# Biochemistry News

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

editor: Bronwyn Carlisle

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**In This Issue**



## View from the Corner

Welcome to the last Biochemistry Newsletter of 2010. The holiday season is now fully here and to me the year has gone by quite quickly. As we finish out the year it's a good time to reflect on the last several months. In many respects it has been a banner year for Biochemistry and we have much for which to be thankful. The Department has been busy and productive as we carry out our missions of teaching, research and service. We are looking ahead to our future as we search for new staff. Teaching and grant income has been good this year, and we are playing key roles in a number of initiatives. Of these I would particularly like to mention New Zealand Genomics Ltd and the exciting approval of a PC3 facility for Microbiology.

A number of our staff deserve special mention for the awards they have received. Catherine Day received the Life Technologies Award at the NZSBMB meeting this year and Iain Lamont the equivalent honour from NZMS. Tony Zaharic received for the third time the OUSA Best Teacher award. Peter Dearden took home the Best Use of Humour Award in the same competition. Of course nothing can top the special moment this year when Warren received the Rutherford and the entire Department collectively cheered. There were strong achievements in the Marsden and HRC competitions but in particular I would like to mention the new Fast Start won by Martin Hohmann-Marriott and the Hercus Fellowship won by our erstwhile colleague Anita Dunbar. It's exciting to be in a Department that has such a strong group of scientists and teachers and I am pleased to warmly congratulate them on a job well-done.

There was some sadness this year in the Department as we sent Kevin and Mary off to retirement. We are grateful for their years of service and in my view this service underpins our success just as much as any award but their work was done in a quiet and often unheralded way. We look forward to their keeping us fully posted on all retirement-type activities.

Outside of the University the year was eventful as a major earthquake struck Christchurch with remarkable force. Later we learned about a new organization called Wikileaks that showed us that secrets today are never quite secret anymore. Who could have imagined that for weeks this year we would follow steady progress to reach a brave group of Chilean miners trapped deep underground, or that this event would be followed so quickly by an incomprehensible tragedy involving our own minors at Pike River. As a relative newcomer, I was struck by the strong sense of community in New Zealand and how the nation watched and mourned these events as one.

cont'd over …

For me, I am close to finishing one year as HOD and am very grateful for the opportunity to serve. During this year I have learned a lot, and I appreciate fully the heavy lifting done by John and Warren in their stint, as well as their personal help offered during this year. I appreciate my Exec for their sage advice and support. I appreciate Frances and Teena along with the entire front office staff without which the Department could not function.

When we get started again next year we will be welcoming a new PVC Health Sciences and shortly thereafter we will await the announcement of our new VC. It is hard to imagine a new person in that position, but I am sure an outstanding choice will be made that will surprise and please us. It has been a hectic year and I am looking forward to spending some time with my family and finally finishing that model of the Titanic with my son Nick that I gave him over two years ago!

Happy holidays to everyone.

## Recent Publications

As found by literature search, please let me know if I've missed your paper out.

**David J Young, Christina D Edgar, Jennifer Murphy, Johannes Fredebohm, Elizabeth S Poole, Warren P Tate.**

*RNA* (New York, NY) (2010) vol. 16 (6) pp. 1146-55

Bioinformatic, structural, and functional analyses support release factor-like MTRF1 as a protein able to decode nonstandard stop codons beginning with adenine in vertebrate mitochondria.

Vertebrate mitochondria use stop codons UAA and UAG decoded by the release factor (RF) MTRF1L and two reassigned arginine codons, AGA and AGG. A second highly conserved RF-like factor, MTRF1, which evolved from a gene duplication of an ancestral mitochondrial RF1 and not a RF2, is a good candidate for recognizing the nonstandard codons. MTRF1 differs from other RFs by having insertions in the two external loops important for stop codon recognition (tip of helix alpha5 and recognition loop) and by having key substitutions that are involved in stop codon interactions in eubacterial RF/ribosome structures. These changes may allow recognition of the larger purine base in the first position of AGA/G and, uniquely for RFs, only of G at position 2. In contrast, residues that support A and G recognition in the third position in RF1 are conserved as would be required for recognition of AGA and AGG. Since an assay with vertebrate mitochondrial ribosomes has not been established, we modified *Escherichia coli* RF1 at the helix alpha5 and recognition loop regions to mimic MTRF1. There was loss of peptidyl-tRNA hydrolysis activity with standard stop codons beginning with U (e.g., UAG), but a gain of activity with codons beginning with A (AAG in particular). A lower level of activity with AGA could be enhanced by solvent modification. These observations imply that MTRF1 has the characteristics to recognize A as the first base of a stop codon as would be required to decode the nonstandard codons AGA and AGG. -

**Gemma C Dickson, Russell T M Poulter, Elizabeth W Maas, P Keith Probert, Jules A Kieser.**

*Forensic science international* (2010) pp.

Marine bacterial succession as a potential indicator of postmortem submersion interval.

The process of decomposition of bodies in the marine environment is poorly understood and almost nothing is currently known about the microorganisms involved. This study aimed to investigate the microbes involved in decomposition in the sea and to evaluate the potential use of marine bacterial succession for postmortem submersion interval (PMSI) estimation, for which there is currently no reliable method. Partial pig remains were completely submerged during autumn and winter and were regularly sampled to document marine bacterial colonisation and the changes in community composition over time. Five stages of decomposition were recognised, some of which exhibited characters specific for partial carrion. Marine bacteria rapidly colonised the submerged remains in a successional manner. Seasonal differences were observed for the rate of decomposition and also for several groups of colonising bacteria. Marine bacteria specific for particular PMSIs were identified. This study provides an insight into the involvement of saprophytic marine bacteria in the decomposition of mammalian remains in the sea and is the first to explore the use of marine bacterial colonisation and succession as a novel tool for PMSI estimation. We propose that with further study, marine bacterial succession will prove useful for determination of the length of time a body may have been immersed in a marine environment. -

**David J Young, Christina D Edgar, Elizabeth S Poole, Warren P Tate.**

*RNA* (New York, NY) (2010) vol. 16 (8) pp. 1623-33

The codon specificity of eubacterial release factors is determined by the sequence and size of the recognition loop.

