Bundles of nerves and arteries provide wealth of new stem cell information

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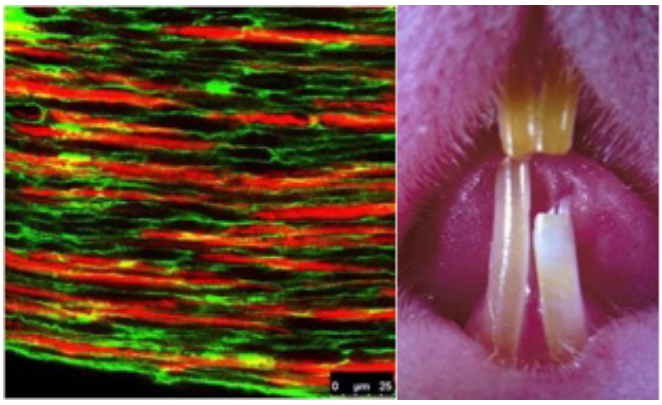

The inferior alveolar nerve provides a niche for stem cells that maintain incisor homeostasis. When the nerve is severed, homeostasis is disrupted and within one month the affected incisor becomes chalky and breaks. Image on the left shows inferior alveolar nerve (green) that produces Shh protein (red). Image on the right shows incisor defect following denervation. Credit: University of Southern California

A new Ostrow School of Dentistry of USC study not only uncovers new details on how bundles of nerves and arteries interact with stem cells but also showcases revolutionary techniques for following the cells as they function in living animals.

Principal investigator Yang Chai, director of the Center for Craniofacial Molecular Biology at the Ostrow School of Dentistry, and research associate Hu Zhao authored the article, which appears February 6, 2014 in the journal *Cell Stem Cell*.

The study focused on neurovascular bundles (NVB) – groupings of nerves and blood vessels intertwined throughout the body – and their interactions with mesenchymal stem cells, or MSC. The team specifically examined how the cells operated in the incisors of mice; those teeth continually regrow over a mouse's lifespan, indicating that stem cells are present.

Typically, MSC are studied in vitro, or harvested from animals and examined outside of their natural environment. However, Chai and his team used a different molecular marker to highlight the cells' expression of the protein Gli1 and follow MSC in living mice. They discovered that the bundles are rich in stem cells – including MSC that wouldn't have been detected using conventional markers and techniques.

It turns out that this newly uncovered population of MSC helps maintain a normal cellular environment, while stem cells normally detected by the more well-known markers focus on injury repair, Chai said.

"We have basically developed a system in which we can follow MSC in their natural environment and see how they contribute to homeostasis," he said.

The study revealed that the MSC populations within NVB are located around arterioles, or small arteries that branch off to bring blood to tissues. Sensory nerves within the bundles secrete a protein called Shh to regulate the stem cells, demonstrating a practical reason for the bundling of the nerves and blood vessels. Such bundles are a ubiquitous anatomical feature and are found in every organ in humans, Chai said.

The study not only highlights the need to cast a wider net in order to identify all stem cells but also emphasizes the need to understand the environment around the cells, he added.

"This study has great implications for tissue regeneration in general," Chai said. "If you want to regenerate tissue, you have to not only provide stem cells but also the proper neighborhood for them to carry out their function."

More information: "Secretion of Shh by a

neurovascular bundle niche supports mesenchymal stem cell homeostasis in the adult mouse incisor," *Cell Stem Cell*, 2014.

Provided by University of Southern California