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Dr. Julian A. Martinez-Agosto

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Assistant Professor of Human Genetics and Pediatrics and A Researcher

Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA

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Employment History

Assistant Professor
UCLA

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"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," said UCLA's **Dr. Julian A. Martinez-Agosto**, the senior author of the study. "In particular, we wondered how the blood progenitor cells sense that change and know when it's time to make more blood cells."

To answer this question, **Martinez-Agosto**, an assistant professor of human genetics and pediatrics and a researcher with the **Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA**, and his colleagues examined a signaling pathway called TOR that the cells use to gauge nutrition levels and stress.

"We found that the TOR pathway uses these two genes to regulate its function and, when activated, it expands or increases the number of blood progenitor cells in the fly's blood," **Martinez-Agosto** said.

...

The precursors, **Martinez-Agosto** said, were producing ROS all the time, and when TOR was activated, the levels increased dramatically. Too much ROS caused them to divide more than normal. The researchers found that if they treated the flies with antioxidants, which reduce ROS levels, the cells would develop normally.

The finding could be important because the TOR pathway is abnormally activated in many cancers, 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 may be able to target therapies that reduce ROS to significantly improve the condition," **Martinez-Agosto** said, adding that specifically targeted antioxidants might be a potential treatment in certain subsets of blood disorders.

"Sometimes that pathway is working more than it should, and we need the right amount of ROS for balance," he said. "It's like Goldilocks - there can't 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 are coming from and perhaps discover an enzyme that may be a good target for therapeutics.

Julian A. ...

[www.newsroom.ucla.edu, 6 Sept 2012 \[cached\]](http://www.newsroom.ucla.edu, 6 Sept 2012 [cached])

Julian A. Martinez-Agosto

... **Julian Martinez-Agosto** UCLA stem cell scientists have found 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. "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," said **UCLA's Dr. Julian A. Martinez-Agosto**, the senior author of the study. "In particular, we wondered how the blood progenitor cells sense that change and know when it's time to make more blood cells." To answer this question, **Martinez-Agosto**, an assistant professor of human genetics and pediatrics and a researcher with the **Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA**, and his colleagues examined a signaling pathway called TOR that the cells use to gauge nutrition levels and stress. "We found that the TOR pathway uses these two genes to regulate its function and, when activated, it expands or increases the number of blood progenitor cells in the fly's blood," **Martinez-Agosto** said.

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[The researchers examined a signaling ...](#)

[www.eurekalert.org, 5 Sept 2012 \[cached\]](#)

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"[The cells in the niche provide ...](#)
newsroom.ucla.edu, 4 Jan 2012 [cached]

"The cells in the niche provide a safe environment to support blood progenitor cells," said co-senior author **Dr. Julian A. Martinez-Agosto**, an assistant professor of human genetics and pediatrics and a researcher with the **Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research 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 niche cells are removed, blood progenitor cells differentiate unchecked. Ultimately, the fruit fly runs out of progenitor cells and is not able to make new cells to mount an immune response to infection or injury, **Martinez-Agosto** said. **Martinez-Agosto** and co-senior author Utpal Banerjee, a Broad Center researcher and the Irving and Jean Stone Professor and chairman of molecular, cell and developmental biology in the UCLA Division of Life Sciences, identified the additional signals coming from the daughter blood cells - a surprising discovery, Banerjee said.

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Martinez-Agosto and Banerjee 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 and did not multiply.

...

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." The team used the fruit fly because it is a very accessible model organism in which genes can be easily manipulated and their effects on cells monitored, **Martinez-Agosto** said.

"The cells in the niche provide ...
www.eurekalert.org, 22 Dec 2011 [cached]

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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 findings by **Martinez-Agosto** and study co-senior author Utpal Banerjee, a Broad center researcher and the Irving and Jean Stone Professor and chairman of molecular, cell and developmental biology in Life Sciences, identified additional signals not coming from the niche cells.

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Martinez-Agosto and Banerjee 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.

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