Paterson
Institute for Cancer Research

Paterson Institute
newsletter

The Newsletter for the Paterson Institute for Cancer Research

Drug Discovery: Full Speed Ahead

Issue 22 - July 2011

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The University of Manchester

CANCER RESEARCH UK

Senior Management Team's Introduction

The Senior Management Team (SMT) Caroline Dive, Iain Hagan and Pippa McNichol have enjoyed their first few months overseeing the Institute whilst the search for a new Institute director builds momentum. Thankfully our ex-director, Nic Jones is in the institute for a part of each week to provide valuable support and advice.

Iain and Caroline are meeting with each of the group leaders in turn to make sure they are up to date with the group's activities, news and needs. After bidding Jenny Varley farewell as Assistant Director for Research at the end of March, we have reorganised our management structure and we welcome Caroline Wilkinson as our new Scientific Operations Manager and Stuart Pepper as our new Head of Research Services. As we expected, both have taken to their new roles like ducks to water! As part of our reorganisation Margaret Lowe now ably oversees Estates and Central Services.

There has been a blaze of recruitment recently in the Drug Discovery Group. We welcome Dr Ian Waddell as the new Head of Biology, who joins us after 18 years as a Director of Discovery Medicine at AstraZeneca and will oversee 10 biologists working with a portfolio of early phase drug targets. In all there have been 23 new appointments in drug discovery, a healthy mix of chemists and biologists working side by side as drug targets are selected and validated, biological assays of drug action are developed and medicinal chemistry programmes driven forward. The team now has an impressive blend of experience gained from the academic and pharmaceutical industry/biotech sectors and already has a strong project portfolio. The HR team have certainly been kept very busy as the Drug Discovery Group has expanded and we thank them for doing a great job. Donald Ogilvie, Leader of Drug Discovery tells us about the excitement of this emerging Institute activity in this newsletter (Page 4).

We also welcome Dr Ged Brady as the new Deputy Group leader of CEP. Ged joins the Paterson after stepping down as the Research and Development lead for Epistem, the Manchester based biotech company set up by Prof Chris Potten after he left the Paterson. Ged brings significant expertise in the area of nucleic acid biomarkers and is already making his mark finding the interactions with Stuart Pepper and Crispin Miller's Bioinformatics Group a great place to start. Ged and Caroline previously worked together in the then School of Biological Sciences, at the University of Manchester, in the 1990s.
Student recruitment has also been very successful in the past three months, ten PhD projects were available, seven students have been accepted and a second round of interviews is about to take place. The quality of the applicants has been extremely high.

Congratulations to Georges Lacaud and Valerie Kouskoff who have recently been awarded a very substantial five-year grant from the Biotechnology and Biological Sciences Research Council (BBSRC) to study the establishment of the haematopoietic transcriptional programme which will further our understanding of leukaemogenesis.

We are pleased to announce that the Manchester Cancer Research Centre (MCRC) was successful with its bid to become a Clinical Centre as part of Cancer Research UK's national Stratified Medicines Initiative (SMI). We will be contributing high quality lung cancer biopsies over the coming two years, an effort coordinated by Jane Rogan, Fiona Blackhall and Noel Clarke through the MCRC Biobank.

With fundraising increasingly important in the current climate, it was great to see so many Paterson Institute staff involved in the highly successful *SHINE* walk held recently in Manchester. Almost 3,500 cancer sufferers and fundraisers lit up Manchester in a bid to collect £2 million for Cancer Research UK and set off on 26 or 13 mile routes around the city. Paterson staff were also participants in the annual Keswick to Barrow walk, and in *Relay for Life* events. A big thank-you is also due to the IT team who pulled out all the stops to get us back on track as quickly as possible when all three air conditioners failed this month.

Finally, we are all looking forward to the Paterson colloquium that will be held in Lancaster between the 26th and 28th September. We also hope to see Institute staff in numbers at the annual National Cancer Research Institute (NCRI) conference in Liverpool 6–9 November, where Nic Jones is the conference chairman.

Professor Iain Hagan, Professor Caroline Dive and Pippa McNichol
The Paterson's SMT

Proposals for new state-of-the-art cancer research building announced

The Manchester Cancer Research Centre (MCRC) has announced proposals for a new state-of-the-art research building, which will be crucial in helping the MCRC to develop and improve cancer treatment.

