Biochemistry News

The newsletter of the Department of Biochemistry at the University of Otago

editor: Bronwyn Carlisle

December 2014

In This Issue

View from the Corner

Welcome to the December 2014 Biochemistry newsletter; many thanks to Bronwyn for putting it all together! The holidays are bearing down on us with rapidity and its a great time to catch up with family and friends. Probably just about the time this newsletter is released it will be time for our Departmental Christmas party with strawberries and ice cream all around.

This year's December newsletter and holiday party are particularly special for me because they will be my last as HOD. Wow five years sure do go by fast! The department has accomplished a lot in the last 5 years in terms of our core business of teaching, research and service and we have ranked highly on external metrics like publications and citations and PBRF scores. We are strong in grants and overheads and we have an enviable workload. As Catherine takes over as our new HOD, I know we will move from strength to strength.

Holiday time is always a good time for expressing gratitude and as I step down I want to be sure and thank you all for the opportunity to serve as HOD. It's been hard work and challenging for me, but I have enjoyed it immensely, and I hope I have grown a bit. The job would, of course, have been impossible for me without all the help and support I have received. I want to thank a few specific groups. First my HOD Advisory Group for sage advice and wonderful discussions, and our Committee Chairs for their good ideas and strong leadership. I would like to thank all the general staff from the store and workshops to the prep room and the IT crew and our wonderful front office staff. To Teena, Frances and now Debbie I owe many, many thanks! I have to especially thank Julian for all the long hours and late nights he served as Deputy HOD.

And finally, I need to thank my group and family for putting up with my being away for so much of the time. All my best for 2015! Happy Holidays! Kurt

Kurt Krause

Recent Publications

Screening in planarians identifies MORN2 as a key component in LC3-associated phagocytosis and resistance to bacterial infection.

Prasad Abnave, Giovanna Mottola, Gregory Gimenez, Nicolas Boucherit, Virginie Trouplin, Cedric Torre, Filippo Conti, Amira Ben Amara, Catherine Lepolard, Benjamin Djian, Daniel Hamaoui, Amel Mettouchi, Atul Kumar, Sophie Pagnotta, Stefano Bonatti, Hubert Lepidi, Alessandra Salvetti, Laurent Abi-Rached, Emmanuel Lemichez, Jean-Louis Mege, and Eric Ghigo

Dugesia japonica planarian flatworms are naturally exposed to various microbes but typically survive this challenge. We show that planarians eliminate bacteria pathogenic to *Homo sapiens*, *Caenorhabditis elegans*, and/or *Drosophila melanogaster* and thus represent a model to identify innate resistance mechanisms. Whole-transcriptome analysis coupled with RNAi screening of worms infected with *Staphylococcus aureus* or *Legionella pneumophila* identified 18 resistance genes with nine human orthologs, of which we examined the function of MORN2. Human MORN2 facilitates phagocytosis-mediated restriction of *Mycobacterium tuberculosis*, *L. pneumophila*, and *S. aureus* in macrophages. MORN2 promotes the recruitment of LC3, an autophagy protein also involved in phagocytosis, to *M. tuberculosis*-containing phagosomes and subsequent maturation to degradative phagolysosomes. MORN2-driven trafficking of *M. tuberculosis* to single-membrane, LC3-positive compartments requires autophagy-related proteins Atg5 and Beclin-1, but not Ulk-1 and Atg13, highlighting the importance of MORN2 in LC3-associated phagocytosis. These findings underscore the value of studying planarian defenses to identify immune factors.

Cell Host & Microbe, 2014 vol. 16 (3) pp. 338-350

Purine biosynthetic intermediate-containing ribose-phosphate polymers as evolutionary precursors to RNA.

Harold S Bernhardt and Roger K Sandwick

The RNA world hypothesis proposes that RNA once functioned as the principal genetic material and biological catalyst. However, RNA is a complex molecule made up of phosphate, ribose, and nucleobase moieties, and its evolution is unclear. Yakhnin has proposed a period of prebiotic chemical evolution prior to the advent of replication and Darwinian evolution, in which macromolecules containing polyols joined by phosphodiester linkages underwent spontaneous transesterification reactions with selection for stability. Although he proposes that the nucleobases were obtained during this stage from less stable macromolecules, the ultimate source of the nucleobases is not addressed. We propose that the purine nucleobases arose in situ from simpler precursors attached to a ribose-phosphate backbone, and that the weaker and less specific intra- and interstrand interactions between these precursors were the forerunners to the base pairing and base stacking interactions of the modern RNA nucleobases. Further, in line with Granick's hypothesis of biosynthetic pathways recapitulating evolution, we propose that these simpler precursors were the same or similar to intermediates of the modern de novo purine biosynthetic pathway. We propose that successive nucleobase precursors formed progressively stronger interactions that stabilized the ribose-phosphate polymer, and that the increased stability of the parent polymer drove the selection and further chemical evolution of the purine nucleobases. Such interactions may have included hydrogen bonding between ribose hydroxyls, hydrogen bonding between carbonyl oxygens and protonated amine side groups, the intra- and interstrand coordination of metal cations, and the stacking of imidazole rings. Five of the eleven steps of the modern de novo purine biosynthetic pathway have previously been shown to have alternative nonenzymatic syntheses, while a sixth step has also been proposed to occur nonenzymatically, supporting a prebiotic origin for the pathway.

Journal Of Molecular Evolution, 2014

The ubiquitin-associated domain of cellular inhibitor of apoptosis proteins facilitates ubiquitylation.

Rhesa Budhidarmo and Catherine L Day

The cellular inhibitor of apoptosis (cIAP) proteins are essential RING E3 ubiquitin ligases that regulate apoptosis and inflammatory responses. cIAPs contain a ubiquitin-associated (UBA) domain that binds ubiquitin and is implicated in the regulation of cell survival and proteasomal degradation. Here we show that mutation of the MGF and LL motifs in the UBA domain of cIAP1 caused unfolding and increased cIAP1 multimonoubiquitylation. By developing a UBA mutant that disrupted ubiquitin binding but not the structure of the UBA domain, we found that the UBA domain enhances cIAP1 and cIAP2 ubiquitylation. We demonstrate that the UBA domain binds to the UbcH5b~Ub conjugate, and this promotes RING domain-dependent monoubiquitylation. This study establishes ubiquitin-binding modules, such as the UBA domain, as important regulatory modules that can fine tune the activity of E3 ligases.

The Journal Of Biological Chemistry, 2014 vol. 289 (37) pp. 25721-25736

A bioinformatics workflow for detecting signatures of selection in genomic data.

Murray Cadzow, James Boocock, Hoang T Nguyen, Phillip Wilcox, Tony R Merriman, and Michael A Black

The detection of "signatures of selection" is now possible on a genome-wide scale in many plant and animal species, and can be performed in a population-specific manner due to the wealth of per-population genome-wide genotype data that is available. With genomic regions that exhibit evidence of having been under selection shown to also be enriched for genes associated with biologically important traits, detection of evidence of selective pressure is emerging as an additional approach for identifying novel gene-trait associations. While high-density genotype data is now relatively easy to obtain, for many researchers it is not immediately obvious how to go about identifying signatures of selection in these data sets. Here we describe a basic workflow, constructed from open source tools, for detecting and examining evidence of selection in genomic data. Code to install and implement the pipeline components, and instructions to run a basic analysis using the workflow described here, can be downloaded from our public GitHub repository: http://www.github.com/smilefreak/selectionTools/

Front Genet, 2014 vol. 5 p. 293

A sequence-specific interaction between the *Saccharomyces cerevisiae* ribosomal RNA gene repeats and a locus encoding an RNA polymerase I subunit affects rDNA stability.

