

Project 9.3 Influence of environmental factors related to maternal infection during pregnancy on the development of neuropsychiatric disorders in offspring with Tuberous Sclerosis Complex in the zebrafish model. (NCN/SONATA BIS)

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Background:

Tuberous Sclerosis Complex (TSC) is caused by mutations in genes encoding TSC1 or TSC2 proteins and manifests by tumours, epilepsy and TSC-associated neuropsychiatric disorders (TANDs), such as autism spectrum disorder (ASD), anxiety, and intellectual disability. In TSC patients, TANDs exhibit variable expressivity and do not fully correlate with the hyperactivation of mTORC1, which is thought to be responsible for the development of tumours and epilepsy. This suggests that environmental factors play a role in the pathogenesis of neuropsychiatric disorders. Our data indicates that white matter and long-distance inter-hemispheric connections regulate anxiety-like behaviour in the zebrafish model of TSC. Also in the TSC patients with diagnosed ASD, connectivity of white matter fibres across multiple regions was impaired within the first two years of life. It indicates that environmental factors may influence the development of white matter fibres to produce neuropsychiatric disorders like anxiety or ASD.

Aim:

The project aims to answer how various environmental insults related to infection during pregnancy interact with changes caused by genetic mutation and how these interactions shape connectivity development and brain function to regulate specific behaviours related to neuropsychiatric disorders. With the use of an integrative, multi-level, and unbiased approach, we aim to unravel environmental influence on early brain development with the primary focus on ASD, anxiety, and ASD- and ID-related learning disabilities using zebrafish semi- and high-throughput behavioural tests, cutting-edge microscopy, and computer vision techniques.

Requirements:

- Master's degree in biology, biochemistry or related field,
- solid knowledge in at least one of the following disciplines: neuroscience, developmental biology, molecular biology, biochemistry, or microscopy and novel imaging techniques,
- solid understanding of the principles of brain development,
- basic hands-on experience in one of the fields: molecular biology, cell biology, fluorescent microscopy,
- willingness to work with a zebrafish animal model,
- prior experience in working with animal models (mouse or zebrafish), as well as basic programming skills would be an advantage but not essential,
- keen interest in neurodevelopment, connectivity development, and molecular mechanisms underlying behavior,
- written and spoken fluency in English,
- willingness to learn and take new challenges, ability to work independently, analytical thinking,
- good interpersonal skills and a collaborative attitude.

Number of positions available: 1

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