

The sixth South West Fly Meeting was held at the Biomedical Sciences Building, University of Bristol on Wednesday 13 June 2018. Dr Angelique Lamaze (Dr James Jepson's lab) (UCL) spoke about the circadian integration of environmental changes in *Drosophila*. She looked at the longest sleep bout response of flies after exposure to 30°C and showed the response was clock dependent and mediated by TrpA1 and Dorsal Neuron posterior (DN1p) clock neurons. Using a range of opto/thermo-genetic approaches she found the DN1p projected to the Anterior Optic Tubercle and noted that the flies' day and night sleep were very different. Dr Owen Peters (Cardiff University) spoke about his lab's work on the functions of conserved Alzheimer's Disease (AD) risk genes in the *Drosophila* nervous system. He compared the effect of overexpression of human AD causal genes with RNAi mediated loss of function of fly orthologs of a number of AD risk genes nominated from GWAS performed at Cardiff Dementia Research Institute (DRI). They compared the effect of neuronal and glia misexpression of the genes, measuring lifespan, neurodegeneration, locomotor and ERG electrophysiological defects. Another freshly minted DRI lecturer, Dr Gaynor Smith spoke about the genetics of axonal mitochondrial biology, this process is fundamentally important but also relevant to Parkinson's disease (PD) which is associated with a range of mitochondrial genes and defects e.g. Pink and Park PD genes controlling mitochondrial fission. Harnessing the power of *Drosophila* forward genetic screens, she imaged mitochondria in wing neurons with *OK371-Gal4>uas-tomato, uas-mito-GFP* and performed a MARCM based embryonic lethal screen using Next Generation Sequencing to identify mutants with interesting mitochondrial phenotypes. She went to identify some of her hits, performed genetic rescue and verified results with orthologues in human cell culture.

Dr Katia Jindrich from Prof Helen White-Cooper lab at Cardiff University described her cutting edge molecular biological characterisation of non-canonical nucleosome positioning in *Drosophila* testis. In the latest MNaseSeq she set out to map nucleosome positioning in wildtype and Meiotic arrest mutant testes, find 816 genes that lost their expression which is following up on. Jack Curran from Dr James Hodge lab at University of Bristol spoke about his thesis work using *Drosophila* to determine the effect of ageing on circadian rhythms and sleep. He showed like humans, flies have progressively weaker and longer rhythms as they age and this was accompanied by more sleep and change in clock neuron excitability and structural plasticity. He also performed a screen of rhythmically expressed clock neuron ion channels revealing specific effects on circadian rhythms and sleep. He has therefore elucidated key components of the mysterious membrane clock which can be considered future targets for treatments for ageing insomniacs. Following on nicely from the earlier talks of the day, James Higham presented his work determining the effect of pathological isoforms of human tau associated with AD. James elegantly showed that like in AD, tau results in loss of fly memory, circadian rhythms and sleep. He showed that he was able to take clinically relevant drugs to reverse some of the hyperexcitability caused by neuronal expression of tau, using a clever combination of calcium imaging of memory neurons and pharmacology. He showed for the first time the effect of human tau on neuronal excitability of clock neurons which include increasing firing at night, thereby removing the circadian change in firing across the day, preventing the AD fly from sleeping at night.

After the talks, there was refreshments kindly provided by the Genetics Society and SLS, and *Drosophila* researchers continued to discuss their results, planned experiments and role of the fly in science and beyond. If you are interested in attending or presenting at this meeting please contact james.hodge@bristol.ac.uk.



Spot the four humanised *Drosophila* mutants (left to right) at the launch of the new Invisible Worlds building at the Eden Project. Answered will be revealed next time.