in patients who have cancer or some healthy people, but is often elevated in small amounts in the blood of most people. CEA is normally found in the breast, lung, pancreas, stomach, cervix, bladder, kidney, thyroid, liver, and ovary. Thus, this targeting of T-cells against CEA may be suitable for the treatment in many cancers and has led to the proposal of a clinical trial later this year. Will this strategy work? At the National Cancer Institute, USA, they have already trialed the use of adoptive T-cell therapy after non-myeloablative chemotherapy for the treatment of refractory metastatic melanoma with what appears to be promising results with 51% of patients exhibiting an objective clinical response. This bodes well for the Medical Oncology trial and for patients in the future.

Stressed Out in Cell Division!

The paper entitled “Polo kinase links the stress pathway to cell cycle control and tip growth in fission yeast” was recently published in Nature by Janni Petersen from the work that she did in the Cell Division group. The paper marks the culmination of ten years work in the group that has followed a lucky break made by the Cell Division group into how cells regulate cell division. This break was the realisation that a component of the spindle pole (centrosome in human cells) plays a critical role in regulating the timing of cell division. The analysis of this molecule over the last decade by Iain’s group has shown that the decision for cells to divide comes from the spindle pole and involves a protein kinase called polo. This ties in well with work in Human cells from Jon Pine’s CR-UK funded group in the Gurdon Institute in Cambridge that shows that the same is true in human cells.

As is invariably the way with advances in understanding cell cycle control it is the genetics of the yeast system that has enabled Janni and Iain to make a very important link between the stress response pathway and cell cycle control. Several groups, including Nic Jones’s group while at ICRF, have shown that yeast cells that are most deficient in the MAP kinase cascade that constitutes the stress response pathway in fission yeast (equivalent of the p38 pathway in humans) do not enter mitosis at the correct time. There is a considerable delay in the decision to divide. This shows that the stress pathway somehow impinges upon the control of cell division. It is the nature of this link that Janni and Iain address in their paper.

So why is all of this of interest to the general community and, in particular, the cancer community? A major goal in seeking new therapeutic approaches, or ways of better exploiting existing treatments, is to find novel means with which to differentiate between tumour and normal tissue. A common distinction between the two is that the disorganisation and poor blood supply in the tumour tissue means that the transformed cells are more highly stressed than normal cells (e.g., tumour tissue is invariably hypoxic). Understanding how such stresses would impinge upon cell cycle controls will clearly guide us to ways of trying to exploit this link to specifically target the tumour cells. Thus findings like Janni’s will help optimise the design of the clinical trials of polo kinase inhibitors that are currently being instigated at a number of centres around the world.

Jain Hagan
Cell Division Group

CR-UK carried out a comprehensive review of the microarray facility on the 1st June. This is the only national CR-UK-wide facility to be based outside London, and is housed within the MBfC in the Paterson. The review went extremely well, with the staff involved here (Stuart Pepper, Yvonne Hey, Gillian Newton and Crispin Miller) being praised for the exemplary service that they provide. CR-UK has increased financial support for the facility, including supporting three posts, some equipment and all running expenses. Many congratulations to all involved in this facility, it really is a flagship example of how a national resource should run, and the credit for this must go to the staff who have made it what it is.
In the last Newsletter I outlined our plans for the development of the Manchester Cancer Research Centre (MCRC) together with the University of Manchester and the Christie Hospital. These are exciting and ambitious plans that will see a huge increase in cancer research activity in Manchester mainly based at the Christie site. The MCRC together with the Christie and other NHS partners will constitute the Manchester Comprehensive Cancer Centre (MCCC).

As you are aware, as part of this development the Paterson Institute will become an Institute of the University although it will retain its current level of operational autonomy. Extensive discussions have been ongoing over the last couple of months to prepare for this transfer. These discussions have proceeded extremely well and we feel we are on schedule with our target date for transfer of October 3rd, 2005. Clearly the work of October 3rd, 2005 is also the target date for establishment of the MCRC and the MCCC. The MCRC Steering Group and the Research Strategy Group will be working hard to develop the strategy of the MCRC, to clarify investment plans and needs, to set up the various committees that will develop and take responsibility for actioning the objectives of the MCRC and MCCC and to finalise the governance arrangements that will oversee these bodies. I see these exciting plans as a logical extension of the overall, major goals of the Institute: to be a world-class centre of cancer research with outstanding scientists and research infrastructure and to build on this platform together with our major research partners, a comprehensive approach to research that encompasses basic, translational and clinical research programmes. I am confident that the development of the MCRC and the strong partnerships it represents, will see these goals being fully achieved.