Inswasti Cahyani, Andrew G Cridge, David R Engelke, Austen R D Ganley, and Justin M O'Sullivan

The spatial organization of eukaryotic genomes is linked to its functions. However, how individual features of the global spatial structure contribute to nuclear function remains largely unknown. We previously identified a high frequency inter-chromosomal interaction within the Saccharomyces cerevisiae genome that occurs between the intergenic spacer of the ribosomal DNA repeats (rDNA) and the intergenic sequence between the locus encoding the second largest RNA Polymerase I subunit and a lysine tRNA gene (i.e. RPA135-tK(CUU)P). Here we used quantitative Chromosome Conformation Capture in combination with replacement mapping to identify a 75 bp sequence within the RPA135-tK(CUU)P intergenic region that is involved in the interaction. We demonstrate that the RPA135-IGS1 interaction is dependent on the rDNA copy number and the Msn2 protein. Surprisingly, we found that the interaction does not govern RPA135 transcription. Instead, replacement of a 605bp region within the RPA135-tK(CUU)P intergenic region results in a reduction in the RPA135-IGS1 interaction level and fluctuations in rDNA copy number. We conclude that the chromosomal interaction that occurs between the RPA135-tK(CUU)P and rDNA IGS1 loci stabilizes rDNA repeat number and contributes to the maintenance of nucleolar stability. Our results provide evidence that the DNA loci involved in chromosomal interactions are composite elements, sections of which function to stabilizing the interaction or mediating a functional outcome.

Mol Cell Biol, 2014

The First Myriapod Genome Sequence Reveals Conservative Arthropod Gene Content and Genome Organisation in the Centipede *Strigamia maritima*.

Ariel D Chipman, David E K Ferrier, Carlo Brena, Jiaxin Qu, Daniel S T Hughes, Reinhard Schröder, Montserrat Torres-Oliva, Nadia Znassi, Huaiyang Jiang, Francisca C Almeida, Claudio R Alonso, Zivkos Apostolou, Peshtewani Aqrawi, Wallace Arthur, Jennifer C J Barna, Kerstin P Blankenburg, Daniela Brites, Salvador Capella-Gutiérrez, Marcus Coyle, Peter K Dearden, Louis Du Pasquier, Elizabeth J Duncan, Dieter Ebert, Cornelius Eibner, Galina Erikson, Peter D Evans, Cassandra G Extavour, Liezl Francisco, Toni Gabaldon, William J Gillis, Elizabeth A Goodwin-Horn, Jack E Green, Sam Griffiths-Jones, Cornelis J P Grimmelikhuijzen, Sai Gubbala, Roderic Guigo, Yi Han, Frank Hauser, Paul Havlak, Luke Hayden, Sophie Helbing, Michael Holder, Jerome H L Hui, Julia P Hunn, Vera S Hunnekuhl, Laronda Jackson, Mehwish Javaid, Shalini N Jhangiani, Francis M Jiggins, Tamsin E Jones, Tobias S Kaiser, Divya Kalra, Nathan J Kenny, Viktoriya Korchina, Christie L Kovar, F Bernhard Kraus, François Lapraz, Sandra L Lee, Jie Lv, Christigale Mandapat, Gerard Manning, Marco Mariotti, Robert Mata, Tittu Mathew, Tobias Neumann, Irene Newsham, Dinh N Ngo, Maria Ninova, Geoffrey Okwuonu, Fiona Ongeri, William J Palmer, Shobha Patil, Pedro Patraquim, Christopher Pham, Ling-Ling Pu, Nicholas H Putman, Catherine Rabouille, Olivia Mendivil Ramos, Adelaide C Rhodes, Helen E Robertson, Hugh M Robertson, Matthew Ronshaugen, Julio Rozas, Nehad Saada, Alejandro Sánchez-Gracia, Steven E Scherer, Andrew M Schurko, Kenneth W Siggens, DeNard Simmons, Anna Stief, Eckart Stolle, Maximilian J Telford, Kristin Tessmar-Raible, Rebecca Thornton, Maurijn van der Zee, Arndt von Haeseler, James M Williams, Judith H Willis, Yuanqing Wu, Xiaoyan Zou, Daniel Lawson, Donna M Muzny, Kim C Worley, Richard A Gibbs, Michael Akam, and Stephen Richards

Edited by: Chris Tyler-Smith

Myriapods (e.g., centipedes and millipedes) display a simple homonomous body plan relative to other arthropods. All members of the class are terrestrial, but they attained terrestriality independently of insects. Myriapoda is the only arthropod class not represented by a sequenced genome. We present an analysis of the genome of the centipede *Strigamia maritima*. It retains

a compact genome that has undergone less gene loss and shuffling than previously sequenced arthropods, and many orthologues of genes conserved from the bilaterian ancestor that have been lost in insects. Our analysis locates many genes in conserved macro-synteny contexts, and many small-scale examples of gene clustering. We describe several examples where *S. maritima* shows different solutions from insects to similar problems. The insect olfactory receptor gene family is absent from *S. maritima*, and olfaction in air is likely effected by expansion of other receptor gene families. For some genes *S. maritima* has evolved paralogues to generate coding sequence diversity, where insects use alternate splicing. This is most striking for the Dscam gene, which in *Drosophila* generates more than 100,000 alternate splice forms, but in *S. maritima* is encoded by over 100 paralogues. We see an intriguing linkage between the absence of any known photosensory proteins in a blind organism and the additional absence of canonical circadian clock genes. The phylogenetic position of myriapods allows us to identify where in arthropod phylogeny several particular molecular mechanisms and traits emerged. For example, we conclude that juvenile hormone signalling evolved with the emergence of the exoskeleton in the arthropods and that RR-1 containing cuticle proteins evolved in the lineage leading to Mandibulata. We also identify when various gene expansions and losses occurred. The genome of *S. maritima* offers us a unique glimpse into the ancestral arthropod genome, while also displaying many adaptations to its specific life history.

Plos Biol, 2014 vol. 12 (11) p. e1002005

Metabolomics of post-mortem blood: identifying potential markers of post-mortem interval.

A E Donaldson and I L Lamont

Metabolomics, 2014

Capturing embryonic development from metamorphosis: How did the terminal patterning signalling pathway of *Drosophila* evolve?

E J Duncan, T K Johnson, J C Whisstock, C G Warr, and P K Dearden

Current Opinion in Insect Science, 2014 vol. 1 pp. 45-51

The structure of alanine racemase from *Acinetobacter baumannii*.

Emily Davis, Emma Scaletti-Hutchinson, Helen Opel-Reading, Yoshio Nakatani, and Kurt L Krause

Acinetobacter baumannii is an opportunistic Gram-negative bacterium which is a common cause of hospital-acquired infections. Numerous antibiotic-resistant strains exist, emphasizing the need for the development of new antimicrobials. Alanine racemase (Alr) is a pyridoxal 5'-phosphate dependent enzyme that is responsible for racemization between enantiomers of alanine. As D-alanine is an essential component of the bacterial cell wall, its inhibition is lethal to prokaryotes, making it an excellent antibiotic drug target. The crystal structure of A. baumannii alanine racemase (AlrAba) from the highly antibiotic-resistant NCTC13302 strain has been solved to 1.9 Å resolution. Comparison of AlrAba with alanine racemases from closely related bacteria demonstrates a conserved overall fold. The substrate entryway and active site of the enzymes were shown to be highly conserved. The structure of AlrAba will provide the template required for future structure-based drug-design studies.

