3D Cell Culture (3DCC) on LifeGel® - characteristics and application in drug efficacy testing, immuno-oncology studies and other biomedical research

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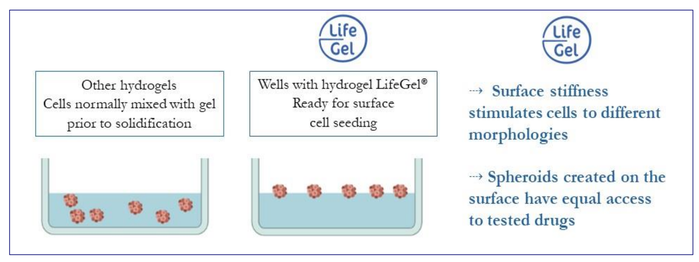
Introduction

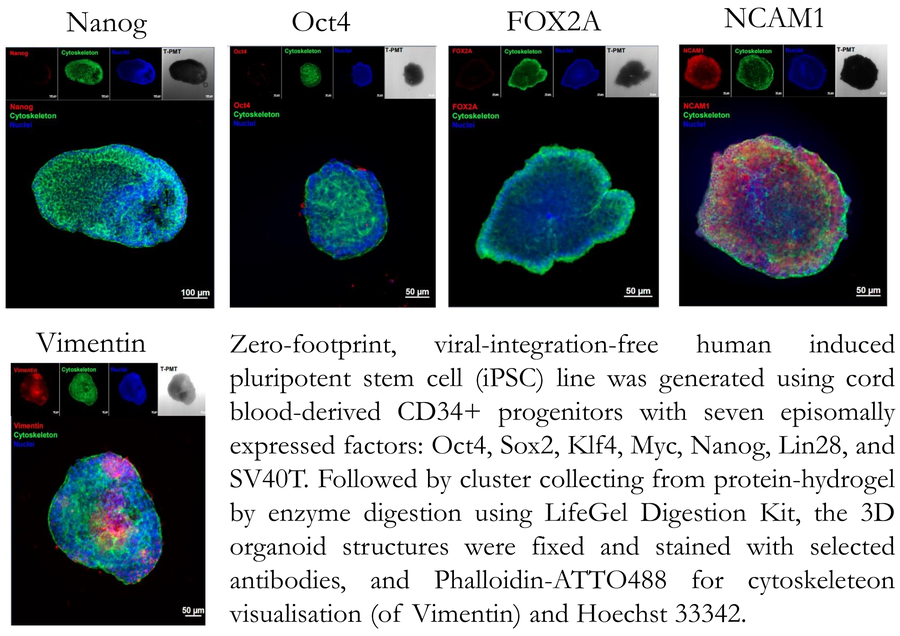
In the ever-evolving landscape of biomedical research, 3D Cell Culture (3DCC) systems have emerged as pivotal tools for mimicking *in vivo* environments and fostering more physiologically relevant cellular responses. It is widely known that 3DCC models may play a crucial role in preclinical studies thus reducing costs of drug testing and avoiding the excessive need for animal models. By providing a biomimetic microenvironment, the hydrogels facilitate the formation of complex cellular structures, enabling reliable representation of tissue architecture and cellular interactions. LifeGels® biophysical parameters can be modified: hardness, density and elasticity, making a solution adapted to every type of organoids and spheroids. The unique characteristic of LifeGel® based 3DCC is the phenomena that the 3D structures grow on top of the hydrogel making them accessible to large molecules like: antibodies, ADC, bi-speciffics, cytokines, CAR-T, oncolytic viruses etc.



3DCC on our protein-based hydrogels – characteristics and application

iPS – DERIVED 3D ORGANOID CULTURE

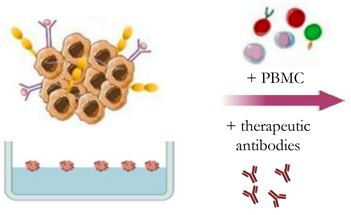
and antibody staining on our protein-based hydrogel



Zero-footprint, viral-integration-free human induced pluripotent stem cell (iPSC) line was generated using cord blood-derived CD34+ progenitors with seven episomally expressed factors: Oct4, Sox2, Klf4, Myc, Nanog, Lin28, and SV40T. Followed by cluster collecting from protein-hydrogel by enzyme digestion using LifeGel Digestion Kit, the 3D organoid structures were fixed and stained with selected antibodies, and Phalloidin-ATTO488 for cytoskeleteon visualisation (of Vimentin) and Hoechst 33342.