On many occasions I have stressed the importance of our research services to the functioning of the Institute, something we are all aware of since we rely on them on a day-to-day basis. Recently (June 1st, 2005) the Unipathmex-based microarray service was externally peer-reviewed by Cancer Research UK. It received glowing reports and results in a commitment to not only continued support, but increased support. So the good news is that donations go to the service and those that run it - Stuart, Yvonne and Gillian, together with the Bioinformatics support from Crispin’s group. They really are doing a fantastic job.

As many of you may know, Elmar Schiebel will leave us towards the end of the year. Elmar is taking up a Professorship with the University of Heidelberg based at the Zentrum fur Molekulare Biologie. Elmar and his group will be a huge loss - his productivity during his time with us has been truly outstanding and he is undoubtedly at the international forefront of his field. He has contributed greatly to the reputation and international recognition of the Institute. I am sure we all wish Elmar well in his new challenge and his return to his home country.

Recruitment for new group leaders will resume shortly - to fill the gap left by Elmar’s departure and in anticipation of new laboratory space when TRF1 is finally completed. One new group leader who will be arriving at the Paterson Institute next Spring is Michael Deininger who has been appointed to a Chair in Haematology. This is a position jointly funded between the University, the Christie Trust and ourselves. Michael who is currently at Oregon State University will provide a big boost to the translational research programme.

In each issue of the Newsletter, we will be featuring a member of staff who will take the “Spotlight” and answer a list of questions that we have put together. The second lucky individual to have this privilege is Martin Dawson

What is your favourite part of Manchester?
My back garden, warm evening, bottle of wine

What is your greatest fear?
Losing my wine collection in a fire when I stop to save the cats

What is your greatest regret?
Not spending more time with my mother; she died when I was 26

Elmar Schiebel in collaboration with Gislene Pereira (University of Manchester) recently had a successful publication in “Kinase Kinetic Cell cycle progression when the spindle is misaligned. Thus, Kin4 is part of a system that prevents chromosome missegregation in polarised cells”. Mol. Cell. In press. Elmar explained that, for many polarised cells, it is critical that the mitotic spindle becomes positioned relative to the polarity axis. Using the model organism budding yeast, we have identified the Atfmetrix-based microarray service was externally peer-reviewed by Cancer Research UK. It received glowing reports and results in a commitment to not only continued support, but increased support. So the good news is that donations go to the service and those that run it - Stuart, Yvonne and Gillian, together with the Bioinformatics support from Crispin’s group. They really are doing a fantastic job.

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What is your most important lesson that you have learnt from life?
No problem is insurmountable!

What is your favourite book?
Revolving Rhymes - Roald Dahl

What is your favourite film?
Groundhog Day (I’d like to be able to get just one day right!)

Do you believe in love at first sight?
Not... However, LUST at first sight....

What three things would you save from your burning house?
Assuming my family can get out by themselves, then it would have to be all my family history documents, my computer and the cats

What is your ideal perfect happiness?
Absolutely nothing, my head sits in the pillow and I’re gone

How would you like to be remembered?
Martin who?

What is your greatest fear?
Losing my wine collection in a fire when I stop to save the cats

What is your favourite part of Manchester?
My back garden, warm evening, bottle of wine

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Revolving Rhymes - Roald Dahl

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Losing my wine collection in a fire when I stop to save the cats

How would you like to be remembered?
Martin who?

University of Manchester Merger

Steve Glover has been meeting with John Rylands Library to ensure that staff have access to both libraries.

Following the staff consultation meeting on 7 June, we have sent a response to the University’s Pensions Manager, Heather Mawson, who is liaising with the NHS Pensions Agency on our behalf. As soon as we receive their reply, we will share it with everyone and act accordingly to ensure that you all have the information you need to make an informed decision about your pensions.

