

Origin of cells for connective tissues of skull and face challenged

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With improved resolution, tissue-specific molecular markers and precise timing, University of Oregon biologist James A. Weston and colleagues have possibly overturned a long-standing assumption about the origin of embryonic cells that give rise to connective and skeletal tissues that form the base of the skull and facial structures in back-boned creatures from fish to humans.

Weston and co-authors from the Max Planck Institute of Immunology in Germany and the French National Scientific Research Centre at the Curie Institute document their potentially textbook-changing case in an article appearing online this week (May 19-23) ahead of regular publication in the *Proceedings of the National Academy of Sciences*.

The cells in question, they argue, do not come from a portion of embryonic neural epithelium called the neural crest, as widely believed, but rather from a distinct thin layer of epidermal epithelial cells next to it. "Our results," Weston said, "could lead to a better understanding of the etiology of craniofacial defects, as well as the evolution of the head that distinguishes vertebrates from other creatures."

The neural crest was first identified by classical embryologists in the late 19th and early 20th centuries and has been one of the most studied embryonic tissues. Conventional wisdom says that the neural crest gives rise to skeletal and connective tissue of the head and face, as well as a wide diversity of other stem cells that migrate to many places in the vertebrate embryo, where they spawn the cells that create the peripheral

nervous system, and pigment cells in skin and hair (or scales and feathers).

The new study is part of research done over 25 years in Weston's quest to understand early development of the neural crest and explore alternative explanations for sometimes differing findings involving its assumed cell lineages. Weston noted that mutations in mice that adversely affected development of the peripheral nervous system or pigmentation did not affect craniofacial structures, whereas mutations that caused abnormal development of skeletal and connective tissue of the head and face did not alter neural crest-derived pigment or peripheral nervous system cells.

This paradox, he said, led him to wonder if different genetic programs were required to function in distinct embryonic precursors of these tissues. "In our new paper," he said, "we finally were able to re-examine some of the underlying assumptions that have led to the conventional wisdom about the source of the embryonic cell lineages that give rise to the skeleton and connective tissue of the head and face."

In the mouse embryo at eight days gestation, Weston and collaborators used high-resolution imaging and immunostaining techniques to identify and track the dispersal of cells known to jump start connective and skeletal tissue development. They were able to see clearly that these cells came from the non-neural layer of cells rather than from the neural crest. The same distinction also exists in chicken embryos during the first few days of gestation, Weston noted. "Looking at the right time is very important," he said.

Weston argues that this non-neural epithelium is indeed distinct from the neural crest, because its cells contain characteristically different molecules. He and colleagues dispute suggestions that this non-neural structure is simply a sub-domain of the neural crest. "These cells emerge

at a different time in development and disperse in the embryo before neural crest cells begin to migrate," Weston said.

"New technologies let us see cell types more clearly than ever before," said Weston, a member of the UO's Institute of Neuroscience. "We previously had discovered that a molecule that marks cell surfaces in the non-neural epithelium reveals a very sharp boundary between this non-neural epithelium and the neural tissue connected to the neural crest. In this study, we took a closer look."

They located a population of cells in the non-neural epithelium that express other molecules that "do not appear to originate from the neural crest," said Weston, who retired in 2001 but continued to teach in the College of Arts and Sciences until 2006. He still collaborates in some research with colleagues at the UO and at various labs around the world.

"I think our results have two important messages," he said. "First, it is important to identify and validate -- rather than ignore -- assumptions; and second, because we identified an alternative embryonic cell lineage as the source of the head and facial structures, we can now more effectively analyze and understand the molecular-genetic mechanisms that regulate the normal and abnormal development of these structures."

Source: University of Oregon

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