The two codon-specific eubacterial release factors (RF1: UAA/UAG and RF2: UAA/UGA) have specific tripeptide motifs (PXT/SPF) within an exposed recognition loop shown in recent structures to interact with stop codons during protein synthesis termination. The motifs have been inferred to be critical for codon specificity, but this study shows that they are insufficient to determine specificity alone. Swapping the motifs or the entire loop between factors resulted in a loss of codon recognition rather than a switch of codon specificity. From a study of chimeric eubacterial RF1/RF2 recognition loops and an atypical shorter variant in *Caenorhabditis elegans* mitochondrial RF1 that lacks the classical tripeptide motif PXT, key determinants throughout the whole loop have been defined. It reveals that more than one configuration of the recognition loop based on specific sequence and size can achieve the same desired codon specificity. This study has provided unexpected insight into why a combination of the two factors is necessary in eubacteria to exclude recognition of UGG as stop.

**Rachel J Brace, Brie Sorrenson, Dmitri Sviridov, Sally P A McCormick.**

*Journal of lipid research* (2010) vol. 51 (11) pp. 3370-6

A gel-based method for purification of apolipoprotein A-I from small volumes of plasma.

We present here a gel-based method for rapid purification of apolipoprotein A-I (apoA-I) from small volumes of human plasma. After isolation of high density lipoprotein from plasma, the apoA-I protein was separated by electrophoresis and the apoA-I band excised from the gel. The apoA-I was then eluted from the gel strip, concentrated, and delipidated ready for use. The structure and function of the gel-purified apoA-I protein was compared against apoA-I purified by the traditional size-exclusion chromatography method. The α-helical content of the gel-purified apoA-I as determined by circular dichroism was similar to chromatography-purified apoA-I. The functional activity of gel-purified apoA-I, as determined by cholesterol efflux assays in primary human fibroblasts and RAW264.7 macrophages, was also comparable with chromatography-purified apoA-I. This method is a valid alternative for apoA-I purification with some advantages over traditional chromatography purification including a much reduced plasma volume requirement, less time and cost, and a higher percentage protein recovery. The method is particularly suitable for applications requiring the purification of apoA-I from multiple human or animal samples of interest.

**M Legge, L M Jones, B J McLeod.**

*Comparative biochemistry and physiology* Part B, Biochemistry & molecular biology (2010)

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

The aim of this study was to investigate the energy substrate requirements of the common brushtailed possum (Trichosurus vulpecula) using intravenous tolerance tests for glucose, alanine, and propionate in five adult male and female animals under standardized conditions. Significant differences ($p<0.01$) were observed for fasting blood glucose values between males (6.3±0.16mmolL(-1)) and females (4.8±0.13mmolL(-1)), and males had a significantly ($p<0.001$) increased response to glucose. All animals returned to fasting glucose levels within 120min after the glucose challenge. No significant change in blood glucose levels was observed for either the alanine or propionate tolerance tests ($p>0.05$). However, following propionate administration, there was a highly significant ($p<0.001$) decrease in blood lactate concentrations over 120min. There was no evidence of ketone formation using β-hydroxybutyrate as a biomarker during any of the tests, indicating that there was no significant switch to lipolysis. In conclusion, the study provides new information on energy substrate utilization in this species and has identified that a gluconeogenic response normally identified in other species is not apparent in the common brushtailed possum.

**L.M McCowan, R.A North, E.M Kho, M.A Black, E.HY Chan, G.A Dekker, L Poston, R.S Taylor, C.T Roberts.**

*Obesity* (2010)

Paternal Contribution to Small for Gestational Age Babies: A Multicenter Prospective Study.

**T.X Pedersen, S.P McCormick, S Tsimikas, S Bro, L.B Nielsen.**

*Journal of lipid research* (2010) vol. 51 (10) pp. 2967-2975

Lipoprotein(a) accelerates atherosclerosis in uremic mice.

**Sharleen M Rae-Whitcombe, Darnell Kennedy, Matt Voyles, Mary P Thompson.**

*Biochemical and biophysical research communications* (2010) vol. 402 (4) pp. 767-72

Regulation of the promoter region of the human adiponutrin/PNPLA3 gene by glucose and insulin.

The adiponutrin/PNPLA3 gene is highly expressed in adipose tissue and liver. Its expression is down-regulated by fasting and rapidly induced by refeeding a high carbohydrate diet. We aimed to determine whether the promoter region of adiponutrin is regulated by glucose and insulin. Endogenous adiponutrin mRNA was increased in mouse 3T3-L1 and human SGBS adipocytes and in human HepG2 cells cultured in 25mM glucose compared to absence of glucose. A 3100bp 5'-upstream region of the human adiponutrin gene was cloned into a luciferase reporter plasmid and used in transient transfection studies. Promoter activity was up-regulated by 25mM glucose, 4.7-fold in HepG2 cells and 2-fold in CHO cells. The effect was shown in CHO cells to be concentration dependent and to depend on glucose metabolism as a non-metabolisable analogue was without effect. In CHO cells constitutively expressing human insulin receptor (CHO-IR), there was a concentration dependent increase of promoter activity by insulin in the presence of glucose. Cotransfection with an expression plasmid for upstream stimulatory factor 2 (USF2), increased promoter activity 1.6-fold in CHO-IR cells. The combined effect of insulin and USF2 (2.3-fold) was greater than the individual effects. Cotransfection of carbohydrate-response element binding protein did not elicit any induction of promoter activity. These results point to potential mechanisms for the observed in vivo nutritional regulation of adiponutrin expression and its up-regulation in fatty liver and by obesity.

