



Paterson  
Institute for Cancer Research

# Paterson Institute

winter newsletter

## MANCHESTER HERALDS NEW ERA IN CANCER RESEARCH



*Pictured left to right:- Professor Mike Richards (Cancer Czar), Professor Alan Gilbert (President & Vice Chancellor, University of Manchester), Professor Joan Higgins (Chair, Christie NHS Trust), Professor Dame Nancy Rothwell (Vice President (Research), University of Manchester), Ms Caroline Shaw (Chief Executive, Christie NHS Trust), Dr Colin Sibley (Associate Dean, FMHS, University of Manchester), Professor Nic Jones (Director, Paterson Institute), Professor Alex Markham (Chief Executive, Cancer Research UK).*

### **A new cancer research centre is set to make Manchester a world leader in the exploration and treatment of the disease.**

The Manchester Cancer Research Centre (MCRC) will bring together scientists and researchers from The University of Manchester, the Paterson Institute for Cancer Research (PICR), the Christie Hospital and Cancer Research UK.

The new centre, which aims to double cancer research activity and significantly increase funding from £30 million to £60million per year, is being launched as the Department of Health's National Cancer Director Professor Mike Richards and Chief Executive of Cancer Research UK Professor Alex Markham visit the city today (11 November 2005).

*.....continues on back page*

**Paterson Institute for Cancer Research**

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I would like to take this opportunity to thank everyone in the Institute for all their efforts over the last year. The refurbishment of the north end of the building has been very disruptive and has created numerous difficulties at

times. However, the refurbishment was badly needed and it will be worth it when complete. There is an end in sight! So, a big thank-you to you all for your patience. I would also like to express my gratitude for the support and understanding that you have shown with respect to our transfer to the University of Manchester. It is a big step for us but one that will provide very exciting opportunities for the future.

We have set a number of goals for next year which will underpin our continuing development:

- Finalise the transfer to the University (expected date January, 1st 2006);
- Work with the University and the Christie Trust to develop the plans for the MCRC including new laboratory-based and clinical research facilities;

- Recruit 4-5 new group leaders (advert now out);
- Complete and occupy the north-end refurbishment;
- Further develop our student programme.

All of these goals are aimed at strengthening the research of the Institute and its reputation.

Finally, I would like to take this opportunity to wish you all a very Happy, Healthy & Prosperous Christmas and New Year and I look forward to a very rewarding and successful 2006!

Nic Jones

## stress in the workplace

### HR Department

In this month's newsletter we wanted to take the opportunity to provide information to you about stress within the workplace.

Many workers within the workplace suffer from stress and it has been defined by the Health and Safety Executive (HSE) as "the adverse reaction people have to excessive pressures or other types of demand placed on them".

In the near future the Institute will be introducing a Stress Policy with the Christie Hospital. This policy will outline our commitment to protecting the health, safety and welfare of our employees and it acknowledges the importance of identifying and reducing workplace stressors.

Whilst stress is not an illness in itself, it can contribute to problems with ill health. Some of the symptoms of a stress-related illness are:

#### • *Emotionally:*

Anxiety, anger, frustration, moodiness, irritability, loss of pleasure and interest, despair, depression and impaired sleep.

#### • *Physically:*

Physical effects may include a weakened immune system, raised blood pressure, tenseness, tiredness, appetite disturbance, nausea, headaches, light-headedness and the emergence or exacerbation of symptoms in any system in the body.

#### • *Mentally:*

Impairment of perception, concentration, memory, judgement, decisiveness, accuracy, motivation and creativity.

#### • *Interpersonally:*

Relationships are likely to be more difficult, both at work and elsewhere.

#### • *At work:*

Attendance can become either exces-

sive or extremely poor. Regular bouts of recurring illness can occur. Time-keeping can become erratic. Performance can be impaired and the levels of accidents rise.

If you would like to talk to someone in confidence about dealing with stress or any other issue, the Employee Assistance Programme (EAP) is available to all staff. The programme provides confidential, professional, free counselling to help staff overcome problems such as anxiety and depression. This service can be obtained by telephoning 0800 282 193 for an appointment. Its services are obtained through self-referral or in some circumstances, a manager may refer an individual if they feel it is affecting their work performance. For further information on the EAP programme please visit <http://info/page.asp?DEPT=17&PID=138>



