Biochemistry News

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

editor: Bronwyn Carlisle

December 2013

In This Issue

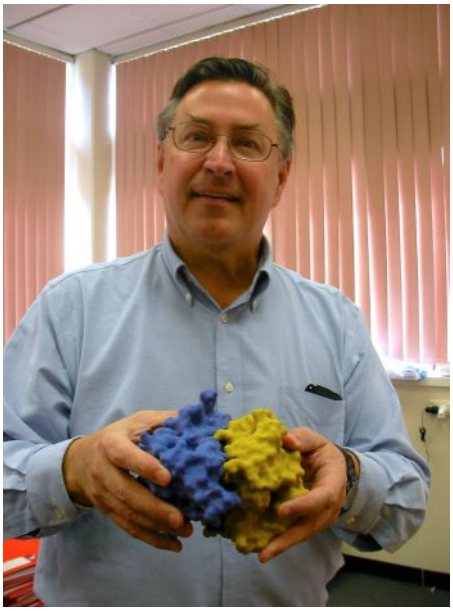
View from the Corner

It's Christmas time and it's a good time to welcome you to the final Biochemistry Department newsletter of 2013! It's been quite a busy year, and at least as far as last week it is showing no signs of slowing down whatsoever. Presumably the winding down will start this week, at least by the time of our Christmas party.

One reason behind why this year has felt so hectic could be the fact that it really *has* been a very busy year, and a year with much change.

To illustrate my point, here are just a few examples of significant developments (I am sure there are many others) listed in no particular order. Near the start of the year, on 21 February, we held our Research Retreat at St. Margaret's and received an inspiring message from Peter Dearden, outgoing Research Committee Chair, on how to improve our research outputs. Simultaneously many were involved in formulating their Marsden and MBIE grant applications as we worked to adapt to a changing external funding environment. Some were exhausted by these efforts and I received one e-mail stating that they were "just sick of the whole thing!", which was a sentiment shared by many!

Next, in April we received some freshly minted PBRF results in which we did very well. We have 9.54 "A" ranked researchers and are the top PBRF-ranked department in the OSMS. There was no time to rest our laurels though, as on 1 May the National Science Challenges were announced. The Government pledged 133.5 M over four years and the scientific landscape over New Zealand was immediately changed. A huge amount of strategic planning has gone into the New Zealand universities' response to these challenges, the rules concerning which seemed to be developed on the fly.



Kurt admires the way a 3D printed protein dimer fits together

One Otago staff member suggested this was akin to "the tracks being laid as the locomotive approached".

But wait there's more! On June 10th of this year the CoRE rebid was announced with an EOI due date of 30 September and a final due date of 6 December. These renewals had been brought forward, in a move that some felt favoured existing centres, but regardless, many new CoRE groups put in their applications along with the rebidders. No wonder it's hard to find time to work on papers!

Student numbers were very good this year, and we had excellent classes at 2nd, 3rd and 4th years. They were an inspiring group for all of us! Late in January this year we decided as a department to reorganise our third-year course, and this has resulted in the merger of BIOC 354 and 352, as well as the merger of BIOC 355 and 353. These were significant changes for many of our teaching personnel, and we hope these changes will revamp and modernise our teaching offerings as we seek to teach the most

cont'd over …

exciting and useful biochemistry to our students. Early student numbers for 2014 look good and the students seem to be adapting to the e-Vision registration system with alacrity. Some of us are dreading this change, and all the preparatory e-Vision training.

There were two Inaugural Professorial Lectures this year from our Department's new Professors and both were outstanding. In October, we heard from Parry Guilford about the coming revolution in cancer therapy based on molecular research. And just last week, we heard from Julian Eaton-Rye who brought us up to speed on Photosystem II, photosynthesis and biofuels.

As always, there are a few personnel changes that take place during the year. After a series of one-year contracts, and standing room-only tutorials, Annika Bokor joined us as a permanent Teaching Fellow. Our research staff had an infusion of youthful intellect when Rutherford Discovery Fellow Peter Mace returned to us from California. This past week we learned that our ace Purchasing Officer, Chelsea Ivey, was leaving us for an OE in Europe - Chelsea you will be missed! Promised postcards are pending. And on another sad note, this year after decades of service to the University, Associate Professor John Cutfield has retired. He was given a splendid sendoff with a dinner on 7 September in the Staff Club, followed later in the year by a morning tea during which he regaled us with his unmatched wit and storytelling and confessed (in jest!) to several clandestine HSNO violations committed over the years! Finally in November he joined with graduate student Matteo Ferla, to host an outstanding quiz night that was huge fun for all of the participants, and won by a nose, in a sing-off by the Marshall-Krause group team.

Amazingly, the developments that I've mentioned in these few paragraphs represent just a few of the many events that occurred over the course of the year. Many more could be listed and some of them will be appearing in the group sections inside. I am hoping that we get to read about summer student projects, summer holiday plans and at least a few words about the 3D printing of protein structures. Enjoy the catch-up with our Biochemistry family and friends, and I am looking forward to seeing you all after the New Year's break.

Latest Publications

Articles published since the last newsletter

Variable Expression of GLIPR1 Correlates with Invasive Potential in Melanoma Cells.

Anshul Awasthi, Adele G. Woolley, Fabienne J Lecomte, Noelyn Hung, Bruce C Baguley, Sigurd M Wilbanks, Aaron R Jeffs, and Joel D A Tyndall

GLI pathogenesis-related 1 (GLIPR1) was previously identified as an epigenetically regulated tumor suppressor in prostate cancer and, conversely, an oncoprotein in glioma. More recently, GLIPR1 was shown to be differentially expressed in other cancers including ovarian, acute myeloid leukemia, and Wilms' tumor. Here we investigated GLIPR1 expression in metastatic melanoma cell lines and tissue. GLIPR1 was variably expressed in metastatic melanoma cells, and transcript levels correlated with degree of GLIPR1 promoter methylation in vitro. Elevated GLIPR1 levels were correlated with increased invasive potential, and siRNA-mediated knockdown of GLIPR1 expression resulted in reduced cell migration and proliferation in vitro. Immunohistochemical studies of melanoma tissue microarrays showed moderate to high staining for GLIPR1 in 50% of specimens analyzed. GLIPR1 staining was observed in normal skin in merocrine sweat glands, sebaceous glands, and hair follicles within the dermis.

Frontiers in oncology, 2013 vol. 3 p. 225

Genetic analyses of bolting in bulb onion (*Allium cepa* L.).

S Baldwin, R Revanna, M Pither-Joyce, M Shaw, K Wright, S Thomson, L Moya, R Lee, R Macknight, and J McCallum

Theoretical And Applied Genetics, 2013 pp. 1-13

Parent peer advocacy, information and refusing disability discourses.

M Bell, R Fitzgerald, and M Legge

Kotuitui: New Zealand Journal of Social Sciences Online, 2013 pp. 1-12

Sequence and structure of naturally-occurring tRNA transcripts and site-directed variants are significant barriers to forming oligomers beyond dimers.

Harold S Bernhardt and Warren P Tate

Advances in Bioscience and Biotechnology, 2013 vol. 04 (05) pp. 1-16

Mutations in genes encoding the cadherin receptor-ligand pair DCHS1 and FAT4 disrupt cerebral cortical development.

S Cappello, M J Gray, C Badouel, S Lange, M Einsiedler, M Srour, D Chitayat, F F Hamdan, Z A Jenkins, T Morgan, N Preitner, T Uster, J Thomas, P Shannon, V Morrison, N Di Donato, L Van Maldergem, T Neuhann, R Newbury-Ecob, M Swinkells, P Terhal, L C Wilson, P J G Zwijnenburg, A J Sutherland-Smith, M A Black, D Markie, J L Michaud, M A Simpson, S Mansour, H McNeill, M Götz, and S P Robertson

Nature Genetics, 2013

Population-specific effects of SLC17A1 genotype on serum urate concentrations and renal excretion of uric acid during a fructose load.

N Dalbeth, M E House, G D Gamble, A Horne, L Purvis, A Stewart, M Merriman, M Cadzow, A Phipps-Green, and T R Merriman

Annals of the Rheumatic Diseases, 2013

Biochemistry changes that occur after death: potential markers for determining post-mortem interval.

Andrea E Donaldson and Iain L Lamont

Death is likely to result in very extensive biochemical changes in all body tissues due to lack of circulating oxygen, altered enzymatic reactions, cellular degradation, and cessation of anabolic production of metabolites. These biochemical changes may provide chemical markers for helping to more accurately determine the time since death (post-mortem interval), which is challenging to establish with current observation-based methodologies. In this study blood pH and changes in concentration of six metabolites (lactic acid, hypoxanthine, uric acid, ammonia, NADH and formic acid) were examined post-mortem over a 96 hour period in blood taken from animal corpses (rat and pig) and blood from rats and humans stored in vitro. The pH and the concentration of all six metabolites changed post-mortem but the extent and rate of change varied. Blood pH in corpses fell from 7.4 to 5.1. Concentrations of hypoxanthine, ammonia, NADH and formic acid all increased with time and these metabolites may be potential markers for post-mortem interval. The concentration of lactate increased and then remained at an elevated level and changes in the concentration were different in the rat compared to the human and pig. This is the first systematic study of multiple metabolic changes post-mortem and demonstrates the nature and extent of the changes that occur, in addition to identifying potential markers for estimating post-mortem interval.

