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Titre du projet : Investigating centriole linkage remodeling during the formation of a primary cilium

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

Centrioles are cylindrical structures involved in essential processes such as **cell division, migration, and signaling**. As components of the **centrosome**, centrioles contribute to the organization of the microtubule cytoskeleton. Centrioles are also necessary for the assembly of c **Investigating centriole linkage remodeling during the formation of a primary cilium**: **primary cilia**, present on most of our cells for signaling, and motile cilia required for generating fluid flows or for cell motility. Abnormalities in the structure of centrioles are associated with **cancer** and genetic diseases called **ciliopathies**, which affect a multitude of organs.

Motile cilia such as those lining the airways or the brain ventricles beat in a directional manner to generate fluid flows. The centrioles at the base of these cilia carry appendages at specific positions, which are necessary for orienting the ciliary beating. We have identified conserved proteins that enable the correct positioning of these appendages. Unexpectedly, we discovered using a recent **super-resolution** imaging technique called **expansion microscopy** that these proteins are localized in a similar manner in the centrioles at the base of primary cilia, which are non-motile and do not have asymmetric appendages (Gaudin et al., 2022). We now want to identify the molecular mechanisms underlying the asymmetric localization of these proteins and their role at the base of primary cilia. We have discovered that some of these proteins are necessary for the formation of a linker between centrioles that forms specifically in cells with a primary cilium. Our data support that the formation of this linker allows to properly position the centrioles, which in turn affects the efficiency of cilium formation. The aim of the project is to determine the molecular architecture of the linker and the mechanisms regulating its assembly, and to identify its functions. It will involve super-resolution microscopy and molecular biology approaches.

Publications de l'équipe relatives au projet de stage

- Gaudin N., Martin Gil P., Boumendjel M., Ershov D., Pioche-Durieu C., Bouix M., Delobelle Q., Maniscalco L., Phan T.B.N., Heyer V., Reina-San-Martin B., Azimzadeh J. (2022). **eLife**, 11:e72382. doi 10.7554/eLife.72382.
- Le Guennec M., Klena N., Gambarotto D., Laporte M., Tassin A.M., van den Hoek H., Erdmann P.S., Schaffer M., Kovacik L., Borgers S., Goldie K.N., Stahlberg H., Bornens M., Azimzadeh J., Engel B., Hamel V., Guichard P. (2020). **Science advances**, Vol. 6, no. 7, eaaz4137. doi: 10.1126/sciadv.aaz4137.
- Pizon V., Gaudin N., Poteau M., Cifuentes-Diaz C., Demdou R., Heyer V., Reina San Martin B., Azimzadeh J. (2020). **Biology of the Cell**, 112(1):22-37. doi: 10.1111/boc.201900038.
- Basquin C., Ershov D., Gaudin N., Vu H.T.K., Louis B., Papon J.F., Orfila A.M., Mansour S., Rink J.C., Azimzadeh J. (2019). **Developmental Cell**, 51:516-25. doi: 10.1016/j.devcel.2019.10.021.