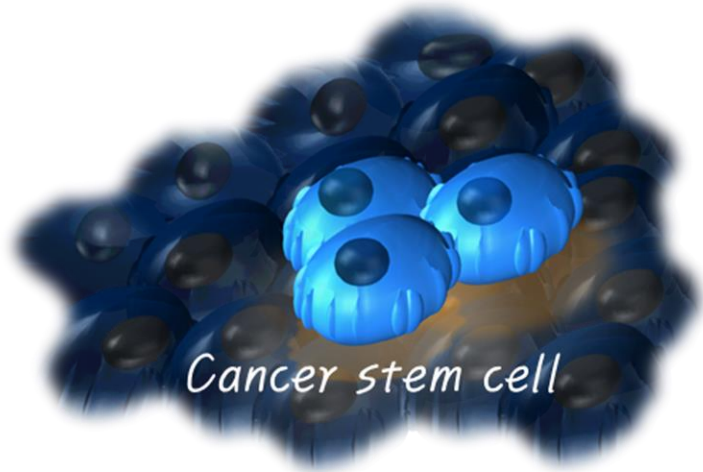


A polymer thin film platform that enables direct transformation of diverse cancer cells to tumorigenic cancer stem cell spheroids

Minsuk Choi, Seung J. Yu, Yoonjung Choi, Daeyoup Lee, Sung G. Im, Sangyong Jon

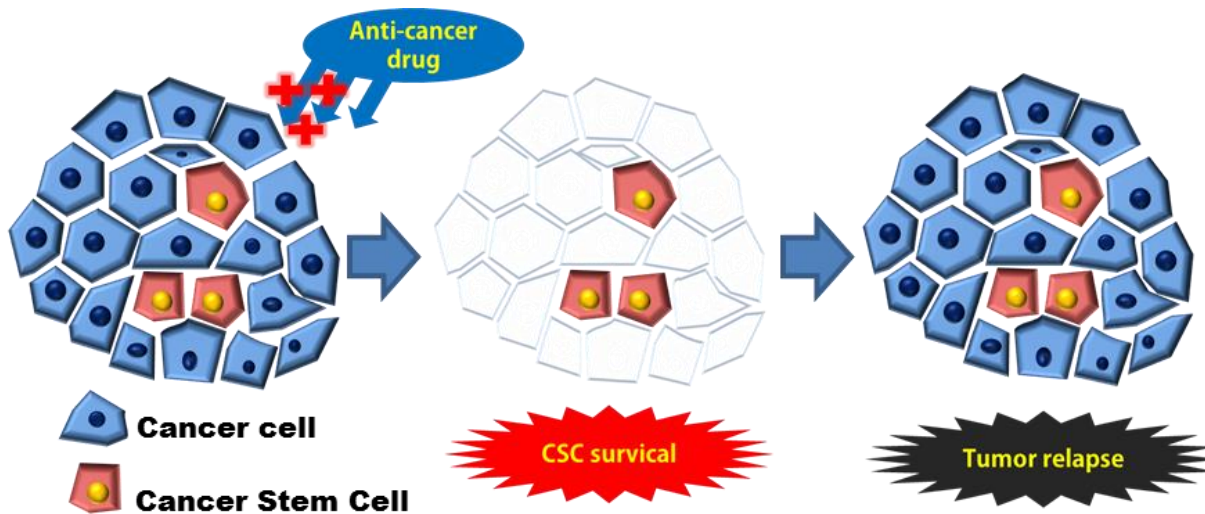


Cancer stem cell

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Cancer Stem Cell !

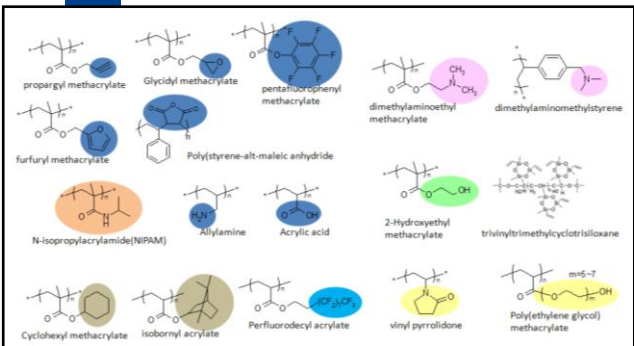
- Minor population in tumor: **0.1-a few %**
- Self-renewing; infinite proliferative potential
- Enhanced **resistance to drugs**, radiation, cell stress
- Tumorigenic; give rise to other cell types in tumor
- Associated with **metastasis** and **relapse**



