Biochemistry News

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

editor: Bronwyn Carlisle

December 2011

In This Issue

View from the Corner

As 2011 winds down I thought it would be a good time to reflect on the major developments taking place in Biochemistry. This year's summary was penned collaboratively by Bronwyn and me. OK, mostly by Bronwyn, and reflects a sample of the events throughout the year.

This year as Director of the Webster Centre for Infectious Diseases, I was fortunate to be part of a team that obtained funding for a PC3 laboratory from the University's large equipment fund. The laboratory is housed in a shipping container. It was made in France, shipped here intact, and lifted onto the Microbiology roof by crane. All air that comes in and out of the laboratory is HEPA filtered, allowing researchers to work on real pathogenic organisms rather than non-pathogenic models. This is one of very first PC3 facilities in a New Zealand academic institution.

In April we began operating a Next Generation Sequencing service, providing high-throughput sequencing on the Roche GS-FLX and Illumina HiSeq2000 instruments. In September this facility officially became a service provider for New Zealand Genomics Limited (NZGL), offering a cost-effective sequencing option to the New Zealand genomics research community.

Over the Christmas break the first and second year labs on the first floor of the Microbiology building are being gutted and completely refurbished. This is only the second time in their forty years that these labs have been renovated so it'll be interesting to see the result in the new year.

While we cannot boast another Rutherford Medal in the Department this

year, staff and students have received a number of lesser scientific awards and a Queen's Birthday Honour.

Warren received the Companion of the New Zealand Order of Merit in the Queen's Birthday Honours list. Warren also did the speaking tour of New Zealand that is part and parcel of his last year's Rutherford Medal award, speaking to packed theatres in Nelson, Wanaka, Dunedin, Auckland, Rotorua, Palmerston North and Christchurch.

Catherine Day, Peter Dearden, Liz Duncan, and Kaye Wilson won major awards at the Otago School of Medical Sciences Awards ceremony at the beginning of the year. Catherine Day won the OSMS Distinguished Researcher of the Year, Kaye Wilson won the Distinguished Teaching Fellow, and Peter Dearden and Liz Duncan won the Best Paper of 2010 Award.

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Distinguished Teaching Fellow, and Peter Dearden and Liz Duncan won the Best Paper of 2010 Award.

Tony Zaharic was given a National Tertiary Teaching Award by the Prime Minister, as well as the prestigious Otago Teaching Award, to round off his collection of three Student Teaching Awards.

In the second annual Genetics Otago/Otago School of Medical Sciences poster evening, Rob Day won the Thermo Fisher Ultimate Postdoc award, while in the student categories, Rowan Herridge and Rhesa Budhidarmo took out the Genetics Otago and NZSBMB prizes respectively.

This year it seems as though we have had a constant presence in the media, with Peter Dearden, Julian Eaton-Rye, Warren Tate, and Tony Merriman each featuring in an episode of TVNZ7's science programme "Ever Wondered", and Stephanie Hughes and Warren Tate appearing in segments of Radio NZ National's "Our Changing World".

Russell Poulter appeared in the news, having led a team who sequenced the kiwifruit pathogens that have appeared on vines around the country. PSA was actually confined to kiwifruit vines in the Bay of Plenty and had not spread to the rest of the country as had been feared - a different, non-virulent, bacterium being the cause of leafspots in the South Island and Eastern North Island. Russell has also been awarded two Grand Challenges Exploration grants from the Bill and Melinda Gates Foundation. Both provide opportunities for substantial further funding after preliminary proof of concept.

Parry Guilford received two project grants and Tony Merriman an extension from the HRC, ensuring that their research (on cancer and autoimmune disease respectively) can continue apace, while Catherine Day and Liz Duncan were successful applicants to the Marsden Fund.

Julian Eaton-Rye finished a massive undertaking this year. He has been editing the 34th volume of "Advances in Photosynthesis and Respiration" since 2005. Herding the 76 international contributing authors from 20 different countries has been a sisyphean task, which is thankfully now over. Anyone interested in purchasing this massive tome can do so at www.springer.com/life+sciences/plant+sciences/book/978-94-007-1578-3.

Mike Legge has retired to the wilds of the West Coast and the great outdoors he and his wife love so much.

We have three new members of academic staff this year. Anita Dunbier and Lynette Brownfield arrived to take up new lecturing positions, and Liz Ledgerwood moved from a research only position to take a half time senior lectureship.

In May the Department held a "Three Minute Thesis" competition under the rules of the University's competition, where Masters and PhD students explained their research in a maximum of three minutes with just one slide and with much encouragement and hilarity from the audience. The winner of this event was Katie Hope, who presented work on her MSc on gene therapy using a sheep model of Batten disease; titled "Cure Batten disease! EWE know I can!" The joint runners up were Meaghan O'Neill (MSc) with "Aphids: not just a pain in your grass" and Sharleen Rae (PhD) with "All you need is a Mouse Brain and a Dream"

Well, that was the year that was. I look forward to seeing you all next year refreshed and ready for another year.

Kurt Krause

At Mike Legge's retirement

Recent Publications

(plus some I missed earlier in the year)

Stephen D Bird, Michael Legge, and Robert J Walker

Thiols stabilize cobblestone morphology of cultured mesothelial cells.

Cellular thiols including GSH (glutathione) and L-Cys (L-cysteine) are essential for cell signalling, growth and differentiation. L-Cys is derived from the extracellular thiol pool and is the rate-limiting compound for intracellular GSH biosynthesis. The present study investigated the effect of thiol-supplemented medium on cell growth, phenotype and total GSH of cultured hPMCs (human peritoneal mesothelial cells). Cells were cultured in medium M199 supplemented with 2% serum, with 'plus' or without 'minus' L-Cys and compared with medium supplemented with either beta-ME (beta-mercaptoethanol) (0.25 mmol/l) or the receptor tyrosine kinase ligand EGF (epidermal growth factor, 100 ng/ml). beta-ME produced a disproportionate increase in total GSH compared with L-Cys and other thiols tested [(procysteine (2-oxothiazolidine-4-carboxylic acid) or NAC (N-acetyl-L-cysteine)], while growth and morphology were identical. Cell behaviour of primary hPMCs is characterized by the transition of fibroblastoid to cobblestone morphology during early passage. L-Cys and beta-ME promoted a rapid MET (mesenchymal-to-epithelial transition) within 3 days of culture, confirmed by the presence of cobblestone cells, intact organelles, abundant microvilli, primary cilia and cortical actin. In contrast, EGF produced a biphasic response consisting of delayed growth and retention of a fibroblastoid morphology. During a rapid log phase of growth, MET was accompanied by rapid catch-up growth. Thiols may stabilize the epithelial phenotype by engaging redox-sensitive receptors and transcription factors that modulate differentiation. These data may benefit researchers working on thiol-mediated cell differentiation and strategies to regenerate damage to serosal membranes.

