AGTA

Australasian Genomic Technologies Association

2017 ANNUAL CONFERENCE

October 29 - November 1

Hotel Grand Chancellor, HOBART

HANDBOOK

www.agtaconference.org

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AGTA17 ORGANISING COMMITTEE

Dr Jac Charlesworth (Convenor)
University of Tasmania

Dr Kathryn Burdon
University of Tasmania

Associate Professor Ruby Lin
University of New South Wales

Ms Vikki Marshall
The University of Melbourne

CONFERENCE MANAGERS

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The University of Melbourne

Mr Liam Williams
The University of Auckland

Image credit: Paul Fleming

WELCOME FROM THE CONFERENCE CONVENOR

On behalf of the Australasian Genomic Technologies Association and the organising committee it is my pleasure to welcome you to the 2017 AGTA Annual Conference at the Hotel Grand Chancellor in Hobart, Tasmania. It is clear from the program that we are in the midst of an exciting time for genomic technologies. The pre-conference workshops on gene editing and single-cell sequencing highlight the emerging technologies that are already reshaping the genomic landscape. The 2017 program is brimming with incredible science and we hope you make the most of having all these inspiring people in one place.

One of the strengths of AGTA conferences is the engagement with our generous sponsors. This meeting would not be possible without their support. Special thanks to our Gold sponsor BGI and Silver sponsor Illumina for their continued support. We also thank our returning sponsors and exhibitors and are pleased to welcome some new faces this year. We recognise that the interface between developers and users of genomic technologies is dynamic and that communication is integral to future advances – so make sure you visit them and take this opportunity to have those important conversations.

I'm excited about so many things this year! We have shaken things up a little – making space in the program for more talks from abstracts, and giving voice to the next generation of genomic scientists. We have also worked hard to flip the gender balance, something this field has struggled with in the past. We have four incredible international speakers joining us this year – all great scientists who also happen to be women – and a well-balanced and inspiring line up of invited speakers representing the thriving Australasian genomics community. We've introduced lightning poster sessions – to give students and ECRs a chance to present their posters in a more dynamic and intense way. Our satchels are made by Freeset – a fair trade organisation providing employment and freedom to women trapped in the sex trade in India. They also feature two local icons – Kunanyi/Mt Wellington and the wedge-tailed eagle.

On the social side, we will kick off with a Welcome Reception at The Hotel Grand Chancellor, our meeting headquarters, on the edge of Hobart's historic waterfront. We're helping you with your bucket list by holding the conference dinner at Mona, the iconic Museum of Old and New Art, known for its artworks, architecture, wine and feasts of fresh Tasmanian produce. We hope you can join us for entertainment, socialising and networking. Please enjoy the meeting and all that Hobart has to offer.

Dr Jac Charlesworth,
University of Tasmania

GENERAL INFORMATION

REGISTRATION DESK

Please direct any questions you may have regarding registration, accommodation or social functions to Leishman Associates staff at this desk.

Registration Desk Opening Times:

Sunday 29 October	2.00pm – 6.00pm
Monday 30 October	7.30am – 5.30pm
Tuesday 31 October	7.30am – 5.30pm
Wednesday 1 November	7.30am – 2.30pm

ACCOMMODATION

If you have any queries relating to your accommodation booking first speak to the staff at your hotel or alternatively Leishman Associates staff at the Registration Desk.

Your credit card details were supplied to the hotel you have selected, as security for your booking. If you have arrived 24 hours later than your indicated arrival day you may find that you have been charged a fee. You will be responsible for all room and incidental charges on check out and may be asked for an impression of your credit card for security against these charges. This is standard policy in many hotels.

DELEGATE NAME BADGES

All delegates, speakers, sponsors and exhibitors will be provided with a name badge, which must be worn at all times within the conference venue as it is required for access to all the conference sessions and social functions.

Proudly sponsored by:

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CONFERENCE PROCEEDINGS

Speaker PowerPoints will be available on the AGTA website following the conclusion of the conference. Speakers will be requested to sign a release form. This is not compulsory.

CONFERENCE WIFI

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Wireless internet will be available throughout the conference venue for the duration of the conference.

Username: AGTA2017
Password: bgiwifi17

TWITTER

Join the Conversation at:
@agtaGenomics #AGTA17

FAMILY ROOM

As an equity and diversity initiative in support of delegates with parenting or caring responsibilities, a private room will be available at the conference venue for parents with young children. This room is also available for delegates to use as a quiet room if they require a breakout space from the Plenary or Trade. Live audio from the Plenary, along with presenter PowerPoint presentations, will be available to view from this room.

GENERAL INFORMATION

DRESS CODE

Dress throughout the day is smart casual or informal business.

EMERGENCY MEDICAL CARE

For any medical emergency please telephone 000. The staff at your hotel will have information if you require contact details for a doctor, dentist or other health professional.

EXHIBITOR PRIZE DRAW

An exhibitor passport is included in the pocket program that will be given to all delegates at registration. The AGTA17 organising committee encourages you to visit each trade exhibitor and have your passport stamped, to go into the draw to win some great prizes!

SATCHEL

Each attendee will receive a tote bag produced by Freeset at registration.

More than a stitched piece of fabric, Freeset bags tell a story of freedom. For hundreds of women trapped in bonded labour and human trafficking. Freeset is in the business of restoring what has been stolen. Women given the opportunity to choose a new job and regain control of their lives in a caring community. Making Freeset Products is part of a women's journey to freedom. To her friends and neighbours among the thousands still trapped in the sex trade, she is a symbol of hope.

BARISTA COFFEE

Barista coffee will be available throughout the conference in the Trade Exhibition

Proudly sponsored by:

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SOCIAL PROGRAM ENTRY

The Welcome Reception is included in the cost of each full conference registration.

The Conference Dinner IS NOT included in any registration type. Social events ARE NOT included in the cost of day registrations or for accompanying partners. Places for day registrants and additional guests for these events may still be available at an additional cost. Bookings can be made at the registration desk subject to availability.

STUDENT FUNCTION

All conference students and early career researchers are invited to a casual function on Tuesday 31 October at Shambles Brewery. If you would like to attend and have not pre-registered, please see Leishman Associates staff at the registration desk. Further information about this event can be found on page 24.

PROGRAM DIVERSITY

We have worked hard to improve the gender balance for the 2017 meeting. 58% of our invited speakers are female (7/12) including all four international invited speakers. This year we have opened the program to more invited abstracts. The program features 33 invited abstract presentations, 48% of which are being given by students or ECRs.

GENERAL INFORMATION

PHOTOGRAPHS, VIDEOS, RECORDING OF SESSIONS

Delegates are not permitted to use any type of camera or recording device at any of the sessions unless written permission has been obtained from the relevant speaker.

SPEAKERS & SPEAKER'S PREPARATION ROOM

All speakers should present themselves to the Speaker's Preparation Room, located at the entrance to the Grand Ballroom at least 4 hours before their scheduled presentation time, to upload their presentation.

A technician will be present in the speaker's preparation room during registration hours. There will be facility to test and modify your presentation as required.

Speakers are requested to assemble in their session room 5 minutes before the commencement of their session, to meet with their session chair and to familiarise themselves with the room and the audio visual equipment. For information on the chairperson attending your session, please see the Registration Desk.

SPECIAL DIETS

All catering venues have been advised of any special diet preferences you have indicated on your registration form. Please identify yourself to venue staff as they come to serve you and they will be pleased to provide you with all pre-ordered food. For day catering, there may be a specific area where special food is brought out, please check with catering or conference staff.

ORAL PRESENTATIONS

Please refer to the program for the time allocated for each presentation, as these do vary. The chairperson for your session will give you a 3 minute warning, however you are asked to stick to your time allocation so that the program remains on schedule.

POSTER PRESENTATIONS

Posters will be displayed in the Federation Ballroom for the duration of the conference. There will be a poster session on Monday 30 October from 2.55pm to 3.45pm and on Tuesday 31 October from 2.55pm to 3.45pm.

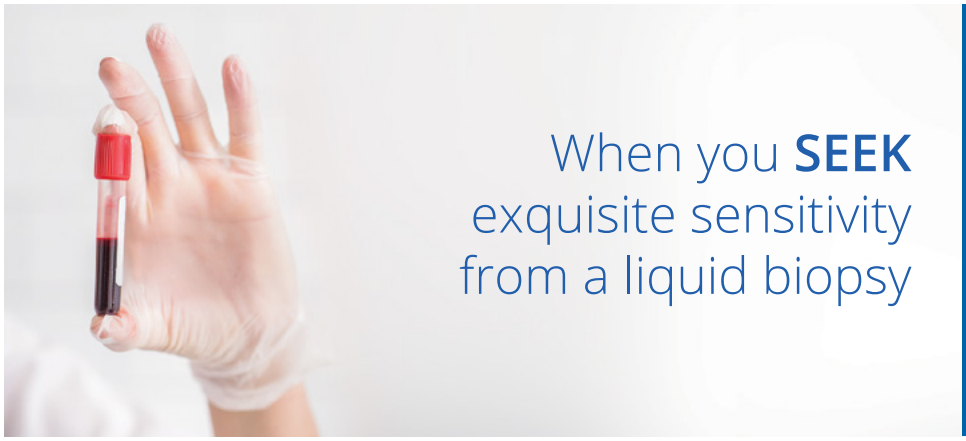
SECURITY

The members of the conference organising committee, Leishman Associates and The Hotel Grand Chancellor accept no liability for personal accident or loss or damage suffered by any participant, accompanying person, invited observer or any other person by whatever means. Nor do we accept liability for any equipment or software brought to the conference by delegates, speakers, sponsors or any other party.

Please protect your personal property. Do not leave laptops, cameras, and other valuable items unsecured. Be conscious of individuals who appear out of place and do not wear a conference name badge. Advise Leishman Associates staff if this does occur.

DISCLAIMER

The 2017 AGTA Conference reserves the right to amend or alter any advertised details relating to dates, program and speakers if necessary, without notice, as a result of circumstances beyond their control. All attempts have been made to keep any changes to an absolute minimum.



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For more information visit us at AGTA 2017 or at **agenabioscience.com**

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Contact us now for more information www.10xgenomics.com

CONFERENCE PROGRAM

Image credit: Tourism Tasmania & Rob Burnett

SUNDAY 29 OCTOBER 2017

PRE-CONFERENCE PROGRAM

1030 - 1200	Workshop Registration Open	
1100 - 1600	**TECHNICAL SOLUTIONS TO SINGLE CELL PROBLEMS**	Harbour View 1
1200 - 1540	**CAN GENOME EDITING FULFIL ITS PROMISE IN THE CLINIC AND THE FIELD?**	Harbour View 2
1400 - 1800	Conference Registration Open	

OPENING ORATION

CHAIR: ASSOCIATE PROFESSOR KATHRYN BURDON

1700 - 1715	**Welcome to Country** **Kartanya Maynard**	Grand Ballroom
1715 - 1800	**Opening Oration** **TECHNOLOGY IMPACT ON OUR VIEW OF TECHNOLOGY** **Dr Deanna Church** 10x Genomics	Grand Ballroom
1800 - 2000	Welcome Reception & Meet the Exhibitors	Federation Ballroom

Image credit: Tourism Tasmania & Stuart Crossett

MONDAY 30 OCTOBER 2017

Today's Refreshment Breaks & Lunch sponsored by: Agilent

0730 - 1730	Registration Desk Open
0800 - 1730	Trade Exhibition Open Barista Coffee Served, *sponsored by:* 华大基因 BGI
0845 - 0900	**Official Welcome and Conference Opening** **Dr Jac Charlesworth** University of Tasmania

SESSION 1: COMPLEX TRAIT GENOMICS

CHAIRS: DR MATT FIELD & PROFESSOR MELANIE BAHLO

0900 - 0945	**PET DOGS, CITIZEN SCIENCE AND THE GENOMICS OF BEHAVIOUR** **Dr Elinor Karlsson** University of Massachusetts Medical School *sponsored by:* IDT INTEGRATED DNA TECHNOLOGIES ●
0945 - 1000	**ENVIRONMENTAL SIGNAL MAXIMIZATION IN HUMAN COMPLEX DISEASES USING GENETIC CORRECTION** **Dr John Blangero** UTRGV-South Texas Diabetes & Obesity Institute ●
1000 - 1015	**IDENTIFICATION OF NOVEL GENES IN LARGE FAMILIES WITH AUTISM SPECTRUM DISORDER** **Dr Kiymet Bozaoglu** Murdoch Childrens Research Institute ●
1015 - 1030	**WHOLE EXOME SEQUENCING AND LINKAGE ANALYSIS OF EXTENDED PEDIGREES TO IDENTIFY GLAUCOMA SUSCEPTIBILITY GENES** **Mrs Patricia Graham** University of Tasmania ●
1030 - 1100	Morning Refreshments & Trade Exhibition

SPEAKER KEY: ● Invited Abstract ● Student ● Early Career Researcher ● National Invited Speaker ● Keynote

SESSION 2: POPULATION GENETICS AND EVOLUTION

CHAIRS: DR KIYMET BOZAOGLU & DR JOHN BLANGERO

1100 - 1130	**USING GENOMICS TO DECIPHER OUR MODERN HUMAN HISTORY** **Professor Vanessa Hayes** Garvan Institute of Medical Research	●
1130 - 1145	**THE MEDICAL GENOME REFERENCE BANK - GENOMICS OF A DISEASE-DEPLETED, ELDERLY AUSTRALIAN COHORT** **Dr Mark Pinese** The Kinghorn Cancer Centre	●
1145 - 1200	**UNTANGLING LIPIDS - A PEDIGREE BASED STUDY OF THE PLASMA LIPIDOME THROUGH WHOLE GENOME SEQUENCING TO ASSESS RARE DELETERIOUS VARIANTS IN 1,025 MEXICAN AMERICANS.** **Dr Nicholas Blackburn** UTRGV-South Texas Diabetes & Obesity Institute	●
1200 - 1215	**LIBRARY-FREE, TARGETED SEQUENCING OF NATIVE GENOMIC DNA AND RNA FROM FFPE SAMPLES USING HYB & SEQTM TECHNOLOGY - THE HYBRIDIZATION-BASED SINGLE MOLECULE SEQUENCING SYSTEM** **Dr Michael Rhodes** NanoString Technologies	●
1215 - 1315	Lunch & Trade Exhibition	

SESSION 3: COMPUTATIONAL BIOLOGY

CHAIRS: DR PENGYI YANG & DR JOSEPH POWELL

1315 - 1400	**USING GENOMIC DATA TO MAP FUNCTIONAL INTERACTIONS IN CELLULAR SYSTEMS** **Dr Kimberly Reynolds** University of Texas Southwestern Medical Center *sponsored by:* BizData® Broader Perspective. Better Decisions.	●
1400 - 1415	**GENOTYPING REPEATS WITH NANOPORE SEQUENCING** **Dr Devika Ganesamoorthy** The University of Queensland	●
1415 - 1430	**BUILDING TRANSCRIPTIONAL LANDSCAPES USING T-SNE BASED DIMENSIONALITY REDUCTION OF PUBLIC DATA** **Dr Traude Beilharz** Monash University	●
1430 - 1445	**GENETIC RISK FACTORS IN A VULVAR CANCER CLUSTER AMONG YOUNG INDIGENOUS WOMEN IN ARNHEM LAND, AUSTRALIA** **Dr Bennet McComish** University of Tasmania	●

SPEAKER KEY: ● Invited Abstract ● Student ● Early Career Researcher ● National Invited Speaker ● Keynote

1445 - 1455

LIGHTNING POSTER SESSION 1

FACILITATORS: MS VIKKI MARSHALL & ASSOCIATE PROFESSOR RUBY LIN

REPRESENTING THE CANCER GENOME WITH MIRROR-DNA SPIKE-IN CONTROLS

Mr Ira Deveson
Garvan Institute of Medical Research

IMPROVING PREDICTABILITY OF CRISPR-CPF1 ACTIVITY

Dr Kaitao Lai
CSIRO

A STRATEGY TO DESCRIBE THE ADAPTIVE IMMUNE LANDSCAPE OF METASTATIC BREAST CANCER LESIONS ON A SINGLE-CELL LEVEL

Mr Ghamdan Al-Eryani
Garvan Institute of Medical Research

THE THERANOSTIC POTENTIAL OF MICRO RNAS IN AGGRESSIVE PROSTATE CANCER

Ms Farhana Matin
Queensland University of Technology

NON-SYNONYMOUS VARIATION IN ADAMTS12 CORRELATES WITH CAROTID ARTERY INTIMA-MEDIA THICKNESS

Mr Juan Peralta
UTRGV-South Texas Diabetes & Obesity Institute

1455 - 1545

Poster Session 1 & Afternoon Refreshments
Poster Session sponsored by:

IDT INTEGRATED DNA TECHNOLOGIES

SPEAKER KEY: Invited Abstract · Student · Early Career Researcher · National Invited Speaker · Keynote

SESSION 4: FUNCTIONAL GENOMICS

CHAIRS: DR SEYHAN YAZAR & DR EVA CHAN

1545 - 1615	**A GENOME-WIDE CRISPR-CAS9 KNOCKOUT SCREEN IDENTIFIES NOVEL ANTI-CANCER DRUG RESISTANT GENES** **Associate Professor Greg Neely** The University of Sydney	
1615 - 1630	**HIGH RESOLUTION TEMPORAL TRANSCRIPTOMICS OF MOUSE EMBRYOID BODY DEVELOPMENT REVEALS COMPLEX EXPRESSION DYNAMICS OF CODING AND NONCODING LOCI** **Dr Brian Gloss** Garvan Institute of Medical Research	
1630 - 1645	**SURVIVAL OF THE FITTEST: THE FIGHT FOR DOMINANCE IN WINE FERMENTATION AND THE GENOMIC ADAPTATIONS THAT UNDERPIN YEAST STRAIN PERFORMANCE** **Dr Anthony Borneman** The Australian Wine Research Institute	
1645 - 1700	**GENETIC AND MOLECULAR ANALYSIS OF TWO NEW LOCI CONTROLLING FLOWERING IN GARDEN PEA, PISUM SATIVUM** **Mr Mainul Hasan** University of Tasmania	
1800 - 2300	**Conference Dinner** *The Conference Dinner is an optional function and is not included in any registration type. Bookings are essential.* *Delegates attending must arrive at the Brooke Street Pier Ferry Terminal by 5:50pm for a 6:00pm departure.*	Museum of Old and New Art (Mona)

SPEAKER KEY: Invited Abstract · Student · Early Career Researcher · National Invited Speaker · Keynote

Today's Refreshment Breaks & Lunch sponsored by:

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0730 - 1730	Registration Desk Open
0800 - 1730	Trade Exhibition Open Barista Coffee Served, *sponsored by:* 华大基因 BGI
0845 - 0900	**Welcome to Day Two** **Associate Professor Ruby Lin** University of New South Wales

SESSION 5: SINGLE CELL 'OMICS AND GENOME ASSEMBLY

DR NICHOLAS BLACKBURN & PROFESSOR VANESSA HAYES

0900 - 0945	**HIGH RESOLUTION BIOLOGY USING 10X** **Dr Deanna Church** 10x Genomics *sponsored by:* millennium® science enabling next-generation research™ ●
0945 - 1000	**DE NOVO GENOME AND TRANSCRIPTOME ASSEMBLIES OF THE BARE-NOSED WOMBAT** **Dr Seyhan Yazar** University of Edinburgh ●
1000 - 1015	**MODELLING BREAST CANCER PROGRESSION USING MASSIVELY PARALLEL SINGLE-CELL RNA-SEQ TECHNOLOGY** **Dr David Gallego-Ortega** Garvan Institute of Medical Research ●
1015 - 1030	**SINGLE CELL RNA-SEQ OF CARDIAC INTERSTITIAL CELLS REVEALS NOVEL POPULATIONS IN HEALTHY & DISEASED HEART** **Mrs Nona Farbehi** University of New South Wales ●
1030 - 1100	Morning Refreshments & Trade Exhibition

SPEAKER KEY: ● Invited Abstract ● Student ● Early Career Researcher ● National Invited Speaker ● Keynote

SESSION 6: SYNTHETIC BIOLOGY AND NOVEL TECHNOLOGIES

CHAIRS: DR BRIAN GLOSS & DR RICHARD TOTHILL

1100 - 1130	**YEAST 2.0 AND BEYOND: BUILDING THE WORLD'S FIRST SYNTHETIC EUKARYOTE** **Professor Ian Paulsen** Macquarie University	●
1130 - 1145	**BIG DATA FROM A SMALL DEVICE: REAL TIME GENOMICS WITH NANOPORE SEQUENCING** **Dr Martin Smith** Garvan Institute of Medical Research	●
1145 - 1200	**PARALLEL ASSAY OF SINGLE-CELL CHROMATIN ACCESSIBILITY AND TRANSCRIPTOME** **Dr Longqi Liu** BGI	●
1200 - 1215	**ONGOING HUMAN CHROMOSOME END EXTENSION DRIVEN BY A PRIMATE ANCESTRAL GENOMIC REGION REVEALED BY ANALYSIS OF BIONANO AND NANOPORE GENOMICS DATA** **Mr Haojing Shao** The University of Queensland	●
1215 - 1315	Lunch & Trade Exhibition	

SESSION 7: BIOINFORMATICS AND DATA ANALYTICS

CHAIRS: DR KAITAO LAI & DR MATTHEW WAKEFIELD

1315 - 1400	**MUTATIONS THAT MATTER** **Dr Pauline Ng** Explorer and Consultant *sponsored by:* ThermoFisher SCIENTIFIC	●
1400 - 1415	**A COMPOSITIONALLY VALID PIPELINE FOR ANY-OMICS DATA** **Dr Thom Quinn** Deakin University	●
1415 - 1430	**USING MACHINE LEARNING TO UNDERSTAND CRISPR-CAS9 ACTIVITY** **Dr Laurence Wilson** CSIRO	●
1430 - 1445	**FUNCTIONAL INSIGHTS FROM RNA-SEQ ARE AFFECTED BY DECISIONS MADE EARLY IN THE EXPERIMENTAL DESIGN, LIBRARY PREPARATION AND SEQUENCING PROTOCOL** **Dr Susan Corley** University of New South Wales	●

SPEAKER KEY: ● Invited Abstract ● Student ● Early Career Researcher ● National Invited Speaker ● Keynote

1445 - 1455

LIGHTNING POSTER SESSION 2

FACILITATORS: MS VIKKI MARSHALL & ASSOCIATE PROFESSOR RUBY LIN

RELIABLY DETECTING CLINICALLY IMPORTANT VARIANTS REQUIRES BOTH COMBINED VARIANT CALLS AND OPTIMIZED FILTERING STRATEGIES

Dr Matt Field
James Cook University

INTRAGENIC ENHANCERS ATTENUATE HOST GENE EXPRESSION

Dr Pengyi Yang
The University of Sydney

DIVERSIFICATION OF INNATE IMMUNE RESPONSES BY TRANSCRIPTIONAL MECHANISMS

Miss Suzanne Butcher
The University of Melbourne

IDENTIFICATION OF SODIUM VALPROATE AND LITHIUM CO-REGULATED GENES IN A SEROTONERGIC CELL LINE

Ms Priyanka Sinha
University of Otago

SLAMSEQ: HIGH-THROUGHPUT METABOLIC SEQUENCING OF RNA

Dr Stephanie Bannister
Lexogen

1455 - 1545

Poster Session 2 & Afternoon Refreshments
Poster Session sponsored by:

IDT INTEGRATED DNA TECHNOLOGIES

SPEAKER KEY: Invited Abstract · Student · Early Career Researcher · National Invited Speaker · Keynote

SESSION 8: EPIGENETICS AND TRANSCRIPTOMICS

CHAIRS: DR HALOOM RAFEHI & ASSOCIATE PROFESSOR ALICIA OSHLACK

Exhibitor Prize Draw 1

1545 - 1615	**SEX SPECIFIC LANDSCAPES OF DNA METHYLATION ON THE MARSUPIAL X CHROMOSOME: THE SHAPE OF SILENCING** **Dr Paul Waters** University of New South Wales	
1615 - 1630	**RNA-CHROMATIN INTERACTOME REVEALS NCRNA FUNCTIONS FOR TRANSCRIPTION REGULATION AND GENOME ORGANIZATION** **Dr Oscar Luo** CSIRO	
1630 - 1645	**SPLICED SYNTHETIC GENES AS INTERNAL CONTROLS IN RNA-SEQ EXPERIMENTS** **Mr Simon Hardwick** Garvan Institute of Medical Research	
1645 - 1700	**DYNAMICS OF CHROMATIN ACCESSIBILITY AND TRANSCRIPTION FACTOR BINDING IN HUMAN AND CHIMPANZEE PLURIPOTENT STEM CELLS** **Dr Irene Gallego Romero** The University of Melbourne	
1715 - 1745	AGTA Annual General Meeting	Grand Ballroom
1830 - 2030	Student Function	Shambles Brewery
1830 - 2030	VIP Function (Invitation Only)	Syra

SPEAKER KEY: Invited Abstract | Student | Early Career Researcher | National Invited Speaker | Keynote

Today's Refreshment Breaks & Lunch sponsored by: ThermoFisher SCIENTIFIC

0730 - 1730	Registration Desk Open
0800 - 1300	Trade Exhibition Open Barista Coffee Served, *sponsored by:* 华大基因 BGI
0845 - 0900	**Welcome to Day Three + Exhibitor Prize 2** **Ms Vikki Marshall** The University of Melbourne

SESSION 9: COMPARATIVE GENOMICS

CHAIRS: DR QUENTIN GOUIL & DR IRENE GALLEGO ROMERO

0900 - 0930	**REPETITIVE DNA: EVOLVING SAFELY IN NUMBERS** **Dr Austen Ganley** University of Auckland
0930 - 0945	**THE OZ MAMMALS GENOMICS INITIATIVE: MAMMAL GENOMICS, EVOLUTION AND CONSERVATION AT A CONTINENTAL SCALE** **Dr Anna MacDonald** Australian National University
0945 - 1000	**POPULATION STRUCTURE OF THE BRACHYPODIUM SPECIES COMPLEX AND GENOME WIDE DISSECTION OF AGRONOMIC TRAITS IN RESPONSE TO CLIMATE** **Professor Justin Borevitz** Australian National University
1000 - 1015	**IDENTIFYING RACIAL DIFFERENCES IN THE MUTATIONAL LANDSCAPE OF AGGRESSIVE PROSTATE CANCER** **Dr Weerachai Jaratlerdsiri** Garvan Institute of Medical Research
1015 - 1045	Morning Refreshments & Trade Exhibition

SPEAKER KEY: Invited Abstract · Student · Early Career Researcher · National Invited Speaker · Keynote

SESSION 10: GENE EDITING AND GENE REGULATION

CHAIRS: DR BENNET MCCOMISH & ASSOCIATE PROFESSOR NICOLE CLOONAN

1045 - 1115	**AUTOMATED CULTURE SYSTEM FOR LARGE SCALE DISEASE MODELLING** **Associate Professor Alice Pebay** The University of Melbourne
1115 - 1130	**EXTENSIVE TRANSCRIPTOMIC AND EPIGENOMIC REMODELING DURING ARABIDOPSIS THALIANA GERMINATION** **Dr Quentin Gouil** Walter and Eliza Hall Institute of Medical Research
1130 - 1145	**PREDICTING THE HDR EFFICIENCY OF CRISPR-CAS** **Mr Aidan O'Brien** Australian National University
1145 - 1200	**SINGLE CELL SEQUENCING REVEALS CHANGES IN THE GENETIC CONTROL OF GENE EXPRESSION THROUGH REPROGRAMMING OF INDUCED PLURIPOTENT STEM CELLS FROM FIBROBLASTS** **Dr Joseph Powell** The University of Queensland
1200 - 1300	Lunch & Trade Exhibition

SPEAKER KEY: Invited Abstract · Student · Early Career Researcher · National Invited Speaker · Keynote

SESSION 11: MEDICAL AND CANCER GENOMICS

CHAIRS: DR DEVIKA GANESAMOORTHY & ASSOCIATE PROFESSOR RUBY LIN

1300 - 1330	**SINGLE-CELL RNA-SEQ: ANALYSIS, SIMULATION AND KIDNEYS IN A DISH** **Associate Professor Alicia Oshlack** Murdoch Childrens Research Institute
1330 - 1345	**WHOLE GENOME SEQUENCING IS IMPROVING THE IDENTIFICATION OF GENETIC CAUSES OF PAEDIATRIC CATARACTS** **Ms Johanna Jones** University of Tasmania
1345 - 1400	**SINGLE-CELL TRANSCRIPTOMICS REVEALS FUNCTIONAL HETEROGENEITY IN BREAST CANCER CELLS** **Dr Daniel Roden** Garvan Institute of Medical Research
1400 - 1415	**GENOME MAPPING ILLUMINATES ARCHITECTURE OF CHAINED FUSIONS IN CANCER** **Dr Eva Chan** Garvan Institute of Medical Research
1415 - 1445	**THE GENOMIC PATHOLOGY OF PANCREATIC CANCERS** **Professor Sean Grimmond** The University of Melbourne
1445 - 1500	Awarding of Prizes, Exhibitor Prize Draw 3, 2018 Conference Launch and Conference Close

SPEAKER KEY: Invited Abstract · Student · Early Career Researcher · National Invited Speaker · Keynote

The 2017 AGTA Conference reserves the right to amend or alter any advertised details relating to dates, program and speakers if necessary and without notice, as a result of circumstances beyond their control. All attempts will be made to keep any changes to an absolute minimum.

