

***The Crawford MacLeod Foundation Fund for Imaging Research Has Funded:***

A Doctoral Postgraduate Scholarship in Pre-Clinical Bacteria Imaging

*Value:* \$40,000 per year for a maximum of four years

*Qualifications:* MSc or MEdSc in Pre-clinical or Medical Imaging preferably in the area of Nuclear Medicine (i.e., Positron Emission Tomography (PET) or Single photon emission computed tomography (SPECT)) and/or in Magnetic Resonance Imaging (MRI).

*The Health Problem:* Antibiotic treatment, before confirming the presence of bacterial infection and identifying the bacterial species involved, damages beneficial bacteria and leads to antibiotic resistance. If this trend continues, it is predicted that by 2050 some 10 million people will die per year of bacterial infections, and chronic conditions, like inflammatory bowel disease.

*How to address this health problem:* Develop a medical imaging method to visualize bacteria in the human body and to identify the specific strain(s) of bacteria.

Using standard medical imaging methods such as x-ray computed tomography (CT) or magnetic resonance imaging (MRI), bacteria are too small to be seen. As a result, the current approach to imaging human infections relies on the accumulation of tissue damage. This is often not an effective approach. Tissue damage is not specific to infection. Also, an infection is well advanced by the time tissue damage occurs. Further, information on bacterial species is not provided.

*The biological basis of our proposal:* A class of viruses, called bacteriophage, attack bacteria but do not attack human cells. Such bacteriophage have been isolated and shown to target select species of bacteria. Several of these bacteriophages have now been safely injected into patients as a microbial therapy.

We have recently shown that bacteriophage can be labeled with a radioactive probe and imaged using positron emission tomography (PET), an approved system for human imaging. Therefore, in theory, any species of bacteria can be imaged by (1) isolating a species of bacteriophage that is specific for the bacterial target; (2) radiolabeling the bacteriophage with our PET probe; (3) injecting the labelled bacteriophage into the patient; and (4) imaging the patient's body. Only the specific bacterial target will provide a PET signal.

Then, after narrow-spectrum antibiotic treatment directed at the particular bacterial infection, the signal from labeled bacteriophage can be re-tested. If the PET signal decreases, then the bacteria in question would have been successfully treated.

*The experiment we propose:* In a pilot experiment using pigs, we will inject two different species of bacteria into the flank muscles, one on each side. Then we will inject radio-labeled bacteriophage, specific for only one of the two bacterial species. Then we will image the PET signal over the course of one week. This will inform us about the best time to image when translated to humans.

*Anticipated impact:* This technology applies to a) animal and human research developing new narrow-spectrum antibiotics, b) patient studies aimed at identifying infections, like those arising from orthopedic implants, and c) patient studies aimed at following fecal bacteria transplantation for treating bowel disease.

The technology was patent protected in April 2021 and has attracted the interest of six private sector partners. If this pilot is successful, two wish to use the technology to develop new treatments for bacterial infections of the gut while the other four will provide funding to further develop the technology, with the intention of licensing it in the future. *Research Group:* The successful PhD candidate will join the Lawson Imaging Research Program (LIRP) at St. Joseph's Hospital, London Ontario. The LIRP has extensive research staff and faculty in Nuclear Medicine and MRI as well as state-of-the-art and leading edge equipment including a PET/CT and PET/MRI with protected and dedicated research time. The bacteria imaging group includes five PhDs, two MDs, one graduate student and three post-doctoral fellows working with four private sector partners.

*Application Process:* Prospective PhD students must apply through the Medical Biophysics Department at Western University. LIRP/SJHCF contact will be through Dr. Frank Prato ([prato@lawsonimaging.ca](mailto:prato@lawsonimaging.ca)).