NEURAL ENGINEERING SEMINAR SERIES

Altered Cerebrospinal Fluid Hydrodynamics are Associated with Impairments to Meningeal Lymphatic Networks and the Glymphatic System in Craniosynostosis

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ABSTRACT: Congenital skull malformations are associated with major vascular abnormalities that can cause complex and serious complications for brain health and fluid balance in the central nervous system. Dr. Max A Tischfield and his team have reported that humans with inactivating mutations in the transcription factor TWIST1 have skull dysplasia (craniosynostosis) and dural venous sinus malformations that are associated with raised intracranial pressure and neurological impairment. New data in Twist1 and Fgfr2 craniosynostosis mouse models now reveals that raised intracranial pressure and altered cerebrospinal fluid (CSF) hydrodynamics can coincide with the failure of meningeal lymphatic vessels to remodel into structured networks. Strikingly, regions specialized for CSF uptake, known as "hotspots", are often poorly formed and/or missing in these animals. Injecting molecular tracers into the CSF reveals significantly less tracer accumulation in meningeal lymphatic vessels, especially near hotspot regions, and in the surrounding dura. These findings suggest that raised intracranial pressure and changes to CSF circulation may affect flow dynamics and mechanical forces necessary for the proper growth and expansion of meningeal lymphatic networks. In addition, Dr. Tischfield and his team have also found widespread changes to perivascular waste clearance pathways in the brain, suggesting that the glymphatic system may be impaired in craniosynostosis, the second most prevalent human craniofacial disorder. Collectively, they propose a novel paradigm whereby they can leverage craniosynostosis models to elucidate functional roles of flow for meningeal lymphangiogenesis, and the chronic effects of raised intracranial pressure on the glymphatic system.

BIOGRAPHY: Dr. Max Tischfield is an assistant professor in the Department of Cell Biology and Neuroscience at Rutgers. He obtained his Ph.D. from the Program in Neuroscience at Harvard Medical School and completed a post doctoral fellowship in the Department of Molecular Biology and Genetics at Johns Hopkins Medical School and the Department of Neurology at Boston Children's Hospital. During this time, Dr. Tischfield discovered the genetic basis of several neurodevelopmental disorders and has broad experience modeling craniofacial, neurovascular, and neurodevelopmental disorders in mouse models. His lab, located at the Child Health Institute of New Jersey, continues to utilize mouse genetics to investigate the underlying neuropathophysiology of Tourette Syndrome, and cellular and molecular mechanisms that control the development and functions of meningeal lymphatic networks and the brain's glymphatic system.

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