# Looking for an internship in Nano-physiology? Come join our lab!

LEIBNIZ FORSCHUNGSINSTITUT FÜR MOLEKULARE PHARMAKOLOGIE

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## The nanoscale molecular organization underlying tight junction properties

Tight junctions (TJs) connect neighboring cells in epithelia, are important for tissue compartmentalization, and create a paracellular barrier that ensures the selective passage of molecules based on size and charge. TJs consist out of transmembrane and cytosolic proteins (*Fig 1A*). The former mediate cell-cell adhesion in the form of a nanofibril-based meshwork, while the latter are important for interaction with the cytoskeleton and signaling. We investigate how TJ barrier properties arise from their nanoscale molecular organization. For this, we mostly focus on the claudin (Cldn) transmembrane protein family, as these proteins form the backbone of the TJ meshwork. We visualize the Cldn TJ meshwork using stimulated emission depletion (STED), so we can image its architecture up to a lateral resolution of ~50 nm (*Fig 1B*).

One question we have started addressing is which molecular principles are behind Cldn organization in strands. Through structural analysis, we have identified a Cldn region that seems of critical importance for meshwork formation. Next to this, we aim to look into the importance and nanoscale organization of another TJ transmembrane protein called occludin (Ocln). While Ocln seems to generally strengthen the barrier function of TJs *in vitro*, loss of Ocln only affects some of the TJ-containing tissues in KO mice and patients with pathogenic *Ocln* mutations. The exact function of Ocln (in TJs) thus remains unclear, but our preliminary data suggest a Cldn-specific supporting role for Ocln, which we now investigate further with functional assays in a KO cell line.

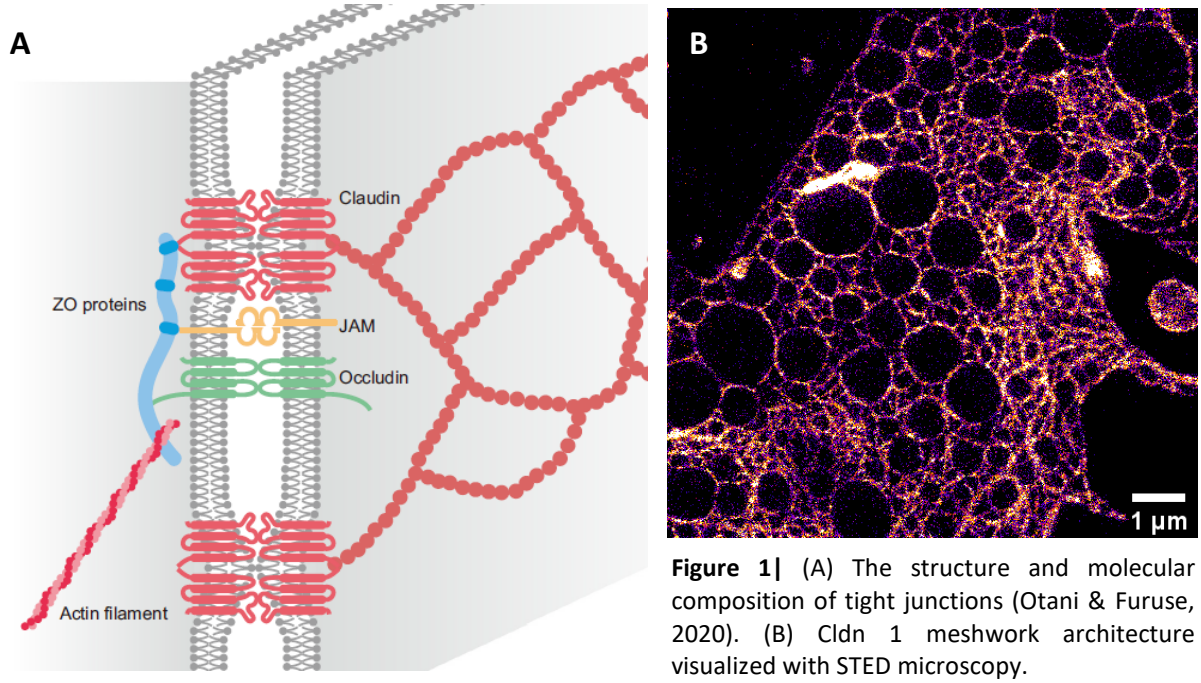


**Figure 1|** (A) The structure and molecular composition of tight junctions (Otani & Furuse, 2020). (B) Cldn 1 meshwork architecture visualized with STED microscopy.

## Available techniques

Confocal microscopy, cell culture, cyst 3D culture, FRET, FRAP, gene-editing (CRISPR), (live)-STED, molecular cloning, structural analysis, Ussing chamber measurements, Western blot

## How to apply

Altogether, there is a wide scope of possibilities for an internship in our group, with room for personal input on preferred methods and research questions. Please write your application (CV + motivation letter) to the supervisors of this project: Dr. Martin Lehmann; (MLehmann@fmp-berlin.de) & Rozemarijn van der Veen (vanderveen@fmp-berlin.de).