Tumor Suppressor Genes Vital to Regulating Blood Precursor Cells in the Fruit Fly

Newswise UCLA stem cell scientists have shown that two common tumor suppressor genes, TSC and PTEN, are vital to regulating the stem cell-like precursor cells that create the blood supply in Drosophila, the common fruit fly.

The researchers examined a signaling pathway called TOR that the cells use to gauge nutrition, said study senior author Dr. Julian A. Martinez-Agosto, an assistant professor of human genetics and a researcher with the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell.

We wondered how an organism knows how many blood cells to make and when to make them in the context of injury and repair to tissue. In particular, we wondered how the blood progenitor cells sense that when its time to make more blood cells, Martinez-Agosto said. We found that the TOR pathway genes to regulate its function and, when activated, it expands or increases the number of blood the flys blood.

The study appears Sept. 5, 2012 in the advance online issue of the peer-reviewed journal Development.

Michelle Dragojlovic-Munther, a graduate student in the Martinez-Agosto laboratory and first found that cells with increased activity of TOR have a competitive advantage, allowing them to more of themselves so they can make blood. These progenitors, Dragojlovic-Munther found, also reactive oxygen species (ROS) -- ions or very small molecules that include free radicals which can predispose humans to aging and heart disease. But in this case, the ROS proved valuable.

The precursors, Martinez-Agosto said, were producing ROS all the time and when TOR was act increased dramatically. Too much ROS caused them to divide more than normal. If they treated antioxidants, which reduce ROS levels, the cells would develop normally.

The finding could be important because the TOR pathway is abnormally activated in many cancerous cells, and it may be possible to target the levels of ROS, which may help regulate the pathway.

What this study may be telling us is that too much ROS is causing more cells to divide and we therapies that reduce ROS to significantly improve the condition, Martinez-Agosto said, adding targeted antioxidants might be a potential treatment in certain subsets of blood disorders. Some pathway is working more than it should, and we need the right amount of ROS for balance. Its like Goldilocks, there cant be too little or too much. We need it just right.

Going forward, Martinez-Agosto and his team will try to determine where the ROS is coming from and discover an enzyme that may be a good target for therapeutics. They know that the higher ROS progenitors are not coming from mitochondria, the cells power source, but have not identified how they are being produced.

This study highlights mechanistic differences between TSC and PTEN on TOR function and demonstrates the multifaceted roles of a nutrient-sensing pathway in orchestrating proliferation and differentiating specific blood progenitors through regulation of ROS levels and the resulting myeloproliferative...
deregulated, the study states.

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