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# Group Leader Spotlight

*structural cell biology*

Compartmentalisation of the eukaryote cell over the course of evolution has brought with it unique mechanisms for the control of multiple activities. The Nuclear Envelope confines replication and transcription to the nucleus and translation to the cytoplasm. Normal metabolism and growth are dependent on controlled molecular traffic across this barrier, mediated via the Nuclear Pore Complexes (NPC). Despite the involved molecular architecture of the pores themselves, as well as the nuclear membranes and the elaborate nuclear lamina on the inner aspect of the nuclear envelope, all of this structure is dismantled at mitosis in vertebrates to allow access to the chromosomes by the spindle apparatus, (termed 'open' mitosis). We are currently investigating NPC reassembly at mitosis and the subsequent NPC proliferation that occurs during interphase. In open mitosis, reassembly of the nucleo-cytoplasmic barrier is initiated as early as metaphase, starting with the association of a NPC precursor protein complex at the chromosome surface, leading to advanced NPC formation (prepores) ahead of NE membrane recruitment. When new NPCs insert into the pre-existing nuclear envelope during interphase, it is at sites of fusion between the inner and outer nuclear membranes. This mechanism is modeled in the *Xenopus* cell free nuclear formation system and the same mechanism occurs in lower eukaryotes which divide with a 'closed' mitosis. Thus it is likely that two distinct mechanisms exist for NPC assembly, with higher eukaryotes using both, whereas lower eukaryotes are restricted to one.

Sheona Drummond is continuing to investigate gp 210, one of only two membrane proteins in the NPC, and is also studying the roles of two recently identified tryptophan-arginine (WD) repeat proteins nup37 and nup43, which are members of the 107-160 Nucleoporin multiprotein complex. HeLa cells have been transfected for expression of Nup 37-EGFP, revealing that during interphase, nup37-EGFP is



left to right: Sheona Drummond, Helen Pickersgill, Sandra Rutherford, Terry Allen,  
Back Row: Steve Murray, Fiona Gardiner

present at the nuclear periphery as part of the NPC. At prophase, upon initiation of chromatin condensation and prior to full disassembly of the nuclear envelope, nup37, (together with the other components of the nup107/160 complex) is lost from the NE. During metaphase nup37-EGFP becomes clearly visible at kinetochores facing the cell poles. Ongoing work aims to determine the contribution of the nup107/160 complex to microtubule-kinetochore association and mitotic progression.

A new project has been started by Fiona Gardiner, who joined us earlier this year, to investigate the roles of condensin and cohesin in the formation and separation of chromatids. This study is part of the Euro DYNA programme together with several other European groups including Jan Michael Peters, Jan Ellenberg and Kim Nasmyth. Cohesin subunits form a huge ring structure which mediates sister chromatid cohesion by embracing DNA duplexes from each chromatid. At metaphase cohesion between sister chromatids is lost following the proteolytic cleavage of the hScc1 subunit of cohesin by the cysteine protease separase in response to passage of the cell through the spindle checkpoint. We are currently investigating the predicted ring structure formed by cohesion in situ using FESEM in combination with Immunogold labelling of specific cohesin subunits and have identified

cohesion at conserved structures associated with mitotic chromatin. Directly related to cohesin is the condensin protein complex. Condensin is involved in the condensation of replicated chromatin which leads to the resolution of chromosome arms. Direct visualisation of mitotic chromatin during condensation and de-condensation using Immuno-FESEM for specific condensin subunits should provide valuable data and insight into the mechanism of this complex. Our current data supports the model in which condensin is proposed to act like a molecular hinge, contacting two chromatin fibres in its open conformation and bringing them into close proximity upon closure.

Although the group has never been a service unit, we have always retained the 'missionary zeal' to spread the gospel of ultrastructure by collaboration with other groups where electron microscopy provides another spectrum of information. This function is performed by Sandra Rutherford and Steve Murray, on top of their group responsibilities, and currently encompasses studies into various mitotic spindle mutants in *S.pombe*, replication complexes and membrane fate in *S. cerevisiae* division mutants, cellular interactions between prostate tumour cells and endothelia, quantum dot visualization, apoptotic pathways and the ES/EB model of Haemopoietic differentiation.



## *Gemma Thornton*

I sat down to write this piece with some trepidation, as I wasn't quite sure where to begin. Four years ago I arrived at the Paterson Institute to begin my studies for my PhD. I was not entirely sure what to expect but was eager for the challenge. I began working on three different projects, all related to different aspects of research within the lab. As the work progressed, I concentrated on a single project studying the role of a previously uncharacterised protein in regulating pleiotropic drug sensitivity. Little did I know what a rollercoaster ride that choice would take me on!