"The rapid expansion of high quality research at the MCRC has reached a point where future growth will be compromised by lack of physical space," said Professor Nic Jones Director of the MCRC and Chief Scientist of Cancer Research UK. "We undertake vital research to develop and improve cancer treatments and urgently need a new purpose-built building to expand and enhance this life-saving research."

The proposals are for a new research building and associated low-rise multistorey car park on The Christie site. The proposed site is directly opposite the main outpatients' entrance of The Christie on Wilmslow Road, between Cotton Lane and Kinnaird Road.

Professor Jones said: "Cancer research and treatment is evolving – we are entering an exciting era where the goal is a personalised approach to cancer therapy. In the future, each patient will be treated according to the specific characteristics of their tumour."

Reaching that point requires research partnerships between laboratory scientists and clinicians, between large academic institutions and major NHS hospitals, and between academia and industry. The MCRC is a partnership that was founded by The University of Manchester (incorporating the Paterson Institute for Cancer Research), The Christie and Cancer Research UK and, with the advent of the Manchester Academic Health Science Centre, has been expanded to include Central Manchester University Hospitals NHS Foundation Trust, Salford Royal NHS Foundation Trust, University Hospital of South Manchester NHS Foundation Trust, Manchester Mental Health and Social Care Trust and NHS Salford (Salford Primary Care Trust).

The MCRC takes an integrated approach to cancer research which is made possible by the immediate proximity on The Christie site in south Manchester of the Paterson Institute for Cancer Research, the Wolfson Molecular Imaging Centre and The Christie clinical trials unit in its brand new £35 million patient treatment centre. By strengthening the research base of the MCRC through provision of more and improved research facilities, the MCRC will be ideally placed to achieve progress through partnership and to deliver research that has life-changing potential for cancer patients.

"Cancer remains one of the major healthcare challenges worldwide, in the UK and here in the North West," said Professor Jones. "The MCRC's vision is the development of personalised cancer treatments, selected based on improved knowledge of each individual patient's disease characteristics, leading directly to better patient outcomes. The proposed new research building will ensure that the MCRC provides outstanding opportunities and a vibrant environment for researchers, clinicians and external partners to work collaboratively towards this vision through a single-site 'bench to bedside' approach."

Group Spotlight - Drug Discovery Centre

By Donald Ogilvie

The last time I contributed to the PICR newsletter was two years ago; I was then the sole member of the drug discovery team and the laboratory only existed on paper as a draft design. We have now been up and running for 18 months, the group has expanded to 21 (soon to be 23) and we are working on a portfolio of novel drug discovery projects.

When I started, the first task was to design and build the laboratory. A key feature of the design is to carry out synthetic chemistry and biological testing in the same space – something not normally seen in drug discovery facilities. The intermingling of those who design and make novel compounds and those who test them has created a real buzz in the team. Due to the sterling efforts of Steve Alcock and an excellent building contractor, the laboratory was completed on time (December 2009) and opened for wet work in January 2010.

While the construction project proceeded, Allan Jordan led the task of building the infrastructure. One of the advantages of starting with a blank canvas was that we were able, within the constraints of our budget, to design an ideal drug discovery workflow from compound design through synthesis, storage and dispensing to testing and data handling. The key feature at the heart of this workflow is the Echo acoustic dispenser which allows accurate handling of tiny (nanolitre) volumes of compound solutions. This means that we need only make small amounts (<10mg) of novel compounds and use them very efficiently (without any plastic pipette tips!). During the equipment procurement process Allan used his initiative, white van and legendary negotiating skills ("How about throwing that in for free?") to obtain ~£2.5m of equipment for £700k. In parallel we have built an informatics platform to support all of these activities. This includes a fully integrated Dotmatics chemo-informatics system, electronic notebooks and the Schrodinger molecular modelling suite. The latter allows virtual screening of a library of >3million compounds in silico, in multiple conformations, against protein structures. The set up phase of this library required considerable computer power at a number of sites including The Paterson and Frankfurt before being completed by Schrodinger in New York.

Recruitment has been a major activity and, with great help from the HR team and also, sadly, the shrinking pharmaceutical industry, we have managed to attract a highly talented team of medicinal, computational and synthetic chemists and molecular and cell biologists.