If anyone has any questions at all about the merger, please send email or pop in and see me. I will send out regular email updates as soon as there is anything concrete to report.
Cells commonly respond to extracellular signals by modulating the activity of specific transcription factors and subsequently the expression of many target genes. We are particularly interested in the response to cytotoxic and genotoxic stress which results in the mobilization of a battery of protective and repair mechanisms or the induction of apoptosis. Failure to respond appropriately can result in cellular damage and thereby drive tumorigenesis.

The laboratory is rather unusual (I am sure for a number of reasons!) in that it approaches the investigation of stress response using two very different, but hopefully complimentary, model systems; mice and fission yeast. At the moment it is quite simple – the boys work on mice and the girls work on yeast though this is set to change with the arrival of a new post-doc, Wolfie Reiter (yes another Wolfie!!), in June.

In mammalian cells the AP-1 transcription factor plays a key role in response to extracellular signals – it is regulated by many physiological and pathological stimuli such as mitogens, hormones, genotoxins, stress signals, viral infections and cytokines. It is a complex factor made up of many dimeric complexes mainly composed of members of the Jun, Fos and ATF protein families. Our specific interest is in the ATF components and asking what role they play in the functions of AP-1. The approach has been to generate a series of genetically modified mice expressing mutant ATF proteins either in all tissues or in specific tissues. Characterisation of these mice is revealing important functions of ATF in mouse development, in regulation of apoptosis in response to certain signals and in susceptibility to tumorigenesis. The major ATF component appears to be ATF-2 which is phosphorylated and activated by multiple MAP kinase pathways including the JNK and p38 pathways that are stimulated by a variety of stress signals.

Furthermore, replacing the normal ATF-2 gene with a mutated version that encodes a protein that can no longer be phosphorylated, shows that the various functions of ATF-2 are dependent upon these signalling pathways. These are frustratingly long-term experiments but are beginning to give us real insights into the functions of these important factors and in the future will allow us to better understand what influence AP-1 might have in tumour formation or maintenance or in the response of tumours to therapeutic agents.

We also use fission yeast as a model system for studying the response to stress. The factors ATF1 and Pap1 co-ordinate most of the changes in gene expression following stress and we are currently trying to understand how these factors are regulated and what target genes they control. ATF1 and Pap1 are related to the mammalian ATF and Jun proteins respectively. ATF1 is phosphorylated by the Sty1 MAP kinase, a homologue of the mammalian p38 kinase. Thus fission yeast serves as a useful model for understanding the role and regulation of AP-1 proteins in mediating the stress response.

In collaboration with Jurg Bahler at the Sanger centre in Cambridge, we have carried out comprehensive global microarray analysis of the transcriptional responses to a variety of different stress conditions. Currently we are focusing on how ATF1 and Pap1 are regulated by post-translational regulation and by interactions with other proteins to orchestrate the appropriate response to various stresses. We have identified a number of proteins using a TAP-tagging procedure which appear to bind specifically to ATF1 or Pap1 upon stress. We are trying to understand how these interactions affect stress-induced transcription of the target genes.

In addition to altering their programme of gene expression, cells also respond to stress more directly through the modulation of post-translational modifications. Some of these responses are mediated by the Sty1 MAP kinase. We have identified new targets of this kinase which are currently being characterised. Previous work has shown that Sty1 also plays a role in cell cycle progression and we are investigating how this kinase interacts with the cell cycle machinery.
Life in Manchester began for me in September 2002, when I was in the Paterson for all of 20 minutes before being whisked off with the other newbies to the delights of the annual Colloquium in Ambleside. Although a touch daunting, I will say it was a good way to be introduced to everyone and for getting to know those in my lab.

I joined John Gallagher’s lab to work on the study of heparan sulphate proteoglycans (wake up at the back those of you snoozing) in mouse embryonic stem cells and their role in the early developmental processes that ES cells lend themselves to studying. Suffice to say it’s been an extremely rewarding project and I feel I’ve helped establish a new wing of the HS field. But that’s enough of the science stuff, apparently I’m supposed to tell you what life has been like for the Paterson PhD student.

The Paterson is unique in that its student community is separate from the University, which means everyone knows everyone, and we can generally be counted on to be found around a pool table in the Golden when life at the bench becomes too much...

