Universität Basel

Research Project

In vivo cell biology of organ morphogenesis

Third-party funded project

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Organisation / **Research unit**
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Department
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Organs and tissues acquire particular three-dimensional shapes during development, which are intimately linked to the particular function(s) an organ has to fulfil. Organ shape is to a large extent determined by cell behaviour, and cell behaviour is to a large extent regulated by cell-cell signalling and cell mechanics. A major interest of my laboratory over the last few years has been to determine how branching morphogenesis restructures epithelial tissues to generate such fascinating structures as the trachea or the vasculature. While we have initially put much effort in understanding this process in vivo in an invertebrate system (tracheal development in Drosophila melanogaster) using state of the art genetics in combination with high resolution live imaging, we have recently moved much of our research efforts to vertebrates, in particular to zebrafish (Danio rerio). Using high resolution in vivo imaging, we have described the cellular activities during angiogenesis, in particular during sprouting, vessel fusion and vessel pruning. To our surprise, we find that the plasticity of developing vessels is accompanied by unexpected cell behaviour; endothelial cells can fission and self-fuse during anastomosis and pruning, respectively.

With the advent of the recently introduced genome manipulation tools (TALEN, CRISPR/Cas9), a genetic dissection of the different steps in angiogenesis is now possible at unprecedented level, and proteins can be tagged at endogenous loci and used as marker for high resolution live imaging. We have recently applied intracellular nanobodies for the first time in developing drosophila embryos to directly manipulate protein function, in particular for protein degradation. We used an anti-GFP nanobody fused to an F-box in degrade GFP-fusion proteins (we called the method “deGradFP” for degrading GFP). In the meantime, we have functionalized the anti-GFP nanobody manifold, so that it can be used for in vivo protein trapping, protein localisation and for post-translation modification of proteins of interest. During the next granting period, we will introduce the use of intracellular nanobodies (and other protein binders) for studying the zebrafish vascular system, in particular to answer the following questions:

Q1: How is the dynamic cell behaviour during sprouting controlled?

Q2: How do endothelial cells recognize each other in order to connect?

Q3: Which molecular processes are involved in luminal membrane expansion?

Q4: Which molecular processes are involved in membrane fusion and membrane fission?

In order to answer these questions, we propose to **undertake the following experimental strategies**:

1) Investigate the role of VE-cad in the dynamic rearrangements of endothelial cells.

2) Generate and use cutting edge in vivo live imaging tools to characterize molecular aspects of cell behaviour during angiogenesis processes.

3) Generate and analyse mutations in candidate genes affecting distinct cellular activities.

4) Generate and use novel tools to manipulate protein function in vivo – a step closer to a synthetic biology approach to organ formation.

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Add publication

Published results

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