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CONFERENCE SOCIAL PROGRAM

WELCOME RECEPTION & MEET THE EXHIBITORS

Date:	Sunday 29 October 2017
Venue:	Federation Ballroom, Hotel Grand Chancellor
Time:	6.00pm – 8.00pm
Dress:	Smart Casual

Join us for the official Welcome Reception for the 2017 AGTA Conference. Enjoy networking with old and new acquaintances, meeting our sponsors and trade exhibitors, whilst enjoying drinks and canapés.

The Welcome Reception is included in a full registration only. Additional tickets can be purchased at $75.00 per person.

CONFERENCE DINNER

Date:	Monday 30 October 2017
Venue:	Mona (Museum of Old and New Art), Berriedale
Time:	6.00pm – 11.00pm (ferry departs Brooke Street Pier at 6.00pm)
Dress:	Smart Casual
Registra-tion:	Tickets to the Conference Dinner could be purchased through the online registration form. Tickets can still be purchased, subject to availability.
Cost:	$165 per ticket. The Conference Dinner is not included in any registration type.

The highlight of the social program will take place at Mona (Museum of Old and New Art). You'll experience a ride on the Mona Roma ferry, followed by a private museum viewing and dinner at Eros and Thanatos. This conference dinner will undoubtedly be one to remember!

STUDENT/ECR FUNCTION

Date:	Tuesday 31 October 2017
Venue:	Shambles Brewery
Time:	6.30pm – 8.30pm

Students and early career researchers are invited to attend the Student/ECR function at Shambles Brewery. Food and a limited beverage service will be provided, don't miss your chance to sample local produce. Bookings are essential.

VIP FUNCTION

Date:	Tuesday 31 October 2017
Venue:	Syra
Time:	6.30pm – 8.30pm
Cost:	N/A Invitation Only

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PRE-CONFERENCE WORKSHOPS

The workshops are optional, tickets can be purchased for $40.00 per delegate and $20.00 per student delegate, ticket price includes lunch and afternoon refreshments. Bookings are essential.

WORKSHOP 1

CAN GENOME EDITING FULFIL ITS PROMISE IN THE CLINIC AND THE FIELD?

Date:	Sunday 29 October 2017
Venue:	Hotel Grand Chancellor Harbour View 2
Time:	12.00pm – 3.40pm

A symposium covering the social, clinical, research and industry applications, potentials and concerns of gene editing.

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Symposium Speakers

Dr Alex Hewitt
University of Tasmania

Associate Professor Alice Pébay
The University of Melbourne

Professor Dianne Nicol
University of Tasmania

Jason Potter
Thermo Fisher Scientific

Dr Kaylene Young
University of Tasmania

Professor Margaret Otlowski
University of Tasmania (Mediator)

Dr Owain Edwards
CSIRO

WORKSHOP 2

TECHNICAL SOLUTIONS TO SINGLE CELL PROBLEMS

Date:	Sunday 29 October 2017
Venue:	Hotel Grand Chancellor Harbour View 1
Time:	11.40am – 4.00pm

This workshop aims to be a technical brainstorming session – comparing and contrasting available technologies, and 'workshopping' the technical issues or tips that directly impact the output and quality of data as well as the advantages and potential pitfalls of specific platforms in different situations.

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Workshop Speakers

Dr Brian Fritz
10x Genomics

Dr David Gallego-Ortega
Garvan Institute of Medical Research

Dr Mark Lynch
Fluidigm

Dr Shalin Naik
Walter & Eliza Hall Institute of Medical Research

Dr Marina Oliva
University of Western Australia

Associate Professor Alicia Oshlack
Murdoch Childrens Research Institute

Dr Joseph Powell
The University of Queensland

Dr Alex Swarbrick
Garvan Institute of Medical Research

ABSTRACTS & BIOGRAPHIES

Image credit: Daniel Tran

ABSTRACT REVIEWERS

Thank you to our AGTA17 abstract reviewers.

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University of Tasmania

Dr Jac Charlesworth
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Dr Robert Day
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Associate Professor Marcel Dinger
Garvan Institute of Medical Research

Dr Kate Howell
University of Western Australia

Dr Carsten Kulheim
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University of New South Wales

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The University of Melbourne

Associate Professor Alicia Oshlack
Murdoch Childrens Research Institute

Mr Kirby Siemering
Australian Genome Research Facility

Dr Helen Speirs
Ramaciotti Centre for Genomics

Dr Richard Tothill
The University of Melbourne

Mr Mark Van der Hoek
South Australian Health and Medical Research Institute

OPENING ORATION

CHAIR: ASSOCIATE PROFESSOR KATHRYN BURDON

1715 – 1800

Guest Speaker
DR DEANNA CHURCH
10x Genomics

Dr. Deanna Church is currently the Senior Director of Applications at 10x Genomics. In this role, she leads a diverse group of scientists who are developing approaches for improved genome analysis, using Linked-Reads, as well as expanding the application space of single cell transcriptome profiling. Previously, she was Senior Director of Genomics and Content at Personalis, where she helped advance the field of genomics based clinical diagnostics. Prior to that, she was a staff scientist at NCBI, where she oversaw several projects concerning managing and displaying genomic data, including dbVar, a database of structural variation, the NCBI Variation Viewer, the NCBI Map Viewer, the Clone database and the NCBI Remap service. Dr. Church was also a founding member of the Genome Reference Consortium (GRC), an international group charged with improving the reference assembly for humans and other model organisms.

TECHNOLOGY IMPACT ON OUR VIEW OF TECHNOLOGY

Technology, tools and methods development are often underappreciated in discussions of breakthroughs in biology. However, it is quite clear that without development in these areas we would not have the insights we have today. For example, our understanding of genome structure and population diversity has changed dramatically as we've progressed from looking at chromosomes through a microscope lens to the myriad of high resolution sequencing and analysis approaches we currently have at our disposal. During this talk, I'll highlight some of transformative technologies and how they have changed our view of biology.

SESSION 1: COMPLEX TRAIT GENOMICS

CHAIRS: DR MATT FIELD & PROFESSOR MELANIE BAHLO

0900 – 0945

Keynote Speaker
DR ELINOR KARLSSON
University of Massachusetts Medical School

Elinor Karlsson uses evolution as a tool for understanding how the human genome works. By combining signals of natural selection with genome-wide association studies, Dr. Karlsson aims to identify genes, pathways, and the functional variants underlying polygenic diseases, and translate these discoveries into advances in human health care. She is currently using this approach to find the genetic risk factors for susceptibility to infectious diseases, like cholera and viral hemorrhagic fevers, as well as psychiatric disorders (using dogs as a model organism). Elinor received her B.A. in biochemistry/cell biology from Rice University, and earned her Ph.D. in bioinformatics from Boston University for research she did on dog genetics at the Broad Institute. She did her postdoctoral research with Dr. Pardis Sabeti at Harvard University.

PET DOGS, CITIZEN SCIENCE AND THE GENOMICS OF BEHAVIOUR

Elinor K. Karlsson[1,2]

[1] Bioinformatics and Integrative Biology, University of Massachusetts Medical School, Worcester MA, USA
[2] Broad Institute of MIT and Harvard, Cambridge MA, USA

Humans have exerted strong selective pressure on dogs, shaping complex behaviours, like guarding, herding, pointing, and retrieving. While this selection drives large effect variants up in prevalence, making them easier to map, it still requires thousands of dogs to map polygenic behavioural traits. To achieve these numbers, we've tapped into a huge population of dogs living in homes with observers of their behaviour: our pets. Our new citizen science dog genetics project called "Darwin's Dogs" that engages directly with dog owners to collect phenotypic and genetic data. This novel approach to dog behavioural genetics — enrolling any dog, regardless of breed ancestry — has allowed us to assemble DNA samples from thousands of diverse dogs, each with detailed behavioural phenotypes. With this resource, we can run statistically robust genomewide studies of complex behaviours, as well as psychiatric diseases shared between humans and dogs.

0945 – 1000

Invited Abstract

DR JOHN BLANGERO
UTRGV-South Texas Diabetes & Obesity Institute

John Blangero is a Professor in the South Texas Diabetes and Obesity Institute at the University Of Texas Rio Grande Valley School Of Medicine. He is a world leader in the area of statistical genetics of complex diseases. He has published over 600 articles and has had competitive grant funding in excess of $100M US. Blangero has been a devoted advocate of large pedigree studies for the identification of complex disease-related genes and for the likely importance of rare variants in normal quantitative variation. His current interests are in epidemiological scale deep cellular phenotyping and in statistical genetic methods to maximize environmental signals in the human disease exposome. He is the driving force behind the SOLAR software package for statistical genetics used by more than 7000 investigators world-wide. In his spare time, he is the lead singer and primary composer for the progressive rock band Harlequin Reborn.

ENVIRONMENTAL SIGNAL MAXIMIZATION IN HUMAN COMPLEX DISEASES USING GENETIC CORRECTION

John Blangero[1], Juan M. Peralta[2]

[1] South Texas Diabetes and Obesity Institute, University of Texas Rio Grande Valley School of Medicine, Brownsville, Texas, USA
[2] Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia

While genetic studies typically focus on gene discovery, we have developed a novel approach that exploits genetics to facilitate discovery of systematic environmental (i.e., non-genetic) factors in disease risk. In our approach, we treat genetics as a confounder that reduces power to detect environmental signals. Pedigree-based designs are a powerful way to obtain statistical control of genetics to enhance the signal-to-noise ratio of environmental factors. Basically, we control for genetic factors in a given disease-related phenotype by estimating individual-level genome-wide additive genetic effects using a Best Linear Unbiased Prediction procedure. The resulting estimated genetic value (EGV) then is subtracted from the phenotypic value to obtain an estimated environmental value (EEV) that is free of the expected additive genetic signal. Conditional on such genetic correction, environmental signals are increased. In this paper, we provide a general framework to show how such derived EEVs should be used in the analysis of systematic environmental factors in disease risk. Using analytical results and simulation methods, we show that the increased environmental signal can be substantial depending upon the focal trait's heritability and the structure of genetic relationships among individuals. We also show how whole genome sequencing information can make this approach useful even when only "unrelated" individuals are available. As an example, we perform an analysis of liver function measures and whole genome sequence data from large Mexican American pedigrees. We demonstrate how we capture and characterize environmentally determined transcriptomic and metabolomic predictors using this approach along with advanced spatial modelling to uncover systematic environmental trends. Our results suggest that this novel approach to controlling for genetics can be employed to enhance the detection of environmental factors in disease risk.

1000 – 1015

Invited Abstract

DR KIYMET BOZAOGLU
Murdoch Childrens Research Institute

Dr Bozaoglu is a senior research officer at the Bruce Lefroy Centre for Genetics Health Research at MCRI. She has a strong background in genetics and molecular biology and her research focus is on understanding the genetics of complex diseases. She has been involved in a number of large human datasets to identify novel genes associated with complex diseases and then characterising these genes using functional genomics. Her work has predominantly been on obesity, diabetes and cardiovascular disease and has more recently expanded her skill set by moving into neurogenetics and focusing on autism spectrum disorder.

IDENTIFICATION OF NOVEL GENES IN LARGE FAMILIES WITH AUTISM SPECTRUM DISORDER

Kiymet Bozaoglu[1,2], Natasha Brown[3,4], Peter Hickey[5,6], Peter Diakumis[5,6], Sarah Wilson[11], Martin Delatycki[1,2], Melanie Bahlo[10,5], Ingrid Scheffer[7,8,9,2], Paul Lockhart[1,2], Miriam Fanjul Fernandez[1].

1 Bruce Lefroy Centre for Genetic Health Research, Murdoch Children's Research Institute, Parkville, VIC, Australia
2 Department of Paediatrics, University of Melbourne Parkville, VIC, Australia
3 Austin Health Department of Clinical Genetics, Heidelberg, VIC, Australia
4 Barwon Child Health Research Unit, Geelong, VIC, Australia
5 Department of Medical Biology, University of Melbourne, Melbourne, VIC, Australia
6 Bioinformatics Division, The Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC, Australia
7 Department of Medicine, University of Melbourne, Austin Health, Melbourne, VIC, Australia
8 Florey Institute, Melbourne, VIC, Australia
9 Department of Neurology, Royal Children's Hospital, Melbourne, Australia
10 Population Health and Immunity Division, Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC, Australia
11 Melbourne School of Psychological Sciences, University of Melbourne, VIC, Australia

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder presenting in childhood, and has a lifelong impact on affected individuals. Children with ASD have deficits in social communication and repetitive behaviours with restricted interests, which can impose a significant burden on children and their families. Over 300,000 Australians have ASD. A broad spectrum of ASD is recognised, ranging from severe social and cognitive impairment to individuals with normal intellect or 'high-functioning' ASD (30% of ASD). ASD has a strong genetic basis with >50% heritability on twin and family studies however the aetiology for ASD remains unknown in ~70% of cases, and a significant challenge is identifying causative and susceptibility genes. Recent research efforts have primarily focused on de novo genetic alterations in sporadic cases. These studies have successfully demonstrated the contribution of these highly penetrant mutations in ASD causality.

We have applied a novel approach to gene discovery in ASD by studying large families. Detailed behavioural phenotyping of individuals with ASD and the Broader Autism Phenotype (BAP) was performed to map ASD traits in large families. Linkage analysis in one family, with 8 affected members across 3 generations identified suggestive linkage (maximum parametric LOD=2.7) to a single chromosomal region. Exome sequence analysis identified a missense mutation within a gene involved in glycogen metabolism that Invited Abstract (Student) segregated with all affected individuals.

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This mutation results in an amino acid substitution that is predicted to be pathogenic by multiple in silico prediction tools. We identified the same mutation in three additional ASD families (n=7 affected individuals). The mutation has a low minor allele frequency in population databases, and is significantly over-represented in the UK10K ASD cohort (OR=2.11, P=0.0037).

Our data suggests that dysregulation of glycogen metabolism may contribute to the pathogenesis of ASD. Targeted validation approaches using patient derived iPS cells are currently being performed to determine how this variant may be contributing to ASD.

1015 – 1030

MRS PATRICIA GRAHAM
University of Tasmania

Patricia Graham is a PhD candidate at the Menzies Institute for Medical Research in Hobart. Her project is focused on finding genes which are involved in susceptibility to glaucoma. Patricia is part of the computational genomics research group which has a particular interest in complex diseases, including blinding eye diseases.

WHOLE EXOME SEQUENCING AND LINKAGE ANALYSIS OF EXTENDED PEDIGREES TO IDENTIFY GLAUCOMA SUSCEPTIBILITY GENES

Patricia Graham[1], Juan Peralta[1,2], Nicholas Blackburn[1,2], John Blangero[1,2], Mary Wirtz[3], Alex Hewitt[1], David Mackey[4], Kathryn Burdon[1], Jac Charlesworth[1]

1 Menzies Institute for Medical Research, University of Tasmania, Australia
2 South Texas Diabetes and Obesity Institute, University of Texas Rio Grande Valley School of Medicine, USA
3 Casey Eye Institute, Oregon Health and Science University, USA
4 Lions Eye Institute, University of Western Australia, Australia

The use of massively parallel sequencing in extended pedigrees has significant potential for identifying functional variants linked with complex disease. We are using whole exome sequencing (WES) of five large, complex families from Tasmania and Oregon (USA) to identify susceptibility genes for primary open-angle glaucoma (POAG), the leading cause of irreversible blindness worldwide. Extended pedigrees, enriched for POAG, provide a powerful tool to search for rare and private genetic variants influencing the disease, where enrichment of rare variants occurs as a function of segregation from the founders. The families in this study range in size from 48 to 201 individuals (28 to 91 sequenced) and span 5 to 7 generations. These families will be used to locate quantitative trait loci (QTLs) for two glaucoma endophenotypes. Intraocular pressure (IOP) and vertical cup to disc ratio (VCDR) are highly heritable (42% and 66% respectively) intermediate traits which are correlated with POAG susceptibility in these families (IOP RhoG = 0.80, p = 9.6 x 10-6 and VCDR RhoG = 0.76, p = 4.8 x 10-10). WES data were generated for 249 individuals from the five pedigrees using the Illumina Nextera Expanded Exome Capture Kit. After alignment to hg19, over 235,000 variants were identified. Multipoint identity by descent will be estimated from a subset of variants using the IBDLD program, which has been specifically developed for dense genotype data. Variance components linkage analysis of IOP and VCDR will be conducted using SOLAR. Variants will be ranked by minor allele frequency in comparable populations and predicted pathogenicity using multiple tools. Genes identified within the QTLs will be validated in large POAG case/control cohorts. Finding genes involved with POAG susceptibility will increase our understanding of the biological pathways involved with the disease process and from that, diagnostic tools and more effective treatments can be developed.

SESSION 2: POPULATION GENETICS AND EVOLUTION

CHAIRS: DR KIYMET BOZAOGLU & DR JOHN BLANGERO

1100 – 1130

National Invited Speaker
PROFESSOR VANESSA HAYES
Garvan Institute of Medical Research

Prof Hayes completed a PhD at the University of Groningen, The Netherlands in 1999, defining the genetic landscape of key regulator genes driving common human cancers. Returning to South Africa briefly, she headed a Genetics Laboratory focused on genetic risk factors associated with HIV/AIDS. Her interest in prostate cancer sparked by the late Prof Chris Heyns (1949-2014).

In 2003, she joined the Garvan Institute of Medical Research where she led a Cancer Genetics group focused on defining prostate cancer genetic risk factors in Australian men. This work awarded her the Cancer Institute of New South Wales Premier's Award for Cancer Research Fellow (2007), an Australian Young Tall Poppy Award for Science (2008) and the Australian Academy of Science Inaugural Ruth Stephens Gani Medal for Human Genetics (2008).

Driven by advances in technology, in 2008 she moved to the Children's Cancer Institute of Australia to establish one of the countries first next generation sequencing research laboratories. She used this technology to drive two large efforts, namely the Southern African Genome Project (Nature 2010) and the Tasmanian Devil Genome Project (PNAS 2011). These efforts resulted in representing Australia as a Fulbright Professional Scholar (Penn State University) and a Professorship at the J. Craig Venter Institute in San Diego.

In 2014, Prof Hayes returned full-time to Australia and the Garvan Institute of Medical Research as the University of Sydney's Petre Chair of Prostate Cancer Research, where she is continuing her research efforts in human comparative and prostate cancer genomics. She has maintained her interest in technology development.

USING GENOMICS TO DECIPHER OUR MODERN HUMAN HISTORY

Eva K.F. Chan[1], Weerachai Jaratlerdsiri[1], Axel Timmerman[2], **Vanessa M. Hayes**[1,3]

[1] Laboratory for Human Comparative and Prostate Cancer Genomics, Garvan Institute of Medical Research, Sydney
[2] International Pacific Research Center, University of Hawaii, USA
[3] Central Clinical School, University of Sydney

While it is clear that modern humans emerged from a single founder population within Africa, the exact origins and timeline of this emergence remains one of the biggest questions of all time. Genomics is providing the tools to begin to unravel the mysteries surrounding early human history. With the richest and oldest fossil record of anatomically modern humans outside of east Africa, southern Africa is a major contender for the birthplace of mankind. Home to the 'oldest' extant contemporary human populations, the click-speaking KhoeSan peoples are arguably the last remaining hunter-gatherers. Having collated the largest KhoeSan resource, we have used mitochondrial and whole genome analysis to redefine not only the timeline of modern human existence (~200 thousand years ago, kya), but importantly provide insights into southern African prehistory. Dating the earliest derived maternal KhoeSan haplogroup to ~170 kya we provide further evidence for environmental changes as the most likely contributor to migrations and geographic isolations that led to significant subpopulation emergence.

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While our Eurasian ancestors were exiting Africa via the northeast end of the continent some 60-70 kya, we provide the first genomic evidence for extensive activity taking place at the most southern tip. We demonstrate the emergence of new human lineages provide evidence for significant migrations, population growths and declines occurring over the last glacial period (110 kya – 11.7 kya). Consequently, we (and others) have shown that southern Africa today has the greatest within and between population genetic diversity globally. Putting this into context, modern Australians have 40% less genetic diversity than the average KhoeSan genome. The KhoeSan people therefore represent the richest source of human genomic variation, with the greatest single potential to add to the catalogue of human genome variation. As such the KhoeSan Genome Project (KSGP) has been initiated.

1130 – 1145

Invited Abstract (Early Career Researcher)
DR MARK PINESE
The Kinghorn Cancer Centre

Dr Pinese completed his undergraduate studies at UNSW Australia on the biology of ageing, before moving to the Garvan Institute to pursue cancer research.

At the Garvan Institute, Dr Pinese was a member of the world's largest sequencing effort in pancreatic cancer, and for his work received a PhD on the molecular determinants of survival of patients with pancreatic adenocarcinoma. Dr Pinese then joined the Kinghorn Centre for Clinical Genomics, where he performed rapid-turnaround genomic analysis for cancer patients, and helped to develop Australia's first clinically-accredited whole genome sequencing test for rare disease.

Dr Pinese is currently a Senior Research Officer in Garvan's Genomic Cancer Medicine Lab, where he is the lead analyst for the Medical Genome Reference Bank, and conducts research into the genetic basis of cancer risk.

THE MEDICAL GENOME REFERENCE BANK – GENOMICS OF A DISEASE-DEPLETED, ELDERLY AUSTRALIAN COHORT

Mark Pinese[1], Paul Lacaze[2], Emma Rath[1], Aaron Chuah[3], Shane Husson[1], Dmitry Degrave[1], the ASPREE Investigator Group[2], the 45 and Up Study Collaborators[4], Margo Barr[4], T. Daniel Andrews[3], Warren Kaplan[1], Marcel Dinger[1] and David M. Thomas[1]

[1] The Garvan Institute of Medical Research, 384 Victoria St, Darlinghurst NSW 2010
[2] The Alfred Centre, Monash University, 99 Commercial Rd, Melbourne VIC 3004
[3] The John Curtin School of Medical Research, 131 Garran Rd, Acton ACT 2601
[4] The Sax Institute, Level 13, Building 10, 235 Jones St, Ultimo NSW 2007

The Medical Genome Reference Bank (MGRB) houses genomic data and rich phenotype information from healthy elderly Australians without cardiovascular disease, neurodegenerative disorders, or cancer. As the most comprehensive 'wellderly' genome cohort in the world, the MGRB provides an unprecedented deep view into the genetic architecture of a healthy Western population, and acts as a universal control population to maximise the efficiency of disease-specific genomic analyses in both the research and clinical settings.

We have completed deep whole genome sequencing of over 3,000 individuals from the MGRB. Here we report our preliminary findings, including patterns of complex variation and the prevalence of apparently 'pathogenic' variants in a well elderly population. To fully leverage our unique high-depth data, we are interrogating the MGRB for latent signals such as mobile element and subclonal variation, and we describe our initial observations. We also discuss challenges in applying genomic technologies at this scale, and the approaches we have taken to resolve them.

To facilitate the use of this public resource by investigators and clinicians, we have created a web-accessible data portal for the dynamic searching and visualisation of MGRB variants, and a GA4GH-compliant data Beacon for integration with the global Beacon variation searching network. Basic demographic and phenotypic information are incorporated into the MGRB data portal, and comprehensive genomic and clinical data are available to researchers internationally.

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MGRB participants have been consented through the contributing studies 45 and Up (Sax Institute, Sydney), and the ASPirin in Reducing Events in the Elderly (ASPREE) clinical trial (Monash University, Melbourne). The Garvan Institute of Medical Research (Sydney) is performing WGS of all samples on the Illumina HiSeq X platform under clinically accredited conditions, leveraging data processing and storage at the National Computational Infrastructure (Canberra).

1145 – 1200

Invited Abstract (Early Career Researcher)
DR NICHOLAS BLACKBURN
UTRGV-South Texas Diabetes & Obesity Institute

Taswegian Dr Nicholas Blackburn completed his PhD in the genetics of hematological malignancies at the Menzies Institute for Medical Research in Tasmania in 2015.

In 2016 he joined John Blangero's group at the South Texas Diabetes and Obesity Institute at UTRGV in Brownsville, Texas. His research now focuses on the application of whole genome sequencing in extended pedigrees to discover genetic factors related to cardiovascular, metabolic, diabetes and other diseases. Specifically he works with data from Mexican American families in the San Antonio Family Heart Study and also Brazilian families in the Posse Family Health Study.

He also maintains close links with researchers in his hometown Hobart at the Menzies and works with them on the Tasmanian devil facial tumour disease, multiple sclerosis, eye diseases and familial cancers.

Twitter: @nickomatics

UNTANGLING LIPIDS – A PEDIGREE BASED STUDY OF THE PLASMA LIPIDOME THROUGH WHOLE GENOME SEQUENCING TO ASSESS RARE DELETERIOUS VARIANTS IN 1,025 MEXICAN AMERICANS.

Nicholas B. Blackburn[1], Juan M. Peralta[1,2], Arthur Porto[1], Marcio A. Almeida[1], Ravi Duggirala[1], Harald H. Göring[1], David C. Glahn[3,4], Peter J. Meikle[5], John Blangero[1], Joanne E. Curran[1].

1 South Texas Diabetes and Obesity Institute, School of Medicine, University of Texas Rio Grande Valley, TX, USA
2 Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia
3 Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA
4 Olin Neuropsychiatry Research Center, Institute of Living, Hartford Hospital, Hartford, CT, USA
5 Baker Heart and Diabetes Institute, Melbourne, Australia

Circulating lipids such as HDL, cholesterol and triglycerides, are routinely used as clinical tools for monitoring human disease risk. These macro scale lipids are constituently made up of a structurally diverse complex of discrete lipid species collectively known as the lipidome. Through the application of mass spectrometry quantification, lipidomic profiling of human samples is identifying new correlations with disease. Specific lipid species have been shown to be important in a range of contexts including major depressive disorder, diabetes and CVD. The genetic basis that drives variation in levels of plasma lipids is relatively unknown and presents an opportunity to understand the genetics of the lipidome and potentially provide new disease insights.

We characterized 319 lipid species in 23 lipid classes and subclasses in plasma samples from 1,025 Mexican Americans in extended pedigrees, each with WGS data. These pedigrees provide the potential to capture sufficient numbers of rare functional variants to permit variant-specific association testing.

Through variance components modelling in SOLAR we identified that all individual lipid species are significantly heritable, ranging from 14%-77% (mean 43%). Using rare, deleterious coding variants (MAF≤0.05 in 1KGP/ExAC, CADD≥15), we used measured genotype analysis to discover potential functional variants driving lipid levels. We identified multiple rare variants significantly associated (accounting for multiple testing) with specific lipid species.

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Variants of specific interest include those of apparent Hispanic origin, LIPC-Q355R, causing large, significant increases (0.57-0.69 SDU) in several phosphatidylethanolamines (p=2.10×10-6 to 9.54×10-9) and DEGS1-L175Q, causing large, significant alterations (0.9-1.3 SDU) in ceramides and dihydroceramides (p=2.00×10-7 to 1.67×10-13).

