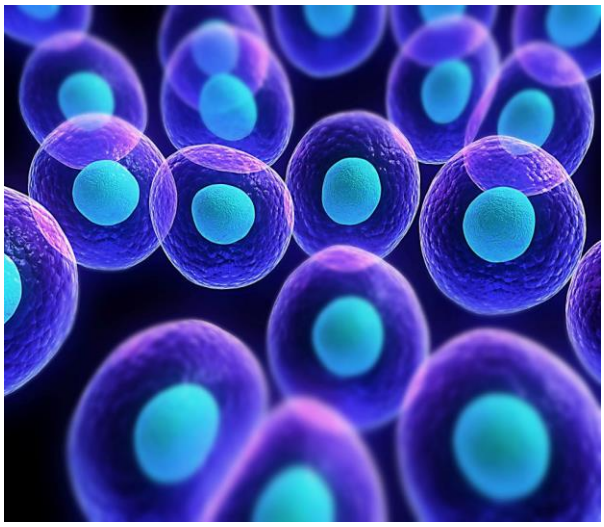
Cellevates nanofibers for complex pancreatic co-cultures

Co-culture systems have long been used to study the interactions between cell populations and are fundamental to cell-to–cell interaction studies of any kind. It is well known that cell to cell contact can engage cellular stimulation, turn on or off gene pathways and/or cellular differentiation, etc. Similarly, indirect contact (cell to cell communication) is known to also have very important effects on eg. cellular stimulation, turning on or off gene pathways and/or cellular differentiation.

Aim



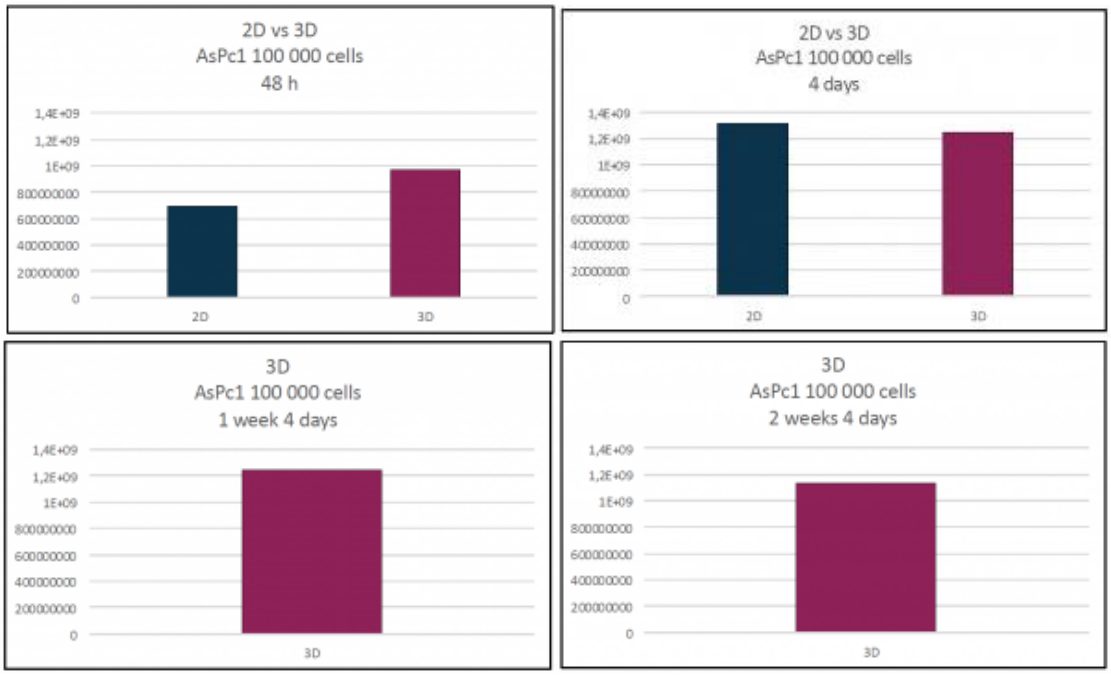
In this customer case Cellevate focused on helping a pre-clinical CRO with one of their in-vitro oncology models. Their model for pancreatic cancer co-cultures, a traditional submerged 2D system had performance issues. Limited space meant contact inhibition was problematic and the system became over confluent around 4 DIV, which was not enough time to develop a disease relevant culture.

Several parameters were evaluated and a network optimized for co-culture of AsPC1 pancreatic cancer cells, CAFs and fibroblasts was developed. The most important readout was viability, which we evaluated through mitochondrial activity using an AlamarBlue™ proliferation assay.

Furthermore, levels of IL-1 beta, IL-6, IL-8 and VEGF-A was measured every day as several of the CROs customers are interested in these for their respective projects.