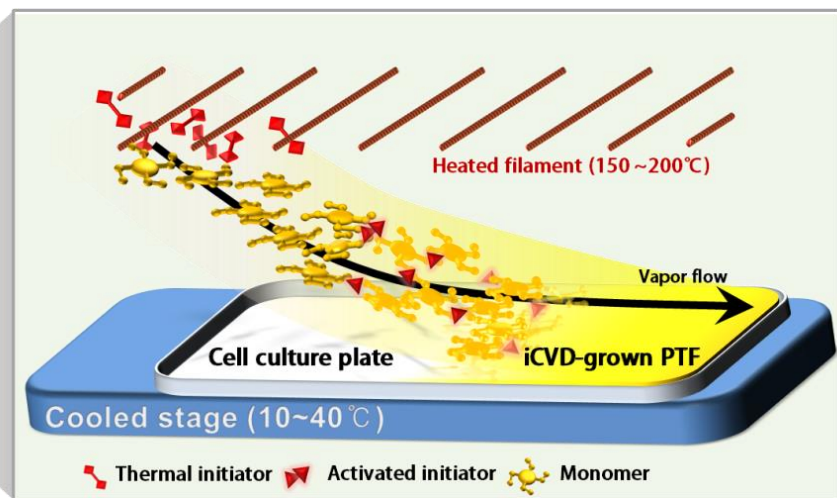
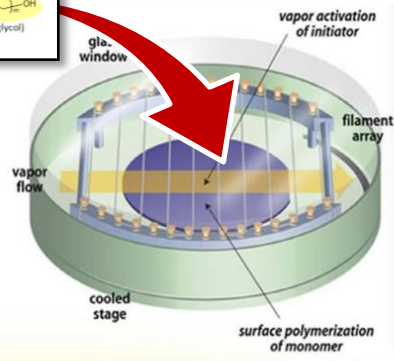
Metastasis and relapse are involved in **more than 90%** of all cancer deaths

Strategies to eradicate CSCs are an urgent topic in cancer research

Library of Polymer-Thin-Films (PTFs)



Searching for new materials by iCVD process

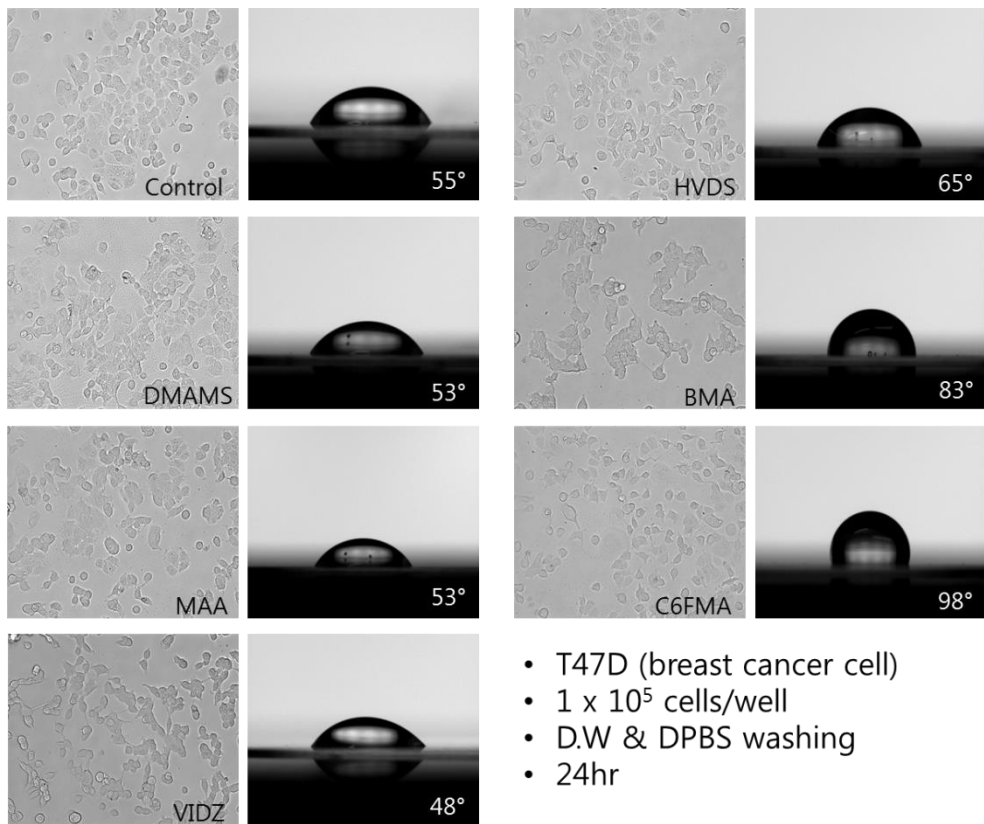


Optimizing process condition for iCVD

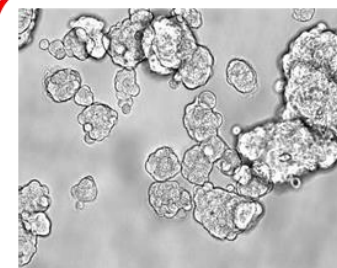


Library of polymer-thin-film coated cell culture plates

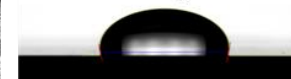
Library of Polymer-Thin-Films (PTFs)



