Blood Progenitor Cells Receive Signals From Niche Cells And Daughter Blood Cells - ($)

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Julian A. Martinez-Agosto

Scientists have determined that two-way signaling from two different sets of cells is necessary for the creation and maintenance of the blood supply in the fruit fly.

That balance both ensures enough blood cells are made to respond to injury and infection, and that the blood progenitor cell population remains available for future needs.

The stem cell-like blood progenitor cells that contribute to the cells of the adult fruit fly's blood supply receive signals from cells that live in a nearby safe zone, or niche.

These signals keep the progenitors in the same stem cell-like state so, when needed, they can begin differentiating into blood cells.

UCLA stem cell scientists also found that the blood progenitor cells receive critical "back talk" signals back from the daughter blood cells they create, telling the progenitor cells when enough blood cells have been made and it's time to stop differentiating.

"The cells in the niche provide a safe environment to support blood progenitor cells," said study co-senior author Dr. Julian A. Martinez-Agosto, an assistant professor of human genetics and pediatrics at UCLA. "When the blood progenitor cells receive signals from the niche cells it creates an environment for those cells to maintain their potential and not differentiate."

Previous studies have shown that when you remove the niche cells, the blood progenitor cells differentiate unchecked. Ultimately, the fruit fly runs out of blood progenitor cells and is not able to make new blood cells to mount an immune response to infection or injury, Martinez-Agosto said.

The new study identified additional signals not coming from the niche cells, but from the daughter blood cells the progenitors were making.

The researchers noted in the four-year study that once the progenitors cells had begun differentiating and the blood cells they were creating became mature, the progenitors became very quiescent, or quiet, and did not multiply. They theorized that there must be a signal coming from the daughter cells that told the progenitors to stop multiplying and differentiating.

The researchers said there was no reason to suspect that the differentiating cells had any role at all in the process. It's always been the paradigm in stem cell biology that all that was needed was the signaling from the niche cells to maintain the progenitor population.

The signaling from the niche cells that maintains the progenitor population is called Hedgehog. In this study, the scientists showed that the daughter cells are sending back a signal to the progenitors that is mediated by adenosine deaminase growth factor A (Adgf-A). The signal regulates extracellular levels

of adenosine, which opposes or counters the effects of Hedgehog signaling.

"We've shown that adenosine as a molecule is really important for regulating the proliferation of progenitor cells in blood. And it requires a delicate balance – just enough signaling to give you more blood cells, but not so much that all the progenitor cells are lost," Martinez-Agosto said. "Maybe other progenitors or stem cells are using the same signaling to determine when to differentiate or not."

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Contact: Dr. Julian A. Martinez-Agosto, 310-794-2405, julianmartinez@mednet.ucla.edu

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