Acta Crystallographica Section F, Structural Biology Communications, 2014 vol. 70 (Pt 9) pp. 1199-1205

Removal of both Ycf48 and Psb27 in *Synechocystis* sp. PCC 6803 disrupts Photosystem II assembly and alters QA(-) oxidation in the mature complex.

Simon A Jackson, John R D Hervey, Asher J Dale, and Julian J Eaton-Rye

The Photosystem II (PS II) assembly factors Psb27 and Ycf48 are transiently associated with PS II during its biogenesis and repair pathways. We investigated the function of these proteins by constructing knockout mutants in *Synechocystis* sp. PCC 6803. In ΔYcf48 cells, PS II electron transfer and stable oxygen evolution were perturbed. Additionally, Psb27 was required for photoautotrophic growth of cells lacking Ycf48 and assembly beyond the RC47 assembly complex in ΔYcf48:ΔPsb27 cells was impeded. Our results suggest the RC47 complex formed in ΔYcf48 cells is defective and that this deficiency is exacerbated if CP43 binds in the absence of Psb27.

FEBS Letters, 2014

Proteomic analysis of chinook salmon (*Oncorhynchus tshawytscha*) ovarian fluid.

Sheri L Johnson, Marsha Villarroel, Patrice Rosengrave, Alan Carne, Torsten Kleffmann, P Mark Lokman, and Neil J Gemmell

Edited by: Josep V Planas

The ovarian, or coelomic, fluid that is released with the egg mass of many fishes is increasingly found to play an important role in several biological processes crucial for reproductive success. These include maintenance of oocyte fertility and developmental competence, prolonging of sperm motility, and enhancing sperm swimming speed. Here we examined if and how

the proteome of chinook salmon (*Oncorhynchus tshawytscha*) ovarian fluid varied among females and then sought to examine the composition of this fluid. Ovarian fluid in chinook salmon was analyzed using 1D SDS PAGE and LC-MS/MS tryptic digest screened against Mascot and Sequest databases. We found marked differences in the number and concentrations of proteins in salmon ovarian fluid across different females. A total of 174 proteins were identified in ovarian fluid, 47 of which were represented by six or more peptides, belonging to one of six Gene Ontology pathways. The response to chemical stimulus and response to hypoxia pathways were best represented, accounting for 26 of the 174 proteins. The current data set provides a resource that furthers our understanding of those factors that influence successful egg production and fertilisation in salmonids and other species.

PLoS ONE, 2014 vol. 9 (8) p. e104155

Ribose-cysteine increases glutathione-based antioxidant status and reduces LDL in human lipoprotein(a) mice.

T Kader, C M Porteous, M J A Williams, S P Gieseg, and S P A McCormick

Atherosclerosis, 2014 vol. 237 (2) pp. 725-733

Functional role of PilA in iron acquisition in the cyanobacterium *Synechocystis* sp. PCC 6803.

Jacob J Lamb, Ryan E Hill, Julian J Eaton-Rye, and Martin F Hohmann-Marriott

Edited by: Wolfgang R Hess

Cyanobacteria require large quantities of iron to maintain their photosynthetic machinery; however, in most environments iron is present in the form of insoluble iron oxides. Whether cyanobacteria can utilize these sources of iron, and the potential molecular mechanisms involved remains to be defined. There is increasing evidence that pili can facilitate electron donation to extracellular electron acceptors, like iron oxides in non-photosynthetic bacteria. In these organisms, the donation of electrons to iron oxides is thought to be crucial for maintaining respiration in the absence of oxygen. Our study investigates if PilA1 (major pilin protein) may also provide a mechanism to convert insoluble ferric iron into soluble ferrous iron. Growth experiments supported by spectroscopic data of a strain deficient in pilA1 indicate that the presence of the pilA1 gene enhances the ability to grow on iron oxides. These observations suggest a novel function of PilA1 in cyanobacterial iron acquisition.

PLoS ONE, 2014 vol. 9 (8) p. e105761

Structural mechanisms in NLR inflammasome signaling.

Bernhard C Lechtenberg, Peter D Mace, and Stefan J Riedl

Members of the NOD-like receptor (NLR) family mediate the innate immune response to a wide range of pathogens, tissue damage and other cellular stresses. They achieve modulation of these signals by forming oligomeric signaling platforms, which in analogy to the apoptosome are predicted to adopt a defined oligomeric architecture and will here be referred to as NLR oligomers. Once formed, oligomers of the NLR proteins NLRP3 or NLRC4 'recruit' the adaptor protein ASC and the effector caspase-1, whereby NLRC4 can also directly interact with caspase-1. This results in large multi-protein assemblies, termed inflammasomes. Ultimately, the formation of these inflammasomes leads to the activation of caspase-1, which then processes the cytokines IL-1β and IL-18 triggering the immune response. Here we review new insights into NLR structure and implications on NLR oligomer formation as well as the nature of multi-protein inflammasomes. Of note, so dubbed 'canonical inflammasomes' [1] can also be triggered by the NLR NLRP1b and the non-NLR protein AIM2, however the most detailed mechanistic information at hand pertains to NLRC4 while NLRP3 represents the quintessential inflammasome trigger. Thus these two NLRs are mainly used as examples in this article.

Current Opinion in Structural Biology, 2014 vol. 29C pp. 17-25

Ethics of mitochondrial therapy for deafness.

Michael Legge and Ruth P Fitzgerald

Mitochondrial therapy may provide the relief to many families with inherited mitochondrial diseases. However, it also has the potential for use in non-fatal disorders such as inherited mitochondrial deafness, providing an option for correction of the deafness using assisted reproductive technology. In this paper we discuss the potential for use in correcting mitochondrial deafness and consider some of the issues for the deaf community.

N Z Med J, 2014 vol. 127 (1405) pp. 78-81

Investigation on the essentiality of Glutamate Racemase in *Mycobacterium smegmatis*.

Yang Li, Roman Mortuza, Daniel L Milligan, Sieu L Tran, Ulrich Strych, Gregory M Cook, and Kurt L Krause

The mycobacterial cell wall has frequently been used as a target for drug development, and D-glutamate, synthesized by glutamate racemase (MurI), is an

important component of peptidoglycan. While the essentiality of the murI gene has been shown in several bacterial species including *Escherichia coli*, *Bacillus anthracis* and *Streptococcus pneumoniae*, studies in mycobacteria have not yet provided definitive results. This study aimed to determine whether murI is indeed essential, and may thus serve as a possible target for structure-aided drug design. We have achieved this goal by creating a ΔmurI strain of *Mycobacterium smegmatis*, a close relative of *Mycobacterium tuberculosis*. Deletion of the murI gene in *M. smegmatis* could only be achieved in minimal medium supplemented with D-glutamate demonstrating that MurI is essential for growth and that glutamate racemase is the only source of D-glutamate for peptidoglycan synthesis in *M. smegmatis*.

Journal of Bacteriology, 2014

Use of E2~ubiquitin conjugates for the characterization of ubiquitin transfer by RING E3 ligases such as the inhibitor of apoptosis proteins.

