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The translational imperative: Making cell therapy simple and effective ☆

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ABSTRACT

The current practice of cell therapy, in which multipotent or terminally differentiated cells are injected into tissues or intravenously, is inefficient. Few therapeutic cells are retained at the site of administration and engraftment is low. An injectable and biologically appropriate vehicle for delivery, retention, growth and differentiation of therapeutic cells is needed to improve the efficacy of cell therapy. We focus on a hyaluronan-based semi-synthetic extracellular matrix (sECM), HyStem®, which is a manufacturable, approvable and affordable clinical product. The composition of this sECM can be customized for use with mesenchymal stem cells as well as cells derived from embryonic or induced pluripotent sources. In addition, it can support therapeutic uses of progenitor and mature cell populations obtained from skin, fat, liver, heart, muscle, bone, cartilage, nerves and other tissues. This overview presents four pre-clinical uses of HyStem® for cell therapy to repair injured vocal folds, improve post-myocardial infarct heart function, regenerate damaged liver tissue and restore brain function following ischemic stroke. Finally, we address the real-world limitations – manufacture, regulation, market acceptance and financing – surrounding cell therapy and the development of clinical combination products.

1. Evolving a culture of impact

The reality of translating biomaterials as research tools in academic laboratories into products that companies sell to physicians for clinical care has taken center stage in the past few years. There is an evolutionary change – some might say a revolutionary change – occurring at universities. Rather than remaining a traditional "ivory tower"– an inward-focused culture that the public views as irrelevant to their lives – many universities are moving towards an open culture based on impact as the unifying metric. To convert academic technologies into products, the inventions at universities require implementation and commercialization; this is true innovation. Indeed, no technology reaches the public unless it is commercialized.

There is, therefore, a translational imperative to implement the creation of products to address real-world needs. The pursuit of this goal by both students and faculty broadens the scope of scholarly activities in an exciting, important way. Participation in translational and transdisciplinary team activities engages and excites students in a way no lecture or laboratory course possibly could. The ultimate deliverable of entrepreneurial student and faculty scholars is to use science to serve the public good by making life better and creating jobs. This overview serves to highlight a case study of how academic research resulted in new products for clinical use in human and veterinary patients. Importantly, it also serves to emphasize how three seemingly independent processes were crucial in this transformation: (i) maturation of the technology, (ii) development of a better commercialization infrastructure within the university and (iii) recognition of the obligation of faculty to help their students do work that will have real impact on the lives of people.

2. Deconstructing the extracellular matrix (ECM)

A synthetic substitute for the ECM should recapitulate the principal functions of the natural ECM in orchestrating cell proliferation, migration, differentiation, angiogenesis and invasion [1]. The design criteria should include: (i) control of composition, (ii) control of compliance, (iii) control of biodegradation in vitro and in vivo, (iv) control of fabrication and physical forms, (v) control of delivery modality, (vi) batch to batch consistency, (vii) ease of use at physiological temperature and pH, and (ix) seamless translation to a clinical product [2]. In addition, perhaps the most important criterion for an ECM substitute should be the clinical imperative: physicians require the material to produce – in conjunction with therapeutic cells – the desired biological and clinical outcome.

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