

## Masters thesis bridging basic science and translational biology in neuroscience

Title: Disease modeling / drug screening in a genetic mitochondrial disorder

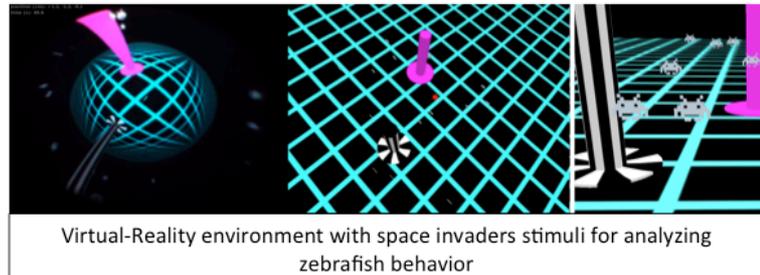
Topic: Genetic diseases causing epilepsy not only affect the patients but also people surrounding them. Wolf Hirschhorn syndrome (WHS) is one of such diseases leading to epilepsy and LETM1 is among the genes deleted in this disorder. Although substantial progress has been made, the molecular and cellular understanding of WHS with respect to LETM1 is far from complete owing to early lethality in homozygous patients [1]. As a result, the field relies on model systems for their better understanding [2, 3]. Zebrafish is emerging as a great tool to identify molecular mechanisms underlying such disorders and provides an opportunity for drug screening.

The goals of the project are:

1.) to establish the zebrafish disease model for uncovering molecular mechanisms and ultimately drug screening.

2.) to understand the cell biology of the disease in primary cells. The thesis

offers excellent opportunities to acquire knowledge in several methods ranging from CRISPR/Cas9 based genome editing, zebrafish genetics, biochemistry, molecular biology, cell culture, high resolution fluorescent microscopy and behavioral assays. Part of the behavioral assays can employ novel virtual reality paradigms, testing higher order brain functions in fish (Fig. and [4])



The Master's thesis will be performed in the groups of Dr Karin Nowikovsky (Specialization: Cell biology of LETM1 at the Medical University) and Dr Kristin-Tessmar Raible (Specialization: Genetics and Behavior in several animal models including zebrafish at the MFPL/ University of Vienna). The Nowikovsky lab is located in Anna Spiegel Center of Translational Research, AKH campus and Tessmar lab is located at MFPL, Vienna Biocenter, providing an interesting blend of stimulating translational and basic research settings for the project. Interested students should contact Dr. Sarfaraz Farooqui (e-mail: [farooquis31@univie.ac.at](mailto:farooquis31@univie.ac.at)), cc'ed to [kristin.tessmar@mfpl.ac.at](mailto:kristin.tessmar@mfpl.ac.at) and [karin.nowikovsky@meduniwien.ac.at](mailto:karin.nowikovsky@meduniwien.ac.at).

Please include a short motivation statement, CV and a short summary of your Bachelor's thesis/ previous practical experience(s), as well as two contact names for possible letters of recommendation.

### Literature:

1. Zhang, X., et al., *Association of mitochondrial letm1 with epileptic seizures*. Cereb Cortex, 2014. **24**(10): p. 2533-40.
2. McQuibban, A.G., et al., *A Drosophila mutant of LETM1, a candidate gene for seizures in Wolf-Hirschhorn syndrome*. Hum Mol Genet, 2010. **19**(6): p. 987-1000.
3. Nowikovsky, K., et al., *Mdm38 protein depletion causes loss of mitochondrial K<sup>+</sup>/H<sup>+</sup> exchange activity, osmotic swelling and mitophagy*. Cell Death Differ, 2007. **14**(9): p. 1647-56.
4. John R. Stowers, M.H., Johannes Griessner, Peter Higgins, Sarfarazhussain Farooqui, Ruth M. Fischer, Karin Nowikovsky, Wulf Haubensak, Kristin Tessmar-Raible, Andrew D. Straw, *Virtual Reality for Freely Moving Animals*. Nature Methods (Under Review), 2016.