Research Project: A QUEST FOR THE MISSING PIECE IN THE PUZZLE OF EPITHELIAL JUNCTIONS

BACKGROUND:

Tight junctions (TJs) in vertebrates and septate junctions (SJs) in invertebrates form diffusion barriers by sealing the paracellular space between plasma membranes of neighbouring cells. Sealing the epithelium at the sites of contact between three cells requires specialized tricellular junctions (TCJs). Despite their fundamental roles in epithelial biology, TCJs are poorly described in terms of their structure, composition, and the dynamics of their assembly and maintenance. The Luschnig group identified Anakonda (Aka), a new transmembrane protein in *Drosophila* that specifically localises to TCJs and is essential for their assembly and function (Byri et al. 2015). Aka has a large extracellular portion with three repeats, each consisting of three domains. Results from the Luschnig group suggest that this unusual triple-repeat architecture may mediate self-assembly at TCJs directed by the geometry of three-cell vertices. Since Aka is not conserved in vertebrates, we are searching for vertebrate membrane proteins that display a triple-repeat architecture in their extracellular portions, as candidates for new TCJ components.

OUTLINE:

The idea for this project is to mine databases for such characteristic domain-patterns and subsequently prune down the results for candidate proteins by scanning the annotations of these candidate proteins. Students will first use existing programmes such as RADS and DoMosaics to look for possible triple-repeat architectures, thereafter to scan for proteins with similar domain arrangements as known TCJs and to analyse all hits in more detail. Finally, remaining hits will be further analysed w.r.t. database annotations using GO-terms and possible spatio-temporal co-expression with other proteins which are known to be involved in the formation of occluding junctions.

Following this computational screen we want to validate selected candidates experimentally, which may encompass generation of tagged expression constructs, transient transfection experiments in mammalian cells, and analyses by high-resolution confocal microscopy.

REQUIRED SKILLS:

Students should have a keen interest in cell biology, structural biology and bioinformatics and be willing to apply or acquire basic skills in scripting, e.g. in PYTHON.

SKILLS THAT CAN BE LEARNED:

- Knowledge about epithelial cell biology, in particular structure and function of occluding junctions
- Knowledge about the modular evolution of proteins
- Familiarity with essential and widely used techniques in bioinformatics
- tissue culture, transfections, fluorescence microscopy

The project is initially available for a FoM (Forschungsmodul, any time) or a PM (Projektmodul/Bsc thesis) and, if successful, can be turned into an MSc project with a stronger focus on either the computational or the experimental side.

Interested candidates should send an email with a short description of their backgrounds and desired starting time to Prof. Erich Bornberg-Bauer ebb@wwu.de and Prof. Stefan Luschnig luschnig@wwu.de

Further information: http://luschnig.uni-muenster.de/ , bornberglab.org

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