'Good' cells can go 'bad' in a 'bad neighborhood'

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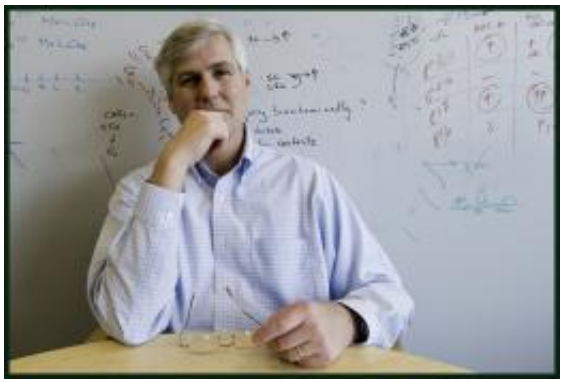

"It [the environment in which the cells develop] can make the system go askew," David Scadden explained.

(PhysOrg.com) -- The general theory of cancer development holds that malignancies occur because of the presence of certain genetic elements within the affected cells.

But a new study by Harvard researchers at Massachusetts General Hospital (MGH) indicates that "good" cells can become cancerous because of exposure to a "bad" environment within the body — similarly to the way a "good boy" may turn to crime when exposed to the pressures of life in a crime-ridden neighborhood.

In their paper in today's edition of the journal *Nature*, David T. Scadden and colleagues report that normal blood stem cells "are dependent upon their environment. They get their cues from the surrounding 'neighborhood' of bone cells," says Scadden, co-director of the Harvard Stem Cell Institute and director of the MGH Center for Regenerative Medicine. "It [the environment in which the cells develop] can make the system go askew," Scadden explained.

Working with mice with normal blood stem cells, Scadden, who is also co-chair of Harvard's inter-School Department of Stem Cell and Regenerative Biology (SCRB), and his team found that when they made a particular genetic alteration in the bone cells surrounding the blood stem cells of the mice, the mice developed a condition called myelodysplasia, a blood disease that is often a precursor of acute myelogenous leukemia (AML), a highly aggressive, usually fatal, form of cancer.

Scadden said it has long been known that a large fraction of patients who develop myelodysplasia "don't have any known genetic abnormality in their bone marrow. But myelodysplasia is called pre-leukemia, so why don't they? That suggests that it's not their blood stem cells that are defective, but rather that there's something wrong with the environment in which their blood cells reside."

According to Marc H.G.P. Raaijmakers, a postdoctoral fellow in Scadden's lab and the lead author of the *Nature* report, "our findings bring new insight into how cancer can emerge, indicating that nearby cells gone bad can facilitate a cell becoming malignant.

"In this case," notes Raaijmakers, "the mice developed fatal AML and were shown to have rapidly developed new genetic injuries in blood cells" after exposure to the defective bone cells in their environment.

Scadden and Raaijamakers both said that the findings might suggest a new approach for developing cancer therapies — targeting interactions between the cells that become malignant, and the "bad" cells in their neighborhoods.

Provided by Harvard University

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