SASKATCHEWAN'S NUCLEAR IMAGING PROGRAM

www.fedorukcentre.ca

A Summary of Achievements

2015-2020

Fedoruk Centre
SYLVIA FEDORUK CANADIAN CENTRE FOR NUCLEAR INNOVATION

Acknowledgements

The Sylvia Fedoruk Canadian Centre for Nuclear Innovation Inc. would like to acknowledge many contributors to Saskatchewan's Nuclear Imaging Program:

- Government of Saskatchewan - Innovation Saskatchewan
- Government of Canada - Western Economic Diversification
- University of Saskatchewan (USask)
- University of Regina (UofR)
- Members of the Research Program Advisory Committee (RPAC)
- Staff of the Saskatchewan Centre for Cyclotron Sciences (SCCS)

Many thanks also for contributions to this summary report:

- Ekaterina (Kate) Dadachova, Fedoruk Centre Research Chair in Radiopharmacy and Professor, College of Pharmacy and Nutrition, University of Saskatchewan
- Aram Teymurazyan, Fedoruk Centre Research Chair in Nuclear Imaging Technologies and Associate Professor, Department of Physics, College of Science, University of Regina
- Gurpreet Aulakh, Fedoruk Centre Research Chair in Imaging Sciences and Assistant Professor, Department of Small Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan
- Dale Schick-Martin, Facility General Manager, Saskatchewan Centre for Cyclotron Sciences (SCCS), Fedoruk Centre
- Humphrey Fonge, Radiopharmacist, Saskatoon Health Region and Assistant Professor of Medical Imaging, College of Medicine, University of Saskatchewan
- Steven Siciliano, Professor and NSERC/FCL Industrial Research Chair in In Situ Remediation and Risk Assessment and Director, CREATE Human and Ecological Risk Assessment Program, College of Agriculture and Bioresources, University of Saskatchewan
- Eric Price, Canada Research Chair in Radiochemistry and Assistant Professor, Department of Chemistry, College of Arts and Science, University of Saskatchewan
- Chris Phenix, Assistant Professor, Department of Chemistry, College of Arts and Science, University of Saskatchewan
- C. Ron Geyer, Professor, Department of Pathology and Laboratory Medicine, and Nutrien Chair in Clinical Research, College of Medicine, University of Saskatchewan

2020 Report on Achievements prepared by Anne T. Ballantyne, Corporate Strategy Advisor,
Sylvia Fedoruk Canadian Centre for Nuclear Innovation Inc., November 2020

Contents

Growing Saskatchewan's Nuclear Capacity

The Nuclear Imaging Program

The Sylvia Fedoruk Canadian Centre for Nuclear Innovation Inc. (Fedoruk Centre) was established to place Saskatchewan among global leaders in nuclear research, development and training.

Nuclear imaging to advance life sciences, agriculture and medicine is a key area of focus, and in 2015, the University of Saskatchewan (USask), University of Regina (UofR) and Fedoruk Centre established the Nuclear Imaging Program. The program leveraged research and development capabilities in medical and life sciences to guide development of the new Saskatchewan Centre for Cyclotron Sciences (SCCS) and advance nuclear imaging tools and applications.

The Fedoruk Centre committed $5.2 million of funding over five years for the Nuclear Imaging Program. This included salary support for three new research chairs, two at USask in the areas of radiopharmacy (Dr. Ekaterina Dadachova) and veterinary imaging sciences (Dr. Gurpreet Aulakh), and one at the UofR in nuclear imaging technologies (Dr. Aram Teymurazyan). Each chairholder also received start-up funding for research, post-doctoral fellows and students. The program also funded new radiochemical and imaging equipment at the SCCS as well as a new clinical research coordinator to support core researchers in translating research from SCCS labs to clinical trials and eventual practice.

USask also hired two new faculty members in radiochemistry (Dr. Eric Price, a Tier 2 Canada Research Chair in Radiochemistry, and Dr. Chris Phenix, Assistant Professor in Chemistry). Drs. Price and Phenix joined Drs. Humphrey Fonge and Ron Geyer (USask College of Medicine), Steve Siciliano (USask College of Agriculture and Bioresources), and Zisis Papandreou (UofR Physics Department) as the program's core researchers.

Both USask and UofR committed a further $3.4 million in support for researchers/chairs as part of the Nuclear Imaging Program and agreed to transition chairholders to permanent faculty positions after funding concluded in 2020. Western Economic Diversification and Innovation Saskatchewan provided resources for equipment and infrastructure expansion of the SCCS.

Through the Nuclear Imaging Program and complementary investments in the SCCS by Innovation Saskatchewan and Western Economic Diversification, the Fedoruk Centre and its partners have established a flexible, versatile scientific resource in a business framework that will maximize societal and economic benefits to Saskatchewan for decades to come. The building blocks have been laid to solidify core nuclear innovation activities in Saskatchewan, concentrating on nuclear imaging for life sciences through the Nuclear Imaging Program.

LOOKING FORWARD

The funded phase of the Nuclear Imaging Program concluded in 2020 with all objectives having been met. The program has established Saskatchewan's leadership capacity in nuclear imaging by attracting established and emerging researchers to produce innovations in nuclear imaging for diagnosis, therapy and isotope production; assembling state-of-the-art infrastructure and equipment to generate new knowledge in life sciences, nuclear medicine, and nuclear imaging tools and methods; and strengthening Saskatchewan's capacity for respectful conversations about nuclear science and technology.

The three Fedoruk Chair holders have transitioned to positions in their home institutions. They continue to be branded "Fedoruk Chairs," and their institutions are providing ongoing support to build a strong cluster of research and education in nuclear imaging. The USask

Clinical Trial Support Unit added a clinical research coordinator to assist researchers in translating their innovations to practical applications in human healthcare. A Research Program Advisory Committee (RPAC) was formed to enable Fedoruk chairholders and other core researchers to advise the Fedoruk Centre on directions for the program as well as developments and practices at the SCCS. The RPAC is continuing in this capacity beyond the funding phase of the program. Responsibility for the sustainable operation of the SCCS is now captured in the Fedoruk Centre business plan.

Having established a foundation of first-class scientific facilities and a cluster of talented research leaders, the Fedoruk Centre can now encourage Saskatchewan people to broaden and deepen their contributions to human wellbeing through nuclear imaging as part of the Fedoruk Centre Strategic Plan (2020-2025).

The Fedoruk Centre has also opened the door for Saskatchewan institutions to propose partnerships to attract high-caliber academic leaders who can exploit nuclear imaging to accelerate contributions to their disciplines, for example in crop or soil sciences, environmental remediation, materials research, or the broad spectrum of topics in human or animal health. Through the foundation established by the Nuclear Imaging Program, its partner institutions and government funding partners, the Fedoruk Centre is positioned to invite users from academia and industry, from across Canada and abroad, to access the specialized capabilities of the SCCS and advance their research or development programs.