PLoS ONE, 2013 vol. 8 (11) p. e82011

Estimation of post-mortem interval using biochemical markers.

Andrea Evelyn Donaldson and Iain L Lamont

Australian Journal of Forensic Sciences, 2014 vol. 46 (1) pp. 8-26

Comparison of PAM50 Risk of Recurrence Score With Oncotype DX and IHC4 for Predicting Risk of Distant Recurrence After Endocrine Therapy.

Mitch Dowsett, Ivana Sestak, Elena Lopez-Knowles, Kalvinder Sidhu, Anita K Dunbier, J Wayne Cowens, Sean Ferree, James Storhoff, Carl Schaper, and Jack Cuzick

PURPOSE Risk of distant recurrence (DR) among women with estrogen receptor (ER) -positive early breast cancer is the major determinant of recommendations for or against chemotherapy. It is frequently estimated using the Oncotype DX recurrence score (RS). The PAM50 risk of recurrence (ROR) score provides an alternative approach, which also identifies intrinsic subtypes. PATIENTS AND METHODS mRNA from 1,017 patients with ER-positive primary breast cancer treated with anastrozole or tamoxifen in the ATAC trial was assessed for ROR using the NanoString nCounter. Likelihood ratio (LR) tests and concordance indices (c indices) were used to assess the prognostic information provided beyond that of a clinical treatment score (CTS) by RS, ROR, or IHC4, an index of DR risk derived from immunohistochemical assessment of ER, progesterone receptor, human epidermal growth factor receptor 2 (HER2), and Ki67. Results ROR added significant prognostic information beyond CTS in all patients (Δ LR-$\chi(2) = 33.9$; $P < .001$) and in all four subgroups: node negative, node positive, HER2 negative, and HER2 negative/node negative; more information was added by ROR than by RS. C indices in the HER2-negative/node-negative subgroup were 0.73, 0.76, and 0.78 for CTS, CTS plus RS, and CTS plus ROR, respectively. More patients were scored as high risk and fewer as intermediate risk by ROR than by RS. Relatively similar prognostic information was added by ROR and IHC4 in all patients but more by ROR in the HER2-negative/node-negative group. CONCLUSION ROR provides more prognostic information in endocrine-treated patients with ER-positive, node-negative disease than RS, with better differentiation of intermediate- and higher-risk groups.

Journal Of Clinical Oncology, 2013 vol. 31 (22) pp. 2783-2790

Macrophage migration inhibitory factor gene polymorphisms in inflammatory bowel disease: An association study in New Zealand Caucasians and meta-analysis.

J D Falvey, R W Bentley, T R Merriman, M B Hampton, M L Barclay, R B Gearry, and R L Roberts

World Journal of Gastroenterology, 2013 vol. 19 (39) pp. 6656-6664

Effectiveness of phages in the decontamination of Listeria monocytogenes adhered to clean stainless steel, stainless steel coated with fish protein, and as a biofilm.

G J Ganegama Arachchi, A G Cridge, B M Dias-Wanigasekera, C D Cruz, L McIntyre, R Liu, S H Flint, and A N Mutukumira

Journal of Industrial Microbiology and Biotechnology, 2013 pp. 1-12

Gout in Maori.

Anna L Gosling, Elizabeth Matisoo-Smith, and Tony R Merriman

Rheumatology (Oxford, England), 2013

Effects of l- and iso-ascorbic acid on meat protein hydrolyzing activity of four commercial plant and three microbial protease preparations.

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

The present study investigated the effects of both l- and iso-ascorbic acid (AA) on the activity of four plant proteases (papain, bromelain, actinidin and zingibain) and three microbial proteases (Bacterial Protease G, Fungal 31,000 and Fungal 60,000) preparations using fluorescent-labelled casein, meat myofibrillar and connective tissue extracts to explore their effects on meat structure components upon treatment with individual proteases. While l-AA in the range 0.8-3.2mM inhibited the activity of papain, bromelain and zingibain, iso-AA acted as an inhibitor of papain but as an activator of zingibain and had no significant effect on bromelain. Both AA isoforms acted as an activator of the actinidin protease and the concentration of AA isoforms appeared to affect the level of activation of the protease. The effect of the two AA isoforms on collagen and myofibrillar protein hydrolyzing activity varied depending on the concentration of the two AA isoforms. The results indicate the ability to up and down regulate the activity of the investigated proteases by using an appropriate concentration of the AA isoform.

Food Chemistry, 2014 vol. 149 pp. 1-9

Construction and analysis of randomized protein-encoding libraries using error-prone PCR.

P Hanson-Manful and W M Patrick

Methods in Molecular Biology, 996, 251-267

Mendelian randomization analysis associates increased serum urate, due to genetic variation in uric acid transporters, with improved renal function.

Kim Hughes, Tanya Flynn, Janak de Zoysa, Nicola Dalbeth, and Tony R Merriman

Increased serum urate predicts chronic kidney disease independent of other risk factors. The use of xanthine oxidase inhibitors coincides with improved renal function. Whether this is due to reduced serum urate or reduced production of oxidants by xanthine oxidase or another physiological mechanism remains unresolved. Here we applied Mendelian randomization, a statistical genetics approach allowing disentangling of cause and effect in the presence of potential confounding, to determine whether lowering of serum urate by genetic modulation of renal excretion benefits renal function using data from 7979 patients of the Atherosclerosis Risk in Communities and Framingham Heart studies. Mendelian randomization by the two-stage least squares method was done with serum urate as the exposure, a uric acid transporter genetic risk score as instrumental variable, and estimated glomerular filtration rate and serum creatinine as the outcomes. Increased genetic risk score was associated with significantly improved renal function in men but not in women. Analysis of individual genetic variants showed the effect size associated with serum urate did not correlate with that associated with renal function in the Mendelian randomization model. This is consistent with the possibility that the physiological action of these genetic variants in raising serum urate correlates directly with improved renal function. Further studies are required to understand the mechanism of the potential renal function protection mediated by xanthine oxidase inhibitors.Kidney International advance online publication, 18 September 2013; doi:10.1038/ki.2013.353.

Kidney International, 2013

Inhibition of storage pathology in prenatal CLN5-deficient sheep neural cultures by lentiviral gene therapy.

Stephanie M Hughes, Katie M Hope, Janet Boyu Xu, Nadia L Mitchell, and David N Palmer

The neuronal ceroid lipofuscinoses (NCLs, Batten disease) are inherited neurodegenerative lysosomal storage diseases caused by mutations in several different genes. Mutations in CLN5 cause a variant late-infantile human disease and some cases of juvenile and adult clinical disease. NCLs also occur in animals, and a flock of New Zealand Borderdale sheep with a CLN5 splice-site mutation has been developed for model studies. Dissociated mixed neural cells from CLN5-deficient foetal sheep brains contained no obvious storage bodies at plating but these accumulated rapidly in culture, mainly in microglial cells and also in neurons and astrocytes. Accumulation was very obvious after a week, as monitored by fluorescent microscopy and immunostaining for subunit c of mitochondrial ATP synthase. Photography at intervals revealed the dynamic nature of the cultures and a flow of storage bodies between cells, specifically the phagocytosis of storage-body containing cells by microglia and incorporation of the storage bodies into the host cells. No storage was observed in cultured control cells. Transduction of cell cultures with a lentiviral vector expressing a C-terminal Myc tagged CLN5 resulted in secretion of post-translationally glycosylated and processed CLN5. Transduction of CLN5-deficient cultures with this construct rapidly reversed storage body accumulation, to less than half in only six days. These results show that storage body accumulation is reversible with enzyme correction and support the use of these cultures for testing of therapeutics prior to whole animal studies.

Neurobiology of Disease, 2013, vol. 62 pp. 543-550

A sequence variant associated with sortilin-1 (SORT1) on 1p13.3 is independently associated with abdominal aortic aneurysm.

