Senior Management Team's Introduction

This issue starts with the wonderful news that Professor Richard Marais is to become the Paterson's new Director. We are delighted by his appointment as it will initiate an exciting new era in the development of the Paterson Institute.

Richard’s research focuses on signalling through the RAS/RAF pathway and the role that this plays in the development and progression of melanoma, the most deadly form of skin cancer. His work was pivotal in determining how mutated BRAF drives function by ubiquitylation.

We were fortunate that Richard was able to join the group leaders at their recent retreat. This was a great opportunity for them to see some of the world class research that is being carried out in Manchester and highlighted why it is so important to support the vital research which could make a significant difference to the 36,100 people diagnosed with cancer in the North West every year.

Speaking after the visit, Sajjad Karim MEP said:

“Each year, there are an estimated 2.45 million new cancer cases receive a large proportion of their funding from charitable sources, with very little funding coming from the European Union. Therefore as a Member of the European Parliament I will be pushing the European Commission for this to be increased in the future and for a greater availability of grant funding for scientists and researchers working in this important area.”

Manchester Team Picks Up Prestigious CR-UK Prize

The Cancer Research UK Translational Cancer Research Prize for 2011 has been awarded to the leaders of the Clinical Experimental Pharmacology team: Caroline Dive and Malcolm Ranson along with Fiona Blackhall, the lung cancer translational research lead within CEP and Andrew Hughes, who is the Head of Early Clinical Oncology Development at AstraZeneca as well as holding a Chair in Translational Medicine at the University of Manchester.

The team have had many successes in using biomarkers – substances that can be measured to determine several factors such as how well a patient is responding to a treatment – to enhance clinical trials. Their biomarker portfolio has been used in over 70 clinical trials since 2004.

Professor Dive said: “We’re honoured to receive the Cancer Research UK Translational Cancer Research Prize. Our collaborations have meant that we’ve been able to make advances that would have been impossible otherwise. Biomarkers have great potential in many areas, and we have championed their use in clinical trials because this can greatly enhance the impact of the trial – for example we are better able to monitor how well a patient is responding to treatment.”

Dr Harpal Kumar, Chief Executive of Cancer Research UK, said: “The team in Manchester fully deserves the recognition of the Cancer Research UK Translational Cancer Research Prize. They’re an excellent example of how team work is essential for translational research, bringing together different backgrounds and expertise to answer some of the biggest questions in cancer.”

The team have also contributed to the training of the next generation of pharmacology researchers through a clinical pharmacology fellowship scheme run by Caroline Dive, Malcolm Ranson and Andrew Hughes. The scheme provides training in ‘biomarker literacy’ through supervision in the pharmaceutical, laboratory and clinical setting.

Local MP’s Dons Lab Coat to Highlight Cancer Research Excellence

Mark Hunter MP, Sajjad Karim MEP and Tony Lloyd MP visited the Paterson recently to learn about the research taking place in the Institute. They met with Professor Caroline Dive to see some research in action and find out more about the future policy priorities for Cancer Research UK.

It was a great opportunity for them to see some of the world class research that is being carried out in Manchester and highlighted why it is so important to support the vital research which could make a significant difference to the 36,100 people diagnosed with cancer in the North West every year.

Speaking after the visit, Sajjad Karim MEP said:

“Each year, there are an estimated 2.45 million new cancer cases and 1.23 million deaths from cancer in the EU. The Paterson Institute and other cancer research centres in the UK currently receive a large proportion of their funding from charitable
New Students – September 2011

Danielle Potter, CEP
Hi, I’m Danielle and I am very excited to be joining the CEP team to study for my PhD. I have just graduated from the University of Manchester with a First in Molecular Biology. Science is a considerable career change for me having worked at Toni & Guy as a senior stylist for several years before returning to education. I am a local girl so know Manchester very well indeed. I love to travel with only South America and Antarctica left to visit. I look forward to meeting everyone.

