During the course of the project I have been characterizing expression profiles of *Drosophila* homologs of human genes, which are considered to cause mental retardation, when their biological function is impaired (MR genes). These human genes were identified in a large genome screen of affected patients and their healthy relatives and the list have been systematically assembled and extended in GENCODYS project (www.gencodys.eu). The list of *Drosophila* homologs of human MR genes currently consists of more than 350 *Drosophila* genes.

I focused on screening of GFP-tagged protein expression in *Drosophila* adult brains and additionally in embryos. I took advantage of FlyFos transgenic *Drosophila* lines that express each GFP-tagged gene under the control of their endogenous genomic regulatory elements. The expression pattern of tagged genes should therefore reflect that of natural (untagged) gene. These lines are currently generated for whole *Drosophila* genome, typically tagged C-terminally. In addition to this, we generated N-terminally tagged lines for selected genes of specific interest. To date we obtained 226 transgenic lines relevant to the project. They cover altogether 145 *Drosophila* genes homologous to human MR genes.

About two third of the so far screened lines have detectable protein expression in adult brain after immunostaining. Interestingly, expression patterns can be categorized into five following groups (based on their intracellular localization and distribution throughout the brain):

1. In nuclei of only some cells (12 % of all screened lines, **fig. 1a-b**).
2. In nuclei of apparently all cells (18 %, **fig. 1c**), expressed at comparable level in all nuclei.
3. In cytoplasm of cell bodies (15 %), detectable either in only some cells (**fig. 1d**) or with strongly enhanced expression in some cells (**fig. 1e-f**).
4. In or close to all cell body membranes (but not around neuronal projections) (15 %, **fig. 1g-h**).
5. In neuropiles (9%), homogeneously expressed in each single neuropile domain with two or more different levels of expression among all domains (e.g. increased in MB neuropile as on **fig. 1i).**

The above categorization is of course strongly simplified and thus somewhat arbitrary. About 12 % of genes with detectable expression combine two of above defined groups (e.g Lis1 protein is localized in cytoplasm of cell bodies and in neuropiles, **fig. 1e-f**) and there are also some proteins which expression pattern does not fit any category, e.g. one line has an exceptional axonal localization restricted to only few axon bundles.

Generally, it is possible to identify genes that are expressed uniformly throughout the brain (e.g. in all nuclei and with the seemingly same expression level). These genes can be important for gene expression or synapse activity and thus their impaired function is deleterious for cognitive processes. The other genes, which are not expressed uniformly (e.g. enhanced strongly in some cell bodies or neuropile domains), deserve future focus and identification of cell types in which they are expressed. Initially, it should be determined whether they are expressed in glia or

neurons. After that, it is possible to identify the specific neuron types, preferably by co-localization with distinct known neuronal type markers. This specification will not only help to characterize the function of studied gene in developed adult brain but also has a potential to provide other clues on the *Drosophila* brain organization.

About 31 % of screened genes have no detectable expression in *Drosophila* adult brain. They probably either play their role during the brain development rather than in maintenance of adult cognitive function or possibly do not form functional protein because of the GFP-tag.

The data collected during the duration of the project will form a base for creation of publicly available 3D atlas of protein expression profiles in *Drosophila* adult brains. We believe that this atlas will contribute to studies of *Drosophila* brain organization and to understanding of the function of studied *Drosophila* genes and their human MR homologs.

Fig. 1. Typical expression patterns of GFP-tagged proteins from our set

Z-stacks projections of confocal images of brains from adult fly Drosophila melanogaster (a-e, h-i) or single slices (f-g) from a brains shown in e and h, respectively. Rectangles on e+f and g+h highlight the same area. Depicted are typical nuclear (a-c), cytoplasmic (d-f; cell bodies are pointed at by arrows), cell body membrane related (g-h), and neuropile specific (i) expression patterns as described in the text above.