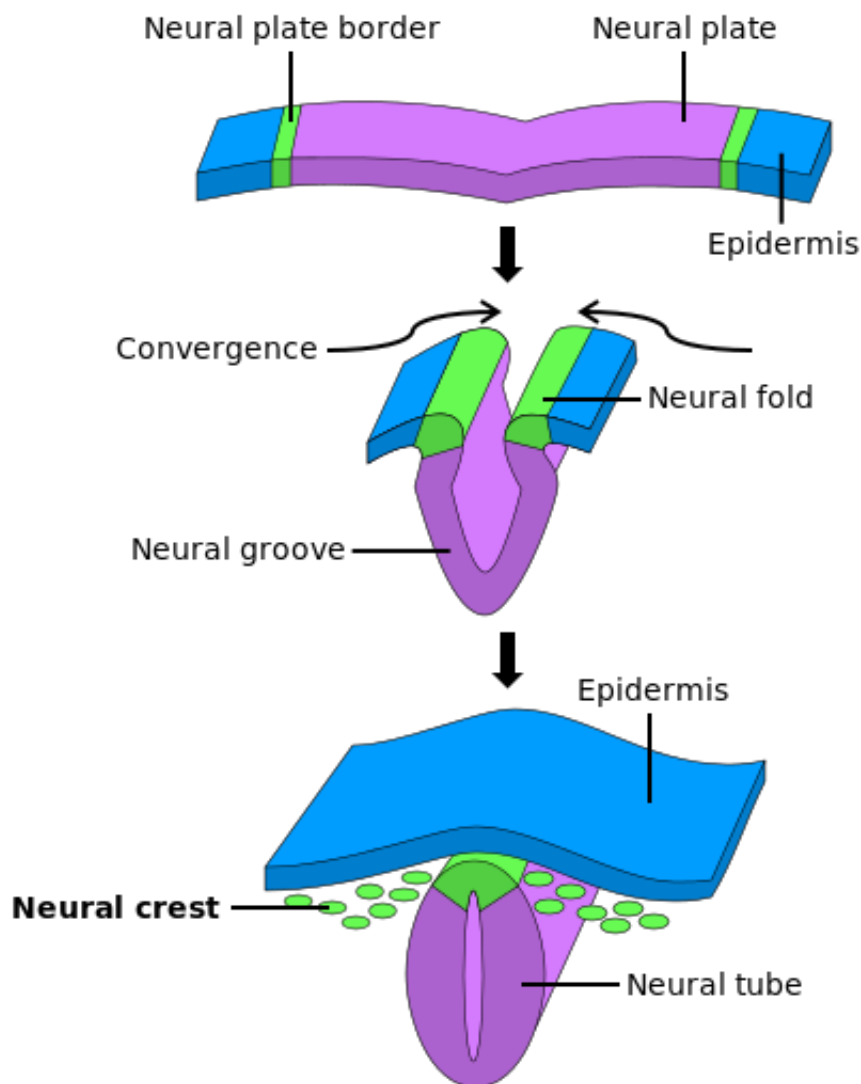


# New origin theory for cells that gave rise to vertebrates

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Neural crest formation during neurulation. Credit: Wikipedia

The vivid pigmentation of zebras, the massive jaws of sharks, the fight or flight instinct and the diverse beaks of Darwin's finches. These and other remarkable features of the world's vertebrates stem from a small group of powerful cells, called neural crest cells, but little is known about their origin.

Now Northwestern University scientists propose a new model for how neural crest cells, and thus vertebrates, arose more than 500 million years ago.

The researchers report that, unlike other early embryonic cells that have their potential progressively restricted as an embryo develops, neural crest cells retain the molecular underpinnings that control pluripotency—the ability to give rise to all the [cell types](#) that make up the body.

"This study provides deep new insights into the evolutionary origins of humans and other vertebrates," said evolutionary molecular biologist Carole LaBonne, who led the research. "It also provides critical new information about the molecular circuitry of [stem cells](#), including [cancer stem cells](#)."

Regenerative medicine scientists now have an updated framework for future studies aiming to harness the power of stem cells to treat human diseases and congenital defects, LaBonne said.

The study also turns conventional thought on its head. Previously, scientists thought neural crest cells had to evolve to gain their incredible properties, but the Northwestern work shows the power was there all along. Researchers now can focus on the molecular mechanisms by which neural crest cells escaped having their potential restricted.

In a study using embryos from the frog *Xenopus*, a powerful model

system used in studies of development, LaBonne and her team found that neural crest cells and the early pluripotent cells present in blastula embryos have surprising similarities, including shared expression of a key set of genes which work together to endow the cells with their unique properties.

The findings will be published today (April 30) as a *Science Express* article by the journal Science. The article also will be the cover story of the journal's June 19 issue.

"Neural crest cells never had their potential restricted at all," LaBonne said. "We believe a small population of early stem cells were set aside, so that when the time came, their immense developmental potential could be unleashed to create new features characteristic of vertebrates."

LaBonne is a professor of molecular biosciences in the Weinberg College of Arts and Sciences. She holds the Arthur Andersen Teaching and Research Chair and is co-leader of the Tumor Invasion and Metastasis program of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Acquisition of neural crest cells more than 500 million years ago led vertebrates to evolve and leave behind less complex life forms (simple aquatic filter feeders, much like today's sea squirts and lancelets). With these cells, animals developed important new features such as a skull to house a complex brain, jaws for predation, a complex peripheral nervous system and many other cell types essential to the vertebrate body.

In their study, LaBonne and her research team studied the genetic toolkit that early embryonic cells use to promote pluripotency or "stemness" and compared it to the one used by neural crest cells. They found that the toolkit used by neural crest cells also is used by pluripotent blastula cells, and they showed that it is essential for pluripotency in both cell types.

The proteins that derive from this toolkit work together to enable a dizzying array of tissues to arise from a population of single cells.

One of these proteins, called Snail1, has been the focus of previous studies by LaBonne's lab. They and others had shown that Snail1 plays key roles in controlling not only the immense developmental potential of neural [crest cells](#) but also their capacity for migratory and invasive behavior.

Cancer cells co-opt the function of Snail1 and other [neural crest](#) regulatory proteins to allow the formation of cancer stem cells and mediate the process of metastasis, whereby [cancer cells](#) disperse throughout the body to form new tumors, LaBonne said. Researchers therefore gain insights into Snail1's role in cancer by studying its function in the developing embryo.

In early blastula embryos, pluripotent cells were thought to exist only transiently; as an embryo develops, cells become restricted into categories of cells called germ layers and then into specialized cell types. The Northwestern study suggests that not all cells get restricted at those early stages. Instead, [neural crest cells](#) may have evolved as a consequence of a subset of blastula cells retaining activity of the regulatory network underlying pluripotency.

The study underscores just how much remains to be discovered about embryonic development. The human body has more than 10 trillion [cells](#) elaborately organized into tissues and organs that are intricate and highly complex, yet it all is self-assembled from a single cell, the fertilized egg.

"It's a fascinating process," LaBonne said. "One of the great frontiers in biology is understanding both how complexity is generated and how it evolves to create what Charles Darwin memorably called 'endless forms most beautiful.'"

**More information:** Shared Regulatory Programs Suggest Retention of Blastula-Stage Potential in Neural Crest Cells,  
[www.sciencemag.org/lookup/doi/ ... 1126/science.aaa3655](http://www.sciencemag.org/lookup/doi/10.1126/science.aaa3655)

Provided by Northwestern University

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