**R.K Weersma, J.B.A Crusius, R.L Roberts, B.P.C Koeleman, R Palomino-Morales, S Wolfkamp, J.E Hollis-Moffatt, E.A.M Festen, S Meisneris, R Heijmans, C.L Noble, R.B Gearry, M.L Barclay, M Gómez-Garcia, M.A Lopez-Nevot, A Nieto, L Rodrigo, T.R.D.J Radstake, A.A Van Bodegraven, C Wijmenga, T.R Merriman, P.C.F Stokkers, A.S Peãa, J Martín, B.Z Alizadeh.**

*Inflammatory Bowel Diseases* (2010) vol. 16 (12) pp. 2080-2089

Association of FcgR2a, but not FcgR3a, with inflammatory bowel diseases across three Caucasian populations.

**Pingsheng Tian, Michael Legge.**

*Cryobiology* (2010) vol. 61 (3) pp. 357-9

Cryosolvent interaction with cellular actin using 3T3-LI cells as a model system.

Previous immunolocalisation studies using intact cells have identified modification of the cytoskeleton by cryoprotectants. In the present study we have used a proteomics approach to directly resolve the interactive effects of 3T3-LI cells exposed to two cryoprotectants, dimethyl sulphoxide (Me(2)SO) and 1,2-propanediol (PROH) in 5,10, 20 and 50(v/v) percent solutions, respectively. Two-dimensional protein electrophoresis and Western blot analysis of the cell extracts identified a range of immunoreactive actin fragments with varying molecular weights and isoelectric points at all cryoprotectant concentrations. The addition of either 10mM l-cysteine or reduced glutathione to the cells prior to cryprotectant exposure modified the actin fragmentation. In this preliminary report, we have provided direct evidence of actin fragmentation when exposed to cryoprotectants and have demonstrated that the use of redox agents can modify the cryprotectant action.

**Megan J Wilson, Benjamin H McKelvey, Susan van der Heide, Peter K Dearden.**

*Development genes and evolution* (2010) vol. 220 (7-8) pp. 179-90

Notch signaling does not regulate segmentation in the honeybee, *Apis mellifera*.

Notch signaling has been implicated in the segmentation of vertebrates but is not involved in segmentation in *Drosophila*. Recent evidence, however, implies that Notch signaling regulates segmentation in some Arthropods, including an insect, and that Notch signaling regulated segmentation in the common ancestor of Vertebrates and Arthropods. Notch signaling regulates clock-like formation of segments in both groups, a phenomenon not seen in *Drosophila*. We present evidence that Notch signaling components are expressed in a pattern implying a role in segmentation in honeybees, where the expression of genes involved in segmentation are modulated in a temporal way. Despite this, pharmacological investigation and RNA interference experiments indicate that Notch signaling does not regulate segmentation in honeybees, but instead regulates patterning within segments after segmentation itself has occurred. Notch signaling thus does not regulate segmentation in holometabolous insects, even when segments appear to form in anterior-posterior sequence.

**E Siakkou, S.M Wilbanks, G.N.L Jameson.**

*Analytical biochemistry* (2010) vol. 405 (1) pp. 127-131

Simplified cysteine dioxygenase activity assay allows simultaneous quantitation of both substrate and product.

**Rebecca L Roberts, Richard B Gearry, Murray L Barclay.**

*Pharmacogenomics* (2010) vol. 11 (11) pp. 1505-8

Allopurinol-thiopurine combination therapy in inflammatory bowel disease: are there genetic clues to this puzzle?.

**L.A Simms, J.D Doecke, R.L Roberts, E.V Fowler, Z.Z Zhao, M.A McGuckin, N Huang, N.K Hayward, P.M Webb, D.C Whiteman, J.A Cavanaugh, R McCallum, T.H.J Florin, M.L Barclay, R.B Gearry, T.R Merriman, G.W Montgomery, G.L Radford-Smith.**

*American Journal of Gastroenterology* (2010) vol. 105 (10) pp. 2209-2217

KCNN4 gene variant is associated with ileal Crohn's disease in the Australian and New Zealand population.

# Book review

This newsletter sees the first of what I hope will be a series of book reviews contributed by readers. Thanks to Sigurd for starting the ball rolling.

### *Plus ça change*

Following a tragic coal mine explosion, government wants science to provide a technological safeguard. The Royal Society promotes science as crucial to the nation's economic ability to compete internationally. Popular debate is animated about the creation of "Frankenstein" life forms. The year is 1815. As glimpsed in the lively stories gathered by Richard Holmes in *The Age of Wonder* the types of challenges facing scientists and scientific institutions have scarcely changed. "Fire damp" explosions in Yorkshire coal mines inspired Humphry Davy to a frenzied set of experiments identifying methane and inventing the safety lamp which allowed a flame to burn without explosion in methane-contaminated mines. The Royal Society was in transition from a gentlemen's club (certainly no lady members) to a professional society. After disappointing early sales, Mary Shelley's "Frankenstein" was adapted for the stage and fuelled the already lively debate on vitalism and the ethics of attempts to create life forms unknown in nature. Sound familiar? Holmes's book explores the origins of some of the institutions and controversies with which we still work.

