size, even modest sex biased dispersal generates a detectable signal. Congruent empirical findings were found in antechinus, which exhibits strong male-biased dispersal during its one-year life cycle. In an extension of this study we are now comparing the genetic expectations under sex-biased dispersal for nuclear, mtDNA and Y-chromosome markers. These analyses suggest that behaviours other than dispersal can contribute to differences in fine scale structure between the sexes. We have also confirmed the generality of these findings by expanding the simulations to species with multi-year life cycles. Simulations parameterised to model the biology of the mountain brushtail possum, in combination with empirical analysis, indicate that despite male-biased dispersal, the extent of male dispersal in this species is insufficient to eliminate the risk of inbreeding. These findings provide a context for exploring other behavioural strategies for inbreeding avoidance, such as mate choice.

5A.2: High genetic diversity is not essential for successful introduction

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Some introduced populations evolve despite the presumed loss of genetic diversity (*GD*) at introduction. We aimed to quantify the amount of *GD* retained at introduction in species that have adapted to introduced environments. Using microsatellite data from native and introduced populations of *Arctotheca populifolia* and *Petrorhagia nanteuilii*, we identified the source for each introduction, estimated *GD* and calculated the amount retained in introduced populations. These values were compared to those from a literature review of *GD* in native, confamilial populations and to estimates of *GD* from a wide range of introduced species showing evidence of evolutionary change. *GD* in the native range of both species was significantly lower than confamilials. We found that, on average, introduced populations showing evidence of adaptation to their new environments retained 81% of native range *GD*. Introduced populations of *P. nanteuilii* had higher *GD* than found in native source populations, whereas those of *A. populifolia* retained only 14% of native *GD* in one introduction and 1% in another. While high *GD* may increase the likelihood of invasion success, the species examined here adapted to novel environments with little neutral *GD*. This finding suggests that even small founding populations have the potential to become invasive.

5A.3: Identifying population structure in Australian foxes (*Vulpes vulpes*)

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The histories of the spread of invasive species are often well-documented, and provide an excellent opportunity to evaluate estimates of demographic and spatial dynamics of species based on molecular data. We are applying this principle to a continent-wide genotypic dataset (3192 individuals; 36 microsatellite loci) for the red fox (*Vulpes vulpes*) in Australia. As the rate of spread, abundance and other life history traits of foxes in Australia are well described it provides a unique opportunity to test the predictions of several recently developed approaches for determining demographic and spatial details of foxes such as dispersal distances, migration rates, and population sub-structuring. As an initial step, we investigated the spatial structure of foxes in Australia using a combination of STRUCTURE and TESS, two Bayesian population clustering models. Preliminary results suggest that the fox population is divided into two main populations by the Nullarbor Plain and the deserts of Western Australia with one population located to the west and the other to the east. On-going work will determine male and female dispersal distances by sub-population, and inter-population migration rates. These results will help to identify the optimal spatial scale for management of this significant environmental and economic pest.

5A.4: Landscape level microsatellite DNA analysis reveals substantial cryptic genetic structure in feral possums in New Zealand

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Population genetic studies of single species can reveal much about population structure, providing inferred information about dispersal and gene flow among sub-populations. Increasingly, such studies are being linked spatially through geographic information systems to provide a finer scale resolution of population interactions. Here we report on a large microsatellite DNA analysis of common brushtail possums from 31 sites in Hawkes Bay, New Zealand. In our initial analysis, we used a non-landscape approach based around sampling on opposite sides of rivers. This showed that major rivers in the area presented a significant barrier to possums that could be ameliorated by the presence of road bridges. However, when viewed spatially, the data revealed much greater complexities in possum population structure and behaviour, including dispersal patterns that appear to favour movement around river head waters in preference to crossing local bridges. More importantly, our analysis shows two distinct genetic groups of possums that appear to abut each other with minimal overlap. These two groups conform to our knowledge of the history of introductions, which involved possums from Tasmania introduced to the north of Hawkes Bay and possums from mainland Australia introduced to the south. This greater complexity of genetic exchange changes markedly our understanding of the dispersal characteristics of possums in the region and more broadly in New Zealand. We discuss the results in the context of incorporating spatial components in population genetic studies.

5A.5: Characterisation of Major Histocompatibility Complex class I in the Australian cane toad, *Rhinella marina*

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The Major Histocompatibility Complex (MHC) class I is an extremely polymorphic gene that encodes cell-surface receptors vital to the recognition of intracellular pathogens and initiation of the immune response. The MHC class I has yet to be characterised in bufonid toads (Order: Anura; Suborder: Neobatrachia; Family: Bufonidae), a highly diverse and widely distributed family of anurans. We identified a large expansion of MHC class I alpha 1 allele variants in the Australian cane toad, *Rhinella marina*. This includes a single classical MHC class I gene and numerous non-classical loci, similar to the genomic organisation of the MHC class I in the distantly related anuran family, Xenopodidae. From 25 individuals sampled from the Australian population, we found only 3 classical MHC class I allele variants with high sequence similarity. This extremely low MHC class I diversity is the likely result of repeated bottleneck events experienced through the cane toad's complex history of introductions as a biocontrol agent.

5A.6: The genetic basis of cryptic female choice in Chinook salmon (*Oncorhynchus tshawytscha*)

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Cryptic female choice, a post-copulatory version of sexual selection little studied in external fertilisers, enables females to favour sperm of one conspecific male over another. In Chinook salmon, we have previously shown that female ovarian fluid differentially affects the sperm velocity of males in a female-dependent fashion, and thus that females may exert cryptic control of male reproductive success. Here we investigate whether this apparent form of cryptic female choice is 1) based on Major Histocompatibility Complex (MHC) dependent sperm selection or 2) influenced by overall genetic relatedness. MHC dependent mate choice is thought to have two main roles: i) to promote offspring with MHC allele combinations that increase immunological competence and/or ii) as a mechanism for differentiating kin, either to avoid inbreeding, or to preserve local adaptations. To reveal whether MHC compatibility is a contributor to the female-dependent sperm performance, we conducted paired-male competitive fertilisation trials with males of different sperm velocity in the focal female's ovarian fluid. After assessing the fertilisation success of each male via microsatellite based parentage assignment, we determined the parental MHC genetic distance at MHC class I and class II loci and examined general relatedness of the parents with 9 microsatellites and a 6000 SNP Chinook salmon array (Clarke, unpublished). We show that sperm velocity is a key determinant for fertilisation success in Chinook salmon and is positively correlated with relatedness between mating pairs when the microsatellite data is considered. While preliminary at this stage, parental MHC genotypic distance, measured by nucleotide difference, does not strongly predict sperm velocity or fertilisation outcomes, but ongoing tests of associations to MHC amino-acid divergence, allelic counts and genome wide relatedness via SNP data might reveal more subtle patterns in cryptic female choice.

5A.7: Genic capture and the evolution of colour-based signalling of genetic quality

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The notion that individuals can advertise genetic quality (i.e. `good genes') through the expression of exaggerated sexual ornamentation has inspired, challenged and frustrated evolutionary ecologists for decades. In the early days, the idea carried such strong conceptual appeal that whole research programs were based around it even despite very little empirical support, and despite concerns regarding the evolutionary stability of indirect benefits signalling. Inevitably, advances in theory have led to more rigorous empirical examinations, which have in turn delivered us a more realistic understanding of when and how genetic quality might be signalled. One outcome of this increased empirical rigour has been the rejuvenation of evolutionary genetics as a tool for testing key predictions at the whole organism level. In this presentation I will introduce the concept of genetic quality signalling and outline my attempts to evaluate prevailing theory using colourful, sexually dimorphic butterflies as a study system. The explicit conceptual context is given by Rowe and Houle's `genic capture' model (Proceedings B 263:1416), which predicts that consistent directional selection will drive ornamental traits to become more exaggerated, more developmentally integrated, and to call upon the effects of an increasingly broad genetic base. The essential breakthrough of this model is how it visualises strong directional selection as a generator of additive genetic variance (rather than an exhauster of variance), which explains the previously troublesome general observation that such traits are indeed highly variable in the wild. My data on butterflies provide varying levels of support for genic capture predictions, with the primary sexual trait -- male wing colouration -- showing high levels of visual exaggeration, sex dimorphism, condition-dependence and genetic variance. Most importantly, wing colour expression is positively genetically correlated with viability correlates such as juvenile developmental and growth rates, and adult body size. However, the strength of these covariances depends upon the nature of the developmental environment, with the strongest `good genes' signature evident among the most nutrient limited males. I discuss the complexities and subtleties of my data, and of the theory, and suggest some intriguing directions for future research.

5B.1: Comparative biology of wRi *Wolbachia* infections in *Drosophila simulans*, *D. suzukii* and *D. subpulchrella*

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There is significant Wolbachia-associated variation in fecundity, cell biology and cytoplasmic incompatibility among wRi-infected isofemale lines from individual orchard populations of Drosophila simulans in northern California. This extensive, multifaceted variation may ultimately be useful for controlling vector-borne diseases. With many collaborators, I am documenting the history and genetic and phenotypic variation of wRi Wolbachia infections in D. simulans and two sister species, D. suzukii and D. subpulchrella, distantly related to simulans. The Wolbachia variant wRi was initially found in southern California D. simulans in 1984 and rapidly spread northward throughout California populations of D. simulans within a decade. The rapid spread of maternally inherited wRi within and among populations was driven by ``cytoplasmic incompatibility'' (CI), increased embryo mortality when infected males mate with uninfected females. As documented by Bill Ballard and his collaborators, the Wolbachia variant wRi is also prevalent among D. simulans in Africa, Australia, Asia, South America and Europe. Analysis of mtDNA variation among wRi-infected lines suggests an African origin of the wRi-simulans association and a greater age than previously suspected. D. suzukii, which is endemic to east Asia, was first detected in North America in 2008. Both D. suzukii and its sister species D. subpulchrella are polymorphic for a Wolbachia infection very closely related to wRi. We have found that wRi is imperfectly maternally transmitted in these species, as in D. simulans; however, wRi causes little if any CI in either D. suzukii or D. subpulchrella. Moreover, preliminary experiments suggest that wRi-infected D. suzukii females are less fecund than uninfected females. Hence, the presence of wRi in all US populations of D. suzukii presents a paradox whose resolution may reveal useful new features of Wolbachia biology.

5B.2: What do we know about host switch frequency of a common maternally inherited insect bacterium?

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Wolbachia is a common endosymbiotic bacterium that can manipulate host reproduction, host fitness and other aspects of host biology. It infects about 40% of insect species where it is primarily maternally inherited, although there is phylogenetic evidence for occasional horizontal transmission between host species. *Wolbachia* can experimentally be transferred between species yet ecological evidence for this, in particular about its frequency, is still limited. Here, I will first report about a recent acquisition of *Wolbachia* by an invasive tephritid fruit fly species from its endemic relative in Europe, and then focus on our study of the diverse group of Australian tephritid fruit flies. Based on *Wolbachia* Multi Locus Sequence Typing, four *Bactrocera* and one *Dacus* species harbour two identical *Wolbachia* strains as double infections, while a fruit fly parasitoid shares identical *Wolbachia* alleles with one of its host species. This is an unprecedented high incidence of four shared *Wolbachia* strains in a total of eight infected out of 26 tested host species across two trophic levels, with all four strains shared by at least one other host species. Horizontal *Wolbachia* transmission in this Australian fruit fly community may be facilitated through the sharing of host plant or parasitoid species, and for some species hybridisation. Frequent host switches by this maternally inherited endosymbiont may be seen as an escape route against infection loss (due to leaky maternal inheritance or host resistance) and genome degradation along the one-way-street of complete host dependency.

5B.3: A molecular method for monitoring *Wolbachia*-infection in the release of *Wolbachia*-infected *Aedes aegypti*

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Wolbachia-infected *Aedes aegypti* have been successfully established in field environments in Cairns in hopes of reducing dengue transmission. Since *Wolbachia* transmit vertically through the matrilineal line, it will potentially sweep all mitochondrial variation that were associated with the founders that were first infected with *Wolbachia*. Here, we exploit this property to develop a method to monitor the *Wolbachia* infection in the field based on mitochondrial background. As expected, we found that the *Wolbachia*-infected mosquitoes had virtually only one or two types of background compared with more variations in uninfected individuals from Cairns. The lack of variation in the mitochondrial background is unlikely to pose a serious threat on fitness, as differences in background within genes only differ by synonymous and silent base changes. This sweep in one or two backgrounds will enable us to ask interesting questions about *Wolbachia* and mitochondria transmission, and other population events.

5B.4: Recent rapid spread of *Wolbachia* variants in east Australian *Drosophila simulans*

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Infection with the maternally inherited intracellular bacterium *Wolbachia* is very widespread amongst arthropod hosts. Although well known for their ability to induce host reproductive manipulations, *Wolbachia* have also been shown to increase host fitness by protecting against infectious microbes or increasing fecundity; and they are expected to evolve towards mutualism in natural host populations.

Recent data from our lab indicates the rapid sequential spread of two *Wolbachia* variants (*w*Au and *w*Ri), only one of which induces significant reproductive parasitism in the form of cytoplasmic incompatibility, amongst Australian populations of *Drosophila simulans* over approximately 20 years. In each case analyses suggest these dynamics are best understood as Fisherian waves of favourable variants, involving net host fitness benefits of a non-trivial magnitude.

The naturally occurring pathogens which significantly impact field populations of *D. simulans* are currently not well characterized. However, we have found that each of the *w*Au and *w*Ri *Wolbachia* variants currently persist within Australia amongst geographically isolated host populations, at quite different infection frequencies. If these *Wolbachia* variants have the effect of promoting host fitness by protecting against infectious microbes, a comparison of different host populations has potential to reveal pathogens that are ecologically significant in a genetically tractable host.

5B.5: Two kingdoms are better than one: genome-scale signatures of bacteria and sponges working together to engineer marine ecosystems

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Animal-bacterial interactions underpin an enormous range of biological disciplines, from human health to terrestrial and aquatic ecology to biomanufacturing. Novel animal functions can be acquired from bacteria in evolutionary time via lateral gene transfer (LGT), or in ecological time via metabolic interplay between animal hosts and their resident symbionts. Marine sponges provide excellent case studies; they have been shaping the heath of the Earth's oceans for more than 600 million years largely due to the diverse microbes with which they associate. Two aspects of sponge biology suggest that LGT could be particularly likely in these animals. First, bacterial DNA is frequently liberated as a result of phagocytotic feeding by sponge cells. Second, there is no germline barrier to LGT, because no dedicated germline is established during embryogenesis. Because both traits probably also apply to the Last Common Animal Ancestor, LGT was likely crucial to the major evolutionary transition from single-celled eukaryotes to multi-celled animals. Here I discuss our accumulating evidence of horizontal gene transfer (HGT) into the genome of the coral reef sponge *Amphimedon queenslandica* and present our novel bioinformatics pipeline to enable rapid and comprehensive detection of LGT in any assembled animal genome of interest.

5B.6: Understanding the causes of virulence in Scedosporium fungi

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Scedosporium aurantiacum is a fungal pathogen of humans and other animals that is highly prevalent in urban Sydney. The variability of virulence between isolates is putatively a result of genetic differences between them. In an effort to establish the genetic factors underpinning virulence we have generated whole genome sequence for 2 high and 2 low virulence S. aurantiacum strains.

We performed de novo assembly and whole genome multiple alignments that included a well annotated relative. Utilising PyCogent and a new tool we have developed, we predict one-to-one orthologs via alignment based projection from the annotated relative.

Our analyses reveal that the high and low virulence strains are more closely related within a group than between groups. Accordingly, for this sample we conclude that the gain or loss of virulence arose since the common ancestor of the different virulence phenotypes, but before the divergences within these groups respectively.

5B.7: Investigating the immune function of the *Drosophila melanogaster* MACPF protein Torso-like

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Membrane attack complex/perforin-like (MACPF) proteins perform roles in vertebrate innate immunity and development. Torso-like (Tsl) is the only known MACPF protein in *Drosophila melanogaster*, and was first identified amongst genes important for early embryonic patterning. To address whether Tsl functions in *Drosophila* immunity, we performed infection survival assays on adult *tsl* null mutants with various strains of bacteria. We have shown that *tsl* null mutants have a susceptibility to gram-positive, but not gram-negative bacteria. This is unexpected, since in mammals the membrane attack complex targets gram-negative bacteria through disruption of the outer bacterial membrane. It therefore seems likely that Tsl performs a different role in the fly immune system. We are currently testing whether *tsl* functions in a humoural pathway, such as the Toll pathway, or in cellular immunity and testing for genetic interactions with known immunity genes. In addition, we aim to identify potential Tsl interactors common to both developmental and immune pathways to determine the similarities and/or differences in Tsl function between these processes.

6A.1: Regional Deregulation of the Cancer Genome involves Epigenetic Remodeling and a Change in Replication Timing

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Epigenetic deregulation is involved in cancer initiation and progression, but most studies have concentrated on gene repression and hypermethylation of tumour suppressor genes. Therefore the mechanism underpinning epigenetic-based gene activation in carcinogenesis is still poorly understood. We reported that epigenetic changes could occur over large domains, resulting in concordant gene repression by Long Range Epigenetic Silencing (LRES) and more recently we reported that concordant gene activation by Long Range Epigenetic Activation (LREA)1 of multiple adjacent genes also is common in cancer. By an integrative epigenome-wide sequencing analysis of prostate cancer and normal cells, we found the epigenetic deregulated domains are characterised by an exchange of active (H3K9ac and H3K4me3) chromatin marks, and repressive (H3K9me2 and H3K27me3) marks. Notably, whilst promoter hypomethylation did not often contribute to gene activation, extensive DNA hypermethylation of CpG islands or ``CpG island borders'' was strongly related to both gene repression and cancer-specific gene activation or a change in promoter usage. We also found that the epigenetic deregulated domains change in the replication timing in cancer, with a clear shift to late replication in LRES regions and conversely early replication in LREA regions. These findings have wide ramifications for cancer diagnosis, progression and epigenetic-based gene therapies.