G T Jones, M J Bown, S Gretarsdottir, S P R Romaine, A Helgadottir, G Yu, G Tromp, P E Norman, C Jin, A F Baas, J D Blankensteijn, I J Kullo, L Victoria Phillips, M J A Williams, R Topless, T R Merriman, T M Vasudevan, D R Lewis, R D Blair, A A Hill, R D Sayers, J T Powell, P Deloukas, G Thorleifsson, S E Matthiasson, U Thorsteinsdottir, J Golledge, R A Ariëns, A Johnson, S Sohrabi, D Julian Scott, D J Carey, R Erdman, J R Elmore, H Kuivaniemi, N J Samani, K Stefansson, and A M van Rij

Human Molecular Genetics, 2013 vol. 22 (14) pp. 2941-2947

***Pseudomonas aeruginosa* uses multiple pathways to acquire iron during chronic infection in cystic fibrosis lungs.**

Anna F Konings, Lois W Martin, Katrina J Sharples, Louise F Roddam, Roger Latham, David W Reid, and Iain L Lamont

Pseudomonas aeruginosa chronically infects the lungs of more than 80% of adult patients with cystic fibrosis (CF) and is a major contributor to the progression of disease pathology. *P. aeruginosa* requires iron for growth and has multiple iron uptake systems that have been studied in bacteria grown in laboratory culture. The purpose of this research was to determine which of these are active during infection in CF. RNA was extracted from 149 sputum samples obtained from 23 CF patients. Reverse transcription-quantitative real-time PCR (RT-qPCR) was used to measure the expression of P. aeruginosa genes encoding transport systems for the siderophores pyoverdine and pyochelin, for heme, and for ferrous ions. Expression of *P. aeruginosa* genes could be quantified in 89% of the sputum samples. Expression of genes associated with siderophore-mediated iron uptake was detected in most samples but was at low levels in some samples, indicating that other iron uptake mechanisms are active. Expression of genes encoding heme transport systems was also detected in most samples, indicating that heme uptake occurs during infection in CF. feoB expression was detected in all sputum samples, implying an important role for ferrous ion uptake by *P. aeruginosa* in CF. Our data show that multiple P. aeruginosa iron uptake mechanisms are active in chronic CF infection and that RT-qPCR of RNA extracted from sputum provides a powerful tool for investigating bacterial physiology during infection in CF.

Infection and immunity, 2013 vol. 81 (8) pp. 2697-2704

Flowering locus T genes control onion bulb formation and flowering.

Robyn Lee, Samantha Baldwin, Fernand Kenel, John McCallum, and Richard Macknight

Onion (*Allium cepa* L.) is a biennial crop that in temperate regions is planted in the spring and, after a juvenile stage, forms a bulb in response to the lengthening photoperiod of late spring/summer. The bulb then overwinters and in the next season it flowers and sets seed. FLOWERING LOCUS T (FT) encodes a mobile signaling protein involved in regulating flowering, as well as other aspects of plant development. Here we show that in onions, different FT genes regulate flowering and bulb formation. Flowering is promoted by vernalization and correlates with the upregulation of AcFT2, whereas bulb formation is regulated by two antagonistic FT-like genes. AcFT1 promotes bulb formation, while AcFT4 prevents AcFT1 upregulation and inhibits bulbing in transgenic onions. Long-day

photoperiods lead to the downregulation of AcFT4 and the upregulation of AcFT1, and this promotes bulbing. The observation that FT proteins can repress and promote different developmental transitions highlights the evolutionary versatility of FT.

Nature Communications, 2013 vol. 4 p. 2884

Numerical identity: the creation of tri-parental embryos to correct inherited mitochondrial disease.

Michael Legge and Ruth Fitzgerald

Inherited mitochondrial disorders affect between 1 in 5000 to 1 in 8000 people. These are a heterogeneous group of maternally-inherited disorders, with an array of outcomes such as heart and liver failure, defects in energy metabolism, blindness, deafness, loss of motor skills and premature death. Recently the Human Fertilisation and Embryology Authority provided advice to the UK Government to permit the use of enucleated donated oocytes with normal (wild-type) mitochondria (a currently prohibited IVF technique) to be used as recipients of nuclear DNA from intending mothers to overcome transmission of mitochondrial disorders. In this short communication we present the basis for this radical new IVF technology, and discuss the implications for its use both in the context of treating a group of inherited disorders and the current New Zealand IVF legislation.

The New Zealand Medical Journal, 2013 vol. 126 (1385) pp. 71-75

Mutational analysis of the stability of Psb27 from *Synechocystis* sp. PCC 6803: implications for models of Psb27 structure and binding to CP43.

Peter D Mabbitt, Julian J Eaton-Rye, and Sigurd M Wilbanks

Psb27 associates with the CP43 subunit of photosystem II during biogenesis of the photosystem. Several models have been proposed for the interaction between Psb27 and CP43. The utility of predictions and hypotheses arising from these models depends on the accuracy of the Psb27 structure used in the model. Two of the Psb27 structures used to model the Psb27-CP43 interaction place residue E98 on the surface of Psb27 and D14 in a position to form hydrogen bonds that stabilise the fold of the protein; however, a third structure questions the surface exposure of E98 and does not identify significant interactions of D14. Here we present evidence that D14 contributes to the thermal stability of Psb27 and that E98 is located on the surface. A D14A mutation was shown to reduce the apparent midpoint of unfolding of Psb27 by 16 °C. Four highly conserved surface residues and E98 were subject to charge-reversal mutations (R54E, R94E, E98R, E103R, R108E). The stabilities of the charge-reversal variants and the unmodified control were similar, suggesting E98 is a surface residue. Placing E98 in the correct, surface position will support more reliable models of the interaction of Psb27 with CP43.

European Biophysics Journal : EBJ, 2013

Gold or silver deposited on layered manganese oxide: a functional model for the water-oxidizing complex in photosystem II.

Mohammad Mahdi Najafpour, Fahimeh Rahimi, Davood Jafarian Sedigh, Robert Carpentier, Julian J Eaton-Rye, Jian-Ren Shen, and Suleyman I Allakhverdiev

Photosynthesis Research, 2013 vol. 117 (1-3) pp. 423-429

Association of the HLA locus and TNF with type I autoimmune hepatitis susceptibility in New Zealand Caucasians.

J H Ngu, M C Wallace, T R Merriman, R B Gearry, C A M Stedman, and R L Roberts

SpringerPlus, 2013 vol. 2 (1) pp. 1-8

The nucleolus: A raft adrift in the nuclear sea or the keystone in nuclear structure?

J M O'Sullivan, D A Pai, A G Cridge, D R Engelke, and A R D Ganley

Biomolecular Concepts, 2013 vol. 4 (3) pp. 277-286

Transient Gene Expression in *Medicago truncatula* Leaves via Agroinfiltration.

Kelsey Picard, Robyn Lee, Roger Hellens, and Richard Macknight

Transient expression is a powerful method for the functional characterization of genes. In this chapter, we outline a protocol for the transient expression of constructs in Medicago truncatula leaves using Agrobacterium tumefaciens infiltration. Using quantitative real-time PCR we demonstrate that the infiltration of a construct containing the LEGUME ANTHOCYANIN PRODUCTION 1 (LAP1) transcription factor results in the strong upregulation of key biosynthetic genes and the accumulation of anthocyanin pigment in the leaves after just 3 days. Thus, this method provides a rapid and powerful way to the discovery of downstream targets of M. truncatula transcription factors.

Methods in molecular biology (Clifton, NJ), 2013 vol. 1069 pp. 215-226

Association of the lipoprotein receptor-related protein 2 gene with gout and non-additive interaction with alcohol consumption.

H Rasheed, A Phipps-Green, R Topless, J E Hollis-Moffatt, J H Hindmarsh, C Franklin, N Dalbeth, P B Jones, D H N White, L K Stamp, and T R Merriman

Arthritis research & therapy, 2013 vol. 15 (6)

Factors determining nematode distributions at Cape Hallett and Gondwana station, Antarctica.

M R Raymond, D A Wharton, and C J Marshall

Antarctic Science, 2013 vol. 25 (3) pp. 347-357

Frequency of CYP2C9 polymorphisms in polynesian people and potential relevance to management of gout with benzbromarone.

R L Roberts, M C Wallace, D F B Wright, M Cadzow, N Dalbeth, P B Jones, L K Stamp, A A Harrison, M A Black, and T R Merriman

Joint Bone Spine, 2013

Time-dependent changes in gene expression induced by secreted amyloid precursor protein-alpha in the rat hippocampus.

M.M. Ryan, G P Morris, B G Mockett, K Bourne, W C Abraham, W P Tate, and J M Williams

BMC Genomics, 2013 vol. 14 (1)

Time-dependent changes in gene expression induced by secreted amyloid precursor protein-alpha in the rat hippocampus.

Margaret M Ryan, Gary P Morris, Bruce G Mockett, Katie Bourne, Wickliffe C Abraham, Warren P Tate, and Joanna M Williams

BMC Genomics, 2013 vol. 14 p.

The N-Terminal Extension of UBE2E Ubiquitin-Conjugating Enzymes Limits Chain Assembly.

Frances-Rose Schumacher, Georgina Wilson, and Catherine L Day

Protein ubiquitylation depends upon the concerted action of ubiquitin-conjugating enzymes (E2s) and ubiquitin ligases (E3s). All E2s have a conserved ubiquitin-conjugating (UBC) domain but many have variable extensions N- and C-terminal to the UBC domain. For many E2s, the function of the extension is not well understood. Here, we show that the N-terminal extension of the UBE2E proteins regulates formation of polyubiquitin chains by the processive UBC domain. Target proteins are therefore monoubiquitylated by full-length UBE2E, whereas the UBC domain alone polyubiquitylates proteins. Although the N-terminal extension of UBE2E1 is largely disordered in solution, these residues have a critical role in limiting chain building, and when fused to the highly processive E2, UBE2D2, ubiquitylation is limited. For some E2s, interaction of ubiquitin with the 'backside' of the UBC domain promotes polyubiquitylation. However, interaction of ubiquitin with the backside of the UBC domain of UBE2E1 does not appear to be important for processivity. This study underscores the importance of studying full-length E2 proteins and not just the highly conserved core domain.

