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Human protein-based biomaterials in preclinical modelling

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Human protein-based biomaterials facilitate the development of preclinical models that integrate predictive value and ethical responsibility. Metatissue uses decellularized extracellular matrix from placenta samples and human blood to create tunable, xeno-free substrates for 3D cell culture, minimizing the reliance on animal models and accelerating translational research.

Poor translatability between preclinical testing and clinical outcomes remains one of the greatest challenges in drug development. Nearly 90% of drug candidates entering phase I clinical trials fail to achieve market approval, primarily because current preclinical models, including 2D cultures and animal models, do not accurately predict human responses[1].

This inefficiency carries substantial costs; developing a single drug typically takes around a decade and investments, ranging from US$314 million to $2.8 billion. Beyond cost, this also delays access to new therapies[2]. Thus, creating more faithful and efficient human-relevant models is a societal imperative.

3D models in preclinical research

Animal models in preclinical research might provide a whole-organism perspective but often fail to predict human drug responses because of genetic, metabolic and physiological differences. According to the most recent European Union (EU) report on animal experimentation, approximately 8 million animals were used in 2020, mainly for human disease studies, whereas only 17% were required for regulatory testing. Therefore, more than 6 million animals were used in research contexts where alternatives could have been applied[3].

Alternatively, dynamic three-dimensional (3D) culture systems can recapitulate the mechanical and biochemical cues of native tissues, offering a physiologically relevant substitute for preclinical animal models. For example, organ-on-a-chip platforms can integrate multiple cell types within microfluidics environments. A study analysing 27 drugs in 870 liver-on-a-chip systems achieved 87% sensitivity and 100% specificity in predicting human hepatotoxicity[4]. Therefore, such 3D systems could not only be applied as research tools but also in regulatory decision-making.

The transition toward non-animal, human-relevant technologies, fuelled by the US Food and Drug Administration (FDA) Modernization Act 2.0, creates an expanding market for such new approach methodologies (NAMs). Accordingly, the 3D cell culture market, valued at $1.7 billion in 2022, is projected to grow at a 16% compound annual growth rate, reaching nearly $12 billion by 2035. Scaffold-based systems represent over half of this market and are expected to reach $4.1 billion by 2035[5].

However, 3D cell culture platforms typically rely on animal-derived materials, such as Matrigel, collagen or porcine or bovine decellularized extracellular matrices (ECM). These substrates raise ethical concerns and introduce variability and xenogeneic risks that compromise reproducibility and cell behaviour. Alternatively, human-derived biomaterials can offer greater physiological relevance, consistency and regulatory suitability.

Human protein-based biomaterials

Human-derived biomaterials, including decellularized ECM from placenta, lung or adipose tissue, as well as plasma-derived proteins, such as albumin and platelet lysates, offer biocompatibility, biodegradability, and, importantly, a strategic advantage, compared with animal-derived materials, by avoiding animal-origin risks (for example, prions, zoonotic viruses and high batch variability). Specifically, proteins derived from platelet lysates or placenta can be obtained from minimally invasive donations without raising ethical concerns. These sources enable access to large donor pools, facilitating industrial-scale production of materials with low batch-to-batch variability.

Human-derived biomaterials could further enable personalized medicine by leveraging patient-derived blood or placenta samples to improve the predictive accuracy of preclinical models. However, moving from pooled tissue sources to individualized biomaterials introduces substantial challenges related to cost, scalability and quality control. Although these personalized materials better reflect physiological conditions, they also introduce greater biological variability, highlighting the importance of establishing robust reference standards for comparing assay results. In addition, the production of 3D models remains labour-intensive and costly. Therefore, without automation, these systems will remain prohibitively expensive for widespread access.

Chemical modification of human platelet lysates

Human platelet lysates are particularly valuable as culture supplements and biomaterial precursors. A blind inter-laboratory study across several European facilities confirmed consistent protein and growth factor content in pooled human platelet lysates, reinforcing their potential for scalable, quality-controlled manufacturing[6]. Nevertheless, although rich in growth factors and adhesive proteins, human platelet lysates lack the mechanical stability needed for long-term assays and dynamic culture systems, such as organ-on-chip platforms.

To enhance the mechanical stability of platelet lysates, they can be chemically modified – for example, by introducing reactive groups such as methacrylates or thiols, which enable controlled crosslinking and the formation of stable, reproducible hydrogel networks[7]. In particular, methacrylation confers photo-reactivity, enabling light-triggered polymerization in the presence of a photoinitiator. This approach provides precise control over stiffness, porosity and degradation rate, thereby influencing cell differentiation, proliferation and matrix remodelling.

