Utilization of 3D Pancreatic Cancer Cell Lines for Analyzing and Evaluating Anticancer Drug Efficacy

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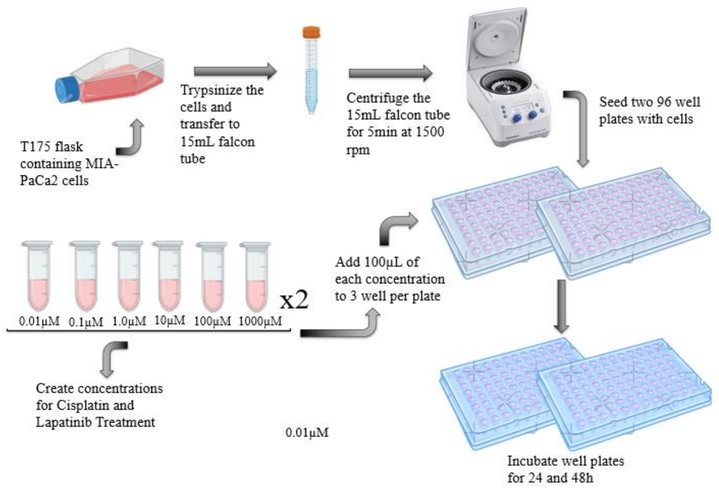
Introduction

The field of three-dimensional (3D) cell cultures holds great promise for mimicking in vivo microenvironments in cancer research. Compared to traditional two-dimensional (2D) models, 3D models offer advantages such as a better understanding of the cell line's microenvironment, increased relevance compared to 2D substrates, and improved direct imaging of changing aspects in each cell line. The scientific debate between 2D and 3D cell cultures for modeling in vivo cancer cell biology and drug screening has been ongoing, with 3D methods showing significant promise in recent years. Despite the century-long dominance of 2D cultures, 3D cell culture methods have demonstrated superior accuracy in representing cells as they would appear in an in vivo tumor, making them more effective for cancer drug screening. In this study we use a pancreatic cancer cell line (MIA-PaCa2), to explore both 2D and 3D culture methods, trying to identify variations in anti-cancer drug responses, aiming to determine which method is better suited for testing cancer drug treatments.

Types	2D models (culture dish, transwell membrane)	3D models (scaffold-based, spheroid, organoid)
Advantages	• Well established methodology • Easy to handle and quantify	• Include cell-cell and cell-ECM interaction • Capture the 3D architecture of tissue culture • Drug sensitivity similar to in vivo
Disadvantages	• Static condition • Lack of physical and biochemical cues • Large reagent volumes • Uniform concentration of nutrients and drugs	• No fluid flow perfusion to create dynamic environment • Inefficient nutrient and waste transport

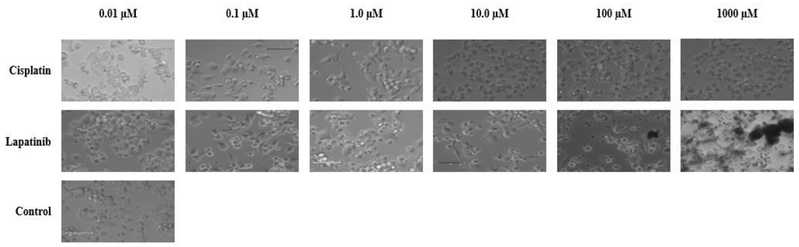
Experimental Methods

Seeding of (MIA-PaCa2) cells in 96-well plates and treated with anti-cancer drugs

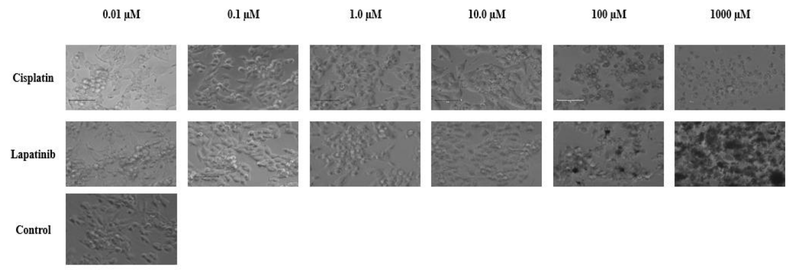


Results & Discussion

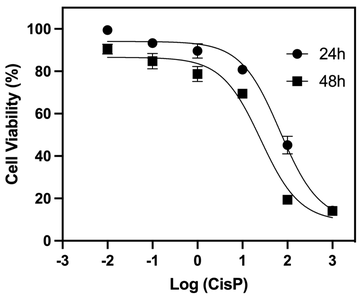
2D Culture of MIA-PaCa2 cells after 24 hours following treatment with anticancer drugs



2D Culture of MIA-PaCa2 cells after 48 hours following treatment with anticancer drugs

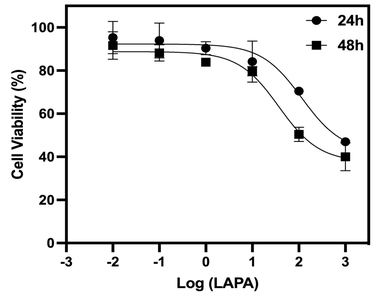


Cytotoxicity Tests for Cell Viability in 2D MIA-PaCa2 culture



IC50 24h - 68.14µM

48h - 25.34µM



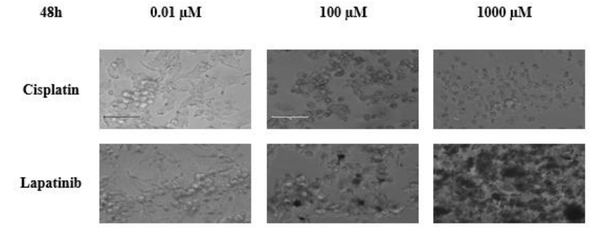
IC50 24h - 115.9µM

48h - 37.24µM

Results & Discussion Cont'd

For 2D MIA-PaCA2 cell cultures:

- Higher concentrations, particularly in the range of 100-1000 µM, resulted in increased effectiveness for all drug treatments, with cell toxicity directly correlating with both drug concentrations and incubation time.
- Both Cisplatin and Lapatinib showed the capabilities of inducing cell death, with Cisplatin being the more effective of the two treatments showing lower IC50 values for both 24 and 48 hours.



Conclusion & Future Work

- It was observed that cell cytotoxicity has a direct relation with drug concentration and the time of incubation.
- Enhanced drug concentration and prolonged incubation time result in increased cell death in both cultures.
- However, 2D cultures are more sensitive to both compounds due to direct exposure to drugs in culture media compared to 3D culture, where micro fibrous scaffolds and cell-ECM interactions limit pharmacokinetic drug diffusion and effects.
- Overall, we presented pancreatic 3D cell culture model as a promising invitro technique to bridge the gap between preclinical and clinical studies for cancer biology and drug screening.

References

Acknowledgements

This work was funded by the National Science Foundation (No. EES-2306449, EES-2219558, EES-2000202) and supported by the NSF FAMU CREST Center award (No. EES1735968). This research work was also supported by The Grainger Foundation Frontiers of Engineering Grant under the National Academy of Sciences Award Number: 200001318. Support was also provided by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number R16GM145595 and by the National Cancer Institute Award Number 2U54CA233396-06. All the work was performed at the National High Magnetic Field Laboratory, which is supported by National Science Foundation Cooperative Agreement No. DMR-1644779 and the State of Florida.