Manchester is also a great city to live in right now; many of you will know that I house-share with Kelly and Aga, and over the years we’ve all had great fun going to various shows, sporting events, concerts and many many bars etc. Can’t recommend it highly enough. (Could be slightly less grey, but that is my only bugbear. Now, if only I could think of something wise and insightful to say with my last thirty words! Ah well, if anyone wishes to know anything else, mine’s a G and T…

\[ \text{Claire Johnson} \]

Martin McQuade(St Bede’s) Ros Whileley (Withington Girls’ School )

On Saturday the 23rd of April, 24 sixth form students from eight local schools spent the day at the institute getting their hands dirty (obviously not literally, Colin) doing some practical experiments. The day was organised by Lez Fairbairn with the intention of enthusing bright youngsters from the area, who might then consider science as a career. Lez admits the sad fact that the idea was concocted in conjunction with his wife (whom some of you may remember as Andrea Campbell – an erstwhile technician in the old Dexter lab), whilst they were having coffee at the Natural History Museum in New York during their honeymoon – talk about a busman’s holiday!

In all, four practicals were set up: Advanced microscopy - run by Steve Bagley, where students got to make time-lapse videos of cells migrating and dividing; Yeast genetics - run by Iain Hagan and his group, with students looking at segregation of traits during meiosis; DNA Sequencing and bioinformatics course - where Stuart Pepper and Claire Wilson took students through the various on-line databases, and also showed off all the cool toys in the Molecular Biology Core Facility; PCR and restriction digestion – based in the KK, with students getting to run their own reactions and gels. A number of our students and postdocs, (Danielle Foulston, Jo Libby, Tom Southgate and Stephen Wharton) provided hands-on help.

The day was a great success, with highly positive feedback both from students and the schools. Several schools have already been back in contact to book their places for next year, and the idea is to have an even bigger and better event next Spring. So, be warned that come September, Lez will be looking for other groups to provide some hands-on experience for students.

\[ \text{Lez Fairbairn} \]

Martin McQuade(St Beate’s) Rosa Whiteley (Withington Girls’ School )
storing several protocols have replaced Leica automated stainer, capable of blade systems and a multi programma-
A cryostat used for cutting frozen sec-
methology much simpler.

The benefit of the platform is that it
also been introduced.

Linked to the new equipment, the unit
now participates in an external quality
assessment program to ensure high
standards are achieved in the key
areas of fixation, processing, microtomy and
staining.

As you are all probably aware the unit
also houses the Arcturus PicoCell II laser
capture microdissection system. With
this we have successfully isolated specif-
ic cell populations based on morphology,
from tissue sections, which then allows
expression analysis on the Affymetrix
platform. In conjunction with the MBCF
we are currently validating protocols and
the kits available that will allow us to use
lower numbers of isolated cells based on
their immunophenotype.

Finally a Leitz double headed teaching
microscope in now located in the histol-

can be contacted on apeerson@picr.man.ac.uk, ext. 3231 or
you can drop by the office to see either of us.

Employee Assistance Programme
The Employee Assistance Programme
(EAP) now includes a new interactive
website. From 1st August 2005, you
and your family household members can
log onto www.ppc-askwell.com 24/7 to
access up to date online health pro-
grames, test your fitness levels and
find out about such things as how to
improve your sleep, diet or work-life bal-
ance. You will find tips on how to incor-
porate changes to your daily life that will
improve health. You can also access top-
cical and practical articles written by
medical professionals. As with all other
EAP services the website is free, totally
confidential and backed up by a 24/7
support help line. Look out for posters

Spotlight On Histology
Laura will be dealing with annual leave
and sickness queries, recruitment
administration such as arranging inter-
views and obtaining references, pre-
employment medicals and accommoda-
tion issues. She will also be providing
assistance to new starters who are relo-
cating to the area by contacting letting
agents, schools, nurseries etc. If you
have any queries on any of these issues,
Laura can be contacted by email on
lhumes@picr.man.ac.uk or by phone on
ext. 3124.