Organo-
silicon



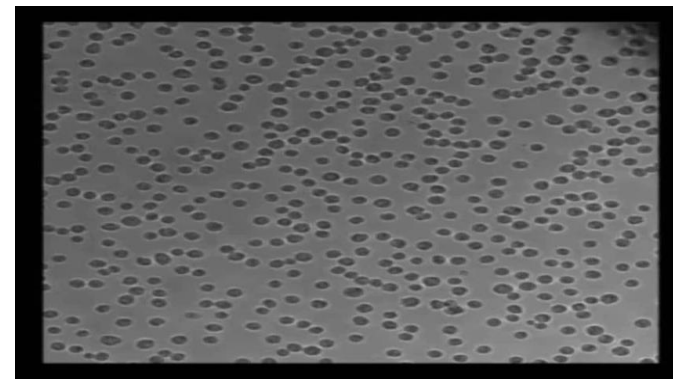
Contact angle: 96°



V4D4

Meth-
acrylate

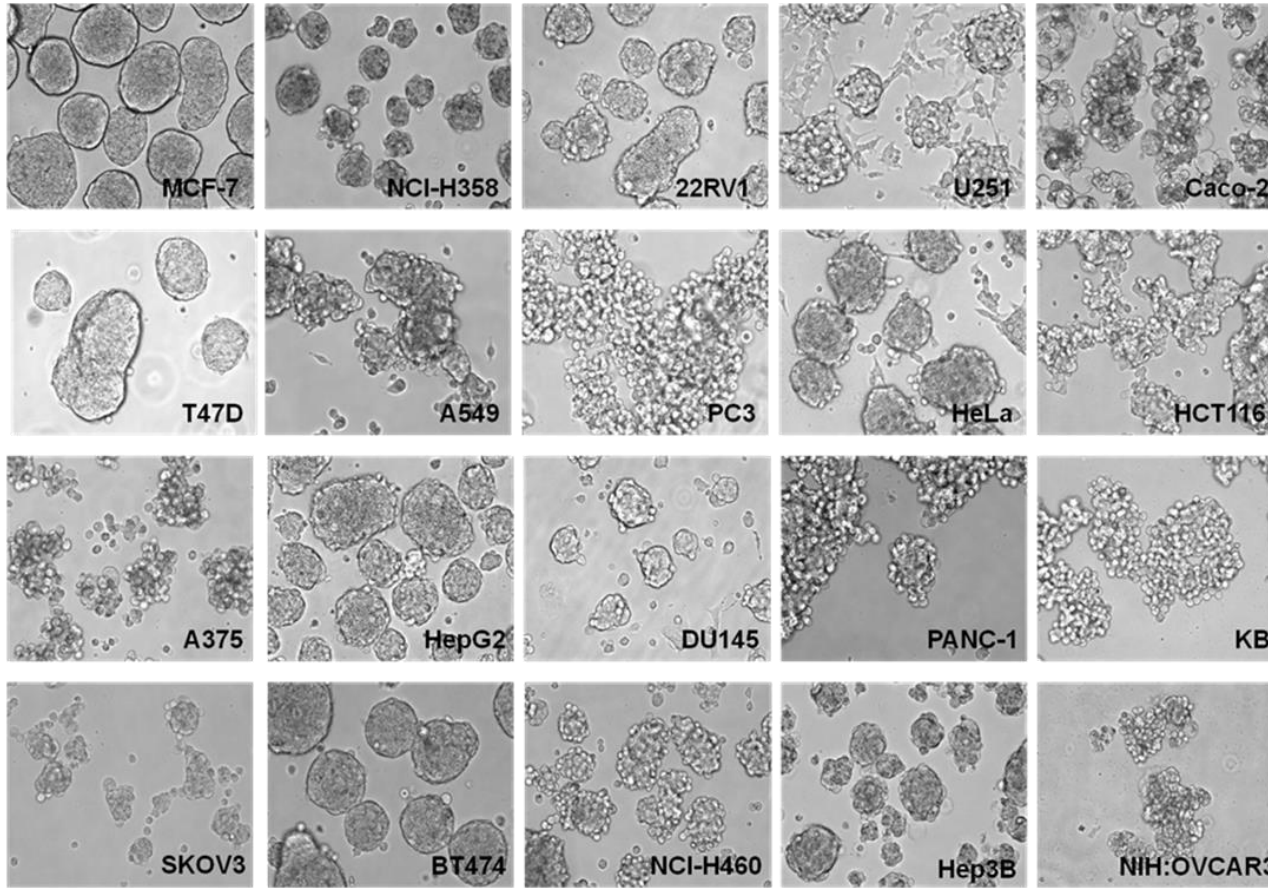
Live imaging: 24 h



- T47D (breast cancer cell)
- 1×10^5 cells/well
- D.W & DPBS washing
- 24hr

Various Cancer Cell Spheroids

Various cancer cell lines



Breast cancer cell

Colon cancer cell

Ovarian cancer cell

Pancreatic cancer cell

Liver cancer cell

