Okayama University Medical Research Updates （OU-MRU） 2020.09 Vol.81

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Okayama University research: Innovative method for determining carcinogenicity of chemicals using iPS cells

(Okayama, 07 October) **In a recent study published in *Scientific Reports* researchers at Okayama University use stem cell models to show how certain chemical compounds can induce cancer.**

Stem cells have the unique ability to grow into any kind of cell within the body. A subtype of these, cancer stem cells (CSCs), reside within tumors enabling the aggressive growth of cancer. Researchers at Okayama University have previously converted ordinary stem cells into CSCs by growing them in tumor milieu. Now, for the first time, Professor SENO Masaharu and Dr. Juan Du from Okayama University and colleagues used this model and developed a method to observe the induction of cancer stem cells to identify potential carcinogens and their mechanisms.

Stem cells of mice were first grown in the microenvironment of lung tumors. Subsequently, these stem cells were treated with 110 different chemical compounds and the effects of these chemicals on CSC induction was measured. Within just a week, three compounds (PDO325901, CHIR99021, and Dasatinib) led to the first sign of CSCs—spherical cluster formation. While other compounds resulted in the stem cells losing their unique properties, PDO325901, CHIR99021, and Dasatinib effectively upheld the integrity of these cells. The stem cells treated with these three compounds where then transplanted into mice and allowed to grow for 6 weeks. As expected, these cells developed into malignant tumors implicating various parts of the mice. Molecular tags which help recognize CSCs were present in these tumors confirming the successful conversion of stem cells into CSCs.

Cancer is initiated when growth signals within a cell are activated indefinitely. When the team took a deeper look into such signals, they found that one cellular pathway, namely, PI3K-Akt-mTOR was especially active in the newly formed CSCs. Genes involved in this pathway were dormant in the original stem cells, but fully functioning in the CSCs. What's more, blockers of PI3K-Akt-mTOR did not result in successful CSC formation. PI3K-Akt-mTOR signaling was thus an important factor in turning healthy stem cells cancerous.

"In the current study, we proposed a simple method to assess the risks of tumor-inducing factors in the presence of chemical compounds that accelerated the conversion of miPSCs into CSCs", conclude the researchers. This study provides a robust model for revealing chemicals with a penchant for cancer initiation, using healthy stem cells. Additionally, this model also unraveled the importance of the PI3K-Akt-mTOR pathway in promoting the conversion of stem cells into CSCs. Therapies which target this pathway might keep cancer cells in check and prevent their spread.

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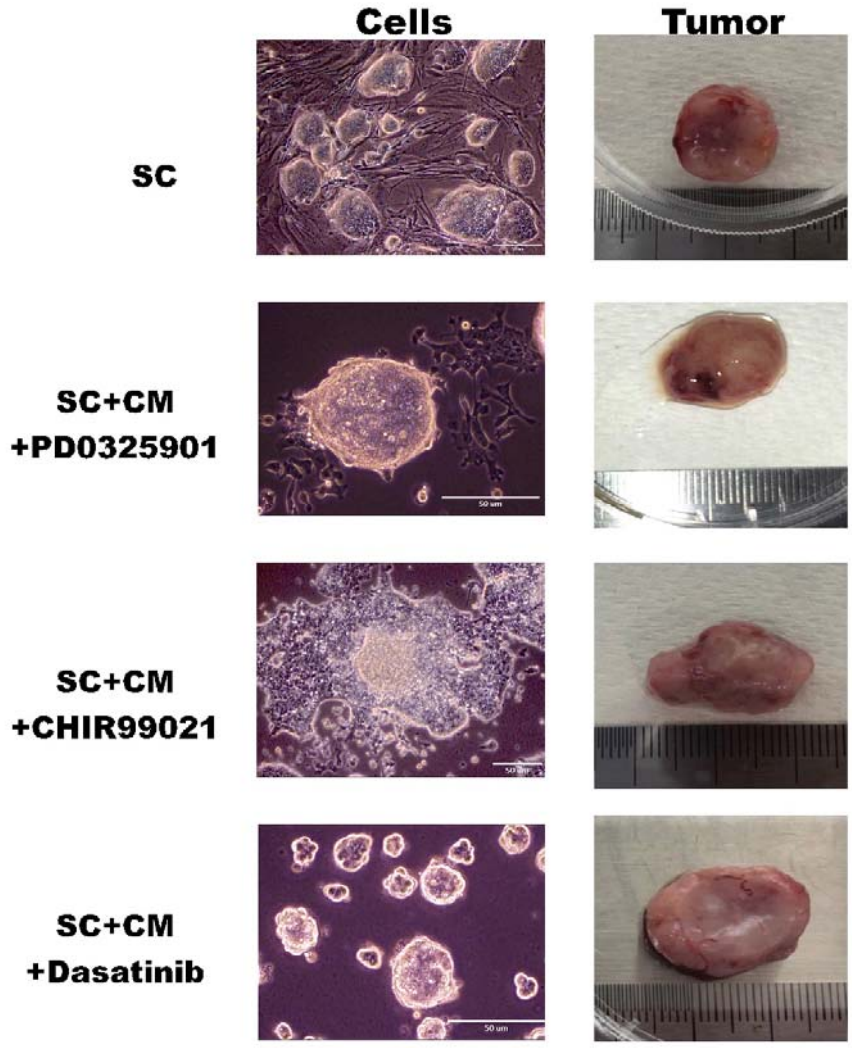
Background

Stem cells and CSCs: Stem cells have two characteristic properties which differentiate them from other cells in the body—they can divide uncontrollably and can grow into any kind of the cell in the body. Given these properties, cancer stem cells (CSCs) are especially dangerous as they multiply easily and contribute to the rapid growth of tumors.

Not too many cellular models enable scientists to visualize the processes at play when healthy, functioning cells turn cancerous; scientists typically rely on existing tumors to study the cells within. Thus, the technique of converting ordinary stem cells into CSCs has opened several research avenues to understand this transition better. Uncovering potential carcinogens, effectiveness of therapies, and underlying pathways are some of the areas researchers can explore with this technique.



Caption

The shapes (Cells) and tumorigenicity (Tumor) of stem cells after 1-week treatment. SC, stem cells without treatment; SC+CM+PD0325901, SC+CM+ CHIR99021 and SC+CM+Dasatinib, stem cells treated with PD0325901, CHIR99021 and Dasatinib, respectively in the presence of the conditioned medium of Lewis lung carcinoma cells (CM). Tumors formed by SCs treated with the compounds showed malignancy while that formed by SC without treatment formed benign teratoma.

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Reference
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Okayama Univ. e-Bulletin: http://www.okayama-u.ac.jp/user/kouhou/ebulletin/
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https://www.youtube.com/watch?v=vQxeL0ztSLA
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◆About Okayama University

Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index_e.html

Japan（日本）

Hirofumi Makino, M.D., Ph.D.
President , Okayama University

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An integrated report is intended to explain how an organization creates value over time through an organic integration of the vision and the combination of financial information and other information. Through this report we hope to promote greater interest in Okayama University among readers everywhere. In order to help us make improvements in future editions, we encourage you to contact us with any comments and suggestions you may have.

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