Human methacryloyl proteins

Building on this functionalization method, at Metatissue, we design and commercialize human protein-based biomaterials for 3D cell culture, drug screening, tissue engineering

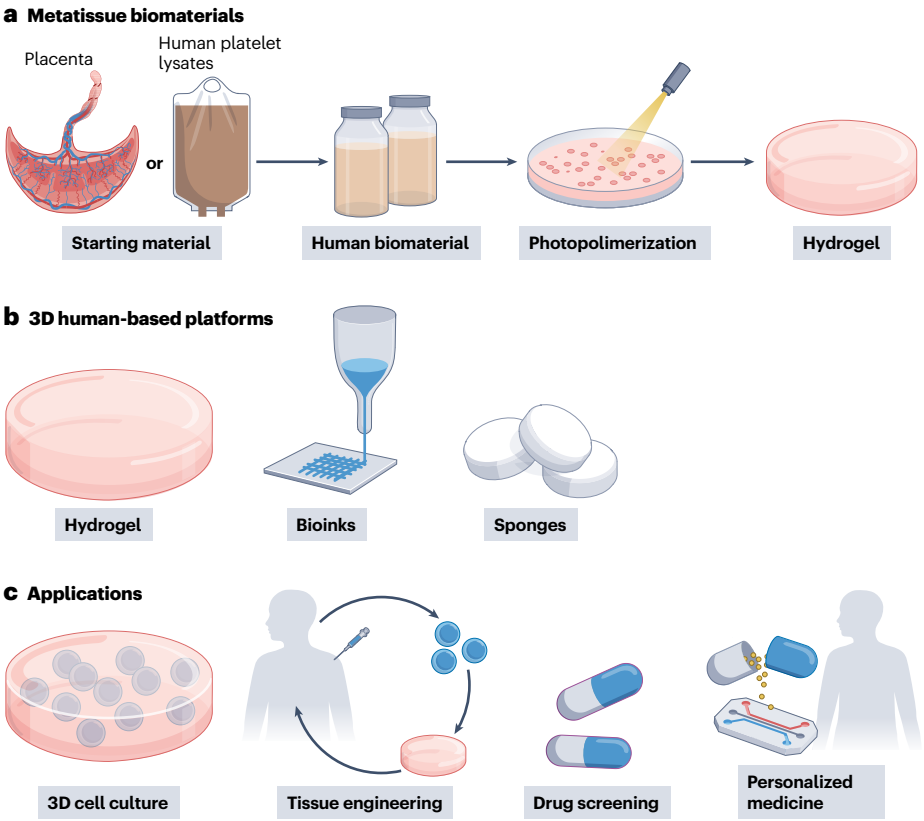

Fig. 1 | Human methacryloyl proteins and their applications. a, Methacrylated human proteins, derived from human platelet lysates and human perinatal tissues, can be cross-linked through light-activated polymerization to form hydrogels with tunable properties. **b**, These human-derived biomaterials can be fabricated as sponges or bioinks. **c**, They can support a range of applications, from 3D cell culture and tissue engineering to drug screening and personalized medicine.

and personalized medicine. In particular, human methacryloyl platelet lysates and human methacryloyl perinatal tissues can be fabricated into matrices that contain a distinct repertoire of bioactive molecules, including albumin, platelet-derived growth factor and vascular endothelial growth factor in human methacryloyl platelet lysates, and collagen or laminin in perinatal tissues[7,8] (Fig. 1a).

These matrices are xeno-free, biocompatible and mechanically tunable. They can be designed as multiple formats, including hydrogels, membranes, sponges and bioinks, and integrated into organ-on-chip platforms (Fig. 1b). These formulations remain functional for at least 9 months when stored at 4 °C, supporting long-term use and streamlined logistics. Importantly, these materials can support 3D cell culture with high viability, low immunogenicity and uniform cell distribution, positioning them as strong alternatives to animal-based matrices[9] (Fig. 1c). Although currently supplied for research use, their Good Manufacturing Practice (GMP)-compatible production pipelines are specifically designed to enable regulatory progression toward clinical-grade applications.

Translational challenges

Translating human-derived biomaterials from research to clinical use remains challenging, and their regulatory pathway requires verified donor consent and traceability, infectious disease screening, consistent batch performance and GMP-controlled sourcing and processing. In addition, stability during storage, transport and long-term use must be ensured for global distribution.

Furthermore, the integration of NAMs in the drug development pipeline is hindered by the lack of standardized protocols and qualification metrics for human-based models. Given the high costs and risks of drug development, companies may be reluctant to adopt unestablished technologies without clear regulatory acceptance. Nonetheless, initiatives led by agencies, such as the National Institutes of Health (NIH), are beginning to bridge this gap by promoting data sharing across 3D models, animal studies and clinical trials, which is essential for protocol standardization and widespread adoption of 3D human models[10].

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Competing interests

C.A.C. and J.F.M. are co-founders of Metatissue. M.D. reports no competing interests.