Journal of Molecular Biology, 2013

Prediction of late distant recurrence in patients with oestrogen-receptor-positive breast cancer: A prospective comparison of the breast-cancer index (BCI) assay, 21-gene recurrence score, and IHC4 in the TransATAC study population.

D C Sgroi, I Sestak, J Cuzick, Y Zhang, C A Schnabel, B Schroeder, M G Erlander, A Dunbier, K Sidhu, E Lopez-Knowles, P E Goss, and M Dowsett

The Lancet Oncology, 2013 vol. 14 (11) pp. 1067-1076

Catalysis product captured in lumazine synthase from the fungal pathogen *Candida glabrata*.

M Shankar, S.M. Wilbanks, Y Nakatani, B C Monk, and J.D.A. Tyndall

Acta Crystallographica Section D Biological Crystallography, 2013 vol. 69 (8) pp. 1580-1586

Mechanistic Implications of Persulfenate and Persulfide Binding in the Active Site of Cysteine Dioxygenase.

Richard J Souness, Torsten Kleffmann, Egor P. Tchesnokov, Sigurd M Wilbanks, Geoffrey B Jameson, and Guy N L Jameson

Describing the organization of substrates and substrate analogues in the active site of cysteine dioxygenase identifies potential intermediates in this critical yet poorly understood reaction, the oxidation of cysteine to cysteine sulfinic acid. The fortuitous formation of persulfides under crystallization conditions has allowed their binding in the active site of cysteine dioxygenase to be studied. The crystal structures of cysteine persulfide and 3-mercaptopropionic acid persulfide bound to iron(II) in the active site show that binding of the persulfide occurs via the distal sulfide and, in the case of the cysteine persulfide, the amine also binds. Persulfide was detected by mass spectrometry in both the crystal and the drop, suggesting its origin is chemical rather than enzymatic. A mechanism involving the formation of the relevant disulfide from sulfide produced by hydrolysis of dithionite is proposed. In comparison, persulfenate {observed bound to cysteine dioxygenase [Simmons, C. R., et al. (2008) Biochemistry 47, 11390]} is shown through mass spectrometry to occur only in the crystal and not in the surrounding drop, suggesting that in the crystalline state the persulfenate does not lie on the reaction pathway. Stabilization of both the persulfenate and the persulfides does, however, suggest the position in which dioxygen binds during catalysis.

Biochemistry, 2013, 52 (43), pp 7606–7617

Environmental pH affects photoautotrophic growth of *synechocystis* sp. PCC 6803 strains carrying mutations in the lumenal proteins of PSII.

T C Summerfield, T S Crawford, R D Young, J P S Chua, R L MacDonald, L A Sherman, and J. J. Eaton-Rye

Plant and Cell Physiology, 2013 vol. 54 (6) pp. 859-874

Quantitative particle microscopy in self-metered fluids.

L V White, I R Cooke, S J Wakes, and S J Sowerby

Journal of Microscopy, 2013 vol. 250 (3) pp. 159-165

Primary hepatocellular neoplasms in a MODY3 family with a novel HNF1A germline mutation.

J S B Willson, T D Godwin, G A R Wiggins, P J Guilford, and J L McCall

Journal of Hepatology, 2013 vol. 59 (4) pp. 904-907

Engineered DNA ligases with improved activities *in vitro*.

R H Wilson, S K Morton, H Deiderick, M L Gerth, H A Paul, I Gerber, A Patel, A D Ellington, S P Hunicke-Smith, and W M Patrick

Protein Engineering Design and Selection, 2013 vol. 26 (7) pp. 471-478

Evaluating accuracy of diagnostic tests with intermediate results in the absence of a gold standard.

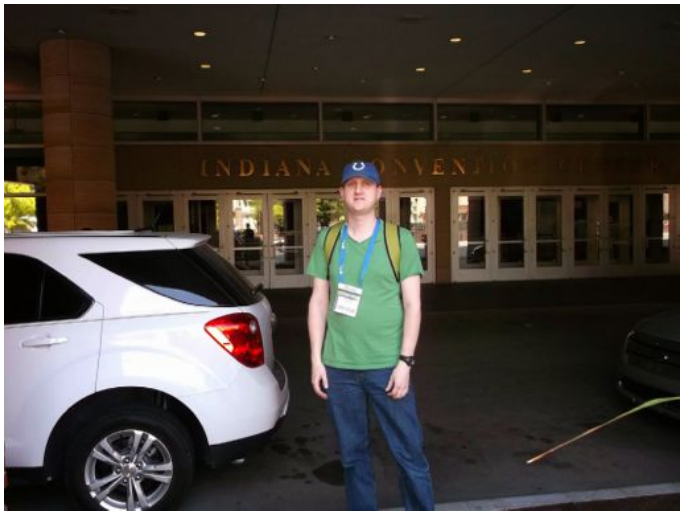
Huiping Xu, Michael A Black, and Bruce A Craig

Statistics in Medicine, 2013 vol. 32 (15) pp. 2571-2584

Conference Report

246th ACS National Meeting & Exposition

September 8-12, 2013 | Indianapolis, Indiana, USA



I am just finishing my second year of my PhD at the Chemistry and Biochemistry Department at the University of Otago working on the enzyme cysteine dioxygenase. This was the optimal time to present my work at an international conference and I chose the American Chemical Society (ACS) National Meeting held in Indianapolis in the USA. The conference had around 10,000 attendees with most of them presenting their work either via a talk or a poster. I got the opportunity to present my work on a bacterial form of the enzyme cysteine dioxygenase orally during the bioinorganic session of the meeting. The talk went well and I got some interesting questions and some good feedback on my presentation. I also attended countless interesting and fascinating talks during the 5 days and often it was hard to choose which session to attend since up to 15 sessions were held at the same time. There was the opportunity to listen to talks about every field of chemistry you can imagine from computational to quantum mechanics and from agriculture to Nano technology. Often the best talks which gave me new ideas and insights for my own PhD were held in small sessions with just a handful of attendees but other talks on more global topics with hundreds of people listening were also interesting. The numerous poster sessions gave the opportunity to check out even more interesting topics and talk to the presenters directly. In addition the meeting has a massive display of chemistry and related companies and I took the opportunity to not only extend my knowledge on equipment we already use in our lab but also on the industry in the US in general, maybe a workplace of the future for me. There were a lot of workshops to attend as well; some even free to improve on a variety of personal skills. I took the opportunity to get my cv screened and to perform a mock job interview where the feedback was a good indication that I am going in the right direction with my PhD at the University of Otago.

After the conference I took the opportunity of being in one of the most exciting countries of the world and spent some weeks as a tourist visiting many cities and got a good feel for the country in general. All this was possible by the funding I received and I want to thank the Division of Science and the Chemistry and Biochemistry Department for contributing to my trip! Summarising my experience I can just recommend an ACS conference in general no matter what part of chemistry you are working on, you will find excellent talks and posters at these meetings that will contribute to your own work.

Matthias Fellner, 7.10.2013

Dunedin Marathon

6am Alarm goes off. Time to get up. Sunday started with a glance out the window to check the weather. Good to see the beginning of a gorgeous day. With a subtle amount of dread the marathon ahead. Pre-race nourishment then making sure everything was ready. Multiple times. Ready to leave.

The drive out to the end of the peninsula was terrible. Such a slow drive among the other vehicles watching the marathon signs as we went. Slowly putting more kms between us and the finish line. Listening to the wind blow past the car. Wondering how much of a problem it would be. Finally we see lines of cars parked and realise we are here. Start line. I jump out of the car and join the line for the toilets. Many nervous runners. The start line of a marathon is a quietly nervous yet friendly place. Everyone knows what they've got into. Most have fears of not enough training. Me especially. I find the guy one number up from me and give him a fist bump. This means I am ahead of the real game. Fist bumping both people with adjacent numbers. Just generally waiting around. Keeping warm in the early morning wind. The man on the speakers gradually counting down the minutes.

Bang goes the gun and everyone starts a slow steady pace down the road. With his final words the man on the speakers said "this is the final countdown" so I now had my race song stuck in my head. Thanks guy on the speakers. I glance over to the right and see a boat sitting at Port Chalmers. Finish line. General banter includes "it's probably just easier to swim" and retrospectively it probably would have been. First sign we pass says 2km. Only 40 more to go. Was a surprise to go past it so quickly but I was feeling like the pace was nice so just continued. The 5km drink station also caught us by surprise. Not too bad a race. Gorgeous day. Nice people. Little bit of wind to help cool off but nothing too horrid. Very good. At 10km I open a delicious race sugar goo thing. So sweet. Washing it down with as much water as I can grab and carry on. Feeling good. Just going through the motions.

We carry on. Winding down the road. Water stops every 5km. Juicy goo thing every 10. Halfway sign comes up and I glance at my watch. An hour 50min. Not a bad half marathon time for me. Still looking good to conquer my 2 goals. Get under 4 hours and beat Meaghan O'Neill.