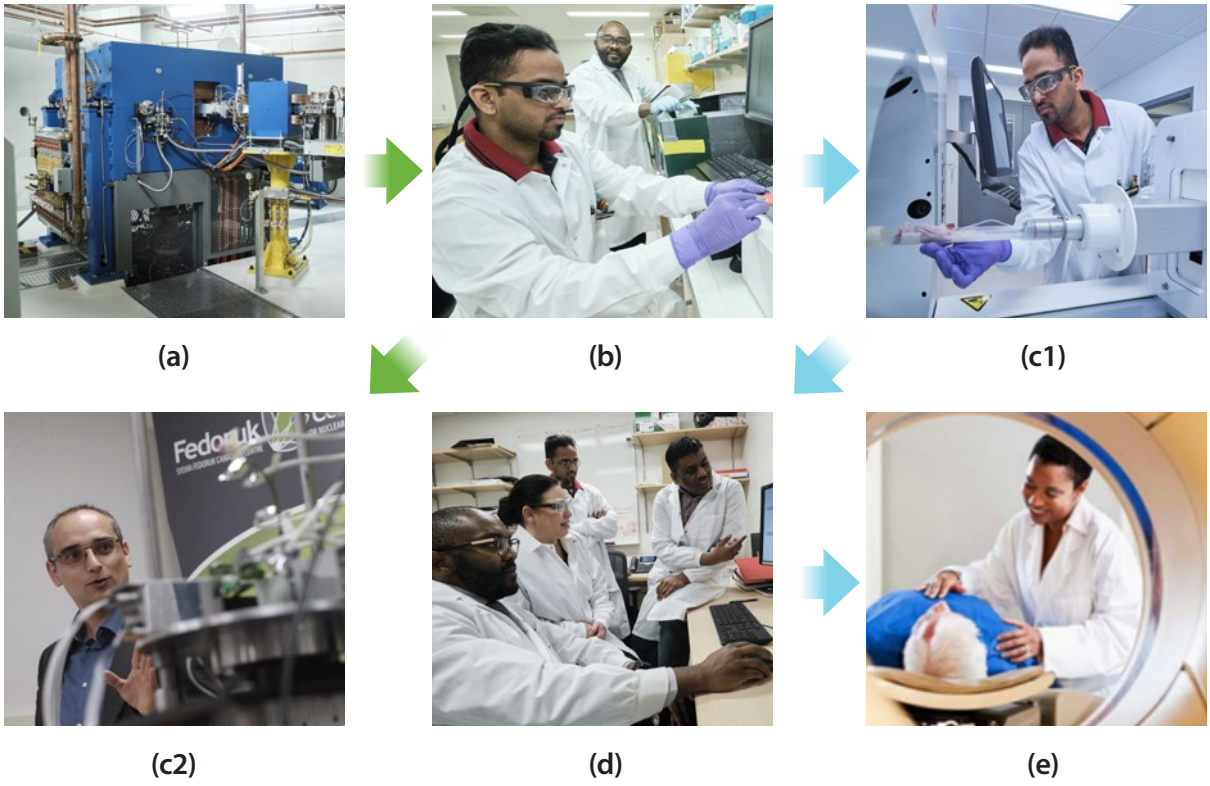


Figure 1 - The SCCS and Nuclear Imaging Program have created a pathway to new nuclear imaging and therapies in Saskatchewan, including (a) generating isotopes with a 24MeV cyclotron; (b) safely exploring new methods to produce radiochemicals and radiopharmaceuticals; (c1) testing the effectiveness for imaging diseases in small animals or (c2) applying nuclear imaging to learn about the metabolism of plants; (d) acquiring nuclear images in living specimens; and (e) supporting clinical trials of new radiopharmaceuticals to target and treat disease.

SASKATCHEWAN CENTRE FOR CYCLOTRON SCIENCES

DALE SCHICK-MARTIN, M.Sc.,
Facility General Manager, SCCS

Dale is a cyclotron engineer with experience in designing, operating, commissioning and maintaining cyclotron-based facilities. He is also familiar with radiation safety protocols, Good Manufacturing Practice (GMP), radiopharmaceutical production, project management and targetry. Dale obtained a Master of Science, Physics degree from the Guelph-Waterloo Physics Institute, where he was involved in the implementation of Canada's first high-resolution microscope.

The Fedoruk Centre partnered with Innovation Saskatchewan and Western Economic Diversification to construct the Saskatchewan Centre for Cyclotron Sciences (SCCS) to supply the nuclear imaging agent fluorodeoxyglucose (FDG) to Royal University Hospital for PET-CT scanning and to support innovation in nuclear imaging applications for life sciences.

In 2013, the Fedoruk Centre assumed responsibility for operating the cyclotron and nuclear-substances laboratories on the USask campus, compliant with regulations of the CNSC and Health Canada.

In 2014, USask and UofR researchers submitted a proposal[1] to the Fedoruk Centre to establish faculty positions and acquire equipment for radiochemistry and imaging of live specimens.

In 2016, the SCCS commenced manufacturing of radiopharmaceutical fluorodeoxyglucose (FDG) for sale to regional hospitals. Since then, FDG manufacturing has quickly ramped up to support PET-CT scanning for patients in Saskatchewan, Calgary, Edmonton and Winnipeg.

The Innovation wing of the SCCS was originally operated by USask. In 2017, a partial renovation by the USask College of Medicine included creation of a pre-clinical imaging laboratory to allow PET, SPECT and CT imaging of small animal specimens and construction of a radiochemical lab. A CNSC licence was issued in 2017 for the university to begin operating in the space.

In 2018, the Fedoruk Centre assumed responsibility for operation of the Innovation Wing. Western Economic Diversification, Innovation Saskatchewan and the Fedoruk Centre jointly funded a $4.4 million renovation of the Innovation Wing into a suite of labs suited for nuclear imaging and radiochemistry. The renovation was complete by March of 2020.

Today, the Saskatchewan Centre for Cyclotron Sciences (SCCS) gives users access to comprehensive nuclear research resources, including the Cyclotron Wing, labs for handling nuclear isotopes, radiochemicals and radiopharmaceuticals, and the fully equipped Innovation Wing, which offers a suite of labs for radiochemical research and imaging living specimens.

Bringing these resources together in a single facility operated by a single operator—the Fedoruk Centre—the SCCS opens the door to the full range of nuclear research, from basic science and radiochemical discovery right through to preclinical investigations of potential medical products.

Figure 2 - The Hon. Ralph Goodale observes a demonstration of radiological handling equipment at the re-opening of the renovated Innovation Wing in 2019.