Zoe Edwards, Signalling Networks in Cancer
In 2009 I graduated from the University of York with a BSc in Biochemistry. Since my degree I have been working in a commercial laboratory in Manchester using analytical chemistry techniques. I am about to start a PhD in John Brognard’s Signalling Cancer Networks Group, and will be looking at the role of a novel MLCK protein in cell migration.

Erinn-Lee Ogg, Cell Signalling
Hi my name’s Erinn-Lee, but most people just call me Erinn. I’m from Glasgow and I completed my undergraduate degree at The University of Glasgow where I studied genetics. I spent a work placement year at The Institute of Medical Technology in Finland where I was involved in prostate cancer research. I have also spent some time at The Beatson Institute for Cancer Research as a summer intern. I am now starting my PhD with Angeliki Malliri and I can’t wait to become one of the team at The Paterson.

Michael Tallis, DNA Damage Response Group
Hi, I’m Mike and I’m undertaking a PhD in the DNA Damage Response Group with Ivan Ahel. I did my degree in Molecular Genetics at the University of Warwick, where I have since worked in a lab for the last 18 months. At the Paterson Institute I will be studying the role and pathways of Poly ADP-Ribosylation in DNA repair. I am very excited to work in such an excellent research environment and also to live in the vibrant city of Manchester, where I hope to see a lot of music and play a lot of sport!

Tim Somerville, Leukaemia Biology
Hi, my name is Tim Somerville and I am from Stockport. I received my undergraduate degree in Anatomical Science from the University of Manchester in 2009 and I have since worked at the Manchester-based biotechnology company Epistem where I have been developing protein biomarkers from plucked human hairs. This September I will be starting a 4 year PhD in Tim Somervaille’s lab (just to cause the most amount of confusion) and I am looking forward to getting started.

Magdalena Florkowska, Stem Cell Biology
My name is Magda and soon enough I will enlarge an already numerous group of Polish postgraduate researchers working under the supervision of Georges Lacaud in the Stem Cell Biology lab. After getting MSc degrees in Chemistry and Biotechnology from Jagiellonian University in Cracow I started working for a biotech company located in the Netherlands. When making the decision to come back to academic research I knew I would have to choose not only a stimulating working environment but also a place where I could bet on beautiful sunny weather all year long. Therefore, the Paterson seemed to be the only choice. Moreover I hope to use the opportunity of being here to develop my extracurricular interests in street art and cinema.

Vania Baldan, Medical Oncology
Hi everybody I am Vania and I am from Italy. I studied Medical Biotechnology at the University of Padua and I got my MSc last year. Soon after I realised that I had enough of sunny weather and warm summers and decided to move to Manchester for my PhD. I have joined the Medical Oncology group where I am doing my project in the field of adoptive cell therapy under the supervision of Dave Gilham. It is an exciting environment and a great opportunity and I will try to make the best of it.

Laura Cove-Smith, CEP
Hi, I’m Laura and I have just started a PhD looking at circulating and imaging biomarkers of cardiotoxicity from cancer treatments in CEP with the lymphoma clinical team at The Christie. I am a Medical Oncology trainee and have been based at The Christie for the past 3 years working as a specialist registrar but I did my undergraduate degree at Sheffield University - the city of steel. I am currently spending a lot of my time doing cardiac MRI scans at Manchester Royal Infirmary so I am getting fit cycling between there and the Paterson, I am not looking forward to the winter months....bring on the Gore-Tex!

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Danish Memon, Bioinformatics
My British connection is rather old having studied in a school of Anglican-origin called Barnes School in the beautiful garrison town of Devlali in India. Upon finishing my studies I moved to the bustling city of Mumbai to study Biotechnology and then to Pune to pursue a master’s course in Bioinformatics, only to return back to Mumbai to work on microbial evolutionary genomics in IIT Bombay. My latest move to the UK for PhD studies is a great opportunity to work in Crispin Miller’s lab on an exciting project on the cancer systems biology of the non-coding genome. A place known to offer something for everyone, Manchester may just turn out to be my perfect home away from home.