However, I was extremely fortunate that I wasn't the only one on that rollercoast-

er. There were a number of people within the group who provided me with technical support and general encouragement when I wasn't sure from my results which direction to follow. Outside the group, I also found a community of people who were eager to share their expertise to help me further my goals.

Four years seems a long time, but has passed in what seems a blink of an eye. As I sit here and prepare for the final exam, I can look back and appreciate the direction the project took – despite the hairy moments when we discovered another group working on the same protein and about to publish, or the long days trying to get the perfect western blot with a membrane protein!

All I can say is thanks to all those who have taken this ride with me and taught me so much, and I hope I will find others like you to join me on the future journeys I will take in my career.



## student social

The new academic year meant that it was time for Becki, Kelly and Laura to hand the student representative baton on to some new volunteers. Hiroko, Claire and Helen have stepped up to the challenge so they'll be responsible for organising student social events and acting as a point of contact for Paterson students for the next year. We asked them to tell us a bit about themselves and also provide a report of their first event as reps; a trip to Belle Vue Dogs.

*I'm Hiroko Morohashi* and I'm in the 2nd year of my PhD in the Cell Cycle group (formerly known as Functional Genomics). The new reps are all a little crazy...come find us in the Red on Friday aftern--- er - evenings.

*Hi, I'm Claire Rooney*, and having been a rotation student last year, I have finally settled down in the Cell Signalling group. We had a great laugh at the dogs earlier on this year, and we're all looking forward to plenty more stu-

dent social activities, so we'll see you there!

*Hi I am Helen Spencer*, and in the second year of my PhD in Immunology. As for Hiroko's accusation of us being crazy, there is no evidence to support that theory. The three of us are very quiet individuals!!!! I'm sure you'll have found this out on the 8th of December – BAR RALLY!!!

### *Student Social*

To welcome the new PhD students, the three of us organised a night out at Bellevue Greyhound Stadium on the 11th November. For most of us it was our first time at the dogs...which meant the main criterion for choosing which dog to bet on was their names, 'Snog the Dog' being a popular choice! There were lots of cheers (and tears?) with some getting a little bit more carried away than others; not to point the finger at our Spanish post-docs! A great night was had by all and, amazingly, a few of us managed to come away with a little more money in our wallets (its called beginner's luck, Flor!)



left to right: Claire, Hiroko and Helen at the student outing they organised to Belle Vue Dogs on 11th November



**Congratulations to:**

**Laura Hollins** (PhD Student in Gene Therapy and Bioinformatics Groups) and Ryan Edwards who got married at Wolstanton Methodist Church, Newcastle-under-Lyme, Staffs on 1st October, followed by a reception at The Upper House, Barlaston, Stoke-on-Trent. Afterwards Laura and Ryan had a short stay in London where they saw Les Miserables before moving on to Iceland where they travelled around for two weeks!



**Pippa McNichol** (Associate Director - Administration) who was recently appointed to the Board of Rodney Housing Association, as a non-Executive Director. Rodney House is a Liverpool-based housing association working with people who are socially excluded.

**Good Luck to:**

Sumia Ali, Hui Jiang (both from Immunology - must be something in the water!) and Angeliki Malliri (Cell Signalling) who are all due to give birth soon. Happy nappy changing!!

**A Warm Welcome to:**

**Michelle O'Hara** who joined the Core Facility in August to provide extra support for the sequencing, genotyping and miniprep services.

**Pranee Quigley**, a chemistry graduate originally from Thailand, who will be joining Medical Oncology for six months at a junior level to be trained in the area of tissue culture and biochemistry.

**A Fond Farewell to Ken McGivern** who worked at the Paterson for over 5 years in Central Services and was, many would say, fortunate enough to discover a heart problem before it became too serious. As a result he underwent a quadruple heart bypass in April 2005 and after a long recuperation period and having given it lots of thought, Ken decided to retire from work. He is keeping very well and active, making the most of his time off! We would all like to wish him well for the future!