The most important thing is, of course, to generate a portfolio of novel cancer drug discovery projects, some of which will hopefully progress to clinical testing. With this in mind, we have developed target selection criteria which emphasise "line-of-sight" to the clinic. There are many hurdles to cross in drug discovery and most projects do not make it all the way so we need continually to replenish our portfolio with new target opportunities. In order to increase awareness of our programme in the MCRC, we have taken our Drug Discovery Roadshow presentation around group leaders and clinicians in the Paterson, The Christie and the wider University. Encouragingly we are now being approached by group leaders with ideas for drug discovery targets. We now have a portfolio of four projects in "hit-finding" phase - in which we seek to identify initial compounds which interfere selectively with target molecules. For two of these projects we have run high throughput screens (HTS) with the Cancer Research Technology Development Laboratory in London. In HTS, a simple biochemical assay is interfaced with a large (~100k) collection of diverse compounds in order to try and identify some hits. These hit molecules serve as starting points for medicinal chemists to optimise potency, selectivity and many other parameters to identify compounds for preclinical testing of a novel drug concept.

Underpinning these projects is a large network of collaborations within the Paterson and beyond. These range from key technologies (e.g. mass spectrometry with Martin Dawson in CEP) to novel, pre-publication target structures (e.g. Ivan Ahel) for virtual screening. The Paterson, and broader MCRC community, is proving to be a great location for doing drug discovery.

In the future we look forward to progressing our projects further in preclinical testing and ultimately, for some, into clinical trials.

Professor Nic Jones awarded Cancer Research UK Gibb Fellowship

Professor Nic Jones, Director of the Manchester Cancer Research Centre, has recently been awarded the Gibb Fellowship - a well-deserved accolade in recognition of his achievements in cancer research. This is the most senior honour granted by the Gibb Fund and recognises outstanding researchers who have given, and continue to give, considerable service to the wider area of cancer research.

There are currently four Gibb fellows: Professor Nic Jones; Professor Sir David Lane, Chief Scientist of A*STAR in Singapore; Professor Chris Marshall, Director of the CR-UK Programme on Tumour Cell Signalling Networks at the Institute of Cancer Research; and Professor Sir Bruce Ponder, Director of the CR-UK Cambridge Research Institute.

Walkers brave rain to take part in Keswick to Barrow

The Paterson team recently joined thousands of people, who braved pouring rain to set out on the Keswick to Barrow walk.

While the rest of South Cumbria lay asleep, around 2,000 were in the countryside of Keswick in the early hours limbering up to take part in the 40-mile fundraising trek. Those who were running the race set off at 5.30am, while the wave of remaining participants began to set off at 6am.The starting line was a sea of rain macs, hoods and ponchos as wet weather poured on to those taking part in the 45th annual event.

The first man in was Ian Symington, 31, from Manchester with a time of 4 hours 31 minutes and 52 seconds, while the first woman in was Kathleen Aubrey, completing the race in 5 hours 20 minutes and 20 seconds and coming fourth overall.

Due to the difficult conditions there was a record amount of withdrawals during the event. Congratulations to the team for completing the walk. The following people took part and have already raised over £2,000 for Cancer Research UK:

Chong Tan, James Lynch, James Dunphy, Xu Huang, Rebecca Foulger, Priti Kalra, Ayse Latif, Sara Cuvertino, Emily Holmes, Marija Maric, Monika Stefanska, William Harris, Filippo Ciceri, Avinash Patel, Suzanne Johnson, Shameem Fawdar.

Shine for Cancer Research UK

By Mandy Watson

A 26 mile night-time walk around Manchester might not seem like the ideal way to spend a bank holiday but that's exactly how my daughter, Ellie, and I spent ours. This is our SHINE story.

We began training in earnest at the beginning of February. However, my highly fashionable choice of footwear, walking sandals with socks (sometimes very brightly coloured!), proved just too embarrassing for Ellie so we agreed to train separately.

Of course the purpose of SHINE is to raise funds and awareness so we came up with a couple of fundraising ideas; cake sale at the Paterson and BBQ for friends and neighbours at home. Both events proved to be great successes, with many people getting involved in the cake sale, and around 40 people coming to the BBQ. My parents and in-laws raised further sponsorship by asking their friends and neighbours. In total we collected over £1000, brilliant! It is inspiring to experience such generosity and obvious appreciation of the work carried out by CR-UK.