Cell Biology International, 2011 vol. 35 (8) pp. 857-867

Elisabeth Cramer Borde, Yasmine Ouzegdouh, Elizabeth C Ledgerwood, and Ian M Morison

Congenital Thrombocytopenia and Cytochrome c Mutation: A Matter of Birth and Death.

Thrombocytopenia (TP) Cargeeg is a unique autosomal dominant disorder, affecting a seven-generation family, caused by cytochrome c (CYCS) mutation that dysregulates platelet formation. The CYCS mutation in this disorder is a glycine 41 replacement by serine, which yields a cytochrome c variant with enhanced apoptotic pathway activity in vitro. The deregulated apoptosis in this disorder affects megakaryocytes (MK) during platelet formation, leading to early and ectopic platelet release in the bone marrow (BM). Notably, the family has no other phenotypic indication of abnormal apoptosis, implying that cytochrome c activity is not a critical regulator of physiological apoptosis in most cells. The pathophysiology of this unique inherited TP, with unaltered platelet survival and normal MK content in the BM, has implications for physiological and pathological mechanisms altering MK apoptosis, with implications for other unexplained thrombocytopenic disorders.

Seminars in Thrombosis and Hemostasis, 2011 vol. 37 (6) pp. 664-672

Ashwini L. Chand and Michael Legge

Amino acid transport system L activity in developing mouse ovarian follicles.

BACKGROUND: Little is known about metabolic processes in the developing ovarian follicle. Using mouse ovarian follicles, we investigated uptake of L-leucine by follicles at varying stages of maturity in the presence of insulin-like growth factor (IGF)-1.METHODS: Mouse ovarian follicles were cultured in vitro for 5 days in increasing concentrations of IGF-1, and follicle diameter and atresia measured as endpoints for growth. Uptake of H-3-leucine was measured in follicles at different stages of development. In optimal IGF-1-mediated growth conditions, competitive inhibition of H-3-leucine uptake by 2-aminobicyclo-(2,2,1)-heptane-2-carboxylic acid (BCH), a non-metabolizable substrate analogue of L-leucine, was performed to demonstrate specificity of influx, via system L transporters. To test whether uptake rates were dependent on intracellular amino acid availability, follicles from in vitro cultures were pre-treated with L-phenylalanine prior to H-3-leucine uptake.RESULTS: Follicle development ($P < 0.001$) and survival ($P < 0.001$) increased with IGF-1 treatment. As pre-antral follicles progressed to late antral stage, we observed an increase in L-leucine uptake, which was reduced in pre-ovulatory follicles. BCH decreased L-leucine uptake rates in early antral ($P < 0.05$), antral ($P < 0.001$) and pre-ovulatory follicles ($P < 0.01$). L-leucine influx increased in follicles preloaded with phenylalanine (trans-stimulation). In follicles lacking free intracellular amino acids (zero-trans suppression), uptake rate was reduced ($P < 0.05$).CONCLUSIONS: These results demonstrate, for the first time, evidence of specific system L amino acid transport in intact, mouse ovarian follicles and profile L-leucine uptake during folliculogenesis. A better understanding of ovarian follicle metabolic pathways is necessary for improved in vitro maturation as well as determining the impact of altered metabolism on fertility.

Human Reproduction, 2011 vol. 26 (11) pp. 3102-3108

T.M. Bricker, J.L. Roose, R.D. Fagerlund, L.K. Frankel, and J. J. Eaton-Rye

The extrinsic proteins of Photosystem II.

Biochimica et Biophysica Acta - Bioenergetics, 2011

Toni Daly, X. Sylvia Chen, and David Penny

How Old Are Rna Networks?

Some major classes of RNAs (such as mRNA, rRNA, tRNA and RNase P) are ubiquitous in all living systems so are inferred to have arisen early during the origin of life. However, the situation is not so clear for the system of RNA regulatory networks that continue to be uncovered, especially in eukaryotes. It is increasingly being recognised that networks of small RNAs are important for regulation in all cells, but it is not certain whether the origin of these networks are as old as rRNAs and tRNA. Another group of ncRNAs, including snoRNAs, occurs mainly in archaea and eukaryotes and their ultimate origin is less certain, although perhaps the simplest hypothesis is that they were present in earlier stages of life and were lost from bacteria. Some RNA networks may trace back to an early stage when there was just RNA and proteins, the RNP-world; before DNA.

RNA Infrastructure and Networks, 2011 vol. 722 pp. 255-273

R.C. Day and C.W. Beck

Transdifferentiation from cornea to lens in Xenopus laevis depends on BMP signalling and involves upregulation of Wnt signalling.

BMC Developmental Biology, 2011 vol. 11

M.J. Denton, G. Kumaramanickavel, and M Legge

Cells as irreducible wholes: the failure of mechanism and the possibility of an organicist revival.

Biology and Philosophy, 2011 pp. 1-22

N Dickerhof, T Kleffmann, and R Jack

Bacitracin inhibits the reductive activity of protein disulfide isomerase by disulfide bond formation with free cysteines in the substrate-binding domain.

FEBS Journal, 2011

JJ Eaton-Rye

Contributions of Govindjee, 1970–1999.

Photosynthesis

Richard C Draper, Lois W Martin, Paul A Beare, and Iain L Lamont

Differential proteolysis of sigma regulators controls cell-surface signalling in *Pseudomonas aeruginosa*.

Cell-surface signalling systems are widespread in Gram-negative bacteria. In these systems gene expression occurs following binding of a ligand, commonly a siderophore, to a receptor protein in the outer membrane. The receptor interacts with a sigma regulator protein that extends from the periplasm into the cytoplasm to control the activity of a cognate sigma factor. The mechanisms of signal transduction in cell-surface signalling systems have not been determined. Here we investigate signal transduction in the pyoverdine, ferrichrome and desferrioxamine siderophore systems of Pseudomonas aeruginosa. When pyoverdine is present the sigma regulator FpvR undergoes complete proteolysis resulting in activation of two sigma factors PvdS and FpvI and expression of genes for pyoverdine synthesis and uptake. When pyoverdine is absent subfragments of FpvR inhibit PvdS and FpvI. Similarly, subfragments of the sigma regulators FoxR and FiuR are formed in the absence of desferrioxamine and ferrichrome. These are much less abundant when the siderophores are present and downstream gene expression takes place. In all three systems RseP (MucP/YaeL) is required for complete proteolysis of the sigma regulator and sigma factor activity. These findings indicate that regulated proteolysis is a general mechanism for signal transduction in cell-surface signalling.

Molecular Microbiology, 2011

Jade E Hollis-Moffatt, Peter J Gow, Andrew A Harrison, John Highton, Peter Bb Jones, Lisa K Stamp, Nicola Dalbeth, and Tony R Merriman

The SLC2A9 nonsynonymous Arg265His variant and gout: evidence for a population-specific effect on severity.