(1) Bert SA, Robinson MD, Strbenac D, Statham AL, Song JZ, Hulf T, Sutherland RL, Coolen MW, Stirzaker C, Clark SJ. Regional Activation of the Cancer Genome by Long Range Epigenetic Remodelling (2013) Cancer Cell 23: 9-21

6A.2: Reassembly of nucleosomes at the MLH1 promoter initiates resilencing following decitabine exposure

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Hypomethylating agents reactivate tumor suppressor genes that are epigenetically silenced in cancer. However, their therapeutic effects are transient and drug resistance inevitably develops. While resistance is associated with resilencing of genes initially demethylated by the drug, the mechanism underlying this resilencing is unknown. Using the MLH1 tumour suppressor gene as a model, we show that decitabine-induced re-expression is dependent upon demethylation and eviction of promoter nucleosomes. Following decitabine withdrawal, MLH1 was rapidly resilenced despite persistent promoter demethylation. Using single molecule analysis at multiple time points, we show that gene resilencing was initiated by nucleosome reassembly at the transcription start site on demethylated DNA and only then was followed by remethylation and stable silencing. Taken together, these data establish the importance of nucleosome positioning in mediating resilencing of drug-induced gene reactivation and suggest a role for therapeutic targeting of nucleosome assembly as a mechanism to overcome drug resistance.

6A.3: Linking Inflammation and Epigenetics in Cancer

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The capacity of the immune system to elicit epigenetic change has major implications for human inflammatory diseases and cancer, but as a process remains largely unexplored. Gastric cancer has the second highest mortality rate of all cancers worldwide and is strongly associated with underlying hyperactivation of gastric immunity (chronic inflammation) following infection with the bacterium Helicobacter (H.) pylori. However, clear molecular mechanisms linking gastric inflammation and cancer development are lacking. We have investigated the impact of H. pylori-dependent inflammation upon the epigenetic state of key tumour suppressor genes (TSGs) in the gastric epithelium. Using human gastric tissue cohorts and mouse genetic models of gastric preneoplasia, tumourigenesis and H. pylori infection we show that inappropriate epigenetic silencing (promoter methylation) of the gastric TSG, trefoil factor (TFF)2 arises in the setting of chronic inflammation and is dependent on the activity of specific pro-inflammatory cytokines. In addition we show that genetic ablation of Tff2 leads to accelerated tumourigenesis in a mouse model of gastric cancer, illustrating how epigenetic loss of TFF2 might promote gastric tumour progression in humans. Finally in translational studies we have explored the utility of inflammation-associated TFF2 promoter methylation as an early biomarker of gastric cancer risk. In summary, our studies elucidate inflammation-associated perturbation of epithelial epigenetic inheritance as a key event driving TSG loss and neoplastic progression in the stomach. Our ongoing work aims to translate TFF2 methylation, as well as other inflammation related epigenetic signatures, into novel diagnostic tools to aid gastric cancer prevention and treatment.

6A.4: Defining the tumourigenic function of a novel epigenetic oncogene required for the development of acute myeloid leukaemic stem cells

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Acute myeloid leukaemia (AML) can originate from a leukaemic stem cell (LSC), which are able to initiate and maintain the leukaemic hierarchy. The prognosis for AML patients remains poor and relapse rates are high. Epigenetic therapy has the potential to be more effective and less cytotoxic than traditional therapy. Together, this suggests that LSC-targeting epigenetic therapies may allow for a cure of AML with fewer adverse effects for patients. Our microarray data identified a novel epigenetic regulator that is significantly overexpressed in LSC compared to normal haematopoietic stem cells (HSC). Overexpression of this gene promoted the proliferative and self-renewal capacities of pre-LSC and also altered the epigenetic landscape. In contrast, its knockdown severely impaired the stem cell properties to the extent that differentiation was induced. Subsequent genome-wide gene expression analysis identified key downstream target genes and pathways, whose deregulation has been implicated in tumour development. Our data strongly suggest that this epigenetic regulator is a key driver in the development of an aggressive form of AML. Targeting this oncogene has the potential to reverse specific abnormal epigenetic marks in LSC, thereby allowing the development of new epigenetic treatment strategies that will enable us to directly target and eradicate LSC in AML.

6A.5: RNA-Seq of Bovine Blood and Liver Transcriptomes Reveals Allele Specific Expression

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Allele specific expression (ASE) occurs when alleles of a single nucleotide polymorphism (SNP) show differential levels of expression. Advances in sequencing technology have allowed RNA sequencing to accurately quantify the level of allelic expression at heterozygous SNP positions throughout the transcriptome. This study investigated whether ASE occurs in the bovine liver and blood transcriptomes. Whole blood and liver biopsy samples were collected from 20 first lactation Holstein dairy cows located at the Victorian Department of Environment and Primary Industries Ellinbank site in Gippsland Victoria. Total RNA was extracted from the tissue samples and RNA-Seq libraries were prepared for each sample. Multiplexed libraries were sequenced on a HiSeqTM 2000 (Illumina, USA) in a 105 bp paired end run. Between 2.35 Gb and 5.37 Gb of raw sequencing data was obtained for each RNA-Seq library. ASE of heterozygous SNP was analysed in each tissue for each cow, revealing the presence of ASE in both the bovine blood and liver transcriptomes.

6B.1: LandPopGenReport - a landscape genetics tool to analyse the effects of landscape features on population structure using genetic data

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Rapid advances in genotyping technology combined with a rapid decrease in costs have vastly increased the availability of SNP and microsatellite data for ecological researchers. By combining individual genotypes with detailed spatial data, it is possible to use least-cost modeling to determine the effects of landscape features on spatial population structures by developing resistance matrices and comparing them with genetic distance matrices using partial mantel tests. Despite the power and usefulness of this method as it potentially sheds light on the fragmentation effect of landscape features, we see a lack of publications applying least-cost modelling within a landscape genetic context. A literature search revealed that until now around 56 papers have been published since 2004, equalling a publication rate of 10-15 manuscripts a year. One explanation for this low number of publications given the amount of data available is the required expertise. An analysis encompasses the integration and exchange of data between three specialised types of software packages (population genetics, geographic information systems and statistical). We present a newly developed R package that incorporates all of the necessary steps into a single framework and demonstrate its application using population genetic data on endangered reptile species within the ACT.

6B.2: MHC class II diversity of koala (*Phascolarctos cinereus*) populations across their range

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Major histocompatibility complex class II (MHCII) genes code for proteins that bind and present antigenic peptides and trigger the adaptive immune response. Here we present a broad geographical study of MHCII DA 1 (DAB) and DB 1 (DBB) variants of the koala (*Phascolarctos cinereus*) from twelve populations across eastern Australia. We identified greater MHCII variation and, possibly, additional gene copies in koala populations in the north (Queensland and New South Wales) relative to the south (Victoria), confirmed by STRUCTURE analyses and genetic differentiation using analysis of molecular variance. The higher MHCII diversity in the north relative to south could potentially be attributed to (i) significant founder effect in Victorian populations linked to historical translocation of bottlenecked koala populations, and/or (ii) different MHC evolutionary pathways between the two regions with increased pathogen-driven balancing selection in the north. Low MHCII genetic diversity in koalas from the south could reduce their potential ability to respond to disease, although the three DAB variants found in the south had substantial sequence divergence between variants.

6B.3: Low MHC diversity in the Tasmanian devil pre-dates European settlement

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The Tasmanian devil (Sarcophilus harrisii) was once widespread on mainland Australia but today is restricted to Tasmania. The devil is currently at risk of extinction due to the emergence of a contagious cancer known as Devil Facial Tumour Disease (DFTD). The emergence and spread of this disease has been linked to low diversity in the devil Major Histocompatibility Complex (MHC). Devils have survived several population crashes in the last two centuries which may have caused a loss of MHC diversity. Alternatively, MHC diversity may have been lost prior to European colonisation. The aim of this project was to determine whether loss of MHC diversity was caused by human impacts or whether it predates European settlement in Australia. MHC class I alleles were cloned and sequenced from nine museum samples spanning the last 200 years since European settlement, a single Tasmanian sample from pre-European colonisation and four mainland devil samples which are at least 3000 years old. The 3000 year old MHC alleles are the oldest ever sequenced. Our results reveal no additional diversity in the Tasmania samples. The mainland devils had common modern alleles as well as novel alleles which are not present in modern Tasmania. However, these novel alleles are highly similar to existing alleles. We conclude that low MHC diversity has been a feature of devil populations for over 3000 years and that a history of population crashes is consistent with a paucity of genetic diversity in key immune response genes.

6B.4: Emperor Penguins and Weddell Seals: ice-dependent animals in a warming climate

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Weddell Seals and Emperor Penguins are both ice-dependent and highly vulnerable to climate change. One approach to understanding the implications of future climate change for such species is to consider how they responded to historical climatic events. We aimed to use phylogeographic methods to discover if these animals have been affected by past environmental change. The mitochondrial control region and cytochrome *b* were sequenced for 110 Weddell Seals and 120 Emperor Penguins from colonies in East Antarctica. Ancient DNA samples were also sequenced, and the time-stamped sequences were used as additional calibration points for a strict molecular clock. BEAST phylogenetic analyses identified three ancestral lineages among the seals, one of which exhibited signals of a refugium. The most recent common ancestor of this lineage was dated at approximately 78,000 years ago (95%CI=7-144KYA), coinciding with a period of global climate fluctuation. Four penguin lineages were identified, with a range in divergence time of 148-230KYA, concurrent with a period of global cooling. Our results will be discussed within the context of both past and future climate change. This is the first study investigating interglacial refugia for Antarctic ice-dependent species, and we hope that refugia may eventually be utilised in Antarctic conservation plans.

6B.5: Predicting demographic responses of rainforest trees to climate change

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A changing climate has caused species to shift in range from ancestral to present-day distributions. The corresponding changes in genetic diversity and structure are known to follow climatic patterns. Linking past intraspecific divergence patterns to well-defined environmental realms of tolerance will allow the forecasting of future threats from anthropogenic-induced climate change. This research aims to determine the level of genetic diversity/structure within naturally occurring rainforest tree populations and establish if this is more strongly influenced by historic or contemporary drivers; via (1) climate envelope modelling of the past-current-future distributional dynamics, (2) the observed fossil record and (3) molecular observation and inference. Using coalescent-based models we estimated ancestral population demographic parameters and divergence times between current genetic disjunctions. Also, we investigated potential distributions of tree species closely associated with different rainforest types and model the effect of post-glacial warming on spatial distribution and altitudinal range shift. The results show the inferred demographic changes are congruent with the observed fossil record. The three population isolation-with-migration analysis together with the palaeodistribution models (i.e. abundance) allows the estimation of ancestral demographic processes among population groups. This has facilitated the prediction of demographic responses to future climate change, which show that anthropogenic-induced climate change and contemporary drivers may be influencing the evolution of these tree species.

6B.6: Ecological and evolutionary limits to species distributions in *Eurema* butterflies

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Species with restricted distributions make up the vast majority of biodiversity. Recent evidence from Drosophila suggests that species with restricted distributions may simply lack genetic variation in key traits, limiting their ability to adapt to conditions beyond their current range. Specifically, tropical species of Drosophila have been shown to have low means and low genetic variation for cold tolerance and desiccation tolerance. It has therefore been predicted that these species will be limited in their response to future climatic changes. However whether these results extend beyond Drosophila is not known. We assess levels of genetic variation for cold tolerance in three species of butterfly from the genus Eurema that can be classified as tropically restricted (E. laeta), tropical/subtropical (E. hecabe) and widespread (E. smilax) in their distribution. Compared to the more widely distributed species, we show that the tropically restricted E. laeta has significantly lower mean cold tolerance and lacks genetic variation for this trait. Our study is the first to empirically confirm that an absence of genetic variation in a key ecological trait may indeed play a role in limiting the distribution of tropically restricted species.

6C.1: Enhancing deep learning in an introductory molecular biology course

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Students studying courses in genetics and molecular biology are often confronted in numerous complex concepts. Learning activities that promote the transition from surface learning to deep understanding play a crucial role in enhancing genetic education, particularly in the learning and application of core ideas in genetics and molecular biology. In this presentation, I will discuss some learning activities that have been used successfully to enhance the learning of complex and abstract concepts. These efforts have focussed on learning gains made by students enrolled in introductory courses in these fields.

6C.2: Effectiveness of using Peer Assessment in assessing Graduate Capabilities in a third year Genetics Subject

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The third year Human and Molecular Genetics (GEN3HMG) subject in La Trobe University is a final year undergraduate subject. It is a capstone subject designed to provide an effective culmination point to prepare students for graduation, in addition to teaching the discipline specific concepts and skills. It is to incorporate the teaching of specific graduate attributes or ``core capabilities required for successful careers, meaningful contributions to their communities, and effective lifelong learning'' and to orientate them to opportunities for further study, employment and future career development. This is a task that is initiated across universities in Australia, but at present without an easy and valid way to assess the effectiveness of such efforts. The nine key graduate capabilities include writing, speaking, numeracy, inquiry/research, critical thinking/analysis, creative problem solving, teamwork, ethical awareness, professional conduct and discipline specific graduate capabilities. We report on the design and implementation of a peer based assessment of these graduate capabilities. The peer assessment used to assess the graduate capabilities is based on a genetics learning activity and was designed with the intention of not only to assess the individual's progress toward graduate capabilities but also to help them recognise how the learning activity helps them reach these goals. It is intended to minimise staff resources and at the same time to place the students at the centre of the learning activity. We also present data showing the validity, the effectiveness and the challenges faced in the trial of such a system.

6C.3: Evaluation of live simulations for the teaching of threshold concepts in first year genetics

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Threshold concepts transform student understanding but students often find them extremely difficult. The teaching of threshold concepts in large classes is therefore challenging. We have evaluated the efficacy of live simulations and associated tools (e.g. edited videos of lectures) for the teaching of threshold concepts in large first-year Science and Medicine classes with an enrolment of approximately 1300 students. Our results provide information on the most effective approaches for teaching threshold concepts in the lecture context, and also indicate how threshold concepts might be taught in other large-class contexts such as massive open online courses (MOOCs).

6C.4: My student is on Twitter: should I be worried?

Steven Hamblin[1]

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Social media has had a transformative effect on society at large and has inspired a new wave of science communication and communicators, but little is known about the true value of social media to scientists and science communicators. In this talk, I will take a critical look at use of social media by scientists and attempt to highlight its benefits (and costs) to practicing academics and students. I will discuss the use and misuse of social media venues such as Twitter, Facebook, blogs, and podcasts and attempt to provide practical advice to students and faculty on how to use these tools to effectively communicate their science to the public and each other.

6C.5: YouTube as an educational resource for visual and kinesthetic learners: A study of DNA replication

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Learning styles can be classified into visual, aural, read-write, and kinaesthetic. Lecturing traditionally caters for aural and read-write learners. Educators can now easily access resources that assist visual and kinesthetic learning via YouTube. This study examined how YouTube has been utilised in the demonstration of DNA replication. A search of www.youtube.com using the criterion ``DNA replication animation" was performed. Videos uploaded between February, 2005 and December 31, 2010 were included. Date of video upload, number of times viewed, and length of video were collected. A general linear model was used to test for associations, with a significance level of $p<0.05$. A total of 127 unique videos, viewed a total of 21,264,244 times, were analysed. The number of views per video ranged from 15 to 2,891,443, with an average of 41,787 views per video, per year. There was a significant association between the time since upload and the number of views, with an additional 360.8 views for each additional day the video had been online ($p<0.001$). YouTube has been extensively utilised to demonstrate the fundamentals of human genetics. It has enabled students and educators to easily access resources for visual and kinesthetic learners to study processes occurring at the molecular level.

7A.1: Mapping biodiversity via DNA metabarcoding

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Ecosystems across the globe are threatened by climate change and human activities. New rapid survey approaches for monitoring biodiversity would greatly advance assessment and understanding of these threats. Taking advantage of next-generation DNA sequencing, we implemented an approach we call DNA metabarcoding: high-throughput and simultaneous taxa identification based on a very short (usually less than 100 base pairs) but informative DNA fragment. Short DNA fragments allow the use of degraded DNA from environmental samples. We applied this approach to tropical ecosystems. We collected 361 samples of surface soil (0-10 cm depth), on a 1 hectare plot with a 5 x 5 m grid system, in the Nouragues Field Station (French Guiana). Extracellular DNA was extracted in the field station within a few hours after collection. DNA amplifications were carried out using several metabarcodes targetting all eukaryotes, plants, and termites. The results obtained with the eukaryote metabarcode show that plant, fungi, metazoa, and unicellular organisms represent 6%, 41%, 47%, and 6% of the sequence reads, respectively. Several hundreds of maps showing the distribution of different taxa over the plot. Such results demonstrate that high-throughput biodiversity data collection is possible via a standardized DNA metabarcoding approach.

7A.2: Using next generation sequencing to explore phylogeographic dynamics of rainforest flora

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A multispecies landscape-level study of phylogenetic patterns and population dynamics across one or more species can reveal the genetic signatures of contrasting temporal responses to environmental change among diverse functional groups. Chloroplast DNA has proved a useful tool to investigate phylogeographic patterns across many plant species. With high quantity and quality data production and low cost, next generation sequencing has the potential to provide new opportunities for plant phylogeographic studies. We developed a simple method to extract cpDNA and detect variation in silicio from Illumina paired reads of whole genomic sequence data. Here we discuss the current results of a study in which we apply this method to multiple Australian rainforest tree species representing a range of functional groups and phylogenetic lineages. The Australian Rainforest biome has a complex history of contraction and fragmentation and the flora is a product of dispersal from the indo-Malaysian archipelago and older Gondwanan relicts. A combination of genetic data and functional trait data of multiple species can enable a critical understanding of how species are distributed, how communities are assembled, and in recognising different susceptibilities to threats and change.