Melanoma cancer cell

Prostate cancer cell

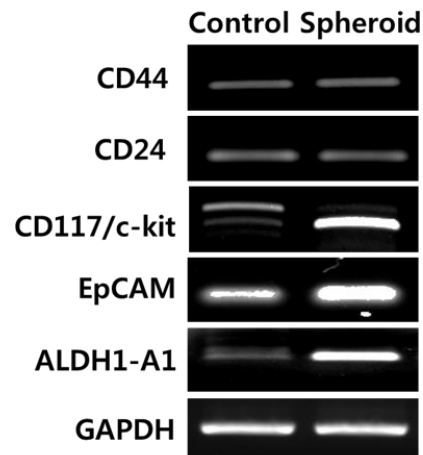
Lung cancer cell etc.

Scale bar = 100 μ m

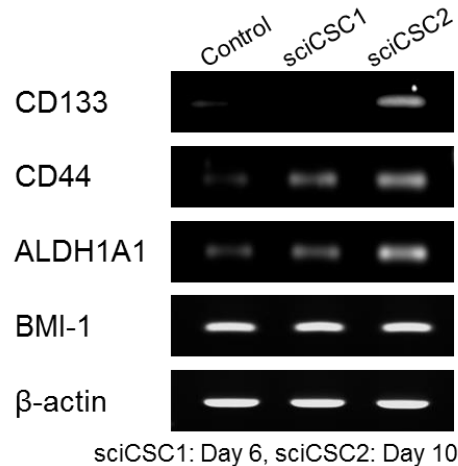
CSC Marker Gene Expression

RT-PCR

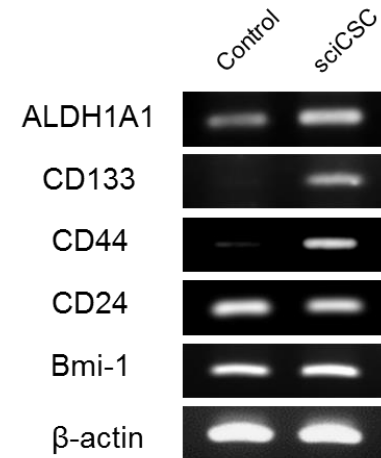
NCI-H358 (Lung cancer)



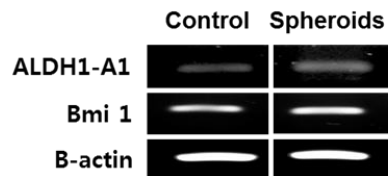
NCI-N87 (Gastric cancer)



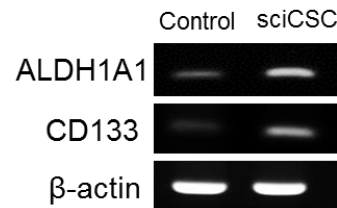
SW480 (colon cancer)



