Katja Röper: Deciphering tissue origami

Katja Röper investigates how cytoskeletal behaviour controls tissue morphogenesis.

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Katja Röper

As a teenager growing up in West Berlin, Katja Röper witnessed the fall of the Berlin Wall from Checkpoint Charlie, and the opening of the Brandenburg Gate, amazing moments in history that reshaped her home country. During these years, her parents—a mineralogist and a nurse—were also shaping her future career as a scientist by encouraging her fascination with biology.

Röper went on to study biochemistry at the Free University of Berlin—in the building where Lise Meitner and Otto Hahn discovered nuclear fission. The biochemistry classes provided an intense first research experience as an undergraduate where she forged many lifelong friendships. Wieland Huttner's group at the University of Heidelberg was her next educational home, as a postgraduate student studying how the multipass transmembrane protein, Prominin, controls asymmetric division of polarized neuroepithelial cells in mouse embryos. Wanting to spread her wings farther during her postdoc, Röper joined Nick Brown's lab at the University of Cambridge to "learn *Drosophila*" and investigate how a spectraplakin protein called Shot interacts with and coordinates different cytoskeletal systems. With a BBSRC fellowship in hand, Röper then set up her own lab in Cambridge, bringing together the power of fly genetics and advanced microscopy techniques to watch and understand the reshaping of flat epithelial sheets into tubular structures in developing embryos. We contacted her to learn more.

What was it that first drew your interest to the cell biology of embryogenesis?

Embryogenesis is an amazing process. Our lab pet, the fly, goes from a fertilized egg to a complete organism that can move and react within 24 hours. How is this feat of coordination achieved? Over the last 20 years, we have come to understand more about the gene regulatory networks and nuclear processes that determine the fate and identity of groups of cells, but how this is turned into a morphogenetic program that controls tissue shape is much less understood. This is where we come in. *Drosophila* is a superbly accessible model system, in terms of genetics, imaging, and cell biology, to address this question and will eventually help us elucidate how related processes in humans are achieved.

What is your lab actively working on?

We want to understand how simple epithelial sheets are deformed in a highly concerted manner into tubular tissues. Tubular tissues form most of our internal organs, including the vasculature, lungs, kidneys, and intestines. Many diseases arise when tube formation or homeostasis goes wrong, such as spina bifida, polycystic kidney disease, and some cancers. We need to understand how these processes occur in a healthy individual and how the changes in cell shape and position that drive tubulogenesis are controlled by the underlying cell biology, especially of the cytoskeleton and cell–cell adhesion receptors.

> "How is this feat of coordination [during morphogenesis] achieved? ...This is where we come in."

The model process we analyze is the formation of the salivary gland tubes from two flat epithelial placodes in the fly embryo. We realized recently how much the different cytoskeletal systems work together to achieve cell shape changes in 3D and that the microtubule cytoskeleton is crucial for the functioning of the actomyosin cytoskeleton (1, 2). Apical actomyosin is the key player in changing cell shape, constricting the apex of epithelial cells and thereby driving tissue bending. But we could show that this is not possible without the support of microtubules, and this applies not only to the salivary gland placode, but also other tissue bending events (3). Curiously enough, this work linked straight back to my postdoctoral work, because our favorite cytolinker protein, Shot, is what connects microtubules and actomyosin apically in the salivary gland placode.

Another important realization was what a profound effect cell surface receptors, and in particular cell–cell adhesion receptors, have on the organization and activity of the underlying cytoskeleton. This was already well established for E-cadherin, but we showed that the apical polarity regulator, Crumbs, works in a similar way to cadherins, binding to itself through homophilic interactions. Changes in Crumbs levels have direct effects on the patterning of actomyosin activity at the apical surface of epithelial cells (4). This work established a crucial link between regulation of apical-basal polarity of epithelial cells, which is key to their functions in any tissue, and the patterning events that drive coordinated morphogenesis of epithelial tissues (5). We suspect that morphogenetic processes in all organisms tap into a toolbox of modules, such as the two described above, that allow many variations of events in tissue formation to take place, and that the particular choice of module combination made will depend on the upstream gene regulatory networks and hence lead to different outcomes. Flies are a great model in which to identify and dissect these modules.

