Another much talked about topic was that of target prediction. It is a stumbling block in our analysis of miRNA function that we find it difficult to accurately predict biologically relevant targets of miRNAs. Although target prediction algorithms have been developed and many hundreds of targets have been predicted for each miRNA, there are still relatively few validated miRNA-target interactions. The current methods depend on conservation and the presence of a seed sequence and some recent work carried out independently by both David Bartel and Nikolaus Rajewsky, using SILAC to measure changes in the proteome in response to alterations in miRNA levels, appears to go some to way to confirming that this is important in many cases. However, it also seems there are many non-conserved target sites and, in addition, sites need not be located in the 3'UTR since some apparently functional sites are found within ORFs. This confirmed my suspicions that by only looking for target sites in the 3' UTR of genes and considering only those that are conserved as worthy of functional testing we are then creating a self-reinforcing (but possibly misleading) cycle which means that only conserved 3'UTR sites are validated! This then apparently reassures us that our models are correct and so on and so forth. It had been shown already by Joan Steitz's group that miRNA binding sites in 5'UTRs of genes are able to cause silencing but until we start looking for endogenous sites in all regions of the mRNA then we will not know how relevant this is.

There were many talks on the use of RNAi and also miRNAs in therapy and with advances in cellular delivery techniques no doubt we will soon see these products coming to market. However in the particularly memorable final talk of the meeting on the use of LNAs to silence miRNA in primates, Morten Lindow urged us to stay single and naked – at least with regard to therapeutic short oligionucleotides! It seems that a single stranded molecule is better than a double stranded molecule at entering cells, possibly as a result of the greater exposure of hydrophobic groups.

Finally, there were an abundance of miRNA and short RNA profiling projects presented in the poster sessions: the technologies for this have advanced rapidly, especially with the advent of deep sequencing. So I am sure that in the next few years we will see an explosion in the discovery of non-coding RNA-mediated regulation in a wide variety of processes and the over-subscribed Keystone symposia on RNAi, miRNA and Non-coding RNA will no longer be viable. Instead we will see a splintering of the field as it expands. I just hope the quality of the research does not suffer because this was one of the best meetings I have been lucky enough to attend – and we had chance to do some skiing! So I guess the take home message from the meeting is that we are only just discovering the tip of the RNA iceberg. Watch this space!

EURASNET Symposium and Workshop on Alternative Splicing and Disease

18th – 23rd February 2008, University of Montpellier, France

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Alternative pre-mRNA splicing increases the coding capacity of the genome and proteomic diversity of eukaryotes. Global studies suggest that at least three quarters of human genes are alternatively spliced, and many aberrant splicing events are associated with human disease. In 2006, a European Alternative Splicing Network (EURASNET) was established with funding from the European Commission Sixth Framework Programme (FP6), bringing together several splicing research groups from different countries. Part of the EURASNET mission is to "promote understanding of the complex regulation of alternative splicing in different systems" and to "establish an active and vibrant network to share and exchange information, methods and material among the network partners" through a series of workshops and conferences.

This EURASNET workshop was held in the university town of Montpellier on the south coast of France. A plenary symposium on Alternative Splicing and Disease was held on the first day, and included invited speakers from several European EURASNET groups. The Speakers introduced concepts and presented findings from their own research into alternative splicing and disease, and also discussed the potential clinical application of aberrant splicing detection and modulation. Of particular relevance to my research in cancer biology were two talks delivered in a session entitled Splicing and Cancer: Professor Guiseppe Biamonti discussed the effect of aberrant splicing events on cancer phenotypes and epithelial to mesenchymal transition; and Professor Elmar Stickeler detailed his own translational research programme in gynaecological oncology.

The rest of the week was dedicated to a practical "hands on" workshop covering a variety of techniques for study of alternative splicing and disease. I was fortunate enough to be part of a small group of 26 students selected to take part. The workshop commenced with a series of short talks from Affymetrix on the use of their GeneChip Exon Array system for the detection of alternative splicing. Participants were able to try two software packages (Affymetrix Expression Console and Biotique XRAY) for analysis of a publically available colon cancer dataset. Pierre de la Grange (INSERM, Paris) hosted an excellent seminar demystifying alternative splicing bioinformatics for non-specialists and explored a number of public splicing databases. He also demonstrated his own database (www.fast-db.com), which very easy to use and can also visualise Affymetrix Exon Array data.

Other techniques covered during the workshop included the design, generation, and transfection of reporter minigenes for study of alternative splicing, RNA purification and RT-PCR, localisation of GFP fusion splicing factors by microscopy, and siRNA. Of particular interest were practical sessions using two different technologies to correct mis-splicing in disease models. In the first, we used morpholino oligonucleotides to modulate splicing of the *Ron* proto-oncogene in cancer cells and in the second, we used antisense U7 snRNA to mask a splice site mutation in the β-*globin* gene and correct aberrant splicing.

Despite intensive 12-hour days in the lab, we had sufficient time to explore Montpellier's historic town centre, vibrant nightlife and even make a trip to the Mediterranean Sea! The workshop was a great opportunity to meet the experts, and try out some of the most up-to-date molecular and cellular techniques in alternative splicing. This was an excellent introductory workshop, which I would strongly recommend to researchers in the field of alternative splicing and disease. I would like to thank the organisers for hosting the event, and the Genetics Society for sponsorship towards this worthwhile and extremely enjoyable trip.

Hands on experience at the Montpellier alternative splicing workshop (courtesy Julia Kiosz)