The narrative is book-ended by two astronomical milestones: the 1769 transit of Venus and the 1840 de-commissioning of William Herschel's forty foot telescope. At its core are the stories of two presidents of the Royal Society, Sir Joseph Banks (president 1778-1827) and Sir Humphry Davy (1820-7), and some of their protégés. This provides an institutional focus, but with a human face for the emergence of science as a profession. This approach is less strong on explaining the technical basis of experimental advances which accompanied the rise of the professional scientist. The term "scientist" was coined at the end of the period (by William Whewell at the newly 1834) and the story of its introduction rounds off the final chapter. The book itself describes how the need for term arose and how that need fostered institutions which still direct our professional lives.

One of the strengths of *The Age of Wonder* is the vivid personal details; it opens with Banks in Tahiti, an enthusiastic participant in activities which gave lively double meaning to the name of the Captain Cook's Fort Venus. Part bon vivant, part natural historian, part diplomat, Banks exemplifies the gentleman scientist of the passing generation. His independent means allow him to remain president of Royal Society for almost five decades as he helps usher in the age of big science and professional scientists. Two chapters are devoted to musician-turned-astronomer William Herschel, including his quest for means to build ever larger telescopes. He obtains them by royal patronage but, not for the last time in the history of science, overspends the grant and has to beg more funds to finish the project. The book concludes with the upright Michael Faraday in the ascendant – depicted as a driven, morally irreproachable and socially dull scientist.

The intellectual advances complement the personal and institutional history. Jenny Uglow's *The Lunar Men,* describing the circle of Erasmus Darwin and Josiah Wedgewood in Manchester, left me with the impression that, barring the difficulty about the age of the earth, the intellectual foundations for *The Origin of Species* had been laid mare than a generation before Charles Darwin embarked on The Beagle. *The Age of Wonder* illustrates that much happened in the

intervening decades. William and Caroline Herschel are looking deep into space to chart new nebulae and comets, and at the same time are realising that the immense size of the universe implies deep time. In 1806 William Herschel writes of the "two million years" that light has travelled to reach his telescopes, declaring the immense age of the universe decades before Lyell's geology provided Charles Darwin the time needed for the mills of natural selection to grind out biological evolution. These decades also saw the discovery of the elements sodium, potassium and iodine as well as methane and other gases, the planet Uranus and infrared light. Europeans mapped the interior of Africa and surface of the moon. The galvanic battery was invented and electricity shown to have biological as well as purely physical manifestations. Holmes creates an engaging account of scientists coming to grips with the size, complexity and grandeur of the universe, and recalls their accomplishments in an age easy to dismiss as transitional between giants such as Newton and Darwin.

*The Age of Wonder* was published by Pantheon and is available in paperback at the University Book Store.

## Good bye from Judy Broom

As most people know, I am leaving Dunedin at the end of the year, and moving to Auckland. Thanks all of you for being such good colleagues over the years. I've been in the Department a long time (I'm not telling how long!) in various capacities. It's been a busy year and December will be a busy month – you'll see me trekking to the skip a lot as I clean out loads of stuff. It's amazing what you accumulate.

I wish you all the very best, and hope some of you will get in touch if you are up in Auckland. I'm moving to the School of Biological Sciences, continuing my work on algal biodiversity and systematics. Look me up if you are visiting.

Judy Broom

Lab 316

### Reminder:

Judy's farewell morning tea will be on Tuesday 21st December, at 10.30, in the Reading Room. Not on Thursday 16th as originally planned.

# Lab News

## The Krause Lab

(profuse apologies from the editor for having omitted their article from the last newsletter)

There have been quite a few comings and goings in the Krause Lab in the past few months. We are very lucky to have Becky Laurie sharing her cloning expertise with us for four months. Sadly we said farewell to Yang Li, who is off to find a PhD position in the UK or USA. His departure left the Y-chromosome count in the lab at an all-time low, although the situation has been temporarily improved with the arrival of Joshua O'Sullivan as a summer student. Gabby Watson has also joined our ranks over summer, and Helen is continuing her research with us for this time as well. Steffi Wachner, an undergraduate from Heidelberg University joined us for a brief 2-week stint, learning some protein expression and purification with Sylvia.

In other recent news, congratulations to Helen for doing so well with her honours degree results. Miriam announced her and Nick's latest project, a sibling for Max, due early March. And finally, Emma, Sylvia and Kurt had a successful but exhausting trip to the Australian Synchrotron in November, collecting vast quantities of data, which we are still sorting through.


*Yang Li's Farewell Tea complete with Mallow Puffs and toxigenic E. coli plush toy.*


*Sylvia and Emma check out some of Melbourne's hottest nightlife.*

## Cancer Genetics

Lots of happy news from the Cancer lab this month. Parry has successfully won an HRC-A* Grant to identify the molecular bases of drug resistance in ovarian cancer and has also secured a Lottery Health grant to identify genetic predictors of capecitabine resistance in colorectal cancers. Luckily Tanis's parents will be reminded who she is during their visit this Christmas before this next project keeps her here to do more mad mountain biking events!

Smiling faces are growing in numbers in 326.We owe a belated welcome to Augustine Chen who has joined us to work on a commercial project to develop a new test for HPV. We're also joined by 2 summer students: Otago 3rd year Bryony Telford who will be trying to understand the tumor specificity observed in HDGC, and Canberra graduate Peng Zhang who is looking into the DNA repair mechanisms in HDGC.

Sujatha has just returned after a very wet month in India catching up with friends and family but has yet to share the photos! Donghui is looking forward to seeing family over Christmas too. Fishing trips, exploring and relaxing with family seem to be the main summer plans!

## Christmas news from the Brown lab

Ambarish has joined us from India, after several years working as a bioinformatician at the National University of Singapore. He begins a PhD working on integrating the tools developed in Brown lab for the Galaxy browser.

Andrew Sarman rejoins the lab to look at candidate post-transcriptionally regulated breast cancer genes. Sherief will contribute to this project over summer. Augustine has moved up in the world to work with Parry Guilford.