Adam J Middleton, Rhesa Budhidarmo, and Catherine L Day

Ubiquitylation of proteins is a versatile posttranslational modification that can serve to promote protein degradation, or it can have nondegradative roles, such as mediating protein-protein interactions. The Inhibitor of APoptosis (IAP) proteins are important regulators of pathways that control cell death, proliferation, and differentiation. A number of IAP family members are RING E3 ubiquitin-protein ligases, which promote direct transfer of ubiquitin from charged E2 enzymes, or E2~ubiquitin (E2~Ub) conjugates, to substrate proteins. This results in the attachment of nondegradative ubiquitin signals to other proteins, or the autoubiquitylation and degradation of IAPs. Modulating ubiquitin transfer by IAPs is the focus of a number of drug development initiatives and these studies require a detailed understanding of ubiquitylation. Here, we describe preparation of stable E2~Ub conjugates that can be used in biochemical and biophysical experiments to examine RING domain function. In the last 2 years, the availability of these conjugates has helped unveil a molecular understanding of the process of ubiquitin transfer by IAPs. The approaches described here will be suitable for studying other RING E3 ligases.

Methods In Enzymology, 2013 vol. 545 pp. 243-263

The CNVrd2 package: Measurement of copy number at complex loci using high-throughput sequencing data.

H T Nguyen, T R Merriman, and M A Black

Recent advances in high-throughout sequencing technologies have made it possible to accurately assign copy number (CN) at CN variable loci. However, current analytic methods often perform poorly in regions in which complex CN variation is observed. Here we report the development of a read depth-based approach, CNVrd2, for investigation of CN variation using high-throughput sequencing data. This methodology was developed using data from the 1000 Genomes Project from the CCL3L1 locus, and tested using data from the DEFB103A locus. In both cases, samples were selected for which paralog ratio test data were also available for comparison. The CNVrd2 method first uses observed read-count ratios to refine segmentation results in one population. Then a linear regression model is applied to adjust the results across multiple populations, in combination with a Bayesian normal mixture model to cluster segmentation scores into groups for individual CN counts. The performance of CNVrd2 was compared to that of two other read depth-based methods (CNVnator, cn.mops) at the CCL3L1 and DEFB103A loci. The highest concordance with the paralog ratio test method was observed for CNVrd2 (77.8/90.4% for CNVrd2, 36.7/4.8% for cn.mops and 7.2/1% for CNVnator at CCL3L1 and DEF103A). CNVrd2 is available as an R package as part of the Bioconductor project: http://www.bioconductor.org/packages/release/bioc/html/CNVrd2.html.

Front Genet, 2014 vol. 5 (AUG) p. 248

ITCHY: Incremental Truncation for the Creation of Hybrid enzYmes.

Wayne M Patrick and Monica L Gerth

Incremental Truncation for the Creation of Hybrid enzYmes (ITCHY) is a directed evolution technique for randomly recombining two genes. The chief advantage of ITCHY is that there is no requirement for the two genes to share any sequence similarity. This distinguishes ITCHY from directed evolution methods that are based on homologous recombination, such as DNA shuffling. In ITCHY, *Escherichia coli* exonuclease III is used to incrementally truncate one of the parental genes from its 3' end and the other from its 5' end. Ligation of the randomly truncated gene fragments yields a combinatorial library of chimeras. In this chapter, we provide detailed protocols for constructing libraries using both the user-friendly thio-ITCHY method and also time-dependent incremental truncation. We illustrate the protocols with the data that we obtained when we recombined two alcohol dehydrogenase genes that only share 47 % sequence identity.

Methods Mol Biol, New York, NY 2014 vol. 1179 (Chapter 16) pp. 225-244

Twenty-eight loci that influence serum urate levels: analysis of association with gout.

A J Phipps-Green, M E Merriman, R Topless, S Altaf, G W Montgomery, C Franklin, G T Jones, A M van Rij, D White, L K Stamp, N Dalbeth, and T R Merriman

OBJECTIVES:Twenty-eight genetic loci are associated with serum urate levels in Europeans. Evidence for association with gout at most loci is absent, equivocal or not replicated. Our aim was to test the loci for association with gout meeting the American College of Rheumatology gout classification criteria in New Zealand European and Polynesian case-control sample sets.

METHODS:648 European cases and 1550 controls, and 888 Polynesian (Maāori and Pacific) cases and 1095 controls were genotyped. Association with gout was tested by logistic regression adjusting for age and sex. Power was adequate (>0.7) to detect effects of OR>1.3.

RESULTS:We focused on 24 loci without previous consistent evidence for association with gout. In Europeans, we detected association at seven loci, one of which was the first report of association with gout (IGF1R). In Polynesian, association was detected at three loci. Meta-analysis revealed association at eight loci-two had not previously been associated with gout (PDZK1 and MAF). In participants with higher Polynesian ancestry, there was association in an opposing direction to Europeans at PRKAG2 and HLF (HLF is the first report of association with gout). There was obvious inconsistency of gout association at four loci (GCKR, INHBC, SLC22A11, SLC16A9) that display very similar effects on urate levels.

CONCLUSIONS:We provide the first evidence for association with gout at four loci (IGF1R, PDZK1, MAF, HLF). Understanding why there is lack of correlation between urate and gout effect sizes will be important in understanding the aetiology of gout.

Annals of the Rheumatic Diseases, 2014

Mendelian Randomization Provides No Evidence for a Causal Role of Serum Urate in Increasing Serum Triglyceride Levels.

Humaira Rasheed, Kim Hughes, Tanya J Flynn, and Tony R Merriman

BACKGROUND:-Triglycerides and their lipoprotein transport molecules are risk factors for heart disease. Observational studies have associated elevated levels of serum urate (SU) with triglycerides (Tg) and risk of heart disease. However, owing to unmeasured confounding, observational studies do not provide insight into the causal relationship between SU and Tg. The aim of this study was to test for a causal role of SU in increasing Tg using Mendelian randomisation that accounts for unmeasured confounding.

METHODS AND RESULTS:-Subjects were of European ancestry from the Atherosclerosis Risk in Communities (ARIC; n=5237) and Framingham Heart (FHS; n=2971) studies. Mendelian randomization by the two-stage least squares regression method was done with SU as the exposure, a uric acid transporter genetic risk score as instrumental variable and Tg as the outcome. In ordinary linear regression SU was significantly associated with Tg levels (β=2.69 mmol/L change in Tg per mmol/L increase in SU). However, Mendelian randomization-based estimation showed no evidence for a direct causal association of SU with Tg concentration - there was a non-significant 1.01 mmol/L decrease in Tg per mmol/L increase in SU attributable to the genetic risk score (P=0.21). The reverse analysis using a Tg genetic risk score provided evidence of a causal role for Tg in raising urate in men (PCorrected=0.018).

CONCLUSIONS:-These data provide no evidence for a causal role for SU in raising Tg levels, consistent with a previous Mendelian randomisation report of no association between SU and ischaemic heart disease.

Circulation Cardiovascular Genetics, 2014

Characterisation of novel fungal and bacterial protease preparations and evaluation of their ability to hydrolyse meat myofibrillar and connective tissue proteins.

Kate Ryder, Minh Ha, Alaa El-Din Bekhit, and Alan Carne

The catalytic capability of four commercially available food-grade fungal and bacterial protease preparations (AFP, FPII, F60K and HT) was evaluated over a range of pH, temperature and substrate conditions using esterase and caseinolytic activity assays and time course hydrolysis over 120 and 60min of myofibrillar and connective tissue proteins, respectively. The protease preparations displayed similar casein hydrolysis kinetics and were active in hydrolysing BODIPY-FL casein to varying extents at postmortem aging meat pH (5.0-6.0). All of the four proteases exhibited selective hydrolytic activity towards meat myofibrillar proteins including myosin and actin. Significant hydrolysis of two meat tenderisation protein markers troponin T and desmin by the four proteases was detected by western blot. The results obtained indicate that the new fungal protease preparations AFP and FPII, bacterial protease preparation HT and the new source of fungal protease preparation F60K have potential for use in meat tenderising applications.