INTRODUCTION:The C allele of the nonsynonymous Arg265His (rs3733591) variant of SLC2A9 confers risk for gout in Han Chinese, Solomon Island and Japanese samples, with a stronger role in tophaceous gout. There is no evidence for an association with gout in Caucasian populations. In the present study, we tested rs3733591 for association with gout in New Zealand (NZ) Māori, Pacific Island and Caucasian samples.

Arthritis research & therapy, 2011 vol. 13 (3) p. R85

SM Hook, AJ Phipps-Green, and F Faiz

Smad2: A Candidate Gene for the Murine Autoimmune Diabetes Locus Idd21. 1.

Journal of Clinical Endocrinology and Metabolism, 2011

J. Hazlett, L K Stamp, T Merriman, J Highton, and P.A. Hessian

IL-23R rs11209026 polymorphism modulates IL-17A expression in patients with rheumatoid arthritis.

Genes and Immunity, 2011

Berit Packert Jensen, Rebecca Lee Roberts, Ritva Vyas, Gitte Bonke, David L Jardine, and Evan James Begg

Influence of ABCB1 (P-glycoprotein) haplotypes on nortriptyline pharmacokinetics and nortriptyline-induced postural hypotension in healthy volunteers.

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT • A single nucleotide polymorphism in ABCB1, which encodes P-glycoprotein, has retrospectively been associated with symptoms of nortriptyline-induced postural hypotension in depressed patients. • This finding needs to be replicated in independent studies before recommendations regarding pharmacogenetic testing can be made. WHAT THIS PAPER ADDS • In a prospective study of healthy volunteers homozygous for ABCB1(1236-2677-3435, TTT/TTT or CGC/CGC), a single dose of nortriptyline was administered, plasma exposure was determined, and blood pressure and heart rate were monitored during posture change. • No differences between ABCB1 haplotype groups were found in plasma exposure of nortriptyline and its active metabolites, E- and Z-10-hydroxynortriptyline. The heart rate response to posture change was increased with nortriptyline, whereas there was no difference in blood pressure response. However, no differences between haplotype groups were observed except that the pre-dose heart rate response to standing was greater in the TTT than CGC homozygotes. • The association between ABCB1 polymorphisms and nortriptyline-induced postural hypotension found in a previous study could not be confirmed. The results raise the possibility of a predisposition in heart rate response in the TTT homozygotes rather than an effect of nortriptyline. SUMMARY: Aims To investigate the influence of ABCB1(1236-2677-3435) polymorphisms on nortriptyline pharmacokinetics and nortriptyline-induced postural hypotension in healthy volunteers. Methods Genetic screening of 67 healthy volunteers identified 8 CGC homozygotes and 9 TTT homozygotes of ABCB1(1236-2677-3435), who were administered a single dose of nortriptyline 25 mg. Plasma exposure of nortriptyline and its active metabolites, E- and Z-10-hydroxy-nortriptyline, was determined over 72 h. Heart rate and blood pressure responses to posture change (active standing and passive head-up tilt) were measured continuously using finger plethysmography. Results There were no differences in plasma exposure between ABCB1 haplotype groups, as the geometric mean (95% CI) AUC(0-72h) ratios were 0.98 (0.94-1.03), 1.02 (0.96-1.09) and 0.95 (0.80-1.10) for nortriptyline, E- and Z-10-hydroxynortriptyline, respectively. The pre-dose heart rate response to standing was greater in the TTT than CGC homozygotes (mean (95% CI) difference 7.4 (1.5, 13.4) bpm, P = 0.02). At t(max) at 8 h post-dose, nortriptyline increased the heart rate response to posture change in all subjects with mean (95% CI) delta heart rate values of 7.4 (3.6, 11.3) bpm on active standing (P = 0.0009) and 4.8 (2.0, 7.6) bpm on head-up tilt (P = 0.002), but no difference was observed between haplotype groups. There was no difference in blood pressure response to posture change in either group. Conclusion The association between ABCB1 polymorphisms and nortriptyline-induced postural hypotension found in the previous study could not be confirmed. The results raise the possibility of a predisposition in heart rate response in the TTT homozygotes rather than an effect of nortriptyline.

British Journal Of Clinical Pharmacology, 2011

Roslyn A. Kemp, Michael A Black, John McCall, Han-Seung Yoon, Vicky Phillips, Ahmad Anjomshoaa, and Anthony E Reeve

T cell subpopulations in lymph nodes may not be predictive of patient outcome in colorectal cancer.

Background: The immune response has been proposed to be an important factor in determining patient outcome in colorectal cancer (CRC). Previous studies have concentrated on characterizing T cell populations in the primary tumour where T cells with regulatory effect (Foxp3+ Tregs) have been identified as both enhancing and diminishing anti-tumour immune responses. No previous studies have characterized the T cell response in the regional lymph nodes in CRC. Methods: Immunohistochemistry was used to analyse CD4, CD8 or Foxp3+ T cell populations in the regional lymph nodes of patients with stage II CRC (n = 31), with (n = 13) or without (n = 18) cancer recurrence after 5 years of follow up, to determine if the priming environment for anti-tumour immunity was associated with clinical outcome.Results: The proportions of CD4, CD8 or Foxp3+ cells in the lymph nodes varied widely between and within patients, and there was no association between T cell populations and cancer recurrence or other clinicopathological characteristics. Conclusions: These data indicate that frequency of these T cell subsets in lymph nodes may not be a useful tool for predicting patient outcome.

Journal of Experimental & Clinical Cancer Research, 2011 vol. 30 pp. -

TR Merriman

Population Heterogeneity in the Genetic Control of Serum Urate.

Seminars in Nephrology, 2011

Rebecca E Laurie, Payal Diwadkar, Mauren Jaudal, Lulu Zhang, Valerie Hecht, Jiangqi Wen, Million Tadege, Kirankumar S. Mysore, Joanna Putterill, James L Weller, and Richard C Macknight

The Medicago FLOWERING LOCUS T Homolog, MtFTa1, Is a Key Regulator of Flowering Time.