Stephanie Harrison, Children’s Cancer
Hi, I’m Steph. I’m from Blackpool, and have done a BSc and MRes in Biomedical Science at Lancaster University and am joining Prof Saha’s group as a PhD student to work on the pathogenesis of CNS disease in childhood acute lymphoblastic leukaemia. I am looking forward to starting at the Paterson and to living in a bigger city.

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Relay for Life

On the 2nd of July earlier this year, a team composed of staff from the Paterson Institute took part in the Stockport Relay for Life. Every year, communities in towns and villages throughout the UK stage Relay events, with 45 Relays taking place in 2011. Relay for Life is an opportunity for groups of people from a given area to work together both to raise money and to share their experiences of cancer.

The Stockport Relay for Life is organized entirely by a group of highly dedicated volunteers. Once registered, each team then raises money for CRUK either through sponsorship or other fund-raising events. On the day of the Relay, all the teams gather together to complete a 24 hour walk. Although this may sound like a gruelling task, in fact the Relay has an inspiring, festival-like atmosphere in which the teams celebrate their achievement. Relay for Life is a unique and rewarding way to support CRUK. Teams typically originate in places of work such as schools and supermarkets, but can also form around churches, large families, pubs and sports clubs. So, there is a real sense of community about this event, and the sense of a shared purpose is tangible too. The Stockport Relay for Life is totally dependent on the commitment of people who live and work in the South Manchester area, and since the Paterson Institute is part of this community, it’s important that we acknowledge everyone’s efforts by taking part.

On the day of the event we demonstrated DNA extractions to the general public and answered questions about the work of CRUK – as well as completing the 24 hour walk! The Stockport Relay raised approximately £37,000. The Paterson Team has raised an estimated £1500 so far, and this is still rising. Your local heroes were:

Ahmet Acar, Georges Lacaud, Gonia Gozdecka, Hadir Marei, Rasila Vaghjiani, Saki Kondo, Steve Lyons, Ula Polanska, Zuzhana Koldekova.

I’d like to take the opportunity to thank everyone on the team. They all worked really hard and were excellent ambassadors for the Institute. Thanks also, to James Dunphy whose assistance on the day of the Relay was invaluable! Finally, thank you to everyone who supported our fund-raising efforts!

Paterson Institute Colloquium

This year’s Paterson Institute Colloquium was held during the final week of September at the new venue of Lancaster University. It got off to a slightly inauspicious start - a crash on the M6 resulted in many people arriving late having endured up to four hours on the motorway. Once underway, though, the usual mix of talks, posters and social interactions ensued enjoyed by over 100 members of the institute.

One advantage of the new venue was the spacious areas available for poster presentations which led to two particularly vibrant sessions. The posters were assessed by a panel of eight judges who decided that there should be two prizes this year and also in the future; one for students and one for everyone else. These were judged mostly on the data but other considerations were the overall layout and appearance of the poster, in combination with how well the presenter explained their work. The student prize was awarded to Monika Stefanska from Stem Cell Biology for her work on tracking the emergence of primitive erythrocytes during mammalian embryogenesis. She shared the prize of Amazon vouchers with Shameem Fawdar, a post-doc from the Signalling Networks in Cancer Group, for her poster describing the identification of novel driver mutations in non-small cell lung cancer using a siRNA screening platform.

The colloquium took place amidst some unseasonably good weather which meant that everyone enjoyed their free time during the second afternoon with trips into the town of Lancaster and to the beach at Morecambe. Others made use of the excellent sports facilities on campus with games of five-a-side football, tennis and badminton, whilst members of Drug Discovery organised a five mile run.

Inevitably comparisons will be made with our previous colloquium venue. Lancaster is never going to compete with the Lake District in terms of beauty but it did have a lot of advantages. I would be interested to get feedback on this year’s event and the new venue, so if you have any comments or suggestions, please contact Caroline Wilkinson (cwilkinson@picr.man.ac.uk).

