Despite significant interest in tissue engineering and regenerative medicine and the success of many tissue engineering technologies in pre-clinical studies, there has been limited success in translating these technologies to the clinic (with the possible exception of some engineered skin products). What do you see as the major hurdle to translating tissue engineering/regenerative medicine products from bench to bedside and why?

A major hurdle in this translation process is achieving proper vascularization and angiogenesis in tissue-engineered products. This is especially problematic when scaling up from animal models to humans. The complexity of human vascular networks and the need for precise blood supply to sustain newly formed tissues are often not adequately mimicked in smaller animal models.

Scale also has major implications on forces exerted on the ECM, especially on muscles and bones; and the growth of the tissue changes the dynamics and composition of the ECM, particularly the basement membrane which is in contact with the surface of many more cells not fully represented in vitro.

In 2D or 3D cell culture, not all cell subtypes are present; therefore, the full interaction of the host inflammatory and immune cells in transplanted cells and tissues, with the fluxes of hormones and other circulating molecules (e.g., growth factors, chemokines, cytokines, nutrients, exosomes, etc.); is poorly replicated in pre-clinical models. Adding to these unknown parameters, drastic changes in ECM occur after injury or disease.

Other major hurdles reported in the literature concern the risk of tumorigenicity, poor cell engraftment and survival.

One strategy to facilitate the transition from models to patients is to design products that can self-assemble within the recipient's body. For instance, artificial blood vessel grafts have been developed using sialic tubing into the peritoneum, which then becomes populated by the patient's own cells and ECM [1].

[1] K. M. Blum *et al.*, "Tissue engineered vascular grafts transform into autologous neovessels capable of native function and growth," *Commun. Med.*, vol. 2, no. 1, p. 3, 2022, doi: 10.1038/s43856-021-00063-7