Our results suggest that WGS in extended pedigrees is useful for the detection of putative functional variants of relevance to the lipidome. Given the large effect sizes of these variants and their apparent Hispanic specificity this study highlights the benefits of studying rare variants in families from different ancestry backgrounds.

1200 - 1215

Invited Abstract
DR MICHAEL RHODES
NanoString Technologies

Graduated from York University with a degree in Genetics, did a Ph.D. in Bioinorganic Chemistry at University of London. After a post doc in Chicago working on genetics of metal transport in P. aeruginosa, returned to UK to work at United Kingdom Human Genome Mapping Project Resource Centre finishing as Operation Manager in charge of four teams: - Mouse resequencing, linkage Hotel, Academic Services and Custom services. Joined Applied Biosystems in 1999, worked on Genotyping, qPCR and finally Next Generation Sequencing. Joined Nanostring in 2012 after seeing the potential of the nCounter technology to take the discoveries from NGS and apply them to translational research. At Nanostring he has worked on many new applications, including 3D biology and advanced analysis for nSolver and is now helping develop Hyb & Seq™.

LIBRARY-FREE, TARGETED SEQUENCING OF NATIVE GENOMIC DNA AND RNA FROM FFPE SAMPLES USING HYB & SEQTM TECHNOLOGY – THE HYBRIDIZATION-BASED SINGLE MOLECULE SEQUENCING SYSTEM

Michael Rhodes[1], Liz Manrao[1], Rustem Khafizov[1], Matt Walsh[1], Mithra Korukonda[1], Mark Gregory[1], Margaret Hoang[1], Sunghee Woo[1], Tushar Rane[1], Yi Deng[1], Dae Kim[1], Joseph Beechem[1]

[1] NanoString Technologies, Inc.

DNA sequencing is an enabling tool for personalized medicine research, but widespread implementation is hindered by complexities in sample preparation and sequence analysis. Hyb & Seq™ technology is a library-free, amplification-free, single-molecule sequencing technique that uses cyclic nucleic acid hybridization of fluorescent molecular barcodes onto native targets. Hybridization-based sequencing enables the simplest sample-to-answer workflow; both DNA and RNA are directly sequenced with almost no manipulation of the input material. The advantages of single molecule sequencing include simple error correction and digital counting to elucidate DNA copy numbers and RNA levels.

Here we describe an end-to-end Hyb & Seq sequencing process that consists of:

i) Sample preparation including rapid gene capture directly from formalin-fixed paraffin embedded (FFPE) tissue.
ii) Library-free targeted sequencing of oncogenic mutations.
iii) Data analysis using a Hyb & Seq assembly algorithm (ShortStack™) for variant calling.

Targeted sequencing of oncogenic mutations was performed on NanoString's prototype Hyb & Seq system.

Highlights of Key Results:

- Total time from FFPE curls to start of sequencing was under 60 minutes, with total hands-on time of less than 15 minutes
- Simultaneous capture of 100 DNA gene targets and 20 mRNA from one to three FFPE curls (10 microns thickness) was sufficient for sequencing with no PCR amplification and cDNA conversion
- Dual strand capture and simultaneous sequencing of both strands of DNA, increased accuracy of variant detection by identifying single-stranded damage artifacts common in FFPE templates
- Automated sequencing carried out on a microfluidic cartridge with runs exceeding 400 Hyb & Seq cycles
- Sequencing accuracy reached 99.99% (QV40) when a base from a single molecule was read > 5 times
- All targeted variants including variant as low as 1% were detected

Hyb & Seq's simplicity, flexibility, and accuracy offers an ideal sample-to-answer solution for the translational sequencing research lab.

SESSION 3: COMPUTATIONAL BIOLOGY

CHAIRS: DR PENGYI YANG & DR JOSEPH POWELL

1315 – 1400

Keynote Speaker
DR KIMBERLY REYNOLDS
University of Texas Southwestern Medical Center

Dr. Reynolds received her undergraduate training in biochemistry at Rice University. She completed her Ph.D. in biophysics with Dr. Tracy Handel at the University of California, Berkeley in 2006, where she studied the computational design of protein-protein interfaces. She then completed a postdoctoral fellowship in the lab of Dr. Rama Ranganathan at UT Southwestern, where she studied on the evolution and engineering of allosteric communication between proteins.

USING GENOMIC DATA TO MAP FUNCTIONAL INTERACTIONS IN CELLULAR SYSTEMS

An unknown pattern of epistasis (or functional coupling) between genes limits our ability to understand how cells work and evolve. Because the activity of one gene is often modified by other genes in the genome, it is difficult to predict system behavior as a whole from measurements of each component taken independently. Thus, an ability to globally map epistasis between genes, and identify groups of genes that are relatively independent from each other would present a major simplification. Interestingly, the dramatic recent expansion in genome-scale sequencing of diverse organisms suggests new ideas for solving this fundamental problem. We use statistical analysis of genomic data to infer the pattern of interaction between genes, and to reduce cellular systems into quasi-independent evolutionary modules. As proof-of-concept, we apply this approach to the folate metabolic pathway. We observe a sparse, modular architecture of interactions, with two small groups of genes coevolving in the midst of others that evolve independently. For one such module –dihydrofolate reductase and thymidylate synthase – we use epistasis measurements and forward evolution to demonstrate both internal functional coupling and independence from the remainder of the genome. Mechanistically, the coupling is driven by a constraint on their relative activities, which must be balanced to prevent accumulation of a metabolic intermediate. The results expose an intermediate organization of cellular systems not apparent from inspection of biochemical pathways or physical complexes, and support the strategy of using evolutionary information to decompose cellular systems into functional units.

1400 – 1415

Invited Abstract (Early Career Researcher)
DR DEVIKA GANESAMOORTHY
The University of Queensland

Dr. Devika Ganesamoorthy is an early career researcher at the Institute of Molecular Bioscience in University of Queensland. She completed her PhD in 2014 at University of Melbourne. Her research is primarily focused on development and assessment of high throughput methods to analyse genomic variations. She has extensive experience with the new high throughput sequencing technology - Nanopore and has explored the method for various applications. She also has extreme interest in the analysis of cell-free DNA for biomarker discovery in various applications.

GENOTYPING REPEATS WITH NANOPORE SEQUENCING

Devika Ganesamoorthy[1], Minh Duc Cao[1], Bhuvaneswari Thiruganansambandham[1], Tania Duarte[1] and Lachlan Coin[1]

[1] Institute for Molecular Bioscience, University of Queensland, Brisbane, Australia

Tandem repeats (TRs) comprises significant proportion of the human genome, including coding and regulatory regions. They are highly prone to repeat number variation and nucleotide mutation due to their repetitive and unstable nature, making them a major source of genomic variation between individuals. However, analysis of TRs in the context of complex diseases is hindered by technical limitations and lack of high throughput methods. Recent advances in long read sequencing technologies provides an opportunity for accurate and high throughput analysis of TRs. We developed a novel targeted sequencing method combined with long read Nanopore sequencing to simultaneously analyse hundreds of repeats. We also developed a novel algorithm - 'VNTRtyper' to genotype tandem repeats from long read sequencing data. VNTRtyper first clusters reads from the same locus into two groups and then creates a consensus sequence from reads within each group. Then it counts the repeat multiplicities on the consensus sequences to determine the genotype of the two alleles. We targeted 142 TRs, ranging from 100bp to 25000bp in length in the reference genome and performed targeted capture with Nanopore sequencing. We successfully captured and sequenced more than 50% of the targeted repeats using our method. We validated nine targets by PCR sizing analysis and the genotype estimates on targeted capture sequencing results by VNTRtyper correlated well with PCR results. Furthermore, genotyping estimates from Nanopore whole genome sequencing data correlated well with the capture sequencing data. We also compared the genotype estimates from Nanopore sequencing data with the PacBio sequencing data, and the results were in concordance. Our findings illustrates the feasibility of Nanopore sequencing to genotype TRs. We present a new cost-effective approach to explore previously unrecognized class of repeat variation in GWAS studies of complex diseases.

1415 – 1430

Invited Abstract
DR TRAUDE BEILHARZ
Monash University

Traude Beilharz is an RNA Biologist. She leads a research team focused on RNA-systems biology, with a special interest in the 3'-end dynamics of mRNA. In recent years her team has been teaming up with bioinformaticians and computational biologists to better visualize, analyse and interpret high-content data. Working with the Monash Bioinformatics Platform, her research team is now split 50:50 between wet and dry lab researchers. Research being presented at AGTA17 is the result of a productive collaboration between Dr. David Albrecht from the Monash Faculty of IT, the bioinformatics platform and Traude's interest in the wiring of global gene expression.

BUILDING TRANSCRIPTIONAL LANDSCAPES USING T-SNE BASED DIMENSIONALITY REDUCTION OF PUBLIC DATA

Michael See[1], Paul Harrison[1], David Powell[1], David Albrecht[2] and **Traude Beilharz**[3]

[1] Monash Bioinformatics Platform
[2] Monash Faculty of Information Technology
[3] Monash Biodiscovery Institute; stem cell and development program

Every RNA-seq or microarray expression analysis holds two sets of information: i) the specific response to altered experimental conditions intended by the researcher; and ii) the general output of a native repertoire of transcriptional wiring options. We reason that large public transcriptomic databases now hold such quantities of gene expression data, collected under such a variety of experimental conditions, that we might be able to dissect the fine-detail of transcriptional and post-transcription connectivity in an unbiased manner. That is, the expression of some genes are likely always co-regulated with a set of functionally related genes, because they share either transcription factors, post-transcriptional regulatory elements, or both. Our approach has therefore been to use the t-SNE algorithm to project genes in high-dimensional 'gene-expression' space down to a two-dimensional layout to understand native wiring from across 1000's of public expression datasets. Our first attempts using ~5000 experiments from the highly curated SPELL data for baker's yeast, reveals discretely ordered and biologically meaningful islands of co-regulated genes. These visual landscapes are particularly useful when used as a framework for overlay and interpretation of new data. To this end, we built Shiny apps to overlay, search, explore and annotate the yeast expression landscape. In follow up work we are building analogous landscapes using expression data from the Fantom5 promoterome. Again, highly biologically relevant islands of expression form around co-regulated genes. Importantly, guilt by association can ascribe function to many unannotated genes. We will present our unpublished work in progress using t-SNE for visualisation of the native wiring of gene expression in eukaryotic cells.

1430 – 1445

Invited Abstract (Early Career Researcher)
DR BENNET MCCOMISH
University of Tasmania

Dr McComish completed his PhD in the Allan Wilson Centre for Molecular Ecology and Evolution at Massey University. His thesis focused on several problems in sequence analysis and phylogenetics, covering de novo sequence assembly, likelihood surface analysis in phylogenetic trees, and mutation mechanisms. Dr McComish has since carried out postdoctoral research into the evolutionary dynamics of microsatellite repeats using whole-genome alignments from 63 species and sequence data from a set of ancient samples spanning more than 40,000 years. He currently works as a bioinformatician supporting human genetics research covering a range of heritable diseases.

GENETIC RISK FACTORS IN A VULVAR CANCER CLUSTER AMONG YOUNG INDIGENOUS WOMEN IN ARNHEM LAND, AUSTRALIA

Bennet McComish[1], Rebekah McWhirter[1,2], Debbie Taylor-Thomson[2], James Marthick[1], Joanne Dickinson[1], John Condon[2,3], Jac Charlesworth[1].

1 Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia
2 Menzies School of Health Research, Charles Darwin University
3 Health Gains Planning Branch, NT Department of Health

Vulvar cancer is usually rare, and occurs most often in postmenopausal women. Among young (<50 years) Indigenous women living in remote Aboriginal communities in Arnhem Land, however, the incidence of this malignancy is more than 70 times the national Australian rate for the same age group. Previously, we found that neither excess HPV incidence nor a particularly virulent strain of HPV could explain the very high incidence of vulvar cancer in this population. Reports from the Gynaecology Outreach Service that cases appeared to cluster in family groups suggested that a genetic susceptibility, either to the effects of HPV or another cause of vulvar cancer, may be involved in this cluster.

To investigate the role of genetic risk factors, 30 cases and 61 controls, matched on age and community of residence, were recruited to the study. DNA was extracted from saliva samples, and genotyped using an Illumina HumanOmni BeadChip 2.5, providing information on approximately 2.5 million genetic variants. In addition, whole genomes were sequenced for 23 of the cases, including four siblings, and nine controls. We identified a set of variants shared by all four sibling cases and absent in all sequenced controls, and used these variants to identify genes of interest. These genes were then prioritised according to the total number of variant alleles found across all sequenced cases. Functional studies to further elucidate the roles of these genes in the aetiology of vulvar cancer are currently underway.

SESSION 4: FUNCTIONAL GENOMICS

CHAIRS: DR SEYHAN YAZAR & DR EVA CHAN

1545 – 1615

National Invited Speaker
ASSOCIATE PROFESSOR GREG NEELY
The University of Sydney

Greg Neely completed his PhD in human immunology at the University of Calgary, Canada and went on to train in conserved functional genomics at IMBA in Vienna, Austria. Since 2011, Greg have been running a lab in Sydney Australia using conserved functional genomics approaches to find novel human disease genes and pathways. Greg's main interest is in age-related diseases involving the nervous system, including pain, neurodegeneration, and strategies to extend lifespan while preserving overall health.

A GENOME-WIDE CRISPR-CAS9 KNOCKOUT SCREEN IDENTIFIES NOVEL ANTI-CANCER DRUG RESISTANT GENES

Raymond Man Tat Lau[1], **G. Gregory Neely**[1]

[1] Dr. John and Anne Chong Lab for Functional Genomics, Charles Perkins Centre and School of Life and Environmental Sciences, University of Sydney, Camperdown, NSW 2006, Australia

Cancer drug resistance is the most common cause of death in cancer patients. An understanding of the drug mechanism of action and identification of accurate resistance biomarkers is required to develop rational drug and personalized combinations. We have performed a genome-wide CRISPR/Cas9 knockout screen to identify genes involved in drug resistance for a panel of 29 anti-cancer drugs under clinical and preclinical investigation. Our efforts have identified a collection of known and novel genes whose loss-of-function mutations lead to cancer drug resistance. By comparing the molecular fingerprint of drug resistance for these anti-cancer drugs, and by classifying various drug resistance mechanisms at the molecular level, our work can have an important impact on new drug development and the design of the most effective combinational treatment strategies to cure cancer patients.

1615 – 1630

Invited Abstract (Early Career Researcher)

DR BRIAN GLOSS
Garvan Institute of Medical Research

Dr Gloss has been a postdoctoral researcher in the Genome Informatics research lab at the Garvan Institute under A/Prof Marcel Dinger since 2013. His research interests revolve around unravelling transcriptional complexity in health and disease. Dr Gloss is involved in a number of collaborative projects worldwide using existing and emerging transcriptomic technologies to answer key questions in normal development and disease processes.

HIGH RESOLUTION TEMPORAL TRANSCRIPTOMICS OF MOUSE EMBRYOID BODY DEVELOPMENT REVEALS COMPLEX EXPRESSION DYNAMICS OF CODING AND NONCODING LOCI

Brian S. Gloss[1,2], Bethany Signal[1,2], Seth W. Cheetham[3], Franziska Gruhl[4], Dominik Kaczorowski[1], Andrew C. Perkins[5], Marcel E. Dinger[1,2]

1 Garvan Institute of Medical Research, Sydney, Australia
2 St Vincents Clinical School, Faculty of Medicine, UNSW Australia, Sydney, Australia
3 The Gurdon Institute and Department of Physiology, Development, and Neuroscience, University of Cambridge, Cambridge, United Kingdom
4 Center for Integrative Genomics, University of Lausanne, Lausanne, Switzerland
5 Mater–UQ Research Institute, The University of Queensland, Translational Research Institute, Brisbane, Australia

Cellular responses to stimuli are rapid and continuous and yet the vast majority of investigations of transcriptional responses during developmental transitions typically use long interval time courses; limiting the available interpretive power. Moreover, such experiments typically focus on protein-coding transcripts, ignoring the important impact of long noncoding RNAs. We therefore evaluated coding and noncoding expression dynamics at unprecedented temporal resolution (6-hourly) in differentiating mouse embryonic stem cells and report new insight into molecular processes and genome organization. We present a highly resolved differentiation cascade that exhibits coding and noncoding transcriptional alterations, transcription factor network interactions and alternative splicing events, little of which can be resolved by long-interval developmental time-courses. We describe novel short lived and cycling patterns of gene expression and dissect temporally ordered gene expression changes in response to transcription factors. We elucidate patterns in gene co-expression across the genome, describe asynchronous transcription at bidirectional promoters and functionally annotate known and novel regulatory lncRNAs. These findings highlight the complex and dynamic molecular events underlying mammalian differentiation that can only be observed though a temporally resolved time course.

1630 – 1645

Invited Abstract

DR ANTHONY BORNEMAN
The Australian Wine Research Institute

Anthony obtained his PhD in Genetics from the University of Melbourne and then spent four years as a postdoctoral associate with Prof. Michael Snyder at Yale University, applying 'omics technologies to study gene networks in yeast.

Anthony is currently a Principle Research Scientist at the Australian Wine Research Institute and an Affiliate of the Department of Evolution and Genetics at the University of Adelaide. His research is focused on applying genomics, systems- and synthetic-biology to understand the genetic basis of phenotypic diversity in industrial microorganisms, with particular focus on the such as the wine yeasts Saccharomyces cerevisiae and Brettanomyces bruxellensis.

SURVIVAL OF THE FITTEST: THE FIGHT FOR DOMINANCE IN WINE FERMENTATION AND THE GENOMIC ADAPTATIONS THAT UNDERPIN YEAST STRAIN PERFORMANCE

Simon A. Schmidt[1], Radka Kolouchova[1], Jane McCarthy[1], Angus Forgan[1], **Anthony R. Borneman[1]**

[1] The Australian Wine Research Institute, Urrbrae, South Australia, 5064

The complex interaction between yeasts and their environment is brought sharply into focus when wine fermentations fail to complete. Retrospective analyses of such failures are difficult or impossible because of the many combinations of factors that may lead to this undesirable outcome. These factors include choice of yeast strain, of which there are many, grape juice composition and winemaker intervention. To begin to address this complex interplay between genetics and the environment, a multi-faceted genomics approach was adopted to elucidate the interactions between yeast strains and wine production.

A population genetic survey was performed by whole-genome sequencing over two hundred wine strains of the yeast Saccharomyces cerevisiae, which included both commercial and environmental isolates. Following this, a broadly representative set of ninety-four strains were selected and genomically-tagged with unique DNA barcodes to enable high-throughput functional profiling under competitive growth conditions. Competition experiments were used to evaluate differential fitness in response to environmental challenges enabling the parallel determination of fitness profiles in a range of industrially relevant conditions. While environmental variables such as sugar concentration and temperature were not discriminating factors of yeast strain fitness, levels of copper and nitrogen were powerful contributors to variations in fitness between wine yeast strains.

In order to elucidate the exact genetic determinants of copper tolerance that were observed in the wine yeasts strains, bulk segregant analysis was employed on different combinations of sensitive- and resistant parental strains. Pooled genome sequencing of the F1 progeny of these crosses has identified at least two major genetic loci that contribute to these differential responses to copper and which appear to have occurred as a secondary, suppressive response to an un-related adaptation to the wine environment.

1645 – 1700

Invited Abstract (Student)
MR MAINUL HASAN
University of Tasmania

I am a researcher having very good theoretical knowledge and hands-on experience in the field of molecular plant genetics. My current PhD project at the School of Biological Sciences, University of Tasmania involves functional characterization of two novel pea flowering mutants namely late3 and late4 which flower very late compared to the wild-type.

I completed my Masters in Agrobiotechnology from the Justus-Liebig University, Giessen, Germany in 2011. Prior to that, I studied Botany at the University of Dhaka, Bangladesh and gained B.Sc. (Honours) degree in 2007. After completing masters, I held different scientific positions at the Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany. During my scientific career in Germany, I dealt with different quality and resistant traits in cereals such as barley and wheat.

GENETIC AND MOLECULAR ANALYSIS OF TWO NEW LOCI CONTROLLING FLOWERING IN GARDEN PEA, PISUM SATIVUM.

A.S.M. Mainul Hasan[1], Valerie Hecht[1], Jacqueline K Vander Schoor[1], James L Weller[1]

[1] School of Biological Sciences, University of Tasmania, Hobart, Tasmania, Australia

Flowering is one of the key developmental process in the plant life cycle and is regulated by different environmental factors and endogenous cues. Isolation and characterization of mutants have been a key research strategy in order to identify genes responsible for flowering in agronomically important legume such as pea, Pisum sativum. This project investigates two novel EMS mutants in the background of cultivated pea line NGB5839 namely late3 and late4 that show extremely late flowering indicating that LATE3 and LATE4 are essential for normal promotion of flowering in pea. Through genetic map and candidate gene analysis, LATE3 and LATE4 genes have been identified as the orthologs of Arabidopsis thaliana Cyclin dependent kinase 8 (CDK8) and Cyclin C (CYCC1) respectively. Besides, we have determined alternative splicing and inferred alternative start codon as the genetic consequences of these mutations. Both CDK8 and CYCC1 are components of the CDK8 module of the eukaryotic mediator complex along with MED12 and MED13, which is known to regulate transcription of many genes. CDK8 module is crucial in maintaining optimum transcription level of such genes in living organisms. Expression analysis of key pea flowering genes such as various FTs have revealed that PsCDK8 and PsCYCC1 mediate expression of these genes which is the potential reason of late flowering phenotype in these mutants. Future experiments will test whether PsCDK8 and PsCYCC1 regulate responses to abiotic factors such as drought, salt stress, light, temperature. The nature of interaction between various components of the pea CDK8 module will also be investigated.

SESSION 5: SINGLE CELL 'OMICS AND GENOME ASSEMBLY

CHAIRS: DR NICHOLAS BLACKBURN & PROFESSOR VANESSA HAYES

0900 – 0945

Keynote Speaker
DR DEANNA CHURCH
10x Genomics

Dr. Deanna Church is currently the Senior Director of Applications at 10x Genomics. In this role, she leads a diverse group of scientists who are developing approaches for improved genome analysis, using Linked-Reads, as well as expanding the application space of single cell transcriptome profiling. Previously, she was Senior Director of Genomics and Content at Personalis, where she helped advance the field of genomics based clinical diagnostics. Prior to that, she was a staff scientist at NCBI, where she oversaw several projects concerning managing and displaying genomic data, including dbVar, a database of structural variation, the NCBI Variation Viewer, the NCBI Map Viewer, the Clone database and the NCBI Remap service. Dr. Church was also a founding member of the Genome Reference Consortium (GRC), an international group charged with improving the reference assembly for humans and other model organisms.

HIGH RESOLUTION BIOLOGY USING 10X

Reconstructing individual genomes and understanding the impact on biology remains a significant challenge. While large numbers of genomes and transcriptomes have been sequenced, the resulting resolution of these data remains insufficient for many applications. Traditional reference based, short-read analysis of genomes provides an incomplete picture of individual genome architecture. Likewise, while traditional transcriptomics has provided many biological insights, higher resolution data will allow for new information to be obtained. We have developed a high-throughput microfluidic system that addresses both areas.

For genomic applications, we partition limiting amounts of high molecular weight DNA such that unique bar codes can be added as part of library generation. This approach allows us to couple long-range information with high-throughput, accurate short read sequencing, generating a data type known as Linked-Reads. Coupling this novel datatype with new algorithms allows us to access a greater percentage of the genome as well as identify the full spectrum of variant types. Additionally, Linked-Reads enable de novo assembly with modest amounts of sequencing.

For transcriptomic applications, our microfluidics system partitions single cells and then barcodes their transcriptional content. This high resolution transcriptional profiling allows for the discrimination of discrete cell types from complex mixtures, allowing for the dissection of complex biological processes at high throughput. This opens up new applications for better discriminating immunological processes as well as understanding tumor micro-environment.

0945 – 1000

Invited Abstract (Early Career Researcher)
DR SEYHAN YAZAR
University of Edinburgh

Seyhan Yazar is a NHMRC Early Career Fellow in the MRC Human Genetics Unit with a specialisation in bioinformatics at the University of Edinburgh Institute of Genetics and Molecular Medicine. Seyhan studied Medical Sciences (Physiology and Pharmacology) at the University of New South Wales and completed a Masters of Orthoptics at the University of Sydney before undertaking her PhD studies with Prof David Mackey and A/Prof Alex Hewitt at the University of Western Australia. During her postdoctoral training, Seyhan investigated the genetic and environmental influences on eye disease development and progression. Seyhan was awarded a CJ Martin Early Career Fellowship from NHMRC in 2016 and joined the computational biology lab of Prof Colin Semple at the University of Edinburgh. Her current research interests include engineering high throughput sequence analysis pipelines and performing well-validated and reproducible computational research.

DE NOVO GENOME AND TRANSCRIPTOME ASSEMBLIES OF THE BARE-NOSED WOMBAT

Seyhan Yazar[1,2], Tamieka A Fraser[3,4], Alison Meynert[1], Adnan Moussalli[5], Jeremy J Austin[6], Janine Deakin[7], Alynn Martin[3], Sandy S Hung[8], David A Mackey[2], Oz Mammals Genomics Consortium, Anna J MacDonald[9], Adam Polkinghorne[4], Matthew A Brown[10], Martin Taylor[1], Colin Semple[1], Alex W Hewitt[7,11*], Scott Carver[3*]

1 Medical Research Council (MRC) Human Genetics Unit, Institute of Genetic and Molecular Medicine, University of Edinburgh, Edinburgh, United Kingdom
2 Centre for Ophthalmology and Visual Science, University of Western Australia, Perth, Western Australia, Australia
3 School of Biological Sciences, University of Tasmania, Hobart, Tasmania, Australia
4 Centre for Animal Health Innovation, Faculty of Science, Health, Education and Engineering, University of the Sunshine Coast, Sippy Downs, Queensland, Australia
5 Sciences Department, Museums Victoria, Carlton Gardens, Victoria, Australia
6 Australian Centre for Ancient DNA, School of Biological Sciences, University of Adelaide, Adelaide, South Australia, Australia
7 Institute for Applied Ecology, University of Canberra, Bruce, Australian Capital Territory, Australia
8 Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, Australia
9 Australian National University, Canberra, Australian Capital Territory, Australia
10 Institute for Health and Biomedical Innovation, Translational Research Institute, Queensland University of Technology, Brisbane, Australia
11 School of Medicine, Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia
* These authors contributed equally to this work.

Wombats are among Australia's most iconic marsupials. They represent the world's largest burrowing herbivores and are threatened by a range of processes, including disease, collision with motor vehicles and conflict with land holders. As part of the Oz Mammals Genomics Consortium, we have been working on de novo genome and transcriptome sequencing of the bare-nosed wombat (Vombatus ursinus). Our current datasets include deep Illumina HiSeq 4000 paired-end sequencing data (100x coverage), low-coverage Pacbio single-molecule real time (SMRT) sequencing data (5x) and RNA-seq data generated from six different tissues using Illumina HiSeq 4000 paired-end technology.

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Additional 10X Genomics microfluidics-based linked reads (56x) are currently being sequenced. Initial genome assembly was constructed using 385 Gbp (~82X) short-read data after quality filtering and error correction. The N50 size of the scaffolds is 62 kbp. The total length of all scaffolds is 3.8 Gbp, for a genome estimated to be 3.9 Gbp. Four transcriptome assemblies generated using a total of 862 million reads pooled from five of the six tissues with four different assemblers. A vast majority of the cleaned reads mapped back to each assembly and of those, 89-95% of the mapped fragments were mapped as proper pairs. We used the BUSCO (Benchmarking Universal Single-Copy Orthologs) library of Mammalian orthologous genes for quality assessment and recovered 87-95% of 4101 single-copy mammalian orthologs in four assemblies. A consensus set of unigenes of the four different methods is under construction in order to present as the final representative transcriptome assembly. This presentation will report the updated state of the genome and transcriptome assemblies and discuss assembly approaches applied to date using multiple platforms.