Prize winners Monika Stefanska and Shameem Fawdar

Paterson’s New Starters

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<tr>
<th>Name</th>
<th>Position</th>
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<tr>
<td>Kiran Batta</td>
<td>Postdoctoral Scientist - Stem Cell Biology</td>
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<td>Lucy Brown</td>
<td>Scientific Officer - Stem Cell Biology</td>
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<td>Azmat Chohan</td>
<td>Lab Aide - Central Services</td>
<td>CEP</td>
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<td>Shital Dulabh</td>
<td>QA - CEP</td>
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<td>Alexa Elades</td>
<td>Postdoctoral Scientist - Stem - Cell Research</td>
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<td>Cecile Evrin</td>
<td>Postdoctoral Scientist - Cell Cycle</td>
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<td>Suzanne Faulkner</td>
<td>Scientific Officer</td>
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<td>Lucy Foster</td>
<td>Scientific Officer</td>
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<td>Amy Hatch</td>
<td>Placement Student - Carcinogenesis</td>
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<td>Sarah Holt</td>
<td>Senior Biochemist (SSG) - Drug Discovery</td>
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<td>Matthew Humphreys</td>
<td>Placement Student - Carcinogenesis</td>
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<td>Laura Maigue</td>
<td>Scientific Officer Chemistry - Drug Discovery</td>
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<td>Nikki March</td>
<td>Senior Biochemist - Drug Discovery</td>
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<td>Amy Moloney</td>
<td>Lab Aide - Central Services</td>
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<td>Daniel Mould</td>
<td>Med Chem Student - Drug Discovery</td>
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<td>Amy Palmer</td>
<td>Scientific Officer</td>
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<td>Sarah Pinder</td>
<td>Placement Student - Carcinogenesis</td>
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<td>Andrew Porter</td>
<td>Postdoc - Cell Signaling</td>
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<td>John Sadat</td>
<td>Domestic Assistant - Operations</td>
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<td>Helen Small</td>
<td>Senior Scientist - Drug Discovery</td>
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<td>Anthony Smith</td>
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<td>Judith Thorp</td>
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<td>Ian Waddell</td>
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<td>Stephen Walker</td>
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<td>Mandy Watson</td>
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A Life at The Paterson

I arrived at the Paterson Institute in October 1975 a few months after graduating from University. It was my first real full time job in science and I was overwhelmed by the size and complexity of the Institute and The Christie hospital.

Building equipment was a hallmark of the institute in those days, as often complex specialised equipment just wasn’t available. The Institute even built its own flow cytometer prior to purchasing a commercial one. An instrument it turned out I would spend many long hours using to study drug resistance. Computing was minimal at that time and calculators were rare and very expensive. One PhD student in my lab proudly sported a calculator he had built from a kit.

The Institute then was a mixture of both translational clinical science and basic research. Fern spore, clostridium bacteria and slime moulds were all used to study the effects of radiation on cell growth and resistance. Radiobiology was very strong at that time in keeping with the history of the labs under Edith and others and most of the culture was done in old glass medicine flat bottles and stored in large hot rooms dotted after graduating from University. It was my first real full time job in science and I was overwhelmed by the size and complexity of the Institute and The Christie hospital.

A Fond Farewell

Tim Ward was the first of the ‘happy trio’ to join the institute in October 1975, closely followed by myself in February 1976 then Martin Dawson in January 1978 at that time, all three of us worked under the Experimental Chemotherapy group umbrella headed by husband and wife team Brian and Margaret Fox, and all three sported a good, if not full, head of hair. We worked in washing glassware, preparing basic solutions and blowing glass to make pasture pipettes, mouth pipetting was the norm and cell counts were done using a haemocytometer only. One of the main projects I was involved in back in those days was methotrexate resistance. Drug resistance was an emerging clinical problem and the mechanisms were not fully understood. Radioactive labelling was the norm in almost every experiment and people were skilled in the handling and disposal of radioactivity.