Figure 3 - Radiopharmaceuticals are manufactured with automated chemical equipment inside hot cells that protect employees from radiation. Employees dress to ensure the product is sterile for clinical applications.

Figure 4 – Newly renovated synthesis and labelling radiochemistry lab in the SCCS Innovation Wing.

Development of a User Access Model

The Fedoruk Centre has developed a user access model for researcher access to the SCCS. The SCCS's full direct operating costs were determined from annual public audits for the fiscal years ending March 31, 2017 and March 31, 2018. A rate was then attributed to each of approximately 25 SCCS workstations. If all workstations were fully occupied throughout the year by a single user, the full cost of operating the SCCS would be recovered from that user's access fees.

Fedoruk Centre staff maintain all workstations in a research-ready state and can offer training and guidance on equipment use, waste disposal and other routine operations. Today, the Fedoruk Centre operates the SCCS transparently and provides equitable user access to workstations, specialized personnel support, standard services and radio-isotope products discovery right through to preclinical investigations of potential medical products.

Production of Radioisotopes

In addition to the routine production of radiopharmaceuticals, the SCCS has expanded to produce additional radioisotopes in response to emerging demands from researchers. This illustrates the synergy between the Nuclear Imaging Program's success in attracting core researchers and the development of state-of-the-art infrastructure in alignment with research needs. The SCCS has 23 different isotopes on its operating CNSC licence.

Figure 6 - Hon. Tina Beaudry-Mellor learns how the Fedoruk Centre will enable Saskatchewan researchers to develop nuclear therapeutics to cure disease.

Scientific Highlights

FEDORUK CHAIRS

EKATERINA DADACHOVA,
Fedoruk Chair in Radiopharmacy

Dr. Ekaterina Dadachova joined the University of Saskatchewan in 2016 as the Fedoruk Chair in Radiopharmacy. Formerly a professor at the Albert Einstein College of Medicine in New York, Dr. Dadachova is leading pioneering research into radioimmunotherapy—using radioisotopes coupled to antibodies or other drug molecules to treat cancer and infections caused by fungi, bacteria and viruses like HIV. Dr. Dadachova has built her research program in two major areas: Advances in Radioimmunotherapy and Safety Studies.

Advances in Radioimmunotherapy

Radioimmunotherapy of melanoma: Dr. Dadachova developed the radioimmunotherapy (RIT) for metastatic melanoma based on the delivery of cytocidal radiation to melanoma tumors by the radiolabeled antibody to melanin (Dadachova E. et al. PNAS 2004). Her team completed pre-clinical development of the radiolabeled antibody and advanced to Phase 1a/1b clinical trial in patients with metastatic melanoma. The encouraging results were presented at the American Society of Clinical Oncology and published in the *Journal of Skin Cancer* in 2013.

Dr. Dadachova has established successful collaborations with industry partners as well. She worked collaboratively with RadImmune Therapeutics to advance towards a Phase I/II clinical trial of a second generation of the antibody in combination with immunotherapy in patients with ocular or uveal melanoma. Her group is also performing basic science investigation of the radioimmunotherapy of melanoma (Allen KJH et al. Pharmaceutics 2019; Jiao R. et al. Int. J. Mol. Sci. 2020).

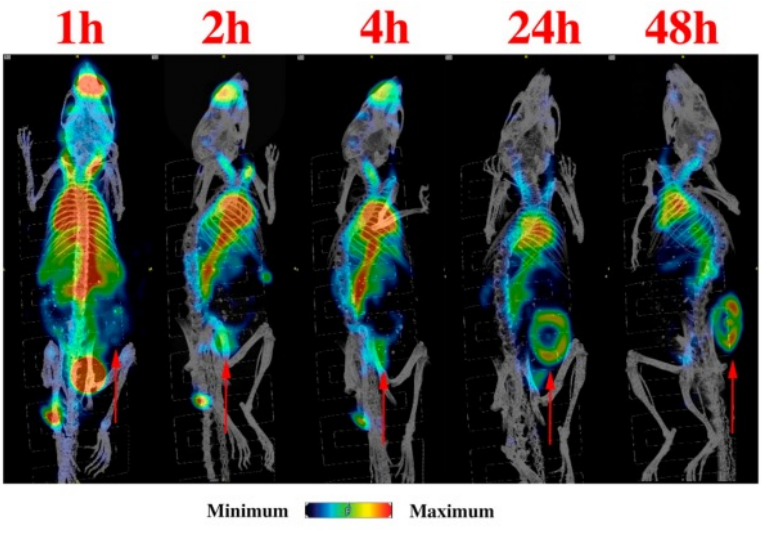


Figure 7 - Microspect/CT imaging of 111In-h8C3 melanin binding humanized antibody in B16-F10 tumor-bearing mice. The red arrows indicate tumor location. Images are presented as maximum intensity projections (MIP) for clarity.

Radioimmunotherapy of osteosarcoma: Another project under Dr. Dadachova's guidance is focused on developing radioimmunotherapy (RIT) of osteosarcoma, a continuation of her successful previous work. The results demonstrated that antibodies to insulin growth factor type 2 receptor (IGF2R) radiolabeled with beta emitters have therapeutic potential in patient derived xenografts (PDX) osteosarcoma models in mice (Geller D. et al. Nucl.Med. Biol 2016; Karkare S. et al. Sci Rep., 2019).

Dr. Dadachova collaborates with Dr. Maruti Uppalapati (USask College of Medicine) and Drs. Ryan Dickinson and Valerie MacDonald-Dickinson (USask Western College of Veterinary Medicine, or WCVM). The project is funded by a Canadian Institutes of Health Research grant to develop novel human antibodies for treatment of osteosarcoma in companion dogs using alpha and beta emitting radionuclide. The study is a comparative oncology approach to finding new treatments for this type of cancer.

Targeting viral antigens on cancers of viral origin: Twenty-five percent of all cancers in humans have viral etiology. Viruses linked to cancers in humans include: Epstein-Barr virus (EBV), which is associated with lymphomas, nasopharyngeal and breast cancer; hepatitis B virus (HBV) and hepatitis C virus (HCV), which are associated with hepatocellular carcinoma; and human papilloma viruses (HPV) which are associated with cancer of the cervix.

Dr. Dadachova is the first scientist to suggest that immunotherapies targeting viral antigens have potential in the treatment of a broad range of virus-associated tumors. She demonstrated the feasibility of treatment of experimental HPV-associated cervical and head and neck cancers. Dr. Dadachova has established and strengthened an international collaboration with oncological surgeon Dr. Rebecca Phaeton (Attending Physician at Hershey Penn State Medical Center, USA), who is Dr. Dadachova's former trainee.