Fund-raising over, training complete, the night of the walk finally arrived. My favourite bit has to be waiting at the start, nerves, adrenalin, bright lights, noise, a tremendous buzz. Although, it is pretty humbling to see all the heartbreaking "I am shining for" photos and dedications on walkers' backs. The first 16 miles passed without incident but then Ellie started to feel the effects of sporadic training; muscle pain and blisters. I was certainly glad to see some familiar faces when we reached the Paterson and for once, no toilet queue! The last few miles into the city centre were pretty difficult; Ellie was really struggling but nevertheless determined to finish. Finally, we turned a corner and Manchester Central was in sight. We crossed the finish line just before 6am, Ellie exhausted and blistered, mum emotional and proud. What a memorable experience; training, fund-raising and taking part. I can highly recommend it.

Snapshots of life at the Paterson

I arrived at the Paterson Institute in October 1992, moving from a University Lectureship at Leicester to lead the molecular aspects of the then Cancer Genetics Group. I vividly remember my first day. I walked into the lab to be shown my bench – which contained several buckets of water and bits of ceiling tile!!

My office was about as far away from the lab as it was possible to be, where the first floor ladies loo is now situated. I did wonder then whether someone was trying to send me a message!!! Those of you who were here while the TRF1 building works were being undertaken may recall my involvement in the Great Coffee Room Refurbishment Saga, with leaking ceilings, pink walls and persistent damp. A message was indeed being sent in that first day I think.

Life did settle down and after a period as head of Cancer Genetics under the then Director, David Harnden, I was appointed as a Section Head by his successor, Mike Dexter. Mercifully the "Section" organisation was short-lived as no-one was quite sure how it was supposed to work!

With the arrival of Nic Jones as Director the Institute went through a period of extensive and much-needed change, and in 2001 Nic asked me whether I would take on the role of Assistant Director. This meant winding down the Cancer Genetics Group and so my decision was not taken lightly, but I have no regrets even if occasionally I did miss the excitement of going into the lab and checking whether my experiments had worked (which of course they always did). As Assistant Director I had many and varied responsibilities including developing and overseeing all the Research Services, managing the Institute's equipment budget, trying to allocate space equitably, helping to co-ordinate space, equipment and often recruitment with newly-recruited Group Leaders, organising the annual Paterson colloquium and annual reports, maintaining publication and space databases, acting on the Education Committee and managing grants and access. This did mean that I had a good overview of what was going on, which hopefully benefitted Nic and the Institute.

I have seen enormous changes in the Institute over my time there. The quality of the science being conducted now is outstanding due to the rigorous recruitment processes from Group Leader through our Postgraduate Students to junior support staff. Many of the constraints on current activities will be alleviated with the completion of the new MCRC building across the road from the Paterson and I am advising on the design of the laboratories, which means that you will still see me around in the Institute for a while yet. I am quite jealous that I won't be around to allocate myself one of the nice new offices!

Away from the Institute I have a number of interests that I will now be able to indulge. We love travelling, and can spend more time visiting places on "the list". "The list" is rather long and as may of you will guess includes wild places with spectacular scenery and wildlife. This allows me to indulge another of my passions, photography, and I have already enrolled on a couple of workshops to expand my camera and processing skills. I also love reading, and am delighting in being able to spend decent amounts of time curled up with a good book and a cup of coffee (or a glass of wine depending on the time of day)! Many of you have asked me whether I miss work. Of course I do, but not enough to make me regret my decision.

Reflections

Gavin White

In my time at the Paterson I have worked with a number of different people and I like to think that I have tried to select their respective best qualities and apply them to my own working life, from the enthusiasm of Jim Heighway to the thoughtful planning of my first supervisor Charlie Ockey. In Jenny's case - she was an achiever – if she said we needed a BAC library or automated sequencing or something else she went out and got it. And as Jenny took on more Institute responsibility I feel this has been her hallmark, where ideas become plans and plans become realities. It must be good when the day comes to retire that you can say 'I did that'. My time working with Jenny was some of the best times and I wish her well.

