

Expertise

Dr. S. Darvesh is a clinician-scientist with 60% protected research time. He is a behavioural neurologist with expertise in assessment, management and clinical research in dementias. He is also a neuroscientist and organic/medicinal chemist with focus on understanding the neurochemistry and neurobiology of butyrylcholinesterase (BChE) in health and disease. He is the *Dalhousie Medical Research Foundation Irene MacDonald Sobey Chair in Curative Approaches to Alzheimer's disease*. He has extensive experience in organic synthesis, radiosynthesis and analysis of inhibitors and substrates of BChE and study of human brain tissues.

Dr. Darvesh has established a multi-disciplinary, multi-institutional pre-clinical imaging program for early diagnosis and treatment monitoring of dementias. This program includes development of alternative metrics for assessment of early metabolic biomarkers of AD and development of novel radiopharmaceuticals for early diagnosis and treatment monitoring of dementias.

He have assembled a specialized team to develop novel radiopharmaceuticals for molecular imaging of BChE in the brain. *Dr. I. Pottie*, Mount Saint Vincent University (MSVU), has expertise in synthetic organic chemistry and will be responsible for preparation of the non-radioactive chemical compounds. His laboratory has access to all necessary equipment needed for synthesizing and characterizing organic compounds. The synthetic procedures for generating radiolabelled molecules will be optimized in his lab prior to radiosynthesis in the Darvesh lab.

Dr. S. Burrell, Dalhousie University is a radiologist with expertise in nuclear medicine. He will be responsible for overseeing pre-clinical imaging and analyzing the results to assess the bio-distribution of the radioligands. He has experience in neuroimaging in patients with dementias⁷⁹ and has played a lead role in developing pre-clinical imaging capabilities at our institution.

Dr. C. Bowen, Dalhousie University, a medical imaging physicist with significant experience in pre-clinical imaging studies and the director of the pre-clinical imaging facility at Biomedical Translational Imaging Centre (BIOTIC), will provide the technical support required for the imaging needs of this program.

Dr. G. Mawko, Dalhousie University, is a clinical radiophysicist with particular interest in cyclotron radiation safety and protection, radiation dose assessment and quality control in nuclear medicine imaging. He will provide medical physics support in this project to those areas related to radiosynthesis.

Resources and Infrastructure

Dr. Darvesh's personnel involved in animal studies and handling radiopharmaceuticals are certified and institutional animal care and radiation safety approvals are in place. Dr. Darvesh's labs house the Maritime Brain Tissue Bank, a CORES facility and are equipped for genotyping, histochemical/immunohistochemical analysis of tissues, radiosynthesis, autoradiography and software for data analysis. Labs contain necessary equipment for experiments (e.g. Agilent 1260 Infinity HPLC, LabLogic radio-TLC/HPCL System, GE Healthcare Typhoon 9410 Phosphorimager). The labs are properly equipped and have institutional ethics approval for the safe use of ^{123}I and ^{18}F for autoradiographic and imaging experiments. Agreements are in place with the Nova Scotia Health Authority, Halifax, Canada, for the production and distribution of ^{18}F . ^{123}I will be obtained from commercial sources (Nordion Canada Inc.). These labelling experiments will be executed in consultation with the

facility radiophysicist, Dr. G. Mawko, and radiochemist A. Bou Laouz. Darvesh has access to Dalhousie's CORES Cellular Microscopy and Digital Imaging Facility that includes a Zeiss Axioplan 2 motorized microscope with Zeiss Axiocam HRc digital camera and AxioVision 4.6 software. Darvesh has full access and approvals to the Carleton Animal Care Facility, Dalhousie University. He has access to ^1H NMR, ^{13}C NMR and HRMS, IR and UV spectrophotometers for compound analysis (Nuclear Magnetic Resonance Research Resource, Dalhousie University).

As an adjunct Professor at MSVU, Darvesh, in collaboration with Dr. I. Pottie, has access of two experimental wet labs and an instrument room capable of conducting synthetic organic chemistry and biochemical analyses of enzymes. The instrument room contains a state-of-the-art GC/MS, Agilent Technologies HPLC, GC/FID and UV/Vis spectrometers. The lab has access to the departmental IR machine and a 60MHZ NMR. For pure compounds, he has access to a Bruker 300 MHz NMR, Saint Mary's University, Halifax, Canada.

In continuing collaboration with Dr. C. Bowen, a radiophysicist with significant experience in pre-clinical imaging studies, of the Biomedical Translational Imaging Centre (BIOTIC), Halifax, Canada, Darvesh has access to dedicated pre-clinical neuroimaging infrastructure including PET/CT (Trifoil Imaging) and SPECT/CT (Cubresa Inc.) scanners and 3.0T MRI (Magnex Scientific/Varian Inc.). This facility can routinely achieve spatial resolutions of $\sim 1.2\text{mm}$ for PET, $\sim 0.8\text{mm}$ resolution for SPECT and $\sim 100\mu\text{m}$ resolution for MRI.

With respect to further development of our synthetic compounds proposed, Darvesh a formal relationship with Treventis Corporation. This is a biotechnology company, of which S. Darvesh is a scientific co-founder, for development of our lead diagnostic agents towards clinical trials.