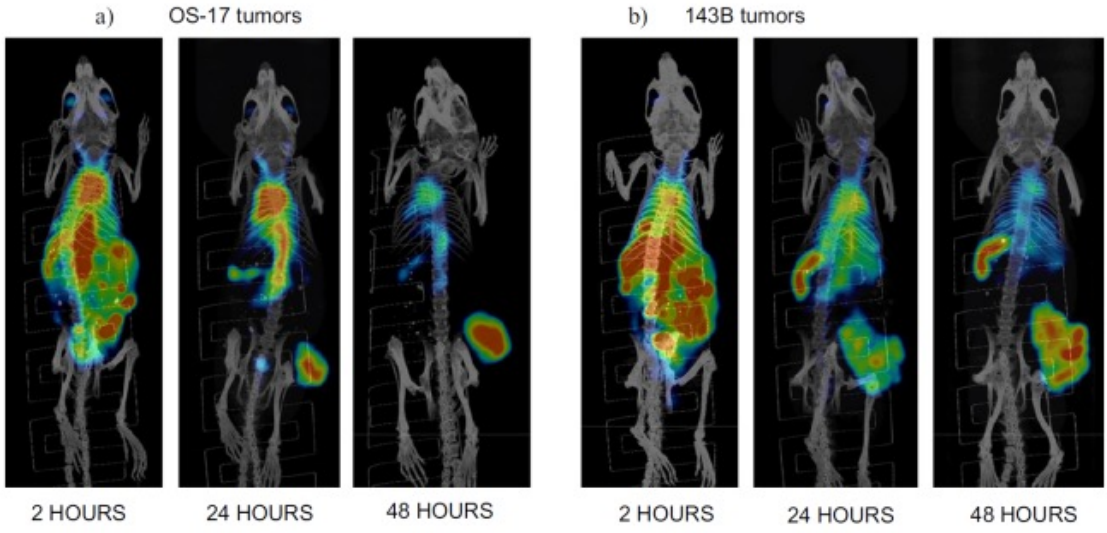


Figure 8 - Microspect/CT imaging of SCID mice bearing human osteosarcoma tumors with 111In-2G11 antibody to IGF2R: (a) OS-17 tumors; (b) 143B tumors.

Translating radioimmunotherapy into the infectious disease arena: There is an urgent need for new antimicrobial therapies to combat drug resistance, new pathogens and the relative inefficacy of current therapy in immunocompromised hosts. Dr. Dadachova is the first to propose that ionizing radiation delivered by the organism-specific monoclonal antibodies can kill microorganisms quickly and efficiently in vitro and in vivo, without acute or long-term toxicity (Dadachova et al. PNAS 2003).

Safety Studies

Developing a cure for systemic and neuroHIV: Dr. Dadachova's group is developing a cure for systemic and neuroHIV using alpha-radioimmunotherapy targeting Gp41 on HIV-infected cells in vivo and vitro (Garg R. et al. Nucl. Med. Biol., 2020).

The group is also undertaking research focused on the development of radioimmunotherapy of blastomycosis infections in companion dogs, targeting beta-glycans on the fungal cells with antibodies armed with 213-Bismuth. The research is being conducted in collaboration with Dr. Elisabeth Snead (USask WCVM) (Helal M. et al. Front. Med., 2020). Recent safety studies of this radiolabeled antibody in healthy dogs have provided encouraging safety data to launch the clinical trial in companion animals with invasive fungal infections at USask (Helal M. et al. Molecules, in revision).

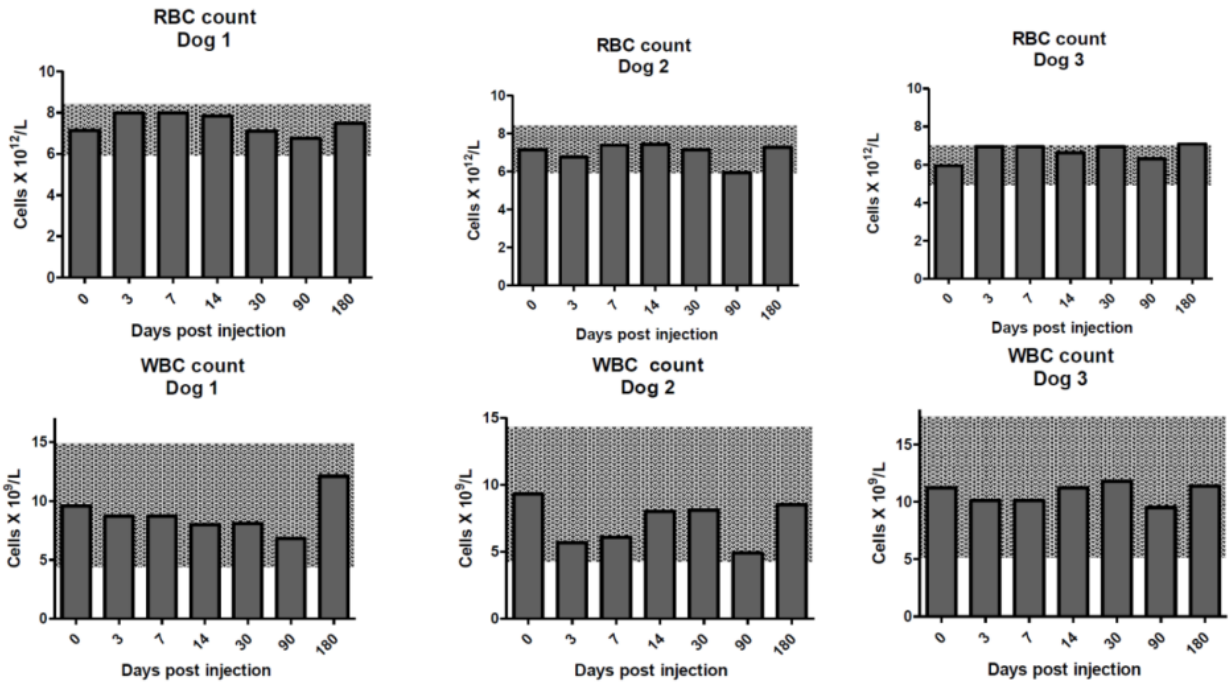


Figure 9 - Red blood cell counts (upper row) and white blood cell counts (lower row) in healthy dogs on days 0-180 post treatment with 213Bi-400-2 fungal beta-glucan targeting antibody. Shaded areas show reference change values (RCVs).

Interaction of melanin pigment with ionizing radiation for development of novel radioprotectors: Dr. Dadachova is working to develop melanin pigment-based radioprotectors for cancer patients undergoing radiation therapy, military personnel, and astronauts. (Pacelli C et al. Astrobiology 2018; Malo ME et al. Fungal Biol. 2018; Malo ME et al. Fungal Biol. 2020).