Food Chemistry, 2015 vol. 172C pp. 197-206

Molecular analysis of the cold tolerant antarctic nematode, *Panagrolaimus davidi*.

Michael A S Thorne, Hiroshi Kagoshima, Melody S Clark, Craig J Marshall, and David A Wharton

PLoS ONE, 2014 vol. 9 (8) p. e104526

Duplication and divergence of the Psb27 subunit of Photosystem II in the green algal lineage.

P D Mabbitt, S.M. Wilbanks, and J. J. Eaton-Rye

New Zeal J Bot, 2014 vol. 52 (1) pp. 74-83

The importance of early life in childhood obesity and related diseases: A report from the 2014 Gravida Strategic Summit.

E C Macaulay, E L Donovan, M P Leask, F H Bloomfield, M H Vickers, P K Dearden, and P N Baker

Journal of Developmental Origins of Health and Disease, 2014 vol. 5 (6) pp. 398-407

Isolation and functional analysis of CONSTANS-LIKE genes suggests that a central role for CONSTANS in flowering time control is not evolutionarily conserved in *Medicago truncatula*.

Albert C S Wong, Valérie F G Hecht, Kelsey Picard, Payal Diwadkar, Rebecca E Laurie, Jiangqi Wen, Kirankumar Mysore, Richard C Macknight, and James L Weller

The zinc finger transcription factor CONSTANS has a well-established central role in the mechanism for photoperiod sensing in Arabidopsis, integrating light and circadian clock signals to upregulate the florigen gene FT under long-day but not short-day conditions. Although CONSTANS-LIKE (COL) genes in other species have also been shown to regulate flowering time, it is not clear how widely this central role in photoperiod sensing is conserved. Legumes are a major plant group and various legume species show significant natural variation for photoperiod responsive flowering. Orthologs of several Arabidopsis genes have been shown to participate in photoperiodic flowering in legumes, but the possible function of COL genes as integrators of the photoperiod response has not yet been examined in detail. Here we characterize the COL family in the temperate long-day legume Medicago truncatula, using expression analyses, reverse genetics, transient activation assays and Arabidopsis transformation. Our results provide several lines of evidence suggesting that COL genes are unlikely to have a central role in the photoperiod response mechanism in this species.

Front Plant Sci, 2014 vol. 5 p. 486

Cont'd from following page

Can molecular genetics ever show what makes us uniquely human? If humanity is revealed in how we act, then any comparison with Neanderthals would seem crippled by lack of information on Neanderthal behaviour. The tools, discarded bones and preserved artwork studied by classical archaeologists and anthropologists would seem to offer our best information on how what our ancestors did defined who we became. Even so, comparative genetics might contribute here as well; although they cannot provide us the climax, penile spines might bring behavioural insight to our story.

Book Review - Neanderthal Man

Sigurd Wilbanks

Personalised Molecular Genetics

Svante Pääbo's *Neanderthal Man* (Basic Books, New York, 2014) is supported by the intertwined backbones of two complementary themes. His unifying subject is the sequencing of the Neanderthal genome and what it told us of human origins. How well Pääbo's ambitious project delivered on the promise to discover our origins is one strand of this tale. Twisted around the first strand is the very personal tale of the inspiration, challenges and triumphs behind the project. That this quest was in the author's genes is the secondary meaning of the title, adding an *ad hominem* aspect to the *ab hominid* investigation. The narrative is driven by ambition, with an unexpected admixture of sex and dynastic rivalry. A third strand to this apparent double helix is cryptic pleading for a Nobel Prize for the author.

As a student, Pääbo became convinced that he could recover genomic sequence from ancient remains and test hypotheses with greater rigour than the classical techniques of anthropology allow. Entwined with his faith in the power of molecular genetics runs a fascination with his own patrimony. Early in the story Pääbo tells us he was "inspired by my father who had been an MD and later became a biochemist." This anodyne detail is later embellished by the revelation that his inspiring father was distant and distinguished - the author was the "secret extramarital son of Sune Bergström, 1982 Nobel laureate for discovery of prostoglandins." Is Pääbo driven to show his family has the dynastic potential of the Langevin-Curies or the Braggs? To underscore how phylogeny becomes personal, Pääbo details his growing desire for children, fulfilled by the birth and childhood of his son. While these personal details titillate and prompt speculation about the role of genetics and Freudian motivation in scientific achievement at the highest levels, they offer little illumination.

Disingenuously, Pääbo deprecates the titillation inherent in sex*:* "I was not in the least interested in sexual practices in the Late Pleistocene unless those practices had left any traces in our genes today." Nonetheless, he makes sure we know that one of the features which set us and Neanderthals apart from the great apes is a lack of penile spines, suggesting that Neandethals would have enjoyed sex much as modern humans do. As for more modern sex, Pääbo's narrative is enlivened with mentions of his bisexuality, details of his seduction of a colleague's wife and gratuitous allusion to sourcing human sperm samples for early Y-chromosome studies. As with hints of his dynastic yearnings, these glimpses prompt questions of how personal passions drive scientific ambition, but his deprecation of interest in this angle cuts it short of affording much insight.

A far stronger complement to the story of scientific discovery is the story of building Pääbo's scientific career. The reader watches as he choses scientific father figures, woos and dumps collaborators, parlays success into a professorship, founds a new Max Planck Institute and finally negotiates a special grant from the Max Planck Society to fund the ambitious Neanderthal genome sequencing project. The balance of teamwork with personal ambition and of loyalty versus expediency are both examined. While not made explicit, the narrative has implicit directions for scientific success. Exploitation of the latest technology is a clear key to success, as is obsessive attention to experimental details. A strong case is also made for the crucial role of organisational acumen; contributions of all fifty authors on the *Science* paper are justified.

Some of his anecdotes show all too human foibles. Long before choosing to publish his most famous results in *Nature* and *Science* to media acclaim, he reports that he is "disenchanted with both those journals because they often seemed more interested in publishing papers that would give them coverage in the *New York Times* ... than in making sure the results were sound and likely to hold up." After choosing to publish an early paper instead in the more rigorous *Cell*, he quotes with irony that paper's conclusion which did not hold up: "The Neanderthal mtDNA sequence thus supports a scenario in which modern humans arose recently in Africa as a distinct species and replaced Neanderthals with little or no interbreeding."

Despite missteps, Pääbo is justifiably proud of his seminal work. However, while he masterfully describes the basis of his success, does less than he might to examine the depth of that success. Sequencing of the Neanderthal genome is clearly presented as a technical tour de force, and an extraordinary feat of organisation. He justifies his early conviction that molecular genetics offers new rigour to aspects of anthropology. In particular, he now offers a robust phylogeny of modern humans, Neanderthals and Denisovans, including insight into the importance of gene transfer between the distinct branches of our family tree. This informs our view of the origin of our species. Our family tree is less informative on the stated question of "what makes us uniquely human". One of the most intriguing genetic differences between us and the great apes is in *FOXP2*, a gene involved in language ability. However, this was identified by comparing the human genome with those of apes; this locus is the same in modern humans and Neanderthals, as is the locus encoding penile spines - nothing uniquely human there, either.