7A.3: Microevolution under climate change

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Species with restricted distributions make up the vast majority of biodiversity. Recent evidence from Drosophila suggests that species with restricted distributions may simply lack genetic variation in key traits, limiting their ability to adapt to conditions beyond their current range. Specifically, tropical species of Drosophila have been shown to have low means and low genetic variation for cold tolerance and desiccation tolerance. It has therefore been predicted that these species will be limited in their response to future climatic changes. However these studies have not considered ecologically realistic stress levels and rearing conditions. Here we show that evolutionary responses to less extreme, but more ecologically realistic levels of desiccation stress are possible in rainforest restricted Drosophila species developing under both wet and dry season temperatures expected in 2030. This suggests that evolution may indeed ameliorate the impacts of climate change in restricted species with low tolerances, provided the extent of climate change is not too extreme.

7A.4: Multi-phyla metagenomics along an altitudinal gradient on a small temperate island

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Some of the most basic questions in ecology remain as intriguing and fundamental as ever. What is the distribution and abundance of a species? How do these relationships relate to other species and what biological and abiotic factors are driving these distributions. With the advent of high throughput metabarcoding, commonly known as metagenomics, the techniques are now becoming available to address these questions simultaneously across multiple phyla. In addition, locations where these studies are being undertaken are becoming reference sites or ``Genomic Observatories'' to develop best-effort pan biodiversity assessments, to monitor temporal changes due to, for instance, climate change, and to define targets for restoration at degraded sites. Here we present a study across ten terrestrial 20x20m plots along a 600m altitudinal gradient on the island of Hauturu (Little Barrier), in the Hauraki Gulf near Auckland, New Zealand. Sampling included soil, leaf-litter, two invertebrate trapping methods, plant material, birdcalls and artificial shelters. Molecular barcoding included metagenomics of bacteria and fungi from soil, while Sanger sequencing of Cox1 was conducted on > 4000 invertebrate samples from pitfall trap and leaf-litter samples. Databases have been built to house the data and analysis pipelines constructed to estimate OTUs and compare plots. Beta diversity increased with spatial distance (horizontal and altitudinal) for taxonomic groups investigated, including bacteria, fungi, invertebrates, trees and birds. Bacterial diversity was strongly associated with soil pH and levels of phosphorus, whereas fungi diversity was more associated with phosphorus levels and tree communities. More recent efforts have focused on expanding the number of plots on the island and the use of metagenomics from soil to assess plant and animal diversity.

http://data.modelecosystem.org.nz/

7A.5: Resilience and adaptive capacity to climate change: an experimental transcriptomics approach

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Understanding the capacity of organisms to respond to climate change is essential for the maintenance of biodiversity and productivity of primary industries. The rate of climate change has exceeded initial predictions. Australia will be hotter and drier with more intense and frequent droughts and heat waves. Extinction events have been predicted based on correlative models. Populations can however persist under novel conditions given the ability to adapt through genetic evolution or acclimatize through phenotypic plasticity. This study takes an experimental transcriptomic approach to determine gene expression and sequence variation among populations (sourced from different climatic regions) and manipulated environmental conditions (temperature and water). The functional significance of differentially expressed genes and genetic variants will be discussed, along with the findings of population genomic analyses.

7A.6: Using next generation sequencing to develop a genotyping assay for the Tasmanian devil.

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Tasmanian devils are threatened with extinction by a rare form of transmissible cancer, Devil Facial Tumour Disease (DFTD). First seen in 1996, the disease has already wiped out 85% of the devil population. To prevent extinction of the species, a captive breeding population has been established. The aim of this insurance population is to maintain 95% of wild genetic diversity in captivity for 30 years. For successful reintroduction to the wild, it is imperative that the genetic diversity of the captive population is adequately assessed and managed. To develop a genome-wide approach to diversity assessment, we have sequenced the genomes of 9 Tasmanian devils. We are using the sequenced genomes to develop a new amplicon-based genotyping assay to assess local haplotypic diversity. Currently, we have surveyed 10 amplicons, each covering approximately 10Kb of devil sequence. The amplicons are being assessed for their utility in detecting genetic variation in both wild and captive animals. Further amplicons are under development and these will be designed to target both genomic regions with expected neutral variation as well as regions that are likely to affect the on-going survival of the species. These regions will include variation near genes involved with immune response, reproduction and behavior.

7A.7: Adaptation to climate in a widespread species of *Eucalyptus* identified through a genome wide scan and phenotypic assessment

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Southern Australia is predicted to become increasingly hotter and drier due to global climate change, with potentially significant impacts on Australia's iconic eucalypt forests and woodlands. Widespread species may occur in a range of environments by diverging into adaptively specialised populations and/or through high phenotypic plasticity. Widespread *Eucalyptus* species growing under a range of climatic conditions may possess adaptations that enhance resilience of restoration plantings to changing climate. We examined genetic divergence and phenotypic plasticity in *Eucalyptus tricarpa* to determine the nature of adaptation to climate in this species. Evidence of genetic adaptation across a climate gradient was obtained from a NGS-based genome-wide scan combined with physiological and morphometric data collected from reciprocal transplant field trials, that revealed significant correlations between outlier loci, climatic variables and phenotypic traits. We also found evidence for phenotypic plasticity that varied along the gradient and appears to be under genetic control. Thus, widespread eucalypts are likely to respond with phenotypic plasticity to a changing climate, but greater climate resilience in populations and long-term plantings would be facilitated by selection of seed sources through climate-adjusted provenancing that takes into account projected climate change.

7B.1: Neuron-specific alternative splicing as a mechanism to increase the diversity of brain wiring proteins

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Down syndrome cell adhesion molecule 2 (Dscam2) is a functionally conserved transmembrane protein expressed on the surface of neurons. Dscam2 mediates self (homophilic) binding between two opposing membranes; this binding event induces repulsion. During Drosophila visual system development, two different neurons, L1 and L2, require Dscam2 homophilic repulsion for forming boundaries between repeated structures in the brain and for specifying photoreceptor synapses. However, these two neurons physically contact each other within the same nerve fibre. Why then, are L1 and L2 not repelled from each other? Given that Dscam2 encodes two alternative isoforms that have unique binding specificities, we hypothesise that L1 and L2 express distinct Dscam2 isoforms. We engineered the endogenous Dscam2 gene to express the Gal4 transcription factor in an isoform-dependent manner. We found exclusive isoform expression in these two neurons; L1 cells express Dscam2 isoform B, whereas L2 cells express isoform A. These data suggest that neuron-specific alternative splicing is a mechanism for increasing the diversity of cell recognition molecules in the brain. Regulation of functionally distinct alternative isoforms may allow for broadly expressed wiring proteins to act specifically in subsets of neurons.

7B.2: The role of a novel epigenetic regulation in a craniofacial and neurological features of Williams-Beuren syndrome

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Williams-Beuren syndrome (WBS) is a neurodevelopmental disorder resulting from a hemizygous microdeletion within chromosome 7q11.23 involving 28 genes. Genotype-phenotype correlations in patients with atypical deletions have mapped the typical craniofacial dysmorphologies, hypersociability and visuospatial problems to a pair of genes that encode the evolutionarily-related transcriptional regulators GTF2IRD1 and GTF2I. The gene GTF2IRD1 was originally cloned and characterized in our laboratory and we have generated Gtf2ird1 knockout mouse lines that show some striking similarities to aspects of the human disease. Similar to WBS patients, knockout mice have large lips and this correlates with the pattern of Gtf2ird1 expression in the developing face. Expression profiling in knockout brain tissue supports a role for GTF2IRD1 in target gene repression and the epigenetic control of experience-induced gene activity. Our biochemical analyses indicate that GTF2IRD1 negatively auto-regulates its own allele though direct DNA binding and utilizes protein interaction domains to cooperate with other DNA binding proteins and regulatory co-factors. These include a set of chromatin modifying proteins that explain GTF2ITD1's observed involvement in gene silencing. These data support the role of GTF2IRD1 in WBS and start to unpick its molecular function in epigenetic regulation and the cellular basis of the craniofacial and neurological features.

7B.3: Functional Genomic Studies of Autism Spectrum Disorders

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Autism spectrum disorders (ASD) encompass a range of neurodevelopmental conditions characterized by language and behavioral deficits. Although ASD are highly heritable, the genetic basis of ASD heritability remains unclear. Both common and rare DNA sequence variants as well as copy number variants (CNVs) are currently implicated in the etiology of ASD, and it is estimated that hundreds of genetic variants contribute to the disease in any given individual. Since ASD are phenotypically and genetically heterogeneous, we are interested to investigate whether the wide variety of genetic variants associated with ASD ultimately dysregulate a common set of molecular pathways. Using co-expression network analyses of transcriptome data from ASD postmortem brain we identified co-expression modules dysregulated in a large subset of ASD cases. We further investigated the effect of CNVs on gene expression in ASD brain and demonstrate frequent CNV dosage compensation.

7B.4: Functional Characterisation of Voltage Gated Chloride Channel Proteins in *Drosophila*

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The membrane-bound proteins of the voltage gated chloride channel family (CLCs) perform crucial roles in stabilising membrane potentials, transepithelial transport, cell volume regulation and acidification of intracellular organelles. Mammals have nine CLCs clustering into three subgroups and four notable human diseases result from disruption of some members; Dent's disease, Bartter's syndrome, osteopetrosis and congenital muscle myotonia. The Drosophila genome encodes three CLCs, corresponding to each of the mammalian CLC subgroups.

This study focuses on the functional characterization of the fly CLC-b (hCLC-6-7) and CLC-c (hCLC-3-5). Null mutations generated in these genes revealed that CLC-c homozygotes cease to develop beyond 2nd instar larvae while CLC-b homozygotes are adult viable with occasional melanotic masses. Mosaic analysis indicated that the CLC-c mutation is cell lethal in a heterozygous background. The two proteins are differentially localized, with ectopic CLC-beGFP found at the early endosomes and CLC-c eGFP localized to the apical membrane. Targeted over expression and RNAi suppression analyses will also be presented along with genetic interactions between these two genes and a detailed characterization of the CLC-c null lethal phenotype.

This research will use the power and flexibility of Drosophila genetics to elucidate the in vivo function of this critical class of Chloride Channel genes and will in future allow us to model the effect of human pathogenic mutations in the fly.

7B.5: Gene expression and the evolution of placental functions in reptiles

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Placentae that provide substantial amounts of nutrients to embryos have evolved rarely in vertebrates. Placentae are formed by both maternal and embryonic tissue and can be classified by the tissues from which they are composed. In the skink, Pseudemoia entrecasteauxii, two placentae are formed, the chorioallantoic placenta and the yolk sac placenta. The function of each placenta has been inferred from their morphology, but very little is known about what occurs at the molecular level. We used next-generation sequencing to examine the transcriptome of the placental tissues of P. entrecasteauxii to compare gene expression patterns in the uterus of the chorioallantoic (n=3) and yolk sac placenta (n=3) of pregnant lizards and the uterus of non-pregnant individuals (n=2). Both the chorioallantoic and yolk sac placenta show substantial gene expression changes (3590 and 1457 differentially expressed genes compared to non reproductive tissue respectively). There is a strong signal of convergent evolution in the differentially expressed genes that facilitate placental functions in mammals. Convergence of genes involved with placental function in lizards and mammals suggests genomic constraints on the evolution of placentation in vertebrates.

7B.6: Systems analysis of developmental gene regulation

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Development of many organs depends on the sequential and reciprocal exchange of various signaling molecules between juxtaposed epithelial and mesenchymal tissue, but the detailed mechanism controlling these epithelial-mesenchymal (E-M) interactions remains unknown. We used the developing mouse molar tooth as a highly tractable model to decipher the gene regulatory network (GRN) that underlies the complex E-M signaling dynamics during organogenesis. Through the extensive profiling of over 100 microdissected embryonic mouse dental E-M tissues, mutant tissues and signaling molecule treated tissues, our analysis reveals two surprising new insights: (1) Despite the reciprocal exchange of signaling molecule expression, the overall temporal genome-wide expression change in E-M tissues is highly concordant, and (2) among key signaling pathways, the Wnt and Bmp pathways are the primary driver of odontogenesis. We developed a statistical approach to integrate our expression datasets with over 1,000 pieces of perturbation evidence from the literature to generate an inter-tissue GRN for early odontogenesis. Within this GRN, we identified a novel feedback circuit that connects the Wnt and Bmp pathways across the E-M tissue compartments through the action of the Wnt and Bmp4 ligands. Moreover, our inter-tissue Wnt/Bmp circuit was validated with two sets of in vivo mouse genetic crosses designed to ``short-circuit" or to ``break" the feedback circuit. Computer simulation demonstrates that the circuit structure alone can explain the observed signaling molecule expression dynamics in wild-type and mutant mice. This work illustrates how complex signaling dynamics like the E-M interactions in organogenesis represent an intrinsic property of the underlying GRN structure. Since E-M interactions in early odontogenesis resemble those in other organs, our findings will advance efforts aimed at multi-tissue organ regeneration. This work was supported by the Systems-based Consortium for Organ Design & Engineering (http://www.SysCODE.org/).

7B.7: Localised control of Torso Receptor Tyrosine Kinase activation in *Drosophila* terminal patterning

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Controlled activation of Receptor Tyrosine Kinases (RTKs) depends on both the presence of the receptor at the cell surface and the availability of its active ligand. In *Drosophila*, the RTK Torso (Tor) is responsible for the specification of the most anterior and posterior regions of the developing embryo. Tor is distributed ubiquitously on the plasma membrane of the embryo but signals only at the termini due to the localised activation of its ligand Trunk (Trk). While it is understood that Trk activation is mediated by Torso-like (Tsl), a molecule present only at the termini of the early embryo, the mechanism by which it occurs and the precise role of Tsl remains unclear. To this end, we have performed *in vivo* structure/function analyses of Trk and have identified a number of regions that are essential for function. Of particular interest, we have found two basic residues N-terminal to the Trk cysteine-knot motif that likely represent a serine-peptidase cleavage site and may be important for conversion of Trk into the active Tor ligand. We are now using epitope-tagged forms of Trk to determine whether Trk is cleaved and, if so, whether this cleavage is Tsl-dependent. In addition, we are performing a deficiency screen to identify the serine-peptidase important for this processing event. Understanding how the Trk protein is activated will provide valuable insight into the spatial control of RTK activation.

7C.1: Targeting Chromosomal Instability

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Advanced tumours frequently show defective regulation of chromosome segregation (CIN), which makes them a moving target for therapy. Our objective is to identify inhibitors that can specifically kill these chromosomally unstable cells. We have depleted genes by RNAi to find those that can generate the best level of apoptosis in cells that have genetically induced CIN, without affecting normally dividing cells. We initially screened the kinase and phosphatase genes from the Drosophila genome and found that our best candidates implicate the centrosome, and responses to DNA damage. Our data suggest that the length of G2 is critical for cells to tolerate the DNA damage associated with chromosomal instabilty, and that this is regulated by JNK signaling in a novel anti-apoptotic role. We have also found metabolic disruption to be implicated in cellular responses to chromosomal instability, with several enzymes that regulate glycolysis or the TCA cycle being critical for the survival of CIN cells. We are characterizing the role of reactive oxygen species and metabolic disruption on the normal progression through mitosis, particularly their effects on the timing and fidelity of anaphase.

7C.2: Netrin-dependent downregulation of the DCC orthologue, Frazzled, is required for the dissociation of the peripodial epithelium in *Drosophila*

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Netrins are secreted chemoattractants with roles in axon guidance, cell migration, and epithelial plasticity. Netrin-1 also promotes the survival of metastasised cells, by inhibiting the pro-apoptotic effects of its receptor Deleted in Colorectal Carcinoma (DCC). Here we report that Netrins can also regulate epithelial dissociation during *Drosophila* wing eversion. During eversion, peripodial epithelial cells lose apico-basal polarity and adherens junctions, and become migratory and invasive - a process similar to an epithelial-mesenchymal transition. Loss of *netrinA* inhibits the breakdown of cell-cell junctions, leading to eversion failure. In contrast, the Netrin receptor Frazzled blocks eversion when overexpressed, while frazzled RNAi accelerates eversion in vitro. In peripodial cells Frazzled is endocytosed, and undergoes NetA-dependent degradation, which is required for eversion. Finally, we provide evidence that Frazzled acts through the ERM family protein Moesin to inhibit eversion. This novel mechanism may also help explain the role of Netrin and DCC in cancer metastasis.

7C.3: Highly conserved zinc transporters performing divergent and specific functional roles in Drosophila melanogaster

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Zinc is an essential dietary nutrient involved in numerous cellular and physiological pathways. Imbalances in zinc homeostasis have been implicated in a number of serious diseases such as Alzheimer's disease, diabetes and asthma. A complex network of zinc transport genes work in a co-ordination fashion to import (ZIP) and export (ZnT) zinc in and out cells, maintaining a strict balance in zinc homeostasis in numerous cell-/tissue-types. In the Burke laboratory we use the vinegar fly, Drosophila melanogaster, which has 17 putative zinc transport genes compared to 24 in mammals, to investigate the function of these transporters. In such a complex system it is difficult to elucidate the function of one single transporter, especially with such scope for functional redundancy. Here I present an investigation into a clade of four highly similar Drosophila ZIP transporters, dZIP89B, dZIP88E, dZIP42C.1 and dZIP42C.2, the most closely related homologs of mammalian ZIP 1, 2 and 3. Analysis of the expression patterns, protein sub-cellular localisation and a detailed functional characterisation of null mutations in two of these genes will demonstrate that although these transporters are dispensable under normal growth conditions they display opposing sensitivities to dietary zinc modulation, indicating even highly related zinc transporters have specific functional roles.

