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A new three dimensional live cell model to screen SERM, based on real time cell growth and death indicators

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Statement of the Problem: Researchers have devised a vast array of model systems to study the complex components of tumors and their treatments. The most simplistic cancer models are cell lines grown as flat monolayers submerged in media. 2D cell culture has contributed tremendous amounts of knowledge about cell growth and cell death. Selective estrogen receptor modulators (SERMs) most often induce growth arrest as well as cell death in the ERα+ cells. Since cell growth and cell death induced by these compounds are very slow, the use of 2D models representing increased cell proliferation is not an appropriate model. Cells in vivo grow and divide very slowly as seen by 3D model system.

Methodology & Theoretical Orientations: The primary objective of the study was to develop better 3D screening approach utilizing florescence based cell death sensors. The cell death sensor consisting of FRET pair of ECFP-EYFP linked in between with caspase specific DEVD sequence was developed and utilized for visualization and quantification of caspase activation in 3D culture by FRET microscopy.

Findings: Developed 3D model has shown significant difference in cell death and cell cycle proliferation determined against a panel of SERMs compared to 2D system and results confirmed closed in vivo similarities. The in vitro models utilizing FRET caspase probe and FACS analysis were also employed for screening of novel compounds in relation to clinically relevant SERMs.

Conclusion & Significance: The primary objective to develop a model of cell growth and cell death in 3D culture system was achieved. The results with known SERMs and novel compounds substantiated the efficacy of model system.

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