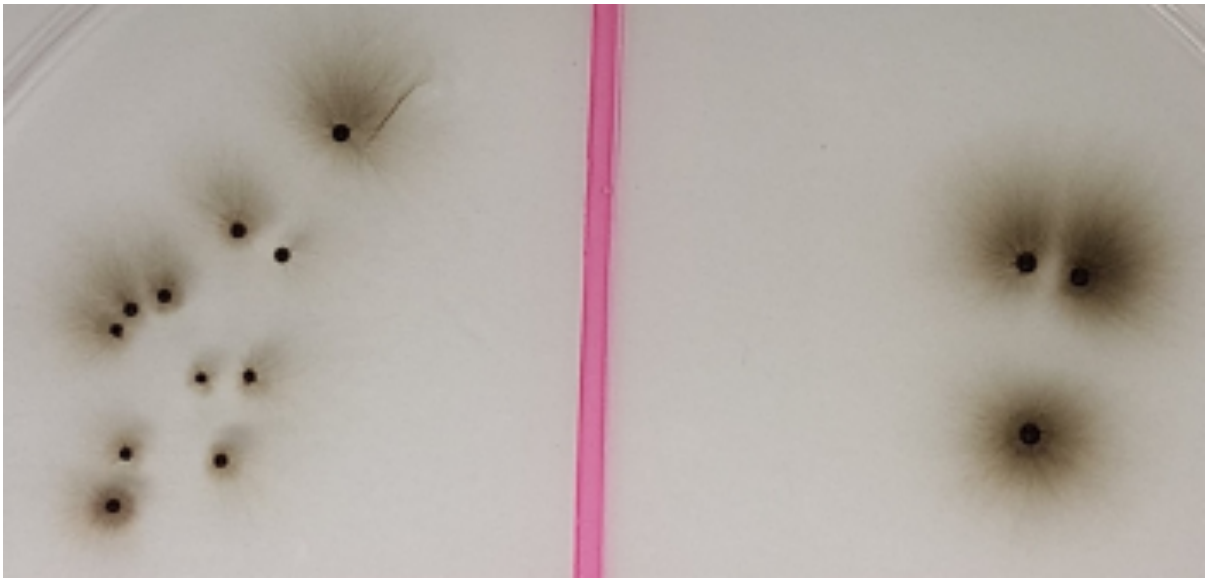


Figure 10 - Black fungus Wangiella dermatitidis is grown in an environment containing radioactive materials. Colonies on the left have had no prior interactions with radiation; colonies on the right have had previous exposure to a mixed source of ionizing radiation. The previous exposure has 'trained' this fungus to 'sense' radiation in its environment through ROS and to respond with increased growth – they have been radioadapted.

Additional Impacts

To support her research, Dr. Dadachova has secured over $5.4 million funding and leveraged resources from the US Defense Threat Reduction Agency, National Institutes of Health (NIH), Canadian Institutes for Health Research (CIHR), Saskatchewan Health Research Foundation (SHRF), Canadian Space Agency (CSA), Wendy Walk Foundation, Sylvia Fedoruk Center for Nuclear Innovation Inc. and private industry.

Dr. Dadachova's current research group at USask has eight members: three postdoctoral fellows, one Master student, one PhD Student, one research associate, one technician and one undergraduate student researcher. Several highly qualified personnel (HQP) have already graduated from her group and moved on to careers in science and medicine.

Dr. Dadachova has 172 published peer-reviewed articles and 46 published conference abstracts. During her years as a Fedoruk Chair, she published 32 peer-reviewed papers and two book chapters.

In April 2020, Dr. Dadachova was recognized by USask with the Distinguished Researcher Award. In addiction to professional presentations, she has actively promoted nuclear science and the Fedoruk Centre mission to the community at large.

ARAM TEYMURAZYAN,
Fedoruk Chair in Nuclear Imaging Technologies

Dr. Aram Teymurazyan holds the Fedoruk Research Chair in Nuclear Imaging Technologies at the University of Regina. His research focuses on development/implementation of novel detector technologies and imaging modalities, and applications of radiation in the diagnosis and treatment of diseases. A more recent addition to his research program is the development of nuclear imaging detectors for plant imaging to improve understanding of factors affecting plant productivity.

Advancing Nuclear Imaging Instrumentation

Dr. Teymurazyan's expertise is in experimental nuclear physics as well as x-/gamma-ray and nuclear imaging instrumentation. He also has extensive experience developing and using Monte Carlo radiation transport simulations to explore advanced detector concepts. During the past five years, the Nuclear Imaging Detector Development Laboratory (NIDDL) he leads at the UofR Department of Physics has established a Saskatchewan program dedicated to the study of plants and soil microbiomes.

The primary focus during this phase was the development of nuclear imaging instrumentation suitable for imaging plants at physiological and structural levels. Research had to be built up gradually and systematically, as nuclear imaging technologies to study plants are far less developed than comparable applications in medical and pre-clinical research. Only about half a dozen groups are working in the field world-wide, and there are currently no commercial solutions available for nuclear imaging of plants.

PhytoPET: 2017 saw the successful test of Canada's first dedicated plant prototype Positron Emission Tomography system (phytoPET). A configuration of four detector modules provides a respectable field of view (~50×15 cm2 H×D). Additionally, the plant within the field-of-view is rotated on a precision motorized platform to allow for complete 3D coverage of the plant. The ability of the scanning PET system to clearly visualize features as small as 1.0 mm in diameter was experimentally demonstrated in 2018.

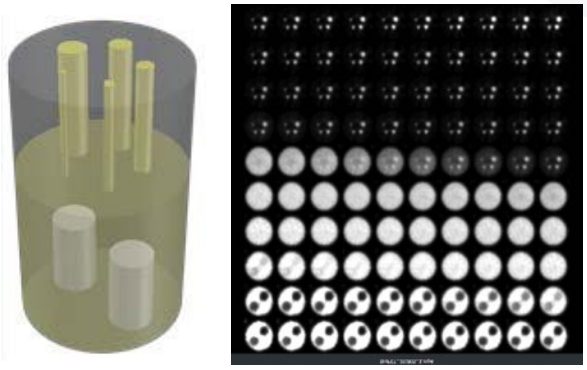


Figure 11 – (Right) Reconstructed cross-sections of the NEMA NU-4 image quality phantom (shown on the left) at various heights. For data acquisition, the phantom was positioned at 0°, 30° and 60° angles with respect to a nominal direction. The additional views significantly improve image quality. Notably, the ability to clearly visualize 1.0 mm thick "hot" cavity and sharp boundaries of "cold" high- and low-density cavities is evident.

The phytoPET was based on a working system developed by Dr. Teymurazyan's collaborators at the Thomas Jefferson National Accelerator Facility in Virginia, USA. Major limitations of the phytoPET system were the limited field of view (without scanning), the fragility of some custom made electronics, and the inability to provide quantitative data at the level theoretically possible by a high resolution PET system, a limitation shared by most plant-dedicated PET devices.