1000 – 1015

Invited Abstract
Dr David Gallego-Ortega
Garvan Institute of Medical Research

David completed his PhD in Biochemistry and Molecular Biology in 2008 at the Spanish National Research Council (CSIC), the largest research organization in Spain. After one year as Postdoctoral Scientist at Translational Cancer Drugs Pharma, a biotechnology company focused in oncology; he joined Professor Ormandy's lab at the Garvan Institute of Medical Research in 2009 to work in mouse models of mammary gland development and breast cancer, obtaining a National Breast Cancer and Cure Cancer Australia Foundation Postdoctoral Fellowship (2012 - 2015). In 2015, David established his own group at the Kinghorn Cancer Centre and he currently holds a Cancer Institute New South Wales Career Development Fellowship (2017-2019). David's group uses highly-parallel single cell RNAseq to study the mechanisms of tumour tolerance and progression driven by tumour infiltrated myeloid cell populations, with the overarching aim of identifying novel molecular targets for the development of immunotherapies.

MODELLING BREAST CANCER PROGRESSION USING MASSIVELY PARALLEL SINGLE-CELL RNA-SEQ TECHNOLOGY

Fatima Valdes-Mora[1,2], Robert Salomon[3], Brian Gloss[4,2], Daniel Roden[5], Yolanda Colino-Sanguino[1], Lesley Castillo[6], Andrew MK Law[6], Samantha R Oakes[5,2], Marcel Dinger[4,2], Christopher J Ormandy[5,2] and **David Gallego-Ortega**[6,2,#].

1 Histone Variants Laboratory, Genomics and Epigenetics Division, Garvan Institute of Medical Research. Sydney, NSW Australia.
2 St. Vincent's Clinical School, Faculty of Medicine, UNSW Sydney, NSW, Australia.
3 Garvan-Weizmann Centre for Cellular Genomics. Garvan Institute of Medical Research. Sydney, NSW, Australia.
4 Genome Informatics, Genomics and Epigenetics Division, Garvan Institute of Medical Research. Sydney, NSW Australia.
5 Cancer Biology Laboratory, Garvan Institute of Medical Research. Sydney, NSW Australia.
6 Tumour Development Laboratory, The Kinghorn Cancer Centre, Garvan Institute of Medical Research, Sydney, NSW Australia.
Corresponding author: d.gallego@garvan.org.au

Breast cancer is the most common malignancy in women, representing one-third of all diagnosed cancer cases and is the second leading cause of cancer-related mortality. Despite the success of targeted therapy for particular breast cancer subtypes, there are still ~1/3 of patients with very limited therapeutic options or who have acquired resistance to conventional treatment. Cancer cell diversity still constitutes a challenge for cancer treatment and deeply impact the outcome of cancer patients.

Transcriptome analysis has been extensively used to understand the heterogeneity of breast tumours, which defines intrinsic molecular subtypes and signatures able to predict response to therapy and patient outcome. This molecular phenotyping has fostered crucial therapeutic advances. A simultaneous overview of cancer cells and associated stromal cells is critical for the design of improved therapeutic regimes.

Single-cell RNA-seq has emerged as a powerful method to unravel heterogeneity of complex biological systems; this has enabled in vivo characterization of cell type compositions through unsupervised sampling and modelling of transcriptional states in single cells. Here we use the high-throughput microfluidic-based single-cell RNA-seq method Drop-seq to elucidate the function and cellular composition of breast tumours.

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We use the MMTV-PyMT mouse mammary tumour model to provide large-scale single-cell transcriptional landscapes of breast tumours that allows unprecedented understanding of breast heterogeneity and deep analysis of the events that result in cancer progression and acquisition of the metastatic disease.

scRNA-seq technology is generating a paradigm-shift in our understanding of biology, applied to tumour biology will lay the first stone for the development of more specific cancer therapies.

1015 – 1030

Invited Abstract (Student)
MRS NONA FARBEHI
University of New South Wales

Nona Farbehi is a third year PhD student at Graduate School of Biomedical Engineering, University of New South Wales (UNSW) and Victor Chang Cardiac Institute. She has completed her Bachelor of Science as an honour student at Research and Science University in Tehran in 2009 majoring Biomedical Engineering. Then she pursued her education towards MSc at Amirkabir University of Technology in biomedical Engineering and was awarded Master of Science in 2011. She was working as a research assistant at UPC in Spain for 1.5 years before she successfully got International Postgraduate Research Scholarship(IPRS) for following her desire towards getting PhD and joined Dr. Robert Nordon's and Richard Harvey's research group in 2014. Her thesis is about single-cell analysis of cardiac stromal and stem cells by applying different technologies and also fabricating novel microfluidics.

SINGLE CELL RNA-SEQ OF CARDIAC INTERSTITIAL CELLS REVEALS NOVEL POPULATIONS IN HEALTHY AND DISEASED HEART

Nona Farbehi[1,2], Ralph Patrick[1], Munira Xaymardan[3], Richard P Harvey[1], Robert E Nordon[2]

i) Developmental and Stem Cell Biology Division, Victor Chang Cardiac Research Institute, Sydney, NSW, Australia
[1] Graduate School of Biomedical Engineering, University of New South Wales, Sydney, Australia
[2] Bioengineering Unit, Department of Life Science, Faculty of Dentistry, University of Sydney, Sydney, Australia

Heart failure following myocardial infarction (MI) is in epidemic proportions and is set to increase. Congestive cardiac failure after MI is a big challenge due to the low level of cardiomyocyte (CM) regeneration after injury.

We hypothesise that Sca1+/PDGFRĐ+/CD31- cells(S+P+) which reside in cardiac interstitium, are analogous to Mesenchymal stem cell (MSCs) isolated from bone but have distinct origins and functionalities (Chong et al., 2011). We propose that they are dedicated to cardiac homeostasis and repair, acting as a reserve for multiple cell types, including smooth muscle cells, adipocytes, and possibly endothelial cells. They may also act as stress sensors to support CM and vascular tissue through dedicated paracrine functions.

To investigate activation of these cells during initial stages of inflammation after MI, single-cell RNA-seq(scRNA-Seq) was performed using GFP+/CD31- cell isolated from a mouse with a H2B-eGFP fusion gene knocked-in to the PDGFRĐ locus. The gene expression(GE) profiles of more than 26000 cells were analysed 3 and 7 days follow MI induce by coronary artery ligation, with identification different clusters across the whole cohort (sham versus coronary artery ligation). Two major differentiation pathways direct cells towards myofibroblast or smooth muscle cell fates. Gene ontology analysis suggests that Wnt signalling is involved in smooth muscle differentiation. scRNA-Seq analysis of freshly isolated S+P+ cells stimulated in vitro with PDGF and bFGF have myofibroblast GE signatures similar to those cells found in vivo following MI.

High content, single cell GE analysis provides extraordinary resolution of the cellular repair process. Our findings highlight the role of resident S+P+ as cardiac progenitor cells in healthy and diseased heart. S+P+ cells are activated following MI, providing a source of differentiated cell types and secretory functions required for cardiac repair. These molecular findings may identify new therapeutic approaches for preserving myocardial contractility following MI.

Reference: *Chong, J. J., Chandrakanthan, V., Xaymardan, M., Asli, N. S., Li, J., Ahmed, I., . . . Harvey, R. P. (2011). Adult cardiac-resident MSC-like stem cells with a proepicardial origin. Cell Stem Cell, 9(6), 527-540. doi:10.1016/j.stem.2011.10.002*

SESSION 6: SYNTHETIC BIOLOGY AND NOVEL TECHNOLOGIES

CHAIRS: DR BRIAN GLOSS & DR RICHARD TOTHILL

1100 – 1130

National Invited Speaker
PROFESSOR IAN PAULSEN
Macquarie University

Professor Ian Paulsen is a Distinguished Professor at Macquarie University and Deputy Director of the Macquarie Biomolecular Discovery and Design Centre. Ian is an ARC Laureate Fellow and an ISI Highly Cited Researcher with more than 250 publications. He received a PhD from Monash University and was an NHMRC C.J. Martin Fellow at the University of California at San Diego. He then took a faculty position at the Institute for Genomic Research (TIGR), where he led many microbial genome sequencing projects. Ian returned to Australia in 2007 as a Professor at Macquarie University and received a Life Science Research Award from the NSW Office of Science and Medical Research. He is the founder and Director of the new Synthetic Biology Laboratory at Macquarie University.

YEAST 2.0 AND BEYOND: BUILDING THE WORLD'S FIRST SYNTHETIC EUKARYOTE

Ian T. Paulsen and the Australian Yeast 2.0 team
Macquarie University

Yeast 2.0 is an international consortium aiming to build the world's first synthetic eukaryote by 2017. Systematic genome wide changes in the synthetic yeast include TAG/TAA stop-codon replacements, deletion of subtelomeric regions, introns, transfer RNAs, transposons, and insertion of loxPsym recombination sites. The Australian Yeast 2.0 team is responsible for the design and synthesis of synthetic versions of chromosomes 14 and 16. Construction is essentially complete at Macquarie, with 100% of the synthetic DNA successfully inserted. Troubleshooting and repairing errors identified through genome sequencing is currently ongoing. One of the most interesting features of Yeast 2.0 is the incorporation of the SCRaMbLE system for generating combinatorial genomic diversity through rearrangements at loxPsym recombination sites. This opens up the possibility of harnessing the SCRaMbLE system for adaptive laboratory evolution experiments. We have developed biosensors that respond to a variety of industrially useful metabolites, and are now seeking to use a combination of SCRaMbLE-ing and flow cytometry to identify strains that can produce higher levels of these metabolites.

1130 – 1145

Invited Abstract (Early Career Researcher)
DR MARTIN SMITH
Garvan Institute of Medical Research

KCCG's Genomic Technologies Group is headed by Dr Martin Smith, who has has 10+ year experience in bioinformatics and 3 years experience developing protocols and analytics for Oxford Nanopore (ONT) sequencing.

BIG DATA FROM A SMALL DEVICE: REAL TIME GENOMICS WITH NANOPORE SEQUENCING

Martin A. Smith[1], James Ferguson[1], Dennis Bunadi[1], Marcel Dinger[1], John Mattick[1]

[1] Kinghorn Centre for Clinical Genomics, Garvan Institute of Medical Research

Oxford Nanopore Technologies offer an affordable and portable sequencing platform that produces ultra long reads, and is capable of identifying epigenetic modifications in native molecules of DNA and RNA. On their own, these data can answer difficult questions in genome biology, but the technology offers more than long, native reads. Here, we elaborate on the real-time nature of nanopore sequencing, where biopolymer subsequences can be interrogated directly as they transit through the pore. To achieve this, we venture into 'squiggle space', a unique nanopore data format that precedes base calling. We describe how squiggles can be processed in real time to de-multiplex barcodes from single cell sequencing and perform transcriptome profiling on the fly. We envision that such real-time analyses will significantly improve turn around times in clinical settings.

1145 – 1200

Invited Abstract
DR. LONGQI LIU
BGI

Dr. Longqi Liu is currently a project leader at BGI. His research interest has focused on how genomic and environmental factors influence epigenome; and how the alterations of epigenome contribute to human diseases such as cancer. He leads a group of scientists who are working at developing bulk and single-cell epigenomic techniques on BGISEQ-500 sequencing platform and applying these approaches to large-scale epigenome-wide studies. He aims to identify key epigenomic signatures associated with specific diseases, where these signatures or their associated trans-factors could be developed as diagnostic biomarkers or therapeutic targets. Dr. Liu completed his Ph.D. in cell biology at Chinese Academy of Sciences, where he adopted epigenomic and transcriptomic approaches to systematically characterize the epigenetic roadblocks during reprogramming of somatic cells into induced pluripotent stem cells.

PARALLEL ASSAY OF SINGLE-CELL CHROMATIN ACCESSIBILITY AND TRANSCRIPTOME

Longqi LIU[1,2,4*], Chuanyu LIU[1,2,3*], Liang WU[1,2*], Yue YUAN[1,2,3], Mingyue WANG[1,2,3], Fang CHEN[1,2,6], Zhouchun SHANG[1,2,5#], Xun XU[1,2#]

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The advances of single cell sequencing technologies have greatly improved our understanding of heterogeneity in terms of genetic, epigenetic and transcriptional regulation within cell populations. We and other groups have developed single-cell whole genome, exome, methylome and transcriptome technologies and applied these approaches to analyzing the complexity of cell populations in tumorigenesis, developmental process and cellular reprogramming. Meanwhile, single-cell epigenome techniques including single cell ChIP-seq, ATAC-seq, DNase-seq and Hi-C, have been developed to decipher histone modifications, chromatin accessibility landscapes, and 3D chromatin contacts respectively in single cells. Integrative analysis of single-cell multimodal data is critical for accurate dissection of cell-to-cell variation within certain cell populations. Recent progress on measuring multi-omics in the same cells has enabled analysis of associations between different layers of regulation on gene expression. So far, the relationship between chromatin accessibility and gene expression has not been investigated at the resolution of one single cell. To address this question, we report scCAT-seq, a technique for simultaneous assay of chromatin accessibility and transcriptome within the same single cell. By applying scCAT-seq to different cancer cell types, we identified trans-factors as bridges linking accessibility variation of cis-regulatory elements to cell-type-specific gene expression across single cells. We further characterized subpopulations within cancer cells and uncovered the regulatory clues that drive transcriptional heterogeneity. Together, scCAT-seq is a promising tool for the joint analysis of multimodal data of single cells, which also offers the potential for clinical applications such as preimplantation screening and cancer diagnosis.

1200 – 1215

Invited Abstract (Student)
MR HAOJING SHAO
The University of Queensland

Haojing Shao completed his bachelor of computer science degree in South China University of Technology at 2010. After that, he worked as a bioinformaticist at Beijing Genomics Institute-Shenzhen from 2010 to 2014 for detecting and analysing indel and structural variations. He started his PhD in the Institute for Molecular Bioscience, The University of Queensland at 2014. His research interest is understanding the human genome from new sequencing technology.

ONGOING HUMAN CHROMOSOME END EXTENSION DRIVEN BY A PRIMATE ANCESTRAL GENOMIC REGION REVEALED BY ANALYSIS OF BIONANO AND NANOPORE GENOMICS DATA

Haojing Shao[1], Chenxi Zhou[1], Minh Duc Cao[1], Lachlan Coin[1]

[1] Institute for Molecular Bioscience, University of Queensland, St Lucia, Brisbane, QLD 4072 Australia

The majority of human chromosome ends remain incomplete due to their highly repetitive structure. In this study, we use BioNano data to anchor and extend chromosome ends from two European trios as well as two unrelated Asian genomes. Two thirds of BioNano assembled chromosome ends are structurally divergent from the reference genome, including both deletions and extensions. These extensions are heritable and in some cases divergent between Asian and European samples. We used long-read nanopore sequence data to validate and fill a 40kb extension sequence on 15q as well as a 10kb sequence on 20p. We identified two sequence families in these extension sequences which have undergone substantial duplication in multiple primate lineages, leading to the formation of new fusion genes. We show that these sequence families have arisen from progenitor interstitial sequence on the ancestral primate chromosome 7. We also identified ancient chromosome ends as subtelomeric interstitial telomere sequences. Comparison of chromosome end sequences from 15 species revealed that chromosome end divergence matches the corresponding phylogenetic relationship and revealed a rate of chromosome extension since the primate divergence of approximately 0.1 bp per year.

SESSION 7: BIOINFORMATICS AND DATA ANALYTICS

CHAIRS: DR KAITAO LAI & DR MATTHEW WAKEFIELD

1315 - 1400

Keynote Speaker
DR PAULINE NG
Explorer and Consultant

Pauline Ng has over 15 years experience in bioinformatics and published over 30 publications with over 10,000 citations. Dr. Ng has developed applied health algorithms for predicting disease mutations such as SIFT. She also designed the content for Illumina's Infinium genotyping microarrays, which are used in the majority of genome-wide association studies. Dr. Ng was an Assistant Professor at J. Craig Venter Institute where she published the first sequenced individual human genome (Craig Venter's) and critiqued personalized genetics companies such as 23andMe. She was a Group Leader ot Genome Institute of Singapore and CIO of its POLARIS program to establish the first CAP-certified NGS lab in Southeast Asia. Dr. Ng is currently an independent consultant.

MUTATIONS THAT MATTER

Much research is conducted and trained on humans. How do we find the mutations that matter? In this talk, I will describe multiple approaches for finding variation that causes phenotypic changes. 1) The SIFT algorithm predicts on missense (nonsynonymous) variants has now been extended to all organisms so that their phenotype-genotype relationships can be explored. SIFT For Genomes will help in agricultural applications. 2) For rare disorders, we have developed Phen-Gen. Phen-Gen can be applied to whole human genomes to find putative causative variants. 3) Finally, we can use the data that is being amassed to distinguish disease mutations from benign variation. I will discuss a federated database-sharing platform so that clinical and proprietary data can be shared.

1400 – 1415

Invited Abstract
DR THOM QUINN
Deakin University

While studying medicine at S.U.N.Y. Upstate in Syracuse, New York, Thom discovered his passion for data. After completing his MD, he joined the Bioinformatics Core Team at Deakin University in Geelong, Australia to pursue a PhD in Bioinformatics. He is primarily interested in learning the best computational methods for disentangling the role of the regulome in human disease through the analysis of high-throughput genomic data. He hopes these insights will someday contribute to advances in medical diagnostics, prognostics, and therapeutics.

A COMPOSITIONALLY VALID PIPELINE FOR ANY-OMICS DATA

Thom Quinn[1], Mark Richardson[1], David Lovell[2], Tamsyn Crowley[1]

[1] Bioinformatics Core Research Facility, Deakin University, Waurn Ponds, Victoria, Australia
[2] Queensland University of Technology, Brisbane, Australia

Correlation is a commonly used method for measuring the association between genomic elements. However, correlation yields spurious (i.e., falsely positive) results when applied to relative data. In contrast to absolute data, relative data only carry meaning proportionally (i.e., [50, 100] is the same as [500, 1000]). Common examples of relative data include anything measured in percent, but can also include biological data sets produced by high-throughput RNA-sequencing, 16S rRNA sequencing, chromatin immunoprecipitation (ChIP), ChIP-sequencing, or Methyl-Capture sequencing. Here, we present propr: an R package implementation of proportionality analysis that provides a valid alternative to correlation that is suitable for any and all data sets. Unlike correlation, proportionality yields the same result for relative data as its absolute counter-part, all without generating spurious results. We show how propr can fit within a larger -omics pipeline to enrich the findings of conventional differential expression analysis. We place specific emphasis on combining the ALDEx2 and propr packages to establish a workflow for differential co-expression analysis that works for any and all -omics data.

1415 – 1430

Invited Abstract (Early Career Researcher)
DR LAURENCE WILSON
CSIRO

Laurence Wilson is a postdoctoral fellow in the Transformational Bioinformatics team, working under Dr. Denis Bauer. His focus lies in computational genome engineering, machine learning, BigData approaches and Cloud Computing.

He received a PhD in Bioinformatics from the Australian National University and undertook Postdoctoral training at the Institut Curie in Paris, focussing on how chromatin dynamics influence cancer progress and weather this information can be leveraged to inform patient treatment decisions.

Laurence's current research focuses on designing computational tools to assist in genome editing applications, focusing primarily on the CRISPR-Cas9 system.

USING MACHINE LEARNING TO UNDERSTAND CRISPR-CAS9 ACTIVITY

Laurence Wilson[1], Aidan O'Brian[1], Robert Dunne[2], Oscar Luo[1], Denis Bauer[1]

[1] CSIRO, Sydney, NSW, Australia
[2] CSIRO, Data 61, North Ryde Sydney

The CRISPR-Cas9 system is one of the most widely utilized genome editing mechanism, allowing the precise targeting of specific genomic loci and has the potential for application in human health. However, the reliable application of the technology requires the identification of the optimal target site as activity can vary substantially between sites. This is currently hampered by our understanding of what factors influence the activity of CRISPR-Cas9.

We analyse over 7500 target sites from 4 studies using a machine learning approach to systematically investigate which factors influence CRISPR-Cas9 activity. Our results identify sequencing-based assays as the most accurate in measuring CRISPR-Cas9 core activity as models trained on this data are predictive across a wide range of differing dataset. From this generalized model, we identify novel sequence features modulating activity. Interestingly, in contrast to what has been reported previously, we also find that histone modifications associated with open chromatin are depleted at high activity target sites. Consistent with this we find that highly transcribed genes, which are typically located in open chromatin regions, are less amenable to CRISPR-Cas9 editing. Suggesting that PolII elongation speed may modulate CRISPR-Cas9 kinetics. Incorporating these novel findings into a predictive model increases accuracy relative to other public models by 30% in cross-validation and up to 15% when tested on an independent datasets.

1430 – 1445

Invited Abstract
DR SUSAN CORLEY
University of New South Wales

Susan graduated with a BSc (Hons) from the University of Sydney in 2005 and then completed her PhD in computational structural biology at the ANU. She joined the Systems Biology Initiative at UNSW in 2012 and has worked on transcriptomic analysis of mammalian tissue in conditions such as schizophrenia, Williams-Beuren syndrome and kerataconus as well as working more generally with high throughput sequencing data.

FUNCTIONAL INSIGHTS FROM RNA-SEQ ARE AFFECTED BY DECISIONS MADE EARLY IN THE EXPERIMENTAL DESIGN, LIBRARY PREPARATION AND SEQUENCING PROTOCOL

Susan M. Corley[1], Marc R. Wilkins[2]

[1] Systems Biology Initiative, School of Biotechnology and Biomolecular Sciences, UNSW Australia, Sydney, New South Wales, Australia

Technical advances in next generation sequencing have resulted in greater output of sequence data, and at a lower cost. This has resulted in the widespread uptake of techniques such as RNA-Seq. With more researchers undertaking transcriptomic analyses, questions arise as to the most accurate and cost efficient way of doing this. Choices must be made whether to use paired-end or single-end sequencing, and whether to use strand-specific or non-specific library preparation kits. Of most importance is whether these choices affect the functional insights that are generated from the resulting data. To better understand the effect of these choices we performed four mammalian transcriptomics experiments and compared the effect of read mapping, feature counting and differential expression analysis using single-end (SE) and paired-end (PE) protocols. For three of these experiments we also compared a non-stranded (NS) and a strand-specific approach to mapping the paired-end data. We found that errors in read counts will occur from use of single-end or non-stranded sequencing, and lead to false negatives and false positives in the analysis of differentially expressed genes. This can and will affect downstream analysis, including in functional GO enrichment analysis. Ultimately, this can affect the biological interpretation of results. At the same time it must be borne in mind that using SE mapping reduces the sequencing cost and that this saving could be used to increase the number of biological replicates. This will increase the power of an experiment, and may be a desirable trade-off.

SESSION 8: EPIGENETICS AND TRANSCRIPTOMICS

CHAIRS: DR HALOOM RAFEHI & ASSOCIATE PROFESSOR ALICIA OSHLACK

1545 – 1615

National Invited Speaker
DR PAUL WATERS
University of New South Wales

Paul's research centres on better understanding epigenetic regulation of transcription in diverse vertebrate representatives, specifically focussing on sex chromosomes dosage compensation. The ultimate goal is to understand how complex epigenetic silencing mechanisms evolved. During his PhD Paul focused on the gene content and evolution of marsupial Y chromosomes, and throughout his first postdoc in South Africa he focused on the genomics of Afrotheria (basal eutherian mammals; which include elephant, aardvarks, etc.).

He was awarded an ARC discovery project to further explore the epigenetics of vertebrate dosage compensation. The next stage of vertebrate genomics and epigenetics for his group involves much use of short read sequencing technologies.

Paul is currently examining dosage compensation in phylogenetically informative vertebrate taxa. He uses ChIP-Seq to understand the chromatin modifications associated with vertebrate dosage compensation, and has also used RRBS to examine the landscape of DNA methylation in the X chromosome in marsupials.

SEX SPECIFIC LANDSCAPES OF DNA METHYLATION ON THE MARSUPIAL X CHROMOSOME: THE SHAPE OF SILENCING

Shafagh A Waters[1], Alexandra M Livernois[2], Hardip Patel[3], Denis O'Meally[4], **Paul D Waters**[1]

[1] School of Biotechnology & Biomolecular Sciences, Faculty of Science, University of New South Wales, Sydney, NSW, Australia
[2] Institute for Applied Ecology, University of Canberra, Canberra, ACT, Australia
[3] John Curtin School of Medical Research, Australian National University, Canberra, ACT, Australia
[4] Center for Gene Therapy, Beckman Research Institute of the City of Hope, Duarte, CA, USA

X chromosome inactivation is the transcriptional silencing of one X chromosome in the somatic cells of females. In eutherian mammals (eg. human and mouse), gene promoters are hypermethylated, which is a late, stabilizing step that maintains transcriptional silence on the inactive X. Contrasting eutherian mammals, analysis of single loci in marsupial models has demonstrated that there was no differential DNA methylation of promoters between the sexes. This had led to the long-standing hypothesis that DNA methylation plays no role in marsupial X-inactivation.

Using reduced representation bisulfite sequencing, we examined the male and female DNA methylation landscape in a marsupial model (grey short-tailed opossum). In contrast to mouse, there was no differential DNA methylation between the males and females at transcription start sites of genes subject to X-inactivation in opossum. Surprisingly, regions that flanked tehse transcription start sites of these genes were hypomethylated in females, "flattening" the DNA methylation profile. This is the first observation of non-random hypomethylation on the X in a female marsupial model, which we propose acts as a silencing signal during X inactivation.

1615 – 1630

Invited Abstract
DR OSCAR LUO
CSIRO

I am a Research Scientist at CSIRO specialise in Bioinformatics and Genomics. Prior to joining CSIRO, I did my Postdoc at The Jackson Laboratory for Genomic Medicine in Dr. Yijun Ruan's lab.

RNA-CHROMATIN INTERACTOME REVEALS NCRNA FUNCTIONS FOR TRANSCRIPTION REGULATION AND GENOME ORGANIZATION

Oscar J. Luo[1]

[1] Transformational Bioinformatics, Health & Biosecurity, CSIRO

Noncoding RNAs (ncRNAs) are an emerging class of regulatory molecules with a broad range of regulatory functions believed to be mediated by ncRNA-chromatin interactions. Genome-wide understanding of ncRNA functions requires precise mapping of all ncRNAs and their target loci. Current methods for studying chromatin-associated ncRNA lack specificity or are limited to singly assessing ncRNAs. To overcome this limitation, we devised an unbiased strategy to identify all RNA Interactions with Chromatin by Paired-End-Taging (RICh-PET), and applied this approach to characterize the Drosophila RNA-chromatin interactome. We discovered that ncRNAs primarily target to promoters and enhancers in open chromatin regions, and are highly co-localized with RNAPII and other TFs, suggesting combinatorial yet specific regulatory instructions for each chromatin locus. Enzymatic nuclear perturbation by RNase-A digestion of single-stranded RNA molecules and followed by examination of individual chromatin loci indicated that ncRNAs collectively help maintain chromatin accessibility, facilitate RNAPII-mediated long-range interactions, and participate in the overall 3D genome organization. Our study demonstrates that RICh-PET and related methods represent a powerful suite of tools to interrogate the genome biology of ncRNAs.

1630 – 1645

Invited Abstract (Student)
MR SIMON HARDWICK
Garvan Institute of Medical Research

Simon A. Hardwick is a PhD student at the Garvan Institute of Medical Research and the University of NSW, in Sydney, Australia. He graduated from Macquarie University, with a combined Science/Law degree, receiving the University Medal for Biology. He then practised commercial law for several years, specialising in intellectual property cases, before commencing his postgraduate studies in 2015. His research involves developing spike-in controls for next-generation sequencing and applying targeted RNA-sequencing to characterise non-coding transcription in the brain.

