

FBM PhD Fellowships Call 2021

Host Laboratory: Prof. Claudia Bagni (Department of Fundamental Neurosciences, University of Lausanne)

<https://www.fbm.unil.ch/dnf/group/cellular-and-molecular-studies-of-synaptic-plasticity-and-cancer-in-intellectual-disabilities/member/bagni-claudia-bagni>

PhD project title: Regulatory mechanisms orchestrating synapse formation, plasticity, and social behaviours

Synapses are key for information processing in the brain. Deficits in synaptic structure or regulation are frequently associated to neurodevelopmental disorders such as autism spectrum disorders (ASD) and schizophrenia (SCZ). The formation and long-term plasticity of synapses requires de-novo protein synthesis, and genetic variants of factors involved in protein translation are risk factors for ASD. Still, the specific translational regulation of proteins involved in synapse formation and/or reshaping remains enigmatic. Using a genetic screen in *Drosophila*, we aim at 1) identifying factors/s that regulate the synthesis of synaptic proteins; 2) explore the role of those factors in social behaviours; 3) use FDA-approved compounds affecting protein synthesis to rescue impaired behaviours caused by mutations in the identified factors. Of note, a preliminary screen has identified interesting candidates linked to ASD. Since important regulatory mechanisms are conserved between *Drosophila* and mammals, the corresponding mouse mutants will be studied for synaptic alterations and ASD-related behaviours. This project will provide important insights into the regulation of synapse homeostasis, social behaviour, and neurodevelopmental diseases and, at the same time, allow the PhD student to grow in the field of neuroscience acquiring molecular, biochemical, genetic, and behavioural tools laying the ground for a successful career in (neuro)science.

4 publications relevant to this project

1. Kanellopoulos A.K., Mariano V, Spinazzi M, Jae Woo Y, McLean C, Pech U, Li KW, Armstrong J.D., A, Callaerts P, Smit A.B., Abrahams B.S., Fiala A, Achsel T and Bagni C (2020). Aralar sequesters GABA into hyperactive mitochondria causing social behavior deficits. *Cell*, 180(6): 1178-1197.e20.
2. Mariano V, Achsel T, Bagni C and Kanellopoulos A.K. (2020). Modelling learning and memory in *Drosophila* to understand Intellectual Disabilities. *Neuroscience*. 445:12-30.
3. Domínguez-Iturza N, Lo A.C., Shah D, Armendáriz M, Vannelli A1, Mercaldo V, Trusel M, Li K.W., Gastaldo D., Santos AR, Callaerts-Vegh Z, D'Hooge R, Mamei M, Van der Linden A, Smit A.B, Achsel T and Bagni C (2019). The autism and schizophrenia-associated protein CYFIP1 regulates bilateral brain connectivity and behaviour. *Nat. Commun.*, 1(10): 3454.
4. Bagni C and Zukin S. (2019). The Synaptic Perspective of Fragile X Syndrome and Autism Spectrum Disorder. *Neuron*. 6: 1070-1088.