Project 9.4. Rac1 contribution to brain connectivity impairments and neuropsychiatric disorders in Tuberous Sclerosis Complex (NCN/OPUS)

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www: https://www.iimcb.gov.pl/en/research/laboratories/5-laboratory-of-molecular-and-cellular-neurobiology-jaworski-laboratory#tab2

Background:

During the brain development specific cellular events, including establishment of neural polarity, axon elongation, and synapse formation, happen in a temporally and spatially controlled manner to establish connectivity. These temporal and spatial boundaries are created by tight regulation of intrinsic and extrinsic factors. One of major components that may perform this regulation during connectivity development is Rac1 as it links plasma membrane receptors with actin dynamics. Also, mammalian target of rapamycin (mTOR) integrates intra- and extracellular factors. The diseases associated with over-expression of mTOR usually exhibit impairments of the brain development and neuropsychiatric phenotypes that do not necessarily correlate with mutation burden or cannot necessarily be explained by levels of mTOR activation. One of the examples is Tuberous Sclerosis Complex (TSC) in which neuropsychiatric disorders like autism spectrum disorder, intellectual disability, or anxiety do not fully correlate with mTOR expression levels, epilepsy, or tumor burden. Therefore, other molecular pathways must interact with mTOR pathway in order to produce these phenotypes. Our results and preliminary data suggest that Rac1 pathway and its diverse inputs may participate in the regulation of neuropsychiatric disorders in TSC through control of connectivity formation during development. The project will be conducted using zebrafish TSC model.

Aim:

The main objective of this project is to unravel how the interplay between various pathways that converge on Rac1 may participate in the brain connectivity and underlie TSC-associated neuropsychiatric disorders. The project will include behavioral testing, extensive microscopy imaging and image analysis, and transcriptome analysis.

Requirements:

- master's degree in Biology, Biochemistry, Bioinformatics, or related area
- solid understanding of the principles of molecular and cellular biology; knowledge on brain development, neuroscience, or computer vision will be a plus
- willingness to work with zebrafish animal model
- previous laboratory experience in basic molecular biology, biochemistry techniques, and/or imaging experience
- prior experience in NGS, and/or working with animal models (mouse or zebrafish), as well as basic programming skills would be an advantage although not essential
- ability to communicate fluently in English and a collaborative attitude