7C.4: Selection maintains heterozygosity at key genes in a clonal population of honey bees (*Apis mellifera capensis*).

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An asexual lineage that reproduces by automictic thelytokous parthenogenesis has a problem: rapid loss of heterozygosity resulting in effective inbreeding. This may contribute to the rarity of thelytoky, despite its theoretical benefits to females. Thus, the circumstances under which rare asexual lineages thrive provide valuable insights into the tradeoffs that have shaped the evolution of alternative reproductive strategies. A socially parasitic lineage of the Cape honey bee, *Apis mellifera capensis*, provides an example of such a lineage. It has been assumed that cytological adaptations slow loss of heterozygosity in this lineage. However, we present evidence supporting an alternative hypothesis: heterozygosity is largely maintained via selection against homozygous recombinants. We examined the genotype of the clonal population at closely linked microsatellite markers along Chromosomes III and IV, and identified regions in which heterozygosity is maintained. One such region contains the complementary sex-determining locus, at which homozygosity is lethal and so selection for heterozygosity is absolute. The observation of other regions on chromosomes III and IV where heterozygosity is maintained suggests that these regions contain functional genes that are deleterious when homozygous. Our results provide a plausible explanation for the maintenance of heterozygosity at multiple loci in a thelytokous lineage.

7C.5: Identification and characterisation of *jam packed* (*jam*), a novel regulator of stem cell development in the *Drosophila* testis.

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In all multicellular organisms, stem cells play essential roles in generating and maintaining tissues. The unlimited growth potential of stem cells requires careful control, via signalling from the stem cell microenvironment, to prevent developmental defects. Stem cell model systems, particularly the *Drosophila* testis, have been instrumental in the study of stem cell dynamics *in vivo*, revealing evolutionarily conserved signals necessary for regulating stem cell self-renewal, differentiation, and proliferation.

Utilising the *Drosophila* testis model system, we conducted a forward genetic screen of pupal-lethal mutants and identified that the orthologue of mammalian *family with sequence similarity 40, member A* (*FAM40A*) acts as a tumour suppressor and is essential for regulating stem cell development. We named this *Drosophila* mutant *jam packed* (*jam*) after the supernumerary stem cell-like cells present in the mutant testes.

RNAi knock-down of *jam* has revealed Jam functions in the somatic stem cell lineage to direct differentiation and control germ-soma cell contact by regulating cytoskeletal development. Further analyses demonstrated Jam acts to non-autonomously restrict germline stem cell proliferation, and limit self-renewal promoting Bone Morphogenetic Protein (BMP) signalling. Therefore, we propose that *jam* is a novel conserved stem cell regulatory factor, necessary for proper intercellular signalling within the stem cell microenvironment.

7C.6: Flies and resistance: A versatile system for studying receptor biology.

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Loss of function of a single nicotinic acetylcholine receptor subunit, Dalpha6, in *Drosophila melanogaster* is sufficient to confer high levels of spinosad resistance. This discovery has provided a versatile system for probing receptor function. Not only can the *D. melanogaster* subunit be studied in closer detail, but we have been able to rescue this phenotype by over-expressing Dalpha6 orthologues from a number of insect pest species. While the receptor's role is critical, there are a number of other proteins that are going to influence the capacity and magnitude of spinosad response of this receptor. These accessory proteins are likely to impact the receptor function in both positive and negative ways that can be detected through alterations in the spinosyn resistance phenotype. We have tested a candidate accessory protein genes from the literature using RNAi to knockdown their expression. Significant spinosad response changes have highlighted genes most likely to interact with Dalpha6. By characterizing these we hope to increase the understanding of insect nAChR biology. From this study we also expect to identify targets with greater variation amongst insects than found for the receptors that may allow development of insecticidal compounds able to target pests more specifically than those currently available.

7C.7: Draft Sequencing and assembly of the New Zealand Giant Weta Genome

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Giant Weta are one of the largest extant insects on earth, however a number of these species are highly endangered. The Poor Knights Giant Weta (*Deinacrida fallai*, Orthoptera) is one such species, and is restricted to a small offshore island. We are using Illumina technology to sequence the genome of this endemic New Zealand insect. The genome of this species is large, with flow cytometry giving a size estimate of 20 GB. Our current draft assembly has been obtained from a mixture of paired-end (200 bp, 500 bp, 1kb) and mate pair (8 kb) libraries using SOAPdenovo2. Additional assemblers, including ABYSS and MSR-CA, will also be trialled in order to obtain a more complete assembly. RNA-seq data has also been obtained from various tissues, to aid genome annotation and candidate gene identification, with the aim of investigating various phenotypic characters, including those involved in reproduction and chemosensing. The draft genome along with comparative SNP and RNA-seq data will be used to investigate a range of evolutionary questions and conservation genetics issues in this and related Weta species.

8A.1: A draft annotated genome sequence for Australia's Bearded Dragon

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New technologies for sequencing the genomes of plants and animals are revolutionizing access to the genetic information that underpins phenotypes and their evolution. Draft whole genome sequences are being generated at an ever increasing rate, and for reptiles we now have at hand unparalleled genomic data for three crocodilians, two turtles, two lizards, two snakes and of course our feathered inclusion to the reptiles, the chicken. The Australian western bearded dragon, *Pogona vitticeps*, is among those that have been sequenced. *Pogona vitticeps* has 2n=32 chromosomes of which 12 are macrochromosomes and 10 are microchromosomes. It has a ZW system of sex determination. Formerly cryptic, the sex microchromosomes were first revealed through comparative genome hybridization (CGH), distinguishable by C-banding on later closer examination. Sexual outcome is also influenced by temperature, with sex reversal of ZZ genotypes to female phenotypes at high temperature - the W chromosome is not required for female development. The *Pogona vitticeps* genome was generated for a wild caught ZZ individual using 13 insert libraries ranging from 0.5 to 40 Kbp to yield 85x sequence coverage. Heterozygosity rate was high at 0.85% (SNPs + Indels) which complicated assembly. Nevertheless, assembly yielded an N50 of 2.3Mbp, with 95% of short insert reads mapping to cover 97% of the assembled genome (average depth 60x), indicating that the genome assembly was good. A total of 19,406 protein-coding genes were annotated in assembly, 63% of them had intact open reading frames with start and stop codons, and most were supported by RNA-Seq signals. Subtraction of the ZZ genome from a ZW genome of lower sequence coverage (62x) has revealed 85 presumptive W chromosome scaffolds and associated gene candidates for sex determination function. No sex determining gene has yet been identified for a reptile.

8A.2: *De novo* Assembly of an Herbal Fungal Genome Using PacBio Long Reads

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Previously we combined several sequencing platforms generating short reads (generally less than 1000 bp) to determine the genomic sequence of an herbal fungal species, *Ganoderma multipileum*. With optical mapping, highly accurate sequences for 13 chromosomes were assembled for the haploid genome of strain BCRC37177. In the current study, we set out to sequence the same haploid genome using the single molecule real time (SMRT) technology of Pacific Biosciences. Taking 41 SMRT cells, we have collected 5.6 Gb raw data with a mean read length of 1,938 bp. A hierarchical genome-assembly process (hGAP) was applied to attempt *de novo* assembly using only the PacBio long reads. Seventy of the 315 contigs were mapped to the nuclear genome sequences of the hybrid assembly. These chromosomally placed contigs added up to 44,760,178 bp, and the maximum and N50 contigs were 4,342,439 bp and 1,354,389 bp, respectively. The PacBio contigs not only helped close the remaining gaps of the BCRC37177 sequences, also it corrected assembly errors and identified unusual chromosomal features. A new type of trio sequences containing conserved fragments of 1,388 bp -550 bp - 478 bp were discovered to be present at near the chromosomal ends. Functions of these unique repetitive sequences are currently unknown. Our sequencing approach yields accurate and complete genomic information and reveals novel chromosome features that are otherwise

8A.3: Exon Expression Analysis Reveals New Levels of Transcriptome Complexity at Upper Thermal Limits and Recovery in Natural *Drosophila*

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While the cellular heat shock response has been a paradigm for studying the impact of thermal stress on gene expression and RNA metabolism, the genome-wide response to thermal stress and its connection to physiological stress resistance remain largely unexplored. Here, we address this issue using an array based exon expression analyses to interrogate the transcriptome in recently-established Drosophila melanogaster⋆ stocks during severe thermal stress and recovery. We first demonstrated the efficacy of exon-level analyses to reveal a level of thermally induced transcriptome complexity extending well beyond gene-level analyses. Next, we showed that the upper range of both the cellular and physiological thermal stress response profoundly impacted message expression and processing in D. melanogaster⋆. As predicted from cellular heat shock research, constitutive splicing was blocked in a set of novel genes; we did not detect changes to alternative splicing during heat stress, but rather induction of intron-less isoforms of known heat responsive genes. We observed transcriptome plasticity in the form of differential isoform expression during recovery from heat shock, mediated by multiple mechanisms including alternative transcription and splicing. This affected genes involved in DNA regulation, immune response and thermotolerance. These patterns highlight the complex nature of innate transcriptome responses under stress and potential for adaptive shifts through plasticity and evolved genetic responses at different hierarchical levels.

8A.4: Microsatellite Tandem Repeats Are Abundant in Human Promoters and Are Associated with Regulatory Elements

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Tandem repeats are genomic elements that are prone to changes in repeat number and are thus often polymorphic. These sequences are found at a high density at the start of human genes, in the gene's promoter. Increasing empirical evidence suggests that length variation in these tandem repeats can affect gene regulation. One class of tandem repeats, known as microsatellites, rapidly alter in repeat number. Some of the genetic variation induced by microsatellites is known to result in phenotypic variation. Recently, our group developed a novel method for measuring the evolutionary conservation of microsatellites, and with it we discovered that human microsatellites near transcription start sites are often highly conserved. In this study, we examined the properties of microsatellites found in promoters. We found a high density of microsatellites at the start of genes. We showed that microsatellites are statistically associated with promoters using a wavelet analysis, which allowed us to test for associations on multiple scales and to control for other promoter related elements. Because promoter microsatellites tend to be G/C rich, we hypothesized that G/C rich regulatory elements may drive the association between microsatellites and promoters. Our results indicate that CpG islands, G-quadruplexes (G4) and untranslated regulatory regions have highly significant associations with microsatellites, but controlling for these elements in the analysis does not remove the association between microsatellites and promoters. Due to their intrinsic lability and their overlap with predicted functional elements, these results suggest that many promoter microsatellites have the potential to affect human phenotypes by generating mutations in regulatory elements, which may ultimately result in disease. We discuss the potential functions of human promoter microsatellites in this context.

8A.5: Microsatellites and genome size

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The occurrence of microsatellites throughout genomes is far greater than expected if the distribution of tandemly repeated nucleotides was random. There is great variability in the relative abundance of different families (i.e. mono, di-, tri-, tetra-, penta-, and hexanucleotides) of microsatellites and also in the abundances of particular motif types (e.g. AC, AT, AG, CG) across the tree of life. Microsatellites form part of the repetitive elements of genomes and several key associations regarding microsatellite relative abundances have been noted. For example, genome size has emerged as a potential indicator of microsatellite abundance with the idea that genomes are augmented by repetitive elements. However, the trends are not uniform across the major branches of the tree of life. Here we revisit the debate regarding correlations of genome size and microsatellite abundance using data generated by second generation shotgun sequencing of partial non-model genomes. We present microsatellite abundance results from over 180 species and over 120 different taxonomic families from across plants and animals and examine the abundance of different motif families with genome size using phylogenetic contrast analysis. We test the hypothesis that microsatellites augment the size of genomes and explore if microsatellite motif family proportions differ with genome size.

8A.6: A *de novo* transcriptome assembly of the black field cricket (*Teleogryllus commodus*)

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Background Rapid advances in next-generation sequencing methods have provided new opportunities for transcriptome analysis (RNA-Seq) in model organisms and non-model organisms. For non-model organisms lacking well-defined genomes, *de novo* assembly is typically required for downstream RNA-Seq data analyses. Although RNA-Seq was successfully used in many non-model organisms to understand transcriptome architecture and various biological processes, strategies for the generation of a reference transcriptome from a genetically heterogeneous and differently treated set of individuals remain under development. **Results** In this study, we used a total number of 489.7 million 101bp PE reads, to assemble the transcriptome of the black field cricket (*Teleogryllus commodus*). Three de Brujin graph assemblers, Trans-ABySS, Oases and Trinity, using multiple k-mers or single k-mer, were used for the assembly. The whole *de novo* assembly process was divided into the following three steps: individual assembly, merging different samples, and removal of redundancy. The influence of each step on the assembly was assessed to optimize transcriptome assembly from short reads. After optimization, the short reads were merged into 71,816 transcripts by Trans-ABySS, 80,476 transcripts by Oases, and 87,065 transcripts by Trinity. Among the three assemblers, Oases produced the longest contig of 49,365 bp, and a highest average contig length of 2,484 bp. At the protein level, Oases produced a total of 47,763 (59.2%) transcripts with significant similarity to *Drosophila melanogaster* isoforms, which is the highest among the three assemblers. We will provide the annotation and the GO analysis of the newly assembled black field cricket transcriptome to the community. **Conclusions** Our work compared the performance of publicly available transcriptome assemblers, and analyzed the factors affecting *de novo* assembly. We document the process for removal of redundancy when dealing with multiple samples from individuals. The strategy for *de novo* assembly of transcriptome data presented here may help guide other de novo transcriptome studies. Our results also provide the de novo assembled transcriptome assembly of the Australian black field cricket for a large ecological and evolutionary community.

8A.7: Plankton to Pooh: Metagenetic approach to investigating plankton community composition and whale diet

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Assessing the role of generalist predators in a community is a difficult yet critical task, particularly in marine environments. The Hauraki Gulf, New Zealand, is a productive embayment that supports a diverse range of marine predators, including a year-round resident population of Bryde's whales. Here we take an ecosystem approach and use high-throughput sequencing and DNA barcoding (18S gene) to metagenetically characterise the plankton community and diet of the Bryde's whale through non-invasively collected scat. Our initial study confirmed that Bryde's whales target krill and copepod species but also found planktonic species (Polychaeta, Hydrozoa and Tentaculata) in the scat and community plankton samples that were not found in the pseudo-control samples (water collected concurrently to scat). This suggests the whales are consuming a wider variety of prey than previously thought and targeting plankton aggregations rather than consumption as a by-product when consuming larger prey. OTU richness was higher in the scat samples (beta diversity = 0.63) than the psuedo-controls (0.07), although not as high as in the plankton community samples (0.85), supporting the theory the species has a diverse diet. This is an effective, non-invasive method to determine prey of generalist marine predators without a priori assumptions on diet composition.

8B.1: Sequence, Assemble, Annotate, Align ... Species Tree?

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Genomic sequences provide the best data we will ever get to resolve evolutionary relationships among species. The reduction in costs of High Throughput Sequencing (HTS) means it is now tractable for many academic groups to de novo sequence entire genomes. Transforming that data into a useful form for addressing questions concerning evolutionary origins is not trivial. In an effort to establish the genetic basis of virulence in fungal pathogens, we have developed two suites of software tools that address (1) the assembly/annotation workflows and (2) the challenge of drawing statistically robust phylogenomic inferences from the resulting data. Here I focus on (2). In particular I will present a statistical measure that allows us to test for each gene whether the evolutionary model employed is suitable and thus whether the subsequent tree can be trusted. I contrast results from analysing a fungal and mammal data set that have substantially different time-depths. We confirm the expectation that time-depth matters. Strikingly, for the more divergent comparisons, results from the most popular reversible model could not be considered reasonable for even one of the hundreds of genes tested. Our results demonstrate the current model selection paradigm that promotes such model choices are seriously flawed.

8B.2: Bison paleogenomics: revealing ancient and modern species and populations

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Advances in sequencing technologies now allow the study of population level samples at the genomic scale for both modern and ancient species. Most notably, commercially available nuclear SNP microarrays hold considerable potential to provide genome-wide data from multiple individuals. However, the ability to generate reliable nuclear SNP genotypes from ancient samples is yet to be explored in detail. The fossil record contains a wide diversity of bison species and/or sub-species distributed across Eurasia and North-America during the late Pleistocene, although only two species remain alive today (the American bison, Bison bison, and the European bison, Bison bonasus). We analysed mitochondrial genomes and ~50k nuclear SNPs from ancient bison samples in Europe, Siberia and North America using both the Illumina BovineSNP50 assay and direct Illumina sequencing. Through comparison with SNP data from modern American bison, cattle and related bovid species, we reveal a range of methodological challenges and limitations to the use of commercial SNP microarrays for phylogenomics studies. The data also reveal an unknown extinct species of bison in Europe that shows a series of paleoecological interchanges with the Steppe bison in the late Pleistocene. Overall the data reveal multiple cases where mitochondrial and nuclear phylogenetic analyses reveal different evolutionary histories.

8B.3: The evolution of a contagious cancer, the Tasmanian Devil Facial Tumour Disease.

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Transmissible animal tumours are informative models to study cancer evolution at genetic as well as epigenetic levels. The Tasmanian devil facial tumour disease (DFTD) is one of the two, clonally transmissible cancers. The first case of DFTD was observed in the east of Tasmania in 1996 and since has led to the dramatic decline of Tasmania devil (*Sarcophilus harrisii*) populations. The cancer causes large ulcerating tumours primarily around the head of Tasmanian devils. Animals generally die within six months of the first appearance of lesions due to starvation or complications from metastases. Devil Facial Tumour cells possess highly rearranged genomes, characterized by tumour specific chromosomal rearrangements. While the clonal nature of DFTs is unequivocal, recently four distinct chromosomal strains have been described. In the present study we investigated the temporal and spatial evolution of DFTD at genetic and epigenetic levels. No spatial genetic or epigenetic variations were observed between strains, but tumour methylation levels decreased over time. Temporal changes were also observed in genes associated with methylation. The variations in gene expression and methylation suggest that this cancer should not be treated like a static entity, but rather as an evolving pathogen.

