Cancer biologists link tumor suppressor gene to stem cells

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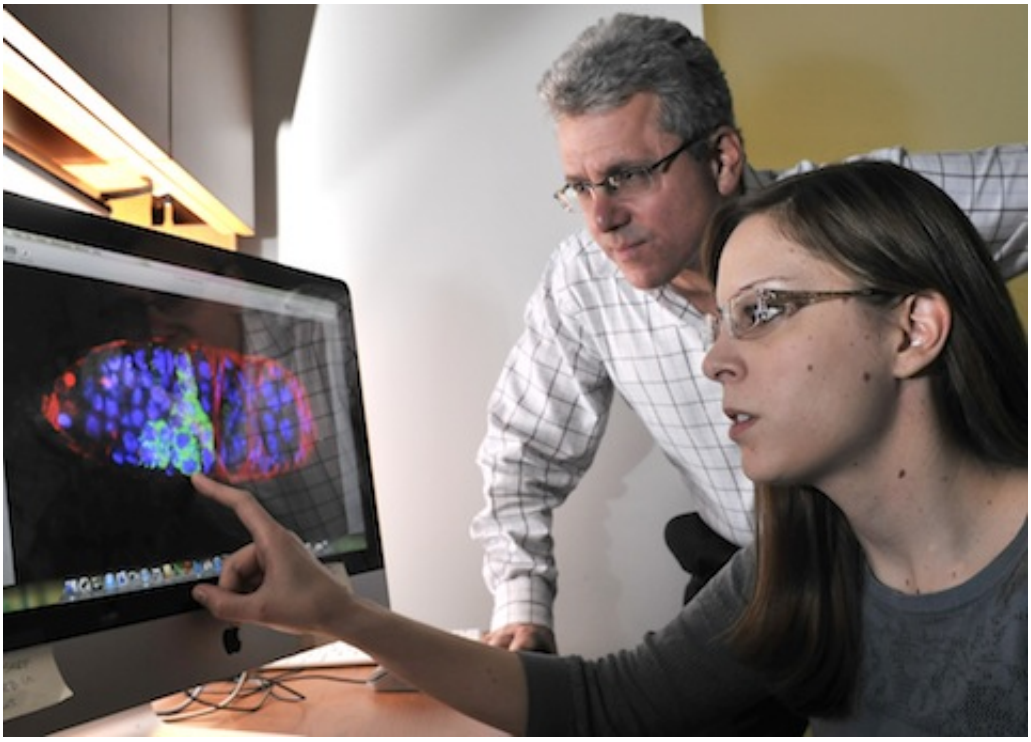

Dr. John Abrams, professor of cell biology (left), and Annika Wylie, a graduate student in genetics and development, discovered that an ancient gene called p53 activates stem cells when damage is present. Credit: UT Southwestern Medical Center

Just as archeologists try to decipher ancient tablets to discern their meaning, UT Southwestern Medical Center cancer biologists are working to decode the purpose of an ancient gene considered one of the

most important in cancer research.

The *p53* gene appears to be involved in signaling other cells instrumental in stopping tumor development. But the *p53* gene predates cancer, so scientists are uncertain what its original function is.

In trying to unravel the mystery, Dr. John Abrams, Professor of Cell Biology at UT Southwestern, and his team made a crucial new discovery – tying the *p53* gene to stem cells. Specifically, his lab found that when cellular damage is present, the gene is hyperactive in stem cells, but not in other cells. The findings suggest *p53*'s tumor suppression ability may have evolved from its more ancient ability to regulate stem cell growth.

"The discovery was that only the stem cells light up. None of the others do. The exciting implication is that we are able to understand the function of *p53* in stem cells," said Dr. Abrams, Chair of the Genetics and Development program in UT Southwestern's Graduate School of Biomedical Sciences. "We may, in fact, have some important answers for how *p53* suppresses tumors."

The findings appear online in the journal *eLife*, a joint initiative of the Howard Hughes Medical Institute, the Max Planck Society, and the Wellcome Trust.

p53 is one of the hardest working and most effective allies in the fight against cancer, said Dr. Abrams. It regulates other genes, marshaling them to carry out an untold number of preemptive attacks and obliterate many pre-cancerous cells before they ever pose a threat. In nearly every case where there's a tumor, *p53* is damaged or deranged, strongly suggesting that it is a tumor suppressant.

Stem cells are one of the body's most useful cells because of their regenerative capabilities. Stem cells produce daughter cells, one that is a

stem cell and another that can become virtually any kind of cell that's needed, such as a blood cell or a kidney cell. Stem cells have received tremendous attention in cancer research because of the stem cell hypothesis. That hypothesis maintains that malignant tumors are initiated and maintained by a population of tumor cells that have properties similar to adult stem cells.

"What this new finding tells us is that an ancient functionality of *p53* was hard-wired into stem cell function," said Dr. Abrams, senior author. "From the standpoint of trying to decipher cancer biology, that's a pretty profound observation."

To study the gene, researchers in Dr. Abrams lab, including Dr. Annika Wylie, postdoctoral research fellow and first author on the paper, developed a transgenic sensor that makes cells glow when they are active in *Drosophila*, or fruit flies. Other UT Southwestern researchers involved included Dr. Michael Buszczak, Assistant Professor of Molecular Biology.

Provided by UT Southwestern Medical Center