BioPet: Dr. Teymurazyan's team is building a new PET system that has 12 new detector modules augmented by the existing four detector modules, effectively quadrupling the field of view. The new detector modules make use of novel GAGG scintillator material, lacking internal radioactivity present in more standard LYSO scintillators, potentially allowing for significantly higher count rates and state-of-the-art solid-state photodetectors (silicon photomultipliers). The system utilizes enterprise level high-throughput electronics both for power supply and for data acquisition, which should offer higher resilience when handled by non-expert users. The new PET system, dubbed BioPET, will move into a commissioning stage at the SCCS in 2020.

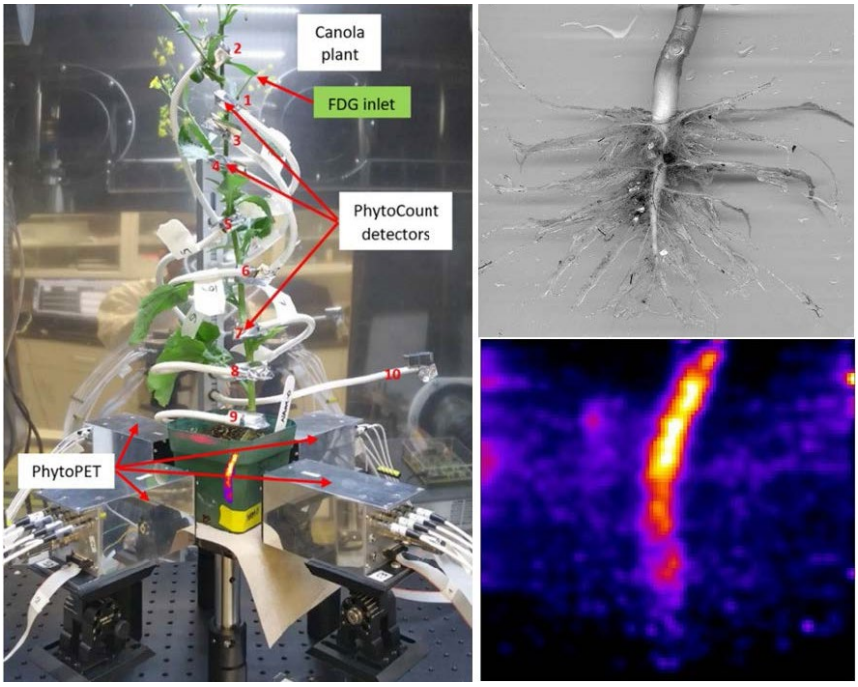


Figure 12 – (Left) Experimental setup for monitoring the 18F-labeled glucose uptake and translocation in canola plant. In these proof-of-concept experiments, the radiolabeled glucose was introduced into the canola plant through a cut point about 5 cm above soil level. PET detectors allow for monitoring of the amount of glucose transported to roots and identification of portions of root architecture participating in the transport. Above ground simple counting detectors (PhytoCount) developed at the UofR monitor the translocation of glucose. (Right top) Photograph of bare root after it has been extracted and washed. (Right bottom) Slice of reconstructed tomograph of the canola root.

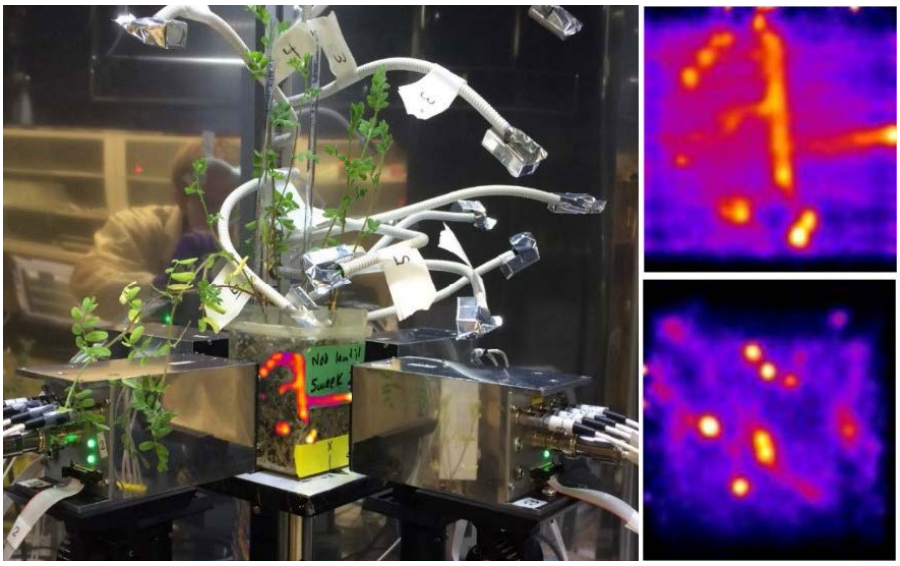


Figure 13 - (Left) Experimental setup for monitoring plant-microbial interactions in lentil roots and two different slices of lentil root tomograph. (Right-top: YZ and right-bottom: XZ) Rhizobial nodules on the lentil roots receiving glucose from the host plant.

Micro-CT system: To take full advantage of the BioPET system's molecular imaging capabilities, the functional images enabled by the systems need to be correlated with structural features of the plants. This is even more important when investigating below ground root morphology and when drawing parallels with above ground plant health. A custom x-ray micro-CT system has been built to allow researchers to study 3-D morphology of plant roots with micron level resolution (down to cellular scale). While it will be possible to operate the proposed micro-CT system independently, it will share its field-of-view with BioPET scanner, allowing researchers to co-register the biological function of plants afforded by PET images with below ground plant structures enabled by the x-ray CT. The team expects the system will be fully deployed in late 2020.

PhytoCount: Dr. Teymurazyan's group has also constructed a prototype of a novel radiation-counting detector system named PhytoCount. The low-cost system allows high-throughput scanning of plants and quantification of radioisotope-labeled molecule uptake and kinetics, opening the door to efficient large-scale plant studies on metabolic regulation and perhaps guidance in gene discovery. The 10-channel PhytoCount prototype can monitor the movement of radiolabeled compounds in an intact plant through direct detection of escaping positrons or electrons with energies above 100 keV at discrete locations along the plant stem, shoots or leaves with resolution of ~2 mm.

