How do cells build organs? Integration of genetic and mechanical information during sea urchin skeletogenesis

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The instructions for constructing the body plan of multicellular organism is encoded in the genome of the species in the form of developmental regulatory networks. One of the fundamental riddles in biology is **how are genomic programs executed during embryogenesis and how do they evolve?** Gene regulatory networks (GRNs) consisting of transcription factors and intercellular signaling control cell fate specification, but this information is not sufficient to make organs. To build an organ, the cells must apply mechanical force on their environment, measure its mechanical properties and make local computation of how to proceed (1). This computation must be also encoded in the genome and is part of the regulatory machinery that drives morphogenesis. In our lab, we aim to decipher **how genetic and mechanical information are processed and translated into the mechanics of organogenesis?** We also investigate **how genetic and mechanical information processing changes during evolutionary innovations where the stiffness of the extracellular matrix changes dramatically?**

To adress these two fundamental question we use the sea urchin larval skeletogenesis as a model. The sea urchin larval skeleton is made of two interconnected frameworks of calcite rods called “spicules”, generated inside a tubular cavity that the skeletogenic cells make. The GRN that drives skeletogenesis is known in great details and shows a remarkable similarity to the GRN that drives vertebrates’ vascularization and is quite distinct from the GRN that drives bone formation (2). The similarity in the GRNs implies a common origin of these two tubulogenesis processes, yet, the vascular lumen is blood, while the spicule lumen is calcite: **how did a liquid lumen that is very soft evolve into a crystal lumen that is very hard?**

The spicules grow by mineral deposition at their tips, which is regulated by differential gene expression at the tips, partially controlled by the **vascular endothelial growth factor (VEGF)**. We discovered that spicule elongation and gene expression depend on mechanical cues provided by **Focal Adhesion Kinase (FAK) and RhoA-associated coiled-coiled kinase (ROCK)**. We revealed that VEGF signaling and FAK-ROCK inputs are both integrated by extracellular-signal regulated kinase (ERK) pathway that controls the activation of gene expression at the tips and shut-down in the back. Interstingly, VEGF-ERK signaling regulates vertebrates’ angiogenesis while the FAK-ROCK-ERK circuit regulates vertebrates osteoblasts differentiation. This could imply that during evolution, FAK-ROCK-ERK circuit was incorporated into the GRN that drives sea urchin skeletogenesis due to the hardening of the lumen from liquid into a crystal. The activity of the FAK-ROCK-ERK circuit in vertebrates bone cells suggests that this circuit serves as a mechanosensing “plug-in that is frequently re-deployed in evolution, when the ECM hardens. Thus, the interplay between genetic and mechanical information processing is essential for the execution of the genomic developmental programs and changes in these interactions support evolutionary innovations.

References

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