GSI - **SEMINAR**

Im Theorieseminarraum, SB3 Raum 3.170a

Darmstadt, Planckstraße 1

Donnerstag, den 19. Mai 2016 14:00 Uhr

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The structure and function of cell-cell junctions visualized by electron tomography

Cells sense, affect and respond to their environment through the fundamental function of adhesion. Several types of adhesion sites are maintained via molecules that are composed of repetitive immunoglobulin (Ig)-folds that anchor extracellular-matrix proteins to the cytoskeleton.

Despite considerable efforts, the long-standing questions of how adhesion sites are formed, structured and regulated remain unanswered. In this presentation I would like to show our latest results on the structure of the adherens junctions of drosophila melanogaster and the structure of the human kidney slit-diaphragm, that despite their biological distance, share amazing similarities, and a stunning applicability.

Vertebrate life depends on renal filtration and excretion of low-molecular weight waste products. This process is controlled by a specialized cell-cell junction called the slit-diaphragm. The molecular arrangement of the junction molecules NEPHRIN and NEPH1 defines the properties of the SD, and these proteins are essential for survival. Interestingly, the repetitive Ig folds composing both molecules present a new picture of the filtration mechanism, which our electron tomographic reconstructions show to be a highly flexible cell-cell junction that forms an adjustable barrier based on a molecular spring-like mechanism. Measuring the biophysical properties of these proteins in several species and a few mutants supports this finding and sketches a new understanding of the structure of the glomerular filtration barrier, and explains why the renal filter does not clog.

The surprising similarities of the adherens junctions to the renal filter are first seen in the similar arrangement of the cadherin-type molecules as well as the general junction configuration. Despite those similarities, they fulfill completely different tasks and have different biophysical properties. We have investigated these differences and similarities by studying the epidermal dorsal closure event in drosophila embryos, which is a model system for wound healing. Our tomographic reconstructions in combination with fluorescence light microscopy visualize the complete junction interplay during the zipping of the epidermis and show the dynamic on-off interplay of attachment and detachment in order to establish a seamless epithelium. The cells coming from each side of the epidermis establish contact through actin-driven exploratory filopodia, then generate stable “roof tile” like overlaps of single lamella, which shorten to produce a pulling force for the final epithelium sealing. To our surprise, microtubules pull in the direct vicinity of these junctions, which causes the junctions to be reinforced and pulls the two sides of the epidermis together.

Einladender: Dr. Michael Scholz

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