**COME ALONG TO THE  
PICR STAFF CHRISTMAS PARTY  
AT 4:00pm ON FRIDAY,  
DECEMBER 16th**

**IN THE  
HOLT LECTURE THEATRE**

**ALL WELCOME!**





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# Moving On

## **Caroline Chadwick**

On the 7th July 1975 a very fresh faced junior technician arrived at the Paterson Institute to start work in Lab 3, intending to stay for 6 months or so. Well that estimate of 6 months was a little bit out – 30 years or 10,950 days or 87,600 working hours later I am leaving to become the Director of Biomedical Services at Birmingham University. Why now? Well that's a good question - maybe it's because I am facing a big birthday in January and after the photos in reception for my 40th I thought I had better get out before the next milestone. In reality it's a fantastic opportunity for me, a big career move and a very exciting challenge, for starters I am going to have to learn to speak Brum (apologies to anyone from there!). At the moment I switch between really excited and really scared – the job is the exciting bit, living away from home for the first 18 months while Sarah completes her GCSE's and leaving behind so many good friends and everything that's familiar is the scary bit. One thing I definitely won't miss will be the ongoing TRF refurbishment – sorry Jenny.

The Institute has seen many changes since 1975 – 4 directors all with very different approaches from Laszlo with his soft suede shoes and pipe – what would Health and Safety say today to the Director walking through the Institute smoking a pipe? - to the present day with Nic and the formation of the MCRC. I am sure that the next few

years will be very exciting for everyone at the Paterson.

Looking back over the years I have very many fond memories of working here, some printable and some not.

### **What was my worst job?**

I started working in Lab 3 (all the Labs had numbers in those days) and I spent the first 2 years looking down a microscope counting cells – before all the snazzy computer assisted microscopes we have today in the advanced imaging facility it was all down to manpower or girl-power in my case. We sat at the microscope all day and counted and counted and counted. The number of silver grains per nucleus was without doubt the worst thing to count, over 150 and you lose the accuracy. One of the worst things for me was that my microscope was on the end of Chris Potten's desk so he knew every minute I wasn't sat there counting. After two years of this I was eventually allowed to do some lab work as well as the counting – never tell me your job is boring.

### **What was my worst moment?**

We had some fantastic Christmas parties and reviews in the old staff club – now the Kinnaird Road car park. My worst moment without any doubt was during a slide show at a Christmas review when a slide appeared on the screen of me topless on the beach – never trust a student in your lab not to find the holiday snaps you have kept hidden in your drawer when showing the rest (censored) to your friends. The

only good thing about the whole evening was that I didn't have to buy a drink all night!

### **What will I miss most?**

Without any doubt it will be the people, I have made some fantastic friends working here and the culture of the Paterson is so friendly and supportive. I will be very sad to leave but as my daughter said when I was trying to decide whether to accept the new job, "Mum you don't lose good friends you just gain more". OK so that tells you who is the mature one in our family.

So after nearly 90,000 working hours I am off into the unknown, taking many happy memories with me – and looking forward to those M6 traffic jams.



## competition winner



Congratulations to Julie Edwards (Cancer Studies) on winning the 'Spot the Ball' competition in the last issue (see picture left).

Although there were quite a few entries (with crosses in some very peculiar places!), Julie came the closest with her 'X' and won a bottle of wine.



In each issue of the Newsletter, we feature a member of staff who will take the 'Spotlight' and answer a list of questions that we have put together. The next lucky recipient of the poisoned chalice is Mick Brown.

***What is your favourite part of the UK?***

Actually it is my home town, Manchester. I enjoy the city life and the ease of everything on your doorstep, great pubs, clubs, restaurants etc

***What is the most important lesson that you have learnt from life?***

Snorting tequila is very bad, but not as bad as chilli vodka.....by any route!!!

***What is your favourite book?***

Colour of Magic, Terry Pratchett. Its just daft!

***What is your favourite film?***

Depends really on the day and mood I am in. Sunday afternoon/evening would be an old Cary Grant / James

Cagney film eg. To Catch a Thief/ the Bishops Wife or Yankee Doodle Dandy, but on a Friday or Saturday need humour or graphic violence, depending on what has happened during the week eg. Ferris Beuller's Day Off or Death Wish!

***If you had to change careers tomorrow, what would you do?***

Pub landlord. I get to laugh and joke, talk politics/sport/rubbish and tell stories all day (nothing new there) whilst having a pint at the same time! So no major career changes there then.

***What three things would you save from your burning house?***

Whiskey Collection, books and a chair. At least I will be able to sit down and relax with a drink.

***What is your greatest fear?***

Turning up at a Urology Clinic and being faced by one of my ex MD students (who will probably still be writing up!).

***How would you like to be remembered?***

Not bad for a Ginge!

***If you could change one thing in your past, what would it be?***

I would have loved the opportunity to study history as well as science subjects at school.

