

Gene Expression and Integrity

Friday 4th April 2008, 10 am – 5 pm

Western Infirmary Lecture Theatre, University of Glasgow

Final programme

10.00 Tea/coffee welcome

4th Scottish Chromatin Group meeting

10.30 - 11.10 **Dr. Marie-Noëlle Prioleau**, Institut Jacques-Monod, Paris

Genome-wide mapping of human replication origins reveals a link to transcription regulatory elements

11.10 - 11.40 **Dr. Grainne Barkess** (Katherine West's group), University of Glasgow

Stimulation of gene expression by the nucleosome binding protein HMGN3

11.40 - 12.25 **Dr. Jesper Svejstrup**, CRUK, London

Contending with obstacles to transcription

12.25 - 13.15 LUNCH (50 mins)

13.15 - 13.45 **Dr. Jacqueline Dickson** (Adam West's group), University of Glasgow

A role for the chromatin barrier protein BGP1 in protection from DNA methylation

13.45 - 14.30 **Prof. Doug Higgs**, MRC, Oxford

Switching genes on and off during blood development

14.30 - 15.10 Tea/coffee (40 mins)

2008 Tenovus-Scotland Medal Lecture

15.10 - 15.20 Introduction by Prof. Sir Roddy MacSween, chairman of Tenovus-Scotland

15.20 - 16.20 **Prof. Darren Monckton**, University of Glasgow

Unstable DNA and human disease: when DNA repair goes bad

16.20 - 16.30 Medal presentation Prof. Paul Hagan, FRSE

16.30 Wine reception

2008 Tenovus-Scotland Medal Lecture

Darren Monckton, University of Glasgow

Unstable DNA and human disease: when DNA repair goes bad

The genetic material, DNA, contains all of the information necessary to build an entire human being, but even one mistake in the six billion bases of DNA that are passed on from one generation to the next can cause devastating inherited disease. Fortunately, millions of years of natural selection has resulted in the evolution of multiple DNA repair systems that act to ensure that DNA is faithfully copied from one cell to the next and from generation to generation, and maintained intact throughout the lifetime of the individual. Thus, DNA is usually accurately transmitted from one generation to the next and disease causing new mutations are usually very rare. However, this paradigm has been shattered by the discovery of the molecular basis of a group of disorders, including myotonic dystrophy and Huntington disease, that share features of wide symptomatic variability and bizarre inheritance patterns. In these disorders, a simple sequence repeat within the gene expands beyond the range usually observed in the general population. Longer repeat tracts are associated with more severe symptoms and an earlier age of onset. Once into the disease associated range, the DNA simple sequence repeats become dramatically unstable and nearly always increases in length when transmitted from one generation to the next. Hence, the symptoms are more severe and appear earlier in successive generations, a phenomenon termed anticipation.

It has also become apparent that expanded repeat tracts are also highly unstable in the somatic tissues of the body in a process that is age-dependent, tissue-specific and highly expansion-biased, properties that contribute toward both the tissue-specificity and progressive nature of the symptoms. Contrary to expectations, these mutations do not occur when the DNA is being copied from one cell to another. Even more unexpectedly, the process of repeat expansion actually requires the activity of DNA mismatch repair enzymes; proteins whose normal function is to prevent the accumulation of mutations. In addition to these trans-acting genetic modifiers, it is also apparent that repeat expansion is subject to major genomic position effects. The precise nature of these cis-acting modifiers has proven more elusive, but it is clear that there is a strong correlation with instability and the GC content of the flanking DNA, with recent data suggesting that epigenetic modifications may also be critical. In addition to the exciting insights into DNA metabolism that these data reveal, they also suggest the genetic instability underlying these disease might be a direct target for therapeutic intervention. Indeed, we have already demonstrated that it is possible to slow the rate expansion using small molecule drugs. Slowing the rate of expansion is expected to be therapeutically beneficial, but our long term aim remains the induction of the contractions that we predict to be curative.

The meeting organisers

Scottish Chromatin Group

The Scottish Chromatin Group was established by Nick Gilbert (Edinburgh) and Adam West (Glasgow) in 2006 to bring together researchers from across Scotland to discuss common interests in chromatin and chromosome structure and function. Meetings are held twice a year in Edinburgh and Glasgow. The aim is to involve and reflect the interests of researchers across Scotland.

Meetings comprise of a number of excellent seminars with plenty of time for questions and discussion followed by refreshments. A speaker from outside Scotland is invited to each meeting. We also invite junior researchers to present work that is close to publication.

www.scottishchromatin.co.uk

Tenovus Scotland and the University of Glasgow

Since 1969, the charity TENOVUS SCOTLAND has supported innovative medical research within Scottish Universities and teaching hospitals. Tenovus Scotland, supported by private donations and fundraising events, funds the full spectrum of medical sciences. Our principle aim is to assist young research staff, who have yet to establish a track record, with small grants to get their research programmes underway.

www.tenovus-scotland.org.uk

Another major activity of Tenovus Scotland is to support high profile lectures and Symposia organised at the University of Glasgow that are focused on basic processes in the broad area of gene biology.

The annual Tenovus Medal Lecture is awarded to a young investigator with a Scottish link who has made a major impact in the field of gene biology. The 2008 Tenovus Medal is awarded to Prof. Darren Monckton of the University of Glasgow.

The triennial Symposia are focussed on basic processes in the broad area of gene biology. The two-day Symposia are held in Glasgow and are aimed at junior scientists, so registration fees are low.

The Tenovus Scotland Symposium Committee are

Co-chairs	Prof. Saveria Campo	Infection and immunity, University of Glasgow
	Dr. Sheila Graham	Infection and immunity, University of Glasgow
Secretary	Prof. David Gillespie	The Beatson Institute for Cancer Research
Treasurer	Prof. Gordon Lindsay	Biochemistry & Molecular Biology, University of Glasgow
Advisory Committee		
	Dr. Nia Bryant	Biochemistry & Molecular Biology, University of Glasgow
	Dr. Gareth Inman	The Beatson Institute for Cancer Research
	Dr. Adam West	Pathology and Gene Regulation, University of Glasgow
	Dr. Joanna Wilson	Molecular Genetics, University of Glasgow
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