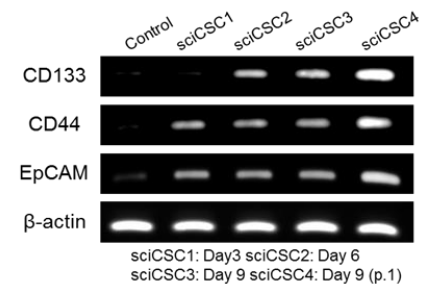
Hela



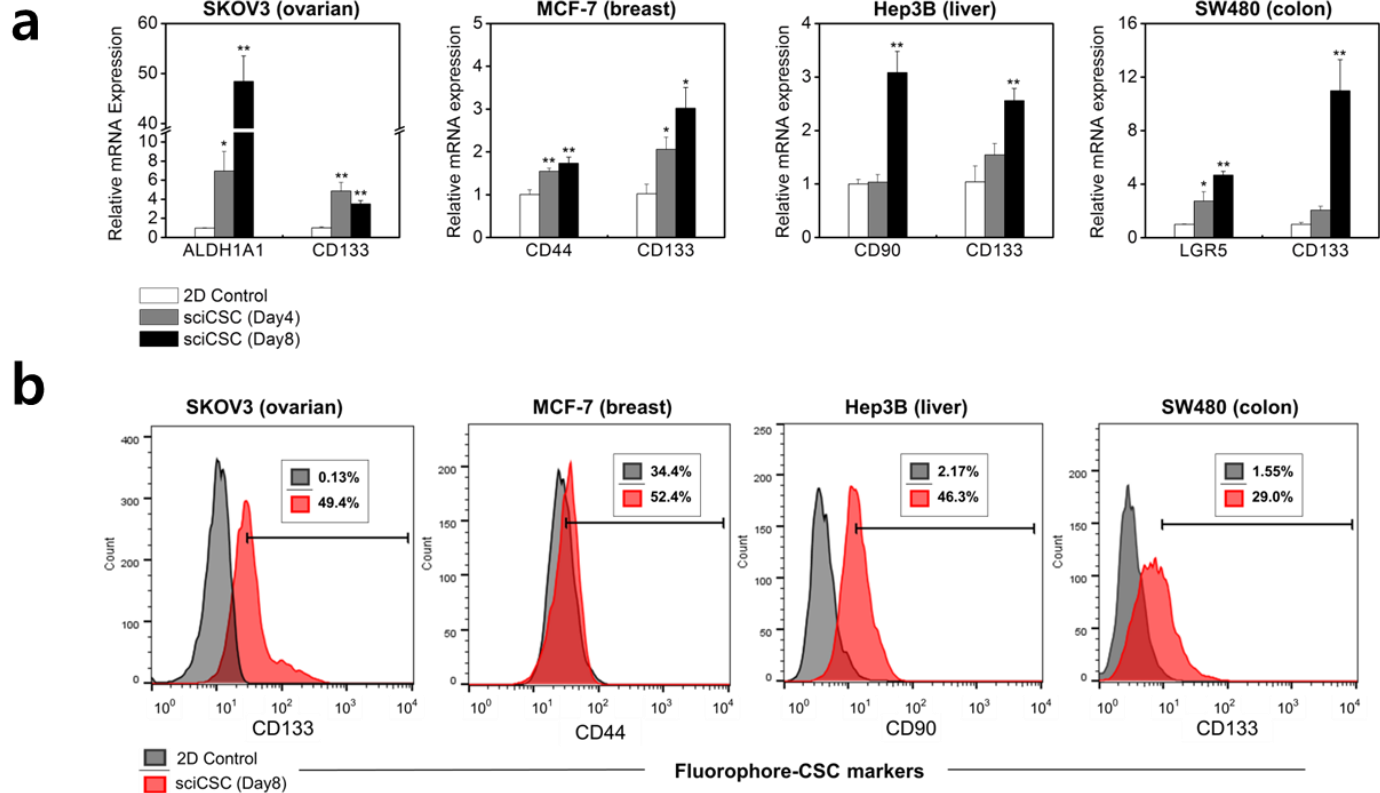
A375 (Melanoma)



Hep3B (Liver cancer)