SPLICED SYNTHETIC GENES AS INTERNAL CONTROLS IN RNA-SEQ EXPERIMENTS

Simon A. Hardwick[1,2], Wendy Y. Chen[1,2], Ted Wong[1], James Blackburn[1,2], Lars K. Nielsen[3], John S. Mattick[1,2] & Tim R. Mercer[1,2]

1 Genomics & Epigenetics Division, Garvan Institute of Medical Research, Sydney NSW 2010, Australia.
2 Faculty of Medicine, University of NSW, Sydney NSW 2010, Australia.
3 Australian Institute for Bioengineering & Nanotechnology, University of Queensland, Brisbane QLD 4072, Australia.

RNA sequencing (RNA-seq) can be used to assemble spliced isoforms, quantify expressed genes and provide a global profile of the transcriptome. However, the size and diversity of the transcriptome, the wide dynamic range in gene expression and inherent technical biases confound RNA-seq analysis. We have developed a set of spike-in RNA standards, termed 'sequins' (sequencing spike-ins), that represent full-length spliced mRNA isoforms. Sequins have an entirely artificial sequence with no homology to natural reference genomes, but they align to gene loci encoded on an artificial in silico chromosome. The combination of multiple sequins across a range of concentrations emulates alternative splicing and differential gene expression, and it provides scaling factors for normalization between samples. We demonstrate the use of sequins in RNA-seq experiments to measure sample-specific biases and determine the limits of reliable transcript assembly and quantification in accompanying human RNA samples. In addition, we have designed a complementary set of sequins that represent fusion genes arising from rearrangements of the in silico chromosome to aid in cancer diagnosis. RNA sequins provide a qualitative and quantitative reference with which to navigate the complexity of the human transcriptome.

1645 – 1700

Invited Abstract

DR IRENE GALLEGO ROMERO
The University of Melbourne

Irene Gallego Romero is a Lecturer in Systems Biology at the Centre for Systems Genomics in the University of Melbourne. She can be found on twitter at @ee_reh_neh.

DYNAMICS OF CHROMATIN ACCESSIBILITY AND TRANSCRIPTION FACTOR BINDING IN HUMAN AND CHIMPANZEE PLURIPOTENT STEM CELLS

Irene Gallego Romero[1], Shyam Gopalakrishnan[2], Yoav Gilad[3]

[1] Centre for Systems Genomics, University of Melbourne
[2] Natural History Museum of Denmark, University of Copenhagen
[3] Department of Human Genetics, University of Chicago

Many human-specific traits have long been hypothesised to be driven by gene regulatory differences between ourselves and our close evolutionary relatives. To test this hypothesis we have generated maps of genome-wide chromatin accessibility using ATAC-seq in induced pluripotent stem cell (iPSC) lines derived from 6 humans and 7 chimpanzees (Pan troglodytes, our closest living relative), and quantified patterns of transcription factor (TF) binding activity in nearly 315 million putative sites across 632 different TFs. As expected, we find that sharing of chromatin accessibility patterns between the two species is strongest near well-conserved orthologous transcription start sites (orthoTSS, r2 = 0.949), and decreases with distance from orthoTSS. Combining these results with RNA-sequencing data from the same cell lines we find that significant inter-species differences in chromatin accessibility near orthoTSS occur more often than expected at differentially expressed genes ($p < 10\text{-}5$). Similarly, when we focus on transcription factor binding patterns in the two species, we find that TF binding sites most likely to be bound in both species are preferentially located close to orthoTSS and tend to have high position weight matrix scores ($p < 2.2*10\text{-}16$). We additionally find that turnover in binding site sequence has a significant effect on transcription factor binding dynamics between the two species. Taken together, our results indicate that changes in chromatin accessibility and transcription factor activity are a likely gene regulatory mechanism through which human-specific traits can arise.

SESSION 9: COMPARATIVE GENOMICS

CHAIRS: DR QUENTIN GOUIL & DR IRENE GALLEGO ROMERO

0900 – 0930

National Invited Speaker
DR AUSTEN GANLEY
University of Auckland

Austen Ganley is a Senior Lecturer in the School of Biological Sciences at University of Auckland. He has wide-ranging interests in genomics, and his work is characterised by the development of novel techniques to address fundamental questions in biology. He is an internationally recognised expert in the genomics of the ribosomal RNA gene repeats in eukaryotes, where he has made seminal advances in the relationship between transcription and recombination, and in the evolutionary dynamics of the ribosomal RNA gene repeats. His research involves a combination of bioinformatics and experimental approaches, and uses a variety of model systems, including yeast, filamentous fungi and mammalian systems.

REPETITIVE DNA: EVOLVING SAFELY IN NUMBERS

Austen R. D. Ganley[1]

[1] School of Biological Sciences, University of Auckland, Auckland, New Zealand

Repeats are persona non grata in the genomic world. They are often conflated with "junk" DNA and actively discriminated against using systems such as repeatmasker. Yet, repeats are incredibly diverse, abundant, and important contributors to eukaryote genomes. Stunning developments in sequencing depth and length over the past decade are making many of the "problems" associated with repeats in genomic datasets obsolete. These developments mean we are now in a position to start taking repeats out of the "black box", and to exploit genomic tools to develop deep insights into the nature of repetitive DNA. Here I will present a novel, general framework for characterizing repeat evolution as a contribution to this goal. I will illustrate this framework with repeat families showing different evolutionary patterns. This work shows how the same molecular processes can interact with selection to produce strikingly different evolutionary outcomes, and how these outcomes can suggest hypotheses for the roles of these repeats. Finally, this work will also highlight important aspects of repeat evolution where our understanding remains limited, and that would benefit from further investigation.

0930 – 0945

Invited Abstract

DR ANNA MACDONALD
Australian National University

Dr Anna MacDonald is the project coordinator for the Oz Mammals Genomics Initiative. Anna's research interests are at the interface between genetics, ecology and evolution, with a focus on the application of genetic and genomic tools to conservation and wildlife management.

THE OZ MAMMALS GENOMICS INITIATIVE: MAMMAL GENOMICS, EVOLUTION AND CONSERVATION AT A CONTINENTAL SCALE

Anna J MacDonald[1], Margaret Byrne[2], Janine Deakin[3], Mark Eldridge[4], Anna Fitzgerald[5], Rebecca Johnson[4], Stephanie Palmer[1], Andrew Young[6], Craig Moritz[1], the Oz Mammals Genomics Consortium

1 Australian National University, Canberra, Australian Capital Territory, Australia
2 Department of Parks and Wildlife, Kensington, Western Australia, Australia
3 University of Canberra, Canberra, Australian Capital Territory, Australia
4 Australian Museum, Sydney, New South Wales, Australia
5 Bioplatforms Australia, Sydney, New South Wales, Australia
6 National Research Collections Australia, CSIRO, Canberra, Australian Capital Territory, Australia

The Australo-Papuan region has a unique mammal fauna, which faces unique threats and poses important evolutionary and ecological questions. Genomics has great potential to advance our understanding of the region's terrestrial mammals and their conservation. The Oz Mammals Genomics Consortium brings together museums, researchers, data specialists and wildlife management agencies to comprehensively tackle mammal genomics at a continental scale and at three different levels of resolution.

There are few published genomes for Australian marsupials. We are developing well-assembled genomes from a broadly representative range of marsupial taxa, to facilitate new insights into evolution and to provide reference data for conservation studies. Genome projects are now underway for eight priority species: the fat-tailed dunnart, brush-tailed rock-wallaby, eastern bettong, mountain pygmy possum, Leadbeater's possum, common brushtail possum, bare-nosed wombat and eastern barred bandicoot.

Our current understanding of evolutionary relationships among many mammal taxa remains incomplete. To improve resolution of genus and species boundaries we are generating comprehensive phylogenies of all extant and recently-extinct terrestrial mammals native to the Australo-Papuan region. We are using exon capture methods to sequence over 1000 genes from around 500 taxa, including marsupials, rodents and bats.

Finally, the availability of reference genomes and phylogenies will provide a solid base for population-level studies. We will develop conservation genomic datasets for a selection of threatened mammal species. Using genome scanning methods we will measure genetic diversity and inbreeding, determine population structures, and identify adaptive variation. Species will be prioritised so that genomic data will contribute directly to urgent conservation management decisions.

0945 – 1000

Invited Abstract

PROFESSOR JUSTIN BOREVITZ
Australian National University

PhD 2002 UCSD
postdoc 2004 Salk
AsProf 2010 UChicago
Prof 2014 ANU

Plant Genomics and Phenomics for Climate Adaptation

POPULATION STRUCTURE OF THE BRACHYPODIUM SPECIES COMPLEX AND GENOME WIDE DISSECTION OF AGRONOMIC TRAITS IN RESPONSE TO CLIMATE.

Pip Wilson, Jared Streich, Steve Eichten, Riyan Cheng, Kevin Murray, Niccy Aitkin, Norman Warthmann, Accession Contributors, **Justin Borevitz**

1 Australian National University

The development of model systems requires a detailed assessment of standing genetic variation across natural populations. The Brachypodium species complex has been promoted as a new plant model for grass genomics with translational to small grain and energy crops. To capture the global genetic diversity within this species complex, thousands of Brachypodium accessions from around the globe were collected and sequenced using genotyping by sequencing (GBS). Samples were initially separated into two diploid or allopolyploid species defining overlapping and invasive ranges and climate niches. A core set of high diversity B. distachyon diploid lines were selected for whole genome sequencing and high resolution phenotyping. Genome-wide association studies was used to identify candidate genes and pathways tied to key fitness and agronomic related traits. A total of 9, 22 and 47 QTLs were identified for flowering time, early vigour and energy traits, respectively. Overall, the results highlight the genomic structure of the species complex and allow powerful complex trait dissection within an emerging model species.

1000 – 1015

Invited Abstract (Early Career Researcher)
DR WEERACHAI JARATLERDSIRI
Garvan Institute of Medical Research

Weerachai completed PhD at the University of Sydney in 2014, focusing on comparative genomics using whole genome sequencing technologies. As an early career researcher, he aims to utilise his proven skills for the advancement of cancer genomics and personalised medicine and has keen interests in the following areas: i) identification of modifiable cancer risk factors to reduce the incidence of cancer; ii) the discovery of biomarkers for earlier detection of cancers; and iii) clinical correlations of the risk factors and biomarkers that can improve cancer outcomes and foster translational cancer research.

IDENTIFYING RACIAL DIFFERENCES IN THE MUTATIONAL LANDSCAPE OF AGGRESSIVE PROSTATE CANCER

Weerachai Jaratlerdsiri[1], Desiree C. Petersen[1,2], Eva K. F. Chan[1,2], Riana Bornman[3], Vanessa M. Hayes[1,2,3,4]

[1] Laboratory for Human Comparative and Prostate Cancer Genomics, Genomics and Epigenetics Division, Garvan Institute of Medical Research, Darlinghurst, NSW, Australia
[2] St Vincent's Clinical School, University of New South Wales, Randwick, NSW, Australia
[3] School of Health Systems and Public Health, University of Pretoria, Pretoria, South Africa
[4] Central Clinical School, University of Sydney, Camperdown, NSW, Australia

African American men are more likely to die from prostate cancer than any other population (2.4- or 5-fold greater than Europeans or Asians, respectively). With no known environmental drivers, this disparity is hypothesised to come from an African ancestral genetic risk upon which somatic mutations drive aggressive disease. However, studies within Africa are lacking. This is the first study using deep whole-genome sequencing of tumour-normal pairs to profile genomic hallmarks of aggressive prostate cancer within six African men. While prostate cancer risk profiling using largely European-derived candidate alleles proved uninformative, we observed significant differences in somatic variation. From 227,289 small somatic mutations, range 9,275 to 169,542 per genome, we describe the most hypermutated prostate tumour to date (14 mutations per Mb). Comparative analyses showed a significant increase in oncogenic driver mutations in men of African versus European ancestry (P-value < 1.84 e-03), yet large genomic rearrangements, especially megabase-sized deletions, are more common in men of European ancestry. The latter included a notable absence of TMPRRSS2-ERG gene fusions in African men. We identified recurrent mutations in 14 putative oncogenes. Clone phylogenetic inference suggested most of these small mutations accumulated at the clonal stage of evolution where all cancer cells were altered (P-value = 9.09e-4). Overall we demonstrate that men of African ancestry are more likely to present with uniquely African mutational signatures. Unlike those common to the majority of European men, with a tendency to be associated with the failure of DNA mismatch repair response, the uniquely African mutational signatures identified are of unknown cause. This study identifies not only a greater burden of small oncogenic drivers in African men with aggressive prostate cancer but suggests a unique as yet unknown cause may be driving the significant racial disparity in disease outcomes.

SESSION 10: GENE EDITING AND GENE REGULATION

CHAIRS: DR BENNET MCCOMISH & ASSOCIATE PROFESSOR NICOLE CLOONAN

1045 – 1115

National Invited Speaker
ASSOCIATE PROFESSOR ALICE PÉBAY
The University of Melbourne

Associate Professor Pébay obtained her PhD in Neurosciences from the University of Paris VI in 2001 and subsequently joined Professor Martin Pera at Monash University to undertake research on human embryonic stem cells (hESC). She then continued her research in this area at the University of Melbourne where she commenced in 2007. Since 2012, Associate Professor Pébay has been appointed to both the Centre for Eye Research Australia and The University of Melbourne. She was a NHMRC Career Development Fellow and is currently supported by an ARC Future Fellowship.

Associate Professor Pébay is the primary inventor of 3 international patents related to stem cell technology. She has published over 70 manuscripts and edited 4 books.

Her research focuses on the use of human induced pluripotent stem cells to model neurodegeneration, including of the retina.

AUTOMATED CULTURE SYSTEM FOR LARGE SCALE DISEASE MODELLING

Induced pluripotent stem cells (iPSCs) generated from somatic cells can be differentiated into specific cell types of interest, as well as into three dimensional cultures of self-organized neural tissue. Together with these recent advances in gene editing technologies, patient-derived iPSCs represent a powerful disease-modeling tool. We established and optimized protocols for the semi-automated reprogramming of human induced pluripotent stem cells (iPSCs), their automated maintenance and differentiation to neural cells for large-scale disease modelling. Our approach using an automated platform shows the advantage of increasing sample size and reducing variability during reprogramming and differentiation.Combining with gene editing technologies, our set-up facilitates the study of complex diseases using iPSCs, including of glaucoma.

1115 – 1130

Invited Abstract (Early Career Researcher)
DR QUENTIN GOUIL
Walter and Eliza Hall Institute of Medical Research

I am interested in genomics and epigenetics. During my PhD I investigated an epigenetic drive known as paramutation, using tomato as a model. I also looked into pathways of DNA methylation in plants. At La Trobe I explored the regulatory networks governing seed germination. I am now pursuing epigenetic research in mammals, with an interest in long read sequencing technologies.

EXTENSIVE TRANSCRIPTOMIC AND EPIGENOMIC REMODELING DURING ARABIDOPSIS THALIANA GERMINATION

Quentin Gouil[1,2,+], Reena Narsai[2,+], David Secco[3], Akanksha Srivastava[3], Yuliya V. Karpievitch[3,4], Ryan Lister[3,4], Mathew G. Lewsey[2], James Whelan[2]

[1] The Walter and Eliza Hall Institute of Medical Research, Parkville VIC, Australia
[2] Department of Animal, Plant and Soil Sciences, School of Life Sciences, La Trobe University, Bundoora VIC, Australia
[3] ARC Centre of Excellence in Plant Energy Biology, The University of Western Australia, Perth WA, Australia
[4] Harry Perkins Institute of Medical Research, Perth WA, Australia
[+] these authors contributed equallly

Seed germination is a developmental progression from complete metabolic dormancy to a highly active, growing seedling. Many factors regulate germination and successful seedling establishment, including environmental sensing, hormone signalling and transcription factor (TF) activity. These interact extensively with one-another, forming a complex network of inputs that control the seed-to-seedling transition. Our understanding of the direct regulation of gene expression on a genome-wide scale during germination is currently limited, as is our knowledge of the dynamic changes in the epigenome and small RNAs (sRNAs). The interactions between genome, transcriptome and epigenome must be revealed in order to identify the regulatory mechanisms that control seed germination.

We present an integrated analysis of high resolution RNA-seq, sRNA-seq and MethylC-seq over 10 time points in Arabidopsis thaliana: from fresh seed, through ripened seed, dark stratification, to germination and post-germination (48 h post-stratification). Extensive transcriptomic and epigenomic transformations were associated with seed germination. We identified previously unannotated loci from which mRNAs are expressed transiently during germination. We also identified widespread alternative splicing and divergent isoform abundance, particularly of genes themselves involved in RNA processing and splicing. These data were integrated to generate the first dynamic transcription factor (TF) network model of germination, which identified known and novel regulatory factors. Expression of both micro-RNA (miRNA) and short-interfering RNA (siRNA) loci changed significantly during germination, particularly between the seed and the post-germinative seedling. These were associated with changes in gene expression and large-scale demethylation observed towards the end of germination, as the epigenome transitions from an embryo-like to a vegetative seedling state. This study reveals the complex dynamics and interactions of the epigenome, transcriptome, sRNAs and TFs during seed germination. This is a necessary step towards a comprehensive regulatory model of the seed-to-seedling transition and its exploitation in plant breeding.

1130 – 1145

Invited Abstract

MR AIDAN O'BRIEN
Australian National University

Aidan O'Brien graduated from the University of Queensland with a Bachelor of Biotechnology (1st class honours) in 2013. With Dr. Timothy Bailey as his honours supervisor, he developed GT-Scan, a CRISPR target predictor. Aidan then started at CSIRO with the transformational bioinformatics team, where he developed VariantSpark, which applies BigData machine learning algorithms to genomic data. Aidan has 4 journal publications (3 first author) with 54 citations (h-index 3). He received the "Best student and postdoc" award at CSIRO in 2015 and attracted $180K in funding to date as AI. Aidan has now started his PhD in the field of genome editing at the Australian National University.

PREDICTING THE HDR EFFICIENCY OF CRISPR-CAS

Aidan O'Brien[1], Nikki Ross[2], Jenna Lowe[2], Jing Gao[2], Nay-Chi Khin[2], Gaetan Burgio[2], Denis Bauer[1]

[1] CSIRO, Sydney, NSW, Australia
[2] Department of Immunology and Infectious diseases, The John Curtin School of Medical Research, The Australian National University.

The CRISPR-Cas system impacts many scientific fields, including reverse genetics, personalised therapies and cancer treatment. While the targeted knock-out of genes using the CRISPR-Cas9 system to cause indels has found many use cases, applying this system to insert or substitute genomic sequences promises an even larger application potential. Here, the homology directed repair pathway (HDR) repairs the double-strand break caused by the Cas9 enzyme by using a provided DNA template to integrate a precise change into the genome. However, the HDR pathway is the less frequently chosen pathway in mammalian cells, and the factors influencing pathway choice are currently not understood.

We hence study a novel dataset that distinguishes sites repaired by HDR from sites where the cut was repaired by Non-Homologous End Joining (NHEJ) leading to indels. Using a Machine Learning approach, we identify sequence features that influence pathway choice and discuss the impact of template choice on the incorporation rate.

From these insights, we develop the first CRISPR target site predictor to advice on HDR efficiency. The cross-validated accuracy is 0.6125. We find location specific sequence feature that promote HDR over NHEJ confirming that the seed region in addition to the template is an important modulator of activity. The resulting framework allows the user to design their CRISPR experiments around targets where HDR is more likely.

1145 – 1200

Invited Abstract
DR JOSEPH POWELL
The University of Queensland

Since 2015 Joseph Powell has been the head of the Single Cell and Computational Genomics Lab at the University of Queensland's Institute for Molecular Bioscience and an NHMRC Career Development Fellow. He obtained his Ph.D. from the University of Edinburgh in 2010 and subsequently completed a postdoctoral position in Peter Visscher's (FAA) group at QIMR. In January 2014, he was appointed as a Team Leader at the Centre for Neurogenetics and Statistical Genomics, located at the University of Queensland. During this time he was instrumental in forming a large international consortium to study the genetic control of gene expression. In 2016 he was awarded the Commonwealth Health Minister Medal for Excellence in Medical Research and awarded an NHMRC prize for the top-ranked CDF applicant in 2015.

SINGLE CELL SEQUENCING REVEALS CHANGES IN THE GENETIC CONTROL OF GENE EXPRESSION THROUGH REPROGRAMMING OF INDUCED PLURIPOTENT STEM CELLS FROM FIBROBLASTS

Joseph Powell[1], Nathan Palpant[1], Sam Lukowski[1], Quan Nguyen[1], Han Chiu[1], Helena H. Liang[2] Duncan E. Crombie[2], Maciej Daniszewski[2], Tejal Kulkarni[2], Alex Hewitt[2,3], Alice Pebay[2]

[1] Institute for Molecular Bioscience, The University of Queensland
[2] Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital
[3] Menzies Institute for Medical Research, University of Tasmania

Induced pluripotent stem cells (iPSCs) are pluripotent stem cells generated from adult somatic cells such as fibroblasts by reprogramming. IPSCs have become as an important element of developmental biology research, and emerged as a model system for studying human traits and disease. A critical, and unanswered, question is whether iPSCs can be used to study the functions of common genetic variants associated with complex human phenotypes and cell fate decisions. Recent, groundbreaking work using data from gene expression measured with bulk RNA-Seq, has shown that gene expression differences between iPSC lines is associated with common genetic variants (Kilpinen et al. 2017 Nature). However, this work is unable to reveal the genetic control of gene expression in sub-populations of iPSCs, or genetic control of cellular gene expression heterogeneity within and between cell lines. Likewise, the changes in genetic control of gene expression that occur during the reprogramming from primary cells such as fibroblasts remain largely unknown.

We generated single cell RNA Sequence (scRNA-seq) data for a total of 194,000 cells from 81 fibroblast cell lines and their reprogrammed iPSCs. The cells lines were derived from healthy, unrelated individuals, and were also genotyped using Illumina Omni arrays containing ~2.5million SNPs. This enabled us to identify common SNPs (MAF > 0.05) associated with both mean gene expression levels and cellular heterogeneity (variance) in both cell populations. Our study outlines the major sources of genetic and phenotypic variation in fibroblasts and iPSC, and identifies changes in genomic control for 1000s of transcripts across cellular reprogramming. Critically, our study design utilising scRNA-seq enabled us to identify 100s of loci that are associated with within-individual transcriptional variation. To our knowledge this is the first demonstration of the affect of allelic differences on transcriptional cellular heterogeneity.

SESSION 11: MEDICAL AND CANCER GENOMICS

CHAIRS: DR DEVIKA GANESAMOORTHY & ASSOCIATE PROFESSOR RUBY LIN

1300 – 1330

National Invited Speaker
ASSOCIATE PROFESSOR ALICIA OSHLACK
Murdoch Childrens Research Institute

Associate Professor Alicia Oshlack is a leader in implementing new bioinformatics methods in the biomedical context. She is a current National Health Medical Research Council Career Development Fellow and the winner of several awards including the inaugural Georgina Sweet Award for women in quantitative biomedical research (2016) and the Australian Academy of Science Gani Medal for Human Genetics (2011).

A/prof Oshlack's bioinformatics expertise is not just in analysis but also in methods development which leads to many independent research projects and publications. She is best known for her work on the analysis of RNA sequencing data but also works in the fields of epigenetics, clinical genomics and cancer.

She started her research career as an astrophysicist before moving to Walter and Eliza Hall as a post-doctoral scholar in the Bioinformatics division. She joined the Murdoch Children's Research Institute as Head of Bioinformatics in 2011.

SINGLE-CELL RNA-SEQ: ANALYSIS, SIMULATION AND KIDNEYS IN A DISH

Alicia Oshlack[1], Luke Zappia[1], Belinda Phipson[1], Alexander Combes[1], Melissa Little[1]

[1] Murdoch Children's Research Institute, Parkville, Vic

Single-cell RNA sequencing (scRNA-seq) is rapidly becoming a tool of choice for biologists wishing to investigate gene expression at greater resolution, particularly in areas such as development and differentiation. Single-cell data presents an array of bioinformatics challenges: data is sparse (for both biological and technical reasons), quality control is difficult and it is unclear how to replicate measurements. As scRNA-seq datasets have become available so have a plethora of analysis methods.

In this talk I will discuss challenges associated with analysis of this data and some important considerations we have identified in making the best use of single-cell RNA-seq. I will demonstrate how simulating data sets can be used in evaluating analysis methods. I will also discuss our analysis of a complex kidney organoid dataset, showing how more cells and different levels of clustering help to reveal greater biological insight.

1330 – 1345

Invited Abstract (Student)
MS JOHANNA JONES
University of Tasmania

Johanna is currently based at the Menzies Institute for Medical Research in Hobart Tasmania. She is a PhD candidate investigating the genetic cause of paediatric cataracts in Australian families.

WHOLE GENOME SEQUENCING IS IMPROVING THE IDENTIFICATION OF GENETIC CAUSES OF PAEDIATRIC CATARACTS

Johanna L. Jones[1], Bennet McComish[1], Jac Charlesworth[1], Mark A. Corbett[2], Jamie E. Craig[3], Kathryn P. Burdon[1]

[1] Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia
[2] School of Medicine, University of Adelaide, Adelaide, South Australia, Australia
[3] Department of Ophthalmology, Flinders University, Bedford Park, South Australia, Australia

Whole genome sequencing is enhancing the ability to identify disease causing mutations in inherited paediatric cataracts (PC), a heterogeneous rare disease that causes visual impairment. We are investigating unsolved families from Australia's largest repository of PC DNA, which contains 191 families. Nine large families, with at least 3 affected individuals each, have been selected for linkage analysis. All available DNA samples (n=96) have undergone genome-wide genotyping using either Illumina OmniExpress or GSA SNP arrays. Parametric linkage analysis, using Merlin software, is being performed using a relevant disease model for each family. Whole genome sequencing of an affected individual from each family was performed on an Illumina X10 platform. The Churchill pipeline was used to align fastq files to Hg19, and variant calling was performed by GATK and SAMtools for SNPs and Platypus for indels. Structural variants will also be considered. Variants within putative linkage regions are filtered for frequency (MAF <0.001) and predicted functionality (using tools such as CADD). Using this pipeline, the PC in family CRVEEH66 have been linked to a 6.8Mb region at Xq24 (LOD=2.53) and two additional regions at 1q42.2-1q43 and 3q26.31-3q26.32 (both LOD=2.48). A Complete Genomics™ whole genome sequence of the proband enabled the identification of a 127kb deletion that truncates the PGRMC1 gene following exon 1 and completely removes a long non-coding RNA gene LOC101928336, located in the chromosome X linkage region. This variant was not detectable by prior exome or Sanger sequencing. This highlights the utility of whole genome sequencing for identifying putative disease causing structural and non-coding variants, which have not been explored in PC. This work will provide these Australian families with a molecular diagnosis and enable genetic screening. The discovery of novel genes will expand the suite of genes available for screening in other patients and improve our understanding of cataract pathogenesis.

1345 – 1400

Invited Abstract

DR DANIEL RODEN
Garvan Institute of Medical Research

I have a background in chemistry, computing and a PhD in bioinformatics from the laboratory of Prof. David Jones at UCL in London. I am currently a senior postdoctoral bioinformatics researcher in the Tumour Progression Laboratory, which is headed by A/Prof Alex Swarbrick, at the Kinghorn Cancer Centre and Garvan institute. My research interests lie in using computational methods to understand the transcriptional regulation of breast cancer development and progression as well as identifying transcriptional drivers of tumour dormancy. This research is becoming increasingly focused on using single-cell transcriptomics and developing computational approaches to explore the impact of tumour heterogeneity on metastatic cancer progression and treatment response.