Gail McGown and Mary Thorncroft

After a period of rumour and great anticipation Jenny arrived at the Institute and certainly did not disappoint. Her enthusiasm for her work attracted people to her and soon a new department was formed. She worked hard and played hard and expected no less from her staff. On the work side she wanted the best for all the members of her group, giving each one the opportunities to develop to their full potential. When she played we all played even if it meant dressing for the evening as fairies, Scooby Doo or even Margaret Thatcher on one of the notorious bar rallies that Jenny entered into with such gusto. When Jenny moved on to become Assistant Director it was a promotion well deserved. We were sorry that it meant the end of the Cancer Genetics but what a productive and enjoyable ten years we spent with Jenny.

Above: Some of the amazing pictures from Jenny's many travels across the globe.

Postdoc Informal Meetings (PIMs)

In February a new series of postdoc informal meetings (also known as PIMs) was started. These meetings are similar to the Thursday lunchtime postdoc seminars but are for postdocs only and the meetings are intended to be informal.

These meetings aim to give postdocs a chance to discuss their data in more detail and show both successful and failed experiments, clean and dirty blots, whatever you like really. You don't have to present a complete story but it's a chance to share ideas with other postdocs. If you're having any technical problems with experiments, you can discuss them at the meeting and hopefully there will be people there who have experience in this area and can help resolve these issues. PIMs are usually held every 4-6 weeks, with the format similar to the current postdoc talks, with 2 speakers per meeting, each having about 30 minutes each. It's not an official talk and the meetings are meant to encourage open discussion. If you are a postdoc and would like to present/attend these meetings but don't receive PIMs emails, please contact James Lynch (Leukaemia Biology) to be added to the postdoc mailing list.

Staff News

Ciara O'Brien, PhD student in the Breast Biology lab gave birth on 15th April to a baby boy; Ruaridh Finlay John Fairbairn, who weighed in at 8lb 10oz.

Dates for your Diary

Paterson Colloquium

26th -28th September 2011

The 2011 Paterson Colloquium will be held at Lancaster University's campus from 26th -28th September 2011.

The 5th International PhD Student Cancer Conference

The 5th International PhD Student Cancer Conference was hosted by the Beatson Institute for Cancer Research on the 15th-17th June.

The conference provides students with the opportunity to discuss their work with other students from leading European cancer research institutes. Students were able to present their work in a series of short talks that covered a range of subject areas including lymphoma and diagnosis, mouse models, and signal transduction. William Harris from the Leukaemia Biology group was selected to give a short talk in the mouse model session and spoke about his work on the inhibition of Lsd1 function abrogating AML leukaemia stem cell self renewal. Students also presented posters at the conference and Sara Cuvertino of Stem Cell Biology was awarded the runner up prize for her poster on the role of Sox7 in leukaemogenesis (as pictured). In addition to the student talks, there were two keynote speakers. Sir Tim Hunt gave an inspiring talk on his research dissecting cell cycle control using *Xenopus* as a model organism. Professor Gerard Evan followed by presenting his fascinating research exploring the possibility of targeting Myc as a treatment for cancer. Sessions were held with Group Leaders at the Beatson Institute in which they spoke about their own research interests along with explaining the qualities they look for in a post-doc. Wednesday evening provided everyone with the opportunity to show off their general knowledge in a Pub Quiz, while Thursday evening gave rise to a more energetic form of entertainment. Following a traditional Scottish meal that included haggis and cranachan, everyone took part in a ceilidh at the National Piping Centre in Glasgow. The Netherlands Cancer Institute will be hosting the 6th conference on the 6th-8th June 2012, and the event promises to be as informative and entertaining as this year's conference.

New Appointments

Head of Research Services – Stuart Pepper

As many readers will know I have been at PICR for over quarter of a century now, and for over a decade have been managing the Molecular Biology Core Facility. During this time I have been involved in developing services on a variety of equipment platforms and have interacted closely with other service units as well as developing a long standing collaborative relationship with Crispin Miller's group.

This is a role that I have always enjoyed immensely - to have the opportunity to support the research efforts of the Institute by providing robust scientific services is very satisfying. With my new role I now have the opportunity to contribute at a higher level and play a part in supporting the ongoing development of all scientific services on site.

How does it feel to make a step up like this? Well the good thing is that thanks to Jenny's tireless support and promotion of the service units I am stepping in to a situation where the scientific services already operate to a very high standard. Of course this is not just down to Jenny's work - I believe the Institute is lucky to have a group of service managers each of whom is a real expert in their field. Despite this there will be some challenges ahead - with the current economic situation funding is tight and it will take some very careful planning to keep all of our service units provided with necessary equipment. Given this challenge it is great to have Caroline Wilkinson to share the equipment purchase decisions with.