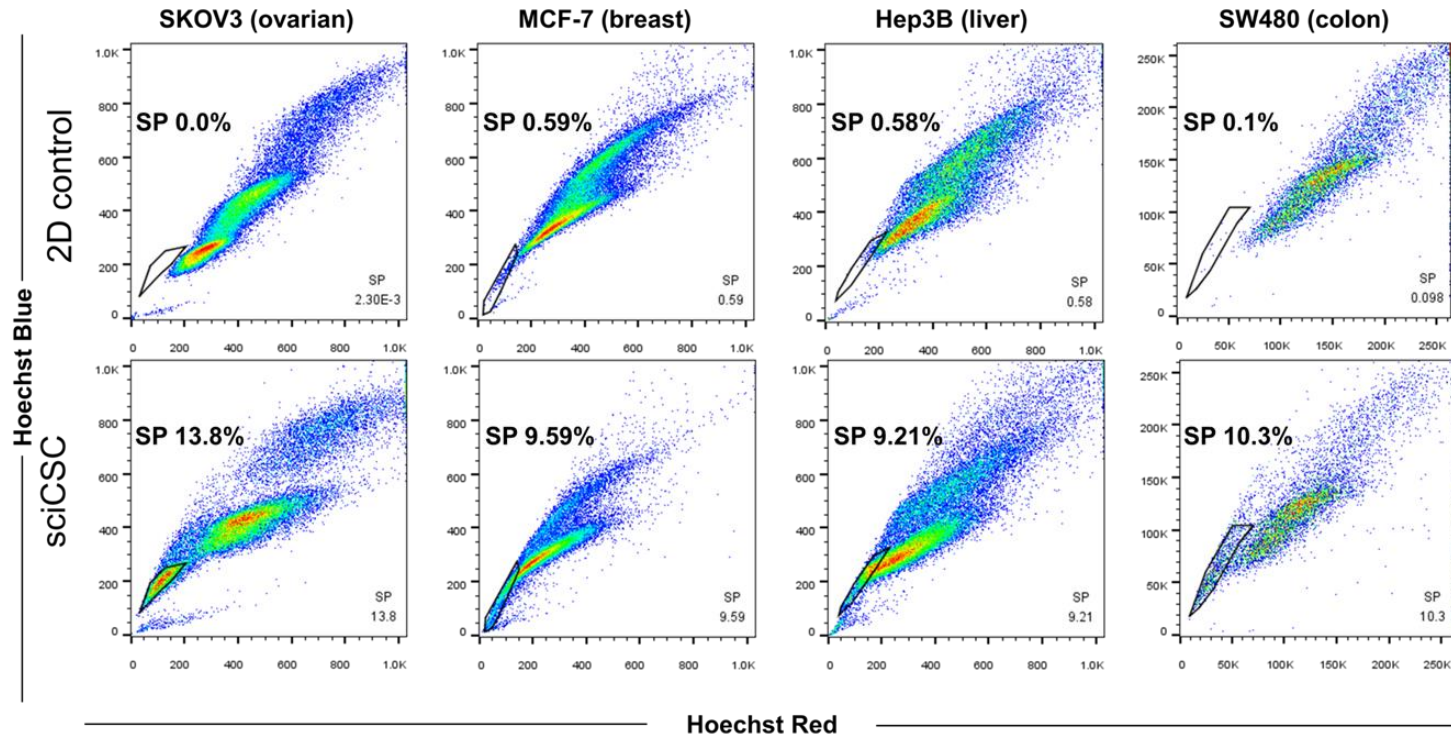


in-vitro Characterization



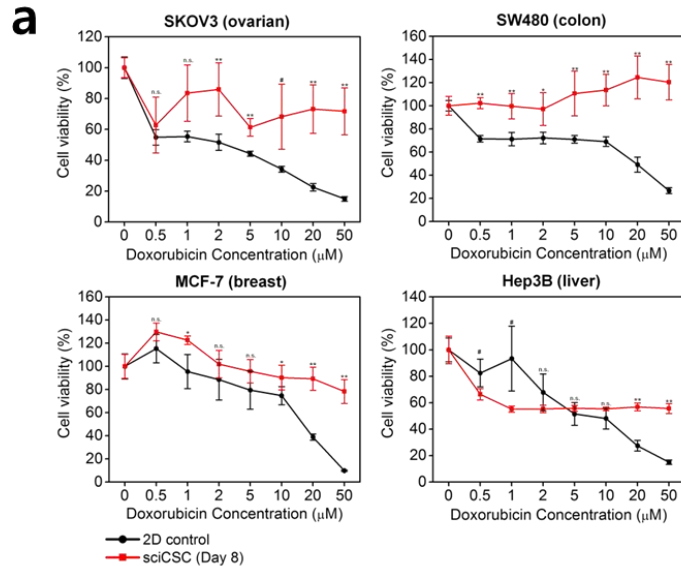
- The expression of cancer stem cell markers of SKOV3, MCF-7, Hep3B and SW480 cell spheroids on pV4D4 was quantified by real-time PCR
- Flow cytometry analysis of the cancer stem cell indicated markers in 2D control cells and sciCSCs.

in-vitro Characterization

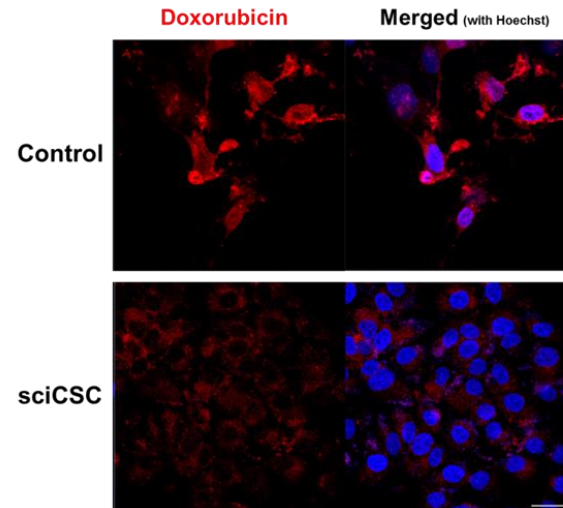
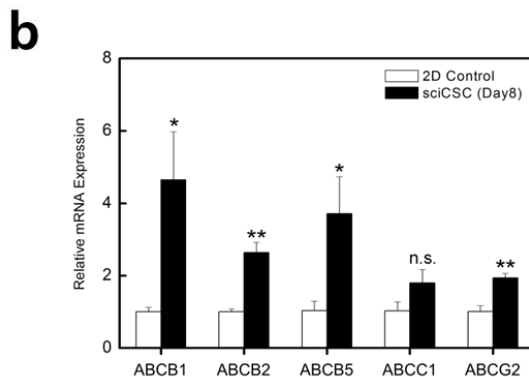


Representative flow cytometry plots for side-population discrimination (SP) assay using Hoechst 33342 staining in 2D control cells and sciCSCs (SKOV3, MCF-7, Hep3B and SW480).