SINGLE-CELL TRANSCRIPTOMICS REVEALS FUNCTIONAL HETEROGENEITY IN BREAST CANCER NEOPLASTIC CELLS

Daniel Roden[1,2], Laura Baker[1], Ben Elsworth[3], Aurelie Cazet[1,2], Chia-Ling Chan[1], Sunny Wu[1], Kate Harvey[1], Radhika Nair[4], Alexander Swarbrick[1,2]

[1] The Kinghorn Cancer Center and Cancer Research Division, Garvan Institute of Medical Research, Sydney, Australia
[2] St Vincent's Clinical School, Faculty of Medicine, UNSW, Sydney, Australia
[3] School of Social and Community Medicine, University of Bristol, UK
[4] Rajiv Gandhi Centre for Biotechnology, Thycaud Post, Poojappura, Kerala, India

Cellular heterogeneity plays a key role in the development, evolution and metastatic progression of many cancers. Breast cancer has long been classified into a number of molecular subtypes (such as luminal A and B, basal-like, and Her2-enriched) that predict prognosis and therefore influence clinical treatment decisions. To date, these subtypes have only been described at a bulk tumour level. Advances in single-cell technologies are providing powerful tools for the isolation and molecular profiling of breast cancers at cellular resolution. To explore the cellular heterogeneity in breast cancer we first used a panel of genes containing the transcriptional markers that define the PAM50 classifier of molecular subtype. Five breast cancer cell line models (MCF7, BT474, SKBR3, MDA-MB-231, and MDA-MB-468) were selected as representatives of the molecular subtypes. The Fluidigm C1 and Biomark systems were used to isolate and quantify the gene expression of single cells from each of these models. To quantify the level of cellular heterogeneity within each, the classifier was applied to isolated single-cells. Using this approach we identified heterogeneity of molecular subtypes at single-cell level, indicating that cells with different subtypes exist within a cell line. This finding was reproduced in MCF7 cells (when using the Chromium 10X system to profile ~1,750 single-cells) and clear clusters of cells with a more aggressive subtype were identified. This approach was extended into more clinically relevant samples from patient derived xenograft (PDX) models. Using the same targeted gene expression approach, as well as high-throughput single-cell RNA-Seq (using 10X Chromium), we again identified significant intra-tumour heterogeneity of molecular subtype as well as sub-populations of cells that showed clinically relevant transcriptional signatures related to proliferative, EMT, and hypoxic phenotypes. These results suggest a high degree of cellular heterogeneity within models of breast cancer that can be functionally dissected using single-cell transcriptomics.

1400 – 1415

Invited Abstract

DR EVA CHAN
Garvan Institute of Medical Research

Dr Eva Chan is a statistical geneticist at the Garvan Institute of Medical Research. She obtained her PhD in Bioinformatics from the University of New South Wales, studying The Genetic Influence of Gene Expression (eQTL-mapping). Eva undertook two postdoctoral trainings focused on Genome-Wide Association Studies. The first was at CSIRO where she learnt the intricacies of cattle breeding and the second was at the University of California-Davis where she dabbled in GWAS of metabolomics. Eva then went into industry where she took up a leadership role in Statistical Genetics at Monsanto Company. In 2013, Eva returned to Sydney to join the Garvan Institute, moving into human medical research, focusing on complex genomic rearrangements in cancer and human diversity.

GENOME MAPPING ILLUMINATES ARCHITECTURE OF CHAINED FUSIONS IN CANCER

K.F. Chan[1,2], Anthony T Papenfuss [3,4,5,6,7], Desiree C Petersen[1,2], Ruth Lyons[1], Benedetta Frida Baldi[1], David M Thomas[8,9], & Vanessa M Hayes[1,2,10,11]

[1] Genomics and Epigenetics Division, Garvan Institute of Medical Research, NSW 2010, Australia
[2] St Vincent's Clinical School, University of New South Wales, NSW 2052, Australia
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[7] Bioinformatics and Cancer Genomics, Peter MacCallum Cancer Centre, VIC 3002, Australia
[8] The Kinghorn Cancer Centre, Garvan Institute of Medical Research, NSW 2010, Australia
[9] Cancer Division, Garvan Institute of Medical Research, NSW 2010, Australia
[10] School of Health Systems and Public Health, University of Pretoria, Pretoria, South Africa
[11] Central Clinical School, University of Sydney, NSW 2006, Australia

Genomic rearrangements are common in cancer, with demonstrated links to cancer progression and treatment response. These rearrangements can be complex, resulting in fusions of multiple chromosomal fragments and generation of derivative chromosomes. Comprehensively detecting complex genomic rearrangements in cancer remains challenging. No single approach can comprehensively identify all SV, as each approach has their strengths and weaknesses. In this study, we demonstrate the utility of whole genome optical mapping in capturing chained fusion events in a well-studied liposarcoma cell line. Using the Irys optical mapping system from Bionano Genomics, we reconstructed 3,338 haploid genome maps, including 101 fusion maps representing the most highly rearranged regions of the cancer genome. These fusion maps clearly revealed chained fusion architectures (content, order, orientation, and size), as well as large rearrangement junctions that are undetectable by sequencing alone. We conclude that optical mapping is an important complement to existing technologies for detecting and reconstructing complex genomic rearrangements.

1415 – 1445

National Invited Speaker
PROFESSOR SEAN GRIMMOND
The University of Melbourne

Sean Grimmond is the founding Bertalli Chair in Cancer Medicine and Director of the University of Melbourne Centre for Cancer Research in the Victorian Comprehensive Cancer Centre. He holds a Genetics degree from University of New England and a PhD in Pathology from the University of Queensland and became a Founding Scientific Fellow in The Royal College of Pathologists of Australasia in 2011. Previous appointments include the Chair of Medical Genomics at the University of Glasgow (2013-2016), the Co-Chair of the Scottish Genomes Partnership (2014-2016), Professor of Genomics at the University of Queensland (2009-2016) and the founding Director of the Queensland Centre for Medical Genomics (2009-2013).

Over the last 20 years, Professor Grimmond's research has focused uncovering the underlying genetics controlling key biological processes and pathological states through integrated omic analyses.

He has pioneered whole genome analysis of cancer patients at scale and led Australia's International Cancer Genome Consortium efforts into both Pancreatic and Ovarian cancers. His current research is firmly focused on real-time omic analysis of recalcitrant cancers, testing the value of personalizing therapies and further cancer genome discovery.

THE GENOMIC PATHOLOGY OF PANCREATIC CANCERS

Pancreatic Cancer is currently the 3rd leading cause of cancer morality in the US and is projected to be the 2nd leading cause of cancer related death within a decade. Frustratingly, while the outcomes for cancers of the Breast, Prostate and Melanoma has steadily improved over recent decades, the median survival of Pancreatic Cancer post diagnosis remains <12 months and 5-year survival remains less than 10%. Since 2009, we have engaged in large scale cohort sequencing programs with the International Cancer Genome Consortium (ICGC) and US Cancer Genome Atlas to systematically resolve what causes somatic mutation, the key events driving tumorigenesis, new molecular taxonomies, and potential druggable targets to all cancers arising in this organ. This presentation will review how these integrated-omic analyses have redefined our understanding of the roots causes and the major driver mechanisms underlying this recalcitrant malignancy. The next phase of this research focusing on refining molecular subtypes of clinical significance and building rapid genomic analysis Pancreatic Cancer in a clinical setting will be discussed.

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POSTER PRESENTATIONS

Image credit: Tourism Tasmania & Garry Moore

#	POSTER TITLE	PRESENTER
1	A STRATEGY TO DESCRIBE THE ADAPTIVE IMMUNE LANDSCAPE OF METASTATIC BREAST CANCER LESIONS ON A SINGLE-CELL LEVEL	Mr Ghamdan Al-Eryani ●
2	AUTOMATED QUANTSEQ 3' MRNA-SEQ LIBRARY PREPARATION FOR HIGH THROUGH-PUT GENE EXPRESSION PROFILING APPLICATIONS	Ms Jekaterina Aleksejeva
3	DIAGNOSING FUSION GENES IN CANCER USING TARGETED RNA SEQUENCING	Dr James Blackburn
4	CREATING A SINGLE CELL GENE EXPRESSION DATA PORTAL AT STEMFORMATICS	Dr Jarny Choi
5	REPRESENTING THE CANCER GENOME WITH MIRROR-DNA SPIKE-IN CONTROLS	Mr Ira Deveson ●
6	UNSUPERVISED DEMULTIPLEXING OF SINGLE-CELL BARCODES FROM RAW NANOPORE SEQUENCING DATA	Mr James Ferguson
7	TECHNICAL ADVANCES IN PLASMA GENOMIC BIOMARKERS FOR MUTATION DETECTION AND MONITORING IN CANCER PATIENTS	Mrs Sandra Fitzgerald ●
8	MODELLING BREAST CANCER PROGRESSION USING SINGLE-CELL RNA-SEQ	Dr Brian Gloss ●
9	COMPARISON OF HIGH-THROUGHPUT SINGLE-CELL RNA SEQUENCING METHODS USING COMPLEX BIOLOGICAL SYSTEMS	Mr Dominik Kaczorowski
10	IMPROVING PREDICTABILITY OF CRISPR-CPF1 ACTIVITY	Dr Kaitao Lai ●
11	THE THERANOSTIC POTENTIAL OF MICRORNAS IN AGGRESSIVE PROSTATE CANCER	Ms Farhana Matin ●
12	WHOLE GENOME- AND TARGETED CAPTURE- SEQUENCING ANALYSIS OF DUAL LUNG METASTASES AND CIRCULATING TUMOUR DNA (CTDNA) IN A RARE PRIMARY ADRENOCORTICAL CARCINOMA (ACC) CASE	Dr Mark McCabe
13	NON-SYNONYMOUS VARIATION IN ADAMTS12 CORRELATES WITH CAROTID ARTERY INTIMA-MEDIA THICKNESS	Mr Juan Peralta ●
14	ROHMER: A TOOL FOR IDENTIFYING RUNS OF HOMOZYGOSITY IN WHOLE GENOME DATA	Ms Clare Puttick ●
15	THE IDENTIFICATION OF RARE VARIANTS IN TASMANIAN PROSTATE CANCER PEDIGREES USING WHOLE-GENOME SEQUENCING	Miss Kelsie Raspin ●
16	EXPLORING THE ECOSYSTEM OF TRIPLE NEGATIVE BREAST CANCER METASTASES AT CELLULAR RESOLUTION	Dr Daniel Roden

AUTHORS: ● Early Career Researcher ● Student

MONDAY 30 OCTOBER 2017

#	POSTER TITLE	PRESENTER
17	LOW FREQUENCY VARIANT DETECTION AND TISSUE-OF-ORIGIN EXPLORATION USING LIQUID BIOPSIES	Mr Andrew Szentirmay
18	MOLECULAR DYNAMICS MODELLING OF A VARIANT OF UNKNOWN EFFECT IN RAD51D	Dr Matthew Wakefield
19	SINGLE-CELL RNA SEQUENCING REVEALS THE HETEROGENEITY OF CANCER-ASSOCIATED STROMAL CELLS IN A MODEL OF TRIPLE NEGATIVE BREAST CANCER	Mr Sunny Wu ●

TUESDAY 31 OCTOBER 2017

#	POSTER TITLE	PRESENTER
20	SLAMSEQ: HIGH-THROUGHPUT METABOLIC SEQUENCING OF RNA	Dr Stephanie Bannister
21	A PHENOTYPE CENTRIC BENCHMARK OF VARIANT PRIORITISATION TOOLS	Mrs Denise Anderson ●
22	DIVERSIFICATION OF INNATE IMMUNE RESPONSES BY TRANSCRIPTIONAL MECHANISMS	Miss Suzanne Butcher ●
23	DNA METHYLATION, A BIOMARKER OF AGE IN A LONG-LIVED SEABIRD?	Mr Ricardo De Paoli-Iseppi ●
24	TIME COURSE GENE EXPRESSION ANALYSIS OF FORENSIC BLOOD SAMPLES	Ms Nadine Dunn ●
25	RELIABLY DETECTING CLINICALLY IMPORTANT VARIANTS REQUIRES BOTH COMBINED VARIANT CALLS AND OPTIMIZED FILTERING STRATEGIES	Dr Matt Field ●
26	UTILISING MIXTURE MODELS FOR UNVEILING PATTERNS IN SCRNA-SEQ DATA	Ms Shila Ghazanfar ●
27	CANCER-ASSOCIATED PTEN MUTATIONS ALTER PTEN CELLULAR FUNCTION	Ms Nahal Haddadi ●
28	FAST, UNBIASED DNA ENRICHMENT RESAMPLING	Mr Antony Kaspi ●
29	HAPLOTYPING AND COPY NUMBER PROFILING OF SINGLE CELLS BY MASSIVE PARALLEL SEQUENCING	Dr Gregory Maes
30	IMPROVING ACCESSIBILITY AND COMPREHENSION IN CONSENT FOR GENETIC RESEARCH: A WEB PLATFORM FOR CONSENT APPS	Dr Rebekah McWhirter

AUTHORS: ● Early Career Researcher ● Student

#	POSTER TITLE	PRESENTER
31	OCCURRENCE OF G-QUADRUPLEXES IN NON-CANCEROUS AND CANCEROUS CELLS IN GENE REGULATORY REGIONS	Mr Arnold Ou ●
32	REPROGRAMMING OF CRITICAL GENE REGULATORY ELEMENTS IN A MOUSE MODEL OF AD	Mr Andrew Phipps ●
33	IDENTIFICATION OF ZBTB7A AND MAZ AS REGULATORS OF GENE EXPRESSION IN DIABETES	Dr Haloom Rafehi ●
34	HOMING IN ON PRECISE DIAGNOSES: THE POWER OF COMBINING MULTI-LAYERED GENOMIC AND HISTOPATHOLOGICAL ANALYSIS IN PANCREATIC CANCER	Ms Tamsin Robb ●
35	COMPARISON OF SHOTGUN DNA LIBRARY PREPARATION KITS FOR SEQUENCING ON ILLUMINA PLATFORMS	Dr Kirby Siemering
36	IDENTIFICATION OF SODIUM VALPROATE AND LITHIUM CO-REGULATED GENES IN A SEROTONERGIC CELL LINE	Ms Priyanka Sinha ●
37	INTEGRATING SEQUENCE VARIATION INTO CRISPR/CAS9 OFF-TARGET DETECTION	Dr Laurence Wilson ●
38	INTRAGENIC ENHANCERS ATTENUATE HOST GENE EXPRESSION	Dr Pengyi Yang ●
39	SYSTEMATIC IDENTIFICATION OF NON-CONVENTIONAL TRANSCRIPTS FROM HUMAN CELLS	Dr Oscar Luo

AUTHORS: ● Early Career Researcher ● Student

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POSTER 1

A STRATEGY TO DESCRIBE THE ADAPTIVE IMMUNE LANDSCAPE OF METASTATIC BREAST CANCER LESIONS ON A SINGLE-CELL LEVEL

Ghamdan Al-Eryani[1,2], Mandeep Singh[1,2], James M. Ferguson[1,2], Daniel Roden[1,2], Sunny Z. Wu[1,2], Chia-Ling Chan[1,2], Katherine Jackson[1,2], David Koppstein[2,3], Tri Phan[1 2], Fabio Luciani[2,3], Simon Junankar[1,2], Chris C Goodnow[1,2], Martin A. Smith[1,2], Alex Swarbrick[1,2]

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Our lab has initiated a project where we will describe the adaptive immune landscape of metastatic breast cancer on a single-cell level. We have successfully captured 8 cancer lesions to date using the 10x Chromium platform, providing an unprecedented snapshot into these tumours intricate immune network. Furthermore, by implementing CITE-Seq, a method by which DNA barcodes conjugated to antibodies are used as surrogates for protein expression when sequenced with cellular RNA, extrinsic effector properties of these immune cells can be studied. Lastly, RAGE-Seq, a novel high throughput method to obtain the T-Cell and & B-cell receptor sequence on a single-cell level is being developed. Using the combined listed methods for each capture, we aim to identify novel targets for immunotherapy with the hope of delivering long-term survival outcomes to metastatic breast cancer patients.

POSTER 2

AUTOMATED QUANTSEQ 3' MRNA-SEQ LIBRARY PREPARATION FOR HIGH THROUGHPUT GENE EXPRESSION PROFILING APPLICATIONS

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RNA sequencing is increasingly used for large-scale, transcriptome-wide, gene expression profiling studies aimed at understanding molecular pathways involved in disease and developmental processes. Enabling cost-effective, reproducible, and automated solutions for RNA-Seq library preparation is therefore an advantage for researchers conducting high volume sequencing projects, including RNA-Seq-based screening studies. QuantSeq is a 3' mRNA-Seq Library Preparation method that produces ready-to-sequence libraries from total RNA, by generating a single 3'-UTR tag per transcript. As a result, fewer reads are needed to determine unambiguous gene expression levels per sample, which facilitates a higher level of multiplexing and reduced sequencing costs. To facilitate the use of QuantSeq for high throughput applications, we sought to automate the QuantSeq 3' mRNA-Seq library preparation system on the Agilent Bravo platform. After careful optimization of liquid handling settings, we could demonstrate good consistency and yields for Bravo-generated libraries compared to manual preps. Using Universal Human Reference RNA (UHRR) with ERCC spike-in controls we have further evaluated sequencing data for manual and Bravo-generated libraries for different total RNA input amounts. The automation of QuantSeq enables consistent and efficient library preparation that will benefit a range of ongoing, high volume RNA-seq-based projects.

POSTER 3

DIAGNOSING FUSION GENES IN CANCER USING TARGETED RNA SEQUENCING

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Fusion genes are created when a chromosomal translocation recombines two distinct genes. These events drive an estimated 20% of all cancer instances. Accordingly, fusion gene identification is essential for patient diagnosis, prognosis and treatment. Despite this importance, current diagnostic technologies (based on FISH and qRT-PCR) suffer from major limitations, including the ability to detect only a single known gene fusion per reaction and the inability to detect novel or variant fusion gene pairs.

RNA sequencing (RNAseq) has more recently been used to detect fusion genes. However, it requires a high library depth, and typically has a limited sensitivity for detecting lowly expressed fusion genes.
To address these challenges, we have developed the use of targeted RNA sequencing (CaptureSeq) to diagnose fusion genes. CaptureSeq uses a panel of biotinylated probes to "capture" the full range of oncogenic fusion RNA transcripts for targeted sequencing, achieving enriched sequence coverage and diagnostic performance. As a single assay, CaptureSeq offers a shortened diagnostic timeline and reduced cost compared to current approaches.

We have designed two CaptureSeq tests that specifically target genes involved in fusion events in blood cancers and solid tumours. Both tests were successfully validated using established cell lines and patient materials with well-characterised gene fusions. To date, the tests have additionally provided a novel molecular diagnosis for several cancer patients, including prostate cancers and inflammatory myofibroblastic tumours (IMT). Furthermore, they have also identified a novel ALK truncation event in synovial sarcoma, leading to the possibility of using kinase inhibitors – such as Crizotinib – as a therapeutic for this disease.

In summary, we have generated two universal tests capable of assessing all known cancer fusion genes and identifying novel fusions and alternative fusion isoforms. Following further validation, we believe that these tests have the potential to be implemented as novel clinical cancer diagnostic tools.

POSTER 4

CREATING A SINGLE CELL GENE EXPRESSION DATA PORTAL AT STEMFORMATICS

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Stemformatics (stemformatics.org) is an established data portal containing over 350 gene expression datasets, with a major focus on stem cells and their stages of differentiation. Rather than simply hosting datasets as they appear in public repositories such as GEO, Stemformatics uses a stringent set of quality control metrics and its own pipelines to process handpicked datasets from raw files - providing a trusted source of stem cell expression data as well as an invaluable resource for meta-analyses across many datasets.

Stemformatics is beginning to host single cell RNA-Seq datasets of relevance, and this is opening up some exciting possibilities for new types of analyses and collaborative framework. We describe our current pipelines for processing the single cell RNA-Seq data from raw counts, as well as proposed visualisation tools for users to view the data. A number of challenges unique to creating a single cell expression dataset portal are discussed.

POSTER 5

REPRESENTING THE CANCER GENOME WITH MIRROR-DNA SPIKE-IN CONTROLS

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Next-generation sequencing (NGS) can be used to identify genetic mutations in tumour samples, and thereby inform diagnosis and therapy selection for cancer patients. However, the analysis of tumour samples by NGS is challenging due to: (1) the sheer size of the human genome; (2) the diversity of mutation types that occur in cancer; (3) tumour impurity, sub-clonal heterogeneity and genomic instability; (4) the influence of technical variables during library preparation, sequencing and bioinformatic analysis.

We recently developed a set of synthetic DNA standards, termed Sequins (sequencing spike-ins) that act as sample-specific qualitative and quantitative controls for NGS experiments [1]. Sequins are mirror-image representations of human DNA sequences (i.e. real sequences arranged in reverse), and can be used to represent almost any feature of the genome, including natural instances of genetic variation or disease-causing mutations. Mirror-DNA standards retain all intrinsic properties of their corresponding human sequences. However, NGS reads derived from Sequins align exclusively to a reverse-orientation copy of the human reference genome, thereby partitioning them from the accompanying sample for parallel analysis.

Here we present a set of Sequin controls purpose-built for cancer genomics. This encompasses 99 recurrent and/or clinically actionable cancer mutations (e.g. BRAF:V600E), gene amplifications (e.g. MYCN), diagnostic microsatellite loci (e.g. BAT26), and a range genetic variants that are difficult to resolve with NGS (e.g. structural variants). Cancer Sequins are assembled into quantitative ladders that emulate copy number variation and heterogeneous somatic allele frequencies encountered in tumours. In this way, Sequins estimate the accuracy with which variants can be detected at different allele frequencies and enable sample-specific determination of diagnostic performance. We provide Cancer Sequins as a standardised resource for the cancer genomics community.

[1] Deveson IW, et al. Nature Methods. 9, 784-91 (2016).

POSTER 6

UNSUPERVISED DEMULTIPLEXING OF SINGLE-CELL BARCODES FROM RAW NANOPORE SEQUENCING DATA

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Single-cell RNAseq (scRNAseq) technology provides the ability to characterise individual cell types from heterogeneous samples, enabling gene expression profiling at deep resolution. In addition to limitations derived from short read sequencing, most scRNAseq technologies only resolve the 3' end of RNA transcripts, making it difficult or even impossible to characterise full molecules. Long-read sequencing platforms offer a solution to these problems, but come with a higher sequencing error-rate than Illumina sequencing and, consequently, make it difficult to accurately demultiplex cell barcodes and unique molecular identifiers (UMI) from scRNAseq data.

Here, we describe an unsupervised method to demultiplex full-length transcripts from single cells using Oxford nanopore sequencing. By vectorising the raw signal corresponding to the cell barcodes with a reference set using dynamic time warping, a growing neural gas can be used to map the topology in N-dimensional feature space and cluster reads accordingly. A similar process for UMIs can generate a more accurate consensus sequence of the transcript, thus overcoming two significant technical limitations, and increasing the resolution and accuracy of scRNAseq.

POSTER 7

TECHNICAL ADVANCES IN PLASMA GENOMIC BIOMARKERS FOR MUTATION DETECTION AND MONITORING IN CANCER PATIENTS

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A sea-change is imminent for cancer medicine, due to the use of non-invasive genomic biomarkers in blood to inform screening, diagnosis and the selection of treatment. This technology may be used routinely in oncology within five years. Although numerous studies, including work in our laboratory, have shown that genomic analysis of blood can detect the presence and even the type of cancer, researchers have only scratched the surface of what this technology can do. There are still many technical challenges that need to be addressed before these biomarkers can be used routinely in the clinic. In our laboratory, we are generating new methods to improve the sensitivity and accuracy of such tests. We have developed a custom QiaSeq Targeted sequencing panel for Neuroendocrine Cancer, and are currently testing the system for mutation detection in the plasma of patients. This system is also being used to investigate the limits of detection to allow for monitoring of mutations in cancer relapse. New methods to assess the sensitivity of plasma genomics assays on a patient by patient basis using spiked-in control nucleic acids are also being optimised.

POSTER 8

MODELLING BREAST CANCER PROGRESSION USING SINGLE-CELL RNA-SEQ

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Cancer cell diversity constitutes a challenge for cancer treatment and deeply impact the outcome of cancer patients. A simultaneous overview of cancer cells and associated stromal cells is critical for the design of improved therapeutic regimes. Single-cell RNA-seq has emerged as a powerful method to unravel heterogeneity of complex biological systems; this has enabled in vivo characterization of cell type compositions through unsupervised sampling and modelling of transcriptional states in single cells.

Here we use the cell type agnostic, high-throughput microfluidic-based, single-cell RNA-seq method Drop-seq to elucidate the function and cellular composition of breast tumours. We use the MMTV-PyMT ± Elf5 mouse mammary tumour model to provide high-resolution landscapes of the disease and highlight cellular events that result in the acquisition of the metastatic phenotype. We show breast cancer cell composition and tumour heterogeneity with unprecedented definition, elucidating the cellular and molecular complexity of tumour progression within the context of a complex multicellular environment.

POSTER 9

COMPARISON OF HIGH-THROUGHPUT SINGLE-CELL RNA SEQUENCING METHODS USING COMPLEX BIOLOGICAL SYSTEMS

Dominik Kaczorowski[1], Nona Farbehi[1], Hira Saeed[1], Lesley Castillo[1], Yolanda Colino-Sanguino[1], David Gallego-Ortega[1,2],Rob Salomon[1]

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Single cell RNA sequencing (scRNA-seq) and specifically high-throughput methods allow the interrogation of biological systems at a specificity and resolution that has not previously been available. New techniques that take advantage of cell sorting, combinatorial barcoding, molecular indexing and microfluidics have allowed this increased resolution to be undertaken in a cost -competitive way, enriching the quality of generated datasets. With the recent launch of the Garvan-Weizmann Centre for Cellular Genomics (GWCCG), we have brought together expertise in flow cytometry, microfluidics, high-throughput sequencing and bioinformatics to focus on major collaborative research programs in melanoma, breast cancer, cancer in bone, diabetes and immune disorders.

In an effort to optimise, refine and offer the best possible service we have compared several of our available highly-parallel scRNA-seq platforms in terms of cost, processing, throughput and output so that we can best address the aims of a given project.

Here we use PBMCs and breast tumours from the MMTV-PyMT mouse mammary cancer model to evaluate 3'-end RNA-seq microfluidic platforms; InDrop, Drop-Seq and Chromium single-cell and FACS-based methods (MARS-seq). Factors such as sensitivity, throughput, reliability, cost and technical accessibility were compared. Additionally, the single-cell results were compared with equivalent bulk RNA-seq to verify that the clustering of single-cell transcriptomic signatures are recapitulated in bulk tissue.

This comparison offers a uniquely local perspective of feasibility, both technical and financial of undertaking large-scale single-cell projects in Australia.

POSTER 10

IMPROVING PREDICTABILITY OF CPRISPR-CPF1 ACTIVITY

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CRISPR-Cpf1 is an alternative endonuclease for the CRISPR system in genome engineering applications. Cpf1 reportedly offers enhanced on-target activity and less off-target activity in comparison to CRISPR-Cas9 technology. Several approaches have measured the activity of individual Cas9/Cpf1 targets through phenotypic assays or indel rate, however a comprehensive predictive tool identifying the features that influence Cpf1 activity is missing.

Here, we evaluate the features from published Cpf1 gRNA data with 1636 events from AsCpf1 and 684 from LbCpf1, two Cpf1 enzymes from different bacteria. Similar to Cas9, the important sequence features include the PAM sequences and GC content. However, we also find Cpf1-specific modulators of activity such as the enzyme type and certain position-specific sequence preferences. From these insights, we train a Random Forests machine learning method achieving an area under the receiver operating characteristic curve (AUROC) of 0.966 and 0.873 (10-fold cross validation) for AsCpf1 and LbCpf1, respectively.

Using this predictor, we identify putative CRISPR-Cpf1 target sites across UCSC HG19 and contrast this activity profile against that of Cas9 with respect to the potential to influence transcription activity (target sites in promotor) as well as the robust knock-out of genes (target sites in the first exon).

POSTER 11

THE THERANOSTIC POTENTIAL OF MICRORNAS IN AGGRESSIVE PROSTATE CANCER

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Background: MicroRNAs (miRNAs) are naturally occurring gene regulators. They are attractive targets for diagnostics and therapeutic intervention due to their stability in blood and altered expression in various cancers, including prostate cancer (PCa). Currently there are no reliable means to predict aggressive PCa and enable patient-specific tailor-made therapies, termed theranostics.

Aims: Our study aims to identify plasma miRNA biomarkers and explore the therapeutic potential of miRNAs in PCa.

