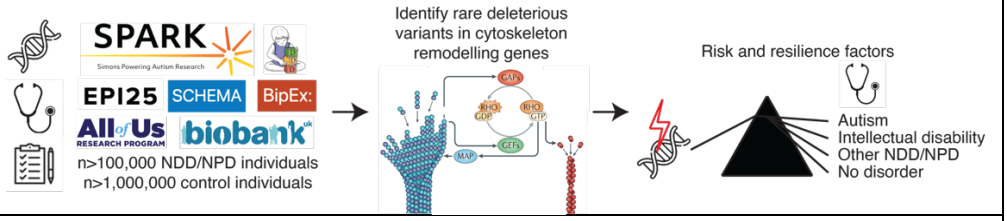
Centre de Recherche de Biologie cellulaire de Montpellier
CRBM / CNRS – Université de Montpellier
1919 Route de Mende, 34293 Montpellier Cedex 05

2027 Internship Offer

Master 1: ~~YES~~/**NO** – Duration: **Master 2**: **YES**/~~NO~~ – Duration: 5/6 months

Team, Contact	Anne Debant, Team Signaling and cytoskeleton dynamics Supervisor thomas.rolland@crbm.cnrs.fr
Title	Cytoskeleton remodelling perturbation in neurodevelopmental disorders
Research Themes and questions	In the past 20 years, important progress has been made in identifying the genetic factors involved in neurodevelopmental disorders (NDD) such as autism spectrum disorder (ASD) or intellectual disability (ID). Close to 2,000 genes can be considered as high-confidence NDD genes. Yet, carriers of rare deleterious genetic variants in NDD-associated genes display highly heterogeneous phenotypic profiles, and the mechanisms associated to this variability remain vastly unknown. NDD-associated genes converge onto a few biological processes, including synaptic development and function. Synaptogenesis is highly dependent on the dynamic remodelling of the actin and microtubule cytoskeletons, regulated by Rho GTPase signalling and by microtubule-associated proteins (MAP). Given their fundamental role, it is not surprising that genes of the Rho GTPase and MAP signalling pathways are found mutated in individuals with NDD. In the human brain, the pathways involved are very complex and dynamic, with at least six Rho GTPases having major roles in brain development, spatially and temporally regulated by more than fifty proteins. In this project, we want to better understand the relationship between genetic variants identified in proteins of the cytoskeleton remodelling pathways and different symptoms associated with NDD.
Methods and experimental approaches	The student will integrate genomic, transcriptomic and clinical data to study the complex relationship between genetic variants in cytoskeleton remodelling proteins and NDD diagnoses. He/she will analyse the expression profiles of genes throughout brain development, and the localisation of the variants in specific functional domains of the encoded proteins. Genotype-phenotype relationship models will be based on machine learning algorithms aiming at the quantification of the association between variants and NDD diagnoses, including logistic/linear regressions and phenotype-wide association studies (PheWAS).
Illustration	
2-3 Publications	Rolland et al. Nat. Med. 2023 Leblond et al. Annu. Rev. Genet. 2024 Bonnet et al. Mol. Psy. 2023