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High Throughput Screening for Selective Inhibitors of Cancer Stem Cells

Eugene Ong

Screens for agents that specifically kill epithelial cancer stem cells (CSCs) have not been possible due to the rarity of these cells within tumor cell populations and their relative instability in culture. We describe here an approach to screening for agents with epithelial CSC-specific toxicity. We implemented this method in a chemical screen and discovered compounds showing selective toxicity for breast CSCs. One compound, salinomycin, reduces the proportion of CSCs by >100-fold relative to paclitaxel, a commonly used breast cancer chemotherapeutic drug. Treatment of mice with salinomycin inhibits mammary tumor growth in vivo and induces increased epithelial differentiation of tumor cells. In addition, global gene expression analyses show that salinomycin treatment results in the loss of expression of breast CSC genes previously identified by analyses of breast tissues isolated directly from patients. This study demonstrates the ability to identify agents with specific toxicity for epithelial CSCs.

紹介論文

Identification of Selective Inhibitors of Cancer Stem Cells by High-Throughput Screening

Piyush B. Gupta,1,3,7,* Tamer T. Onder,1,2,7 Guozhi Jiang,1,3 Kai Tao,4 Charlotte Kuperwasser,4 Robert A. Weinberg,1,2,6,8,* and Eric S. Lander1,2,3,5,8,*

1Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139, USA, 2Whitehead Institute for Biomedical Research, 9 Cambridge Center, Cambridge, MA 02142, USA, 3Broad Institute of MIT and Harvard, Cambridge, MA 02142, USA

4Department of Anatomy and Cell Biology, Tufts University School of Medicine and Molecular Oncology Research Institute, Tufts Medical Center, Boston, MA 02111, USA, 5Department of Systems Biology, Harvard Medical School, Boston, MA 02115, USA

6MIT Ludwig Center for Molecular Oncology, Cambridge, MA 02139

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Studies have identified subpopulations of cells within tumors that drive tumor growth and recurrence, termed cancer stem cells (CSCs). CSCs are resistant to many current cancer treatments, including chemo- and radiation therapy. This suggests that many cancer therapies, while killing the bulk of tumor cells, may ultimately fail because they do not eliminate CSCs, which survive to regenerate new tumors.

参考論文

1. Generation of breast cancer stem cells through epithelial-mesenchymal transition. Morel et al., *PLoS One*. 3(8):e2888 (2008)