As the eighties progressed things got easier and faster as development and instrumental analysis I received in those days could not be surpassed and I was able to put a lot of this experience to good use in later years. The training I received was second to none and the friendships and collaborations will always be with me.

Ian Waddell – DDU head of Biology

I started at the Paterson on the 1st of June and even although it is only 3 months I already feel very much involved. Partly that is due to the fantastic welcome I received from many different people in the institute but also because of the excellent work Donald and Allan have done in building the Drug Discovery Unit.

For the previous 18 years I have worked just down the A34 at AstraZeneca’s Alderley park site but earlier this year I found myself in a position where I could take a redundancy package. Like many I saw this as an opportunity to take the skills I had developed at AZ but use them in a new environment. So when Donald offered me the opportunity to join the DDU as head of biology I was delighted to accept.

So far it has lived up to my expectations. The DDU lab is an excellent example of a well designed functional laboratory. The equipment and facilities are state of the art and will allow us to do modern drug discovery. Most importantly of all we have recruited a fantastic group of scientists who bring many different skills. Equally having the CEP group close by will greatly enhance our ability to prosecute the translational aspects of delivering new therapies to cancer patient including meaningful clinical biomarkers. I am passionate about the target selection and target validation aspects of drug discovery. Therefore one of the things that excited me most about joining the DDU was the opportunity to work alongside internationally recognised groups at the Paterson with a view to developing new targets and hopefully new therapies. It is still very early days but I think I can speak for the whole of the DDU when I say that the first such examples are really starting to show promise.

In my last role at AZ I developed an interest in outsourcing, became a lean six sigma black belt and had to work with groups in Shanghai and Boston to deliver project needs. It is that desire to work collaboratively and complex mix of skills that I am most looking forward to bringing to my role at the Paterson.

On the personal front I am married to Norma and we have two teenage sons, Craig and Ross. None of whom has the ability to get up in the morning. So if I arrive at work in the morning looking stressed, that’s probably the reason. I have a keen interest in cycling both taking part and watching as a sport. As far as rugby goes I think I am keen but then again I support both Sale and Scotland, so on current form maybe that should read disillusioned. In my spare time I read a lot particularly around Soviet history and I suspect I am the only Dundee United supporter in the institute.

The three wise scientists Tim Ward, Martin Dawson and Martin Greaves
Paterson Scientists get a clearer picture of DNA damage and repair

DNA damage is involved in both cancer initiation (by causing gene mutation) and treatment (many current cancer therapies work by damaging DNA). For these reasons Paterson scientists have been studying the molecular mechanisms by which cells recognise and repair damage to their DNA.

One of their studies has been recently published in the journal, Nature. The work by DNA Damage Response group, headed by Dr Ivan Ahel, in collaboration with Prof. David Leys’ group at the University of Manchester, revealed for the first time the 3-dimensional structure of PARG (poly(ADP-ribose) glycohydrolase), an essential enzyme involved in the removal of the chemical signals called poly(ADP-ribose). Poly(ADP-ribose) serves to regulate DNA repair in human cells and it is synthesised by PARP proteins which are already being exploited as targets in cancer therapy.

The insight into the PARG structure provides a vital understanding of how this enzyme works and should facilitate the development of small cell-permeable PARG inhibitors for use in regulating the DNA damage response in patients. The ability to regulate the DNA damage response during cancer therapy will provide benefit to patients by increasing the effectiveness of currently used therapies (if the cell cannot repair the DNA damage caused by the cancer therapy then it will die). This means patients will be able to have lower doses of therapy for the same benefit reducing the side effects often associated with treatment. In future it may also be possible to reduce side effects further by protecting normal tissues and cells by increasing the levels of DNA repair during therapy.