Methods: Plasma samples were collected from PCa patients with <5 years survival (n=12), metastatic (n=14) and non-metastatic (n=16) disease, and 19 healthy controls. We screened 372 cancer-associated miRNAs using PCR arrays and validated 35 shortlisted miRNAs in the discovery cohort (n=61). We further validated 13 miRNAs in a validation cohort (n=58), and performed binary logistic regression analysis in a combined cohort (n=119). Furthermore, we performed functional assays and mass spectrometry for a potential tumour suppressor miRNA, referred to as ProsmiR. Preclinical studies to validate the effect of ProsmiR in vivo are underway.

Results: We identified two combinations of miRNAs capable of diagnosing PCa (AUC=0.89), and predicting aggressive disease (AUC=0.75) at an early stage. We also found that ProsmiR was capable of inhibiting proliferation, migration, invasion and colony formation of PCa cells possibly by targeting genes involved in the cell apoptosis pathways.

Conclusion: Our study demonstrates a promising approach based on the assessment of distinct miRNA expression patterns for improved PCa diagnosis and prognosis, paving the way for the development of a novel therapy by restoring miRNA function.

Translational significance: PCa is a major cause of cancer-related deaths in men worldwide. The current non-invasive method of diagnosis (PSA test) leads to over-diagnosis and over-treatment. Identification of a better diagnostic miRNA signature and a tumour suppressor miRNA (ProsmiR) may lead to development of a novel miRNA-based therapy enabling individualised therapeutic management for PCa patients.

POSTER 12

WHOLE GENOME- AND TARGETED CAPTURE- SEQUENCING ANALYSIS OF DUAL LUNG METASTASES AND CIRCULATING TUMOUR DNA IN A RARE PRIMARY ADRENOCORTICAL CARCINOMA CASE

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Background: Adrenocortical carcinoma (ACC) is an aggressive, rare malignancy with poor prognoses and limited treatment options, which cannot be improved largely due to limited genetic profiling. We hypothesise that whole genome sequencing (WGS) and capture sequencing targeting genes commonly implicated in cancer against DNA derived from the germline, primary/metastatic tumours or freely circulating in plasma, will provide a comprehensive landscape of genomic aberrations causing and/or contributing to disease pathogenesis, while informing novel therapeutic options. We aim to apply these approaches to a 37 year old female, who presented with adrenocortical carcinoma metastasised to lung, for whom we have germline and metastatic tumour DNA, plus ~quarterly plasma-derived ctDNA.

Materials and Methods: HiSeq-X for WGS of germline (~30X) and 2 metastases (~90X), followed by custom panel targeted against >300 cancer-associated genes (~0.9Mb) designed through Roche/NimbleGen and applied to germline (~900X), metastatic-tissue (~570X) and ctDNA (~300X) which had been subjected to KAPA HTP Library Preparation prior to sequencing on a HiSeq-2500. Bioinformatics followed GATK best practices for the identification of variants with additional tools for ploidy, purity, CNV and loss-of-heterozygosity estimates (Sequenza) and microsatellite instability (MSI; msisensor).

Results: No driver mutations or risk-alleles in germline detected. Targeted-capture of one metastasis revealed 916 variants of which 551 were unshared with the other metastasis or 6 ctDNA samples. WGS of the first metastases (68% cellularity) revealed a hyperdiploid cancer with extensive loss-of-heterozygosity but few structural rearrangements. MSI presented at 8.8% of sites. Loss-of-function mutations were identified in cancer-associated genes including TP53 and PTEN, and a drug-actionable splice-site ablation observed in MSH2. Further analyses of the second metastasis and ctDNA are ongoing.

Discussion: We present an extensive WGS/capture-sequencing analysis of an ACC patient with lung metastases for whom we expect ctDNA to confirm detected mutations. Encouragingly, a splice-critical mutation detected in MSH2 appears to be drug-actionable.

POSTER 13

NON-SYNONYMOUS VARIATION IN ADAMTS12 CORRELATES WITH CAROTID ARTERY INTIMA-MEDIA THICKNESS

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The internal carotid intima-media thickness (ICAIMT) is widely used to quantify the extent of subclinical artherosclerosis and a common marker of cardiovascular disease risk. Heritability estimates for ICAIMT have been reported to range between 0.35 to 0.65, suggesting a genetic basis for its phenotypic variation.

We conducted genome-wide kernel-based association analyses of carotid artery measurements, within the variance component framework of SOLAR. Scored genotypes at non-synonymous (NS) variant loci (n=257,063) observed in the WGS of individuals from extended pedigrees of Mexican American ancestry in the San Antonio Family Heart Study (SAFHS) cohort (n=2,621, 1,111 males, 1,510 females) were collapsed into gene-specific covariance kernels (n=14,078). The covariance structure of these kernels is allele-frequency bound with an expectation towards identity-by-descent (IBD) when the NS variation within the kernel is rare, and towards kinship otherwise. The kernel association analysis, in effect, behaves as an empirical linkage test.

We identified multiple genome-wide significant kernel-trait associations. Of specific interest to ICAIMT, which exhibited a high heritability (h2=0.66, p=2.6x10-22) in the SAFHS cohort, we found a genome-wide significant association with ADAMTS12 (p=8.89x10-07, Bonferroni=3.55x10-06) that accounted for 16% of the total phenotypic variation in ICAIMT. The introduction of ADAMTS12 non-synonymous variant scores as covariates (n=15) into the analyses completely absorbed the kernel association signal. Post-hoc measured genotype analysis of the individual non-synonymous variant scores do not yield any significant association signal. In general, ADAMTS enzymes have been previously described to play a wide variety of roles including an involvement in inflammation processes and vascular biology. The ADAMTS12 enzyme, in particular, has been shown to exhibit an angioinhibitory effect.

Our results suggest a role for ADAMTS12 in the etiology of vascular pathologies and highlights the potential that kernel-based approaches have, within the context of extended families, to simplify the analysis of WGS.

POSTER 14

ROHMER: A TOOL FOR IDENTIFYING RUNS OF HOMOZYGOSITY IN WHOLE GENOME DATA

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Diagnosing a genetic disease is critically important not just because it can lead to a change in treatment plan, but also because it can help with prognosis as well as family planning. Whole Genome Sequencing (WGS) provides a wealth of data, however with approximately 5 million variants per genome, including 8500 novel variants, it can be incredibly challenging to identify a variant as being pathogenic, particularly to the level of certainty required in clinical practice.

A Run of Homozygosity (ROH) is a large autozygous segment of the genome, which results from both parents passing down identical sections of DNA. The occurrence of a ROH is significantly more likely when the parents are related, which is why consanguineous populations have a higher rate of autosomal recessive diseases. It can be useful when diagnosing a genetic disease to focus on ROHs, particularly if the proband comes from a consanguineous union.

Current methods to identify ROHs are based on Arrays or Exome data, and are generally not clinician friendly. ROHmer uses Plink's sliding window approach, with WGS data from a VCF file to identify ROH across the entire genome. It outputs IGV compatible BED and VAF files, as well as a clinician friendly report.

To date, ROHmer has helped diagnose patients in several published studies, including a number of patients from India. Given that approximately 20% of the world's population live in communities that favour consanguineous marriages ROHmer is a useful tool for a clinical geneticist.

POSTER 15

THE IDENTIFICATION OF RARE VARIANTS IN TASMANIAN PROSTATE CANCER PEDIGREES USING WHOLE-GENOME SEQUENCING

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Prostate cancer (PCa) is a highly heterogeneous disease with studies suggesting a degree of heritability greater than other cancers. It has been found that as much as 58% of disease risk can be explained by heritable factors. While more than 150 common genetic risk variants have been identified, these variants still only explain a minor portion of risk, are largely of low to moderate effect size, and are functionally ambiguous. There has recently been significant success in the discovery of rare genetic variants contributing to complex disease, including PCa, through next-generation sequencing (NGS) of large families, where rare variants are enriched and there is reduced genetic complexity. Here, we have applied whole-genome sequencing (WGS) to several large Tasmanian PCa pedigrees with the aim of identifying rare genetic variants contributing to the development of PCa.

Thirty-seven individuals from six PCa pedigrees were WGS on the Illumina HiSeq X™ Ten platform. Variants were prioritised on a per-family basis by frequency (<1% in 1KGP, UK10K, ExAC and ESP), segregation with disease, mutation type (missense, nonsense or splice) and predicted functional consequence (CADD, PolyPhen and SIFT scores). Unaffected older male relatives and population controls were also WGS and used to prioritise variants based on non-sharing. After additional genotyping in our larger familial PCa dataset and population-based, case-control study, 15 variants were investigated in an existing familial PCa whole-exome sequencing dataset from the Fred Hutchinson Cancer Research Center (FHCRC). Familial-based association testing has been undertaken for several rare variant PCa candidates that were also present in the FHCRC pedigrees. Functional studies are currently underway to determine the effect of such mutations on gene and protein expression.

This study was designed to identify new biological pathways involved in the pathogenesis of familial PCa and may lead to novel diagnostic and therapeutic targets for PCa patients.

POSTER 16

EXPLORING THE ECOSYSTEM OF TRIPLE NEGATIVE BREAST CANCER METASTASES AT CELLULAR RESOLUTION

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Most cancers display remarkable cellular heterogeneity, both between the neoplastic cells and amongst the many contributing parenchymal cells. It is now clear that the phenotype of the cancer is a function of cell autonomous programs and interactions with the host. For example, recent evidence suggests a critical role for cancer-associated fibroblasts in defining cellular response to therapy. Furthermore, the advent of checkpoint inhibitors has ignited intense interest in the immunobiology of cancer.

To advance our insights into cancer biology and develop improved treatments, we must consider cancers as complex 'ecosystems'. However, we have only a rudimentary understanding of the cellular architecture of solid cancers, in particular lethal metastatic disease, greatly limiting our capacity to rationally design therapies targeting the cancer ecosystem.

Single cell RNA-Sequencing (SCRS) has emerged as a remarkable technology to systematically study the diverse cellular populations within tissues and tumours. In this way, integrative and comprehensive studies of cellular populations and interactions become possible, leading to new mechanistic insights and therapeutic opportunities.

To investigate the cellular ecosystem of metastatic breast cancer, we are using the 10X Genomics Chromium platform to encapsulate thousands of cells into barcoded droplets prior to SCRS on the Illumina NextSeq 500. To date we have sequenced 7 metastases collected through biopsy or autopsy. This analysis has revealed completely novel stromal cell subsets, immune phenotypes and actionable neoplastic cell expression features not identified by conventional pathology. By analysing animal xenograft models also established from these clinical biopsies, we are able to investigate the evolution of tumours over time at single cell resolution.

POSTER 17

LOW FREQUENCY VARIANT DETECTION AND TISSUE-OF-ORIGIN EXPLORATION USING LIQUID BIOPSIES

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The promise of liquid biopsy assays lie in the non-invasive monitoring of diseases, such as cancer, through cellfree DNA (cfDNA) or circulating tumor cell DNA. This may assist in advancing early-stage diagnosis and improving the ultimate prognosis while simultaneously monitoring treatment response over time. Since these materials are often limited, most liquid biopsy assays incorporate targeted sequencing to enable cost-effective deep coverage of target loci for detection of low frequency pathogenic variants, yet a critical aspect in attaining the necessary sensitivity is an assay that produces uniform, comprehensive coverage from low DNA input quantities. We have developed a liquid biopsy workflow to enable low frequency variant detection from a 10 mL blood draw using the Promega Maxwell® RSC combined with Swift Biosciences Accel-NGS® 2S library preparation methodologies. Briefly, whole blood samples were collected in Streck cell-free DNA BCT vials from patients with late stage cancer and cfDNA was extracted with the Promega Maxwell RSC. This instrument yielded DNA outputs ranging from 8 to 32 ng, with a size profile defined by a predominant peak of ~170bp and a mean Alu repeat qPCR integrity score of 0.22 [0.09-0.34], characteristic of high quality cell-free DNA lacking cellular DNA content. A total of 20 ng cfDNA was used to make an Accel-NGS 2S Hyb library followed by hybridization capture using Agilent SureSelect Human All Exon probes. The Accel-NGS 2S Hyb Library Kit exhibits a 90% library conversion rate with cfDNA and provides high complexity libraries with uniform target coverage. In addition, molecular barcodes were incorporated to label each library molecule uniquely prior to PCR amplification. These molecular barcodes were utilized for accurate removal of PCR duplicates while simultaneously preserving naturally occurring fragmentation and strand duplicates to maximize data recovery. Secondly, these barcoded molecules were grouped to generate consensus sequences after removal of false positives originating from PCR and sequencing errors. Variant calling was performed using Vardict and Lofreq enabling highly sensitive and precise detection of variants down to a 0.5% allele frequency. In parallel, we have developed a workflow to determine if the epigenetic status of cell-free DNA can identify tissue-of-origin. This workflow utilizes the Accel-NGS Methyl-Seq DNA Library Kit to enable unbiased characterization from low (5 ng) cfDNA inputs. Through whole genome bisulfite sequencing, using a priori knowledge of differentially methylated regions characteristic of different human tissues, we can identify the predominant tissue source of cfDNA in blood.

POSTER 18

MOLECULAR DYNAMICS MODELLING OF A VARIANT OF UNKNOWN EFFECT IN RAD51D

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High-grade epithelial ovarian carcinomas (OC) containing mutated BRCA1/2 have homologous recombination defects and are sensitive to poly(ADP-ribose) polymerase inhibitors (PARPi). In a clinical trial of the PARPi rucaparib (ARIEL2 Part 1, Clovis Oncology) a patient was observed with a germline truncating mutation in RAD51D (c.770_776del, p.G258Sfs*50) and a secondary mutation (c.770_776delinsA, p.S257_R259delinsK) in a biopsy of a splenic lesion that was progressing on PARPi therapy. Evolutionary analysis and molecular dynamics modelling were used to assess the function of this variant of unknown effect alongside the functional wild-type variant(s). Results indicated that the observed differences in amino acid sequence between the secondary mutation and wild-type RAD51D were unlikely to disrupt normal function and are evolutionarily well tolerated. The secondary mutation (c.770_776delinsA, p.S257_R259delinsK) would likely mirror the function of wild-type RAD51D, thus would restore function and lead to PARPi resistance. This prediction was confirmed by CRISPR directed homology repair introduction of the secondary mutation into a human ovarian cancer cell line, PEO4, which demonstrated a decreased cisplatin and rucaparib sensitivity relative to a PEO4 RAD51D knockout. In conclusion, the secondary RAD51D mutation (c.770_776delinsA, p.S257_R259delinsK) identified in this lesion most likely contributed to or caused the PARPi resistance and lesion progression.

Kondrashova et al 2017 *Cancer Discovery* DOI:10.1158/2159-8290.CD-17-0419

POSTER 19

SINGLE-CELL RNA SEQUENCING REVEALS THE HETEROGENEITY OF CANCER-ASSOCIATED STROMAL CELLS IN A MODEL OF TRIPLE NEGATIVE BREAST CANCER

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Triple-negative breast cancer (TNBC) represents a heterogeneous group of aggressive tumours which exhibit high rates of relapse and poor prognosis. There are currently no effective targeted treatments due to a lack of well-defined molecular targets. Recent therapeutic approaches, including immune-checkpoint blockade, have taken to targeting tumour-stromal interactions in combination with chemotherapy. However, little clinical progress has been made in TNBC treatment. This has been largely impeded by a limited understanding of the cancer-associated stromal cells and their biological mechanisms underlying tumourigenesis.

To gain insights into tumour-stromal heterogeneity and crosstalk mechanisms, we performed single-cell RNA sequencing on murine allograft M6 models of TNBC. In this study, our models are driven with and without hedgehog (Hh) pathway activation to explore the response of the stroma to Hh ligand, as Hh ligand overexpression is associated with poor prognosis in TNBC. We also profiled healthy murine mammary glands to help identify gene expression specific to cancer-associated stromal cells in our models.

We used the droplet-based Chromium Single Cell 3' system (10X Genomics), followed by short-read sequencing on the NextSeq500 (Illumina), to generate transcriptomes for over 10,000 single cells. In the tumour microenvironment, we identified cancer cells, cancer-associated fibroblasts (CAFs), endothelial cells, pericytes and innate immune cells. Unsupervised clustering identified subsets of stromal cells with differential pathway activation that highlights potential mechanisms involved in tumourigenesis and response to Hh signalling. In particular, we observed intra-tumoural CAF heterogeneity, identifying a novel subtype with functional enrichment for immune and cytokine signalling pathways.

This work demonstrates the power of single-cell technologies to understand and unravel the tumour-stromal ecosystem and aims to offer insights into new anti-stromal therapeutic targets in TNBC.

POSTER 20

SLAMSEQ: HIGH-THROUGHPUT METABOLIC SEQUENCING OF RNA

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Standard RNA-Seq methods measure total RNA abundance but cannot resolve the underlying kinetics of RNA transcription and degradation that determine overall steady-state levels. Metabolic sequencing of RNA combines the use of metabolic RNA labeling with RNA-Seq read-out to enable quantitative analysis of newly-synthesized (nascent) RNA. Existing approaches for metabolic RNA-Seq include pulse-labeling of RNA with nucleotide derivatives including 4-thiouridine (S4U), together with biochemical pull-down to separate nascent and existing RNA for library preparation. However, these protocols are time- and labour-intensive, require high amounts of RNA input, and often produce low signal quality. Pull-down efficiencies of individual transcripts also depend on sequence properties, meaning the results are only semi-quantitative. Further, the combination with standard RNA-Seq library preparation methods make these approaches overall costly and analysis-intensive, particularly when time courses and sufficient replicates are considered.

Lexogen has developed a family of protocols based on a new transcriptome-wide, non-invasive, quantitative, and fast method: SLAMseq, thiol (SH)-Linked Alkylation for the Metabolic sequencing of RNA, which was invented at the Institute of Molecular Biotechnology in Austria. SLAMseq enables quantitative analysis of nascent and existing RNA from a single total RNA sample in parallel, without the need for biochemical isolation. SLAMseq workflow can be readily applied to living cell experiments. Compared to standard RNA-Seq the SLAMseq protocol adds only two extra steps: Labeling of the RNA by adding S4U to the culture medium, and pre-processing of the total RNA with iodoacetamide to induce alkylation of the 4-thiol group, before continuing with a standard RNA-Seq protocol. At the level of data processing an algorithm distinguishes between reads from existing and nascent RNA molecules by detecting sites of nucleotide conversion in NGS reads, similar to single nucleotide polymorphism analysis. Additionally, evaluation of all obtained reads provides quantification of total steady-state RNA levels as reported by standard RNA-Seq.

POSTER 21

A PHENOTYPE CENTRIC BENCHMARK OF VARIANT PRIORITISATION TOOLS

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Next generation sequencing is a standard tool used in clinical diagnostics. In Mendelian diseases the challenge is to discover the single etiological variant among thousands of benign or functionally unrelated variants. After calling variants from aligned sequencing reads, variant prioritisation tools are used to examine the conservation or potential functional consequences of variants. We hypothesized that the performance of variant prioritisation tools may vary by disease phenotype. To test this we created benchmark datasets for variants associated with different disease phenotypes. We found that performance of 24 tested tools is highly variable and differs by disease phenotype. The task of identifying a causative variant amongst a large number of benign variants is challenging for all tools, highlighting the need for further development in the field. Based on our observations, we recommend use of five top performers found in this study (FATHMM, M-CAP, MetaLR, MetaSVM & VEST3). In addition we provide tables indicating which analytical approach works best in which disease context. We anticipate that further development into disease focussed tools will lead to significant improvements.

POSTER 22

DIVERSIFICATION OF INNATE IMMUNE RESPONSES BY TRANSCRIPTIONAL MECHANISMS

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Innate immune cells elicit a broad inflammatory program as a first-line defence against infection. As the spectrum of innate cell phenotypes produced by different pathogens has the capacity to drive long term adaptive immunity, it is important that the repertoire of immune responses are understood.

We have used Cap Analysis Gene Expression (CAGE) to characterise the monocyte transcriptomes elicited by ten different pathogenic challenges. CAGE maps the location and expression of distinct transcription initiation events. Engagement of multiple transcription start sites (TSSs) by genes in our dataset was prevalent. Half of the 11113 genes expressed by treated monocytes were expressed from multiple TSSs. Multi-TSS genes constituted a majority of differentially expressed genes (66%) and were enriched for biological functions related to the innate immune response, including cytokine and pattern recognition receptor mediated signalling, and apoptosis. Conversely, single-TSS genes were enriched for housekeeping functions, encompassing metabolic processes, and nucleic acid processing and repair. This implicates multi-TSS genes in adapting to extracellular stimuli and adjusting homeostasis during inflammatory responses to infection.

The patterns of TSS engagement provide insight into transcriptional mechanisms co-opted by the innate immune cell, to amplify the transcriptional activity at key inflammatory loci, as well as set up diversity in downstream signalling events through expression of protein isoforms predicted to alter subcellular localisation, protein partnerships, or activation potential of innate immune pathways. These help provide a mechanism for rapid phenotypic change from monocyte to macrophage in response to pathogenic challenge.

POSTER 23

DNA METHYLATION, A BIOMARKER OF AGE IN A LONG-LIVED SEABIRD?

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Most seabirds do not have any outward identifiers of their chronological age, so estimation of seabird population age structure generally requires expensive, long-term banding studies. We investigated the potential to use a molecular age biomarker to estimate age in short-tailed shearwaters (Ardenna tenuirostris). DNA methylation (DNAm) is a key mechanism for regulating gene expression in animals and levels are known to change with age. Recent studies have used DNAm changes as a biomarker to estimate chronological age in humans and these techniques are now also being applied to domestic and wild animals. Animal age is widely used to track ongoing changes in ecosystems, however chronological age information is often unavailable for wild animals. An ability to estimate age would lead to improved monitoring of (i) population trends and status and (ii) demographic properties such as age structure and reproductive performance. We have quantified DNAm in several A. tenuirostris genes that have shown age-related methylation changes in mammals. In birds ranging from chicks to 21 years of age, bisulphite treated blood and feather DNA was sequenced and methylation levels of 67 CpG sites in 13 target gene regions was analysed. The majority of markers had no clear association with age and statistical analysis using a penalised lasso approach did not produce an accurate ageing model. Due to the difficulties in identifying a conserved bird DNAm age biomarker from mammalian genes, we have recently carried out a pilot study using digital restriction enzyme analysis of methylation (DREAM). Shearwater blood DNA was sequenced using Illumina's MiSeq instrument and analysis yielded data on approximately 11,000 CpG sites. Further experiments will make use of newer sequencing technologies to increase the read coverage for each CpG site. Based on previous evidence, this enzymatic approach should yield a robust global DNAm age biomarker and may lead to further gene targets in birds.

POSTER 24

TIME COURSE GENE EXPRESSION ANALYSIS OF FORENSIC BLOOD SAMPLES

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mRNA expression levels are used to identify body fluids in forensic casework. In real world settings, body fluid stains may be weeks or months old and exposed to various environmental conditions prior to sample collection and analysis. With this study we investigated how gene expression in dried blood samples changes over time, and what effect this has on the reliability of commonly used forensic biomarkers. Small amounts of circulatory blood were left to dry in the lab to simulate aged forensic stains. We extracted RNA at 12 time points ranging from 0 hours to 84 days, sequenced samples on the Illumina HiSeq2500, and performed a time course gene expression analysis. Focussing on six genes used for identifying blood in forensic science, we found that despite decreasing expression levels, all markers included in this study were detectable at 84 days and thus are appropriate markers for blood identification in aged forensic stains. We also compared expression of whole genes to specific RNA stable regions of the blood markers to determine if the latter are more consistently expressed in aged samples, and found that some regions are equally expressed over time.

POSTER 25

RELIABLY DETECTING CLINICALLY IMPORTANT VARIANTS REQUIRES BOTH COMBINED VARIANT CALLS AND OPTIMIZED FILTERING STRATEGIES

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A diversity of tools is available for identification of variants from genome sequence data. Given the current complexity of incorporating external software into a genome analysis infrastructure, a tendency exists to rely on the results from a single tool alone. The quality of the output variant calls is highly variable however, depending on factors such as sequence library quality as well as the choice of short-read aligner, variant caller, and variant caller filtering strategy. Here we present a two-part study first using the high quality 'genome in a bottle' reference set to demonstrate the significant impact the choice of aligner, variant caller, and variant caller filtering strategy has on overall variant call quality and further how certain variant callers outperform others with increased sample contamination, an important consideration when analyzing sequenced cancer samples. This analysis confirms previous work showing that combining variant calls of multiple tools results in the best quality resultant variant set, for either specificity or sensitivity, depending on whether the intersection or union, of all variant calls is used respectively. Second, we analyze a melanoma cell line derived from a control lymphocyte sample to determine whether software choices affect the detection of clinically important melanoma risk-factor variants finding that only one of the three such variants is unanimously detected under all conditions. Finally, we describe a cogent strategy for implementing a clinical variant detection pipeline; a strategy that requires careful software selection, variant caller filtering optimizing, and combined variant calls in order to effectively minimize false negative variants. While implementing such features represents an increase in complexity and computation the results offer indisputable improvements in data quality.

POSTER 26

UTILISING MIXTURE MODELS FOR UNVEILING PATTERNS IN SCRNA-SEQ DATA

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Single cell RNA-Sequencing (scRNA-Seq) has enabled unprecedented insight into the behaviour of individual cells on the scale of the entire transcriptome. Such precision offers an opportunity to explore cell-specific heterogeneity, however two distinct features arise from such data: (1) hyperinflation of identically zero counts for the majority of genes for any given cell, and (2) an apparent bimodal distribution of non-zero counts. Both features are unique to scRNA-Seq, and warrant further development of statistical tools in order to answer biological questions of interest.

We propose a mixture modelling framework to classify cells into three transcriptional states for each gene: (1) no, (2) low, and (3) high gene expression. This approach has the potential to reveal the cell-specific dynamics of RNA transcription (bursting) and degradation, as well as acting as a cross-dataset standardisation. We conducted a comparison of four particular models using either gamma-gamma or gamma-normal mixture models, and either performed independently across genes or constrained to ensure the first gamma component (lowly expressed) parameters are common across all genes. Comparison was conducted using metrics such as the Bayesian Information Criterion (BIC) to identify the most parsimonious mixture model type across all profiled genes. As a result, in addition to a standardised dataset, specific gene features can be obtained via the estimated parameters of each mixture model fit and used for further characterisation of genes, e.g. to identify especially highly or lowly variable genes.

We utilised a number of publicly available scRNA-Seq datasets, stemming from mouse neuronal cell populations, to perform the mixture model comparison, assess highly and lowly variable genes, and to estimate cell networks via a uniqueness thresholding.

POSTER 27

CANCER-ASSOCIATED PTEN MUTATIONS ALTER PTEN CELLULAR FUNCTION

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Background: The phosphatase and tensin homolog (PTEN) is a tumour suppressor that plays an important role in normal cellular function, including regulating the cell cycle arrest, apoptosis, cell adhesion, migration and differentiation. Alterations of PTEN are central to the development of various cancers and other diseases. Previous work in our laboratory demonstrated the occurrence of PTEN gene mutations in 25% of primary human colorectal tumours [1]. Interestingly, all tumours harbouring alterations of PTEN demonstrated either reduced or absent PTEN protein expression. Overall, 10 novel cancer-associated PTEN mutations were described.

Aim: This project aims to determine the effect(s) of these novel mutations on PTEN cellular function.

Methods: Wild type and mutant PTEN expression constructs were prepared and transiently transfection into various cancer cell lines (U87MG glioblastoma, MCF7 breast cancer cells and HCT116 colon cancer cells). The effect(s) of WT and mutant PTEN on cell cycle phase distribution, the rate of cell proliferation and AKT activation were assessed.

Results and Discussion: In contrast to the effects observed with WT PTEN, a number of the tested PTEN mutations were found to decrease the ability of PTEN to (a) bring about cell cycle arrest, (b) slow the rate of cell proliferation and (c) decrease the level of AKT activation. The effects observed were dependent on the cell type as individual mutations did not have the same effect in all cell lines.