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News from Around the Department

Laboratory for Cold Adaptation

Lots of change in the lab this time around. Abhishek is all done and has a lovely blue thesis to show for his time here. He's now working with Peter Mace (and thinking about writing those papers, are you not?). Anna has finished her laboratory work and is now in Germany (via Australia) for attention to her knee and to write up her thesis. We expect her back sometime in the new year with a completed thesis and to do some paper writing of her own. Victor completed his year and is considering research options while taking a well-earned break. A final departure was Yukiko who was a volunteer in the lab for several months and made some good progress working with Michelle on sequencing oyster mitochondrial DNA. Stephen Clarke, who some of you may remember, is about to submit his thesis: something of a milestone after a long time. Persistence brings with it many rewards.

New people in the lab include Amy Smith who is a zoologist by training but keen to learn some biochemical techniques. She is doing work on ice active proteins in an alpine cockroach (to keep the zoological theme). Belinda, who normally works in the Prep Room, is doing things with marine samples of various kinds. So far these have included oysters and tooth fish and dogfish is next on the list. We hope to purify LDH for second year labs that is more stable than our previous stocks. It is good to see new faces replacing those who've left.

I'm on study leave for six months from 1 January and keep threatening to get into the lab: it will happen and chaos will reign.

Craig

Day Lab

How is it already December? This year has flown by. However, a lot has changed in the Day lab. Gene joined us and is now known for his bad-ass negotiation and protein prep skills (so good that he was considering changing his name from 'Gene' to 'Protein'). Alyssa also completed her Honours year and left us for the dream job of creating beer at Cassels and Sons Brewery. Marco, our German exchange student, is part way through his Masters and seeing the most beautiful country in the world while he does it. Eugene is the most recent member to join the Day lab as a summer student, it seems like only yesterday I was in his place!

What a year! Catherine went on sabbatical to Europe, leaving us to fend for ourselves! Thankfully the internet and skype exist, meaning we had still had the guidance of our supervisor. However Catherine wasn't the only one scampering around the globe. Josh also went to Copenhagen to attend the 60th Benzon Symposium on Nuclear Regulation by Ubiquitin. There he met some of the big names in the field, followed by a tour of Europe. Josh further impressed us by solving a library of crystal structures as part of his PhD research.

Big changes are coming in the Day lab. The lab has more people than ever and Catherine will soon be HOD of the department. Like true scientists, we eagerly look forward to the results of this experiment (I guess we might need to see a few replicates).

Mike

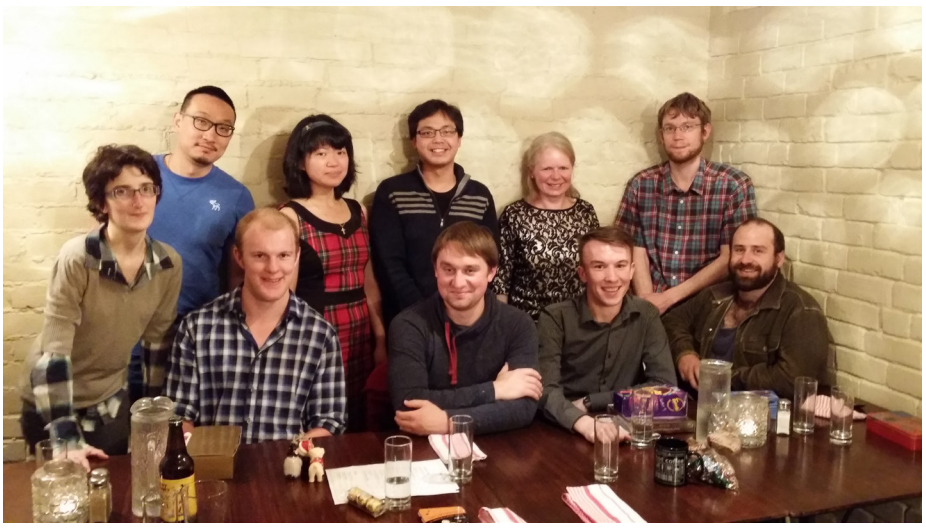


Figure 1: The Day lab Christmas dinner at Ombrellos. We had some great food and awesome craft beer, followed by a cheeky game of Thieving Secret Santa. I think we were all happy with the result, although Marco was not so happy about losing his chocolate!

From left, backrow: Gene, Val, Rhesa, Catherine, Adam. Frontrow: Martina, Eugene, Marco, Mike, Josh.

Regulatory Genomics Lab - Brown

Again a rush to the end of the year, lots done, but still a lot to do. This year several older and 'wiser'? lab members have progressed on.

Earlier this year we bid farewell to Stewart and Ambarish, both having finished their PhDs. Ambarish has taken on a post-doc with Sergio Morales in the Microbiology department, still in collaboration with our lab, he will be partly funded by the new Marsden grant on CRISPR-Cas in the New Year.

Stewart is continuing his Medical studies, but is making a big move up to Wellington, his wife Robina is expecting a baby and they will both do their clinical years there. We wish both of them the best for their futures.

We also saw two of our masters students finish. Gareth and Andrew finished in the early parts of this year, both producing excellent theses. Gareth is currently back as a paid bioinformatics person working on miscellaneous projects in the lab, putting is expertise to good use. His upcoming project will be a collaboration with Botany (David Orlovich and Tina Summerfield) working on novel native truffle like fungal genomes.

This year saw the coming and going of two honours students Brad and Chan. Brad however, does not want to leave, the stress/trauma of doing an honours wasn't enough, so he is coming back to do a masters in early 2015. His project will continue work on viral-antiviral genomic systems (notably CRISPR-Cas) in methanogens from sheep and cattle. This will fit in well with his families' sheep farming background.

Tubo Shi has joined us over the summer while med school is out. He is looking at virus/bacteriophage and CRISPR-Cas in Archaea particularly human and rumen systems.

Earlier this year we also bid farewell to a visiting scientist Atheer Matroud, who has returned to Iraq to Sulimani, in Kurdistan, to take up a faculty position at the American University there. Hopefully he can remain safe and have a prosperous career (http://www.auis.edu.iq/Atheer_Matroud).

This year has also seen great success for our masters' students, with two completing, in addition Scout is almost finished with her masters and seems to be showing a newfound devotion in getting it done.

Rachael has been incredibly busy doing work both here, Anatomy and AgResearch. She won a student scholarship to attend and present at the NGS conference held in Dunedin earlier this year and also invited to speak at MapNet. Her assembly of the genome and transcriptome of the Green Shell mussel is progressing quite well, and she is now in the final stages of her masters.

I (Sam) also have had a busy year, presenting research at the Lorne Genomics conference in February, also getting a student scholarship to present at the NGS conference in Dunedin, and taking care of the honours students. My research is progressing along and I too am nearing the final stages of my masters. With all luck on our side Scout, Rachael and I will all be done in the early parts of next year.

Graham Wood (Statistics) enjoyed most of the early part of the year visiting with us while working on bees with the University of Warwick. He is now gainfully employed as a Statistician at Invermay, and settling in a new house overlooking the harbour in Broad Bay.

As for the mastermind, Chris Brown, his year seems to have been very successful, lots of papers and completions. He has recently returned from a short trip to Sydney where he spoke at the first Japan-Australasian RNA meeting. He is planning for projects around the new Marsden funded research with Peter Fineran (Micro), and we have some students on track. The Marsden funded work on fungal endophytes with Lincoln is near complete and several gene expression studies in human cells are being finished off by us.

We wish everyone a safe and enjoyable holiday season, one which we hope you can take a breather and reflect on the year, let's make 2015 an even better one. Look after each other and we will see you next year.

Cancer Genetics Lab

It's all go at the Cancer Genetics Lab, as we close on an eventful 2014.