in-vitro Characterization



- a. Drug resistance of SKOV3, MCF-7, Hep3B and SW480 cells was analyzed using doxorubicin.
- b. The expression of drug efflux ABC transporter markers of SKOV3, MCF-7, Hep3B and SW480 cell spheroids formed on pV4D4 surface were quantified by real-time PCR



in-vivo Characterization

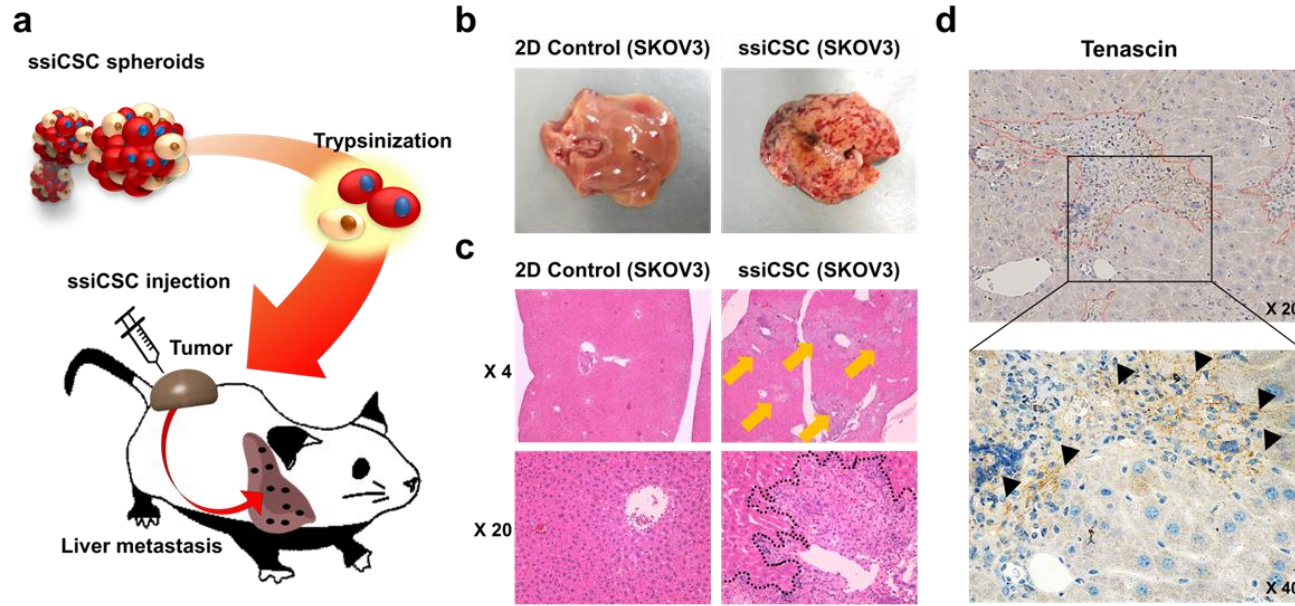


Table 1 | Tumor formation and metastasis of SKOV3 in BALB/c nude mice.^a

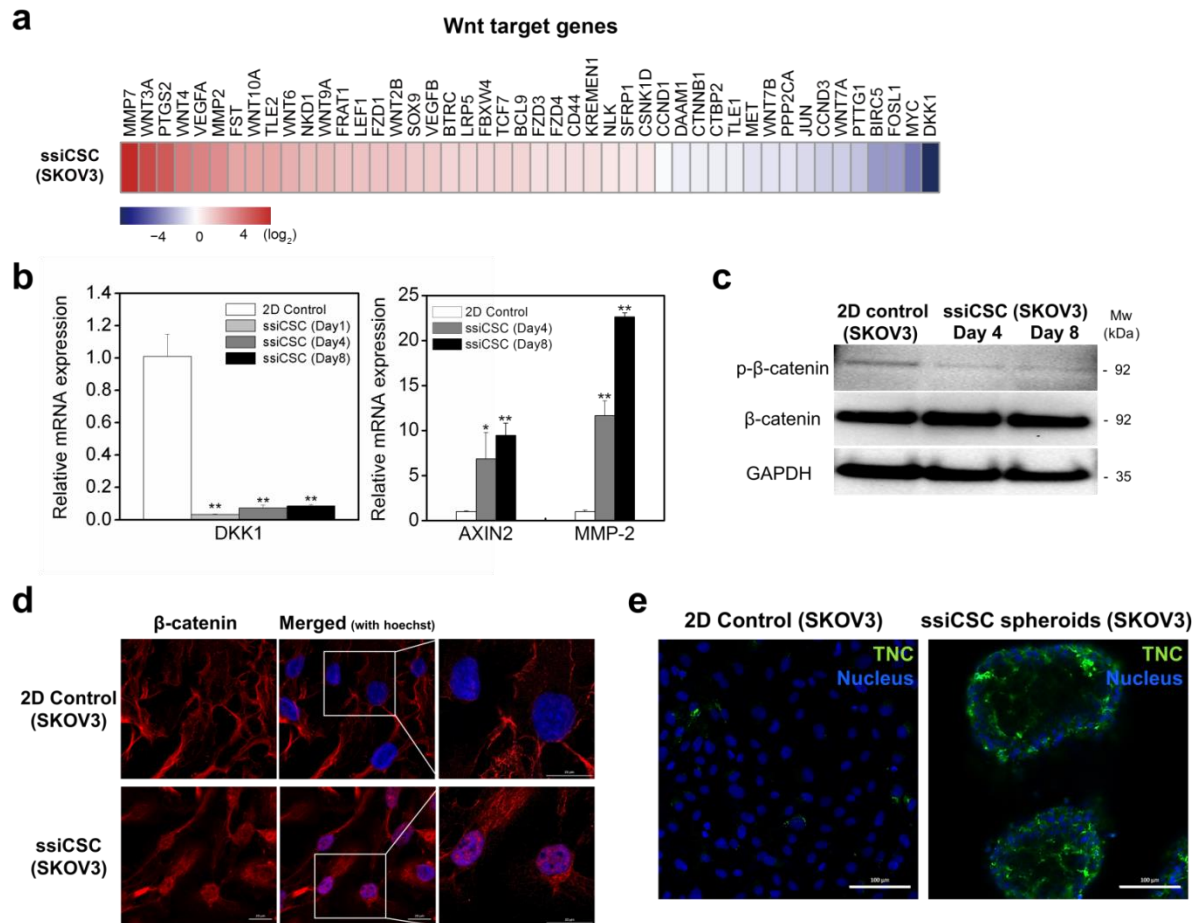
Cell number ^b	Tumor formation		Liver metastasis	
	2D control	ssiCSC	2D control	ssiCSC
100	0/5	0/5	0/5	4/5
1,000	0/5	1/5	0/5	4/5
10,000	0/5	4/5	0/5	4/5
100,000	0/5	3/5	0/5	5/5
1,000,000	2/4	-	0/4	-