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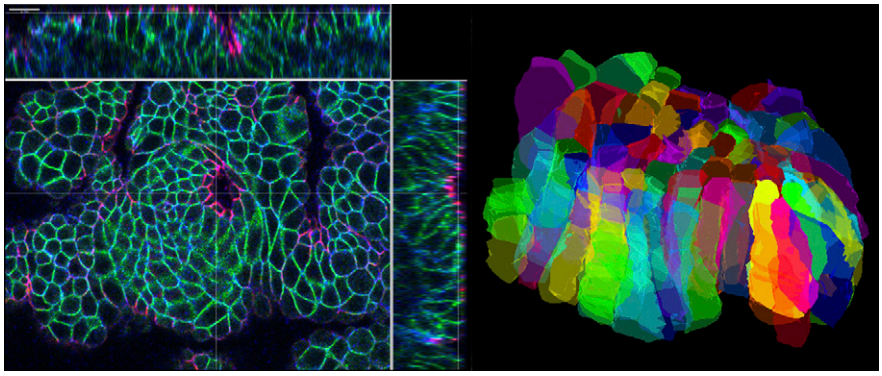

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A salivary gland placode during early tissue bending in a confocal image (left panel) labeled for Crumbs (red), E-cadherin (blue), and Scribble (green), as well as a segmented placode showing 3D cell shapes (right panel).

What kind of approach do you bring to your work?

We are using fly genetics and advanced imaging approaches to dissect the cell biology of tube formation. And imaging is really our forte, especially analyzing epithelial cells in 3D over time. We try to avoid the apico-centric view that a lot of studies of epithelial morphogenesis take. Epithelial cells in many tissues undergoing morphogenesis are very tall and columnar, and so focusing only on apical events ignores most of the cell volume. We have very fruitful collaborations with bioinformaticians to segment and track cells in 4D, allowing us to quantify and compare morphogenetic events in wild-type and mutant situations, deduce strain rates and infer forces impinging on cells.

> "Most importantly, enjoy what you do and make the people working with you enjoy science, too."

What did you learn during your PhD and postdoc that helped prepare you for being a group leader?

I mostly learned what style of "running a lab" I liked and felt comfortable with, and what I felt would not work for me. What comes as a slight shock once you run your own lab, is how much time is easily spent on organizational, administrative, and other duties. I am very lucky, though, to be based at the MRC-LMB in Cambridge, an institute that has always promoted small group sizes and lots of collaboration, so I actually still manage to do some experiments myself, although not as many as I would like.

What has been the biggest challenge in your career so far?

The biggest challenge for me, and a challenge that many young scientists face, is how to combine a successful career in science with having a family. I have two young children, aged 7 and 10, and the older one was born in the year I started my lab. I was helped enormously by a very supportive husband who truly shares all child-related duties. The fact that we are both scientists, and are thus to some extent fairly flexible with our time, also helps a lot in accommodating lab life with family life.

What is the best advice you have been given?

One excellent piece of advice for the early stages of establishing your own research group is, "you are your lab's best postdoc," so don't stop bench work too early, get your own great results, and be a bench role model for the people in your lab! The second one is, "if in doubt, do not hire." Especially in a small group, nothing can be more disruptive to good science than hiring someone who won't gel and fit in, or is unproductive or even messing up equipment and tools. Whereas, in reverse, a happy cohesive lab will usually be productive.

What hobbies do you have?

I have always loved making music, and I have sung in all sorts of different choirs: small or large, a cappella or with an orchestra or band. Singing takes you out and away from the day-to-day mayhem, relaxes you, and cheers you up. Many of my friends from my student times and nowadays have come through music. I've been fortunate to perform in amazing places, such as the Berlin Philharmonie and King's College Chapel—the feeling of standing in these venues and performing wonderful pieces of music is hard to top.

Any tips for a successful research career?

Just go for it: if you want to do it and have the energy, you will probably succeed. But be prepared with a plan B, C, D… for getting to your goal, because the path won't necessarily be straight. And keep in mind that everything always takes much longer than initially expected—applications, paper writing, and submission and so forth. Most importantly, enjoy what you do and make the people working with you enjoy science, too!

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Röper on annual family holiday in Brittany