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“One of the major interests in our laboratory is understanding the molecular mechanisms of cancer and the role of inflammation, which is the underlying cause of many diseases.”

The mouse has long provided researchers with valuable insights about cancer. But the most commonly used technique for producing a cancer mouse model—transplanting human tumor tissue or cancer cell lines in immunocompromised mice—ignores the role of the immune system in cancer. Other animal models either express oncogenes in a tissue-specific manner or shut down the expression of tumor suppressor genes in the whole tissue. But tumors generally develop from a single cell or a small number of cells of a specific cell type, which is one of the major determinants of the characteristics of tumor cells.

To create a better mouse model, researchers in Verma's laboratory turned to gene therapy techniques, using modified viruses to infect cells and ferry activated oncogenes into a small number of cells in adult, fully immunocompetent mice. After initial experiments confirmed that the approach was working, his team injected viruses carrying two well-known oncogenes into three brain regions of mice lacking one copy of the gene

encoding the tumor suppressor p53. They specifically targeted astrocytes, star-shaped support cells that are suspected of being the source of glioblastoma, the most common and deadly human brain cancer. Within a few months, massive tumors that displayed all the histological characteristics of glioblastoma developed in two of the regions.

To test whether the induced glioblastomas contained cancer stem cells, investigators isolated and cultured individual tumor cells in the lab, which looked and behaved just like neural stem cells. Less than 100 and as few as 10 cells were enough to initiate a tumor when injected into immunodeficient mice. These findings show that this cancer model will not only allow scientists to gain new insights into the biology of glioblastoma but will also help them answer many questions surrounding cancer stem cells. Verma and his team are currently using this methodology to investigate lung and prostate cancers.

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

Left to right:

Aaron Parker, Yifeng Xia, Amy Firth, Samantha Serey, Martin Preyer, Narayana Yeddula, Nien Hoong, Quan Zhu, Jesse Fox, Beth Coyne, Tatiana Hurtado De Mendoza, Nina Tonnu, Noam Beckmann, Fei Liu, Dinorah Morvinski, Mark Schmitt, Margaret Lutz, Rajesh Narasimamurthy, Ruben Alvarez, Oded Singer, Yair Pilpel, Travis Berggren, Gerald Pao, Yasushi Soda, Bjarne Woods, Karl-Dimiter Bissig, Inder Verma