Coming into Portsmouth Drive I start to waver. Slowing the pace I think this is where a small amount of training would have come in handy. Meaghan passes me and I think to myself "it's ok. She'll wall soon and I'll get her at the end". It's amazing how delusional one gets when exhausted. Meeting up with the half marathon (only really walkers left now) I get an extra boost of energy. Passing people is always good for the mind, even if they are restricted from running. 30km water station. Final goo. Feeling like it will give me the last little bit to keep a gentle stagger of a jog to the end.

And from here it gets a little hazy... I keep looking at my watch and seeing the time pass. Slowly my jog becomes infected with walk steps. Just one every 20m. Then 10. Then every third step. Starting to walk more and more. I tell myself I can keep up and push on. Run a few steps, shake my head and walk some more. About 35km I have pretty much given up. Time wise I keep trying to tell myself I can make it easily under 4 hours if I run at a similar pace to what I started at. Delusion makes me feel it's achievable. But fairly soon after it's a continuous walk from here. My quads burn so I try to give them a stretch. However this gives the hammies some time to be short and relaxed muscles for a while and they cramp. Bad choice. Keep on walking. All the enjoyment from passing the walkers is sucked away as they all pass me back. Offering advice and telling me not long now. 7km is a long way and I can see how far in the distance.

It's a dark place settling into this "wall". We got talking and decided this running isn't for us. That possibly we should focus on some other ventures. Totally given up now and just a gentle stroll into the finish. Closer to walk to the end and get a ride home than walking straight home.

Coming into Port Chalmers people are starting to gather. A walker behind me cheers on another marathon runner who had also walled and found some new energy. He encourages me to roll on and run with this guy so I give it 5 steps. The walker then watches me run and yells "Wow look at this old man!" and it cheers me up a little. At least now I might be able to smile through the crowds. Finally the finish line approaches and as I enter the speaker man calls out my name and tries to encourage me to run the last 10m. I shake my head and continue my walk. Crossing the line I walk to a place where I can sit down, gather my thoughts and try to be happy with myself.

Comparatively my second half took 2h 50min. 4hr 38min all up. Not quite within my 4hr goal and not quite near Meaghan's 3h 51min. Nearly had her.

Lots of people at the end and I meet up with friends who were among a mixture of full and half runners and supporters. Beautiful day to be out and about and getting to the car is a bitter sweet mix of hobbling at a terrible pace and spending more time in the sun.

All in all not as terrible a day as I was feeling at the time. The thing with long distance running is it never seems that bad hours after the pain. Stupid endorphins. Will be hanging up my running shoes for a while though. Maybe until the November trail running half with Wayne…

James McKellar

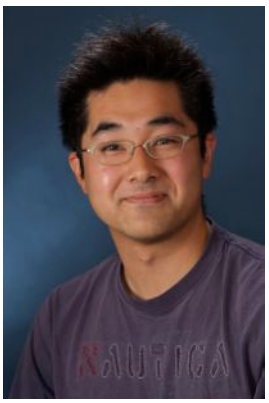
Quiz Report

John's Ultimate Quiz drew a packed house on Friday November 29, with 14 teams slugging it out neuron to neuron, fuelled by beer and pizza. A wide variety of questions was posed, drawing an even wider range of responses, regrettably most of them incorrect. A narrow victory was achieved by *Darwin's Beagles* who just pipped *It's Quizmas Time* followed by *And in Last Place* who tied for third place (after a countback) with *Antibiotic Resistance is Futile*. The karaoke sing-off produced some outlandish performances, particularly by James, Simon and Rhesa Their wild gyrations and primeval utterances did little to disguise the fact that they were off-key, but entertainment value was high and they certainly have futures as entertainers at children's parties.

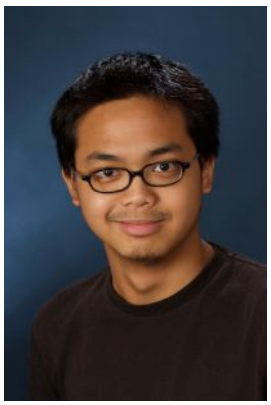
John reports that he was impressed by the contestants' knowledge of ice-creams, Beyonce, Richard III, William Wallace, baby bones and the Hindu Festival of Lights. However he suggests that more homework is needed on African colonial history, Michael Faraday, Emerson's beers, the Davis Cup, and the time difference for the Chatham Islands.

Overall it was a very enjoyable evening and a nice sign-off for John's last (official) day in the department. A big thanks to Matteo, Organizer Supreme, and to DJ for lending his (precious) sound system.

Domo arigato Mr. Roboto



by



by Rhesa Budhidarmo

Most of us have probably seen a tall Japanese man walking around the department. He's well-known for his keen ability to decipher how enzymes work, for his willingness to help others, as well as for his eardrum-popping laughs. He's been around for a while and a large number of us have probably received his help in one way or another. Rumour has it that his time working in Biochemistry department might be significantly reduced next year. It looks like he might be slowly leaving us. Although I realise that his legacy will lie in the success of the students whom he helped, the equipment that he fixed, and the papers that he wrote with colleagues from inside and outside Biochemistry, I feel the need to add to that by sharing some of the things that he told (and taught) me. Why? because I don't think that many people realise what an funny and eccentric guy he is. Therefore, I've assembled a list of quotations. The list contains some of the funniest, whimsical, thought-provoking, and uncalled-for words that ever came out of his mouth. I call this list 'Top 10 things Yoshio said that can make you wiser, laugh or cringe'. Enjoy!

No. 10. "What the f* is this ?!"**

This was what he said when he found out that there were mp3 files containing songs from the English boyband 'One Direction' in his iTunes folder. He said that one of kids must've put them there. Sure, Yoshio ... Suuuuuuureee .... It's one of your "kiiiidddssss". Just kidding ... he listens to another English boyband: The Beatles.

No. 9. "I think people need to understand kinetics"

I think he meant enzyme kinetics ... but I understood it as the need to understand that things constantly change with time because living systems are far from thermodynamic equilibrium, and that we must constantly adapt in the face of impermanence ... but I could have misinterpreted it because I might have been a bit too drunk.

No. 8. "I see proteins as machines"

He explained how he could often see with his mind's eye and predict how proteins move around, jiggle about, and change conformation in solution.

No. 7. "John would never allow me to compromise"

This statement reflects John's influence on him to do things properly. This principle can often be felt outside his scientific pursuits too.

No. 6. "It looks like a penis!"

I was using PyMol to show him a Lys side chain on the surface of my protein that might've been ubiquitylated. To highlight the residue, I displayed it as spheres but I forgot to hide the main chain. He then said the above statement and unleashed his earth-shattering laugh (see no. 1 later). We've since used only wireframe, cartoon, surface, or stick representations ... NOT spheres.

No. 5. "Read the f*ing manual!" a.k.a 'The RFM principle'**

This one is a Yoshio classic. This statement is often followed by a thunderous laugh (see no. 1 later). He's quite proud of this one, even though he never actually said this to anyone's face. However, beginning and advanced researchers often overlook the information that is contained within a product's manuals. I've definitely committed this crime a few times.

No. 4. "The peer review system is not working ... People keep publishing crap data! The data is all fake ... like Korean girls!"

LOL! I couldn't disagree.

No. 3. "Don't worry about money. Money comes and goes. It's good that you guys are alive and safe. That's more than enough."

This (or a similar statement) was heard when he picked Val and I up in the middle of the night from an accident scene where I had crashed my car earlier this year. It was ~20-30 min north of Dunedin and he came straight away after receiving my phone call. We can't thank him enough for that ... Like many people, I often worry about money too much and forget to appreciate what I have. Don't worry too much, people! Start living.

No. 2. "I want to look after young people like John and Sue did"

One day, I asked him what kind of supervisor he'd be like if he had his own lab and had students under him.

No. 1. "HA HA HA HA HA HA HA HA HA HA HA HA HA HA HA HA HA HA HA HA HA !!!"

This infamous laugh can be (painfully) heard after he utters the RFM principle (see no. 5), or after he discovered that there was something wrong with his data (e.g. "It's in the wrong space group. It should be $P42_12_1$ not $P2_12_14$. HA HA HA HA HA HA HA HA!"). The laugh was also heard when, for example, he found out that somebody forgot to add SDS to the SDS-PAGE running buffer, that a construct which was sent by a

collaborator contained a frameshift mutation, that his assays didn't work, that a tube that was supposed to contain a rare restriction enzyme was empty, or when he couldn't find his chopsticks or keys (luckily Bronwyn always had spare chopsticks). The laugh, which I have dubbed "The Transcendent Bliss of the Laughing Buddha", is a reflection of his ability to see the funny side of things even when those things went horribly wrong. I think many of us can use a little bit of that attitude.

There you go. I hope you enjoyed it and have been able to learn something about this man, yourself and the people around you. Let us continue to look after each other, and remember to laugh when things don't go as well as you've planned. If you do the things you do with good intentions and an open mind, there will always be a way out. Peace!