I am responsible for advising on issues
relating to disciplinary and grievance,
respect at work, maternity and paternity,
redundancy and redeployment, terms
and conditions, employment legislation,
pay and grading, improving working
lives, agenda for change and providing a
confidential advisory service to individual
members of staff who wish to seek guid-
ance on employment matters. I am also
responsible for undertaking employment
checks with the Criminal Records
Bureau and for obtaining work permits. I
physiology office. The microscope will soon
have a camera attached and is available to
anybody requiring the use of a basic
light microscope and camera.

In April Cancer Research UK held its annual
regional meeting, this time covering the North
of England. The meeting provided an excel-
ent opportunity for CR-UK funded
researchers across the North of England
to meet each other and potentially develop new
collaborations. PICR was well represented in
the program with talks from Iain Hagan, Arik
Welman, Tom Southgate, Wolfgang
Brötsch and Anghelki Malliri and our newest
group leader, Clemens Schmitt. In the stu-
dent session both Marion Searah and Ada
Gambus gave excellent talks.

The meeting was held within the picturesque
Museum Gardens with lunch provided in the
13th Century Hospitium, which is thought to
be the oldest timber framed building in York
(see picture).

There were many thought provoking talks,
and Herbie Newell provided both a stimulat-
ing opening presentation and a neat sum-
mimg up of the meeting. Despite the high
quality of the science, however, it is likely that
the longest lasting memories were generated
during the dancing after the formal dinner
at the Royal York Hotel.

**Meetings**


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**1st International MGMT Meeting** - 6-8th August, 2005, Keele Conference Centre

This meeting will be the first of its kind, and there will be presentations from many, indeed most, of the leaders in this field.

The deadline for registration has now passed, however the deadline for abstracts is 26th August! If you have any queries or
require any further information, please contact Julie Hallett on x3113.


The National Cancer Research Institute (NCRI) has announced the first in what is planned to be a series of meetings that aim
to provide a major international forum in the UK for the dissemination of research advances in cancer across all disciplines. This
event will be the biggest conference of its kind ever to be held in the UK.

The establishment of the NCRI brought together for the first time the major cancer research funding bodies from the govern-
ment, charity and industrial sectors to form a true partnership. Its purpose is to accelerate and advance improvements for the
benefit of cancer patients, by engaging with the whole UK cancer research community.

The deadline for abstract submission has now passed, however the deadline for discounted early registration is not until 29 July.
Further details of the meeting are available on the NCRI website: www.ncr.org.uk
**Staff News**

**Retrojet**

Bet you didn’t know that we have a rock star in our midsts!!

Jon Deakin (Medical Oncology) plays lead guitar in ‘Retrojet’, along with his friends Dave and Shell Caddick on bass and vocals respectively, Steve Crompton on rhythm guitar and Brian on drums. They play locally, with past venues including The Red Lion, Old Cock Inn, Wheatsheaf in Altrincham and Bakers Vaults in Stockport. They will be appearing at the South Manchester Music Festival in Altrincham in mid-July and Bullstock Festival in Stalybridge in the summer. The music is contemporary rock such as the Manics, Morrisette, The White Stripes, Kravitz and the odd Black Sabbath oldie. All gigs are free to attend and usually involve a half lager (and the rest) at some point in the proceedings! Posters are placed on notice boards around the Institute prior to gigs, so go along and show your support! If you want to hire them for your own event they charge £150 (1% discount for Paterson staff!) - speak to Jon on x3619.

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**Welcome to new members of staff who have recently joined us:**

- Bilal Bham, Immunology
- Stephanie Briers, Stem Cell Biology
- Phil Crossbie, Carcinogenesis
- Lucy Dalton, Structural Cell Biology
- Fiona Gardiner, Cell Signalling
- Claire Graham, Medical Oncology
- Cassandra Hagarty, CEP
- Laura Hughes, Administration
- Robert Lord, Clinical Research
- Tristan McKey, Key Kendall Laboratories
- Michal Okoniewski, Bioinformatics
- Daniela Rosa, Medical Oncology
- Robert Sobczak, BRU
- Sophie Summers, Clinical Research
- Stefano Vernarecci, Mitotic Spindle Function
- Jessica Worthington, Cell Regulation
- Liqun Zhang, Mass Spectrometry