Stewart says the IRE is a very cool element and we love it at the Brown lab. It has Christmas written all over it. I guess AGU in the apical loop must mean Happy Christmas in nucleotide speak. Stewart is working on some new models for this element with Paul Gardiner from the RFam at Sanger (Hinxton). We have some interesting putatives to chase up so the race is going to be on to get to those after the model is published. Stewart has also been seen in a lab coat, just to prove that there is carbon based life outside the world of silicon.

Joshua is developing an integrated work flow for motif discovery in a range of localized mRNAs, as well as some online tools to assist data analysis.

Sylvia is digging up potentially interesting structured elements in 3,Äô UTRs of transcription factors. Things will happen automatically right over during Christmas and some results will magically show up right after New Year. All will contribute to making up some sort of biological pathway.

## The Day Lab

With the Christmas holiday approaching, lab 223 has been quite busy lately. Although you can hear a lot of humdrum noise from our FPLC machines (even in the weekends!), our situation is far from grim.

The arrival of new members especially livens up the atmosphere. First, there's Yoshio who seemed, at first, a bit puzzled by our prolific use of paper towels, acrylamide and PBS. He quickly adjusted and now we can't spend a day without his useful tips and unmistakeably jolly laughs! (In your face, Santa!). There's also Puja. Having recently celebrated her wedding anniversary, Puja bravely tackled some of the most annoying cloning jobs that most of us would be more than happy to avoid.

Talking about challenging cloning jobs, Chu has recently nailed the "snipligate" technique (basically, you snip and ligate DNA all at the same time! It's awesome!). Together with Fran, Chu has also been passing some of our collective knowledge to our summer students, Imogen and Josh, who happily and enthusiastically worked through numerous protein preps.

Sarah also stayed for a few weeks after finishing her honours project to tidy up some lose ends and play around with our light scattering machine which has been maintained brilliantly by the one and only Bodhi "The Bodacious" (Woop! Woop!). Michelle's been a legend in keeping everything clean and tidy. Honestly, we can't live without her!

In the mean time, Rhesa is perplexed by the fact that "White Christmas" is the biggest selling Christmas song of all time ("White Christmas" is overrated. It should be "Snoopy's Christmas"!). After an exhilaratingly busy phase, Catherine is now having a relatively-not-so-hectic period, just in time to prepare for a warm holiday under the sun.

Basically, we are all looking forward to the holidays to spend some quality time with relatives, brilliantly cooked roast meals, some sweet … sweet bakings ("Bang it in the oven! Rock and roll! Happy times!" says Jamie Oliver), good wine and plenty of sunshine! Have a nice holiday from lab 223. Don't drink and drive. Oh … and eat your greens!

## Dearden Lab News.

The Dearden lab has had a brilliant couple of months, Drs Megan Wilson and Liz Duncan were each awarded UORGs for next year, our Honours students wrote-up with much success and very little stress – (not at all acceptable, really; where has all the fear gone?). Rosannah and Megan Leask have attended "Bee Fest" (a meeting of NZ bee researchers) in Auckland to talk about their brilliant work with the super-insect, Sarah is going on an Intensive Writing Retreat in Long Bay, north of Auckland and our two Masters students (Abi and Meaghan – yes we have three Megans!) are back in the lab to settle in to the real work – no more time consuming papers getting in the way of experiments.

To celebrate the end of semester and say goodbye to the Honours students, the entire lab bundled into a van in the middle of November to road trip & picnic at Elephant Rocks followed by fossil hunting in Duntroon We even saw some sunshine and had an absolutely brilliant day! What a way to celebrate the end of the academic year.

Happy holidays everyone!

## Lab 216 news.

The New Zealand Microbiological Society and New Zealand Society for Biochemistry and Structural Biology Annual Joint Meeting (NZMS/NZBMB) in Auckland was a good conference and our lab was well represented. Becky Edgar, who completed her BSc (Hons) in the lab last year, won the NZBMB Student Speaker award; Leo Germoni won the best poster prize for the NZMS; and Iain gave his NZMS oration.

As people know, Andrea has had to deal with very serious health issues. She is on the mend however and looking forward to being back in the lab in early 2011.

The lab honours students this year, Emma and Howard, successfully completed their fourth year projects in the lab, in genetics and biochemistry respectively, as well as contributing a lot to the lab environment. All the best for the future!

Katy has started her summer project in the lab studying the outer membrane proteins of various *Pseudomonas aeruginosa* clinical isolates.

Lois has been working hard as usual and has been helping our new summer student, Katy, with her project.

Xin left us, after almost 2 years as a research assistant, at the start of November to join her partner in the USA. Her contribution to the lab was much appreciated!

## McCormick Lab

It's been another busy year in the McCormick lab this year, although unlike most previous years, we have no new babies to report. Recently we welcomed 3 summer students : 2 new students Hannah and Sijing, plus the return of a relative old-timer (Greg). 2010 was also a busy year travel-wise, with conference and lab visits to Whistler/Honolulu (Rachel and Brie), Kyoto/Germany (Nina), Sydney (Sally/Anne), Melbourne (Sally) and Queenstown (Sally/Greg). These visits have provided some great new contributions to the lab tacky fridge magnet collection which is a compulsory part of any conference trip.

The next few months will see some big changes in the lab. First up is Rachel's wedding on December 18th, after which she will be heading to Adelaide after 5 years in the Department. Greg will also be leaving in February to start a PhD in Sydney with a former student of Mary Thompson. There is a rumour that it may with the former student of Mary, who attended clown school, although this could not be confirmed at time of going to print.