FLOWERING LOCUS T (FT) genes encode proteins that function as the mobile floral signal, florigen. In this study, we characterized five FT-like genes from the model legume, Medicago (Medicago truncatula). The different FT genes showed distinct patterns of expression and responses to environmental cues. Three of the FT genes (MtFTa1, MtFTb1, and MtFTc) were able to complement the Arabidopsis (Arabidopsis thaliana) ft-1 mutant, suggesting that they are capable of functioning as florigen. MtFTa1 is the only one of the FT genes that is up-regulated by both long days (LDs) and vernalization, conditions that promote Medicago flowering, and transgenic Medicago plants overexpressing the MtFTa1 gene flowered very rapidly. The key role MtFTa1 plays in regulating flowering was demonstrated by the identification of fta1 mutants that flowered significantly later in all conditions examined. fta1 mutants do not respond to vernalization but are still responsive to LDs, indicating that the induction of flowering by prolonged cold acts solely through MtFTa1, whereas photoperiodic induction of flowering involves other genes, possibly MtFTb1, which is only expressed in leaves under LD conditions and therefore might contribute to the photoperiodic regulation of flowering. The role of the MtFTc gene is unclear, as the ftc mutants did not have any obvious flowering-time or other phenotypes. Overall, this work reveals the diversity of the regulation and function of the Medicago FT family.

PLANT PHYSIOLOGY, 2011 vol. 156 (4) pp. 2207-2224

M Legge and LM Jones

Energy substrate utilization in the common brushtailed possum (*Trichosurus vulpecula*) using intravenous tolerance tests.

Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology, 2011

EP Tchesnokov and SM Wilbanks

A Strongly Bound High-Spin Iron (II) Coordinates Cysteine and Homo-cysteine in Cysteine Dioxygenase.

Biochemistry, 2011

Lance D. Miller, Lan G. Coffman, Jeff W. Chou, Michael A Black, Jonas Bergh, Ralph Jr D'Agostino, Suzy V. Torti, and Frank M. Torti

An Iron Regulatory Gene Signature Predicts Outcome in Breast Cancer.

Changes in iron regulation characterize the malignant state. However, the pathways that effect these changes and their specific impact on prognosis remain poorly understood. We capitalized on publicly available microarray datasets comprising 674 breast cancer cases to systematically investigate how expression of genes related to iron metabolism is linked to breast cancer prognosis. Of 61 genes involved in iron regulation, 49% were statistically significantly associated with distant metastasis-free survival. Cases were divided into test and training cohorts, and the supervised principal component method was used to stratify cases into risk groups. Optimal risk stratification was achieved with a model comprising 16 genes, which we term the iron regulatory gene signature (IRGS). Multivariable analysis revealed that the IRGS contributes information not captured by conventional prognostic indicators (HR = 1.61; 95% confidence interval: 1.16-2.24; P = 0.004). The IRGS successfully stratified homogeneously treated patients, including ER+ patients treated with tamoxifen monotherapy, both with (P = 0.006) and without (P = 0.03) lymph node metastases. To test whether multiple pathways were embedded within the IRGS, we evaluated the performance of two gene dyads with known roles in iron biology in ER+ patients treated with tamoxifen monotherapy (n = 371). For both dyads, gene combinations that minimized intracellular iron content [anti-import: TFRCLow/HFEHigh; or pro-export: SLC40A1 (ferroportin) (High)/HAMP(Low)] were associated with favorable prognosis (P < 0.005). Although the clinical utility of the IRGS will require further evaluation, its ability to both identify high-risk patients within traditionally low-risk groups and low-risk patients within high-risk groups has the potential to affect therapeutic decision making. Cancer Res; 71(21); 6728-37. (C)2011 AACR.

Cancer Research, 2011 vol. 71 (21) pp. 6728-6737

Yoshio Nakatani, Susan M Cutfield, Nathan P Cowieson, and John F Cutfield

Structure and activity of exo-1,3/1,4-β-glucanase from marine bacterium Pseudoalteromonas sp. BB1 showing a novel C-terminal domain.

Following the discovery of an exo-1,3/1,4-β-glucanase (glycoside hydrolase family 3) from a seaweed-associated bacterium *Pseudoalteromonas* sp. BB1, the recombinant three-domain protein (ExoP) was crystallized and its structure solved to 2.3Å resolution. The first two domains of ExoP, both of which contribute to the architecture of the active site, are similar to those of the two-domain barley homologue ExoI with a distinctive Trp-Trp clamp at the +1 subsite, although ExoI displays broader specificity towards β-glycosidic linkages. Notably excision of the third domain of ExoP results in an inactive enzyme. Domain 3 has a β-sandwich structure and was shown by circular dichroism to be more temperature stable than the native enzyme. It makes relatively few contacts to domain 1 and none at all to domain 2. Two of the domain 3 residues involved at the interface, Q683 (forming one hydrogen bond) and Q676 (forming two) were mutated to alanine. Variant Q676A retained about half the activity of native ExoP but the Q683A variant was severely attenuated. The crystal structure of Q683A-ExoP indicated that domain 3 was highly mobile and that Q683 is critical to the stabilization of ExoP by domain 3. SAXS data lent support to this proposal. Domain 3 does not appear to be an obvious carbohydrate binding domain and is related neither in sequence nor structure to the additional domains characterized in other GH3 subgroups. Its major role appears to be for protein stability but it may also help orient substrate.

The FEBS journal, 2011

GB Petersen

Kenneth Burton. 26 June 1926—22 November 2010.

Biographical Memoirs of Fellows of the Royal Society, 2011

S Burut-Archanai and J Eaton-Rye

Na+-stimulated phosphate uptake system in Synechocystis sp. PCC 6803 with Pst1 as a main transporter.

BMC Microbiology, 2011

Eleni Siakkou, Malcolm T Rutledge, Sigurd M Wilbanks, and Guy N L Jameson

Correlating crosslink formation with enzymatic activity in cysteine dioxygenase.

Cysteine dioxygenase (CDO) from rat and other mammals exhibits a covalent post-translational modification between the residues C93 and Y157 that is in close proximity to the active site, and whose presence enhances the enzyme's activity. Protein with and without C93-Y157 crosslink migrates as distinct bands in SDS-PAGE, allowing quantification of the relative ratios between the two forms by densitometry of the respective bands. Expression of recombinant rat wild type CDO in Escherichia coli typically produces 40-50% with the C93-Y157 crosslink. A strategy was developed to increase the ratio of the non-crosslinked form in an enzyme preparation of reasonable quantity and purity, allowing direct assessment of the activity of non-crosslinked CDO and mechanism of formation of the crosslink. The presence of ferrous iron and oxygen is a prerequisite for C93-Y157 crosslink formation. Absence of oxygen during protein expression increased the fraction of non-crosslinked CDO, while presence of the metal chelator EDTA had little effect. Metal affinity chromatography was used to enrich non-crosslinked content. Both the enzymatic rate of cysteine oxidation and the amount of cross-linking between C93 and Y157 increased significantly upon exposure of CDO to air/oxygen and substrate cysteine in the presence of iron in a hitherto unreported two-phase process. The instantaneous activity was proportional to the amount of crosslinked enzyme present, demonstrating that the non-crosslinked form has negligible enzymatic activity. The biphasic kinetics suggest the existence of an as yet uncharacterised intermediate in crosslink formation and enzyme activation.