8B.4: Accounting for density dependent cladogenesis clarifies comparisons of diversification rates

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Comparisons of species richness between sister clades are often used to test for differences in rates of diversification. This is valid when clades have diversified at a relatively constant rate through time, but may be inaccurate if diversification has slowed or stopped, and diversity has reached an equilibrium level. We simulated the growth of pairs of sister clades under a process of density-dependent diversification to show that the initial difference in diversification rate between clades declines as clades become older. We then used phylogenies of avian and mammalian families to test whether models that relate diversification rate to latitude are improved by adding information on diversification slowdown. We find that diversification slowdown does not recover a latitudinal bias in diversification rate, but this slowdown is more common in clades at higher latitudes. We conclude that commonly used measures of diversification rate obscure differences in the original diversification rate of a clade, while the latitudinal biodiversity gradient is at least in part driven by more extinction or less speciation in temperate regions.

8B.5: Predicting Quantitative Traits from the Metagenome: Applications for Greenhouse Gas Mitigation

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Domestic ruminants such as cattle and sheep have the ability to convert low quality forages into high quality protein in the form of milk and meat via rumen fermentation. However a by-product of the fermentation process is methane, a potent greenhouse gas. Methane from rumen fermentation accounts for 11% of Australia's National greenhouse gas emissions.
We have exploited the emerging field of untargeted (shotgun) metagenomics to profile the rumen microbial communities of 150 dairy cattle. Inspired by techniques used in genomic prediction for livestock breeding, we used the microbial profiles from these samples to predict the amount of methane produced by individual animals. In our preliminary study, we achieved an accuracy of prediction of 0.47, which is higher than could be predicted with genomic prediction, given the number of samples and the moderate to low heritability of methane emission levels. As more metagenomic samples are added to the dataset the accuracy of prediction may increase. We have also successfully employed the same method on public datasets to predict body mass index and inflammatory bowel disorders in humans. This work highlights the importance of the metagenome in complex phenotypes such as methane emission levels from cattle.

8B.6: Quantifying the influence of sequence neighborhood on mutation

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Mutagenesis is the cause of genetic variation and a critical contributor to phenotypic diversity. Understanding the factors influencing mutation can improve detection techniques, identify diagnostic signatures of disease causing mutagens and facilitate development of more accurate models of genetic divergence. As illustrated by CpG hypermutability, neighboring bases can influence mutation in a manner proportional to proximity. We have sought to establish whether characteristic sequence motifs influence the occurrence of the 12 different point mutations.

We developed a novel information theory based statistic that adjusts for the variation in nucleotide composition characteristic of many genomes. Sampling 5,060,154 Human SNPs from Ensembl, we infer the mutation direction by ancestral state reconstruction. A mutation motif logo is then constructed from the new metric.

Our results affirm the well known CpG effect and identify that close neighbors exert a substantial influence over all mutations. Notably, the CpGs effect is relatively weak and varies by genomic location. Some motifs exhibited changes with allele frequency of the segregating variants in a manner consistent with the operation of biased gene conversion. Those influences vary by chromosomal location and sequence coding content.

8B.7: Comparing closely related fruit flies: just how close is close?

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The Queensland fruit fly and the Lesser Queensland fruit fly are economically important pests that also happen to be sympatric species that can easily be distinguished by appearance and behaviour. In captivity however, they readily hybridise to produce fully fertile offspring. Early investigations failed to find any fixed genetic differences between the two species. Consequently, they are referred to as closely related sibling species. But how close is close? We have used a comparative genomics approach to investigate how the two species differ. Our analyses examined single copy regions, repetitive sequences and transcriptomes. Our results show that divergence varies widely between these different types of sequence. The results are highly relevant not only for speciation models but also for practical aspects of pest monitoring and control.

8C.1: Interspecific mating between *Apis cerana* and *A. mellifera*: Does it happen and what does it mean for Australian bees?

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When formerly allopatric species are brought together, interesting genetic consequences may result from interspecific mating. The western honey bee, *Apis mellifera*, and the Asian hive bee, *A. cerana* have been allopatric for over 6 million years, but are similar in morphology and behaviour. During the last century they have been brought into contact anthropogenically in Asia, some Pacific islands, and now in Cairns Australia. When *A. mellifera* and *A. cerana* are artificially cross-inseminated, hybrid offspring are inviable. Thus interspecific mating is of concern to commercial apiarists as brood viability and honey production may be adversely affected. Additionally, interspecific mating may induce thelytokous parthenogenesis, a phenomenon that can cause outbreaks of clonal reproductive parasites. We examined the frequency of natural interspecific mating, analysing spermathecal contents of sympatric *A. mellifera* and *A. cerana* queens from China and Cairns by species-specific PCR. In China, where there are large populations of both species, 10% of *A. mellifera* queens mated with at least one *A. cerana* male. In contrast, no *A. cerana* queens had mated with *A. mellifera* males. While as yet there is no evidence of interspecific mating in Cairns, this may occur with increasing frequency as the invasive *A. cerana* population expands.

8C.2: Genetically identifying dispersers: how many loci are enough?

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Genetic data is increasingly used to quantify contemporary dispersal in wild populations. However, empirical genetic datasets used for these analyses are rarely tested to determine if they are capable of providing accurate results. Correct identification of dispersers is vital to downstream ecological conclusions. We have developed a method to test if a genetic dataset provides sufficient information to accurately identify first-generation migrants. Using microsatellite data from three genetically distinct wild populations of common starlings (*Sturnus vulgaris*), we artificially forced migration of a subset of individuals. We then ran GeneClass2.0 simulations using diminishing numbers of loci, to assess at which point forced migrants could no longer be correctly identified. Our results suggest that with this dataset, at least 20 microsatellite loci are necessary to confidently identify first-generation migrants. Our review of the literature has revealed that studies that have implemented first-generation migrant detection to date have used 10 microsatellites on average. We suggest that future studies increase the number of microsatellite used when possible and employ our approach to determine if their dataset provides sufficient information to conduct these analyses.

8C.3: Functional characterisation of a naturally occurring olfactory receptor variant in *Drosophila melanogaster*

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The insect olfactory receptor (*Or*) genes are a large, rapidly evolving gene family that determine the responses of olfactory receptor neurons (ORNs) that mediate critical behaviours. One member of this family, *Or22a*, shows multiple duplication events across *Drosophila* species, and there are dramatic changes in the response profile of the ORN class, ab3A, in which it is expressed (1). These response changes may be ecologically important, as most other ORN classes have well-conserved response properties across *Drosophila* species. In our standard laboratory strain of *D. melanogaster*, Canton-S, *Or22a* and its closely linked paralogue *Or22b* are thought to be expressed in ab3A neurons, however only *Or22a* mediates the ab3A response (2). Interestingly, at this locus high levels of allelic variation were found in natural populations along the east coast of Australia (3). The major source of this variation is a deletion mutation that creates a fusion of *Or22a* and *Or22b* and is predicted to encode a single chimaeric receptor, *Or22del*. This deletion mutation may be under positive selection as its frequency varies clinally along the east coast. We have shown that flies homozygous for the *Or22del* allele have significant changes in the response profile of the ab3A neuron compared to flies without the deletion. We have further shown that it is the predicted hybrid Or22del protein that underlies this altered profile. We are currently performing behavioural assays to determine if *Or22del* causes changes in olfactory behaviour that may be under selection.

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8C.4: Using lizards to investigate the genetic mechanisms controlling uterine angiogenesis during live birth: consequences for cancer

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In viviparous squamates (lizards and snakes), increased uterine vascularity via angiogenesis during pregnancy coincides with increased oxygen demand by the developing embryo. I aimed to identify genes involved in increases in uterine angiogenesis in viviparous (live-bearing) and oviparous (egg-laying) skinks during pregnancy using the unique skink *Saiphos equalis*, an egg-retaining species with oviparous and viviparous populations, and a closely-related oviparous skink *Anomalopus leuckartii*. An angiogenic gene (VEGF111) known only in tumour-related angiogenesis was recently identified in pregnant uterus of the viviparous population of *S. equalis*, suggesting that the evolution of viviparity and susceptibility to cancer are linked. Using real-time RT-PCR, I tested the hypotheses that 1. VEGF expression increases during pregnancy in an egg-retaining species, 2. other genes (EPAS1, FGF2, and IRE1) indirectly regulate angiogenesis via VEGF expression, and 3. that VEGF111 expression is required for the evolution of viviparity. No significant change in expression in the uterus of either population of *S. equalis* was found. Furthermore, VEGF111 expression was identified in both populations of *S. equalis* and in *A. leuckartii*. Therefore, VEGF111 expression is not essential in the transition from oviparity to viviparity. These results suggest that multiple genetic pathways can be selected to increase uterine vascularity during the evolution of viviparity and that *S. equalis* may use a unique pathway.

8C.5: Characterisation of the toll-like receptors genes in the Tasmanian devil, *Sarcophilus harrisii*

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The Tasmanian devil (*Sarcophilus harrisii*) is the largest carnivorous marsupial in the world, and is restricted to the island state of Tasmania in Australia. Genetic bottlenecks and island effects have resulted in low genetic diversity in this species. The aim of this study was to characterize the level of genetic diversity in a key immune gene family - the toll-like receptors (TLRs). TLRs play a key role in recognising and binding pathogens and triggering innate and adaptive immune responses. Most eutherian mammals have 10 to 15 TLRs and each can interact with specific viral, bacterial, fungal or parasitic pathogens. Ten TLR genes have been annotated in the Tasmanian devil genome, including homologues of eutherian TLR2---10 and TLR13. The TLRs sequence similarity with human and opossum is on an average of 60% and 80%, respectively. So far, I have characterised six of these genes and examined genetic polymorphisms in ten individuals from different subpopulations. Low levels of genetic variability were observed at all loci. Further studies will be carried out to characterize the other four genes and to measure genetic diversity in larger sample size. We will also investigate whether diversity in TLRs plays a resistance or susceptibility to devil facial tumour disease.

8C.6: Novel Defensin Peptides of the Tasmanian Devil (*Sarcophilus harrisii*)

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Defensins are a small antimicrobial peptide (AMP) family that displays a wide range of anti microbial and immunoregulatory functions in a diverse range of species. Known as one of the natural antibiotics of the body this gene family displays extraordinary sequence and bioactivity diversity, reflecting the selection pressures and specific microbial challenges that individual species have faced over millennia. Monotremes and marsupials give birth to immunologically naive young, which need to survive in an environment of high microbial diversity, either the pouch or the burrow. Antimicrobial peptides play a key role in protecting these young during this time period. The Tasmanian devil, a dasyurid marsupial, faces extinction due to devil facial tumour disease. With the recent sequencing of the Tasmanian devil genome it is now possible to characterize the defensin gene family. We have mined the available genome and transcriptome sequence data to identify two alpha and six beta defensins. All defensisn identified thus far, retain the characteristic features of the defensin family including a conserved 6-cysteine motif, cationic charge (between 2+ to 11+) and high proportion of hydrophobic residues (>30 %). Phylogenetic analysis of these sequences reveals lineage specific gene expansion unique to this species, with sequence identity between 10-40%. A beta defensin that is orthologous to a previously reported opossum defensin has also been identified, sharing 100% sequence identity in the mature peptide domain. These finding reveal Tasmanian devil defensin genes that have both diversified over time and retained a high level of homology to other marsupial species.

8C.7: Species from faeces: metabarcoding to detect vertebrate prey from predator scats

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Predation by foxes and cats has been implicated in the declines of several Australian mammals. The recent introduction of foxes to Tasmania has put many more species at risk. Concurrently, the Tasmanian devil has suffered a rapid decline following the spread of facial tumour disease. Both events will significantly alter future predator-prey dynamics in Tasmania. DNA from predator scats constitutes a unique ecological resource and could provide critical information about predation by native versus introduced predators in Tasmania. Scat DNA may also improve understanding of species distributions and the detection of rare or elusive species.

Metabarcoding approaches can detect DNA from multiple species from each scat. Here, we report on the application of Roche 454 sequencing to the analysis of short (<200bp) amplicons from two mitochondrial genes (16S and 12S) using DNA from Tasmanian predator scats. We assigned sequence reads to taxonomic groups using MEGAN, following BLAST against GenBank. We detected multiple species, including rodent, rabbit, pademelon, ringtail possum and skink DNA. This initial study enabled us to refine the analytical approach and highlighted gaps in taxonomic resolution for certain taxa. We will now analyse hundreds more scats, targeting additional genes to improve resolution, while developing a regionally focused sequence database.

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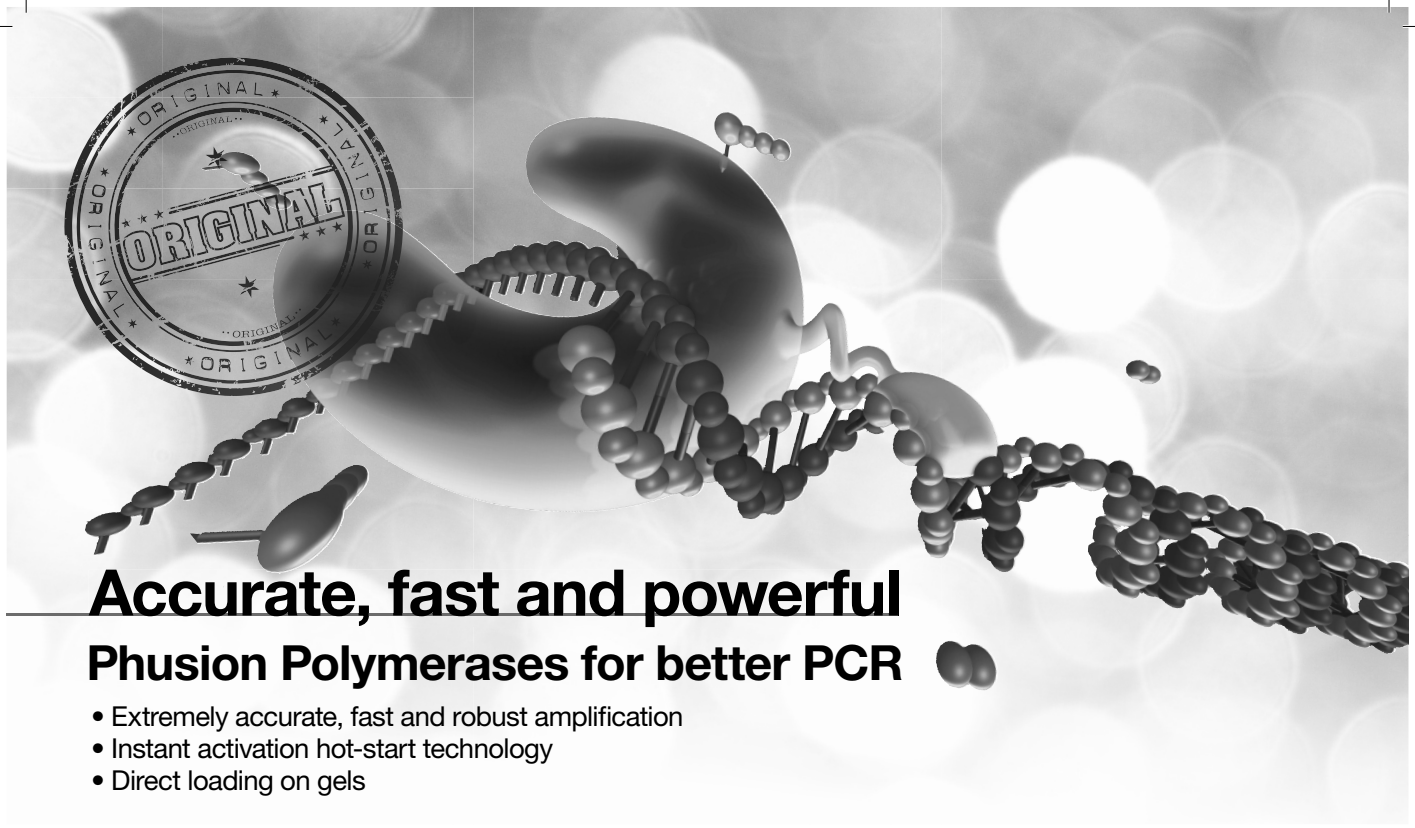

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Posters

1: Phylogeography within the Australian arid zone. Plio-Pleistocene diversification and genetic structure in the skink Tiliqua rugosa revealed by mitochondrial and nuclear DNA

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Palaeoclimatic events and biogeographical processes since the mid-Tertiary have influenced the evolution and distribution of the Australian fauna. However, the effects of climate fluctuations over this period in shaping the present-day genetic structure of animal and plant populations in southern Australia is poorly known, particularly for arid to semiarid biota. Here we investigate the phylogeographic history of an Australian scincid lizard, Tiliqua rugosa (the sleepy lizard), within Australian arid and semiarid regions. We assessed genetic variability within and among regions using mitochondrial DNA and two nuclear markers, the non-encoding intron 7 of β-fibrinogen, and glyceraldehyde-3-phosphate dehydrogenase (Gapd). Phylogenetic analyses reveal three mtDNA lineages for sleepy lizard corresponding to the northern and the southern regions of the Murray River in southern Australia and a western clade spanning the west and east regions of the Nullarbor Plain. In contrast, haplotype networks reveal a lack of concordance between nuclear DNA markers and mtDNA. The observed patterns suggest that the lineages originated during the Plio-Pleistocene with the effect of glacial-interglacial cycles. Future work will incorporate investigating the distribution of variation in 15 anonymous nuclear markers and MHC loci.