## Ledgerwood Lab

The Ledgerwood lab has grown with the addition of two new summer students. Eiren Sweetman (who will be an honours student in 2011) is working alongside Tracy investigating the species-specific role of cytochrome *c* in *Xenopus* and Zebrafish. Joanne Guest (who completed a BSc in Biochemistry this year) has been working alongside Gill on peroxiredoxins. We are also expected a visiting PhD student, Yasmine from the Institut Cochin, Paris in December.

Lab members and partners meet at the Dunedin ice rink for a curling match for this years Christmas function. After a slow start, and very few stones crossing the hog line, the competitive nature came out in Dan Garama and Liz's husband Andrew who became the 'curling enforcers' knocking out Gill, Moira and her husband Mike's stones going on to tie 5 all. The other teams were made up of Liz, Fabienne and Gills husband Peter and the opposition, Tracy, Eiren and Jo with a final score of 3-2. No curling match would be complete with out a couple of falls on the ice; this award went to Moira and Eiren.

New people to the lab are not the only new additions. Moira and Gill have been working very hard through the year to make 5 new cytochrome *c* variants, bringing the total to 9! Many people who use the 2$^{nd}$ floor cold room may have notice their pink masterpieces dialysing in 5 L buckets.

Since the last update Carolyn has been working on top-secret lab stuff (more to be revealed in the next newsletter) and has been enjoying the sunshine on her new deck.

Liz is away in Akaroa attending the free radical conference for the week, but will be back in time for our summer students to give their first lab meeting presentation.
Tracy has been working with a synchrotron goal in sight depleting the aforementioned cytochrome *c* being expressed. She was also awarded a 1st equal prize for her poster at the Division of Health Sciences Research Forum 'Pathways from Discovery to Delivery'. In August she travelled home to New Plymouth as a guest judge in the Taranaki Science fair.
The Ledgerwood lab would like to wish Mary Thompson a very happy and relaxing retirement and to everyone else, a very merry Christmas, Ho Ho Ho.


*The curlers (from left to right) Fabienne, Mike, Moira, Gill, Liz, Andrew, Eiren, Tracy, Dan and Jo.*

## From the Marshall lab

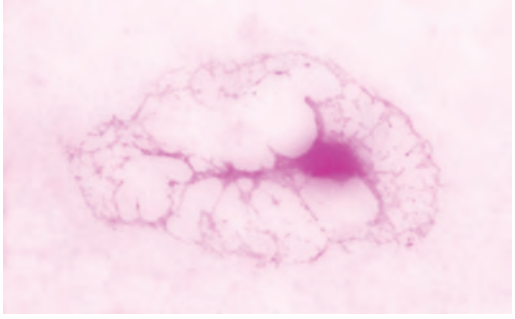
Everything is going well from here. Most of the same as last time except for the addition of two wee summer students. Calum Johnson and Jodi Wall have recently been welcomed into the family and are working on projects assisting James and Melanie respectively. We are looking forward to the holiday with many of us traveling abroad for christmas (or whatever indians celebrate at this time in Abhishek's case). We wish everyone a happy holiday and look forward to more exciting science in the following new year.

## NDD lab news

The Neural Development and Disease Lab has almost doubled its numbers, and gained their second ever male this summer. Sam from the prep room has joined us to learn about cloning, as well as teaching the girls about diversity. Nicole and Eleanor are doing summer studentships in the lead up to their Honours year in 2011. They are both working on the genetics of Autism.

Hollie is working hard to finish her bench work in preparation for writing her Master's thesis. She has developed a particular knack of making art from neural cultures (as illustrated). Erin is planning her big European OE for when her contract finishes. Katie is basking in the glory of some nifty cloning plus an impressive showing of disease pathology in her cell culture model of Batten Disease. Kate has been making a lot of viruses in preparation for the next round of in vivo gene therapy for Batten Disease in sheep, before leaving us at the end of the year (we will miss you K8!). Next year Kate will be working with Reagan Jarvis in the Surgery Department. Here's hoping Reagan will survive the experience! Shar is on holiday and will be back sometime in the New Year.Steph has been very busy with staff and students among her numerous collaborations, and is also getting ready to submit a paper with Kate on Batten Disease.

NDD alumni Sarah and Lorie are both working Research Assistants in Melbourne and loving it. Sarah,Äôs job has been confirmed for 2011. Marten is somewhere in the Pacific and has recently had a third child; a pretty cute son called Lukas.



*Is Hollie growing neurons from brains, or brains from neurons?*

## Trust (but verify) in the Wilbanks Lab

Our title alludes to the aphorism favoured by Ronald Reagan, who claimed it was translated from the Russian Доверяй, но проверяй. Egor, our local Russian, has not allowed himself to be misled recently, but other lab members have spent some time separating fact from fiction.

Peter has sorted out the 3′ and 5′ of PCR primers designed by others. After plenty of analysis both *in vitro* and *in silico* and some serious re-design, he has appropriate amplification and his clones.

Malcolm has been unable to detect any pattern in the labelling scheme of the clones he was sent for expression of tau protein, except that there were the same numbers of clones as labels, and that none were correctly labelled. Bonus question – given nine clones and random labelling, what are the chances *none* were correctly labelled?

Aimée was lied to by her new lab mates about the contents of our – 80 °C freezer – not one, but two of the strains she pulled out of storage already had the antibiotic resistance with which Sigurd had asked her to transform. Ask her about how this sets up a teachable moment for the lesson to trust no one and do all the controls.

Jess's new expression clones have not exactly misled her, they are simply holding out, so she is seeking solace in assays of protein from native sources.

Samuel may have been misled by his traveling companion, who steered him to South Korea for a no tension holiday. On the plus side, he might pick up a tip or two for negotiating with Aimée for sovereignty over "his" bench.