^a Tumor formation and metastasis were monitored up to 120 days.

^b All cells were dissociated into single cells and counted with a hemocytometer before subcutaneous injection.

In vivo metastasis of the sciCSC (SKOV3) cells in liver tissue from primary dorsal tumor

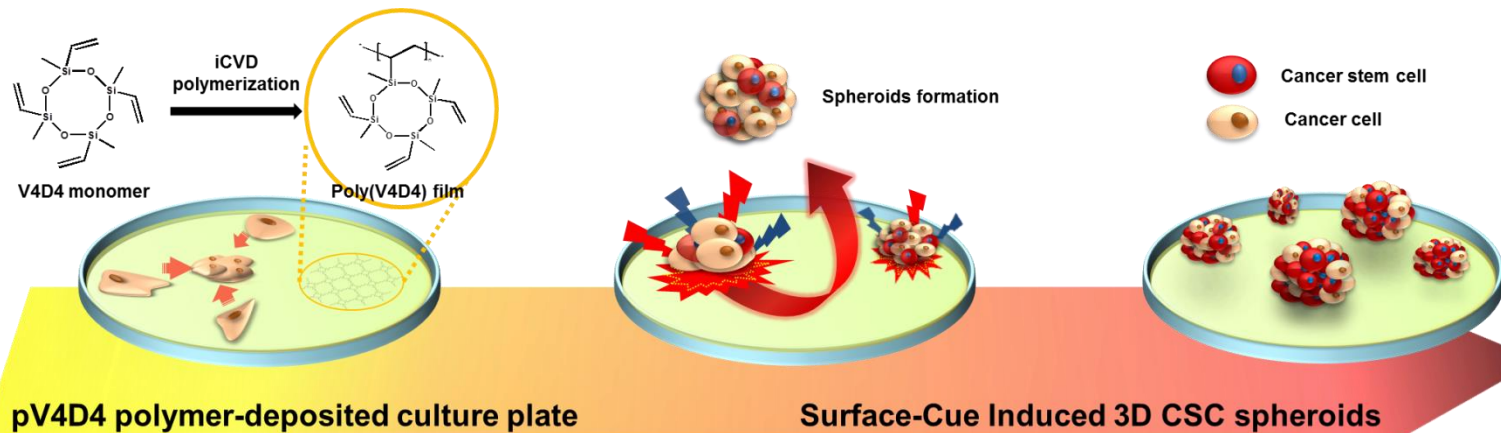
Mechanism Study



Activation of Wnt/ β -catenin signaling pathways in SKOV3-sciCSC spheroids

Conclusion

- The findings presented here clearly demonstrate that a **pV4D4-based cell-culture platform** enables the **conversion of conventional cancer cell lines to highly tumorigenic CSC-like spheroids** with high efficiency, reproducibility, and versatility.



Acknowledgement

This work was supported by a grant from the Samsung Research Funding Center of Samsung Electronics.



iCVD: 생명화학공학과 임성갑 교수님 연구팀

NGS: 생명과학과 이대엽 교수님 연구팀