This year we launched our new name for the Centre of Translational Cancer Research: 'Te Aho Matatū'. It means 'the enduring connection' and conveys weaving strands together to form a strong, enduring bond across generations, and into the future. Dr Karyn Paringatai of Te Tumu, who benefited from the Lab's research in the past, conceived the name.

This year has seen several welcome arrivals. We are pleased to welcome Anita's new summer student, Barry Schmidt, who is an absolute champion. Anna Bundock started her MSc this year, while Adelaide Hopkins has just finished her BSc(Hons). Dr Adrian Laurence, a medical doctor, has taken a break from the clinic to help us with looking at circulating tumour DNA. In terms of equipment, we now have our very own Illumina Mi-seq and Cytell for high-throughput cell imaging.

Three MSc students, James Frick, Tom Brew and Chris Harris are finishing up their research. Meanwhile, the staff are keeping busy. Tanis, Sofie, Jody and Rob continue in the lab, while Augustine and Donghui have just left for overseas holidays.

The PhD students continue to toil tirelessly in the lab. They will all be returning next year where some will be in the process of finishing up.

We are all looking forward to our end of year function of laser tag. It is hoped that Aziz, who is the only one in the lab with real military training, won't massacre us.

Happy holidays!

Lab 118 Migrations to and from the North

To begin with the beginnings, Lab 118 welcomes Yan Jiang and Julius Maggs for their summer projects. Julius is an Otago BSc student and will be attempting new tricks with split inteins. No one, except perhaps Sigurd, will be more surprised if they actually works as designed, but whatever the inteins do, it should be interesting. Yan hails from Jinan, Shandong province, in China by way of the University of Newcastle in Australia. We are indebted to the Otago diaspora, in this case erstwhile Lamont Lab-member Karla Mettrick, , for convincing Yan to join us for the summer. If all goes well with her CD74, maybe we can convince her to stay longer. Gabriel, having earned his first, is lingering in the lab while Sigurd is trying to make a long linger appealing to him.

Two lab members are bound for the frozen north. Aimée has submitted her MSc thesis and departed with Simon to be ski bums in Canada, leaving us with the memories and a nano-Christmas tree. Egor has been appointed as a research associate at the University of Alberta in Edmonton, so will leave us early in the new year. Good travels and best of luck to him, Yesim and the boys!

Much of the rest of the lab are preparing their own completions. Rachel and Matthias are both in the final sprint for thesis submission, and Antonia and Malcolm are also focused on more letters after their names in 2015.

With his thesis not yet impending, Casey used his "spare" time to publish yet another paper. With lots of help from Egor and Matthias, he managed submission in less than a week after hearing rumours of competition, and final acceptance in less than five weeks, with no scoop yet in print - one more aspiration not gone south.

JER news

Wow, where did 2014 go?!

There have been a few comings and goings in the JER group recently. We have said goodbye to our 4th year students, Matt and Lauren, who had a very productive year, and we are about to farewell Chris Williams who has been out from Norway for the last 6 months and leaves Dunedin in the weekend.

Since the last newletter we have welcomed some new faces. Julian Taffner who is here for 6 months from Germany as part of his Masters degree. Our summer student, Jack Forsman, has jumped in the deep end and is collecting heaps of data on all things photosynthesis for his mutants.

Shiny is frantically writing her Masters thesis and hopes to submit before the year is out.

Julian has just returned from a busy 2 weeks in Japan, where he gave a presentation.

Lab 308, which includes JER, RCM and LRB groups, are heading out tonight to Ombrellos for our Christmas dinner. For a change we are doing 'Selfish Santa' (instead of Secret Santa), which should be a laugh. Looking forward to a great night.

Happy holidays, Biochem!!!

Krause Lab

The members of Krause Lab have plunged headfirst into the end of the year and tackled the difficult and dangerous job of cleaning up the lab. Gone are the dust bunnies from behind the centrifuges and the toxic waste waiting for disposal in the fume hood. And in return we get to start the New Year with the lab the cleanest that any of us have ever seen. But wait there's more...

Max Wilkinson and **Ashley Campbell** have both been awarded prestigious scholarships - Max received funding from the Rutherford Foundation Trust for a PhD at Cambridge in structural biology, and Ashley a Fulbright Fellowship for study in the USA. Congratulations to you both.

The **54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)** took place in Washington, DC in early September where our lab was selected for a podium talk. To showcase the lab works, **Kurt Krause**, **Sinothai Poen** and **Roman Mortuza** attended the conference as a group. Kurt presented the talk, highlighting the recent findings by Sinothai and Roman. After the end of the conference, they took the long walk from the Capitol to the Lincoln memorial to visit most of the spots with historical importance along the way. A more detail summary of the conference tour will be published in the upcoming issue of the NZSBMB newsletter 'Southern Blot'. Stay tuned.

Helen Kim Opel-Reading went recently on an extended holiday to see her family and friends back in Germany. Her journey led her to places from the far north to the far south of the country, as well as short trips across the border to France and Switzerland. Halfway around the world, she also met up with other people from the Biochemistry Department including **Anna Gosling**, **Caillan Crowe-McAuliffe** and **Franziska Huschmann**. After eating too much and enjoying the warm autumn in Europe, she's happy to be back in her garden and reunited with her husband and cats!

Josh Donn and **Anton Jackson-Smith** have joined us for the summer for their initial taste of real lab work, and have both been put to work on expressing proteins. Josh is working on fungal glucan synthase for future crystallography and drug design work under the guidance of both Kurt and **Brian Monk** in Dentistry. Anton is playing with some squid luciferase proteins, bravely tackling the baculovirus/insect cell expression system with help from **Miriam Sharpe**.

Sadly, we said farewell to **Emily Davis**, who finished her Masters thesis in record time for the Krause lab (i.e. on time). She is now going to take a break from science over the summer, and may take off for a year in the UK.

We have just heard that **Michele Krause**, whose tissue culture talents are really appreciated throughout the lab, has broken her ankle badly and has required surgery to fix it. Our thoughts are with Michele, Kurt and their kids, and we hope ankle makes a speedy recovery.

Ledgerwood Lab Christmas Newsletter 2014

The Ledgerwood lab has been hard at work burning through lab supplies (everyone) and Liz's sanity (Kirstin). Lab 201/203 has seen a busy and crowded few weeks with three PIs and at least several students sharing the same quaint lab overlooking the majesty of Cumberland St traffic.

As the bewildered new summer student, James has been hard at work asking everyone in the lab where things are, learning that PCR is the sort of mad science that only a hallucinating hippy tripping on LSD could have come up with. He hopes to achieve competency (of cells and self) sometime in the next five weeks.

As for everyone else, Matthew has been setting up cells for shRNA peroxiredoxin knockdown, performing Westerns, and learning the ways of mass spectrometry. Hoping to probe peroxiredoxin catalysis via detection of disulfide exchange intermediates, he assures me it's as simple and easy as mixing the proteins together and putting everything in the plate reader. Famous last words.

In addition to indulging in her penchant for purchases (sartorial and scientific), Kirstin has been enjoying the ethanol ambience of the cell culture room. She has also been quoted on record as 'looking forward to 2015' when, during a trip to the Christchurch campus's Seahorse to do cellular respiration research, she will have an entire regional air flight of captive audience with Liz for 'story time.' This writer suggests the Very Hungry Caterpillar in keeping with the theme of metabolism.

Rinky has been busily traversing the walkway between chemistry and biochemistry, collaborating with Guy Jameson and preparing samples for measurement by Mössbauer spectroscopy. One suspects everyone but her in the lab nods absently at descriptions of this technique with an eyes-glazed-over expression. Something something recoilless gamma ray fluorescence.