Biochimica et biophysica acta, 2011 vol. 1814 (12) pp. 2003-2009

M Chen-Xu, R Topless, C Mckinney, M E Merriman, A Phipps-Green, N Dalbeth, P J Gow, A A Harrison, J Highton, P B Jones, M Nissen, M D Smith, A Van Rij, G T Jones, L Rodriguez-Rodriguez, B Fernandez-Gutierrez, M Teruel, A Balsa, D Pascual-Salcedo, A M Ortiz, M A Gonzalez-Gay, S Steer, M Maehlen, B Lie, B P Wordsworth, L K Stamp, J Martín, and T R Merriman

Replication of association of the interleukin 23 receptor rs1343151 variant with rheumatoid arthritis in Caucasian sample sets.

Annals of the Rheumatic Diseases, 2011 vol. 71 (1) pp. 155-157

Lisa K Stamp and Rebecca L Roberts

Effect of genetic polymorphisms in the folate pathway on methotrexate therapy in rheumatic diseases.

Methotrexate (MTX) is the first-line treatment for rheumatoid arthritis and is frequently used in the management of other forms of inflammatory arthritis. It is currently challenging to predict which patients will achieve adequate disease control and which patients will develop adverse effects while taking MTX. As an analog of dihydrofolic acid, MTX enters cells through the reduced folate carrier-1 protein, and is polyglutamated. MTX polyglutamates inhibit key enzymes in the folate pathway to produce an anti-inflammatory effect. It has been suggested that genetic polymorphisms in the folate pathway may influence intracellular folate and MTX polyglutamates pools, and thus MTX response. However, studies to identify genetic predictors have yielded inconclusive results. Nonreplication across studies has been attributed to insufficient statistical power as well as pharmacological and clinical confounders. Prospective studies, standardizing the definitions of response and toxicity, and application of genome-wide approaches may advance the search for genetic predictors of MTX response.

Pharmacogenomics, 2011 vol. 12 (10) pp. 1449-1463

Judith E. Sutherland, Sandra C. Lindstrom, Wendy A Nelson, Juliet Brodie, Michael D. J. Lynch, Mi Sook Hwang, Han-Gu Choi, Masahiko Miyata, Norio Kikuchi, Mariana C. Oliveira, Tracy Farr, Chris Neefus, Agnes Mols-Mortensen, Daniela Milstein, and Kirsten M. Mueller

A New Look at an Ancient Order: Generic Revision of the Bangiales (Rhodophyta).

The red algal order Bangiales has been revised as a result of detailed regional studies and the development of expert local knowledge of Bangiales floras, followed by collaborative global analyses based on wide taxon sampling and molecular analyses. Combined analyses of the nuclear SSU rRNA gene and the plastid RUBISCO LSU (rbcL) gene for 157 Bangiales taxa have been conducted. Fifteen genera of Bangiales, seven filamentous and eight foliose, are recognized. This classification includes five newly described and two resurrected genera. This revision constitutes a major change in understanding relationships and evolution in this order. The genus Porphyra is now restricted to five described species and a number of undescribed species. Other foliose taxa previously placed in Porphyra are now recognized to belong to the genera Boreophyllum gen. nov., Clymene gen. nov., Fuscifolium gen. nov., Lysithea gen. nov., Miuraea gen. nov., Pyropia, and Wildemania. Four of the seven filamentous genera recognized in our analyses already have generic names (Bangia, Dione, Minerva, and Pseudobangia), and are all currently monotypic. The unnamed filamentous genera are clearly composed of multiple species, and few of these species have names. Further research is required: the genus to which the marine taxon Bangia fuscopurpurea belongs is not known, and there are also a large number of species previously described as Porphyra for which nuclear SSU ribosomal RNA (nrSSU) or rbcL sequence data should be obtained so that they can be assigned to the appropriate genus.

Journal of Phycology, 2011 vol. 47 (5) pp. 1131-1151

Chun K. Wong, Vivienne L. Young, Torsten Kleffmann, and Vernon K. Ward

Genomic and Proteomic Analysis of Invertebrate Iridovirus Type 9.

Iridoviruses (IV) are nuclear cytoplasmic large DNA viruses that are receiving increasing attention as sublethal pathogens of a range of insects. Invertebrate iridovirus type 9 (IIV-9; Wiseana iridovirus) is a member of the major phylogenetic group of iridoviruses for which there is very limited genomic and proteomic information. The genome is 205,791 bp, has a G+C content of 31%, and contains 191 predicted genes, with approximately 20% of its repeat sequences being located predominantly within coding regions. The repeated sequences include 11 proteins with helix-turn-helix motifs and genes encoding related tandem repeat amino acid sequences. Of the 191 proteins encoded by IIV-9, 108 are most closely related to orthologs in IIV-3 (Chloriridovirus genus), and 114 of the 126 IIV-3 genes have orthologs in IIV-9. In contrast, only 97 of 211 IIV-6 genes have orthologs in IIV-9. There is almost no conservation of gene order between IIV-3, IIV-6, and IIV-9. Phylogenetic analysis using a concatenated sequence of 26 core IV genes confirms that IIV-3 is more closely related to IIV-9 than to IIV-6, despite being from a different genus of the Iridoviridae. An interaction between IIV and small RNA regulatory systems is supported by the prediction of seven putative microRNA (miRNA) sequences combined with XRN exonuclease, RNase III, and double-stranded RNA binding activities encoded on the genome. Proteomic analysis of IIV-9 identified 64 proteins in the virus particle and, when combined with infected cell analysis, confirmed the expression of 94 viral proteins. This study provides the first full-genome and consequent proteomic analysis of group II IIV.

Journal of Virology, 2011 vol. 85 (15) pp. 7900-7911

N Panjaworayan and CM Brown

Effects of HBV Genetic Variability on RNAi Strategies.

Hepatitis Research and Treatment, 2011

A Farewell from José Garcia-Bustos

I will take this last chance to bid farewell to the many members of the Biochemistry Department whom I could not personally meet during my last week there. I wish you all the best luck in your professional endeavors and a great holiday season to recharge and renew. My stay among you has been extremely rewarding personally and professionally. I chose to visit New Zealand because it has the reputation of being a special place, and I found that indeed it is. With strengths and weaknesses, like everywhere else, but the outcome of unique geographical and historic circumstances in which the positives certainly outweigh the negatives. And I love the kiwi attitude, for me encapsulated in the usual reply to an expression of thanks: "no worries". It is great, it makes one immediately feel more at ease no matter the business at hand.

