We examined that down-regulation of Miro enhanced the rough eye phenotype associated with AD flies. Further, RT-qPCR showed that AD genes such as Appl and Tau expression level were altered in Miro overexpressing/Downregulating flies. Thus, on the basis of results it was concluded that Miro interacts with AD genes in Drosophila and it could be a new therapeutic target for AD disease.

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PS4.44

The signal regulation of Wnt-Ror-Dsh pathway in neurites outgrowth in C. elegans

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Neurites outgrowth and extension are critical for the precise connection between neurons and their target cells during neural development. Guidance cues act on guidance receptors at the surface of growth cones to regulate the underlying cytoskeleton dynamics. Besides the four well-known families, Netrin, Slit, Ephrin and Semaphorin, classic morphogens including Sonic hedgehog (Shh), bone morphogenetic proteins (BMPs), and Wnts, can also guide axons. However, when axons navigate their way in vivo, at every choice point they are probably confronted with several different signals and many remain to be learned how multiple signals are integrated by the growth cones to make the correct decisions on path-finding.

Through an unbiased genetic screen in *C. elegans*, we previously identified a Wnt-Frz/Ror-Dsh pathway involved in the regulation of RMED/V neurites outgrowth. Specifically, the RTK-like orphan receptor Ror2/CAM-1 functions as Wnt co-receptor in this process. In contrast to complete neurites loss in the full-loss-function *cam-1(gm122)* mutant worms, the *cam-1(ks52)* and *cam-1(gm105)* alleles with the majority of intracellular domain being disrupted display distinctive but much weaker RMED/V neurite outgrowth defect, suggesting that other signal components may facilitate the signal transduction from CWN-2 to DSH-1 together with CAM-1. To reveal the additional regulatory mechanism underlying CAM-1-mediated RMED/V outgrowth, we did yeast two-hybrid screen to seek the interacting partner of CAM-1 protein. From this screen, we identified additional signal receptors and downstream effectors involved in Wnt-Ror-Dsh-mediated neurite outgrowth. Detailed analysis is undergoing and corresponding results will be reported in this meeting.

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PS4.45

Sleep/wake disorders and the hypocretin/orexin system in a zebrafish model of Parkinson's Disease

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Introduction: Sleep/wake alterations are non-motor symptoms present in various neurological disorders including Parkinson's Disease (PD). Hypocretin/orexin, whose deficit is the main cause of narcolepsy, is involved in sleep/wake regulation. Since zebrafish is a suitable model for PD and sleep/wake behaviour, we evaluated the sleep/wake changes associated with alterations in the hypocretin (Hcrt) system in a PD zebrafish model.

Material and methods: We challenged 2 dpf zebrafish larvae with 6-hidroxidopamine (6-OHDA) during 72 hours using WT and Tg(Hcrt:EGFP) lines. Dopaminergic and Hcrt neurones were examined and quantified by anti-tyrosine hydroxylase (TH), anti-GFP immunostaining and confocal imaging. TH neurons and Hcrt receptor were also observed by in situ hybridisation. Locomotor activity during day and night was measured with an automated tracking video system (TrackFish).

Results: The number of expressing TH (protein and mRNA) and Hcrt neurons decreased after 6-OHDA. The diencephalic 5-6-11 groups of aminergic cells, which resemble the mammalian substantia nigra, were sensitive to 6-OHDA. We found defects in zebrafish locomotor activity, i.e. distance travelled and swimming speed and sleep/wake pattern. Locomotion, but not number of TH neurons, improved after two-day recovery following 6-OHDA.

Discussion: Results suggest that 6-OHDA induces a behavioural disorder in zebrafish larvae. Alterations may arise from a reduced 5-6-11 dopaminergic population and/or be secondary to the reduced number and activity of Hcrt neurons.

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PS4.46

Zeb2 controls the output of the young postnatal neurogenic niche

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In the adult mouse brain, the subventricular zone (SVZ) of the lateral ventricle produces immature neuroblasts that migrate along the rostral migratory stream (RMS) to the olfactory bulb (OB), where they integrate as interneurons in the existing cellular network. The bulk of the SVZ niche develops from the lateral ganglionic eminence (LGE), which during embryonic development also generates medium spiny neurons and contributes to the formation of the amygdala. The molecular program that determines the fate and number of the cells generated in this region is currently less well understood.

We used the Gsh2-*Cre* mouse line to conditionally remove the transcription factor Zeb2 from the LGE during embryonic life. In the mutant, proliferation in the SVZ was reduced leading to a decrease in neurons arriving in the OB. As a result, the mutant OBs appeared smaller and disorganized at postnatal day 5. Tracing of early postnatally generated OB interneurons by electroporation revealed a severe defect in migration to the OB, which could be restored by re-introducing full length Zeb2. Transcriptome profiling of Zeb2 KO cells isolated from the young postnatal SVZ clearly indicated an increased striatal interneuron gene expression profile at the expense of medium spiny neuron markers. In particular Sox6, a transcription factor that is absent from most olfactory lobe