(DISCLAIMER: These quotations might not be 100% accurate because I only relied on my memory alone. However, I have tried my best to preserve the message. The interpretations are all mine and do not reflect the opinions of other members of lab 223. I have gained permission to write this piece from the man himself, although he said that he didn't want to see the draft or the final version of it)

News from Around the Department

Tate Lab

We have welcomed Mercy Moxham, as our summer student for 2013 into our family. She is working with our lab's favourite sAPPa protein and variants of it to see if we can elucidate specific regions important for its neuroprotective function. After the successful use of the Christmas decorations for John's last quiz night by our team, "it's quizmass time" (Caillan, Eiren & Ollie, Mercy, Jeremy and ~~Osama bin Laden~~ oops Warren) the xmas decorations have been reclaimed and are lighting up the lab (beating the reading room and prep room to it!) and - we are ready to party (although the quiz team got us off to a good start - Warren's office is full of the wine-ings!). But seriously we have mostly been very good boys and girls this year in the Tate lab so come on Santa! The lab is also going to get into the Christmas spirit at the performance of Handel's Messiah on Dec 10th - supporting Warren and Lyn!

Harold Bernhart has also returned to his favourite computer after being awarded a Marsden Fast Start grant. Yehh! He will be looking at the pre Darwinian chemical evolution of RNA in collaboration with Bill Hawkins (chemistry) & Joel Tyndall (pharmacy) with Warren as mentor, provider and co-supervisor of students. Welcome back Harold! Warren has been super busy as always. Since mid October he has presented at an RNA symposium in Christchurch, an Alzheimers community meeting in Oamaru, an ME/CFS support group annual meeting in Christchurch, given the Brain Health Research Centre's lecture for 2013, and has just returned from Australia presenting an ME/CFS talk at the opening of a National Centre for Neuroimmunology and Emerging Disease at Griffiths University, Gold Coast. And he always(!) seems to be in Wellington at an MBIE Science Board Meeting.

Laboratory for Cold Adaptation

New faces and some gaps in the Laboratory for Cold Adaptation this time. Lincoln Mackenzie has submitted his PhD and will graduate soon (in absentia sadly). Afroza Bulbul from Chemistry who has been doing some work in the laboratory has also completed her PhD and will graduate in person this week. Haoyu Xiong has just started a PhD working on ice active compounds in alpine plants as a joint student with David Wharton in Zoology. Ana Clarke is completing a summer scholarship working on Cd and Zn in oysters, and Brendon Lee, who completed his Honours degree this year, will be finishing some work on supercooling in beetles over the summer before he heads to Canberra and ANU next year.

Abhishek Kumar has just returned from a month in India and his brother's wedding (although that lasted only three days) and all his siblings are now married. Anna Seybold went to the New Zealand Molecular Ecology conference in Paekakariki where she talked about RNAi in nematodes and had a good time. Craig Marshall went to Canada to attend a conference and make some plans for forthcoming RSL which I'll tell you all about some other time.

In other news, the laboratory is tidier than it has ever been since we moved in and the fridges and freezers are due for a going over very soon too. The Departmental DSC (google it) arrived and we have a new place to put it. James McKellar has been exploring its possibilities and it looks to be a very nice thing to have. Our collection of laboratory animals continues to thrive as the beetles and brine shrimp are doing very well.

From the Office

It has been a long year and we are well and truely ready to have a break with our families. First of all a huge thank you to Robyn and Mel in the main office who have helped keep things ticking over. As many of you will know Frances and her family have had a year of Frances' Mum being terribly ill and in November her Mum passed away, and Frances had to have periods of time away to help care for her Mum and support her family in Wellington. Robyn and Mel have helped keep the office up and running during this time which we all appreciate. Frances has also watched her youngest daughter (Natalie) finish her final year at high school, so next year she will have both her daughters at University. Ooh, forgot Frances also had some friends over from the US this year and she took them bungy jumping this in itself is not all that exciting - EXCEPT Frances also did a jump. Mel has had his overseas trip with his family, by all accounts they had a fabulous time - probably saw more trains than any one person could hope to see in a year and even came back with a genuine handmade cuckoo clock all the way from the Black Forest. Robyn has welcomed a beautiful grandson in to her family (Eli) and she managed to time a trip over to Australia at the right time to visit him when he was a newborn and a second trip where she was fortunate to be able to give him his first ice cream - which was a bit of a mess but he looked pretty happy in the photos, Robyn has also become a foster mum to a great little dog Astra. So if you are looking for a new doggie pet for your family get in touch with Robyn and she'll direct you to Dunedin Dog Rescue a good team of people saving dogs and puppes from being put down in Dunedin. I (Teena) have had a reasonably straight forward year (thank goodness) and in my holidays (so far this year and over Christmas) am looking foward to spending time with my children, Mitchell and Emily, biking, kayaking and just relaxing! Although my football team has entered the Masters games (in Feb) so I guess I better do some training as well. We hope everyone has a happy and safe holiday with their families and see you all next year. From the office team

Frances, Mel, Robyn and Teena

Brown Lab

It's currently full steam ahead for everyone in the Brown lab.

We are pleased to welcome a visiting Statistics/ Bioinformatics Professor, Graham Wood, currently working on the "Saving the bees" project Systems Biology at Warwick, but still affiliated with Statistics at Macquarie University. He will give a seminar in the new year. For more information see http://www2.warwick.ac.uk/fac/sci/systemsbiology/staff/grahamwood/

Dan has fully left us after returning for a month in October. Managing to finish off the remaining couple of cool science-ey things while being incredibly busy. He now has a position at Monash.

Stewart having just handed in his PhD thesis, while juggling med-school during the year. He is now off on a well-deserved break. Travelling around Milford Sounds with his parents, hopefully coming back a whole lot more relaxed.

Ambarish, nipping at Stewart's heels, submitted his PhD thesis on Tuesday. Never seeming to take a break, which I'm sure will all pay off in the end. He also has a paper under review in the journal Bioinformatics, on his new tool called CRISPRDirection, the next should be submitted when that is accepted.

Rachael after finally being pried away from her computer, is currently extracting RNA from mussels. Leaving half of the lab with the unmistakable odour of rotting shell-fish. There is no problem she informs me because, "it doesn't smell in the area of the lab which does all the bioinformatics".

Gareth, another member of the lab who never seems to take a break, will soon complete his MSc. He has recently made available, the annotated transcriptome of the Kina on NCBI's GenBank and through a website mrna.otago.ac.nz/kina. His paper got good reviews from BMC genomics, on the transcriptome of the kina, including the first ever phylogenetic analysis involving kina to other sea urchins. Thanks particularly to Jodi and the Carne lab.

Andrew is in the process of writing his master's thesis, which at last contact was coming along nicely, but slowly. I have the utmost faith that he will produce a great thesis.

Scout has been incredibly busy with matters in and out of the lab. Her side project "Footsteps NZ" won the top 15 prize at this year's Audacious student business challenge. Despite all this she still perseveres in the lab.

I (Sam) have recently finished my honours year, and heading into the arduous time of being a master's student next year. Recently being awarded a Genetics Otago travel grant, enabling me to present research at next year's Lorne Genomics conference. Still researching hard up until the break, trying to get a head start for next year.

And as for our glorious commander and chief Chris. Despite being buried in paperwork and all the flood of incoming thesises to look over. He is still managing to undertake research and even recently submitting an invited review on regulation in hepatitis B virus, with Augustine and Joy, former PhD students.

So all in all, business as usual. We look forward to any new people joining the lab next year, and would like to wish everybody a joyous Holiday season and a good new year. Stay safe everyone.

Day lab

It's that time of the year again; the time be jolly and festive. Some would say that this is also a good time to reflect. This year has certainly been quite interesting for us. There were many ups and downs, but all is well now. As usual, people come and go. It felt like it was only yesterday that we said goodbye to Mat. Judging from the photos that he posted on Facebook, Mat seems to be living the good life in Nelson with his family.

Not so long ago, Yoshio's time with us also came to an end. As many of us know, he now enjoys his quiet new nest on the first floor, where he can do some serious thinking and have the freedom to fart whenever he wants (just kidding).

Georgina will also be leaving us. She is probably the only person in our lab who can do 47-56 things in a day (for comparison, on average, I can only do 3.14 things in a day). Her departure will be quite a loss for us. Rumour has it that she's looking for new adventure overseas. We wish her good luck and we hope that she'll find what she's been searching for.

It's not all sadness and tears, though. A few weeks ago, we welcomed a new summer student, Michael. Mike is continuing on a project which I left a few years ago. As a starter, he has cloned the expression constructs that I didn't have time to make in 2010. He has expressed and purified the proteins from those constructs and has been enthusiastically learning different biophysical techniques. All that in only 3-4 weeks!! At this rate, it looks like there are many more good things to come.

Josh made a breakthrough. He's solved his very first crystal structure! (AWWYISSSS!!!) Now, there are a few more experiments that he needs to do to validate the crystal structure. Apart from that, he's also been making more mutants and Frankenstein's monster-style fusion proteins to get more crystals.

It is now Martina's turn to fight with computers. In learning to understand the magic of turning diffraction spots into ribbon diagrams, one often needs to swear (a lot), bash the computer, and go look for DJ whenever the computer can't find the right directories. It's all fine, Martina. It's normal and it's all part of the learning process. There's no need to break Adam's arms :)

Speaking of Adam, he recently discovered that there's a protein fold called the 'hotdog' fold (for example, PDB code: 3D6L). We suggest that a new classification scheme be developed to group the hotdog fold together with the well-known jelly roll fold, β-sandwich domain, and the spaghetti of intrinsically disordered proteins.

