

Merial Student Research Program
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Research Interest: Knee Meniscal Tissue Engineering

Tissue engineering is a means of producing living tissues and organs in the laboratory to replace lost or damaged ones. This field of research was inspired by the complications and inherent limitations of organ transplant, bone and joint implants and replacements, and to avoid nefarious activities such as illegal organ harvest and underground organ/tissue trade. In order to produce new, living replacement tissues in the laboratory, cells must be cultured under special biological and mechanical conditions to rebuild the target tissue. Determining the ideal conditions for in vitro tissue synthesis and finding ways to integrate new tissue with the patient are the two principal areas of research in tissue engineering currently.

The focus of this laboratory is to produce fibrocartilage tissue found in knee meniscus. The menisci are C-shaped fibrocartilages located in the knee joint, and are crucial for knee joint shock absorption and stability.⁵ Tears within the axial, avascular 2/3 of the meniscus do not heal,^{6,7} and complete healing and restoration of the avascular meniscus has not been accomplished.^{10,12,13} To ameliorate patient discomfort, joint locking, and popping, avascular meniscal injuries are treated with partial meniscectomy. While removing the torn fibrocartilage improves short term patient comfort, articular cartilage is lost at a rate of 6.9% per year, resulting in irreversible knee arthritis.¹⁵

Between 30% and 50% of dogs with cranial cruciate ligament have concurrent damage to the medial meniscus.^{1,16-19} An increasing, ageing population of dogs have received the meniscal release procedure, which inhibits normal meniscal function,^{20,21} and causes cartilage damage and lameness.²² Even following stabilization, 6-13.8% of dogs with cranial cruciate ligament deficiency can still develop post surgery meniscal tears, which require surgical treatment.²³⁻²⁵ For the equine athlete, only 47% of horses return to their intended function post partial meniscectomy.⁴ Meniscal tears are the most common knee injury in people with a prevalence of acute tears at 61 cases per 100,000 persons.^{2,3} Arthroscopic meniscectomy is the most common human orthopedic surgery performed annually, and represents approximately 9 billion dollars in medical expenditures each year.^{26,19}

In response to this clinical problem, we are looking at ways to form meniscal replacement tissue in the laboratory, using tissues that are normally removed and discarded for other purposes during routine clinically indicated surgery. Ongoing research includes:

- Testing safety of tissue engineered neo-tissues
- Bioreactor design: designing machines that can “exercise” cells in culture to help form and strengthen tissue matrix.
- Testing of different biological stimuli (such as growth factors) and scaffold stimuli (such as collagen or gel scaffolds) to induce cells to form meniscal fibrocartilage in vitro.

A student working on one of these projects will learn about canine knee surgery and arthroscopy, learn cell culture techniques and tissue analysis techniques including spectrophotometric assays, micro materials testing, and RT-PCR. The tissues you will grow will come from cells harvested arthroscopically from canine patients in the clinics (who you will meet and observe their surgery). Tissue Engineering research involves cell culture; to keep the cells alive they need to have daily sterile media changes. The cells need this daily attention for culture periods of 3-5 weeks per patient. All research in the lab is done with the intent of getting a published manuscript. To make your contribution to patients who need replacement tissues possible, we require a student with initiative to follow through and write up their research. The discussions, readings, and scientific training and mentoring you will receive will provide an introduction to the kind of research that can be done for graduate degrees, or graduate degrees during residencies, and particularly could be beneficial to students investigating a future in surgery.