2024 Multidisciplinary Research Program in Medicine Project*: Etiopathogenesis of capsular contracture: Novel application of mathematical model*

Hypothesis or Research Question(s): Our previous research confirms that Capsular Contracture is caused by a deranged immune recruitment in response to mechanical and architectural properties of the developing capsule. For this project, we intend to expand our preliminary mathematical model to better account for bio-mechanical factors and test hypotheses generated from the mathematical model with vitro and in situ experiments.

PROJECT BACKGROUND & SUMMARY

Breast reconstruction following mastectomy is an essential component of comprehensive breast cancer care. Patients interested in undergoing reconstruction may experience a potentially enhanced quality of life in the long term. The majority of Canadian patients undergoing breast reconstruction choose to have a breast implant. Capsular contracture (CC) is a common and morbid complication of implant-based breast reconstructive surgery. CC is defined by abnormal collagen deposition, resulting in a thick and contracted capsule that is firm, deformed, and painful. CC is associated with reconstructive failure, reoperations, and long-term morbidity. In these circumstances, CC can negate the anticipated benefits of breast reconstruction in survivorship. Extensive studies have been conducted on the development of CC, covering cellular, biochemical, surgical, and biomaterial factors. The causes and development of CC remain unclear, with seemingly disparate etiological theories related to the body's immune response, mechanosensitivity, and implant properties. Divergent theories have led to a multi-pronged clinical approach to decreasing CC incidence, involving both preventative and therapeutic measures, such as meticulous infection control and rigorous surgical planning. Despite these efforts, a 40% incidence of CC persists for breast cancer patients following implant-based reconstruction. Based on evidence to date, we developed a foundational mathematical model of capsule formation and explored model variants of conjectured cellular and biomechanical mechanisms underlying CC formation. Our modeling supports the hypothesis that CC is a consequence of a deranged immune recruitment in response to mechanical and architectural properties of the developing capsule. For this current project, we will develop a mathematical model to test the mechanosensitive cellular responses leading to CC. With this model, we will generate a list of hypotheses for testing the responses of mechanosensitive cells to tissue stress through experiments. Based on hypothesis testing, we will validate or refute hypotheses and augment our understanding of capsular disease. Our project uses expertise in mathematics, immunology, and biomechanics to tackle a complex issue in breast cancer care. The expected outcomes go beyond theoretical insights, aiming to contribute practical solutions for reducing CC incidence and improving the success of breast reconstructions. By bridging these disciplines, our research has the potential to revolutionize the understanding and management of capsular diseases. This interdisciplinary approach is crucial for addressing the complexity of CC, making our project uniquely positioned to bring about meaningful advancements in breast cancer care.

BENEFIT TO THE STUDENTS

The students' main role will involve supporting a crucial interdisciplinary research project focused on breast cancer care and the prevention of capsular contracture (CC) following breast reconstruction. Specifically, we aim to enhance our understanding of CC by exploring the immune-related aspects of capsule formation through a mathematical model and experiments.

Students' roles:

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- Conduct literature search on capsular contracture development and causes, specifically bio-mechanical factors.

- Support the development of mathematical models based on data generated by previous research. - Draft papers and a short communication on theoretical pathogenesis of capsular contracture, the defective outcome of breast prosthesis implants after breast cancer surgery.

- Support the supervisors in protocol development for the experimental phase of the project. - Perform biological experiments under the supervision of a lab technician.

- Communicate project findings in research conferences. Support and additional opportunities: - Students will be required to attend weekly meetings. This will include opportunities for reflection and receiving support from the research team.

- Students will have support from the lab clinical research coordinator if they have questions or concerns that may arise. - Students will be given monthly feedback on their progress and work performance. This will help students be accountable for their work.

- Students will have the opportunity to interact with other students, research assistants and clinicians in the lab.

- Students will be invited to plastic surgery grand round lectures. This will give the students an opportunity for a more holistic understanding of the research in our department and an opportunity to meet other trainees, clinicians, and researchers in the department.

- The students will be encouraged to contribute their own ideas to the design of the research project. There are no limitations on the scope of involvement of the students. As they progress, they will be welcomed to take on more responsibility.

- At the end of their contract, the students will be supported in training the next student who joins this project.

This opportunity will help the students learn how scientific research is conducted using previous research and how new knowledge is generated. The project also requires students to collaborate with researchers from different disciplines and communicate effectively. This will help students understand the significance of interdisciplinary research and encourage them to have an interdisciplinary approach to their own learning and work. The opportunity will allow the students to develop a sense of responsibility, project ownership, self-confidence, pride in their work and strengthen their connection to UBC.