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Editorial: Biomaterials for Brain Therapy and Repair

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Editorial on the Research Topic

Biomaterials for Brain Therapy and Repair

Acute or chronic alterations of brain function, either in the form of brain disorders, including developmental, psychiatric, neurodegenerative, and autoimmune diseases, cancer or injury represent a tremendous social and economic burden that has increased considerably over the last 20 years (Feigin et al., 2017). Technologies to repair or induce regeneration of brain tissue are still in early stages of development, but the use of induced pluripotent stem cells (iPSCs) have opened the possibility of modeling and reconstructing brain circuits (Barker et al., 2018). Recent efforts have begun to consider the explicit development of tools to analyze brain composition and function as a means to better diagnose, prevent, or treat brain diseases. Artificial models of healthy and diseased brain tissue may eventually help decipher patterns of regional cell diversity and connectivity and allow the precise manipulation of cells and extracellular conditions to mimic neural microenvironments. In this context, biomaterials can act as a dynamic stimulatory platform that can recreate the native cerebral tissue, deliver growth factors or immune-modulating components to support neural growth and allow detailed analysis of therapeutic outcomes.

Over the last 30 years we have witnessed advances in biomaterials technologies supporting regeneration of a range of tissues, from skin to heart valves, urinary bladder and cartilage (Langer and Vacanti, 2016). However, central nervous tissues such as the brain remains a challenge due to their native complexity. Recently, increasingly interdisciplinary efforts are combining fields such as chemical and functional imaging, developmental biology, animal models and behavioral studies, and tissue engineering to develop new understanding regarding mechanisms of homeostasis and disease progression in the brain, as well as to discover and validate new therapeutic strategies.

This collection of research articles highlights recent biomaterials-centric approaches to study and treat disorders, diseases, and injuries to the brain. Topics span diverse areas of interest, such as tissue engineering, targeted drug delivery, *ex vivo* disease models, dynamic biomaterials, neurovascular diseases, molecular imaging, neurobiology, proteomics, systems biology, protein biosensors, and biomimetic scaffold design.

One area of significant effort is the development of biomaterials to examine the progression and treatment of brain cancer. Efforts highlighted here seek to model influential regulators of the glioblastoma tumor microenvironment (Cha and Kim) that may yield clinically-actionable data (Cornelison and Munson), including using cytokines to direct angiogenesis, improving drug delivery and increasing the circulation of immune cells at the tumor site, as well as manipulating biophysical properties to control cell phenotype and migration. Such platforms also facilitate study of cellular level heterogeneity associated with brain cancer, such as the role played by

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a subpopulation of glioblastoma stem-like cells (Heffernan and Sirianni) and heterogeneity of tyrosine kinase receptor density (Chen et al.) on tumor recurrence and therapeutic resistance. They also examine the role of matrix composition, such as the molecular weight of hyaluronic acid, on glioblastoma cell invasion capacity (Chen et al.).

This virtual issue also includes an exciting compilation of research describing biomaterials to recapitulate native neural behavior *in vitro*. Biomaterial environments can guide controlled differentiation of neural cells and support neuronal processes (Farrukh et al.) and may serve as a platform to culture embryonic neuronal cells in a brain-mimetic hydrogel matrix (Magariños et al.). The microscale architecture of biomaterial culture platforms can directly affect the efficacy of neural cell transplants (Meco and Lampe), while the precise manipulation of topographical, chemical, electrical, and mechanical cues enhance control over directionality of regenerating neurites (Cangellaris and Gillette). Recent advances in 3D bioprinting may ultimately provide the resolution necessary to replicate the native complexity of the neural environment tissue (Thomas and Willerth). Precisely embedded bioactive signals may alternatively provide a pathway to direct migration and differentiation of neural stem cells (Matta and Gonzalez) as a means to regenerate the subventricular zone following stroke. This issue also provides an overview of delivery systems that support the repair of the stroke-damaged tissue (Tuladhar et al.).

Changes in the neural vascular environment play a critical role in acute brain damage and chronic neurodegenerative disorders. Such injuries are characterized by inflammatory reactions that include possible alterations of the extracellular matrix and modifications of the blood-brain barrier (BBB) (Nih et al., 2018). Here, a review article compiles efforts employing iPSCs in biomaterial models of the BBB to analyze mechanisms of neurovascular diseases (Bosworth et al.), while a research article examines the role of BBB integrity on the functional behavior of intracortical electrodes (Falcone et al.).

Together, this Research Topic illustrates the current state-of-the-art and future opportunities for the development of biomaterials to sustain and support differentiation of cells involved in neurological conditions. Due to the complexity of the brain, further progress in this area will presumably be related to technological advances at multiple scales and from multiple disciplines. However, it is clear that biomaterial platforms will play an essential role in these ongoing and future efforts. They may: aid the development of models to study the dysregulation and degradation of neuronal architectures; act as templates to promote neural regeneration; facilitate study of the progression of a wide range of brain related diseases including trauma and cancer; and play a central role in the optimization and delivery of therapeutic strategies. As a result, we have been excited to help organize this Research Topic *Biomaterials for Brain Therapy and Repair* and hope it serves as a relevant and useful resource to our colleagues.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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