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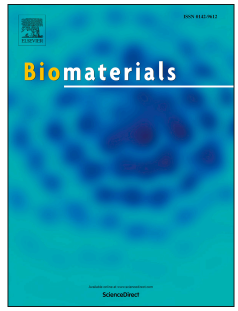

Induced neuro-vascular interactions robustly enhance functional attributes of engineered neural implants

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Title

Induced neuro-vascular interactions robustly enhance functional attributes of engineered neural implants

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Abstract

Engineered neural implants have a myriad of potential basic science and clinical neural repair applications. Although there are implants that are currently undergoing their first clinical investigations, optimizing their long-term viability and efficacy remain an open challenge. Functional implants with pre-vascularization of various engineered tissues have proven to enhance post-implantation host integration, and well-known synergistic neural-vascular interplays suggest that this strategy could also be promising for neural tissue engineering. Here, we report the development of a novel bio-engineered neuro-vascular co-culture construct, and demonstrate that it exhibits enhanced neurotrophic factor expression, and more complex neuronal morphology. Crucially, by introducing genetically encoded calcium indicators (GECIs) into the co-culture, we are able to monitor functional activity of the neural network, and demonstrate greater activity levels and complexity as a result of the introduction of endothelial cells in the construct. The presence of this enhanced activity could putatively lead to superior integration outcomes. Indeed, leveraging on the ability to monitor the construct's development post-implantation with GECIs, we observe improved integration phenotypes in the spinal cord of mice relative to non-vascularized controls. Our approach provides a new experimental system with functional neural feedback for studying the interplay between vascular and neural development while advancing the optimization of neural implants towards potential clinical applications.

Keywords: Tissue engineering; Engineered neural implants; neuro-vascular interactions; induced neural activity; functional neural activity monitoring; Biomaterials