

Centre for Health & Bioinformatics

Visiting Speaker

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8th February 2018

16.00 – Lecture Theatre West Wing ICfL

The Landscape of Alternative Splicing during Ageing and Calorie Restriction across the Mouse Lifespan

This presentation will provide a snapshot of gene expression and alternative splicing analysis carried out on RNA-seq data from mouse liver tissue at multiple ages across the life span. The samples analysed were part of the Newcastle Main Study carried out at the Institute for Ageing, and consist of a cohort that aged normally, and one that aged slowly as a result of being placed under 40% calorie restriction.

I will use this dataset to illustrate the analysis of time-course data including clustering analyses and functional annotation to uncover patterns of co-regulated gene expression that are perturbed during ageing, and rescued by calorie restriction. Furthermore, I will present recent results showing that age-related gene expression changes, especially in very old age are primarily driven by alternative splicing switches.

Followed by:

Post lecture networking – ICfL

To attend the lecture, please book a place at:

<https://forms.ncl.ac.uk/view.php?id=1199983>

Sushma Grellscheid



Biography

Sushma Grellscheid received her PhD in RNA Biochemistry in 2004 from the University of Cambridge, UK. Her post-doctoral work at the University of Cologne and Newcastle University was on RNA biology in Human Genetics, and Ageing followed by research fellowships at the European Bioinformatics Institute (EMBL-EBI, Cambridge, 2011-2012), and Durham University (Addison Wheeler 2012-2015). She was appointed Assistant Professor in RNA Genomics at Durham University in October 2015.

Research

We are interested in understanding the regulation of gene expression during ageing and senescence, with a focus on RNA alternative splicing and translation control by RNA binding proteins. We employ a combination of wet-lab and informatics approaches to interrogate the regulatory networks controlling gene expression from transcription (RNA-seq), through to RNA processing (RNA-seq, CLIP) and translation (ribosome profiling). We focus especially on cellular stress responses to oxidative stress in young versus senescent cells.

Selected Publications:

- Mikolaj Ogronik et al, *Cellular senescence drives age-dependent hepatic steatosis*. **Nature Communications**. 2017 Jun 13; PMID: 28608850
- Feracci M et al, *Structural basis of RNA recognition and dimerization by the STAR proteins T-STAR and Sam68*. **Nature Communications**. 2016 Jan 13; PMID: 26758068.
- Ghosh P et al, *A tale of two paralogs: human Transformer2 proteins with differential RNA-binding affinities*. **J Biomol Struct Dyn**. 2016 Sep; PMID: 26414300.
- Invited Book Chapters “*Differential mRNA Alternative Splicing*” by Albert Lahat and **S. Grellscheid***, and “*Ribosome Profiling*” by Anze Zupanic and **S. Grellscheid***, in: *Field Guidelines for Genetic Experimental Designs in High-Throughput Sequencing*, edited by Ana M. Aransay, José Luis Lavín Trueba, Springer.
- Holly AC et al, *Comparison of senescence-associated miRNAs in primary skin and lung fibroblasts*. **Biogerontology**. 2015 Aug; PMID: 25700689.
- Zupanic A et al, *Detecting translational regulation by change point analysis of ribosome profiling data sets*. **RNA**. 2014 Oct; PMID: 25147239.
- Thedieck K et al, *Inhibition of mTORC1 by astrin and stress granules prevents apoptosis in cancer cells*. **Cell**. 2013 Aug; PMID: 23953116
- **Grellscheid S et al**, *Identification of evolutionarily conserved exons as regulated targets for the splicing activator tra2b in development*. **PLoS Genet**. 2011 Dec; PMID: 22194695
- **Grellscheid S et al**, *Molecular design of a splicing switch responsive to the RNA binding protein Tra2b*. **Nucleic Acids Res**. 2011 Oct; PMID: 21724598