



Geoffrey M. Wahl

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“We are studying the genetic basis of the origin and progression of cancer and developing new strategies to tailor-make drugs based on the genetic signature of a patient’s tumor.”

Cancer is the second leading cause of death in the United States, but the revolution in our understanding of cancer etiology holds the promise for significant therapeutic advancements in the future. There are, however, two significant impediments to effectively treating cancer. First, cancer is often detected when it is very advanced. Second, cancer cells are often genetically unstable, enabling them to develop resistance to anti-cancer drugs at alarming rates. Wahl and his team showed that cancer cell genetic instability often involves disabling a stress response pathway controlled by the key tumor suppressor, p53. P53, a transcription factor that regulates the activity of genes, is activated by many of the stresses, such as DNA damage, that promote cancer cell development. Once activated, it stops cell division or, if the damage is too severe, induces a cell death program.

Recently, a collaborative study led by Geoff Wahl and Juan Carlos Ispizúa Belmonte uncovered that the tumor suppressor p53 not only stops cells that could become cancerous in their tracks but also controls somatic cell reprogramming.

In cells genetically engineered to lack p53, reprogramming efficiency was increased at least tenfold compared to control cells, demonstrating that p53 clearly played an important role in reining in cells trying to revert back into a stem-like state. Their findings not only bring iPSCs technology a step closer to fulfilling its promise as a source of patient-specific stem cells but also are forcing scientists to rethink the development of cancer.

The idea that cancer arises through the de-differentiation of fully committed and specialized cells had been around for decades, but eventually it was discarded in favor of the currently fashionable cancer stem cell theory. Now that Wahl and his colleagues have shown that p53 prevents de-differentiation, they believe it is time to reconsider the possibility that reprogramming plays a role in the development of cancer since virtually all cancer cells lose p53 function in one way or another. They have begun to investigate whether mutation of p53 promotes acquisition of a stem-like state during tumorigenesis in vivo, with encouraging preliminary results.

For more information, please visit
salk.edu/faculty/wahl.html



Left to right:

Rose Rodewald, Jennifer Lin, Justin La, Samantha Cheung, Jennifer Green, Dannielle Engle, Geoffrey Wahl, Mark Wade, Vivian Wang, Daphne Chen, Benjamin Spike, Leo Li, Taneashia Morrell (at top)