IMPRS Honorable Mentions

Intravital Microscopy Optimization for Murine Tail Lymphedema Model

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Background: Lymphedema is limb swelling caused by lymphatic dysfunction. It occurs in 30% of patients that undergo axillary lymph node dissection in the treatment of breast cancer. It can cause pain, impair function, and decrease quality of life. Lymphedema is treated with compression, excisional procedures and microsurgical physiologic procedures. There is no cure for this disease. The murine tail model of lymphedema is an established animal model for lymphedema. Visualization of lymphatics and functional assessment remains a challenge.

Project Rationale: Immunohistopathology and qRT-PCR are two commonly used in vitro techniques for molecular assessment of lymphatics in animal tissues. These methods provide incomplete information about the structure/function of lymphatics and introduce the confounder of harvested tissue. Methods of functional evaluation such as lymphoscintigraphy or lymphangiography show transit of dyes through lymphatics without high resolution imaging of the lymphatic vessels. Intravital two-photon microscopy (IVM) addresses these disadvantages through real-time imaging of subcellular level biological processes in live animals. The goal of this project is to optimize IVM methods for the assessment of functional lymphangiogenesis in the murine tail lymphedema model.

Methodology Development: A full-thickness skin excision is performed near the base of the tail in C57BL/6 mice. The lymphatic trunks are then surgically transected. Gene-based therapy is delivered to the tail at the surgical site. At 10 days post-treatment, a second full-thickness skin excision is made distal to the site of occlusion. FITC-Dextran (2000 kD) is injected at the distal tail for lymphatic uptake. Lymphatic vessels are visualized at the second skin excision site with the Leica SP8 Confocal/Multiphoton Microscope and assessed for number of branching points. Images are captured with Leica Application Suite Advanced Fluorescence Software and analyzed with Imaris Microscopy Image Analysis Software. This results in the ability of functional assessment of lymphatics and visualization of lymphangiogenesis following gene-based therapy.

Changes in Cortical Composition during Gyrification in the Developing Brain

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Background and Hypothesis: Abnormal brain folding has been implicated in neurodivergent conditions such as schizophrenia and autism, yet the mechanical and biological processes responsible for this process are not well understood. One current hypothesis is that cortex growth outpaces growth of the underlying white matter to drive mechanical buckling. However, mechanical stresses, such as those resulting from buckling, can also influence cellular behavior. In this study, we hypothesized that mechanical stresses from cortical folding influence processes of biological growth within the cortex, such as dendrite arborization within the neuropil and neuronal differentiation.

Methods: To quantify change in cell body size and neuropil over the period of cortical folding, sections of the developing ferret brain (postnatal days 20, 26, 32, and 38) were stained with FluoroNissl dye, imaged with confocal microscopy, and analyzed using Fiji software. Change in percent neuropil, cell area, cell density, and overall length were quantified at upper, middle, and lower thirds of the cortex to assess the influence of bending stresses within gyri and sulci during development.

Results: Preliminary analysis revealed a substantial increase in neuropil over time in the upper layers of the cortex. However, gyral regions expected to experience mechanical tension and increased expansion did not exhibit the hypothesized differences in neuropil or cell size. Though there was an overall increase in neuropil volume fraction and cell body size over time, throughout all layers of the cortex, these factors only accounted for roughly 2/3 of the physical growth quantified throughout these cortical layers.
Potential Impact: Findings indicate that neuropil and cell body expansion are insufficient to fully explain the growth observed during cortical folding. These results highlight a potential role for alternative cellular processes, such as the migration of other cell types into the cortex, to induce cortical growth and folding in gyrencephalic species.

Grounded Practical Theory Analysis of Patient-Provider Communication with Black Women Participating in Breast Cancer Clinical Trials

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Background: Previous literature suggests breast cancer clinical trial participation among Black women has declined in recent years by as much as 35%. Though the literature identifies barriers to participation for this population, little has been studied about how researchers can address these barriers. This study investigates the communication between healthcare providers and Black women to illuminate how providers and researchers can positively influence their perceptions of breast cancer clinical trial participation.

Methods: Fourteen women (n=14) who self-identified as Black, Black American, or African American, were interviewed about their communication experiences with healthcare providers regarding breast cancer clinical trial participation. Each transcribed interview was coded using thematic analysis. Grounded Practical Theory was introduced to give insight into the patient-provider communication needs of Black breast cancer research participants.