When the new building is ready we will see a further expansion of the amount of scientific activity on site, and the service units will need to be ready to support this larger number of scientists. Clearly this will present some challenges and maybe some difficult decisions, but rest assured that the focus of the service units will always be providing world class support for scientific the programs carried out at PICR.

Scientific Operations Manager – Caroline Wilkinson

The last decade has seen a significant amount change at the Paterson. Throughout this time, Jenny Varley has played a vital role in helping to bring about the necessary re-organisation and development of the institute and her contributions will be sorely missed.

Her departure has resulted in some re-structuring within the operations department, culminating in the new post of Scientific Operations Manager, which I began at the end of May. This role covers a number of Jenny's previous responsibilities including reviewing all grant applications involving institute resources as well as working with the senior management team to develop the institute operating plan, which annually secures core funding from CR-UK. Other tasks will include organising the colloquium, tenure reviews, post-doc seminars and annual report while equipment requests and the management of institute space will be jointly considered by me and Stuart Pepper, the new head of Research Services. An important requirement for this post is an understanding of research and operations right across the institute. Serving on the education committee for the last two years has provided a good starting point for me in this regard, and I will continue to be a member of the EC as well as sitting on the ethics committee, clonal sequencing group and the Biobank approval board.

Taking on this new role was a tough decision as it means leaving behind life in the lab. Working as an associate scientist for Nic Jones has been hugely enjoyable. Fortunately, I am not cutting ties with the bench completely and will continue to work in Cell Regulation one day a week for the foreseeable future. I am, however, looking forward to the challenges that this new position will throw at me as well as the opportunity to contribute to the continued success and development of the institute.

CEP Deputy – Ged Brady

Ged has recently joined Caroline Dive's group as CEP Deputy where he will work with the group to further develop and apply biomarkers which are aimed at benefiting clinical practise and patient outcome.

Previously Ged has spent over 30 years developing advanced molecular biological methods and using them to further the understanding of a variety of key biological areas including DNA replication control, cancer initiation and stem cell regulation. In the course of his scientific career he has carried out research in the Max Planck Institute for Molecular Biology (BERLIN), the German Cancer Research Centre (HEIDELBERG), the European Molecular Biology Laboratory (HEIDELBERG), the Ontario Cancer Institute (TORONTO) and has held positions of Lecturer and AstraZeneca Special Fellow at the University of Manchester. More recently, Ged joined Epistem (a spin out company from the PICR founded by Chris Potten and Cath Booth) shortly after its inception where he was responsible for setting up research and developing the underlying science for Epistem's Novel Therapies and Biomarker divisions. Of particular relevance to the scientific and commercial development of both the biomarker and therapeutics program at Epistem is his expertise in single cell gene analysis. While continuing to maintain collaborative links with Epistem, he will be working with the CEP team to continue and develop their internationally recognised excellence in biomarker development and delivery.

New Starters

Alexander Boakes
Senior Bioscientist, Drug Discovery

Ged Brady
Senior Staff Scientist, CEP

Samson Chinien
QA Auditor, CEP

Laura Cove-Smith
Clinical Fellow, CEP

Julia Draper
Postdoc, Stem Cell Biology

Roberta Fiume
Research Fellow, Inositide Laboratory

Nicola Hamilton
Bioscientist (SO2), Drug Discovery

Gemma Hopkins
Bioscientist, Drug Discovery

Amanda Lyons
Chemist (SO2), Drug Discovery

Alison McGonagle
Senior Chemist (SSO), Drug Discovery

Jessica Mitchell
SO2, BRU

Rosa Morra
Postdoc, DNA Damage

Rebecca Newton
Senior chemist, Drug Discovery

Radoslaw Polanski
Postdoc, CEP

Kate Smith (nee Clapham)
Senior chemist, Drug Discovery

Mailys Vergnolle
SSO, Cell Division

Bohdan Waszkowycz
Computational Chemist, Drug Discovery

Julie Watson
SO2, MBCF

Kuan Yoow Chan
Postdoc, Cell Division

Paterson Research Covered in Blood

Research by two groups at the Paterson Institute has recently yielded papers in the journal Blood. The first of these by the Stem Cell Biology and Stem Cell Haematopoiesis groups identifies a key step in haematopoiesis, whereas the second paper by the Children's Cancer group identifies factors involved in the metastatic spread of ALL to the CNS.