2: Phylogenetics and evolution of Australian *Nasutitermes*F231

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In Australia, termites are keystone species and ecosystem engineers in many environments, particularly in arid areas. Australia contains a total of 260 termite species, representing 5 of the 7 generally recognized families worldwide. One important genus in Australia is Nasutitermes. There are 19 representative species in Australia (of over 200 species worldwide), which are found all across the Australian continent in various ecoregions including temperate forests, semi-deserts, savannah woodland and others. Australian Nasutitermes are particularly known for their variability in nest architecture and construction. Despite the ecological and economic importance of the Australian termite fauna, their systematics and evolution is poorly understood. We are constructing a comprehensive phylogeny of the Australian Nasutitermes based on mitochondrial and nuclear gene markers and will report our most recent results.

3: The powerhouse of our body

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Mitochondria are small organelles in cells. They produce energy. If you want to run fast like Usain Bolt feed your body, your cells and your mitochondria healthy food. Train hard to produce more mitochondria.

If you stop exercising and eat unhealthy food you can get fat and unfit. If you are fat and unfit you have less fun and can catch more colds.

4: Group theoretic formalization of Double cut and join model of chromosomal rearrangement

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The ``double cut and join'' model of chromosomal rearrangement has received attention as this operator is a universal operator and can model inversions, translocations, fusion and fission. We translate the DCJ (double cut and join) operator into its algebraic realization as a group action on the space of multichromosomal genomes. We study this group action, deriving some properties of the group, and finding group-theoretic analogues for the key results in the DCJ theory. There are very few examples of an algebraic approach to modeling biological phenomena. Adopting an algebraic viewpoint may in fact reveal deep insights. This paper attempts to translate the problem of finding the rearrangement distance between genomes into a problem in group theory. Moving this known problem into a different space may lead to the development of a novel approach.

5: Detest the pest: Understanding Spinosad - *Drosophila* interactions

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Spinosad is a widely used insecticide targeting nicotinic acetylcholine receptors (nAChRs) in the insect nervous system. The study of resistant mutants in *D. melanogaster* showed that spinosad targets the nAChR D6 subunit. However, beyond the target, little is known about the biological interface between spinosad and the insect.

For an insecticide to be effective it must be activated by or bypass metabolic enzymes and then be transported to the target where it generates its toxic effect. Resistance can theoretically occur from mutations in genes involved in any of these processes. To identify some of these genes we have performed a Genome Wide Association Study (GWAS) on spinosad resistance in the Drosophila Genome Reference Panel (1). In identifying genes associated with resistance, we expect to identify the key biological processes that interface with spinosad. Of particular interest are genes that produce accessory proteins responsible for the assembly and function of nAChRs.

Our GWAS has identified a large number of candidate genes. As a first step we are examining the level of resistance in RNAi lines for each of the candidate genes identified.

An understanding of the insect-insecticide interface will facilitate the design of more effective insecticides.

1 - MACKAY, T. F. C., S. RICHARDS, E. A. STONE, A. BARBADILLA, J. F. AYROLES et al., 2012 The Drosophila melanogaster Genetic Reference Panel. Nature 482: 173-178.

6: Are Macropodiformes in Tasmania genetically distinct from their mainland counterparts?

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In Australia, numerous extinctions of native mammals have been caused by human disturbances to land management and direct interactions with introduced predators. Tasmania is one of the last safe havens for several of Australia's marsupial species, with relatively few extinctions compared to the Australian mainland. There are five extant Macropodiformes in Tasmania, two of which (the Tasmanian bettong and the Tasmanian pademelon) are extinct on the mainland. These species are now at risk of predation by introduced cats, dogs and foxes in Tasmania. DNA detection of Macropodiformes from predator scats has the potential to improve conservation management of these native species, but relies on the availability of diagnostic genetic markers suitable for the analysis of degraded DNA. To this end, we are developing a reference database of mitochondrial DNA sequences from Tasmanian Macropodiformes and their mainland relatives. We will generate robust phylogenies and use these to identify short diagnostic markers for application to next generation sequencing surveys of predator scats. We aim to identify Macropodiformes found within scats to species level, to demonstrate the Tasmanian provenance of the Macropodiformes detected and to investigate the ability of these markers to assign DNA sequences to specific regions within Tasmania.

7: GTF2IRD1 is an epigenetic regulator of gene expression important in developmental facial skin patterning

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Williams-Beuren Syndrome (WBS) is a genetic disorder associated with multisystemic abnormalities, including craniofacial dysmorphology. It is caused by a deletion of 28 genes on chromosome 7q11.23. Atypical deletions have implicated two evolutionary-related transcription factors GTF2I and GTF2IRD1 as prime candidates for the cause of the facial dysmorphology. Here we investigated the involvement of GTF2IRD1, a transcriptional repressor discovered in our laboratory that acts as an epigenetic regulator, in the control of epidermal proliferation and differentiation and its role in the causation of the typical WBS craniofacial features. Using *Gtf2ird1* -targeted knockout mouse models, we have mapped the expression of *Gtf2ird1* in the skin and tracked its expression from embryo to adult. Our results also show that the lack of *Gtf2ird1* in mice produces striking similarities to aspects of the human disease including enlarged lips caused by an extreme thickening of the epidermal layer. We conclude that *Gtf2ird1* plays an important role in how facial skin is patterned during development, being a crucial component of the transcriptional machinery for proper cell proliferation and differentiation in specific regions of the skin. Finally, comparative RNA-seq analysis from lip skin samples has provided important clues concerning the molecular mechanisms involved.

8: A gene implicated in the neurobehavioral abnormalities of Williams-Beuren syndrome, *GTF2IRD1*,is a novel epigenetic regulator

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Williams-Beuren syndrome (WBS) is an autosomal dominant disorder resulting from a hemizygous microdeletion within chromosome 7q11.23. Genotype/phenotype correlations in patients with atypical deletions implicate a gene discovered in our laboratory *GTF2IRD1*, as responsible for the distinctive neurocognitive profile of WBS. However, the molecular and cellular consequences of *GTF2IRD1* haploinsufficiency remain unknown. *Gtf2ird1* knockout mice recapitulate many of the defects of WBS, including hyperactivity and ataxia. To identify any transcriptional changes arising in the brain, we performed microarray transcript profile analyses in corpus striatum tissue from these mice followed by qRT-PCR validation. We found increased expression of genes involved in neuronal development and a cluster of immediate-early response genes that correlate with hyperactivity, ADHD and the response to psychostimulants. We combined these analyses with biochemical studies to reveal the molecular interactions of GTF2IRD1. Using a yeast two-hybrid screening system, we identified a panel of novel interacting partners that constitute functional groups, such as DNA binding proteins, post translational modification machinery (SUMO and ubiquitin ligation proteins) and chromatin modifying factors. Our data is consistent with a role for GTF2IRD1 as an epigenetic regulator of gene repression that coordinates interactions with transcription factors, DNA binding proteins and components of the chromatin modification machinery.

9: BloodChIP: An Atlas of Genome-wide Transcription Factor Binding Profiles in Human Haematopoietic Stem/Progenitor Cells

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Haematopoiesis serves as a model system for the multi-lineage differentiation of adult stem cells. There is a growing emphasis on transcriptional drivers that assign cell states by altering the epigenomic landscape. Cell type specific expression of transcription factors, and cell type specific accessibility of enhancer elements, control gene expression profiles to give blood cells of various lineages their distinct identities. It has now been established that a core set of transcription factors work in combination to regulate gene expression in human stem/progenitor cells (HSPCs).

BloodChIP is a database integrating genome-wide binding profiles of seven core haematopoietic transcription factors in primary HSPCs with histone modification profiles and gene expression in normal and leukaemic stem/progenitor fractions. An interactive web interface allows users to query BloodChIP and ascertain the relative expression level of their genes of interest across normal and leukaemic stem/progenitor fractions. Importantly, the user is then able to associate expression levels in these cell fractions with histone modifications and transcription factor binding profiles allowing exploration of how the core transcription factors cooperate to regulate gene expression during HSPC differentiation. BloodChIP will be an invaluable resource to help researchers better understand leukaemogenesis, normal blood development and stem cell biology.

10: Do DNA sequences influence recruitment of histone variants?

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WITHDRAWN

11: Developing a genetic test for haemophilia A in Australian Kelpies

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Haemophilia A is the most severe inherited bleeding disorder of the domestic dog. The X-linked, recessive disease affects the animal's ability to control bleeding due to low levels of coagulation factor VIII (FVIII). Severity of disease is affected by the type of mutation present in the FVIII gene. Some canine populations are prone to sporadic mutations in the FVIII gene. The mutation that causes haemophilia A in Australian Kelpies has yet to be characterized. Ten individuals of a family including two severely affected males were genotyped using the Illumina high density canine genotyping array. Further, Illumina HiSeq 2000 sequencing data from one affected male was obtained and this revealed two non-synonymous, single nucleotide polymorphisms (SNPs) in exons 12 and 26 of the FVIII gene relative to the canine reference genome (CanFam2.0). The genotyping analysis unexpectedly revealed that the phenotypically normal maternal-grandsire of the affected pups shares the same FVIII haplotype as the affected males. Genome-wide analyses are ongoing including analyses to understand this observation.

12: An Essential Role for a Neural Receptor during Insect Development

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Nicotinic acetylcholine receptors (nAChRs) are key players in the nervous systems of vertebrates and invertebrates alike. They have gained much attention, being targets for some common insecticides, and also being linked to human neurodegenerative diseases. Mature nAChRs are pentamers that function as ligand□gated ion channels in the plasma membrane of post-synaptic cells. Ten different nAChR subunits are encoded in the *Drosophila melanogaster* genome, but only one of them appears to be essential for development: D□5. RNAi knockdown and deletion of the D□5 subunit results in larval lethality during the 3rd instar stage. Surprisingly, this lethal phenotype is seen when D□5 is knocked down specifically in the prothoracic gland; the gland responsible for the production of the insect moulting hormone, ecdysone. It appears that this lethality in D□5 mutants is due to a disruption in moulting. We hypothesise that D□5 is forming cation channels in the prothoracic gland, facilitating the influx of Ca2+ ions that occurs when various tropic factors stimulate the gland throughout development. Given that the prothoracic gland and its known functions are insect specific, current research into this gland, and the role of D□5, will provide exciting opportunities to design safe new insecticides for pest management.

13: Genomic conflict and the uniparental inheritance of mitochondria

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Why are the mitochondria of male gametes destroyed shortly after fertilisation? Theory predicts that within-individual genomic conflict is the answer. If a cell contains multiple mitochondrial lineages that differ in replication and respiration rates, within-cell selection should favour mitochondrial lineages that replicate quickly, while cell-level selection should prefer mitochondrial lineages that respire efficiently. `Selfish' mitochondria increase replication rate at a cost to cell fitness, and thereby create a conflict between the mitochondrial and nuclear genomes. Uniparental inheritance is a nuclear-mediated mechanism that alleviates this theoretical conflict by preventing the mixing of, and competition between, different mitochondrial lineages. *Physarum polycephalum* is an ideal organism for empirically testing the genomic conflict theory. In *P. polycephalum*, nuclei and mitochondria replicate without cell division, creating an ideal environment for selection of selfish genomes. Nevertheless, evidence suggests that biparental inheritance can occur in certain crosses between specific *P. polycephalum* strains. This provides us with the opportunity to examine the fitness costs, if such costs exist, of biparental inheritance of mitochondria. If we find negative fitness effects of biparental inheritance experimentally, we intend to explore mechanisms that *P. polycephalum* may use to counteract the deleterious effects of these selfish organelles.

14: RNA-Seq analysis of the Dorsolateral Prefrontal Cortex in Schizophrenia

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Schizophrenia is a complex disorder. As such, identification of specific genes involved in the disease process is challenging. Massively-parallel sequencing of mRNA (RNA-Seq) allows genes of interest to be identified in the transcriptome and can provide exquisite insights into the proteins likely to be active within a tissue. We have analysed RNA-Seq data from dorsolateral prefrontal cortex (DLPC) obtained post-mortem from 19 schizophrenia patients and 19 controls. The reads were previously produced on the SOLiD platform and mapped with XMATE [1]. We performed alternative mapping using TopHat. Differential expression analysis was performed using DESeq. Our results indicate potential dysregulation of nuclear receptors and differential expression of the genes activated by these transcription factors. In particular, we confirm differences in immunity related processes, and see expression changes in genes involved in the ubiquitin-proteasome pathway and GABAA signaling. Our results show that RNA-Seq is a powerful tool for identifying aberrant pathways or networks in complex disorders such as schizophrenia.

Fillman, S.G., et al., Increased inflammatory markers identified in the dorsolateral prefrontal cortex of individuals with schizophrenia. Mol Psychiatry, 2012.

15: Comparative genomics of *Campylobacter concisus* isolates reveals genetic diversity and provides insights into disease association

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In spite of its association with gastroenteritis and inflammatory bowel diseases, the isolation of *Campylobacter concisus* from both diseased and healthy individuals has led to controversy regarding its role as an intestinal pathogen. One proposed reason for this is the presence of high genetic diversity among the genomes of *C. concisus* strains. In this study the genomes of six *C. concisus* strains were sequenced, assembled and annotated including two strains isolated from Crohn's disease patients (UNSW2 and UNSW3), three from gastroenteritis patients (UNSW1, UNSWCS and ATCC 51562) and one from a healthy individual (ATCC 51561). The genomes of C. concisus BAA-1457 and UNSWCD, available from NCBI, were included in subsequent comparative genomic analyses. The Pan and Core genomes for the sequenced *C. concisus* strains consisted of 3254 and 1556 protein coding genes, respectively. Genes were identified with specific conservation in *C. concisus* strains grouped by phenotypes such as invasiveness, adherence, motility and diseased states. Phylogenetic trees based on ribosomal RNA sequences and concatenated host-related pathways for the eight *C. concisus* strains were generated using the neighbor-joining method, of which the 16S rRNA gene and peptidogylcan biosynthesis grouped the *C. concisus* strains according to their pathogenic phenotypes. Furthermore, 25 non-synonymous amino acid changes with 14 affecting functional domains, were identified within proteins of conserved host-related pathways, which had possible associations with the pathogenic potential of *C. concisus* strains. Finally, the genomes of the eight *C. concisus* strains were compared to the nine available genomes of the well-established pathogen *Campylobacter jejuni*, which identified several important differences in the respiration pathways of these two species. Our findings indicate that *C. concisus* strains are genetically diverse, and suggest the genomes of this bacterium contain respiration pathways and modifications in the peptidoglycan layer that may play an important role in its virulence.

16: Investigating the genetic basis of amyotrophic lateral sclerosis using next-gen techniques

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Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease, occurring as familial or sporadic disease. Mutations in over 15 genes have now described in ALS; including ``SOD1", ``TARDBP", ``FUS", ``C9ORF72", and ``UBQLN2". Nevertheless, the genes are yet to be identified in 30-40% of familial ALS. We aim to identify novel genes involved in ALS using next-generation sequencing techniques. We performed exome capture and massively parallel sequencing on DNA samples from four ALS families. Bioinformatic analysis of exome data identified several candidate variants. Segregation analysis in one family reduced the number of potential causative variants to two. Analysis of large control cohorts is underway to validate these variants. Using exome and Sanger sequencing we have also determined the prevalence of known ALS genes in Australian familial and sporadic ALS cohorts. Mutations in known ALS genes account for 57.2% of familial ALS and 5% of sporadic ALS. The familial mutations comprise of``SOD1" (13.9%, n=26), ``FUS" (2.7% n=5) ``TARDBP" (2.1% n=4), ``C9ORF72" (38% n=71), ``OPTN" (0.5% n=1), ``UBQLN2" (1.1% n=2), and ``SS18L1" (0.5%, n=1). Additional exome sequencing projects are underway in Australian familial index patients to identify novel ALS genes in the remaining FALS and SALS cases.

17: *Wolbachia* modulates *Hira* gene expression in *Drosophila melanogaster*

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It is estimated that the intracellular bacterium *Wolbachia pipientis* infects up to 60% of all insect species. *Wolbachia's* success is due to its ability to reproductively manipulate its host to ensure transmission. One of the most common reproductive manipulations is cytoplasmic incompatibility (CI) where *Wolbachia* infection in father induces the embryonic lethality of its offspring when mated to an uninfected female. In *Drosophila melanogaster*, CI is influenced by factors such as male age and larval development time of males, termed the ``younger brother'' effect. We have found that the strength of CI associated with the ``younger brother'' effect is correlated with a transcriptional downregulation of *Hira*, a Histone H3.3 chaperone. We have also found that *D. melanogaster* males mutant for *Hira* induce a CI-like effect that can be partially rescued when mated to females infected with *Wolbachia*. We are currently examining *Hira* levels in other Drosophila species to determine if *Hira* RNA modulation can more broadly explain all aspects of CI such as incompatibility between different *Wolbachia* strains.

18: eDNA Detection Parameters

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The utility of environmental DNA (eDNA) for low-density species detection has been demonstrated in a number of studies and offers great potential for the control of invasive species or the conservation of endangered species. To determine the value of this relatively new technique as a management tool, detailed studies are required to evaluate detection probabilities for various species under a range of environmental conditions. Controlled aquarium manipulation experiments allow us to measure the influence of variables contributing to changes in eDNA concentration and detection probabilities. We have selected several taxa that are listed as invasive in Australia and for which low-density detection is likely to provide economic and/or environmental benefits. These taxa will be used to parameterise a detection framework. We will present data from initial aquarium experiments on the Oriental weatherlaoch, *Misgurnus anguillicaudatus*, that examine the relationship between the number of individuals and eDNA production, the distribution of eDNA throughout the water column and eDNA accumulation and degradation over time. We aim to develop a framework for eDNA detection probabilities that will ultimately provide information for natural resource managers on the utility of eDNA to address environmental questions.

