MedicalXpress

Engineered cancer cells can fight primary and metastatic cancer

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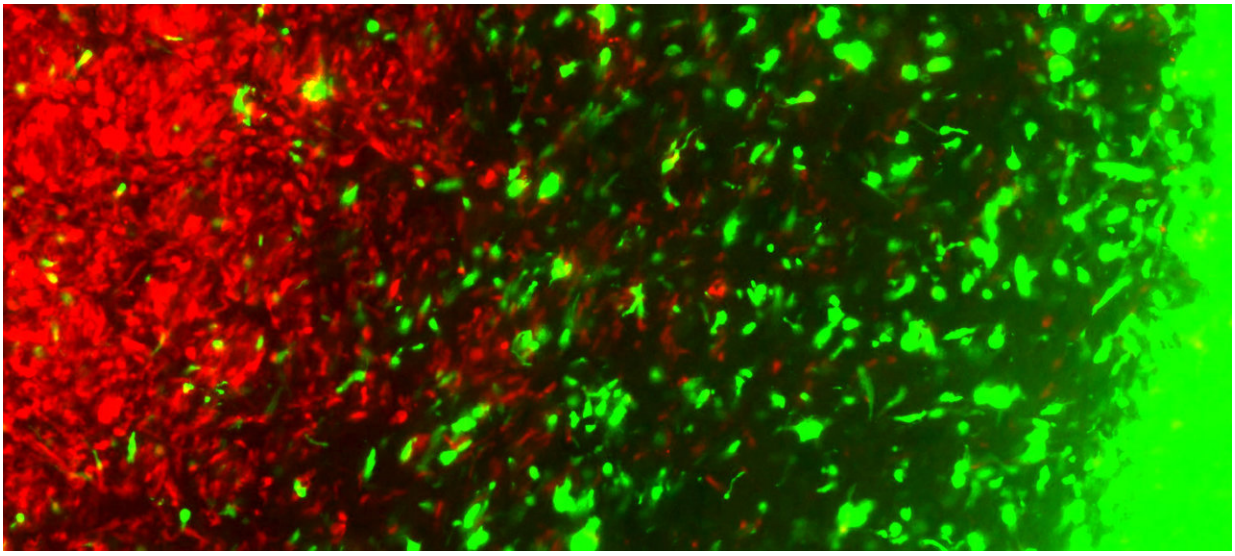


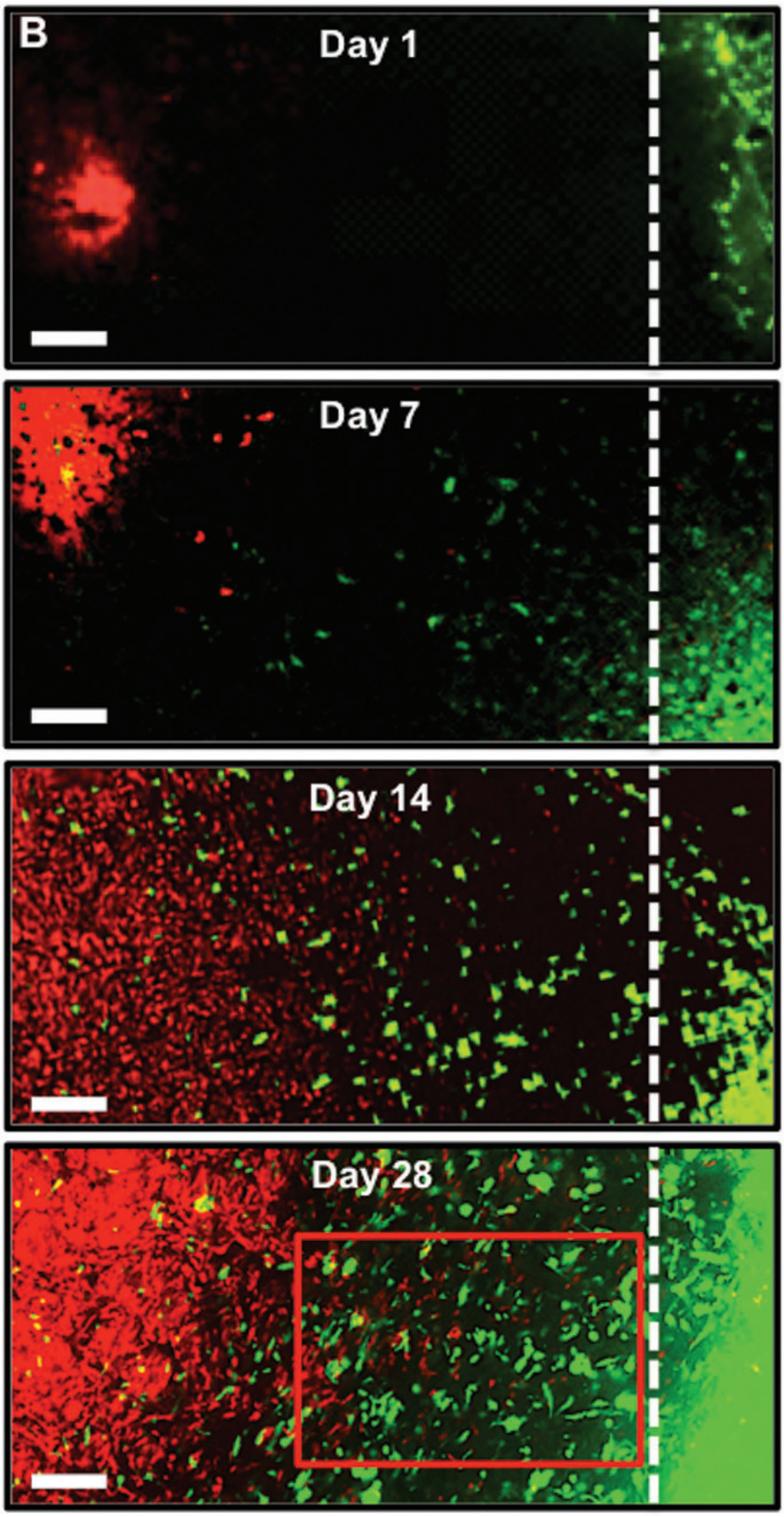
In this image, CRISPR-engineered therapeutic cancer cells (green) track primary cancer cells (red) in the brain. Credit: CSTI/Khalid Shah lab

