Wnt/Dkk negative feedback loop regulates sensory organ size in the lateral line system of fish

Summary
Organ growth is tightly regulated during development. Some organs stop growing at a predetermined size, while others keep growing in proportion to the body size. The mechanosensory organs of the lateral line system in fish (neuromasts) are composed of sensory hair cells surrounded by non-sensory support cells. Superficial neuromasts on the surface of the skin retain the same size all along fish life, and they bud off new neuromasts, which will grow until they reach the same size again. By contrast, canal neuromasts become embedded under the skin, and increase in size in proportion to the body size. Thus, neuromasts use opposing strategies to grow depending on their positions, which provides an excellent opportunity to study mechanisms underlying organ growth control.

In this study, by creating a system to visualize and manipulate Wnt signaling activities in zebrafish, we demonstrate that Wnt signaling promotes cell proliferation to increase neuromast size, whereas Dkk2 secreted by the sensory cells suppresses cell proliferation by inhibiting Wnt signaling. Moreover, this Wnt/Dkk negative feedback loop also acts during hair cell regeneration to achieve size constancy. We further demonstrate that axonal innervation is required for activation of Wnt signaling during neuromast budding, suggesting that the Wnt activator is provided by axons that innervate neuromasts. We propose that a simple negative feedback mechanism accounts for various aspects of organ size regulation in the lateral line system.