HSCs, which could be abrogated by dose dependent inhibition of PDGFRA signalling.

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PS2.10

Rho differentially regulates the Hippo pathway by modulating the interaction between Amot and Nf2 in the blastocyst

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The Hippo pathway modulates the transcriptional activity of Yap to regulate the differentiation of the inner cell mass (ICM) and the trophectoderm (TE) in blastocysts. Yet, how Hippo signaling is differentially regulated in ICM and TE cells is poorly understood. Through an inhibitor/activator screen, we identified Rho as a negative regulator of Hippo in TE cells, and PKA as a positive regulator of Hippo in ICM cells. We further elucidated a novel mechanism for Rho to suppress Hippo, distinct to the prevailing view that Rho inhibits Hippo signaling through modulating cytoskeleton remodeling and/or cell polarity. Active Rho prevents the phosphorylation of Amot Ser176, thus stabilizing the interaction between Amot and F-actin, and restricting the binding between Amot and Nf2. Moreover, Rho attenuates the interaction between Amot and F-actin by binding to the coiled-coil domain of Amot. Through blocking the association of Nf2 and Amot, Rho suppresses Hippo in TE cells.

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PS2.11

Identifying the Alternative Receptor of ELABELA in hESCs

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ELABELA (ELA) is a highly conserved hormone required for heart development and vasculogenesis. These processes are mediated by its cognate GPCR, the Apelin Receptor (APLNR, APJ). Surprisingly, in human embryonic stem cells (hESCs), which do not express APLNR, ELA is abundantly secreted and is essential for maintaining pluripotency and self-renewal. Endogenous ELA is taken up by hESCs in a paracrine manner through an unknown receptor, and signals through the PI3K/AKT pathway, to promote survival and priming toward mesendodermal lineage. Consistently, ELA is highly enriched in the blastocyst, implying that it may play a similar function in pre-implantation human embryos. In order to identify ELA's second receptor in hESCs, we utilized an unbiased ligand-receptor capture crosslinking approach on cultured cells. Through this endeavour, several candidates have been identified and are being validated.

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PS2.12

Asymmetric morphogenesis of the parapineal organ in the embryonic zebrafish brain

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Introduction: The establishment of asymmetry in the embryonic zebrafish brain begins with the left-sided asymmetric positioning of the parapineal organ (PpO), an event that is required for further development of asymmetries in neighbouring diencephalic nuclei. Previous studies have shown that PpO asymmetric morphogenesis requires Nodal and Fgf8 dependent signalling but the cellular behaviours that are controlled by these signalling pathways are still unclear. Here we investigated these behaviours.

Material and Methods: We developed and applied mathematical computational image processing tools for *in vivo* 3D microscopy datasets, which were combined with indirect immunofluorescence to unravel the transformations of neuroepithelial cell morphology and organisation underlying PpO formation in *Tg(flh::EGFP)* zebrafish embryos.

Results: We found that precursor cells of the PpO display early left-right differences in cell behaviour during the process of nucleogenesis. Left-sided precursors contract their axis of elongation while right-sided precursors move across the midline to assemble with left-sided precursors and form a left-sided compact cluster organised in a 3 dimensional rosette. This process precedes the detachment of the PpO from de pineal complex.

Discussion: Establishment of asymmetry in the PpO involves the concerted organisation of precursor cells into a rosette-like structure on the left-side, which is the seed for further transformation of PpO precursors into an asymmetric nucleus. These results will be contrasted with conditions devoid of Nodal and Fgf8 signalling.

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PS2.13

Mitochondrial dynamics and oxidative phosphorylation in neuroblast differentiation in the Drosophila brain

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Neuroblasts differentiation gives rise to the cells of the nervous system in Drosophila melanogaster. This process is tightly regulated by variety of signaling pathways such as Notch-Delta pathway. Here we have assessed the role of mitochondrial dynamics and oxidative phosphorylation (OxPhos) in neuroblasts differentiation. We found that depletion of mitochondrial membrane fusion protein and two components of OxPhos caused reduction of ganglion mother cells (GMCs). Lineage specific analysis of type II neuroblasts showed reduction in mature intermediate neural precursor (INP) and GMC number together showing that differentiated cells are depleted. Mitochondrial fusion and OxPhos downregulation caused subsequent increase in cytochrome C and reactive oxygen species (ROS) level, however polarity and neuroblast proliferation remained unaffected. Increased cytochrome C levels in these mutants indicated a role of cristae morphology in neuroblast differentiation. Further analysis of the Notch signaling pathway showed that the Notch Intracellular domain was depleted from ganglion mother cells and present in vesicular pools in neuroblasts indicating a possible lowering of Notch signaling in these cells. Future analysis of changes in Calcium, ROS and Cytochrome C will allow a dissection of the mechanism by which Notch mediated differentiation is affected by perturbing mitochondrial morphology and activity in neuroblasts.

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