Gene thought to make heart tissues turns out to make blood and muscles as well

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New research out of the Lillehei Heart Institute at the University of Minnesota shows that by turning on just a single gene, Mesp1, different cell types including the heart, blood and muscle can be created from stem cells.

The study was published today in the journal *Cell Stem Cell*.

"Previous research indicated that this gene was the "master regulator" for development of the heart, and that its activity prevented the differentiation of other cell types," said Michael Kyba, Ph.D., associate professor in the University of Minnesota Medical School Department of Pediatrics and a Lillehei endowed scholar. "Our work reveals that this gene acts differently, and that it plays a role in the development of blood and skeletal muscle as well. The outcome depends on the chemical signals that cells expressing this factor sense in their environment."

The research was conducted in the Kyba Lab by lead author Sunny Chan, Ph.D., a postdoctoral associate in the lab.

Stem cell researchers have been trying to generate different cell types for regenerative medicine for years. The gene Mesp1 was particularly interesting to cardiac researchers because it was believed to be a master regulator, sitting at the pinnacle of a gene hierarchy driving cardiac differentiation, blocking the differentiation of other cell types.

However, this research turns that assumption on its head.

A carefully designed study, aimed at understanding precisely what Mesp1 does at different points in time as stem cells develop, revealed that the gene can do so much more than previously thought.

By turning Mesp1 on and off at specific time windows and fine-tuning the culture environment, stem cells can be coached to become not just heart cells, but also blood and muscle cells.

"This is totally out of the blue, but our discovery brings some conflicting findings about Mesp1 together," said Chan. "Some previous studies reported Mesp1 could not make heart cells in certain contexts. We now know why."

The Kyba team further shows Mesp1 is present in the cells that go on to become adult stem cells in the bone marrow which form new blood cells, and stem cells in the skeletal muscles, which form new muscle fibers.

"We are amazed at what a single gene can do," said Chan. "By understanding what Mesp1 does, we are more likely to make different cell types from stem cells more efficiently. We are one step closer to using stem cell technology for regenerative medicine."

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