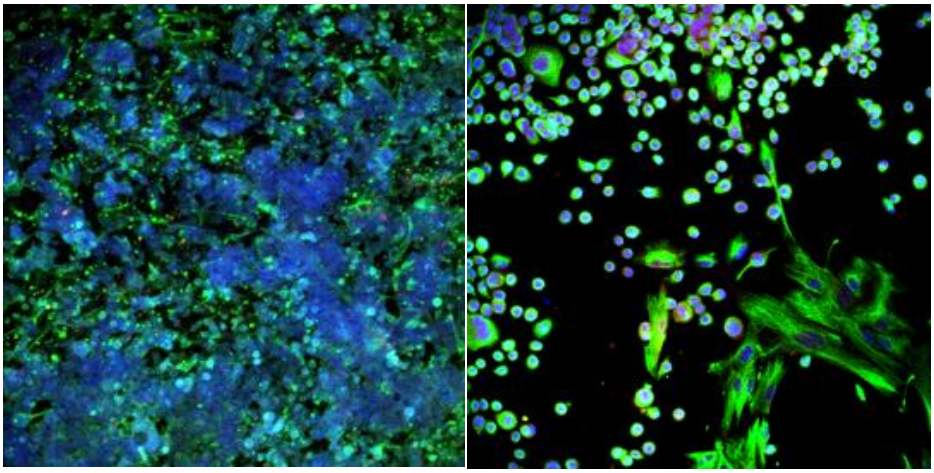
Increased viability

After optimization, the scaffold platform developed by Cellevate increased the viability of the co-culture. For the purpose of this evaluation the viability was examined at 2, 4, 11 and 18 DIV respectively, with viability in the 3D culture remaining constant throughout the full experimental time.



Morphology

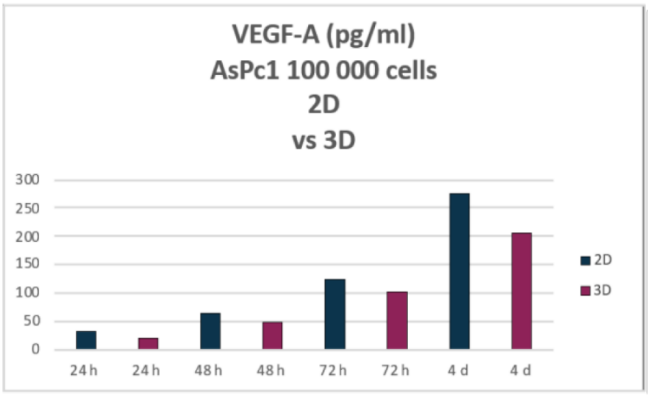
Furthermore, morphology was evaluated through confocal microscopy. The resulting images show formation of in-vivo like clusters of AsPC1 pancreatic cancer cells intermingled with supporting CAFs in 3D culture (left), these formations are not found in traditional 2D monolayer culture of the same cell types (right).

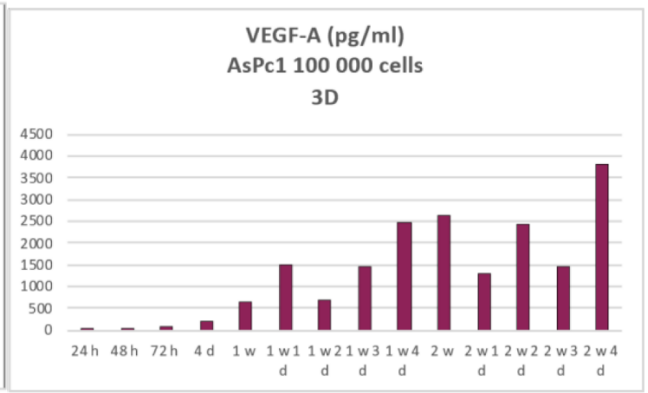


Biomarker expression

Additionally, although initially comparable, biomarker concentrations are significantly higher past the 2D cell culture limit. This was the case for all measured biomarker concentrations.

The expression increases over time and is high even though media was changed in 3D indicated by the dips in concentration at 4, 8, 12, 14, 16 DIV respectively. This likely indicates an up-regulation of biomarker production as cell viability measurements show that the culture is stable from 4 DIV. This phenomenon is currently being investigated further.





Conclusions

For our CRO-customer we managed to design a model that firstly solved the problem of over confluent cells. This led to a significant increase in cell viability. Since the cells could be cultured for a longer period of time the model could let the different cells intermingle to create true in vivo like relations and features. Further more, this model is currently being used to give reliable results when investigating drug sensitivity and cytotoxicity.

Contact Iwai North America Inc. (info@iwai-chem.com) for more information.