19: The role of Nanog in Germline Development and Spermatogenesis

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The homeobox gene Nanog has been described as the ``gate keeper'' of pluripotency because it is only expressed in pluripotent cells and is capable of driving LIF independent stem cell self-renewal 1. With Oct4 and Sox2, Nanog is part of the core transcriptional network that maintains stem cell pluripotency in vitro and in-vivo. Nanog null mutant mice die at implantation due to a failure of the pluripotent epiblast 2. Previously, we reported human and mouse expression of Nanog in pluripotent inner cell mass cells, primordial germ cells, embryonic stem cells and germ cell tumours 3,4. Here, we utilize mice carrying a knock-in ⊠-galactosidase reporter and floxed Nanog allele to study the expression and function of Nanog during germ cell development and spermatogenesis.

1 Silva J, et. al., Cell. 2009. Aug 21;138(4):722-37. 2 Mitsui K, et. al., Cell. 2003. May 30;113(5):631-42. 3 Hart, A. H., et. al., Developmental Dynamics, 2004. 230, 187-198. 4 Hart, A. H., et al., Cancer. (2005)104(10): 2092-2098.

20: Dermatoglyphics: Genetics at your fingertips

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Dermatoglyphics is defined as the scientific study of dermal ridges on the distal phalanges, palms, and soles of primates. These ridges form discrete patterns that can be categorized according to their landmark structures. Some characteristics of these dermal ridges such as their permanence and uniqueness, have led to the use of fingerprint patterns as a way of identification in forensic investigations. The current study aims to identify the genetic influences on fingerprint patterns across ten fingers on both hands, utilizing genome-wide association and meta-analysis. The three samples consisted of 2296 twins from the QIMR Brisbane Adolescent Twin Study, 1859 twins from the QIMR studies of alcoholism in adults (SSAGA), and 7000 individuals from the Avon Longitudinal Study of Parents and Children (ALSPAC). Results of meta-analyses across all three samples revealed one significant SNP in a gene region in chromosome 3. A post-hoc TATES analyses was also conducted on the QIMR and ALSPAC samples, which also showed highly significant results. As the gene region identified has previously been associated with type 2 diabetes and waist-hip ratio, these results suggest the lasting effects of genetic variants influencing earlier growth on later development.

21: Identification of genes encoding proteins that interact with the Drosophila MACPF protein Torso-like

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Many members of the membrane attack complex / perforin (MACPF) protein family are pore forming proteins involved in vertebrate immunity. Of the ~500 MACPF proteins that have been identified so far, *torso-like* (tsl) is the single MACPF protein found in *Drosophila* and, unlike many other members of this family, is involved in development. Specifically Tsl is required for patterning the ends of the early embryo via localised activation of the ubiquitous receptor tyrosine kinase Torso. The mechanism by which Tsl achieves this, and whether unidentified partner proteins are involved, remains unclear. To address these questions, we are performing a genome-wide screen for suppressors of the phenotype generated by unrestricted tsl expression, known as `splice'. Using the Bloomington Deficiency kit, we have identified over 60 regions that contain suppressor genes. We are identifying the causative suppressor genes by first mapping these regions further using other genomic deficiencies and then testing mutant alleles of candidate genes. This approach has already identified 10 suppressor genes that had not previously shown to function in terminal patterning. Further work is being conducted to elucidate the roles of these genes in terminal patterning and nature of their interactions with Tsl. We hope that the genes identified will provide valuable insight into the mechanism of Tsl action in terminal patterning and more broadly, address how MACPF proteins function in development.

22: New insights into the role of MHC diversity in Devil Facial Tumour Disease

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Devil facial tumour disease (DFTD) is a fatal contagious cancer that has decimated Tasmanian devil populations. The tumour has spread without invoking immune responses, possibly due to low levels of Major Histocompatibility Complex (MHC) diversity in Tasmanian devils. Animals from a region in north-western Tasmania have lower infection rates than those in the east of the state. This area is a genetic transition zone between sub-populations, with individuals from north-western Tasmania displaying greater diversity than eastern devils at MHC genes, primarily through MHC class I gene copy number variation. It has been previously proposed that the reduced effects of DFTD at this site are due to this copy number variation of MHC class 1 alleles. We tested the hypothesis that animals that remain healthy and tumour free show predictable differences at MHC loci compared to animals that develop the disease. Comparison of MHC class 1 sequence and MHC-linked microsatellites of long-lived, healthy devils to those of diseased devils at this location revealed no predictable differences in MHC class 1 copy number. Microsatellite data was equivocal and identified genomic areas for further study.

23: DNA methylation to exon 2 of DNA polymerase gamma A suppresses mitochondrial DNA copy number in fast replicating cells

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We have previously shown in undifferentiated and differentiating mouse embryonic stem cells that DNA methylation is negatively correlated with the expression of PolgA and mtDNA copy number. However, the relationship between DNA methylation and the regulation of mtDNA copy number in human cancer stem cells has yet to be determined. We examined the enrichment of 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC) within exon 2 of PolgA in various fast replicating cells, such as human cancer stem cells and embryonic and adult stem cells. Immunoprecipitation of methylated DNA (MeDIP) showed that the enrichment of 5mC is at least twice as high as 5hmC in all fast replicating cells with low mtDNA copy number, whilst in post-mitotic tissues, such as placenta, the ratio was closer to 1 and these cells contained significantly higher mtDNA copy number. We also show in Glioblastoma Multiforme cancer stem cells (HSR-GBM1) that had been progressively depleted of their mtDNA that they had higher levels of 5hmC during replenishment of mtDNA as these cells formed tumours in mice. Finally, using MeDIP analysis, we demonstrated that enrichment of 5hmC is higher than 5mC within the mtDNA-encoded genes, suggesting that mtDNA is DNA methylated but this is negated by active demethylation.

24: Testing whether L1 neurons functionally require a specific DSCAM2 isoform

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In Drosophila, Down syndrome cell adhesion molecule 2 (Dscam2) is a cell surface protein expressed in the developing brain. Dscam2 is alternatively spliced to generate two biochemically distinct isoforms that convey isoform-specific homophilic binding. Dscam2 establishes structural boundaries between different parts of the brain and specifies synapses in the visual system through a homophilic repulsive mechanism. Dscam2 is essential for the normal development of L1 and L2, two intimately associated neurons occupying the same nerve fibre. The repulsive function of Dscam2 sets up a paradox in these cells. How do L1 and L2 neurons stay in physical contact with each other when they express the same repulsive protein? Dscam2 isoform specific reporter lines demonstrate that L1 and L2 neurons express distinct isoforms, which seemingly resolves this paradox. However, L1 neurons show relatively normal morphology in flies engineered to express the same isoform in both L1 and L2. Photoreceptors in these single-isoform expressing flies exhibit a looping phenotype that is indicative of the loss of a proximal boundary element, suggesting that some neurons do require distinct isoforms. These observations indicate that multiple mechanisms are in place to prevent repulsion between L1 and L2 neurons. Potential models will be discussed.

25: Molecular phylogenetics of isopod crustaceans and the colonisation of fresh

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Isopods are a remarkably diverse group of crustaceans that can be found in virtually all environments. The colonisation of land, freshwater, and deep sea promoted the diversification of isopod morphology and species numbers. Their morphological and taxonomic diversity makes the study of their relationships and evolution challenging. This study aims to provide a timeframe for isopod colonisation of the freshwater and terrestrial habitats, to test the phylogenetic position of several major suborders (Phreatoicidea, Oniscidea, Asellota and Cymothoida), and to estimate the rates of evolution among different habitats. We conducted phylogenetic analyses of nuclear 18S and 28S and mitochondrial COI and 16S using a molecular clock. The origins of the terrestrial fauna at 299 Mya (95% CI: 226-368 Mya) and the freshwater fauna at 314 Mya (95% CI: 307-336 Mya) coincide with the formation of the supercontinent Pangaea and with the reduction of seaways. These date estimates are far older than those based on the terrestrial fossil record. The suborders Oniscidea, Asellota and Cymothoida were found to be paraphyletic, conflicting with the classical views based on morphology. Finally, we found no effect of environmental temperature on evolutionary rates in isopods, with freshwater rather than deep-sea clades (coldest) having the slowest rates.

26: Investigating the molecular basis of protogynous (female-to-male) sex change in fish

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Investigating the molecular basis of protogynous (female-to-male) sex change in fish Most vertebrates, especially mammals, are born as either males or females and remain the same sex throughout their life history. Fishes, by contrast, display an extraordinary diversity of sexual expression including socially controlled sex change (also termed as sequential hermaphroditism). While the selective advantage of such flexibility is well established, the molecular and neuroendocrine mechanisms by which sex change is regulated remain poorly understood. Using the Caribbean bluehead wrasse (*Thalassoma bifasciatum*), a well studied sequential hermaphrodite that can be experimentally induced to reverse sex in nature, together with new state-of-the-art gene expression analyses and comparative genomic approaches, we seek to elucidate both the primary trigger and subsequent genetic cascade that result in female-to-male sex change in fishes. We expect to obtain a set of candidate genes being up- or down-regulated in the brain and gonad across the course of sex change that we can test their roles and interactions in sex reversal and differentiation. This study will enhance our knowledge on sex reversal and sex determination, and also provide insights into the lability of developmental programming and phenotypic plasticity in response to the environmental signals.

27: RIC3 - analysis of its critical role in neurological receptor function

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Neurotransmitter receptors generally require several accessory proteins for correct localization and functioning. RIC-3 is one such protein, playing a role in correct folding and assembly of nicotinic acetylcholine receptors (nAChRs). Most studies have focused on its ability to enhance or inhibit functional expression of receptor subtypes in heterologous systems. However, no study has been done to identify any other functions RIC-3 has in vivo. Our lab has generated RIC-3 putative deletions in *Drosophila melanogaster* by mobilizing a Minos element that was inserted within the RIC-3 genomic region. Two deletions have been identified and confirmed using PCR and sequencing. An automated locomotion monitoring system is being used to assay behavioural changes, if any, in these two lines. Specifically, activity level, longevity, negative geotaxis response and aging effects are being examined. Additionally, as increased insecticide resistance is expected if receptor cell surface expression is affected as a result of partially deleted RIC-3, toxicology assays on larvae using three different insecticides are also being carried out to examine their resistance levels. Later on, *dmric-3* will be over-expressed to attempt to rescue any significant phenotypes, as well as to determine if mis-expression leads to a phenotypic effect.

28: Testing for Conflicts in Reproduction and Genetic Polyethism in the Polygynous Termite *Nasutitermes exitiosus*

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Insect colonies are often thought to have a single queen. However, in some species, colonies are headed by multiple, unrelated queens (polygyny). Given the assumed importance of high-relatedness among colony members for the evolution and maintenance of eusociality, this phenomenon requires explanation. Some termite species including *Nasutitermes exitiosus* are facultatively polygynous (the population has colonies that are polygynous and monogamous). Two possible consequences of polygyny are: 1) genetic polyethism i.e. an influence of genotype on task performance and division of labour, and 2) reproductive skew i.e. conflict among queens over whether and how to divide up the reproduction. We are sequencing mitochondrial genes and using microsatellites to gather genetic data from *N. exitiosus*. The data will then be used to identify the prevalence of polygyny and to investigate the consequences of polygynous colonies. The results could provide evidence to account for the maintenance and evolution of polygamous colonies.

29: The Cellular trafficking of a Tagged Nicotinic Acetylcholine Receptor.

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Nicotinic Acetylcholine receptors (nAChRs) are pentameric ionotropic channels that mediate fast synaptic transmission and are evolutionarily conserved across taxonomies, ranging from *C. elegans* to humans. The nAChR literature focuses on vertebrate nAChRs which are more readily expressed in vitro, whereas insect receptors have difficulties forming due to absent endogenous factors. We have labeled the *Drosophila D6* subunit with YFP and CFP fluorescent tags to track receptor trafficking and localization. To demonstrate the tagged receptor subunits function, a prerequisite for using them in this research, we have used insecticide susceptibility as a proxy for wild type function. *D6* tagged subunits are able to complement the *D6* null mutation by restoring susceptibility to Spinosad. Drosophila larval brains were dissected and D6 expression visualized using confocal microscopy. The expression pattern observed was compatible with *D6 in situ* hybridization data and the receptors were found to localize at the cell membrane. The *D6* tagged subunit, despite being unable to rescue the null mutation as efficiently as its wild type counterpart, retains a high degree of its functionality. This system will allow us to analyse trafficking and environmental influences on nAChRs in *vivo*.

30: Sequence and functional divergence of CEP signalling peptides in eudicots and monocots

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Small posttranslationally modified peptides, including the well-studied CLE family and the less-characterised CEP family, are small signalling peptides which are cleaved from precursor peptides, posttranslationally modified and secreted. They have been implicated in the regulation of root architecture and development, including root growth and lateral root organ development [1], and act as non-cell-autonomous, short-range signals. Using bioinformatics tools we identified and characterised *CEP* genes in 68 reference genomes and 6 transcriptomes spanning the plant kingdom, and found that specific residues can distinguish monocot from eudicot CEPs. This distinction is supported by a phylogenetic analysis that illuminates the evolutionary history of the CEP family, and is in contrast with CLE peptides, which are largely conserved between Arabidopsis (a eudicot) and rice (a monocot) [2]. Monocots and eudicots are two flowering plant (angiosperm) clades, and can be distinguished by many architectural differences. This includes root systems, which in monocots are dominated by adventitious roots from the stem, whereas eudicot root systems normally develop from the radicle. To assess the functional impact of the divergence of monocot and eudicot CEP sequences on root systems, the effects of exogenous addition of synthetic peptides and overexpression of *CEP* genes in Arabidopsis and *Brachypodium distachyon* - a new monocot model organism - have been assayed. These results will be presented, revealing differences in the action and activity of monocot and eudicot CEPs. Ultimately, we aim to determine if the evolution of distinct monocot and eudicot CEPs is part of the molecular basis for the divergence of angiosperm root system architectures. [1] Murphy, Evan, Stephanie Smith, and Ive De Smet. ``Small signaling peptides in Arabidopsis development: how cells communicate over a short distance." *The Plant Cell Online* 24.8 (2012): 3198-3217. [2] Kinoshita, Atsuko, *et al.* ``Gain-of-function phenotypes of chemically synthetic CLAVATA3/ESR-related (CLE) peptides in *Arabidopsis thaliana* and *Oryza sativa*." *Plant and cell physiology* 48.12 (2007): 1821-1825.

31: Comparative phylogeography of 33 freshwater species in southeast Queensland

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Phylogeographic studies often only consider one or two species, but does such a small sampling of the biota really reflect the biogeography of a region, or merely idiosyncratic species-specific patterns? We used mitochondrial data from 33 freshwater species of fish and crustaceans in south-eastern Queensland to look for larger scale patterns between groups of species and groups of river catchments. We used standard single-species methods, such as Analyses of Molecular Variance and haplotype networks, to detect individual species patterns. We also did simultaneous coalescent multi-species analyses to test if divergences across multiple species between adjacent catchments were likely the result of a single or multiple vicariant events using hierarchical approximate Bayesian computation (msBayes). Further we did regional scale analyses using msBayes to investigate whether the deep divergences seen in many species across the area could be explained by a single event, such as a particular episode of climate change. Unsurprisingly, we found that the river basin is a key determinant in the phylogeographic patterns of most freshwater species, but that certain catchments divides seem to delineate larger scale and more ancient multi-species divergences, which are likely explained by particularly influential periods of past climate change.

32: Re-mapping for the cerebellar abiotrophy disease gene/s in Australian Kelpie dogs using Illumina high-density 172K canine SNP arrays and candidate gene sequencing

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The Australian Kelpie is a local dog breed developed for herding. Cerebellar abiotrophy (CA) is a movement disorder first documented by Thomas *et al.* (1989) in the Kelpie, which results in early onset ataxia. CA in Kelpies has been previously mapped by homozygosity analysis using the 128,000 marker Affymetrix canine genotyping array to a 5 Mb region on chromosome 3. Sequencing across the previous candidate region failed to identify any functional variants associated with the CA phenotype.

A whole genome association study with 25 CA affected and 16 related unaffected Kelpies, was conducted using the Illumina high-density 172K canine SNP array. An analysis performed with the PLINK software (minor allele frequency > 0.15, missing SNP genotypes < 0.1, and individual Kelpie genotyping rates > 0.9, 10,000 permutations) identified a SNP marker on chromosome 22 with genome-wide significance (p-value *genome* = 0.04, p-value *raw* = 6.82×10ˆ-7). No signal was observed for chromosome 3. Subsequent homozygosity analysis on chromosome 22 has identified a 103 kb region (containing 16 markers) that is homozygous among 32% of cases, and is not observed as homozygous in any unaffected individuals. Positional candidate genes are currently under investigation using qRT-PCR and Sanger sequencing.

33: Enhancement of a DNA Vaccine against Colon Cancer through the use of Chitosan-DNA Nanoparticles and Ultrasound

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While conventional cancer therapies such as chemotherapy, radiotherapy and surgery are becoming more effective, many cancers are still resistant or recalcitrant to such interventions and therefore novel treatments are needed. One such strategy is the use of DNA vaccination. DNA vaccines are essentially recombinant DNA plasmids taken up and expressed by host cells. When targeting cancers, the products encoded by DNA vaccines can be associated either with reactivating a tumour suppressor gene or inducing an immune response against a tumour associated antigen. Their use in the past has been hampered by poor immunogenicity due to low levels of vaccine uptake and expression. We aim to enhance the immunogenicity of a DNA vaccine developed against the c-MYB antigen which is associated with about 80% of colorectal cancers. To do this, we use chitosan-DNA nanoparticles (CDNs) conjugated to a nuclear localisation signal (NLS) delivered in combination with ultrasound. We show preliminary data indicating enhancement of plasmid uptake of a GFP reporter using a modified SV40 T antigen NLS for nuclear targeting and ultrasound at 1Mhz and 0.5 W/cm2. The results provide a basis to develop a strategy for enhanced DNA vaccine delivery *in vivo* to a murine colon cancer model.