What if cancer cells could be re-engineered to turn against their own kind? A new study led by researchers at Brigham and Women's Hospital leverages the power of gene editing to take a critical step toward using cancer cells to kill cancer. The team reports promising results in preclinical models across multiple types of cancer cells, establishing a potential roadmap toward clinical translation for treating primary, recurrent and metastatic cancer. Results are published in *Science Translational Medicine*.

"This is just the tip of the iceberg," said corresponding author Khalid Shah MS, Ph.D., director of the Center for Stem Cell Therapeutics and Imaging (CSTI) in the BWH Department of Neurosurgery and faculty at Harvard Medical School and Harvard Stem Cell Institute (HSCI). "Cell-based therapies hold tremendous promise for delivering therapeutic agents to tumors and may provide treatment options where standard therapy has failed. With our technique, we show it is possible to reverse-engineer a patient's own cancer cells and use them to treat cancer. We think this has many implications and could be applicable across all cancer cell types."

The new approach capitalizes on cancer cells' self-homing ability—the process in which cancer cells can track the cells of their kind that have spread within the same organ or to other parts of the body. Harnessing this power could overcome drug delivery challenges, helping get therapeutics to tumor sites that may otherwise be difficult to reach.

The team developed and tested two techniques to harness the power of cancer cells. The "off the shelf" technique used pre-engineered tumor cells that would need to be matched to a patient's HLA phenotype (essentially, a person's immune fingerprint). The "autologous" approach used CRISPR technology to edit the genome of a patient's cancer cells and insert therapeutic molecules. These cells could then be transferred back into the patient.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Day 1
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The CRISPR-engineered cancer cells (green) migrated towards an established glioblastoma tumor site (red) over the course of 28 days in a mouse model. Credit: C. Reinshagen et al., Science Translational Medicine (2018)

To test both approaches, the team used mouse models of primary and recurrent brain cancer and breast cancer that has spread to the brain. The team saw direct migration of engineered cells to the sites of tumors and found evidence that the engineered cells specifically targeted and killed recurrent and metastatic cancer in the mice. The researchers report that the treatment increased the survival of the mice. Engineered cells were equipped with a "kill switch" that could be activated after treatment—PET imaging showed that this kill switch worked to eliminate the cells.

"Our study demonstrates the therapeutic potential of using engineered tumor cells and their self-homing properties for developing receptor-targeted therapeutics for various cancers," said Shah.

More information: C. Reinshagen el al., "CRISPR-enhanced engineering of therapy-sensitive cancer cells for self-targeting of primary and metastatic tumors," *Science Translational Medicine* (2018). stm.sciencemag.org/lookup/doi/ … scitranslmed.aao3240

Provided by Brigham and Women's Hospital

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