Group Spotlight – Signalling Networks in Cancer Group

By John Brognard

I moved to Manchester just over a year ago from San Diego and quickly realized the weather was not going to be the only major change. My capabilities for driving on the left-hand side of the road have been tested and indeed have warranted more than a few angry glares and words not worthy of print from other drivers! However, as in life, I have embraced the challenges and now my driving only warrants one evil stare a month and a couple of screams from my wife a week. Onto the business at hand....

The lab has quickly taken shape and we were off and running with experiments only a couple of months after my arrival. We have developed an optimistic and energetic team that includes Wendy Trotter (SSO), Shameem Fawdar (Postdoc) and Anna Marusiak (Postdoc). We will have our first graduate PhD student joining us this fall, Zoe Edwards. The lab is located on the second floor, just down from the director’s office, and we have office space located in close proximity to the lab. Feel free to stop by at any time for a chat and often times we will have left over cake from morning lab meetings or journal clubs.

For the research in the lab, the overarching goal of the lab is to identify novel kinases harbouring driver mutations that can be therapeutically targeted for the treatment of cancer, particularly focusing on lung cancer. These are exciting times for cancer biologists as we have entered the golden age of cancer genomics, where prices associated with sequencing normal and cancer exomes from cancer patients have dropped dramatically in the last few years. This makes it possible to sequence every cancer patient’s exome to identify somatically mutated enzymes, which harbour “driver” mutations and this is a main focus of the lab. Using bioinformatic tools we identify kinases with putative driver mutations and then test to determine if mutations alter kinetic activity and drive cancer phenotypes both in normal cells and in cancer cells harbouring somatic mutations in a putative cancer kinase. We have some exciting leads and hope to progress these further along and some may even end up as novel targets for therapeuticists in the clinic. We have received a warm welcome from many at the Paterson Institute and we are grateful for these interactions particularly with the groups in the CSI meeting, the Drug Discovery Unit, and the lung cancer focus group. We have also established some exciting collaborations with investigators at the University of Manchester and look forward to teaming up with other groups in the future. In conclusion our group is excited to be part of this first-rate institute and will work hard to contribute to our understanding of cancer for the benefit of cancer patients in the clinic. Please stop by and say hi at anytime!
In the spotlight with Helen Whalley, Cell Signalling

1. What is your favourite part of the UK?
That’s a tricky one, I like the countryside so most of the national parks, especially in the north. If I had to choose I’d probably say the Lake District, it is beautiful.

2. Which website do you always check, and why?
BBC Weather – I don’t know why, it’s normally wrong!

3. What is your favourite film?
For pure escapism I like cheesy action films with lots of explosions, so maybe Con Air! I don’t know whether I should admit it but I also seem to be very fond of Love Actually (I have to watch it every Christmas).

4. If you had to change careers tomorrow, what would you do?
I’d probably try to be an artist or a chef.

5. What is the most important lesson that you have learnt from life?
Don’t chop chillies & then rub your eyes.

6. Name three things you would take with you to a desert island?
Can ‘things’ be people or animals? If so I’d take my husband, my goldfish and some love-hearts (the sweets - I’m addicted to them).

7. What is your greatest fear?
Bad things happening to people I care about. And daddy longlegs!

8. How would you like to be remembered?
Why, is someone planning to kill me?

9. If you could change one thing in your past what would it be?
I wouldn’t spend so much time worrying, it doesn’t help achieve anything.

10. What is your signature dish to cook?
I have a few. I asked my husband and he said my slow baked lamb shanks. Mmmm.

11. You’ve just won the lottery and have £5 million pounds to spend. What do you buy first?
A nice cold beer.

12. What is your idea of perfect happiness?
A nice cold beer.... and £5 million pounds!

13. What keeps you awake at night?
If I have a big talk or an interview I get nervous & generally don’t get much sleep the night before. Also I can’t stop thinking about work if there’s something important going on. In general though, I am quite good at sleeping.