Catherine has been enjoying a few weeks without too many meetings. This time of the year seems to be a good time for her to sort out the lab, figure out if we need new reagents and/or computers, and look around PubMed to see what's new in the ubiquitin world.

As for me, I'm just happy that I've survived this year. There were some turbulent periods. The only reason I got through them is because there are some wonderful people around me who are willing to spring into action to help me organise my life, often on short notices: the lovely people at the office, the computer and graphics wizards, the equipement menders, present and past members of lab 223, my friends and relatives, and many others. I'm sorry I cannot mention all of you by name simply because there are so many of you. I just want to say a thousand thanks to all of you. I really appreciate what you did. I hope one day I'll be able to repay you and do the same for others.

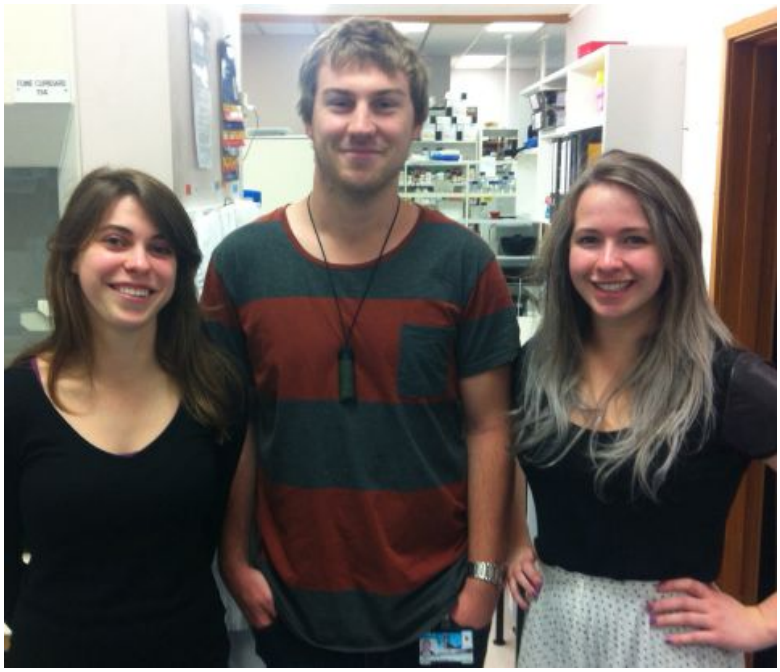
Happy holidays everybody. Drive safe.

Rhesa (for lab 223)

Walking the Dinosaur with the E^3 Lab

The last time we wrote a newsletter column, the Laboratory for Enzyme Engineering and Evolution comprised Monica, Wayne, Matteo and Jordan. How times have changed! PhD students Matilda and Danni are practically Dunedinites already, hardened locals James and Yoshio have been recruited, and two Honours students (Hannah & Shereen) have been, taken their first-class degrees, and gone. The arrival of summer has also heralded the arrival of our enthusiastic summer students: Cecilia Chambers (engineering ligases with Wayne); Tom Wiggins (evolving acylases with Monica); and Liz Prentice (making Psa mutants with Monica, Wayne and Peter Fineran).

In short – the lab is rocking! We even managed to secure the domain www.enzymes.org.nz for a new lab website – check it out for more information on what we've been up to.



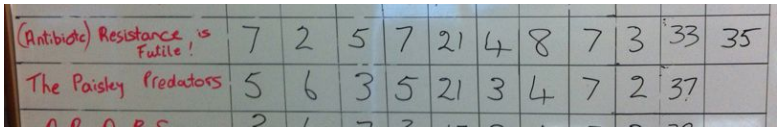
Summer students Liz, Tom and CC. Don't they look happy to be here

Nationally, the E^3 Lab announced our arrival by sweeping to victory in the QMB Fashionomics competition. Using the power of phylogenetics, ancestral sequence reconstruction and gene synthesis, we created…DinoZyme! Whilst a team effort, chief designer Matilda Newton, and model James McKellar, deserve particular credit. The very same day, Monica and Wayne learned that their MBIE Smart Idea grant had been funded…so cocktails were consumed in celebration (after waiting for the flames to die down, in Danni's case).

DinoZyme. Note the MPI/EPA-approved hazard labelling.

Back home, we sallied forth in strength to the Departmental Quiz Night. Matteo put in a sterling effort as John Cutfield's right-hand man, while two lab teams (originally named 'Naturally Selected' and 'Intelligently Designed') went head-to-head. At first glance, 'The Paisley Predators' looked to have sewn up the bragging rights…but wait… doesn't the score for '(Antibiotic) Resistance is Futile' actually add up to 45, not 35? We sense scandal and demand an Inquiry…though we all agree that James should not be given any more encouragement to sing Michael Jackson covers…

Finally, as Christmas approaches, so too does the end of Matteo's PhD. In fact, he is bidding to be the third of Wayne's PhD students to submit their thesis in 2013 – an amount of proofreading that Wayne, specifically, is keen never to repeat again. Thanks to one of Matteo's chapters (namely, Chapter 3) being in press at *PLoS One* already, we're hopeful that the examination process will go smoothly!



Quiz Night scandal!

JER news

Wow, yet another year is coming to a close!

The lab is at capacity as we welcomed our summer students, Jack Hervey who is staying on after putting his exams behind him and having a great honours year with us. The new-comers are Lauren Nicol and Matthew Prouse who have settled in nicely. A few months ago, now, we welcomed Afshan Rani to the JER lab, she is learning some molecular biology techniques with lots of PCR and cloning.

Everyone else is chugging along. Asher handed in the first draft of his Masters thesis for Julian to 'red pen'. Shiny is becoming an expert in SDS & BN-PAGE, Harvinder is looking forward to his trip back to India to visit family over the break, and Tim has submitted his paper and is hoping to wind up bench work soon to concentrate on writing his PhD thesis.

This week we attended Julian's Inaugural Professorial Lecture, which was brilliant and was followed by a few drinks and nibbles at the Staff Club. Very enjoyable, although I'm sure Julian's glad it's all over.

We haven't had Jared Fudge here to organize our end of year function, but amazingly we have coped without him and the dress code is somewhat more relaxed. So, to end the year the whole lab - which includes JER, RCM and LRB groups in 308 - are off to Del Sol on Friday, which should be grand as always, and with a few ex-lab members tagging along too, namely Rowan Herridge, Jake Lamb and Kelsey Picard. Looking forward to catching up and hearing about their new lives abroad. (Worryingly, happy hour is beforehand).

Have a safe and happy holiday!

Lab 216 ...

BIG congratulations to Andrea and Leo who both had very satisfactory oral defences to their PhDs. Leo is in the process of making some corrections requested by the examiners, we look forward to seeing Dr Germoni in his graduation garb next year. Andrea graduates on Saturday, having been very busy submitting two manuscripts for publication as well as packing up to move home to Hamilton where she has a job. Well done both!

Congratulations also to Astra and Jess for their great results in their fourth year exams. Both are staying in the lab as summer students, carrying on from their Honours projects. In between times they are having fun with their respective animals …

Lab 216 has had two new students arrive; Adam from Australia to carry out a summer project working on aspects of iron uptake by the kiwifruit pathogen PSA, and Nathan, working on different aspects of the same topic after finishing his BSc in Biochemistry at Otago. Both have settled in very quickly. Enjoy your time in the lab guys!

Older hands continue to keep busy. Annabelle is looking forward to Christmas with her family, if not the Brisbane warmth. Georgi attended the biennial Pseudomonas conference in Switzerland, as well as taking the opportunity to see parts of Europe, and has returned even more inspired about her project. Lois is on a mission to increase our waistlines with ongoing delicious baking. Iain also went to the Pseudomonas conference, then had 3 weeks in Italy taking part in another conference as well as spending time with collaborators in Rome - all very worthwhile though he seems to have been playing catch up ever since.

Lab 216 wishes you a fantastic holiday season!

Stocking the stockings in lab 118

Dear Santa,

While a pony would be nice, other things are further up our lists this year. So, if it is not too much trouble, could you please load these on your sleigh this December 24th?

At the top our list, we would like a half dozen or so fair and enthusiastic reviewers, please. Egor could use two with expertise in single turnover kinetics, Matthias would like a couple with a penchant for new assays and Antonia would like some with a fascination for urea metabolism. If they work out, we could recycle them in the new year for our description of bacterial CDO, Jess's SAXS story and Aimée's structures of inhibitor-bound macrophage migratory inhibitor factor.

Malcolm would like the exams he completed last month to truly be the "last exams I will ever take." Four times saying that should be enough! He also wants his clones back.

Shereen just wants a nice vacation at home for a few weeks before getting back to Dunedin and choosing a home lab for doctoral study.

Egor would like a mutant that accumulates a reaction intermediate. Matthias wants a phenotype for the cysteine dioxygenase knock out strain of *Pseudomonas* - it's fine with him if you deliver it to Lois in Iain's lab, please. Aimée wants a few more residues to be in the "favourable" region of the Ramachandran plot of her DnaK structure. Jess would like another pig brain, pretty please.