I must admit early September in Dunedin was tough. Climbing the dark streets of Opoho hill in the rain lugging groceries from the Gardens New World was no fun. The drastic reduction in bus frequencies at times when the evening rush hour would be starting in Madrid conflicted with my work habits. And I am all against energy waste and light pollution, but having to walk along the center of the road to avoid hitting trash bins hidden in the shadows of trees and shrubs seemed a bit too much. Despite the low lighting, to this day I have not been able to see the Southern Cross, one of my very few regrets from this visit. Oh well, at least unlike Madrid the way was not a mine field of dog poo. Then spring started and I began to look forward to my morning walk through the botanical garden. That was quality of life. Going back in the evening was still less enjoyable, so I moved to Dunlop House, part of Arana College. That allowed me a much shorter walk to and from work through the beautiful Otago campus. Those of you accustomed to such surroundings may not notice them anymore but for me, crossing the Leith among cherry blossoms, towering beech trees and beautifully preserved XIX century buildings was an everyday treat. I kept shopping at New World, mostly to admire the spring bloom. First the rhododendrons and later everything else, reaching its climax at the rose garden. I literally took hundreds of pictures in the gardens but will refrain from boring anybody here by flashing them in quick succession. They are beautiful, but it is the experience of being there, the landscape, the smells and sounds that make them special.

My grocery shopping trips also allowed me to literally walk among Otago student culture. I regret no having had more time to reconcile my image of students in the Department, hard working and intellectually engaged, with that of the young people walking bare footed around broken beer bottles and burnt couches. Could they possibly be the same species?

Finally, summer weather arrived and I took a short trip to the West Coast. Unable to find a travel mate, I gave up learning to drive on the "wrong" side of the road by myself and took the bus to Queenstown. A long trip but one which allowed me to take in the human and natural landscape in a way I could never have done while driving. I would have never stopped at places like Roxburgh, where the Clutha river flows turquoise and powerful, with its quaint brightly painted hotel, "The Commercial", reminiscent of gold-rush times. I also saw my first deer farms and sheep in quantities to explain all the kiwi lamb in the supermarkets here. Queestown, the Milford Track (just one day, mind you) and the Milford Sound, all of them in glorious weather (see photo) rounded off what have been fantastic three months.

I will conclude this summary adding to what we learned in the past Newsletter about ways to make trips more enjoyable to our air travel companions. You need two children between 10 and 14 years of age. Get yourself a business seat and, since the children will not sleep anyway, put them down the next cabin aft. Why waste money? Just so that they do not get bored and keep coming forwards to exchange their peanuts for your macadamias, give them game consoles connected so that they can play against each other, with headphones. This way they will need to shout out what they will do to each other's game characters and the rest of us in the same cabin will get frequent reports on the game status all night long, distracting us from the uncomfortable seats.

Happy holidays.

News from Around the Department

Eaton-Rye Lab

So the end of another year is upon us, and I think its safe to say we are all in need of a holiday.

So what's been happening with us I hear you ask? Well it wouldn't be a JER newsletter without mentioning Simon Cabout. This time he tripped over his shoes laces on a fishing expedition and dislocating his knee. One would think that having walked an hour from the car to get to their fishing spot, before the aforementioned knee injury, would warrant calling the rescue helicopter … but no! In true Southern Man style, Simon hobbles for 4 hours back to the car to drive to A&E and sit there for a further 2 hours before being seen to. Needless to say, Ryan, leaving Simon to get around by lab chair, was constantly stealing his crutches. He also used his knee injury as an excuse not to finish up his uptake assays, wasting perfectly good isotope! No dedication ;-)

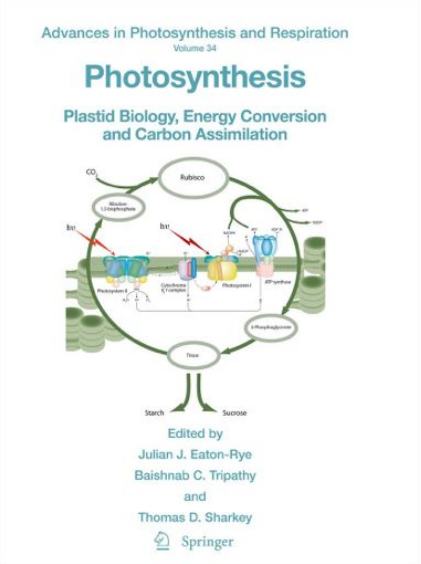
Our 4th year students have put their talks and exams behind them, so the lab had been quiet for a number of weeks as they prepared for those. The talks went well, and luckily so did the exams. This has seen us farewell Josh O'Sullivan from the lab, however Jake and Asher are staying on over the summer. (Umm, yay).

Simon Jackson has returned from an amazing climbing expedition … He missed our Xmas dinner to climb Mount Cook!!! Definitely worth missing a meal for. Great weather and an 18-hour climb to the top. Big tick off your bucket list.

And as Simon stood atop Mt Cook, the rest of us were nice and warm at the Crown Mill restaurant having our Xmas function. The evening begun with pre-dinner drinks and nibbles at Jared Fudge's flat, and then we wondered around the corner to the Crown Mill for an impressive 3-course meal. It was an excellent evening, and we highly recommend the venue! Secret Santa presents were distributed, between the main and dessert courses, and this always proves to be in good humor as people put a lot of thought into their gifts for fellow lab members. The 308 guys made an effort having suited up, some in their tuxes (no less), very dapper. It was an evening of chest baring and falling off chairs … not so dapper. After leaving the Crown Mill, most headed off into town to the usual bars and it's safe to say the rest of the weekend was quiet.

To finish with, and it is on a sad note, that we farewell Martin from 308. He has taken up a position in Norway and is shifting over there. Martin has been great to have in the lab, his helpfulness and advice is going to be missed. All the very best to him and his family!!

Merry Xmas to you all, and happy holidays! See you in 2012.



Julian's book is finally done.

Ledgerwood Lab

In the absence of our resident cartoonist we are back to mere words for our news. The Ledgerwood lab is feeling very prestigious as we have been joined for the summer by Hannah (recipient of a Health Sciences Prestigious Summer Scholarship) and Aziz (recipient of an OSMS Dean's Prestigious Summer Scholarship). They are working hard and keeping us on our toes with all their questions.

Overseas adventures have been the main feature of the last few months – Gill traveled to Rarotonga to help Carolyn celebrate a birthday, Hannah managed a long weekend in Sydney (and learnt that she really was meant to bring us back chocolates), and now Tracy has headed off to Antarctica as one of Craig Marshall's trusty field assistants. She is intending to return refreshed and ready to tackle thesis writing in earnest.

In lab alumni news PhD graduate Reagan Jarvis is heading to Germany in January to take up a postdoctoral position at the German Cancer Research Center (DKFZ) in Heidelberg. Henry Hampton (Honours student in 2009) has embarked on a PhD at the Garvan Institute in Sydney after spending a year working there as a research assistant.

