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MODELLING MENTAL RETARDATION IN FLIES: DISSECTING MOLECULAR NETWORKS UNDERLYING COGNITIVE FUNCTION

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Functioning of the brain relies on the ability of neurons to organize into complex networks and to remodel these networks in response to learning and experience. Studying monogenic causes of Mental Retardation (MR) provides an excellent starting point into understanding these processes. To date, more than 420 MR genes have been identified. Despite this advance, little is known about the function of most of these genes. Our research aims at providing an overview on MR gene function in the nervous system using *Drosophila melanogaster* as a model organism. In order to study the function of MR genes in *Drosophila*, large scale RNA interference (RNAi) screens are performed. MR gene knock-down flies can be investigated for defects, for instance in neuronal architecture, function and cognitive behaviour of the fly. Because genes that cause similar phenotypes likely operate together, the functional data generated by our screens will be subjected to bioinformatic phenoclustering to predict groups of MR genes acting in the same pathway. We aim to dissect these pathways and identify novel molecular players and interactions. In my PhD project, I systematically dissect the role of all fly orthologues of human MR genes in neuronal function and development. My RNAi screen is focused on *Drosophila* photoreceptor neurons, for which I have established a phototaxis assay. Adult flies walk towards light, if their photoreceptors are functionally intact. The ability of flies to see light can be quantitatively assessed with high resolution in my assay, which is used as a simple read out to measure photoreceptor functionality. Using this method we already identified some first exiting genes that give a phenotype in photoreceptor functionality in development, amongst others: TBCE, Lis-1, TUBA and SNAP29. I will present these and other interesting findings and my strategy to identify different phenotypic groups amongst MR genes.