Sigurd has misled Jodi about only one or two of their seaweed samples; the rest really are red algae and have yielded various amounts of gorgeous, day-glo phycoerythrin.

Richard may have been too trusting of initial Mössbauer spectra, but is cranking out the new samples needed to verify the result. Eleni has verified that cysteine dioxygenase does indeed go faster as the assay progresses, just in time to present her results at the free radical meeting in Akaroa.

## Tate Lab

A long long time ago a young Warren Tate… [insert life story here]. Ok so I am neither brave enough, nor know enough about the illustrious history behind Warren Tate to even attempt this "life story" task. We hear many snippets in the lab from time to time (broken centrifuges, Head of Department stories etc). I will gladly collect these all together for a biography on the man in question for the next issue. For now however, huge congratulations are in order for the remarkable scientific achievements recently honored by the Rutherford medal. It has been an exciting time for the Tate Lab since this news came to light, and we will be buzzing (sorry for stealing what could be a good Dearden lab pun…) for many months to come!

*Spot the anomaly: This piece of Photoshop above is almost unrecognizable, can you spot the odd person out? No prizes to the winner, I just think it's rather clever!*

Although Warren has deserved the limelight for the past month, we have many other things to celebrate. In our last Tate Lab issue, we touched on the subject of the many comings and going we experience on a regular basis. This month we say a very sad farewell to one of the longest standing Tate Lab members, David Young. David has been with us since 2003, and although we are sad to see him go, we wish him the best of luck in his new Post-Doctoral position in the U.S. working with Alan Hinnebusch at NIH.

On a brighter note, we welcome our new summer students to the lab. Caillin Crowe-McAuliffe has decided he just couldn't get enough of our company and has signed on for more entertainment this summer. He is working with the human gene encoded PEG 10 protein. PEG 10 is cleaved up just like the polyprotein of a retrovirus and Caillin wants to know where the pieces end up in the cell. Liz Poole has made it through to the second round of the HRC reviews for this project. Clare Ogilvy has joined the group, activating the Chronic Fatigue Syndrome project, and is working to develop molecular markers that might be used in CFS diagnosis. Warren talked at his first international CFS scientific meeting just two weeks ago on the Gold Coast. Katie Appleyard is working with the pesky molecules involved in Alzheimer's, and finally Sarah Hunt has flown all the way from ANU to join us. Sarah is using a Schizophrenia rat model to see how immediate early genes respond to a new environment (namely Arc). Welcome and good luck to all of you (even if you are already half way through!).

And finally, introducing:

*Pun of the Month:* (This may yet become a monthly tradition if I have anything to do with it…which I do!). If you know Warren you know he's pretty handy with the odd pun. It's been a long time coming putting some of these into print, and I vividly remember I wasn't going to let this particular one slide…

The "Rubberford" pun: Warren has promised to make his Rutherford medal available for those needing a "lucky rubb" in the lab from time to time. In typical Warren style, it was proposed that if this were to happen we would then need to rename it the "rubberford" medal. Instant Classic.

Angriff auf das Getriebe

Wettlauf zwischen Mensch und Mikrobe: Der Molekularbiologe Daniel Wilson arbeitet an einer neuen Generation von Antibiotika

Von Martin Thurau

München – Die Boulevard-Medien sind längst auf die Skandal-Rhetorik eingeschwenkt, sie schreiben von „Killer-Keimen" und senden Beiträge über den „Tod aus dem Krankenhaus". Tatsächlich haben deutsche Kliniken derzeit ein massives Problem: Bald 1500 Menschen, so schätzen Deutschlands oberste Seuchenwächter vom Robert-Koch-Institut in Berlin, sterben hierzulande pro Jahr, weil sie sich im OP oder auf Station mit Erregern infizieren, gegen die gängige Antibiotika nichts mehr ausrichten können. Andere Schätzungen gehen sogar von noch viel höheren Fallzahlen aus. Und die meisten Experten sagen voraus, dass sich die Lage noch zuspitzen wird, denn die multiresistenten Mikroben rüsten weiter auf. „Es ist immer wieder dieselbe Geschichte", sagt Daniel Wilson, „auf dem Markt für Antibiotika tut sich nicht eben viel."

Eigentlich arbeitet Daniel Wilson an ganz anderen Fragen, nicht an solchen der Krankenhaushygiene stammelnd. Am Genzentrum der Universität München (LMU) erforscht er absolute Grundlagen der Biologie: Funktion und Steuerung der sogenannten Ribosomen, die in jeder biologischen Zelle arbeiten. Wie setzen diese Riesenmoleküle, Maschinen gleichsam, nach den Bauplänen der Erbgutes die Eiweiße zusammen? Von solchen Fragen aus der Grundlagenforschung allerdings ist der Weg zur Suche nach neuartigen Antibiotika gar nicht so weit. Schließlich legen viele dieser Wirkstoffe gerade die Eiweißsynthese der bakteriellen Erreger lahm. Und vielleicht kann die Medizin mit solchem Wissen im Wettlauf zwischen Mensch und Mikrobe wieder Boden gutmachen.

So hat Wilsons Team beispielsweise herausgefunden, wie Linezolid wirkt. Das ist nicht irgendein Bakterienmord, sondern die Substanz, die Mediziner als ihre derzeit schärfste Waffe betrachten. In Deutschland ist sie seit acht Jahren auf dem Markt und begründete damals eine neue Wirkstoffklasse. Die Substanz dockt im Zentrum der Maschine an, die in Bakterien etwas anders konstruiert ist als beim Menschen, und blockiert so die Montage der Eiweiße regelrecht.