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**Anyone For Rugby**

Sale FC 1st XV (not the Sharks!) won the South Lancashire and Cheshire 3 (League) and were promoted as Champions. They currently play at Heywood Road, Sale (former Sale Sharks ground) and have all the Sale Sharks professional equipment (very impressive Clubhouse, including new gym, squash courts, dart team and a brand new multi million pound rugby training facility down the road). They are currently looking for fresh blood (met literally) - training is on Mondays and Thursdays, with indoor training for cold/cold winter nights! All standards are catered for and there are 3 teams playing in various leagues and at various standards (ranging from former professionals to beginners). It is an excellent set up with professional facilities and les and there are regular celebrity coaches including Sale Sharks professional coaches, current professional players and England Academy coaches. The season is finished for the moment but pre-season starts in July, so if anyone is interested in joining or wants further information, please contact Martin Chadwick (x3137).

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**Women’s Running Network**

For anyone that is interested in boosting their fitness levels, Claire Wilson is involved with the South Manchester Group from the Women’s Running Network (http://www.wrn-north.co.uk/). It is based at the Northern Lawn Tennis Club on Palatine Road and a beginners walk to run group has recently started on a Monday and Thursday evening at 6:30pm. Two other sessions are run as well, aab on Monday and Thursday evenings and if you want any more information, please contact Claire on x8618.

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**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 new format of our Newsletter or ideas for future issues, then we would really like to hear your views! Please contact Elaine on x3101, or via emercer@picr.man.ac.uk.

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**Great Manchester Run**

Congratulations to all those members of staff who were amongst the 20,000 people taking part in the Great Manchester Run on May 22nd, running a very impressive 10K! Many thanks to everyone who sponsored them, helping to raise lots of money for numerous good causes, including of course, cancer research!

**Well done to:**

- Wolfgang Brettwieser - 51:25
- Kelly Chiang - 59:28
- Jon Chung - 45:13

and everyone else who was brave enough to enter....

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**Barrow To Keswick Walk**

Very many congratulations to all those who took part in the Keswick to Barrow walk recently (40 miles in a single day through the Lake District). 1212 people started the walk and 1018 finished this year, with the whole event hopefully raising over £100,000 for local and national charities, with the Paterson team raising over £1000 for Cristies against Cancer. The team came 44th out of 171 in the overall team competition (pretty impressive!). They also came 16th out of 49 in the “Outsiders” team competition for non-Cumbrian teams.

**The final position and times were:**

238  Gavin Wilson (09:28:54)
239  Anek Weilman (09:29:15)
373  Eduardo Castaneda Saezco (10:24:05)
965  Chris Lamanna (14:44:32)
966  Lourdes Ponce Perez (14:44:42)
967  Darren Roberts (14:44:56)
968  Helen Sanderson (14:45:04)
969  Stephen Wharton (14:45:07)

With two retirements due to injury - Chris Morrow (27 miles) and Dan Tennant (33 miles).

Grateful thanks go to Martin Dawson who drove the support minibus on the day, Starlabs, Bioline and everyone who sponsored the team! More information on the walk (history, route, fastest time etc.) is on the website (www.keswick2barrow.co.uk). Many (if not all) intend to try to better this year’s performance next time round when it will be the 40th anniversary of the walk. So if you feel the urge to join in, please feel free to contact Darren on x3036.

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**Congratulations To:**

- Cassandra Hagarty (CEP) who got engaged to Adam Hodgkinson (of Central Manchester and Manchester Children’s University Hospital) on 15th March, 2005. They plan to wed early in 2006 in Cassandra’s home town of Dubbo, NSW, Australia.
- Anna Pearson (HR Manager) and Justin Haylock on their engagement on 20 May, 2005. Justin whisked Anna off to Vienna for her birthday and got down on bended knee outside the Hofburg Palace to ‘pop the question’! Naturally Anna said ‘yes’ and they will be getting married in the next couple of years!!
- Steve Lyons (Cell Regulation) and his wife Jo (a Registrar working at the Christie Hospital) on the birth of their beautiful baby girl Hannah on 24th April, 2005, weighing in at a healthy 7lbs. As you can see from the photo, she seems very content with her lot!!

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**Photography by:** Steve Royle, Jenny Varley & Geoff Margison