The Summer Undergraduate Research Fellowship (SURF) Symposium
7 August 2014
Purdue University, West Lafayette, Indiana, USA

Tissue Engineering: Applications in Developmental Toxicology

Stephanie N. Thiede, Nimisha Bajaj, and Kevin Buno
Weldon School of Biomedical Engineering, Purdue University
Sherry L. Voytik-Harbin
Weldon School of Biomedical Engineering & Department of Basic Medical Sciences, Purdue University

ABSTRACT

In vivo toxicology assays are expensive, low-throughput, and often not predictive of a human response. Three-dimensional *in vitro* human cell-based tissue systems incorporating cell-cell and cell-matrix interactions have promise to provide high-throughput, physiologically-relevant information on the mechanism of the toxin and a more accurate assessment of the toxicity of a chemical before progression to human trials. Quantification of the disruption of vasculogenesis, the *de novo* formation of blood vessels from endothelial progenitor cells, can serve as an appropriate indicator of developmental toxicity since vasculogenesis is critical to the early development of the circulatory system. The current routinely used *in vitro* angiogenesis assays are 2D and thus not physiologically-relevant and analyzed semi-quantitatively. Recently, a 3D *in vitro* model of vasculogenesis, involving a type I collagen oligomer matrix and endothelial colony forming cells, was described to be capable of producing and maintaining lumenized blood vessel networks up to 14 days. Here we utilized this model to develop a 3D vasculogenesis assay. We quantified the performance of this assay with a set of known angiogenesis modulators (imazamox, thalidomide, 2-methoxyestradiol, levamisole) through cytotoxicity testing and 3D image analysis. Preliminary data suggests a difference in the drug sensitivity and response when measured with the 3D vasculogenesis assay and compared to a well-established 2D angiogenesis assay. We expect our model to more closely mimic results from *in vivo* studies, but further validation is needed. This new 3D vasculogenesis model can provide a physiologically-relevant, high-throughput screening and mechanistic assay for applications in pharmaceutical development and developmental toxicology.

KEYWORDS

vascuolgenesis, developmental toxicology, in vitro, type I collagen, oligomer, quantification, 3D

REFERENCES

Sarkanen, J.R., et al. (2010). Intra-Laboratory Pre-Validation of a Human Cell Based in vitro Angiogenesis Assay for Testing Angiogenesis Modulators*. Front Pharmacol*, *1,* 147.

Whittington, C.F., Yoder, M.C., and Voytik-Harbin, S.L. (2013). Collagen-polymer guidance of vessel network formation and stabilization by endothelial colony forming cells in vitro*. Macromol Biosci*, *13*(9), 1135-49.