

AVAILABLE POSITIONS

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PROJECT INFO	
Title of the proposed project:	Primary cilia structure, composition, function in health and ciliopathies
Short description of the project	Primary cilia are signalling organelles present on nearly every human cell, and their dysfunction causes most known ciliopathies. Yet they remain the least understood of all cilia: small, sparse and buried within tissues, they still lack a molecular description of their structure and composition in disease-relevant human contexts. This project will build an integrated structural and compositional map of primary cilia across healthy and diseased states and link it to ciliary function. The student will combine three complementary approaches used in the lab: expansion microscopy to localise and quantify ciliary components in intact cells and tissues, cryo-electron tomography to resolve their native three-dimensional architecture in situ, and AI-aided spatial proteomics to define their protein composition within native tissue. These methods will be applied in parallel to wild-type and ciliopathy-model organoids, and ultimately to patient-derived material. By defining what primary cilia are made of, how they are built, and how these features change in disease, the project will provide the first mechanistic framework for primary cilium structure and function in human tissue, opening routes to understanding and treating ciliopathies. The student will gain cross-disciplinary training spanning structural biology, advanced imaging, organoid models and computational proteomics.
Main research area for the project	Cell biology
Second research area for the project	Structural Biology
3 key words for the project	Primary cilia, spatial proteomics, cryo-electron tomography

LAB INFO	
Main topic/s of the lab	Cilia biology in health and disease
Short description of the lab activity	In our research, we integrate structural biology methodologies with advanced cell biology techniques to uncover the molecular mechanisms governing the assembly and function of motile and primary cilia—microtubule-based organelles essential for eukaryotic life and human health. Over the years, my team has expanded its expertise to encompass a diverse array of cutting-edge tools, including genome engineering, in situ cryo-electron tomography (cryo-ET), single-particle cryo-EM, AlphaFold2-based structure prediction, structural proteomics, correlated

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	light and electron microscopy (CLEM), expansion microscopy, high-resolution fluorescence imaging, in vitro reconstitution assays, mechanical manipulation of cells and cytoskeletal components, and mass spectrometry. By leveraging this multifaceted approach, we have elucidated the molecular structure, dynamics, and mechanisms of Intraflagellar Transport (IFT)—the universally conserved bidirectional transport system required for cilia and flagella assembly across all ciliated cells. Understanding the structural and functional complexity of IFT - and of other processes involved in ciliary assembly and functions- is critical, as defects in this system can lead to severe ciliopathies. Perhaps the most audacious aspect of our research is the relentless pursuit of visualizing dynamic cellular processes at the highest possible resolution, often pushing technological boundaries and developing custom methodologies to capture these intricate molecular events in unprecedented detail.
Recent bibliography	Kiesel P, Alvarez Viar G, Tsoy N, Maraspini R, Gorilak P, Varga V, Honigmann A, Pigino G. The molecular structure of mammalian primary cilia revealed by cryo-electron tomography. <i>Nat Struct Mol Biol.</i> 2020 Dec;27(12):1115-1124. doi: 10.1038/s41594-020-0507-4. Epub 2020 Sep 28. PMID: 32989303; PMCID: PMC7610599. Müller, A., Klena, N., Pang, S. et al. Structure, interaction and nervous connectivity of beta cell primary cilia. <i>Nat Commun</i> 15, 9168 (2024). https://doi.org/10.1038/s41467-024-53348-5. Lacey SE, Pigino G. The intraflagellar transport cycle. <i>Nat Rev Mol Cell Biol.</i> 2025 Mar;26(3):175-192. doi: 10.1038/s41580-024-00797-x. Epub 2024 Nov 13. PMID: 39537792. Lacey SE, Graziadei A, Pigino G. Extensive structural rearrangement of intraflagellar transport trains underpins bidirectional cargo transport. <i>Cell.</i> 2024 Aug 22;187(17):4621-4636.e18. doi: 10.1016/j.cell.2024.06.041. Epub 2024 Jul 26. PMID: 39067443; PMCID: PMC11349379. https://rupress.org/jcb/article/220/9/e202108043/212596/Gaia-Pigino-Inside-the-cell
Group composition	1 Master student, 2 PhD students, 5 Postdocs, 1 PI
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