

Stem Cell Vaccine Protects Mice From Cancer

Stem cells and cancer cells have enough molecular similarities that the former can be used to trigger immunity against the latter.

By Ruth Williams | February 15, 2018

With their pluripotency and ability to self-renew, some cancer cells have been likened to stem cells. Now, researchers show that the similarities between the

cells are in fact sufficient for induced pluripotent stem cells (iPSCs) to serve as anti-cancer vaccines in mice. A paper in *Cell Stem Cell* today (February 15) reports

that injections of irradiated iPSCs protect mice from developing breast, lung, and skin cancers, and prevent surgically removed cancers from regrowing. "The approach, at first glance, seems simplistic and naive," cancer researcher [Robert Weinberg](#) of MIT's Whitehead Institute for Biomedical Research writes in an email to *The Scientist*. "Why should an early embryonic cell or a cell closely related to such an embryonic cell display markers that would provoke the immune system to attack certain types of cancer cells?"

But while it may not be intuitive to use an unrelated cell type to trigger immunity against cancer, hints that the scheme might work were dotted here and there throughout the literature. For example, cancer cells and embryonic cells have similar gene-expression and antigen profiles, and studies from almost a century ago showed that injecting embryonic material into animals protected them from transplanted tumors. More recently, embryonic stem cells have been shown to protect mice from cancer. It "isn't totally novel" to imagine stem cells as cancer vaccines, says oncologist and immunologist [Willem Overwijk](#) of the University of Texas MD Anderson Cancer Center, "but it's not widely discussed."

The new results have turned what was essentially "idle twaddle," says Weinberg, into something "highly credible and exciting."

While control animals developed sizable tumors over the weeks following cancer cell injection, mice that received the vaccine tended to have smaller tumors, or tumors that regressed.

Using embryonic stem cells as vaccines, as was done in the previous studies, poses problems, says [Nigel Kooreman](#), a surgical resident at the Haaglanden Medical Center in the Netherlands. For one thing, there are ethical and feasibility constraints. For another, the cells would not be genetically identical to the patient and so may not provide a matching repertoire of cancer antigens, he explains. "If the cell line comes from yourself, then it will likely be the best representation of whatever the cancer cells might look like."

The use of iPSCs circumvents these issues, says Kooreman, a coauthor of the study. The ultimate goal, he says, would be to isolate blood or skin cells from a patient, create iPSCs, irradiate the cells so they themselves cannot form tumors, and then inject them back into a patient already suffering from cancer. Or, says Stanford University's [Joseph Wu](#), who led the research, the iPSCs could be used as a prophylactic in older people to protect against the possibility of developing cancers. "By the time we reach 70 there's a higher prevalence of cancer, so it's possible in the future that anybody who is 70 years old will have iPSCs generated and be vaccinated to prevent future cancer formation," Wu says.

To find out if such concepts might actually work, the researchers turned to mice. Having first determined that mouse and human iPSCs have gene-expression profiles similar to those of cancer cells, the researchers used mouse iPSCs developed from fibroblasts together with an immune-boosting molecule called CpG to vaccinate the animals. A few weeks later, the mice were injected with breast, skin, or lung cancer cells. While control animals developed sizable tumors over the weeks following cancer cell injection, mice that received the vaccine tended to have smaller tumors, or tumors that regressed, showing that the vaccine worked prophylactically.

To confirm that the vaccine conferred specific anti-cancer immunity, the team transferred T cells from vaccinated animals into non-vaccinated animals with breast cancer, and they too experienced tumor regression.

Lastly, the team showed that while the vaccine could not eliminate established skin cancers in mice, it could prevent the regrowth of tumors that had been partially removed by surgery.

"That was a really exciting finding . . . because it is a realistic setting," says Overwijk. Often, surgeries to remove tumors from patients are unable to eradicate all cancerous cells, he explains. So a follow-up iPSC vaccination to boost the patient's own anti-cancer response would be highly valuable.

Using a patient's own cells as a vaccine might be expected to run the risk of inducing autoimmunity, but in the mice at least, says Kooreman, no signs of increased inflammatory signals nor any self-reactive antibodies were detected. Instead, "what we saw in our vaccination studies is that these mice thrive over time, they grew, they gained weight and had healthy-looking fur . . . We have not seen any signs that it is not safe."

Whether the vaccine will show similar efficacy and safety in humans remains to be determined, but these animal studies provide "a solid basis from which to go forward with real clinical potential," Overwijk says.

N.G. Kooreman et al., "Autologous iPSC-based vaccines elicit anti-tumor responses in vivo," *Cell Stem Cell*, doi:10.1016/j.stem.2018.01.016, 2018.