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Three-Dimensional *In Vitro* Co-Culture Model of Breast Tumor using Magnetic Levitation

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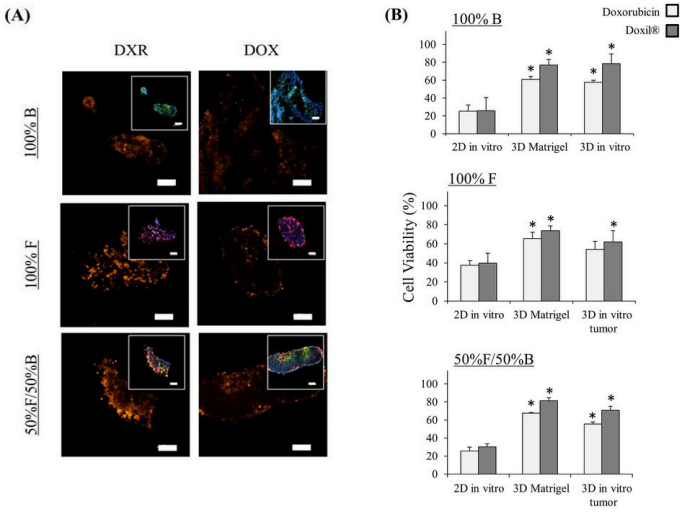
Abstract: In this study, we investigate a novel *in vitro* model to mimic heterogeneous breast tumors without the use of a scaffold while allowing for cell-cell and tumor-fibroblast interactions. Previous studies have shown that magnetic levitation system under conventional culturing conditions results in the formation of three-dimensional (3D) structures, closely resembling *in vivo* tissues (fat tissue, vasculature, etc.). Three-dimensional heterogeneous tumor models for breast cancer were designed to effectively model the influences of the tumor microenvironment on drug efficiency. Various breast cancer cells were co-cultured with fibroblasts and then magnetically levitated. Size and cell density of the resulting tumors were measured. The model was phenotypically compared to *in vivo* tumors and examined for the presence of ECM proteins. Lastly, the effects of tumor stroma in the 3D *in vitro* model on drug transport and efficiency were assessed. Our data suggest that the proposed 3D in vitro breast tumor is advantageous due to the ability to: (1) form large-sized (millimeter in diameter) breast tumor models within 24 h; (2) control tumor cell composition and density; (3) accurately mimic the *in vivo* tumor microenvironment; and (4) test drug efficiency in an *in vitro* model that is comparable to *in vivo* tumors.



Distribution and therapeutic efficacy of doxorubicin and Doxil on 3D *in vitro* tumors. (A) Fluorescent images of 3D in vitro tumors composed of mono- or co-culture of fibroblast (in red) and breast cancer cells (in green) –inset images, comparing 72 h treatment with doxorubicin and Doxil ®, blue – nucleus and orange – fluorescent emission from doxorubicin, Scale bar = 100 μm, (B) Viability assay treated with either doxorubicin or Doxil ® (100 nM) for 72 h, comparing on three different in vitro systems: (1) 2D in vitro (grown for 1 day), (2) 3D in vitro (grown for 1 day), and (3) 3D Matrigel™ (grown for 7 days) * = statistically significant difference to 2D in vitro with the same treatment, n = 4, $p < 0.05$.

- **BiO Assay combines the in vivo-like environment of 3D cultures, with a simple, real-time, and quantitative metric**
- **The iPod system improves throughput and efficiency**

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