Identification and characterization of a novel transcriptional target of RUNX1/AML1 at the onset of haematopoietic development

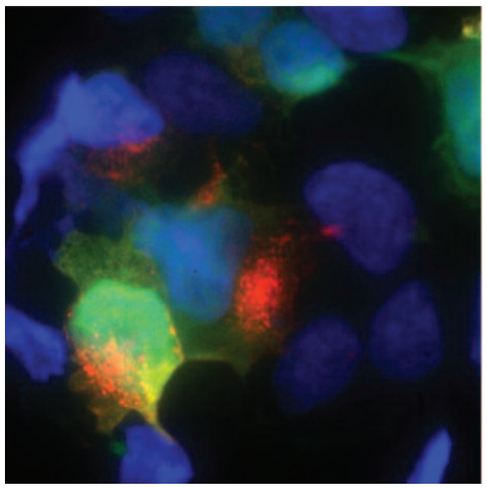
By Cristina Ferreras

AML1 (Acute Myeloid Leukaemia 1) encodes a transcription factor that regulates the expression of haematopoietic genes and alterations in the activity of the protein AML1/RUNX1 is a frequent initiating event leading to leukaemia. To better understand this it is important to define the downstream transcriptional targets of AML1/RUNX1 in normal haematopoietic differentiation.

In this work, we took advantage of the absolute requirement of AML1/RUNX1 for the development of the blood system to identify new transcriptional targets of AML1/RUNX1. We compared gene expression between AML1/RUNX1$^{+/-}$ and AML1/RUNX1$^{-/-}$ cells at the stage where blood development is halted in the absence of AML1/RUNX1 activity. Several genes were found to be differentially expressed and one, AI467606, encodes a protein with no known function and with no homology to other proteins. We validated the difference in AI467606 expression and demonstrated the direct regulation of AI467606 expression by AML1/RUNX1. We further established that AI467606 is specifically expressed in the haematopoietic system from its establishment early in ontogeny to its maintenance throughout adult life. All haematopoietic cell lineages, except for mature erythrocytes, express AI467606. Taken together our findings indicate that AI467606 is a novel transcriptional target of RUNX1/AML1 at the onset of haematopoietic development that is widely expressed within the haematopoietic system.

This suggests that AI467606 expression might be affected by alteration of AML1/RUNX1 at the onset of leukaemia and that these changes could be implicated in the impairment of haematopoietic differentiation. To test this hypothesis we are currently evaluating whether AI467606 expression is altered in leukaemia cells and are further investigating the function of this intriguing novel protein in haematopoiesis.

Ref: Identification and characterization of a novel transcriptional target of RUNX1/AML1 at the onset of hematopoietic development. Cristina Ferreras, Christophe Lancrin, Michael Lie-A-Ling, Valerie Kouskoff, and Georges Lacaud. Blood 2011 blood-2010-06-294124; published ahead of print April 15, 2011, doi:10.1182/blood-2010-06-294124



Cells stained to show the localisation of AI467606 (RED), characterised in Ferreras et al. DNA is shown in BLUE

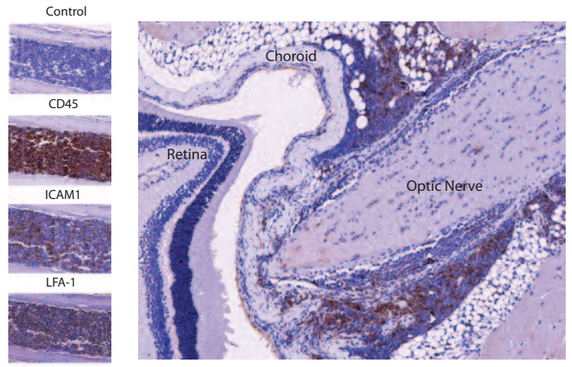
Clues to how ALL cells invade

By Darren Roberts

In a demonstration of the benefits of a research institute environment the Children's Cancer group recently led research involving the Immunology group, the Stem Cell and Leukemia Proteomics Laboratory, the Applied Computational Biology and Bioinformatics group and the Mass Spectrometry, Histology, Flow Cytometry and Advanced Imaging Services into the mechanism of ALL invasion into the CNS.

