Purified biomaterials improve reliability of 3D *in vitro* cancer models

A recent study demonstrates the critical role low endotoxin biomaterials play in achieving credible results in 3D disease models.

IMMUNOTHERAPY IS a rapidly developing therapeutic approach that has revolutionised cancer treatment and revitalised the field of tumour immunology research.[1] In particular, 3D *in vitro* models are emerging as a powerful tool in oncology, creating optimal conditions to study the tumour microenvironment (TME) and test the potential efficacy of novel immunotherapies.

The unique advantages of 3D models

Historically, 2D cell culture systems have provided an invaluable means of investigating tumour biology and supporting the preclinical development of many anti-cancer drugs, however they have several limitations. They do not fully reflect the complex physiology of the original tissue, lacking tissue-specific architecture and biochemical signals.[2] On the other hand, animal models are expensive, associated with ethical issues[3] and not always representative of human-specific conditions. Thus, 3D *in vitro* models represent an interesting solution to this unmet scientific need, providing a simple and low-cost method of accurately reproducing the TME.

How to choose the right biomaterials for accurate disease models

One crucial factor often overlooked in the development of 3D models is the role of biomaterial purity in producing accurate results.

A recent study led jointly by the University of Twente, the Netherlands, and Rousselot, global leader in collagen-based solutions, has shown for the first time that the reliability of 3D *in vitro* cancer models is significantly impacted by the presence of endotoxins.[4] Researchers investigated the effect of endotoxins on 3D breast cancer models, looking both at the crosstalk between macrophages and cancer cells, and the effect on the measured efficacy of immunotherapies.

Standard, commercially available gelatin with naturally high endotoxin levels was compared with Rousselot's X-Pure® gelatin methacrylate (GelMA) – a purified biomaterial with low endotoxin levels.

Endotoxins impact the reliability of therapeutic outcomes

Endotoxins, or lipopolysaccharides, are large, highly immunogenic molecules that form the major component of the outer membrane of gram-negative bacteria. Consequently, endotoxins are everywhere in the environment, making them hard to avoid. The study found that materials with high levels of endotoxins produced a larger inflammatory reaction than those with lower endotoxin levels.[4] In addition, high endotoxin gels resulted in significant gene inhibition and reduced the crosstalk between macrophages and cancer cells, making the macrophages less responsive to the cancer stimulus.

Crucially, the researchers found that endotoxins impacted the reliability of therapeutic outcomes, emphasising the growing need for purified biomaterials. The high endotoxin environment artificially increased the measured efficacy of the therapy that was designed to inhibit the expression of anti-inflammatory markers, while in the therapy designed to induce pro-inflammatory markers it showed limited efficacy. Overall, the results show that the presence of endotoxins can lead to the misinterpretation of the safety and potency of novel therapeutics.

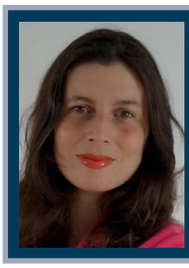
Upgrade your 3D *in vitro* models with purified biomaterials

For drug developers looking to explore alternatives to animal testing, Rousselot's X-Pure range of highly purified, GMP-grade pharmaceutical gelatins are designed to support researchers in recreating *in vivo* conditions and leveraging the power of 3D cell culture. Not only do they offer ultra-low or controlled endotoxin levels and batch-to-batch consistency, but they are also fully compliant with relevant US Food and Drug Administration (FDA) and EU quality and safety regulations.

Beyond 3D models: the potential of gelatin to accelerate biomedical innovations

Gelatin's unique ability to mimic the natural composition and mechanical properties that each cell type requires makes it ideal for a wide range of innovative biomedical applications, from organs-on-a-chip to embolisation, tissue engineering, implants and wound healing. Rousselot's team of dedicated experts applies cutting-edge technology and combines it with 130 years of experience to create customised gelatin solutions for every application.

Purified and customisable biomaterials not only help to reduce the costs, time and ethical concerns, such as animal testing, associated with drug development, but can also increase the accuracy of pre-clinical testing, helping new and improved immunotherapies reach patients sooner.



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