RESEARCH SCHOLAR PROGRAM – 2018

SUPERVISOR & PROJECT INFORMATION FORM

Please complete and return, via email only (crems.programs@utoronto.ca) by ***November 3rd 2017*** *(forms received after this date will not be posted).*

Supervisor Information

Name: Aaron Nauth

Email:NauthA@smh.ca

Degree: MD, MSc

SGS Appointment (IMS, IHPME, LMP etc..): IMS

Academic Rank: Assistant Professor

Field of Research: Orthopaedic surgery

Research Institution Affiliation (if applicable): St. Michael's Hospital (Keenan Research Centre for Biomedical Science)

Allocation of student contact time (number of hours per week YOU are available to the student for any concerns or to review progress): 2

Project Information

Title: Effectiveness of Endothelial Progenitor Cell (EPC) Therapy as Part of the Induced Membrane Technique – a Comparison with Bone Grafting in an Animal Model of Segmental Bone Defect

Description (max 500 words):

Management of large segmental bone defects remains a major challenge for orthopaedic surgeons. The induced membrane (Masquelet) technique (IMT) has been gaining popularity as a therapeutic option for these complicated cases. In this two-stage technique, the affected bone is first stabilized and the defect is filled with bone cement. During a second intervention, the cement is removed, leaving intact the membrane that has formed by foreign-body reaction. The induced membrane creates a defined, closed space for the final step of bone grafting. The membrane is also assumed to provide biological stimulation and local vascularization, which support survival and maturation of the graft and ultimately facilitate bone healing. Successful treatment of large segmental defects, up to 25-cm long, has been reported with this technique.

Nevertheless, autologous bone grafting is associated with significant shortcomings. For instance, patients can suffer from various complications at the harvest site. The development of alternative treatments overcoming these issues has recently been the focus of active investigation. In this context, our team has demonstrated the potential of endothelial progenitor cells (EPCs) for promoting healing in a small animal model of critical-size bone defect. These cells can initiate and stimulate the formation of blood vessels, an essential element of the healing process. However, an EPC-based therapy has never been tested as part of the IMT.

Consequently, the goal of the proposed project is to evaluate the effectiveness of EPCs in a small animal model of femoral defect treated with IMT. The EPC-based therapy will also be compared to autologous bone grafting, the current standard intervention for the second stage of IMT.

In brief, a 5-mm defect will be created in the right femur of rats. After stabilizing the bone with a miniplate and screws, the defect will be filled with bone cement. Three weeks later, the cement will be carefully removed to avoid disrupting the induced membrane, and the defect will be filled will either cancellous bone graft or with a gelatin scaffold seeded with EPCs. Bone graft will be obtained from donor rats during the same surgical session. Cells will be derived from bone marrow of additional donor rats and kept in culture for 7-8 days before implantation. Bone healing will be assessed through radiographic evaluation and scoring, micro-computed tomography, and biomechanical testing.

If successful, the proposed investigation will help refine the IMT and create a new potential application for EPC-based therapy. Above all, this project could lead to a much needed alternate strategy for the treatment of nonunions in high-energy trauma patients.

If human subjects are involved, have Ethics been obtained?

☐ YES ☐ NO ☐ Application Submitted ☒ N/A

Do you expect this work will be published within the 20 months?

☒ YES ☐ NO ☐ Uncertain

Student's roles and responsibilities (please be specific)

Please indicate who will serve as the student's direct report (PI, PhD student, technician etc…)

The successful applicant student will:

-Review and summarize the literature relevant to the research topic.

-Contribute to the planning and supervision of the project.

-Complete animal handling training.

-Learn proper cell culture techniques.

-Perform isolation, culture, and preparation of endothelial progenitor cells.

-Assist during surgeries (with a possibility to perform surgeries).

-Acquire data (e.g., radiographic assessment, micro-computed tomography, biomechanical testing).

-Contribute to data analysis (data compilation, statistical analysis).

-Write and prepare for submission the abstract(s) and manuscript resulting from this project.

-Participate in the lab meetings and journal club.

A research associate and a technician will provide the required training, supervision, and help on a daily basis. The student will also have the opportunity to meet regularly with their supervisor, Dr. Nauth, to provide guidance and mentorship on the project and their career.