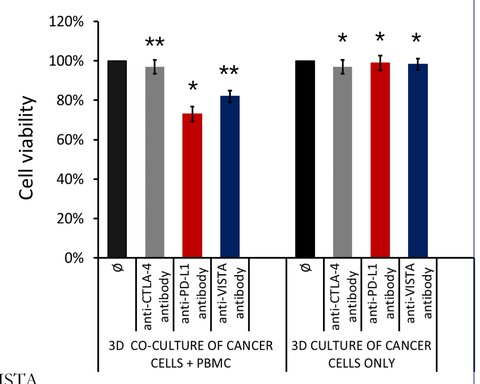
3D IMMUNO-ONCOLOGY MODEL

Veryfing of the potency of immune checkpoint inhibitors using 3D co-culture model

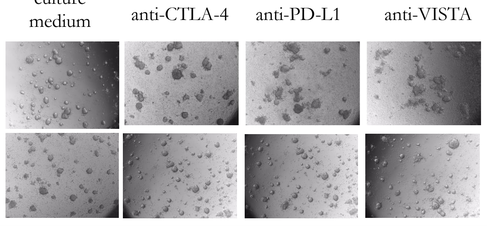


3D culture of cancder cells expressing immune checkpoints ligands PD-L1 and VISTA

- 3DCC surface staining of immune checkpoint proteins on cancer cells.
- Mesurement of viability of 3D cancer cells after co-culture with PBMC and antibodies.



Cell viability was measured using CellTiter-Blue reagent (Promega) using the protocol optimized for 3D cell culture. The data are presented as a mean value for three PBMC donors. Error bars are represented bv SD. * p<0.05, * * p<0.01

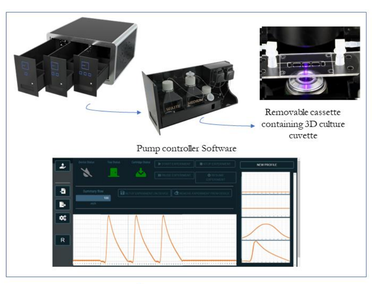


3D co-culture of cancer cells and PBMC

3D co-culture of cancer cells only

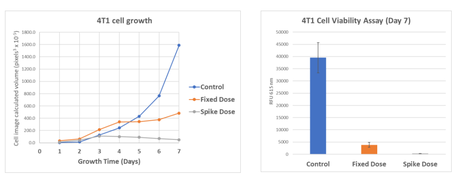
In collaboration with recepton affinity to science

PHARMACOKINETICS STUDIES ON 3DCC



ADVANCED PHARMACOKINETICS STUDIES

- Predicting efficacy of different treatment schemes for animals or patients by mimicking PK profiles in the lab.
- Opportunity to measure metabolites and image cell growth in response to different treatment regimes.

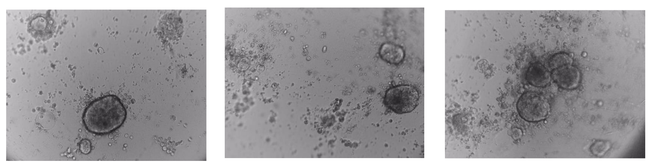


Despite the same total drug quantity being administered, the dose profile may make a significant difference in efficacy, depending on mechanism of action.

