abstracts: poster presentations

ASCB | EMBO
2017 meeting

Pennsylvania Convention Center

Philadelphia, USA | December 2-6

ascb-embo17.ascb.org | **#ascbembo17**

President: Pietro De Camilli
Program Co-Chairs: Laura Machesky
and **Tobias Walther**

Download the Meeting App
Search for "ascbembo17"

has proven to be a particularly powerful system to dissect the function of novel cilia genes because cilia are exclusively found in post-mitotic neurons, which are dispensable for viability and fertility. The availability of a wide range of ciliary markers, together with the stereotypical pattern of nematode development, makes it easy to characterize the role of novel proteins involved in cilium biogenesis. Of the 386 human genes whose inheritance pattern is characteristic of cilia, 135 are conserved in C. elegans including a set of 60 novel genes. Preliminary characterization of available mutants revealed a number of additional cilia genes. This poster will present the primary data from our screen, as well as more detailed characterization by light and electron microscopy of several of these novel proteins, including an apparent regulator of cilium biogenesis conserved across eukaryotes.

P2027

Board Number: B167

TrypTag.org – Genome wide protein localisation reveals organelle sub-domains, with functional consequences in the flagellum.

J.D. Sunter[1], R.J. Wheeler[2], S. Dean[2], B. Edwards[2], K. Gull[2];
[1]Department of Biological and Medical Sciences, Oxford Brookes University, Oxford, United Kingdom,
[2]Sir William Dunn School of Pathology, University of Oxford, Oxford, United Kingdom

Organelles have highly organised, complex internal structures that enable them to perform a diverse set of biological functions. Analysing this complex structural organisation on a genome-wide scale, using methods like mass spectrometry is typically extremely challenging and often loses fine-scale structural resolution. To address this, we are determining the localisation of every protein encoded in the *Trypanosoma brucei* genome using our high-throughput tagging methodology and automated quantitative image analysis of cell ultrastructure. Trypanosomes are ideal for this study as they combine an exquisitely ordered cellular architecture with conserved core eukaryotic biology. Trypanosome organelles have precisely defined positions/distributions in the cell, and inter-organelle contact occurs at specific positions; crucially they have greater internal order than yeast cells or typical human cell lines. To date we have localised over 80% of the 8129 proteins encoded in the genome and the data we are generating is made freely available on our website http://tryptag.org. We have shown many proteins localise to specific organelle sub-domains and this organelle asymmetry/inhomogeneity applies to all organelles, including the flagellum, endoplasmic reticulum and mitochondrion. Here, as one example, we concentrate on our comprehensive molecular cartography of the flagellum and the role of protein asymmetry within the flagellum. So far, we have found 43 proteins that localised to the proximal region of the flagellum only, 29 to the distal region only, 62 flagellar tip proteins and 289 proteins in the basal body or transition zone. Comparable asymmetry of protein localisation was also observed for flagellar membrane proteins. The cohort of distal flagellum proteins included orthologs of the docking complex proteins DC1 and DC2, required for attaching the outer dynein arms to the microtubule doublets of the axoneme. We showed there are also proximal flagellum DC1-like and DC2-like orthologs. This proximal/distal asymmetry is important for flagellum beat control in trypanosomes, and predicts tissue-specific control of flagellum beat by DC1 and DC2 orthologs in humans. This one example of exploiting the Tryptag dataset has identified a new candidate ciliopathy gene and produced a map at molecular detail of the entire flagellum. TrypTag is a rich dataset that will help define organelle sub-domains and therefore refine overall organelle function with implications for the entire eukaryotic cell biology field.