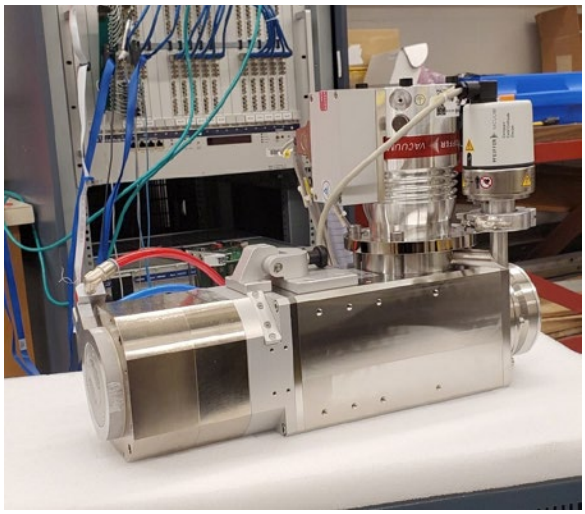


Figure 14 – Prototype of PhytoCount system.

A fruitful collaboration has been established with Dr. Steven Siciliano (see Core Researchers), an early adopter and proponent of nuclear imaging technologies for plants and soil microbiomes at USask. Together, Dr. Siciliano's and Dr. Teymurazyan's teams have worked towards production of plant relevant radiotracers ([^{11}C]-CO_2, [^{13}N]-N_2 and [^{13}N]-ammonia) at the SCCS. The prototype system passed preliminary testing and the associated intellectual property (IP) is being transferred to the SCCS/Fedoruk Centre.

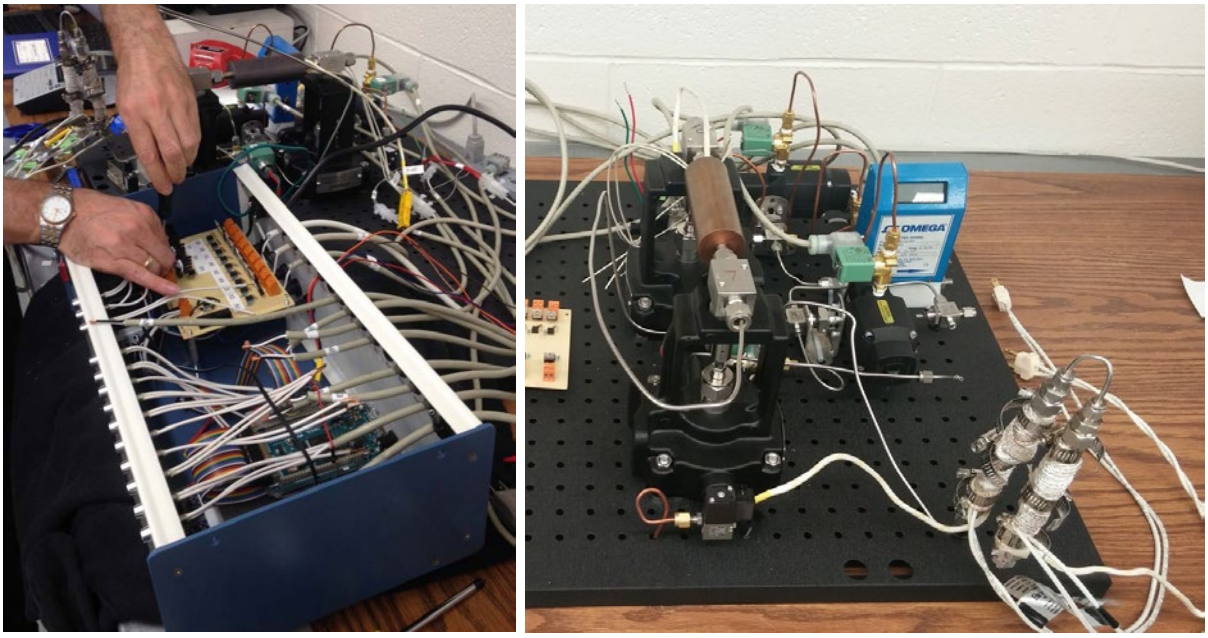


Figure 15 - (Left) Control for the [^{11}C]- CO_2 / [^{13}N]-N_2 system. (Right) An early rendering of mechanical components of the CO_2 trap and the NO_x scrubber developed by Dr. Steven Siciliano's group.

Collaborations: Dr. Teymurazyan is collaborating on applications of radiation in the diagnosis and treatment of disease, in particular with Dr. Alla Reznik at Lakehead University and Dr. Geordi Pang of the Odette Cancer Centre and Sunnybrook Research Institute in Toronto. He and his group have tested a proof-of-concept high quantum efficiency MV x-ray imaging detector.[2] X-ray conversion layer efficiency of the prototype detector is >12 percent, about a factor of 4 higher compared to clinically used imagers. This progress in MV x-ray imaging instrumentation is a direct translation of technology from fundamental particle/nuclear physics into an applied arena.

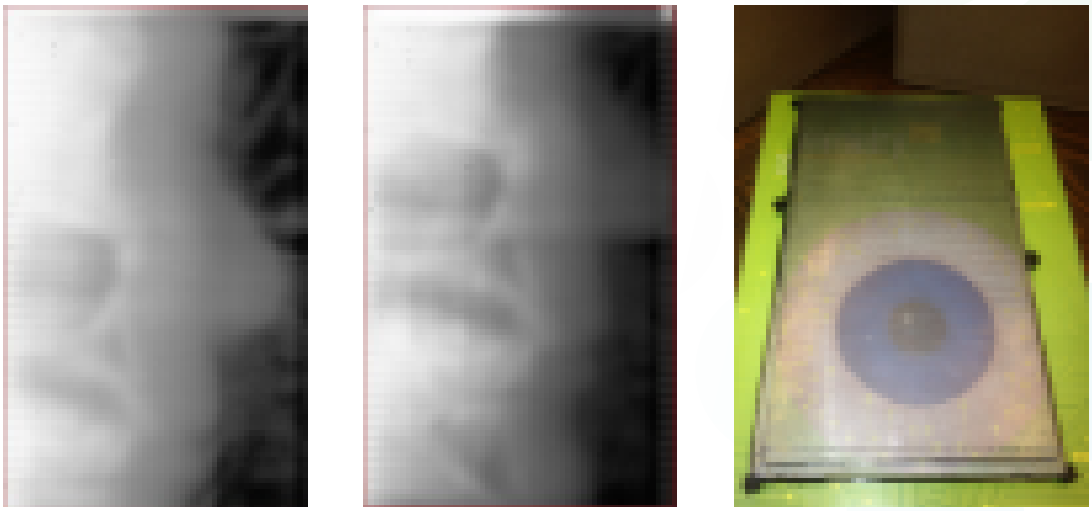


Figure 16 - Images of the head-phantom are shown alongside a photograph of the prototype high-efficiency x-ray conversion layer.

