

Non-coding RNAs in development

The BioPark Hertfordshire, Welwyn Garden City, AL7 3AX: 1st April 2011

PLEASE NOTE THAT THE DATE OF THIS MEETING HAS CHANGE TO APRIL 1st 2011

Eukaryotic gene expression is modulated at many layers of regulatory control. It is becoming apparent that differentiation and development involve the action of numerous regulatory non-protein coding RNAs (ncRNAs). This meeting will focus on the discovery and characterization of ncRNAs in the context of embryogenesis and organismal development, highlighting recent technological advances for high-throughput functional genomics. Meeting Chair: Paul Bertone, European Bioinformatics Institute, Cambridge, UK

This event has CPD accreditation and a troubleshooting panel session.

On registration you will be able to submit your questions to the panel that will be asked by the chair on the day of the event

- 9:00 – 9:45 **Registration**
- 9:45 – 10:00 **Introduction by the Chair:** *Paul Bertone*, European Bioinformatics Institute, Cambridge, UK
- 10:00 – 10:40 **The non coding code of the breast**
Dr Anna Git, Cancer Research UK Cambridge Research Institute (CRI), Li Ka Shing Centre, Robinson Way, Cambridge, UK
Breast cancer is a heterogeneous disease loosely reflecting the hierarchy of stemness and differentiation of normal breast epithelium, itself poorly understood. Using a custom microarray, we are investigating the expression of numerous classes of non-coding RNAs in a large cohort of breast tumours and cell lines as well as in normal breast epithelium and non-breast normal tissues. I shall be presenting the work that led us to select the microarray platform, the process of its customisation and preliminary results of the study itself.
- 10:40 – 11:20 **Title to be confirmed**
Dr Anton Enright, EMBL - European Bioinformatics Institute, Cambridge, UK
- 11:20 – 11:30 **Speakers photo**
- 11:30 – 12:20 **Mid-morning break**
- 12:20 – 13:00 **The complex life of small RNA**
Dr Eric Miska, Gurdon Institute, Wellcome Trust/Cancer Research UK Gurdon Institute, The Henry Wellcome Building of Cancer and Developmental Biology, Cambridge, UK
MicroRNAs (miRNAs) are 22 nucleotide small RNAs that act as endogenous regulators of gene expression by base-pairing with target mRNAs. Here we analyse the function of the six members of the *C. elegans* miR-51 family of miRNAs (miR-51, miR-52, miR-53, miR-54, miR-55, miR-56). miR-51 family miRNAs are broadly expressed from mid-embryogenesis onwards. The miR-51 family is redundantly required for embryonic development. miR-51 family mutants display a highly penetrant pharynx unattached (Pun) phenotype, where the pharyngeal muscle, the food pump of *C. elegans*, is not attached to the mouth. Unusually, the Pun phenotype in miR-51 family mutants is not due to a failure to attach, but a failure to maintain attachment during late embryogenesis. Expression of the miR-51 family in the mouth is sufficient to maintain attachment. The Fat cadherin ortholog CDH-3 is expressed in the mouth, and is a direct target of the miR-51 family miRNAs. Genetic analysis reveals that miR-51 family miRNAs act in part through CDH-3 to regulate pharynx attachment. This study is the first to assign a function to the miR-51/miR-100 miRNA family in any organism.
- 13:00 – 13:15 Oral presentations
- 13:15–14:00 **Lunch and Poster Viewing**
- 14:00 – 15:00 **Question and Answer Session**
Delegates will be asked to submit questions to a panel of experts. Questions can be submitted before the event or on the day
- 15:00 – 15:30 **Afternoon Tea/Coffee and Last Poster Viewing**

15:30– 16:10

MiR-155: a microRNA of all trades?

Dr Tilman Sanchez-Elsner, Southampton General Hospital, UK

microRNA-155 is one of the currently most studied microRNAs. Roles for this 22 nt noncoding RNA have been already proposed by several different groups, usually involving important and disparate functions in regulating the immune system. These roles range from the modulation of the expression of antibodies in B-cells to T-cell polarisation. We have shown for the first time that, by targeting three different genes, PU.1, IL13R α 1 and SMAD2, miR-155 is able to affect pathogen binding in dendritic cells, dampen the IL13 signalling pathway and reduce the profibrotic effects of TGF- β in macrophages, respectively. We thus found that, by mildly affecting several physiological roles, miR-155 might have a profound effect on the immune function of myeloid cells.

16:10 – 16:50

Connectivity Mapping of small RNAs

Dr Gerome D Breen, Kings College, London, UK

The effect of drugs on miRNA expression and the drug like action of miRNAs themselves are potentially interesting targets for both therapy and examination of miRNAs as mediators of environmental effect on mRNA and thus protein expression. I will present a pilot experiment where we have examined the effects of drugs and hormones on miRNA expression as well as the effect of miRNA in altering the response of cells to drugs and on mRNA gene expression..