Our sad news is that the funding for Gill's position runs out at the end of the year and so she will be leaving us and looking for new opportunities. Gill has been in the department for around 40 years and has made many important contributions to the smooth running and research output of the department over that time. We will miss her.

Macknight Lab news

Cup Fever

This spring coincided with at least three important happenings – Movember, Melbourne Cup, flowering time, oh and of course the Rubgy World Cup. Several of the 308 Boys cultured moustaches to varying degrees of masculinity during Movember, including Rowan Herridge. His was sufficient to warrant his Secret Santa carefully assembling a 'moustache care kit', comprising wax, a comb, scissors and compact mirror. Although that moustache wouldn't be at home at Flemington. Perhaps Wingatui instead ?

The Melbourne Cup was more disappointing than the election turnout for any of our lab members that placed a bet and enjoyed a beverage at a nearby establishment with TAB facilities. Dunadin dun it though for Calum Johnstone (Kina research group) whom simultaneously collected the departmental sweepstake and a moderate dividend from a cheeky bet.

Moving now from Cup Day to Cup Year, RWC 2011 (mandatory topic) seems to have been quickly forgotten about by now by most people. Several lab members attended various qualifying matches in Dunedin. Unforgettable however was the effort made costume-wise for the England vs Romania game, which had a distinct Eastern European flavour.

A new PhD student, Manda Safavi, has arrived from Iran. She is working on a Medicago flowering time project and is already flourishing - having identified some exciting flowering time mutants in a Tnt1 insertion screen. We also welcome two summer students, Kelsey Picard and Wenn Han Bong. They are investigating responses to daylength and vernalisation in Medicago, respectively. Speaking of cool stuff – Mau Jaudal is graduating with her PhD on December 17, so congratulations to her.

The Lab 308 Christmas bash was held on December 9, once again a memorable occasion - more so for some than others. A pre-dinner party was held at Jared Fudge's place, then off to the Crown Mill restaurant for a tremendous dinner and musical chairs. Some thoughtful (read: hilarious) Secret Santa presents were abound, with Julian acting as the Santa. Manda celebrated her first Christmas with us and had a marvellous time. Importantly, no animal attacks were reported that night, meaning a fun night was enjoyed by all.

Jared Fudge

In the Wilbanks lab . . .

…the women come and go, assaying with Steady-Glo.

Well, not all of them. Eleni is the only one to go far, with plans to depart early next year for a post-doctoral position in Bremen, working on environmental chemistry. She submitted her thesis in July, just about three years and a month after starting (!) and just had her second paper accepted, this one in BBA. With a third manuscript under review, one more to write, and graduation this December, she is busy to the end.

Jess and Aimée have only gone as far as Nelson and Rarotonga, respectively, to walk upon a beach - no word on whether they dare to eat a peach. Jess has made sense of her SAXS data and Aimée is through with exams (forever, so she says) so the vacation is well earned.

Peter is staying put for the duration, so there will be time to murder some cyanobacteria and create Psb27 variants and a bewildering array of double mutants with other chaperones and components of PSII. Let me clarify: bewildering for the rest of us, not for Peter; he knows how they all lead to an overwhelming question.

Only one woman has come, Erica, joining to assist with the DnaK project over the summer. She has already purified two variants with Malcolm and is starting on the Steady-Glo assays with Sam. Sorting out our luciferase assay has been just one milestone passed in Sam's sprint to the finish of his bench work. He looks on track for submission this summer, followed by departure for Europe and doctoral study in Copenhagen, involving more single molecule studies.

We are not solely an exporter of talent. Matthias Fellner has joined us from Austria, seemingly to replace Eleni on the CDO project. Also in CDO news, Richard and Egor have completed new structures and have manuscripts underway, working towards that hundredth revision and resolution of the last indecision. This is in quick follow-up to Egor's recent Biochemsitry paper, with the first characterization of the enzyme's iron binding.

Besides success as a co-author on the BBA paper, and introducing others to the lab, Malcolm has grown spectacular crystals of MIF, which give diffraction off the edge of the image plate in the downstairs X-ray suite and yielded electron density maps with gorgeous density for the isothiocyanate inhibitor. Now if we can only make the HRC as excited about the result as we are, we can relax and have time for toast and tea.

Krause Lab

We celebrated a fantastic 2011 this week with a delicious Christmas pot luck dinner and some good ol' board games.

Kurt recently squeezed in a trip to Taiwan. Here's an excerpt from his email to the lab last week:

> Dear All,
>
> Hello to you from Taipei, Taiwan. 24 million people in a country that is much smaller then NZ. It is real trip! Lots of fun, though very scary to drive on a tiny scooter holding onto my son in traffic with buses, taxis, cars and other scooters!! I just attended yesterday a dragon smoke offering in the hills around Taipei - first time for everything, right? - and a large butterfly descended from the sky during the dragon smoke offering to spend time on my arm and shoulder. Ebony and indigo wings, black body with white spots. I was told this was auspicious.
>
> Thinking about all of you everyday. Take care, Kurt

Kurt and his son, Jonathan in Taipei.

Kurt cleaned up at the Krause lab ten-pin bowling competition in September, introducing us all to the concept of a "Turkey", or three strikes bowled consecutively. The origin of this dates back to before the turn of the 20th century; during Thanksgiving or Christmas week, the proprietor would present a live turkey to people who scored three consecutive strikes [Wikipedia]. Unfortunately/fortunately none of us had any spare turkeys to present to Kurt.

Sadly we have had to farewell our visiting fellow José Garcia-Bustos. It has been a pleasure to have him with us these past months and we have learned a lot from him. We had some farewell drinks for him at the Staff Club last week.

Food and Christmas cheer at Michele and Kurt's house.

Listening to some of James's wisdom at José's farewell.

In other news, Emma, Sylvia and Kurt have had a paper on the structure of alanine racemase from S. aureus accepted into Acta Crystallographica D.

Ashley, Victoria and Hugh, the fourth-year students, have had their exam results back, and they all "did awesome". They're scattering across the country for Christmas with their respective families, and happily will all be coming back for another year at Club Krause.

Helen and Sylvia have both had early December holidays, Helen enjoying the sunshine in her beautiful garden, and Sylvia on a tiki tour round Wellington and the South Island. Thankfully Sylvia survived a gold panning sandfly massacre and has returned to the department to continue learning how to use the Biacore.

Miriam has returned to work, part time for now, and is learning how to juggle two kids, many sleepless nights and some frozen glowworms.

Rob is diligently purifying A3G, making good progress, and has promised Kurt some crystals really soon (!).

Merry Christmas and a Happy New Year!