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POSTER 28

FAST, UNBIASED DNA ENRICHMENT RESAMPLING

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Resampling methods, such as cross validation and bootstrap remain powerful techniques in the development of robust bioinformatic models. Unfortunately, these methods are very computationally expensive for large 'omics data sets, restricting their use in large clinical studies. An important requirement for resampling methods to be valid, is that out of sample data, such as test data, is hidden during model generation. Genome wide enrichment sequencing protocols such as ChIP-seq and MBD-seq, are commonly analyzed by peak finding, followed by summarization (counting sequence tags within a peak), then statistical detection of differential enrichment. Given that repeating the summarization process is computationally expensive when resampling from a large sample group, a possible analysis strategy would be to generate a single summarization result based on peaks from all samples, then resampling from that result. We show that using the peaks from all samples to generate a single sequence count summarization biases the results towards overly optimistic models. In order to make comprehensive unbiased resampling methods available for epigenomics without the computational expense of repeated summarization, we developed a method using a partially precomputed index of summations. Having calculated the summations for all possible peak sub-regions, the summarization step consists of subsample peak determination, followed by subsample peak summation. From our tests, using this index speeds up subsample summarization data generation by at least 20 times, making epigenomic resampling available to a larger range of computer systems and larger clinical studies.

POSTER 29

HAPLOTYPING AND COPY NUMBER PROFILING OF SINGLE CELLS BY MASSIVE PARALLEL SEQUENCING

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Introduction: Genome-wide haplotyping (such as karyomapping or haplarithmisis) enables the reconstruction of genome-wide haplotypes and copy-number profiles and is able to determine the parental origin of haplotypes at the single cell level. This methodology is being implemented as a generic method for preimplantation genetic diagnosis (PGD) in many IVF laboratories. The method can be applied on blastomeres biopsied from cleavage embryos or trophectoderm sampled from blastocysts. This allows the diagnosis of disease alleles, numerical and structural chromosomal abnormalities genome-wide. Current methods use SNP arrays to deduce the haplotype. The resolution of SNP arrays is limited and the platform is costly. The ultimate genetic screen of a single cell would be whole genome sequencing. However, this is currently too expensive. To overcome these limitations, we developed a single cell based genotyping-by-sequencing (GBS) method.

Materials and methods: Proof-of-principle experiments were performed on cells from the HapMap cell lines. DNA is amplified by RepliG. Three different restriction enzymes were used to digest the DNA and reduced representation libraries were generated. The fragments were sequenced on Illumina HiSeq2500. Subsequent haplotyping was performed by haplarithmisis. To allow for sequencing based genotyping, the siCHILD computational workflow was amended.

Results: We first demonstrate that a median coverage of 20 allows for a genotyping accuracy of 99.9 % for bulk DNA. Across informative SNPs covered in both single cell and genomic DNA from the same individual we obtain up to 94 % concordance for the single cell genotype compared to the bulk DNA genotype. Preliminary results show a confidence of 99% within a distance of 18 informative SNPs flanking a homologous recombination site for correct single cell haplotype inference compared to the haplotype derived from bulk DNA. Subsequently a validation study is performed by comparing the GBS based haplotypes with the SNP array based haplotypes which were derived on embryos from clinical PGD cycles. Results of this ongoing study will be presented.

Conclusions: Here, we present a novel methodology for genotyping single cells through next-generation sequencing. By applying the GBS protocol as a method for genome reduction and the advancing sequencing technologies, we foresee this methodology as a valuable alternative for genotyping using SNP arrays

POSTER 30

IMPROVING ACCESSIBILITY AND COMPREHENSION IN CONSENT FOR GENETIC RESEARCH: A WEB PLATFORM FOR CONSENT APPS

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Informed consent is fundamental to ethical research with human participants. Yet in many cases, consent is still undertaken using long written documents that do a poor job of explaining the study and its risks to potential participants. This approach can be particularly problematic for genetic research, where it can be challenging to concisely explain the study rationale (why do you need controls? What is a genetic variant?) and the relevant risks (how will my privacy be protected? What are incidental findings? Will you return my results? What will the results mean for my health, or for my insurance?) to a lay audience, including a significant proportion with poor literacy skills or for whom English is not their first language.

As part of the Tasmanian Reference Genome Project, in which 200 healthy Tasmanians will be recruited to provide control data for a range of disease genetic studies, we developed a web platform for creating informed consent apps. iCAR (Informed Consent Apps for Research) addresses these issues and is designed to improve the informed consent experience for potential participants. This platform allows researchers to easily and affordably create their own customised informed consent app, including multimedia and interactive components to improve participant accessibility and comprehension. It also makes it easier to include multiple languages, and provides consistency of participant experience. The functionality of the platform was designed based on the findings of quantitative and qualitative studies involving stakeholders (HRECs, researchers, and vulnerable participant groups), and is being tested through the development of a pilot app for the Tasmanian Reference Genome Project.

POSTER 31

OCCURRENCE OF G-QUADRUPLEXES IN NON-CANCEROUS AND CANCEROUS CELLS IN GENE REGULATORY REGIONS

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G-quadruplex DNA (G4) are non-canonical secondary DNA structures that are often found in regulatory regions of the human genome e.g. gene promoters and 3'-end of telomeric DNA.1 These structures have roles in gene regulation and have been implicated in a range of diseases such as cancer and neurodegenerative diseases.2 Oncogenes (VEGF, BCL2, MYC, KRAS, RB1, TERT and PDGFA) that contribute to the six hallmarks of cancer (sustained angiogenesis, evasion of apoptosis, self-sufficiency, insensitivity, limitless replication potential, and tissue evasion and metastasis) contain G4 forming sequences in their promoters. The identification of G4s are important, as they are attractive targets for drug therapy of "undruggable" genes.5

Hansel-Hertsch et al. (2016) utilized a newly developed G4 Chromatin Immunoprecipitation (G4-ChIP) method combined with ATAC-seq and FAIRE-seq to demonstrate that G4s are over-represented in nucleosome-depleted regions of the human genome and they are enriched in the promoters of highly transcribed genes and 5'UTRs3

In this work, we developed a combined method termed ATAC-G4-ChIP-seq to map G4s in chromatin accessible regions of cancerous and non-cancerous breast cancer cell lines (MCF7 and MCF10A, respectively). We also utilize a previously reported early breast cancer model4 using human mammary epithelial cells (HMEC) which are then transformed to variant human mammary epithelial cells (vHMEC) to study how G4-formation sites are altered during this transformation.

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POSTER 32

REPROGRAMMING OF CRITICAL GENE REGULATORY ELEMENTS IN A MOUSE MODEL OF AD

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Introduction: Alzheimer's disease (AD) is a terminal progressive neurodegenerative disorder, yet the underlying cause of sporadic AD cases remains unknown. Epigenetics allows for dynamic regulation of chromatin structure, and complex interaction between the DNA and our environment, and underpins neuronal diversity and function. Epigenetic alterations such as DNA methylation, post-translational histone modifications, and nucleosome occupancy may contribute to the pathological pathways implicated in the onset and progression of sporadic AD.

Methods: APP/PS1 AD mice closely recapitulate the pathology present in human early-AD cases of beta-amyloid plaque deposition and plaque-associated synapse loss. APP/PS1 mice enable us to examine the earliest pre-pathology epigenetic changes that occur in AD, as well as a time course of disease progression. Neuronal nuclei from the forebrain of APP/PS1 mice and age-matched wild-type control mice (n=5 per genotype at 3,6,12 months of age) were isolated, then purified with FACS and subject to chromatin immunoprecipitation and next-generation sequencing (ChIP-seq) with antibodies detecting H3K4me3, H3K27me3, and H3K27Ac.

Results: Enhancers (H3K27Ac) and promoter (H3K4me3, H3K27me3) marks are lost from regulatory regions in APP/PS1 mice compared to age-matched controls ($p<0.05$). Specifically, both enhancer and promoter marks were lost from key risk factor genes for sporadic AD (PICALM, BIN1; $p<0.05$) or at known differentially expressed genes in sporadic human cases and transgenic AD mice (PICALM, TBXA2R, F2RL2, SORBS3; $p<0.05$).

Conclusions: These data show that epigenetic reprogramming occurs in a mouse model of early AD, affecting both enhancers and promoters. Epigenetic dysregulation may be a key aspect of AD onset and pathology.

POSTER 33

IDENTIFICATION OF ZBTB7A AND MAZ AS REGULATORS OF GENE EXPRESSION IN DIABETES

Haloom Rafehi[1], Harikrishnan Kaipananickal[1], Jun Okabe[1], Mark Ziemann[1], Ishant Khurana[1], Antony Kaspi[1], Assam El-Osta[1]

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Background: Endothelial dysfunction is the critical early step that lead to the development of atherosclerotic plaques in diabetes. To date, the regulation of transcriptional events in endothelial dysfunction remain poorly defined. Furthermore, while recent evidence shows anti-inflammatory effects of histone deacetylase (HDAC) inhibitors in healthy primary human endothelial cells, the effects in diabetic cells have yet to be defined.

Materials and methods: we studied genome-wide gene expression (RNA-seq) and histone acetylation (ChIP-seq) profiles of primary human aortic endothelial cells (HAECs) derived from healthy and T1D individuals, before and after exposure to an anti-inflammatory histone deacetylase (HDAC) inhibitor SAHA (n=3, conc. 2 μM, for 12 or 16h).

Results: we identified wide-spread increases in histone acetylation at gene promoters in diabetic HAECs following SAHA exposure, consistent with the paradigmatic action of HDAC inhibitors. In contrast, SAHA lead to both increases and decreases in healthy HAECs, which correlated with gene expression. Unexpectedly, gene promoters deacetylated in healthy cells, but acetylated in diabetic cells, were enriched for the transcription factors (TFs) ZBTB7A and MAZ, suggesting altered activities of these TFs in diabetic HAECs. Analysis of TF binding sites from ENCODE shows that up to 90% of ZBTB7A binding sites genome-wide intersect with MAZ. Validation by RNA-seq of healthy and diabetic HAECs cultured in hyperglycaemic conditions for 15 days identified activation of multiple genes regulated ZBTB7A and MAZ, such as TRIB1, an inflammatory regulator implicated in atherosclerosis and glucose homeostasis. Re-analysis of public datasets identified strong binding of ZBTB7A at the promoter of TRIB1, and increased TRIB1 expression following ZBTB7A deletion in immortalised human erythroblasts.

Conclusions: our data suggests a role for ZBTB7A and MAZ in gene regulation by chronic hyperglycaemia. Further work, including ZBTB7A and MAZ ChIP and deletion studies in hyperglycaemic cells, are in progress to validate the generality of these findings.

POSTER 34

HOMING IN ON PRECISE DIAGNOSES: THE POWER OF COMBINING MULTI-LAYERED GENOMIC AND HISTOPATHOLOGICAL ANALYSIS IN PANCREATIC CANCER

Tamsin Robb[1], Ben Lawrence[1], Cherie Blenkiron[1], Kate Parker[1], Peter Tsai[1], Sandra Fitzgerald[1], Paula Shields[1], Mee-Ling Yeong[2], Nicole Kramer[2], Michael Findlay[1], Cristin Print[1]

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In a study of 60 patients with pancreatic neuroendocrine tumours (pNETs), multi-layered genomic and histopathological analysis led to refined diagnosis for four patients (7%). Targeted deep DNA sequencing and RNA expression data alongside pathological examination were employed to search for molecular drivers in pNETs, and incidentally provided valuable evidence for re-diagnosis. This poster focusses on the reconsidered diagnosis of two patients' tumours as pancreatic solid pseudopapillary neoplasms (SPNs), which share some cytological features with pNETs but are genomically distinct. pNETs and SPNs each have a discrete clinical course, staging and follow-up programme.

Histological review had diagnosed two tumours within this study as pNETs by morphological and immunohistochemical criteria but also noted uncertainty due to some variable SPN-like morphological features. DNA sequencing revealed activating CTNNB1 variants in these tumours, mutations pathognomonic for SPNs. These variants were both predicted to be dominant positive activators of Ð-catenin function. The diagnosis was strongly supported at the RNA level by undetectable expression of pNET marker CHGA, and at the protein level by cellular relocalisation of Ð-catenin to the nucleus. In accord with the known activating effect of the CTNNB1 single nucleotide variants in both tumours, subsets of RNAs known to be up-regulated by Ð-catenin activity in colorectal cell lines were also highly expressed (≥2 SD above the mean of all pNETs). Taken together, this study highlights the enhanced value of considering genomic and pathological findings together when making rare tumour diagnoses, which will lead to more accurate clinical decision-making.

POSTER 35

COMPARISON OF SHOTGUN DNA LIBRARY PREPARATION KITS FOR SEQUENCING ON ILLUMINA PLATFORMS

Jafar S. Jabbari[1], Lavinia Gordon[1], Matthew Stephen[1], Matthew Tinning[1], **Kirby Siemering[1]**

[1] Australian Genome Research Facility, Melbourne

Library preparation methods are evolving with advances in next generation sequencing platforms. Early shotgun DNA library preparation protocols were labour intensive involving many steps. Ongoing innovations to increase library preparation efficiency, lower inputs, and simplify protocols have resulted in a rapid expansion in the number of kits on the market from multiple vendors. In this study, we have prepared and sequenced libraries across three different input quantities using kits from four leading suppliers. We compare library characteristics and analysis results and discuss the suitability of kits for different applications.

POSTER 36

IDENTIFICATION OF SODIUM VALPROATE AND LITHIUM CO-REGULATED GENES IN A SEROTONERGIC CELL LINE

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Sodium valproate and lithium are drugs of very different chemical classes that are widely prescribed in the treatment of bipolar disorder and other conditions. Molecular and pharmacological studies have revealed some relevant properties and targets of these drugs but their precise modes of action are not yet understood1-2. Genes displaying specific regulation by either or both of these drugs are relevant to the mechanism of action, and co-regulated genes highlighting the common pathways are of greatest interest. Most mood disorders appear to involve the serotonergic system, so we are using a serotonergic cell line called RN46A3 that represents a relevant model for the neurological effects of valproate and lithium.

RNA-Seq analysis of cells treated with valproate (0.5mM) and lithium (0.5mM) for 72 hrs yielded 145 genes (log2 fold change >1.5 and FDR < 0.05) significantly changed after exposure to valproate, and none with lithium. High correlation (r2=0.75) is observed between RNA-Seq and Nanostring for chosen 23 genes. 8/23 genes, ADAM23, *CDKN1C, CNTN1, LSP1, MAOB, MMP13, SERPIN2B* and *WNT6* are regulated by lithium when the dose is increased from 0.5mM to 2mM. None of these 23 validated genes are regulated by lamotrigine, another mood stabilizer.

9/23 genes, *CACNA1B, IGF2, LZTS1, MPP3, NOTCH3, LINGO1, SHANK3, SNAP91* and *VGF* are upregulated by both valproate and valpromide, a non-histone deacetylase (HDAC) valproate analog, suggesting non-HDAC regulation. *ADGRB2, ERBB3, GNAI1, NGFR, PAK3* and *ZCCHC12* are upregulated only by valproate.

CI994, HDAC 1 inhibitor, regulates *LSP1, MAOB, NGFR, CDKN1C, CNTN1, WNT6* and *ZCCHC12*. None of these 23 genes are regulated by HDAC 3 (RGFP966) and HDAC 8 (PCI34051) inhibitors.

Protein expression of these genes are being investigated in valproate-treated rats using immunohistochemistry. Our results show novel shared targets of lithium and valproate which may play an important role in mood regulation.

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2. Atmaca, M. (2009). *Valproate and neuroprotective effects for bipolar disorder.* International review of psychiatry. 21: 410-3.
3. White, L., et al. (1994). *Distinct regulatory pathways control neurofilament expression and neurotransmitter synthesis in immortalized serotonergic neurons.* The Journal of Neuroscience 14, 6744–53.

POSTER 37

INTEGRATING SEQUENCE VARIATION INTO CRISPR/CAS9 OFF-TARGET DETECTION

Sara Hetzel[1], **Laurence Wilson[1]**, Denis Bauer[1]

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Genome engineering is increasingly used in applications where incorporation efficiency is crucial because biological samples or time is limited, such as in human health. Sequence variation, such as mutations and indels, can effect this efficiency. This is because target scoring is typically done on a fixed reference genome and the 3 million base pairs that are different between any two individuals can create new targets or render off-targets inactive in the edited genome.

For each individual approximately 20000 SNPs lie in coding regions, which are typically the main focus of genome engineering applications. As even a single substitution can impact on the CRISPR/Cas9 target system, we develop a new algorithm that takes a variable genome into account when designing targets.

We compare our SNP-aware off-target detector against traditional approaches when scoring the genomes of individuals or population, and demonstrate the efficiency gain obtained from adopting this practice. In addition, a machine learning model following the off-target screening predicts the activity of the detected off-targets and provides a ranking based on those scores. In addition, we integrate our previously published on-target activity predictor to provide the most complete prediction for CRISPR-Cas9 activity. We will highlight the implementation details of using AWS Lambda functions, which makes the tool highly scalable.

POSTER 38

INTRAGENIC ENHANCERS ATTENUATE HOST GENE EXPRESSION

Pengyi Yang[1,2*], Senthilkumar Cinghu[1*], Justin Kosak[1], Amanda E Conway[1], Dhirendra Kumar[1], Andrew J Oldfield[1], Karen Adelman[3], Raja Jothi[1]

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Gene transcription in eukaryotic organisms is regulated at multiple rate-limiting steps, including RNA Polymerase II (RNAPII) recruitment, transcription initiation, promoter-proximal RNAPII pause release, and transcription termination. However, transcriptional regulation during productive elongation remain poorly understood. Enhancers, which activate gene transcription, themselves undergo RNAPII-mediated transcription, but our understanding of enhancer transcription and RNAs (eRNAs) remain incomplete. Here we show that transcription at intragenic enhancers interferes with and attenuates host gene transcription during productive elongation. While the extent of attenuation correlates positively with nascent eRNA expression, the act of transcription at intragenic enhancers, but not the transcript itself, explains the attenuation. Through CRISPR/Cas9-mediated deletions, we demonstrate a physiological role for intragenic enhancer-mediated transcription attenuation in cell-fate determination. Our findings suggest that intragenic enhancers not only enhance transcription of one or more genes from a distance but also fineÐtune transcription of their host gene through attenuation, facilitating differential utilization of the same regulatory element to perform disparate functions.

POSTER 39

SYSTEMATIC IDENTIFICATION OF NON-CONVENTIONAL TRANSCRIPTS FROM HUMAN CELLS

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Identification of non-conventional RNA molecules such as fusion and read-through transcripts is a challenging task in the effort to comprehensively characterize the functional readout of the human genome. RNA sequencing by Paired-End diTag (RNA-PET) analysis possesses the unique capability to accurately and efficiently characterize the 5′ and 3′ ends of RNA fragments, which makes it an ideal tool for this problem. Previous studies have reported promoter and enhancer transcription, a lot of which display bidirectional transcription. Fusion transcripts have been identified with RNA-PET in human cancer cell lines which directly correspond to gene fusions resulting from genome structure variation and lead to disease. Similarly, read-through transcripts and trans-spliced transcripts were reported in mammalian genomes, however, a comprehensive characterization of all these types of transcripts and how they function is still far from complete.

Here, we use RNA-PET data from IMR90 (fetal lung fibroblast) cells from the ENCODE project. Out of 20.6 million PETs 19.2 million are concordant. Reads in close proximity are clustered together resulting in 137822 clusters, whereby the cluster count can be used as a proxy for the transcript's expression level. Overlapping RNA-PET clusters which have a cluster count higher than one with known exons, we find that 33% match known transcripts, 16% are fusion products mostly using internal exons, another 44% have alternative start or stop sites and the remaining 6% represent novel transcripts. By including an RNA-PET replicate, histone marks, TFBSs, DNase activity, termination sites and overlap with known transcripts as support we can distinguish real sites from transcriptional noise and experimental errors. Aggregation plots of these marks around TSSs and TTSs help us identify which marks are actually involved in transcription. Lastly, we compare our results to transcripts in other cells to find a possible functional relationship between non-conventional transcripts and diseases.

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Scientifix

Scientifix represents Takara Bio, Rubicon Genomics and Wafergen Biosystems; the specialist in low input NGS. Selection includes RNA-seq, smRNA-Seq, ChIP-seq, Methyl DNA-Seq, DNA-seq, Plasma-seq, TCR profiling, WGA and comprehensive tools for CRISPR/Cas9 workflow. Takara's Long ssDNA Production System for CRISPR/Cas9 knock-in experiments, and Wafergen's ICELL8 Single-Cell System for high throughput single-cell analysis are examples of our newest products. We also offer solutions for DNA/RNA extraction from challenging samples and plasma.

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Tecan is a leading global provider of automated laboratory instruments and solutions. Our systems, components and support help people working in clinical diagnostics, basic, translational research and drug discovery bring their science to life.

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Total Genomics Solution

Total Genomics Solution (TGS) is an emerging NGS company based in Melbourne. It provides high quality genomics and bioinformatic services to the Australasian scientific community. TGS is an expert in integrating multiple NGS platforms and delivering systematic NGS solutions. It aims to be a 'One-Stop' NGS centre and enables the scientists to focus on their questions.

TGS provides a broad range of NGS sequencing for genome, transcriptome, single cell, targeted regions, epigenetics etc. using one or mixed Illumina, PacBio, Nanopore platforms. It also provides customised bioinformatic solutions.

www.tgstech.com

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Niccy Aitken	EcoGenomics Lab Manager	Australian National University	ACT
Jekaterina Aleksejeva	Senior Marketing Manager	Lexogen	Austria
Ghamdan Al-Eryani	PhD Candidate	Garvan Institute of Medical Research	NSW
Denise Anderson	Biostatistician	Telethon Kids Institute	WA
Melanie Bahlo	Division Head	The Walter and Eliza Hall Institute of Medical Research	VIC
Stephanie Bannister	Application Scientist	Lexogen	Austria
Marco Barsanti	Account Manager	QIAGEN	VIC
Brant Bassam	Product Manager	Bio-Strategy	VIC
Anthony Beckhouse	Field Applications Specialist	BGI	QLD
Traude Beilharz	Group Leader	Monash University	VIC
Dan Belluoccio	Field Application Scientist	Agilent Technologies	VIC
Tony Bhalla	Sales Leader Oceania Ag	PerkinElmer	VIC
Jim Blackburn	Senior Postdoctoral Researcher	Garvan Institute of Medical Research	NSW
Nicholas Blackburn	Assistant Research Scientist	UTRGV -South Texas Diabetes & Obesity Institute	United States
John Blangero	Professor	UTRGV-South Texas Diabetes & Obesity Institute	United States
Justin Borevitz	Professor	Australian National University	ACT
Anthony Borneman	Principal Research Scientist	The Australian Wine Research Institute	SA
Kiymet Bozaoglu	Senior Research Officer	Murdoch Children's Research Institute	VIC
Kathryn Burdon	Principal Research Fellow	Menzies Institute for Medical Research	TAS
Dave Burt	Director, UQ Genomics	The University of Queensland	QLD
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Eva Chan	Senior Research Officer	Garvan Institute of Medical Research	NSW
Jac Charlesworth	Computational Genomics	Menzies Institute for Medical Research	TAS

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Ming Chen		Menzies Institute for Medical Research	TAS
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Rebecca Craythorn	Account Manager	Merck	VIC
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Glenn D'Cunha	Account Manager	Australian Genome Research Facility	VIC
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Craig Don Paul	Account Manager	Pathtech	VIC
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Owain Edwards	Group Leader	CSIRO	WA
Nona Farbehi	PhD Student	University of New South Wales	NSW
James Ferguson	Genomic Systems Analyst	Garvan Institute of Medical Research	NSW
Matt Field	Senior Bioinformatics Fellow	James Cook University	QLD
Lynn Fink	Director of Research	BGI	QLD
Sandra Fitzgerald	PhD Student	The University of Auckland	New Zealand
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David Gallego-Ortega	Group Leader	Garvan Institute of Medical Research	NSW
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Austen Ganley	Senior Lecturer	The University of Auckland	New Zealand
Brooke Gardiner	Genomic Services Coordinator	The University of Queensland	QLD

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Joel Geoghegan	Manager	SA Pathology	SA
Shila Ghazanfar	PhD Student	The University of Sydney	NSW
Brian Gloss	Postdoctoral Researcher	Garvan Institute of Medical Research	NSW
Agnieszka Golicz	Research Fellow	The University of Melbourne	VIC
Cynthia Gong	Sales Director	Novogene	China
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Patricia Graham	Student	Menzies Institute for Medical Research	TAS
Sean Grimmond	Director & Bertalli Chair in Cancer Medicine	The University of Melbourne	VIC
Nahal Haddadi	PhD Student	University of Technology Sydney	NSW
Simon Hardwick	PhD Student	Garvan Institute of Medical Research	NSW
Ivon Harliwong	Facility Manager	BGI	QLD
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Longqi Liu	Project Leader	BGI	China
Ivan Lukic	Field Application Scientist	Partek	Croatia
Oscar Luo	Research Scientist	CSIRO	NSW
Anna Macdonald	Oz Mammals Genomics Initiative	Australian National University	ACT
Gregory Maes	Project Manager	KU Leuven	Belgium
John Markham	Researcher	Peter MacCallum Cancer Centre	VIC
Vikki Marshall	Operations Manager	The University of Melbourne	VIC
Farhana Matin	PhD Candidate	Queensland University of Technology	QLD
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Cath Moore	Market Development Manager	QIAGEN	VIC
Greg Neely	Associate Professor	The University of Sydney	NSW
Pauline Ng	Explorer and Consultant	Explorer and Consultant	Singapore
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Fabrice Odefrey	Application Scientist	Thermo Fisher Scientific	VIC
Marina Oliva	Research Associate	The University of Western Australia	WA
Alicia Oshlack	Head of Bioinformatics	Murdoch Children's Research Institute	VIC
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Alice Pébay	Principal Research Fellow	The University of Melbourne	VIC
Juan Peralta	Programmer Analyst IV	UTRGV-South Texas Diabetes & Obesity Institute	United States
Andrew Phipps	PhD Candidate	University of Tasmania	TAS
Mark Pinese	Senior Research Officer	Kinghorn Cancer Centre	NSW
Joseph Powell	Group Leader	The University of Queensland	QLD
Cristin Print	Professor	The University of Auckland	New Zealand
Clare Puttick	Research Assistant	Garvan Institute of Medical Research	NSW
Thom Quinn	PhD Student	Deakin University	United States
Haloom Rafehi	Research Fellow	Monash University	VIC
Kelsie Raspin	PhD Candidate	Menzies Institute for Medical Research	TAS
Nadav Rayman	Director - Sales and Marketing	BizData	VIC
Kimberly Reyolds	Assistant Professor	University of Texas Southwestern Medical Center	United States
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Tim Semple	Molecular Genomics Core	Peter MacCallum Cancer Centre	VIC
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Yang Shen	Research Scientist	Genome Institute of Singapore	Singapore
Kirby Siemering	Executive, Science and Technology	Australian Genome Research Facility	VIC
Priyanka Sinha	PhD Student	University of Otago	New Zealand
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Martin Smith	Head of Genomic Technologies	Garvan Institute of Medical Research	NSW

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Helen Speirs	Deputy Director	Ramaciotti Centre for Genomics	NSW
Stephanie Sun	Marketing Coordinator	BGI	QLD
Andrew Szentirmay	Director	Gene Target Solutions	NSW
Stone Tang	Director of BD	Genewiz	China
Richard Tothill	Group Leader	The University of Melbourne	VIC
Vito Trifilo	General Manager	Tecan Australia	VIC
Peter Tsai	PhD Student	The University of Auckland	New Zealand
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Mark Van der Hoek	Genomics Fellow	South Australian Health & Medical Research Institute	SA
Matthew Wakefield	Research Fellow	The University of Melbourne	VIC
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Paul Wang	Bioinformatician	SA Pathology	SA
Bill Wang	Client Manager	Total Genomics Solution	VIC
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Adam Werner	Technical Sales Representative	Integrated DNA Technologies	NSW
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Seyhan Yazar	Postdoctoral Research Fellow	University of Edinburgh	United Kingdom
Chengzhong Ye	Masters of Research Student	The Walter and Eliza Hall Institute of Medical Research	VIC
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