34: Characterisation of the role of Wiz in development

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There is increasing evidence that the establishment of aberrant epigenetic states can be associated with human disease. The activity state of a gene changes depending on its epigenetic state. For the last decade we have been identifying molecules that act to control these epigenetic marks in order to understand more about the establishment and maintenance of the epigenetic state. To better our understanding, I will be studying a mutant mouse line, MommeD30 which was produced in a random ENU (N-ethyl-N-nitrosourea) mutagenesis screen. MommeD30 has a mutation in Wiz (widely-interspaced zinc finger motifs). Little is known about the Wiz protein except that the homology domains reveal six widely interspaced Kruppel (C2H2) type zinc finger motifs and that it forms a tripartite complex with two histone methyltransferases, G9a and G9a-like protein (also called GLP). Humans heterozygous for a loss of both G9a and GLP, suffer from Kleefstra Syndrome.

The aim of this study is to (i) increase our understanding of the role of Wiz in the Wiz/G9a/GLP tripartite complex; (ii) to observe any phenotypic (behavioural) abnormalities in MommeD30 mice; (iii) and to investigate the DNA methylation state of embryos (heterozygous and homozygous for a mutation in Wiz). The mouse model of Wiz may help us to understand the underlying events in Kleefstra Syndrome.

35: A candidate gene for worker sterility in the honey bee: development of an RNA interference protocol

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In honey bee (*Apis mellifera*) colonies the queen monopolises reproduction, while the workers are `altruistically' sterile. A mutant `anarchistic' strain, in which the workers activate their ovaries, has enabled investigation of the mechanisms that have evolved to enforce worker sterility. Mapping and gene expression studies of the anarchistic strain have yielded a short list of candidate genes for worker sterility. *Anarchy1* (GB13621), a peroxisomal membrane protein, is the strongest candidate gene based on map location and differential expression between anarchistic and wildtype workers; and workers with activated and non-activated ovaries. To determine whether there is a causal relationship between expression of Anarchy1 and ovary activation we experimentally manipulated expression of *Anarchy1* using RNA interference. We injected two-day-old workers with dsRNA and then determined expression of *Anarchy1* over time. Expression of *Anarchy1* was successfully reduced in treated workers relative to controls. This new protocol will help establish the molecular pathway that regulates functional sterility in honey bee workers.

36: Characterisation of plasmid stability systems in Haloarchaea

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Plasmid partitioning (*par*) systems enhance the equal distribution of genetic material to daughter cells during cell division. *Par* systems have been well studied on bacterial plasmids, but not in Archaea, despite the existence of mega-plasmids expected to carry genes ensuring their stable maintenance. This study aimed to investigate the distribution of putative archaeal plasmid *par* systems and to identify a possible candidate for further study. To accomplish this, the P1 ParA sequence from *Escherichia coli*, a model type I *par* system, was used to search translated archaeal genomes. Results included five possible ParA candidates encoded on plasmids carried by the model organism *Halobacterium salinarum* NRC-1. Further features of putative *par* systems were investigated, including identification of a Walker-type ATPase motif within the predicted ParA proteins and putative *parB* genes as immediate downstream open reading frames. Putative DNA-binding ParB proteins found shared no similarity to that of characterised bacterial ParB proteins, but aligned with other such archaeal proteins. Direct repeats, indicating a possible *cis*-acting centromere like site, were located upstream on three of the seven putative systems of the predicted *parA-parB* genes and downstream on one. Two *par* systems appeared excellent candidates for experimental studies.

37: Influence of *Wolbachia* on *Drosophila melanogaster* sleep behaviour and circadian rhythm

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Sleep is a highly conserved behaviour essential for optimal performance of an organism. Drosophila melanogaster is a model organism that displays a behavioural state, which exhibits traits consistent with mammalian sleep. This includes periods of immobility accompanied by an increased arousal threshold and reduced sensitivity to stimuli. As with other animals, if D. melanogaster have disrupted sleep consolidation of newly formed memoriesare inhibited and lifespan is reduced.

D. melanogaster are naturally infected by the endosymbiont Wolbachia - infections by some strains have been shown to modify complex behaviours, reduce lifespan or protect against viral pathogens. While Wolbachia are known to infect adult brains, very little is known about the impact Wolbachia have on complex behaviours such as sleep. Using whole organismal and molecular techniques we have assessed the impact Wolbachia have on sleep

38: Molecular phylogenetics of Australian native burrowing cockroaches

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Australian native burrowing cockroaches are currently recognised as comprising two subfamilies: the wood-burrowing Panesthiinae and the soil-burrowing Geoscapheinae. Previous work questions the monophyly of Panesthiinae, with evidence that soil-burrowers evolved from wood-burrowing ancestors that migrated from Asia through Wallace's Line. We aim to build a comprehensive phylogeny to test the monophyly of the soil-burrowing Geoscapheinae, using various molecular markers including a gene from the *Blattabacterium cuenoti* symbiont present in cockroaches. Using molecular clock analyses, we aim to test the hypothesis that the widespread aridification of Australia during the Miocene promoted the evolution of soil-burrowing. We will present our latest results from this project.

39: Recurrent Somatic Mutations in Loss of Heterozygosity Regions of Hepatocellular Carcinoma

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BACKGROUND Hepatocellular carcinoma (HCC), the most common liver malignancy, is characterized by frequent loss of heterozygosity (LOH) at multiple chromosomal locations. Genetic alterations in these LOH regions have not been systematically examined.

METHODS We investigated 58 target genes in the LOH regions by using Agilent SureSelect enrichment technology in 12 HCC paired samples. Eight candidate genes identified by capture sequencing were further examined by TruSeq custom amplicon sequencing technology to uncover mutation hotspots in 95 HCC tumors. DNA mass spectrometry was used to validate the findings in independent cohorts.

RESULTS Initially we discovered 15 nonsynonymous mutations in 7 genes by capture sequencing. Then 113 variants were identified by amplicon sequencing, including 5 nonsense mutations. Among them, only 11 were reported in the dbSNP137. Eight missense mutations in 4 genes and one nonsense mutation in a gene occurred in at least two patients. One of them is a known tumor suppressor gene and 9/95 HCCs contained the mutation at sites that are critical for protein-protein interactions. Furthermore, a single mutation in another gene occurred in 8/95 HCCs.

CONCLUSIONS Focused investigation of selected genes in the LOH regions revealed frequent and recurrent somatic mutations. Genetic alterations discovered by this approach can be used to identify distinct HCC subtypes for developing patient-specific management.

40: Transcriptome comparison of lymphoblast cell lines and human brain by RNA-seq and deepCAGE

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Autism spectrum disorders (ASD), are highly heritable, yet genetically heterogeneous conditions. Hundreds of genetic variants have been implicated in ASD (State et al. 2011), but the majority of these variants is incompletely penetrant, and occur in a small number (<2%) of ASD cases. Thus dissecting out the genetic basis of ASD, and neurodevelopmental disorders in general, requires further evaluation of the functional consequences of genetic variation. Simultaneously assessing DNA sequence variants and their functional effects on brain gene expression has proven effective in genetically complex disorders (Li et al. 2012). However, the availability of brain tissue from ASD patients is very limited. By contrast, large numbers of lymphoblast cell lines (LCLs) have been archived and are readily available. We thus set out to test which genes and transcript variants are reliably detected in both human brain and LCLs by next-generation sequencing. We deeply sequenced total RNA from LCLs and four distinct brain regions: frontal cortex, temporal cortex, occipital cortex and cerebellum using two independent methods: RNA-seq and deepCAGE. We characterize the expression levels of ASD susceptibility genes and their transcript isoforms in LCLs and brain and identify a set of genes for which LCLs represent a good surrogate of brain tissue.

41: Investigating the source of *Thaumastocoris peregrinus* invasions in South Africa and South America using mitochondrial DNA

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The sap-sucking bug *Thaumastocoris peregrinus* is an Australian endemic species that has been introduced invertebrate pest of non-native Eucalyptus plantations in Africa and South America during 2003-2005, and more recently into Italy and New Zealand (during 2012). Since their introduction populations have grown explosively. For example, *T. peregrinus* has attained an almost ubiquitous distribution over several regions in South Africa on 26 Eucalyptus species. A recent mitochondrial DNA study by Nadel et al (Biol Invasions (2010) 12:1067-1077) investigated the source of these invasive populations by comparing them with those collected from urban areas in Southeast Queensland, and Sydney, as well as nearby rural areas. At least three distinct introductions were identified. As yet, no representatives from areas outside Australian cities have been investigated to further understand the origins of the source population. We are sequencing additional Australian *T. peregrinus* samples and will report phylogenetic comparisons of these with previously reported sequences.

42: Exudative cloacitis in the endangered Kakapo (Strigops habroptilus) linked to human Escherichia coli infection

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New Zealand kakapo *Strigops habroptilus* are critically endangered and currently only 124 birds remain in the wild. In 2002 a potentially catastrophic disease, exudative cloacitis (Crusty Bum Disease), was discovered and has been observed in nine birds so far. To date no cause has been identified. While there exist robust molecular tests for known microbial pathogens for some diseases, the discovery of novel pathogens raises a complex set of challenges. Here, we employ metatranscriptomics techniques to reveal potential aetiological agents for Crusty Bum Disease in a `pathogen discovery' study. Our results suggest the presence of a bacterial phage from a known food-borne human pathogenic *E. coli* strain in diseased kakapos, but absent in their healthy counterparts. This result is putatively supported by a contrasting *E. coli* community profile between conditions. Our study suggests a human origin of Crusty Bum Disease in kakapo, will ultimately lead to preventative management and treatment, and represents one of the first studies to employ pathogen discovery in wildlife for wildlife sake.

43: Applying NGS to familial ALS cohorts to identify novel genes

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Amyotrophic lateral sclerosis (ALS) is a rapidly progressive neurodegenerative disorder. Familial ALS accounts for ~10% of all ALS cases, with mutations in known genes explaining 60% of familial ALS in Australia. We aim to combine genetic linkage analysis, exome sequencing, high-throughput genotyping and bioinformatic strategies to identify novel causative genes across three different ALS family types.

Type 1 families (n=3, sample n=9) contain DNA samples from multiple family members including affected, unaffected, and at-risk individuals. Linkage data was coupled with exome data to identify 1, 2 and 4 variants respectively. Type 2 families (n=3, sample n=10) have DNA samples from either two affected individuals plus a `married-in' control or >2 affected individuals. Following exome sequencing and filtering, 18, 28 and 37 potential causative variants remained. To reduce the number of variants, we are performing high-throughput iPLEX genotyping through population controls. Each candidate gene was screened through exome data from family Type 3 index cases (n=60) to search for additional variants in these genes. Scripts are being developed to identify related individuals among Type 3 index cases. If related individuals are identified, they will be combined to create a Type 2 family, and reduce the number of potential causative variants.

44: Targeting chromosomal instability for the specific killing of cancer cells

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Chromosomal INstability (CIN), a common feature of advanced tumors, is linked to drug resistance, metastasis, relapse and lower survival rates of patients in clinical settings. CIN describes cells with the tendency to progressively gain and lose large sections of DNA. This feature is often observed in cells with defects in chromosomal segregation, a process monitored by the **spindle assembly checkpoint** (SAC). Using *Drosophila melanogaster* carrying a weakened SAC, a genetic screen was carried out to identify genes that induce lethality specifically in animals with CIN. From this screen the c-Jun N terminal kinase (JNK) pathway was identified as a modifier of CIN cell fate. Knockdown of the JNK pathway was found to induce apoptosis and DNA damage specifically in CIN cells. Evidence is presented implicating that the duration of G2 is crucial in the protection of CIN cells from death and DNA damage: shortening G2 but not G1 phase in CIN cells mimics the apoptosis induced by knockdown of JNK, while lengthening G2 but not G1 phase rescues the apoptosis. Based on these observations, JNK is proposed to play a role in the regulation of G2 length following chromosome missegregation.

45: Genome sequencing of the New Zealand endemic stick insect *Clitarchus hookeri*

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Within New Zealand there are ten genera of stick insect (Plasmatiadae), containing at least 23 species, all of which are thought to have originated from New Caledonia approximately 24 million years ago. Today members of the family are found throughout southern temperate New Zealand, unlike most other stick insects which are commonly found in tropical or subtropical regions. Several phylogenetic studies have been conducted to investigate the origin and evolution of these insects; however, there is a shortage of genomic data. Genome-wide sequencing of the most common New Zealand species Clitarchus hookeri will allow expansion into genomic datasets. The genome size of Clitarchus hookeri has been estimated at 10 GB. We have obtained approximately 70-fold depth of short read sequence reads from libraries of various insert sizes and have produced preliminary assemblies. The best of these will be further gene-annotated and used to as a reference genome together with RNA-Seq data to detect gene expression divergence among the New Zealand, some Caledonia, Australia and Pacific stick insect species in order to understand adaptive evolution.

46: Wolbachia-associated bacterial protection in the mosquito

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WITHDRAWN

47: DNA methylation state of repetitive elements in sperm from obese and control rats

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Obesity is one of the great health problems of our time. Around 1 in 4 Australians are obese, a figure that is projected to rise in the coming decades. It has long been known that whether an individual develops obesity is a consequence of complex interactions between the environment (such as diet and exercise) and the genome. In addition to this, we and others have shown that the life-time experience of an individual's parents also influence the risk of developing obesity. The impact of maternal obesity on offspring metabolism is well documented. However, our lab recently demonstrated that metabolic defects from the father can be passed on to the F1 generation. Female rat offspring from high fat diet (HFD) fed fathers developed glucose intolerance and defective insulin secretion. The main explanation for the paternal effect is an epigenetic modification in the sperm of obese rats that alters the development of offspring. The major challenge is identifying which type of epigenetic modifications are involved (e.g. DNA methylation or histone acetylation) as well as what regions of the genome are affected. Here we describe the DNA methylation state of different classes of repetitive elements in the sperm of obese and control rats.

48: Characterisation of the MHC class II beta diversity in the endangered New Zealand frog, *Leiopelma hochstetteri*

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The Leiopelmatid frogs of New Zealand are amongst the most archaic frogs in the world and all four species are endangered or vulnerable. *Leiopelma hochstetteri* is a semi-aquatic species and the most widespread of the endemic New Zealand frogs. However, populations are fragmented, of variable sizes and densities, and scattered over an extensive area of the northern half of the New Zealand North Island. The Major Histocompatibility Complex (MHC) is a popular adaptive genetic marker used in conservation genetics. The MHC class II is involved in the recognition of extracellular pathogens with the beta chain contributing peptide binding residues. We found evidence for a single MHC class II beta gene (DAB) in *L. hochstetteri* from a spleen transcriptome sequenced on a Roche GS Junior 454 Sequencer (Landcare Research, Auckland). Gene sequences were verified through PCR amplification from cDNA and Sanger sequencing prior to investigating the DAB gene diversity across *L. hochstetteri* populations. We found 11 DAB allele variants across 18 individuals from Brynderwyn, a population previously found to have high neutral genetic diversity. These allele variants share between 0.846 and 0.995 sequence identity and showed strong positive selection across the sequenced peptide binding domain.

49: Estimation of selective constraint in viral populations

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Methods for estimating selective constraint (negative selection) on a gene have been developed for analysing sequences sampled across divergent populations, or sequences sampled from within a single population. However, differences in sequences sampled from viral populations consist of both within-population polymorphism and between-population divergence. The typically high viral mutation rate increases the supply of polymorphisms, but the expected time until a mutation is lost by drift is not affected by the mutation rate. Consequently, the contribution of deleterious polymorphisms to observed sequence differences can be large, which is known to cause underestimation of selective constraint. Here, we examine the effect of deleterious polymorphisms for time-structured sequence data using forward simulation of a Wright-Fisher population. We present diagnostics that indicate when deleterious polymorphisms will affect commonly-used phylogenetic methods, leading to underestimation of selective constraint and sample-size dependency. In addition, we present a coalescent-based method for estimation of the strength of selection which can be used when population size dependency and weak deleterious effects have a strong effect. With the increasing availability of viral sequence data, methods that use both polymorphism and divergence can provide further insight into how selection has shaped viral populations at both short and long time-scales.

*The plenary presentation by **Professor Michael Turelli** and the **Computational & Mathematical Genetics Session** are supported by Mathematics of Planet Earth Australia 2013*

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The Ramaciotti Centre has recently purchased the Fluidigm C1 Single-Cell Autoprep and BioMark HD Systems. Using these systems, the following high throughput microfluidic-based PCR assay services are now available at The Ramaciotti Centre: qRT-PCR for mRNA and miRNA analysis, allele-specific SNP genotyping, copy number analysis, rare mutation detection, library preparation for targeted resequencing libraries and automated single-cell isolation and genomic preparation.

With the Fluidigm technology, The Ramaciotti Centre can now accelerate the validation phase and expand the sample screening phase of a project. The speed of data generated with Fluidigm will allow some projects to be turned around 20 times faster compared with some other approaches. The BioMark HD can complete 30,000 PCR data points per day, proving it has scalability to suit a range of sample and target numbers The Ramaciotti Centre was wishing to provide its users.

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The Ramaciotti Centre for Gene Function Anlaysis

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