PREDICTIVE RAPID THROUGHPUT ASSAY FOR BONE, CARTILAGE, ANGIOGENESIS ASSESSMENT AND MATERIAL BIOCOMPATIBILITY FOR REGENERATIVE MEDICINE

"We provide rapid and predictive bioassays that reduce the need for animals in your regenerative medicine research"

The development of new cartilage and bone formation strategies offers tremendous therapeutic opportunities in a variety of musculoskeletal diseases. However, assessment of the efficacy of these new approaches, has typically required animal models.

We have developed a number of alternative chick *ex vivo* models, the organotypic and chorioallantoic membrane (CAM) with the capacity to recapitulate, in part, the complex *in vivo* scenario while providing an ethically acceptable framework. The chick CAM provides a unique assay for biomaterial/tissue engineering evaluation given its comparative ease of access, the under-developed immunocompetent system and rapid vascular development. In combination with the organotypic model (bone culture in a dish) these models offer a cost-effective approach prior to evaluation in animal models with the ethical constraints that must be addressed.

Organotypic and chorioallantoic (CAM) models offer the following key advantages:

- **Sample throughput** – opportunity to screen relatively large numbers of compounds, growth factors and material/cell constructs over an 8-day time frame in an *ex vivo* model
- **Reduction in animal use –** the organotypic and CAM models provide a predictive *ex vivo* approach that reduces use of sentient animal models
- **Cost reduction –** significantly reduced cost in comparison to standard animal models
- **Micro Computed Tomography** allows in-depth analysis of data sets as required
- **75 year history of research** in developmental biology and more recently in tumour, toxicity and angiogenesis biology
- **Diverse applications –** potential to develop custom assays (specific defects)

Case studies:

Moreno-Jiménez *et al.* The chorioallantoic membrane (CAM) assay for biomaterial testing in tissue engineering: a short term in vivo preclinical model, Tissue Engineering (2018)

Hulsart-Billström *et al.* A surprisingly poor correlation between in vitro and in vivo testing of biomaterials for bone regeneration: Results of a multicentre analysis, Eur Cells Mater (2016)

Moreno-Jiménez *et al.* The chorioallantoic membrane (CAM) assay for the study of human bone regeneration: a refinement animal model for tissue engineering, Scientific Reports (2016)

Smith *et al.* The Effects of 1α, 25-dihydroxyvitamin D3 and Transforming Growth Factor-β3 on Bone Development in an Ex Vivo Organotypic Culture System of Embryonic Chick Femora, PLOSone (2015)

Smith *et al.* A new take on an old story: chick limb organ culture for skeletal niche development and regenerative medicine evaluation, Eur Cell Mater (2013)

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