# Stem Cells' Janus Faces

Cynthia Fox

The ability of HIV to linger in the body for decades may be due to the simple fact that it hides in stem cells that live for decades.

This is according to a January 2014 *Nature Medicine* [1] paper by Harvard immunologist Mathias Lichterfeld et al. The news was striking to immunologist Nicholas Restifo of the National Cancer Institute, the man who actually isolated [2] the memory T stem cells Lichterfeld tagged as HIV's biological safe house. Restifo told us: "It is fascinating and at the same time sort of horrifying to read in the

(Lichterfeld) paper that the HIV virus takes advantage of this stem cell-like activity to survive and propagate for long periods of time. It is reminiscent of the concept that cancer too can take on stem cell-like properties to propagate itself forever. Indeed cancer in some cases might actually be transformed stem cells."

He continues: "Thus the biology of stemness is Janus-faced. Stem cells offer the chance for regeneration. They are why even old people can rejuvenate and heal their own tissues. But these same cells can have a dark side as well." Restifo is, ironically, using the memory T stem cells he isolated to attack cancers--some of which arose from stem cells in the *first* place. He is finding that those “T stem cell” armies are more potent [3] cancer-killers than the “mature T cell” armies of most cancer immunotherapies. (See more from both Lichterfeld and Restifo in a related story in an upcoming [4]*Drug Discovery and Development* article.)

The "Janus Faces" of stem cells unveiled themselves further in a January 2014 *Stem Cell Reports* [5] paper. Breast cancer stem cells may transition between two different stem cell states, according to the team of University of Michigan oncologist Max Wicha. One stem cell state helps tumors mobilize; another stem cell state helps them grow. This may also explain the different kinds of breast cancers-- say "luminal" vs. "triple negative" cancers.

Georgia Regents Cancer Center molecular oncologist Hasan Korkaya, who has worked with Wicha on cancer stem cells, tells us: "I think this paper is demonstrating a contrary view to that of MIT's Robert Weinberg, who suggested a spontaneous conversion [6] of non-stem cells to stem cells." That is, Wicha’s paper emphasizes cancers arising from stem cells gone awry, where Weinberg, in a 2011 paper, emphasized a “bidirectional” effect, where cancers arise from both stem cells, and mature cells trying to revert to a stem-cell-like state. "Max is also trying to conclude that cancer stem cells in the "mesenchymal epithelial transition" state may represent luminal tumors and may be driven by the expression of the receptor HER2 (on the tumor cells), while cancer stem cells in the "epithelial mesenchymal transition" state may be representing the triple negative breast cancers. There may also be a transition between these two states even in the clinical settings." (See upcoming [7] *Bioscience* story, in which both Wicha and Weinberg elaborate.)

Stem cells are the most potent cells in the body. But they can also become, it seems increasingly clear, the most dangerous cells in the body.



**Links:**
[1] http://www.nature.com/nm/journal/vaop/ncurrent/full/nm.3445.html
[2] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3192229/
[3] http://www.nature.com/nrc/journal/v12/n10/full/nrc3322.html

[4] http://www.dddmag.com/articles/2014/04/stem-cells-hide-hiv-may-bring-new-therapies
[5] http://www.cell.com/stem-cell-reports/abstract/S2213-6711(13)00149-5
[6] http://www.pnas.org/content/108/19/7950.full.pdf+html
[7] http://www.biosciencetechnology.com/articles/2014/03/cancer-stem-cell-camps