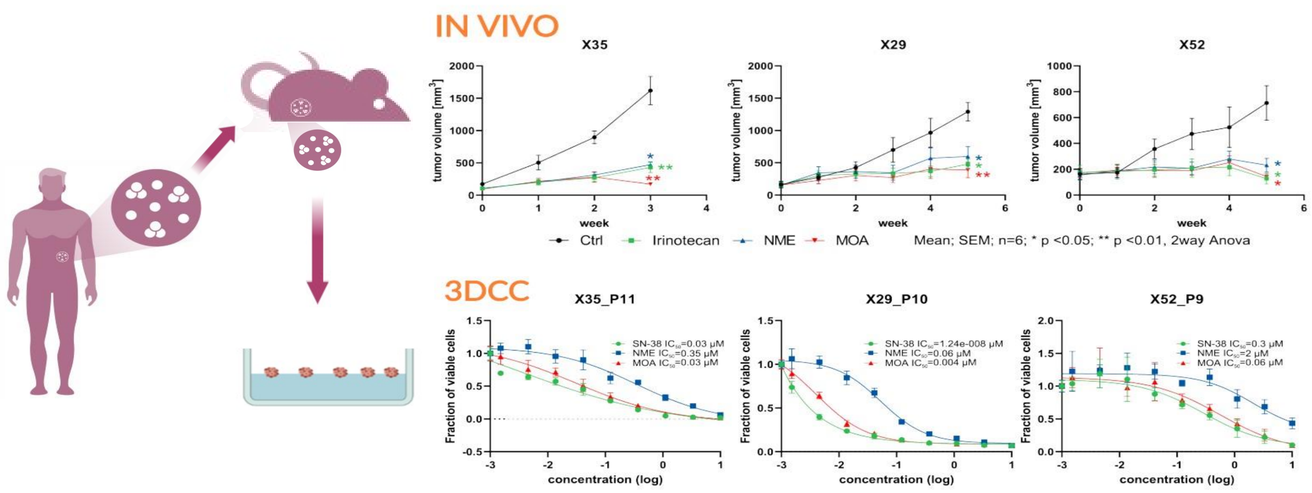
DRUG DEVELOPMENT

- *in vitro* 3DCC offers reliable predictive models for *in vivo* outcomes

In collaboration with Maria Sklodowska-Curie National Research Institute of Oncology



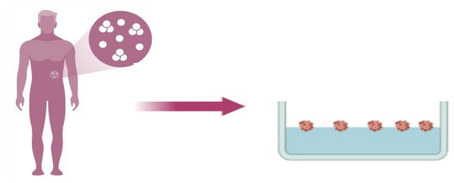
3DCC on of *ex vivo* culture of PDX-derived cells (colorectal cancer)



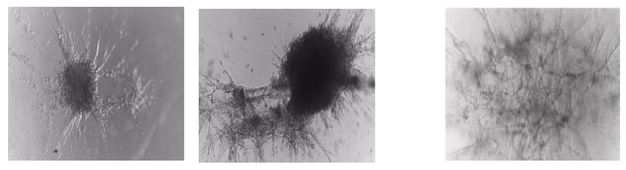
The study demonstrated that the results obtained from 3DCC of PDX-derived colorectal cancer tissues/cells align closely with those observed in *iv vivo* colorecral cancer PDX models, solidifying 3DCC role as a reliable predictive tool of drug response.

- *in vitro* 3DCC of patient-derived cells

canvas



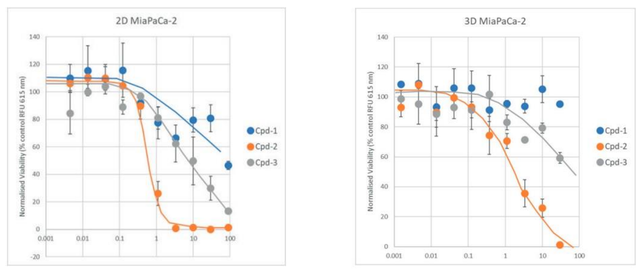
3D cell structures of patient-derived non-small cell lung carcinoma cells – different LifeGel® hardness and elasticity



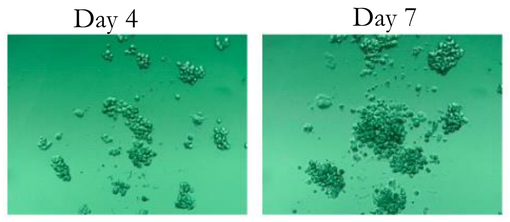
- 3D Cell Cultures expand drug development

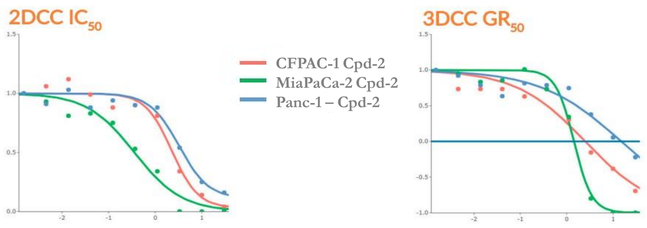
In collaboration with SEED THERAPEUTICS

2D vs 3D cell culture IC_{50} or GR_{50}



3DCC of MiaPaCa-2 pancreatic tumor cells





Compound - 2	2D		3D	
	IC_{50}	GR_{50}	IC_{50}	GR_{50}
CFPAC - 1	2.4	2.6	5.2	0.4
MiaPaCa - 2	0.4	0.2	0.8	0.9
Panc - 1	3.9	3.0	4.9	1.6

Conventional IC_{50} data for Cpd-2 presents significantly more activity on one of the cell lines in 2DCC, but on 3DCC GR_{50} parameters for two compounds have similarly high potency, and even the least active is much more active than in 2DCC.

Conclusion

In the realm of cancer research, 3D cell cultures showcase a predictive power in assessing the anticancer effects of drugs that rivals traditional *in vivo* research models. In our study, we presented a wealth of 3D forms grown on LifeGel® and indicated their use in further stages of 3D organoid culture, drug efficacy testing, immuno-oncology studies and other biomedical research.

Find us

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Acknowledgement

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