16:50 - 17:00 **Chairman's summing up**

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About the chair

Paul Bertone received the PhD from Yale University and is currently a Group Leader at the EMBL European Bioinformatics Institute in Cambridge. He also holds joint appointments in the Developmental Biology and Genome Biology Units at the EMBL in Heidelberg. His work to date has included the development of novel technologies for large-scale genome annotation, protein functional analysis and computational biology. His research group is applying state-of-the-art experimental platforms and computational methods to the characterisation of stem cell lineage commitment, differentiation and reprogramming. This includes the elucidation of transcription factor-mediated gene regulatory pathways, functional characterisation of non-coding RNAs, and comprehensive transcriptome analysis using next-generation sequencing technologies.

About the Speakers

Michael Barnes is a team leader in GSK Computational Biology. His group is actively engaged in bioinformatics approaches that have shown impact across the various phases of drug discovery and development with a focus on neurosciences. Working externally, Michael has worked closely with industry and academic bioinformatics organisations to champion pre-competitive collaboration to build public tools and resources for bioinformatics. Michael has published widely and holds a visiting Senior Lecturer position at the Institute of Psychiatry, Kings College London. He is currently co-supervising a PhD student at Kings, investigating the role of miRNA in neurotransmission

Anna Git completed her B.Med.Sc. and M.Med.Sc. in Haddassah Medical School (Jerusalem, Israel), proceeding to a Ph.D. and first postdoctoral position at the Department of Biochemistry in Cambridge, UK. For the last 7 years she has been working in the laboratory of Prof. Caldas at the Department of Oncology (University of Cambridge), which recently relocated to the Cancer Research UK Cambridge Research Institute. Her research always revolved around RNA metabolism in development and disease, including regulation of translation, localisation and stability, interaction with RNA binding proteins and cytoskeleton, and more recently, the interplay between coding and non-coding RNAs.

Eric Miska received a BA in Biochemistry from Trinity College, Dublin, Ireland in 1996. He received his PhD in pathology from the University of Cambridge, Cambridge, UK in 2000. He was a postdoctoral fellow in the laboratory of Bob Horvitz at the Massachusetts Institute of Technology, Cambridge, MA, USA from 2000 to 2004.

Tilman Sanchez-Elsner studied Biology at the Universidad Complutense of Madrid, Spain, pursuing the PhD in the same University at the Department of Biochemistry and Molecular Biology (June 2002). During his PhD, Tilman focused on the transcriptional control of angiogenesis and repair in human, describing the co-operation between two transcription factors, HIF-1 α (Hypoxia Inducible Factor) and Smad3 (which mediates TGF- α inducible responses). After his PhD, he worked a postdoctoral fellow (2002-2006) at the University of California at Riverside, where he described a novel non-coding RNA, crucial for the epigenetic control of the fruit fly development. He was then interested in applying the acquired knowledge to the human model, and more specifically, to work in Immunology and hematopoietic development. He started working in the field of microRNAs since 2006, in the lab of Dr A.L. Corbi, as a senior postdoc. In this lab, he acquired expertise in the immunological techniques, as well as in the field of MicroRNAs. He decided to develop his own independent research joining University of Southampton, as a Lecturer in Biomedical Sciences of the Division of Infection, Inflammation and Repair (School of Medicine) in August 2007. He is currently engaged in several projects related to microRNA expression and function interested both in basic scientific questions as well as more clinical oriented projects. He is also involved in several cross-

disciplinary projects as the functionalisation of nanoparticles as anti-angiogenic agents, as well as developing a new sonoporation chamber that proved to be useful for delivery of plasmid DNA into cells.

Gerome Breen is the genetics coordinator of the NIHR BRc for Mental Health and a lecturer at the MRC Social Genetic and Developmental Psychiatry research centre at KCL. His research interests in bioinformatics and the genetics of common mental disorders and the aetiological links between them, and is using molecular, statistical, and bioinformatic genetic approaches to help tackle this problem. He has published over 70 papers. His core publications have been on common mental disorders such as cocaine addiction, ADHD, depression and manic depression. His most significant findings illustrated both how variants can contribute to seemingly different psychiatric disorders and how they can interact with different environmental insults/pathogens in the forms of stimulants and alcohol..

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POSTERS

An Ensembl-based pipeline for microRNA prediction and expression profiling using Next Generation Sequencing data

Nick James¹, Madhu Donepudi¹, William Spooner¹ and Michael Watson²

¹Eagle Genomics Ltd, Babraham Research Campus, Cambridge CB22 3AT, ²Bioinformatics Group, Institute for Animal Health (IAH), Compton, Newbury, RG20 7NN, UK

We have developed a workflow appliance for predicting miRNA loci and profiling miRNA expression based on short read sequences generated from small RNA libraries. Our pipeline runs on the Ensembl eHive distributed processing system for which we have built wrappers for a number of best-in-class, open-source miRNA analysis software including RNAfold, MiPred, miRDeep and DroshaSVM. Ensembl databases are used for data storage, automatically integrating results with the latest genome annotations and providing an excellent and widely used interface for data access. The workflow system is compatible with several cluster architectures, including Sun Grid Engine, Condor, Platform LSF, Amazon Web Services or standalone.

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