Johannes has been split commuting between the Ledgerwood lab and the Mace lab, a full four metres of bench away, often seen taking the scenic route via the cell culture room. This arrangement has given him the 'unique pleasure' of attending twice the normal number of lab meetings. Presently, Johannes has been trying to get his peroxiredoxin His tags to cleave. Nth time lucky, Johannes!

Lily lives in the postgrad writeup room, working on her thesis and emerging occasionally for coffee and cell culture, as well as showing James where we keep pipette tips.

Rewi has been practicing his filleting skills with our cytochrome c mutant mice, making some lovely coronal sections of mouse brain that really accentuate the massive intracranial haemorrhage our murine colleagues have experienced.

Liz has spent her time marking, mentoring, and getting the last couple of papers written up for the year, and is pleased to have had her UORG grant approved. She, like everyone else, looks forward greatly to the curling tournament arranged for the lab Christmas party.

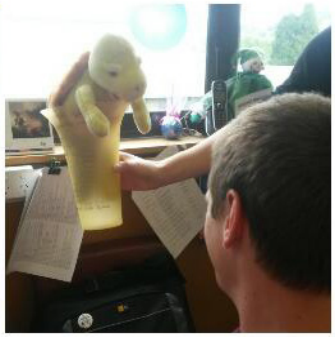
James

The Merriman Lab 12 Days of Christmas:

1. Baby on the way – Congratulations to Murray and Hana!
2. Of Ruth's photos printed in the latest OSMS calendar.
3. Days of wedding celebrations for Tahzeeb and Awais. Wishing them the Best.
4. Hours before their Melbourne Airport departure time would have been a better time for Humaira and Monica (from Sally's lab) to leave their hotel – they arrived at the airport as their flight back to NZ was taking off!
5. Summer students recently welcomed to our group (some shared with Mik).
6. New computers bought to keep up with our research needs.
7. Staff members are still employed thanks to International and Programme grants funded by the Health Research Council NZ.
8. Years of combined PhD study by Rebecca and Hoang has paid off – Congratulations to them both for finishing.
9. International trips throughout the year – Africa, America, Australia, France, Pakistan, Switzerland, USA and more!
10. Different studies send blood to our lab for DNA extraction – we're experts!
11. Is only half our publication count for the year – not a bad haul so far.
12. Years since the Supreme MerriAward cup was created – won by Murray at this year's lab Christmas function.

Whatever you are up to, we wish you all a wonderful time over Christmas and the New Year – see you all in 2015!

The Merriman Lab



E^3: New Zealand's First ~~XV~~ XIV for Enzyme Engineering and Evolution

We begin by congratulating Prof. Philippa Howden-Chapman on becoming the first woman to win the Prime Minister's Science Prize. Here in the E^3 Lab, we fully support all research into the effects of overcrowded living conditions. In fact, with Lab 114's population density now exceeding 150,000 per km^2, we believe we can offer an interesting case to compare with the slums of Kolkata (44,458 per km^2 in 2001[1]).

On the bright side, the arrival of four summer students and one technician has turned the lab into a hive of activity. We're also inching closer to Wayne's stated goal of being able to field an entire rugby team. The team's locking stocks have been strengthened considerably by the arrival of 2+ metre Sean Boult, while Chony King and Kelsi Hall have already emerged as a dynamic 9/10 duo, more than capable of directing the traffic. Meanwhile, the Ghost[2] like skill sets of Alison McGhie and Liz Prentice have made them invaluable additions to the team's back three. In short, we're one front rower away from being a genuine threat at the 2015 World Cup[3]. Applications are open!

The growth of the lab largely reflects Monica's awesome run of recent grant successes. The biggie was a Marsden Fast Start on bacterial chemoreceptors[4]. Seed funding from the Webster Centre has allowed her to buy a fancy microscope and kick off a new project on *Phytophthora*. And in recent days, she has won the 2014 Division of Health Sciences Translational Research Grant, for her anti-biofilm enzymes project. In the immortal words of Timbuk3, "$50,000 a year will buy a lot of beer…"

In other news, Matilda is now officially writing up (translation: her bench has been reassigned), and wins the prize for World's Most Efficient Postdoc Job Search. She'll be off to A/Prof. Burckhard Seelig's lab at the University of Minnesota, just as soon as she is able. Jordan is also in write-up mode, although somehow he has managed to hold onto his lab bench. Danni stormed through her PhD confirmation, and then wowed the crowd with her talk at the recent Otago Energy Research Centre Symposium. Shereen is getting stuck in to her literature review, while counting down the sleeps until her holiday in Malaysia. Miguel is also looking forward to visiting his sister in Italy – though it is even more exciting that he has crystals of untagged ADH at last! CC is back after surviving Honours, and is now leading the ancestral sequence reconstruction part of Wayne's Marsden. She also showed off her cocktail-making skills at the lab Christmas party – thanks CC! Last but not least, James divides his time between putting the finishing touches on manuscript revisions, trying to stop YejG from aggregating, and putting Wayne to shame with his superior activity feed on Strava. The lesson, as always: Wayne must try harder…

Merry Christmas from the E^3 Lab – just go easy on the cocktails!

[1] Kundu, N. (2003). Understanding slums: case studies for the Global Report on Human Settlements 2003. Available at: http://www.ucl.ac.uk/dpu-projects/Global_Report/pdfs/Kolkata.pdf

[2] Yes, that is a Ben Smith reference.

[3] A genuine threat to the Uruguayan practice squad…unless it is the World Cup of Enzyme Kinetics that we're talking about, of course…

[4] Featured here: http://www.royalsociety.org.nz/2014/11/04/positively-psa-what-psa-can-teach-us-about-sensing-the-environment/

Tate Lab Newsletter – August 2014

Warren is awaiting his very first grandson in January- he is super excited and cannot wait to buy him a Stadium season ticket for the Rugby!

Neuroscience student Hayden Smith has joined our lab for 10 weeks over the summer. He produced the best looking lambda markers we have ever seen in his first days, and asks so many intelligent questions that we are all challenged!

Warren's pilot ME/CFS Dunedin study is well underway with Tina having isolated and purified blood cell fractions and plasma from a group of selected patients and controls. Warren recently gave a talk on the study to the AGM of MEISS (Otago and Southland) and they seem to get it, apart from understanding what a 'transcriptome' was!

Our lab is a bit like a Masters games. The three newest students are a tight Genetics trio - Alex, Chris and Jack. They have settled into Tate lab life well and are happy to have finished exams! We hope they will become our 'McCaw, Keino and Read' all Stars. The established Biochemistry trio Eiren, Josh, and Geremy are keen to pass the baton, hang up their boots and get their masters projects written up.

A tearful, departure occurred when Caillan, after graduating with an MSc with distinction, left for the UK to begin his PhD at Oxford University. While we shall miss his brains and his lovely self (and he will miss us!), we wish him all the best for this exciting new chapter in his life. Warren has already had several skype sessions with him (desperately pleading with him to come back!).

Yosuke is getting close now to submitting his PhD thesis. Like Caillan we do not want to lose him from our lab family. He is so knowledgeable technically and so helpful but it seems we will have him still with us in 2015. Moreover, his writing up next to Warren's office means he is able to keep Warren under control.

The lab enjoyed a trip out to Waitati for a pot luck Xmas feast (see photos), Santa turned up and aliquoted gifts, we drank bubbles & blew bubbles and played a thrilling game of biochem charades! The highlight was the depiction of primer design – done with the pizazz of a Kapa haka hand shimmer!

Happy holidays everyone from the Tate Lab!