Keele University

Case Study | Academic Research | Staffordshire, UK

At the multidisciplinary Bioengineering and Therapeutics Group at Keele University there are multiple research projects within Postgraduate Research that focus on cell and tissue engineering and the enabling technologies involved in their introduction to the clinic. One of those areas of research is Regenerative Mechanisms, led by Professor Alicia El Haj, Director of the Institute of Science & Technology in Medicine.

The Challenge

With a focus on tissue engineering of connective tissues including bone, cartilage, tendons, and ligaments, Professor El Haj and her team – Post-Docs Dr. Yvonne Reinwald and Dr. James Henstock, and PhD candidate Joshua Price – needed a more complex system to perform hydrostatic stimulation on cells and tissues. Their current mechanical compression system was unable to reproduce physiological pressures on tissues in multi-well tissue culture plates for testing different model tissues and allowing larger numbers of samples in experiments. They knew that to create such a bioreactor in-house would not only be time-consuming, but would require an interdisciplinary team and be difficult to recreate in other laboratories. Along with being an easier solution than a home-grown system, they needed a bioreactor from an industry partner that demonstrates reliability, ensures repeatable results, increases throughput and offers the flexibility for use by multiple departments. Most importantly, this system needed to keep the cells alive and healthy during these novel experiments.

Purchasing a new hydrostatic bioreactor meant that Professor El Haj would have the ability to perform a different type of stimulation than their current tests allowed. But with change comes uncertainty.

“Because this is a different type of stimulation it’s going to produce results which need to be carefully compared to previously published data,” says El Haj. “Additionally, increasing the sample numbers can be risky – it has the potential to introduce more variability if the system isn’t well controlled.”

Keeping these risk factors in mind, El Haj looked to purchase from a well-respected manufacturer that produces high-end equipment. Finding the right partner and purchasing their solution would need to outweigh the possible risks of investing in such a novel system.

The Solution

Using grant money from the BBSRC, Professor El Haj designed with Instron a bioreactor which could be produced commercially. The CartiGen HP bioreactor

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provides static or dynamic hydrostatic pressure to mimic physiological conditions and induce natural cell development in up to 192 separate, simultaneous samples on the bench. After gathering benchmark data, she was able to determine that there was some evaporation occurring in the multi-well cell culture plate used in the HP bioreactor system.

"One essential requirement of utilizing a new system is for the cells to stay alive," says El Haj. "Cells need to stay hydrated and fed, and excessive evaporation can be very damaging."

Knowing the importance of the fix, the Instron team made a small change to ensure consistent and continuous hydration of the cells. They added an off-the-shelf film that sticks to the top of the chamber to minimize evaporation while still allowing for gas transfer to occur and keep the cells alive.

The Results

The bioreactor has opened the door to many possibilities for the Regenerative Medicine team at Keele. Because hydrostatic forces play an important role in many biological systems, the new bioreactor allows researchers to recreate the necessary environment on the benchtop where developmental biology can be observed, understood and used to improve TERM therapies in the future.

"We couldn't do what we're currently doing without this system. It's revolutionized our ability to study physiological forces on our 3D models," says El Haj.