Casey wants everyone to have a safe Christmas - which includes latching the doors on flammables cabinets!

We would also like some mammalian proteins, please. I know it sounds greedy, but Antonia wants her insect cells to make more myeloperoxidase and Malcolm wants more CD74 from his bacteria. Rachel just wants her HEK293 cells to continue slurping up AlexaFluor-labelled Hsc70. Transducing protein instead of DNA - how cool is that?

As to whether or not we have been bad or good, for goodness sake ignore that unfortunate episode with the cow brains and consider, instead, that Jess, along with Shereen, Casey, Laura, Matthias, Egor, Antonia, Sigurd and Aimée all were very good at QMB. In the poster sessions, anyhow. Also remember that Aimée, Matthias and Antonia all made very nice presentations at overseas conferences this year (see Matthias's report elsewhere in the newsletter). Finally, we also would like you to consider the goodness of former lab members Anshul, Peter, Richard and Tracy, who each had a paper published this year, and together have a few more in revision or proofs.

Oh, yes! And a BLItz! Sigurd very much wants a BLItz bio-layer interferometer, please. He promises he will be very good and revise everyone's manuscripts and structures really, really soon if he gets one. He also promises he will share with other labs.

Sincerely yours,

Members of the Wilbanks Lab

P.S. Thanks very much for the early gift of a heat pump - we are most grateful and appreciate the out of season sleigh trip for delivery.

The Mace lab,

…nestled between the McCormick and Ledgerwood labs above the one way on the 2nd floor has been home to three occupants in the past few months. The leader of the pack Peter Mace, who is fresh from San Diego is spending the holidays with the family and plans to do some camping within the greater Otago area this summer.

The second occupant, Sam Jamieson is being welcomed and farewelled within the same newsletter, leaving for greener pastures on the first floor to return to his post as a senior technician. Sam plans to be in Dunedin with the family and carry out some home renovations. You will be missed!

So where do I, Adam Graham, fit in as summer student of the University of Otago? Its early days, but I plan to stick around with postgraduate study in the Mace Lab for a while yet (sorry in advance Peter). I will be returning to family in Auckland for Christmas, but expect to be travelling within the North Island during the break.

Seasons greetings from all in the Mace Lab.

Peter, Sam & Adam.

Krause Lab News

The big news of the year is, of course, that our team won John's final quiz evening. Kurt, Ashley, Emily, Roman, Miriam and our excellent honorary lab member Craig, with superb general knowledge, astounding geographical nous, and highly trained vocal chords, trumped the Tate lab and landed some fine wine.

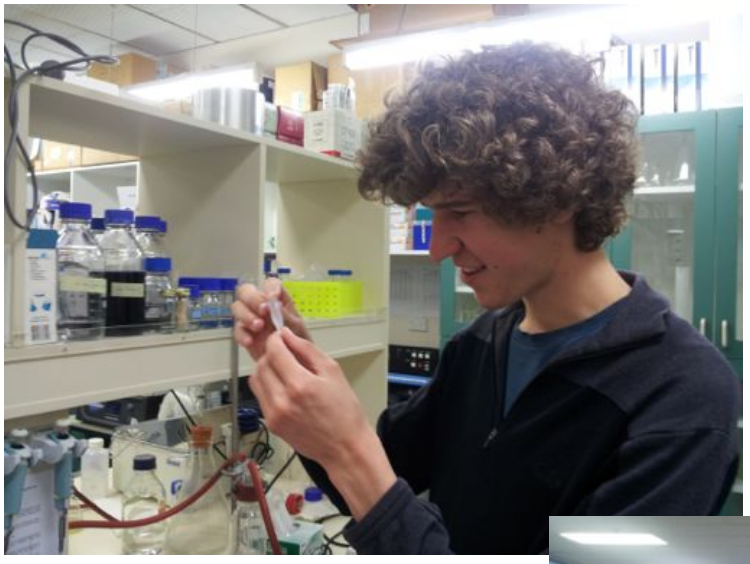
Continuing the competitive spirit, Kurt organised a 'Most Perfect Gel Competition' for the lab last week. Ashley and Michele took first place, with a gel of such clarity and perfection that it was worthy of framing and hanging on the wall.

We have some comings and goings as we wrap up 2013. Sailesh will be leaving us for the warmer shores of Adelaide where he starts medical school in the new year. Best of luck to Sailesh for his future adventures. And we welcome Max Wilkinson, who is studying CAS/Crisper proteins during a summer studentship, partly in the Krause Lab, and partly with the Fineran Group in Microbiology.

Michele and Kurt provided us with a warm example of American hospitality when they hosted the lab for a Thanksgiving dinner late November. The food was excellent; the turkey, prepared outside thanks to a recalcitrant oven(!), was moist and flavorful, and accompanied by some delectable apple and pumpkin pie.

Sinothai has been getting all technical on us, organising for his glutamate racemase structure to be printed out in 3D. This will help him figure out how the protein might best form a dimer, but we suspect it's also an excellent excuse for getting really sidetracked.

We are now seeing out the year with the unenviable task of defrosting and cataloguing our -80 freezer. Fortunately the prospect of strawberries and ice cream at the end of the week is helping to get us through the chore, and, of course, being able to start the new year with a clean, organised freezer that closes without us having to swear at it.



McCormick Lab

The McCormick lab has been ticking over quietly over the course of 2013. Between battling HRC grant application deadlines and jet-setting to Melbourne Sally has been making sure the lab has been running smoothly – she was even caught a few times doing the hard yards in a lab coat! Rumour has it she requested her own bench space and a new set of pipettes (citation needed). Better dig up the old protocols eh?!

Carolyn has been a fantastic addition the McCormick lab, joining the team at the start of the year. She fitted in smoothly and quickly asserted her matriarchal dominance in both the lab and write-up room. After many months battling with BioRad over a dodgy FPLC, Anne has emerged on the other side successful and is now back on track with labwork.

After three (long) years, Tom has finally decided to pull finger and submit his attempt at a Masters thesis. The McCormick lab harem will be sad to see the only male figure to walk its floors in years depart in such an abrupt fashion. When asked about how she felt about the aforementioned submission, Sally (or someone in Sally's lab (clearly a female!) responded, "I forgot we even had a Masters student to be honest, he didn't really come in that much." Well done Tom!

2013 also brought with it the addition of a new PhD student and a new BiomedSc student in Monika and Tanjina, respectively. Having skills in the kitchen as well as the lab, Monika has treated the team at lab meetings with her impressive Indian cuisine – the onion bhajis probably were the fan favourites! A huge congratulations to Tanjina for recently graduating! After having a stressful time around the deadline for thesis submission, she pulled through to get top marks. Doesn't she look happy (figure 1)? Even through the tough times, Tanjina still managed to keep smiling and provide snacks in the form of snickers and kit-kats to everyone, and for that we thank her.

Have a good xmas and new years everyone! Bring on 2014!!

Christmas greetings from the Merriman Lab

Well, we nearly missed out on getting this update in. This year has probably been like yours - a very busy one and much accomplished over the year; which we celebrated at the weekend with a pot luck dinner at the Merriman's home, along with our annual awards - this year Ruth won our supreme award.

In October, Hoang presented his PhD work at the American Society of Human Genetics meeting in Boston followed by a short visit to New York. Tony visited San Diego to present at the American College of Rheumatology meeting and discovered it has an "extremely good craft beer" industry there. His email read, "Very busy with work. This conference is always full on, meeting with collaborators and going to talks." A bit later in the same email……. "I walked around San Diego - Balbao Park and Coronado on Sat - hunting out brew pubs." Needless to say Tony came back with lots of project ideas, new ways to deal with our large amounts of data and more work for us all. At one place (The Hopping Pig) there was a dessert menu with 'Pig Licker Ice cream' which is actually 'vanilla bean custard, with chocolate bacon and peanut butter' - only in the USA!!

Back at base the rest of us have all been working hard on our various projects and James has joined us as full-time staff member for a while which is really helpful to us. We also have a few summer students; however you probably haven't seen them as Vidya is in a collaborator lab in Christchurch, Kimberley is mostly in the Psychology Dept with another collaborator and Marama is putting together information to present lab information to the Community in a short movie as part of our translational science work. Jarrod has gone to Samoa and Humaira has gone to Pakistan to visit family, whilst Tanya, Anna and James are off to visit their families in the North Island. James is in for significant brownie points from his Mum for being the only kid at home this Christmas. Cushla has been doing alterations at their home, shifting and doing the solo Mum thing (all at once) whilst her husband was away for work. Mansour and Tahzeeb have been busy making yummy food again (well we actually thinking Z which we all enjoy and will also enjoy time off although Tahzeeb is hoping her husband will be able to visit NZ sometime soon. Meanwhile Murray is enjoying not having to study and work at once and Ruth even has a Christmas tree at her home this year. Mandy, Marilyn & Tony has been enjoying the end of year festivities their children are involved in and finally the building work is finishing in time for Christmas at Marilyn and Tony's.

We also recently had a major lab clean out (and clean up) and reckon we have the best Christmas decorations out (thanks Tanya and Ruth). We hope this year has been a good one and wish you all a very enjoyable Festive Season.