***What would be your perfect meal?***

This is a real tough one as my perfect meal varies with the mood I am in and there is such an array of fantastic tastes and sensations out there still to try. I suppose with winter coming on I would go for cream of winter vegetable soup with crusty wholemeal bread followed by game pie or haunch of veni-

son with seasonal vegetables followed by treacle toffee pudding with vanilla ice cream and custard.

***What trait do you most deplore in others?***

Passing the buck. If you make a mistake, admit it. Don't try and blame somebody else or ignore it. I also hate with an equal passion the current inconsiderate trend of parents taking their single fat child to school in a 4x4/SUV/ 20 seater people carrier! You supposedly live in the appropriate catchment area, walk to school. Its better for your kid, reduces the burden on the NHS due to obesity related illnesses, better for the environment and cuts my journey time in to work by half!

***If you had to spend £1,000,000 tomorrow, what would you do with the money?***

I would first return to the Four Seasons Restaurant in Manhattan for a meal washed down with a few bottles of Chateau Lafite Rothchild Pauillac 1986. I would then take a risk and visit the ancient world regions where civilisation began eg. Mesopotamia. Unfortunately this is not the most stable of regions, covering Syria, Iraq, Iran, Southern Turkey etc. so all the money would have to go on bodyguards, but a chance to see all the ancient wonders would be too good to miss.

***Which words or phrases do you most overuse?***

B\*\*\*\*\*s, not again!!!!!!!!!!!!

***What is your idea of perfect happiness?***

Being able to do what I want to do.

***What keeps you awake at night?***

What are those MDs up to now?

## items for the newsletter

If anyone would like to submit an article to the newsletter or has information for the 'Staff News' section, we would love to hear from you. Equally, if you have any feedback about the format of our newsletter or ideas for future issues, then we would really like to hear your views!



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# Photo Competition

## Jenny Varley

Once the coffee room had been refurbished we decided to run a Photo Contest, and to display the winning images around the walls of the coffee room. The response was excellent, and the quality very high. The eventual choice of winner was left to Anne Murtagh in Medical Illustrations, and to my embarrassment (as I had organised the contest) one of my photos was the winner. Runners up were Steve Royle, Adam Dangoor and Andy Sims.

I have been asked to say a little bit about the photo, and to do that I need to describe the area where it was taken. This summer we took a trip on a Russian Icebreaker to areas of the High Arctic, a trip that was quite indescribably awesome for its beauty, remoteness, weather, scenery, geology, wildlife, splendour and people. It is tragic to think that we are steadily destroying this wonderful place. We travelled up the centre of Ellesmere Island to Tanquary Fjord, and visited Chapman's Glacier where the photo

was taken. The weather was amazing and the sea completely calm, and once the ship had anchored this gave tremendous opportunities for a good reflection photo with a wide-angle lens. This cliff is around 1000 feet high, and shows some dramatic effects of glaciation, as well as impressive stratification. I have another

2,500 photos from the trip if anyone is interested.....

At some stage once the coffee room dries out, and is all repaired, we will be exhibiting all the short-listed photos, and we do plan to repeat the competition in a year or so.



## cover story continued

The University of Manchester's Board of Governors has now approved bringing the Paterson Institute into the University. Bringing the two organisations together will not only build on their internationally renowned strengths, it will also allow strategic development of their work to have an even greater impact on cancer research.

Researchers from the University's Faculty of Life Sciences and the Faculty of Medical and Human Sciences will also play major roles in the MCRC, but the hub of the Centre will be at the Paterson/Christie Hospital site in Withington, to help promote close interaction between those dedicated to basic research into the causes and progression of cancer, those involved in the translation of new knowledge into novel treatments and those who provide

state-of-the-art patient care.

The Centre will have a multi-disciplinary approach and research programmes will include existing work on breast cancer; paediatric cancer; cell proliferations, death and genome stability; experimental cancer therapeutics; and tumour microenvironment. New research programmes are likely to include other disease-focussed programmes; radiation related research; and chemical biology.

The MCRC's five-year plan also includes:

- The recruitment and development of at least ten world-class researchers across the whole spectrum of cancer research, from basic studies through to clinical work, to build on existing

strengths and also develop key new areas. There will also be leaders for 25-30 new research groups and the recruitment and development of young research leaders.

- A plan to increase funding from £30 million to £60 million per year to enable strategic investment in research infrastructure, such as new laboratories and clinical research facilities, and a major investment in the supporting technology (mass spectrometry, expression and SNP arrays, molecular imaging and bioinformatics).

- International "Centres of Excellence" in four or five areas of cancer research through the creation of multidisciplinary teams designed to enhance collaboration between clinical investigators and laboratory scientists.