The Tate Lab

The Tate lab wishes everyone a very merry Christmas! We had a lovely breakfast party to celebrate the festive season. Warren struggled to realise he was actually Mother Theresa and secret Santa delighted us with his special trash sack, fun and games! This summer we have welcomed in to our lab Abbey Burgess (2nd year student) who is learning the ancient art of ribosomology. Gary Morris will graduate as Masters with distinction this coming week and will be leaving us for a well deserved holiday. He plans to do a PhD overseas but that lucky lab is yet to be chosen. Simon McKensie-Nickson has secured a PhD position in Melbourne and by the time you are reading this he plans to have his Masters thesis finished and be in Wellington enjoying a break. Gary and Simon have been a joy to work with and will be missed in the group; we wish them both a happy and successful future. Another huge loss to the lab will be Dr Lucia Schoderbock from Austria who has been working in the group as an ARF on a fixed term contract. She has contributed hugely to the Memory project in the 6 months she has worked with us with her incredible skills, great ideas, and fantastic personality. We will miss you Luci. The Tate lab also supported Warren's choir group fund-raiser with a visit to the Fortune Theatre: A short cut to happiness, an hilarious play by Roger Hall, depicting the tale of a Russian Lady trying to make a life in New Zealand as a music teacher but unable to get a visa due to her lack of perfect English. Struggling to survive she is a dance teacher, finds cleaning jobs and eventually love...ahhhh.

Cancer Genetics Lab

The cancer genetics lab is slowly but surely on the rise again with the addition of two newbies. Myself (Jackie) and Briar are new summer students working under Anita. Briar is looking at immune responses in breast cancer under oestrogen deprivation before fleeing to medical school next year. I will be working on characterising methylation patterns upstream of the oestrogen receptor and being the newest addition I was involuntarily given the pleasure of writing this caption. All going well I will be staying on next year for my Masters project (tbc). Parry has also acquired a summer student. Jo, who is already doing her Masters in the cancer genetics lab, has been given a reprieve from the stressful student life to spend 10 weeks working with Augustine on a commercial project for HPV.

On another note, after years of anticipation, Sujatha is very excited as she has been given the go ahead to write up her thesis on 'genomic and transcriptomic association studies in colorectal cancer'. All in all everyone is looking forward to a relaxing break with relatives and in-laws. From everyone in the Cancer genetic lab, hope everyone has a merry Christmas and happy New Year.

The Dearden Lab

This final quarter has gone by with a whiz and a bang – The brilliant Elizabeth Duncan was super successful in obtaining her Marsden and will be a fully fledged Research Fellow with her name on her office door and everything. Big ups for being so awesome.

The National Research Centre for Growth and Development (NRCGD) annual symposium was held in Dunedin this year, organized by Liz and Peter, and the whole thing went off amazingly well – Rosannah took out second place in the student poster competition. The conference dinner was held at the Savoy and was both delicious and hilarious – a savage night had by all. The Executive Board of the NRCGD took the opportunity to visit and had a tour of the lab, our beautiful research space had been given a savage cleaning and both equipment and scientists were sparkling for the event.

The Genetics Otago annual symposium was also held this quarter at the Mecure, with brilliant plenary speakers (including Coral Warr from Monash University and our own Stephen Robertson). Our MSc and youngest 2 PhD students presented their work, and all did a lovely job. This was, as always, a great symposium and really highlights the breadth of genetics research both across the campus and within this department!

Our two oldest PhD students have embarked on the epic thesis-writing journey this quarter, with much swearing and consumption of chocolate for inspiration. Tread carefully, very very carefully!

Lab Day O' Fun this year (to celebrate Hons students finishing up, the end of a fantastic academic year, the onset of bee season and just general awesomeness) was held at the Dunedin ice rink where a savage curing competition played out. Several of the group were inducted into the bums-on-ice club, with Megan inducting herself twice, and her chin once. Lunch at Starfish followed and good times were had, as usual.

Cris came second in the National Grappling competition, so if you need a lab enforcer, drop us a line. In other news Megan got an iPhone and (arguably more importantly) Bee season is a go (go gadget adrenalin shot! – hopefully not).

That is all, what up with you, homes?

The curling teams! Note that the contrary to appearances Team Peter did NOT savage Team Sarah, rather Abi took some creative license with the score-card just prior to the photo being taken and the ever observant astute photographer (Liz) did not notice. (Actual score was 7 vs 3 to Team Sarah).

Merriman Lab

Once upon a time, not so very long ago, was a group of gout researchers trying to learn all there is to know.
The lab workers and students got along famously and the boss was a man who gave out compliments shamelessly.
All of the mothers were content with their brood, with no-one expecting or in such a mood.
But the lab was still growing at a steady rate, attracting students from every state.
Humaira came from across the sea, eager to start on her PhD.
And three of the students were happily engaged, all planning weddings in summer for a change.
Write-Ups for others had been a great headache, but all were finished and ready to graduate.
The rest of the lab was ticking along, when suddenly an evil wind blew so strong.
Most people it passed with just a slight niggle, adding a bit of frustration, anger or evil giggle.
But this wind affected the boss so profoundly that the lab was no longer a place to work soundly.
For weeks this wind blew and conditions got worse as the bosses demands grew, things started to get terse.
He ranted and raved all through the day, he demanded new results. "I want answers!" He would say.
And all those poor workers and students would reply, "We're sorry, we're trying, SNPMax has crashed, we don't know why."
This of course sent the boss crazy "Calculate it by hand then, don't be so lazy!"
The lab members were all at the end of their tether, but while the evil wind blew things wouldn't get better.
Even exotic trips to Rarotonga, Paris and The Bay couldn't keep the bosses evil away.
Until one day with Christmas growing nearer, something magical happened that made things all a bit clearer.
The answer of course was in front of them you see, the evil wind was coming from the A/C!
The lab members were horrified, they knew how to stop him, but to fix it some poor soul would have to cross him.
"I'll do it," said Tanya, the brave technician, I'll save us all from this horrible villain.
Quietly she snuck away from her desk, hidden behind eppendorfs and pipettes.
She made her way right to the wall, when out stormed the boss nostrils flaring and all!
"What do you think you're doing out of your seat? When did I say you could get to your feet?"
Tanya, legs trembling looked the boss in the eye, and boldly told him a barefaced lie.
"I just came over to make the A/C colder, I thought it might keep everyone awake for longer"
"Ah!" Said the boss, "what a great idea, carry on lets watch them all shiver with despair"
And with that Tanya pushed the button on the A/C, as the evil wind stopped everyone shouted with glee.
The workers set about with elation covering the lab in Christmas decorations.
Then they all had a brilliant party, full of families and children and laughter a plenty.
The boss was sorry for his evil ways, and wished everyone the best for their Christmas holidays.
And off they all went with smiles on their faces, to visit their family and friends in all kinds of places.
Happiness of course reigned forever more, and never again were lab conditions so poor.

Merry Christmas from the Merriman Lab!
The events depicted in this story are based on actual events. Some aspects have been altered for dramatic purposes.

Christmas Party photos