The work used a model of ALL to investigate how the disease invades the CNS, of particular interest during relapse when involvement goes from <2% of cases to >30% of cases. After extending their previous work to show that the protein AEP was involved in how ALL cells invade, the group went on to identify other proteins involved in the process by comparing the proteins found in the membrane of invasive cells with those of non-invasive cells. This identified both RAC2 and ICAM1 as proteins associated with the invasive nature of the cells and by manipulating levels of these proteins their role in invasion was confirmed. Finally by analysing cells from healthy donors and comparing them to those from ALL patients either before treatment or upon relapse they confirmed that a sub-population of cells expressed significantly higher levels of the proteins identified in their studies (RAC2, AEP, ICAM1) in the relapsed patients. This work could help identify therapies to prevent or treat relapse in patients with ALL.

Ref: RAC2, AEP, and ICAM1 expression are associated with CNS disease in a mouse model of pre-B childhood acute lymphoblastic leukemia. Mark Holland, Fernanda V Castro, Seema Alexander, Duncan Smith, Jizhong Liu, Michael Walker, Danny Bitton, Kate Mulryan, Garry Ashton, Morgan Blaylock, Steve Bagley, Yvonne Connolly, John Bridgeman, Crispin Miller, Shekhar Krishnan, Clare Dempsey, Ashish Masurekar, Peter Stern, Anthony Whetton, and Vaskar Saha. Blood 2011 blood-2010-09-307330; published ahead of print May 23, 2011, doi:10.1182/blood-2010-09-307330



Tumour cells invading bone marrow in the skull. Tumour cells are labelled brown in the ICAM1 and LFA-1 boxes.

Plain Speaking

Haematopoiesis
The process of producing new blood cells.

Ontogeny
Describes the origin and the development of an organism - for example: from the fertilized egg to mature form

Erythrocytes
Red blood cells

Metastasis
The process by which tumours spread from the original site to other sites in the body.

ALL
Acute lymphoblastic leukemia

CNS
Central nervous system – composed of the brain and spinal chord

Relapse
Reoccurrence of cancer after initial treatment has reduced the disease

In the spotlight with Steve Morgan, Security Coordinator and Receptionist

1. **What is your favourite part of the UK?**
   Without a doubt, the Lake District and in particular the village of Grasmere

2. **What is your favourite book?**
   The first book that I read was Jeffrey Archer's Kane and Abel and that gave me the reading bug. My all time favourite is Richard Llewellyn's How Green Was My Valley

3. **What is your favourite film?**
   It has to be John Wayne's The Quiet Man, but more than happy to watch anything by Tarantino

4. **If you had to change careers tomorrow, what would you do?**
   That's an easy question to answer! I'd be a professional singer, but at my X Factor audition they didn't see my true potential. Philistines!

5. **What is the most important lesson that you have learnt from life?**
   Treat everyone as you would like to be treated

6. **What three things would you save from a burning house?**
   The picture of my son and daughter, a shaving mug given to me by 'the King' Denis Law and my Swiss army knife

7. **What is your greatest fear?**
   Manchester City winning 20 league titles

8. **How would you like to be remembered?**
   As the life and soul of the party

9. **If you could change one thing in your past what would it be?**
   The Little sparrow said it all 'Non, je ne regrette rien'

10. **What would be a perfect meal?**
    Roast lamb, mint sauce, Yorkshire pud, roast potatoes, cauliflower, carrots and lots of thick gravy, and if a dessert is classed as part of the meal then let's finish with sticky toffee pudding and Cornish ice cream.

11. **What trait do you most deplore in others?**
    Arrogance and ignorance

12. **You've just won the lottery and have £5 million pounds to spend. What do you buy first?**
    A Chevrolet corvette zr1. 0-60 in 3.4 seconds!

13. **Which words or phrases do you most overuse?**
    'At the end of the day', 'mate' and 'love'

14. **What is your idea of perfect happiness?**
    Being with special people at special times in very special places

15. **What keeps you awake at night?**
    A bottle of 'Maccallan's' 15 year old malt whisky

16. **What question would you have like to be asked?**
    Steve! Would you like either a pay rise or an all expenses paid holiday to Mauritius?

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