Schlagkräftig ist Linezolid vor allem, weil es bislang nur sehr sparsam eingesetzt wird. Als Reserve-Antibiotikum bekommt man es nicht in der Apotheke auf Rezept, sondern nur nach strenger Indikation in Notfällen in der Klinik. Denn je breiter und unkontrollierter ein Antibiotikum eingesetzt wird, desto wahrscheinlicher ist es, dass widerstandsfähige Erreger auftauchen. Jeder Kontakt, der die Keimpopulation nicht ganz ausradiert, begünstigt resistente Erreger, die per Zufall durch kleine genetische Veränderungen entstehen. In einzelnen Fällen, so bestätigt das Robert-Koch-Institut, gab es sich schon Resistenzen gegen Linezolid. Dafür braucht es vermutlich nur eine kleine Änderung im räumlichen Aufbau des Ribosoms, fand Wilson heraus, die Substanz kann dann nicht mehr ins Getriebe der Maschine und verliert so ihre Wirkung. Vielleicht lassen sich aber auch Abkömmlinge von Linezolid effektiv einsetzen. Wer also lernt, wie die Ribosomen im Detail aufgebaut sind und wie sie arbeiten, findet womöglich Angriffspunkte für neuartige Antibiotika, erklärt der 39-jährige Wissenschaftler, der am Genzentrum eine eigenständige Nachwuchsgruppe leitet. Und wer erkennt, wie die Substanzen die Eiweißsynthese blockieren, erfährt auch etwas über die Mechanik der zellulären Maschinen.

Wilsons Arbeiten jedenfalls sind gefragt. Vor kurzem bekam er einen Nachwuchspreis der europäischen Organisation der Molekularbiologen (Embo), in der vergangenen Woche zeichnete ihn die Robert-Bosch-Stiftung in München mit einem Stipendium aus. Und ebenfalls letzte Woche veröffentlichte das hoch angesehene Fachblatt Nature Forschungsergebnisse, an denen Wilsons Team maßgeblich mitgearbeitet hat. Darin lieferten sie entscheidende Details, wie die Matrone für die Montage durch die Eiweißmaschine gefaltet wird.

Dafür allerdings müssen die Forscher ein ziemlich genaues Bild vom räumlichen Aufbau der Ribosomen haben, die dreiviertel aus großen Eiweißmolekülen bestehen. Wilsons Team unterwarf sie mit Methoden der sogenannten Röntgenkristallographie, wofür sie die Riesenmoleküle als reine Kristalle gewinnen müssen – keine ganz einfache Prozedur. Erst dann lassen sich die Moleküle analysieren und die Daten am Rechner zu dreidimensionalen Modellen zusammensetzen. Nicht umsonst haben in vergangenen Jahr drei Ribosomenforscher unter anderem für ihre Analysetechniken den Chemie-Nobelpreis bekommen. Einer der Laureaten wiederum hat lange am Max-Planck-Institut für Genetik in Berlin gearbeitet, an dem auch Wilson sechs Jahre war.

Als Wilson dort im Jahr 2000 anfing, hatte er einen Doktortitel der Otago-University in Dunedin (Neuseeland) in der Tasche und ein Jahr bei einer kleinen Pharmafirma in London hinter sich. Er hatte sich entschieden müssen, zwischen einem gut dotierten Job bei einem Pharmakonzern und einem Humboldt-Stipendium für das Max-Planck-Institut in Berlin. „Ich habe die Freiheit der Wissenschaft gewählt", sagt Wilson, „und das bis heute nicht bereut." Auch zuvor schon, während seiner Doktorarbeit, war er einige Zeit an dem Berliner Institut – es war eher eine Art Faszenfüller zwischen sportlichen Wettkämpfen, wie Wilson erzählt. Damals war der Nachwuchsforscher Mitglied der neuseeländischen Nationalmannschaft im Florettfechten. Seit 2007 nun ist der 38-Jährige am Genzentrum am Rande von Großhadern und leitet eine fünfköpfige Arbeitsgruppe.

Wilson kennt also beide Seiten – die Institute und die Firmen, nicht zuletzt auch von vielen Kongressen und aus der Zusammenarbeit mit kleineren Pharmaunternehmen. Die Großen, sagt Wilson, hätten sich weitgehend aus der Forschung an Antibiotika zurückgezogen. Frische Wirkstoffe lassen auf sich warten. Linezolid war die erste neuartige Substanz seit 34 Jahren. Die Entwicklung ist teuer und langwierig, viele Stoffe scheitern in den klinischen Studien, weil sie erhebliche Nebenwirkungen haben. Und kommt tatsächlich mal eine Substanz auf den Markt, wirft sie nicht genug ab. Die Mediziner dürfen sie nur sparsam einsetzen, damit sie möglichst lange wirksam bleibt, die Patienten müssen sie nur kurze Zeit einnehmen, nicht wie Betablocker oder Blutverdünner oft für den Rest des Lebens.

Wilson hofft auf eine Wiederbelebung der Antibiotikaforschung, andernfalls laufen die Mediziner Gefahr, den Wettlauf zu verlieren, denn die Resistenzen entwickeln sich rasant. Im Falle der Klinikkeime handelt es sich meist um ein weit verbreitetes Bakterium mit dem Namen Staphylococcus aureus, das Wundinfektionen, Lungenentzündungen und Blutvergiftungen auslösen kann. Vor zwanzig Jahren, rechnen Mikrobiologen vor, waren zwei Prozent der Erreger resistent. Heute sind es gut 20 Prozent.

Forscht im Genzentrum darum, wie Zellen nach der genetischen Information der DNS Eiweiße bauen: Daniel Wilson. Foto: Alexandra Schellingerr

*While Warren was getting photos (with molecular models draped around him) in various publications, his ex – student Daniel Wilson was not to be upstaged and coupled this with a paper in Nature (2nd December issue). Who's the master?!*