The development of novel gamma and x-ray detectors and systems required building in-house competencies and capabilities, since custom electronics design and prototyping is lacking in the province. As a result of these activities, NIDDL has designed fast amplifiers for on-Semiconductor SiPM array readouts that in many aspects exceed capabilities of commercially available solutions. Dr. Teymurazyan and his team are exploring commercialization avenues to capitalize on these newly acquired capabilities and hardware developments.

Additional Impacts

Dr. Teymurazyan has leveraged over $1M in additional research funding through the Fedoruk Centre and Western Economic Diversification Canada. His current research group consists of two Master level students and two postdoctoral fellows at the UofR. He routinely employs one or two undergraduate students every summer to provide exposure to a research environment. Over the years, he has supervised a number of undergraduates, graduate students and postdoctoral fellows who have gone on to careers in academia and research.

At the UofR, Dr. Teymurazyan has designed an undergraduate course in Introductory Radiation Science and Biophysics and a graduate level directed reading course on computerized tomographic imaging with an emphasis on positron emission tomography. He also revised the UofR Bachelor of Medical Radiation Technology program, which is offered in partnership with Saskatchewan Polytechnic's Radiological Technician program.

Dr. Teymurazyan and his team's efforts to develop nuclear imaging technologies for plant research was featured on CBC News as well as Global News.[3, 4]

Dr. Teymurazyan, his students and collaborators have 13 published peer-reviewed articles and conference abstracts directly related to his tenure as the Fedoruk Chair in Nuclear Imaging Technologies. He and his colleagues (A. Reznik and O. Bubon) have a U.S. patent pending for their invention of tileable block detectors for use in nuclear medicine applications.

GURPREET AULAKH,
Fedoruk Chair in Imaging Sciences

Dr. Gurpreet Aulakh is the Fedoruk Chair in Imaging Sciences and an assistant professor at the Western College of Veterinary Medicine at USask. Dr. Aulakh earned her Ph.D. at USask and was a post-doctoral fellow at the University of Calgary. She uses a variety of optical microscopic, synchrotron and nuclear imaging tools to understand how tissue inflammation works at the cellular level.

Prior to her appointment, Dr. Aulakh was involved in pre-clinical research using animal models and in vitro assays to investigate the role of angiostatin in neutrophil biology and lung inflammation. She also developed synchrotron and intravital imaging protocols for murine lungs. Since assuming the Fedoruk Chair, she has focusing on the development of advanced imaging tools for animals.

Advancing Nuclear Imaging Sciences

To advance the development of better therapeutics for inflammatory conditions, Dr. Aulakh is endeavouring to bridge molecular imaging techniques with immunological and pharmacological analysis of clinical endpoints. She is targeting her program on inflammation research and validation of nuclear imaging probes in relevant animal disease models by working closely with small animal clinicians, cyclotron scientists, radiopharmacists and chemists.

Fundamental pulmonary research: In collaboration with Drs. Elisabeth Snead and Jaswant Singh at the WCVM, Dr. Aulakh worked to develop a physiologically and clinically relevant murine model of low-dose ozone induced acute lung injury, with the possible long-term vision of scaling up the model to a clinically pre-disposed feline species. By establishing comprehensive read-outs of lung injury and cellular and molecular markers of inflammation, the team has characterized the adaptive response of lung alveolar dynamics to environmentally relevant levels of ozone. The study is a critical step in establishing the lab's expertise in the field of fundamental pulmonary research. [5] Dr. Aulakh and her students have clarified the role of a novel chemokine receptor, CX3CR1, in regulation of the lung neutrophil migration induced by ozone.

Nuclear imaging strategies: Dr. Aulakh has prioritized efforts to develop a foundation for sound nuclear imaging protocols and analysis routines. Along with the animal model development, she developed a nuclear imaging strategy for the murine ozone lung inflammation model. Her team has successfully set-up an imaging protocol using FDG as the prototypical radiochemical, which is currently under review at *Scientific Reports*. The paper[6] presents deep phenotyping of lung inflammation showing ozone induced lung metabolic upregulation and analyzed CT data-sets have been deposited in the online repository.[7] Current findings highlight increased murine lung FDG uptake despite extensive lung damage upon two hours' exposure to 0.05 ppm ozone or tri-oxygen (O_3).

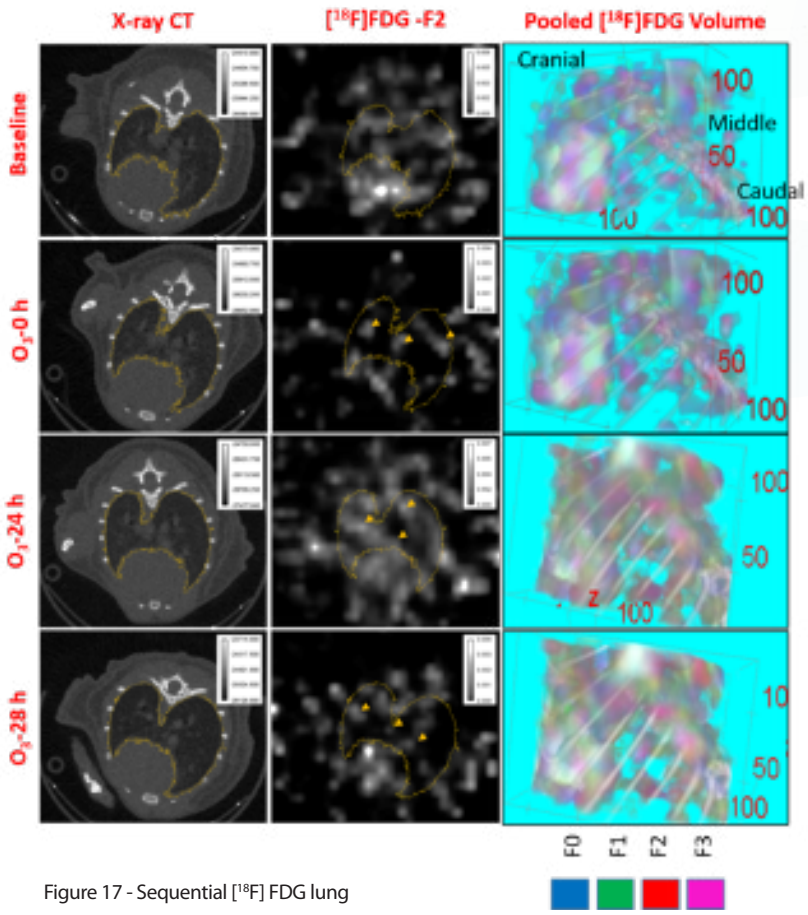


Figure 17 - Sequential [18F] FDG lung distribution using X-ray ROI.

Figure legend: Sequential lung [18F]F-FDG distribution using X-ray region-of-interest:

Representative lung X-ray CT slice, FDG slice in the fourth frame (F4) and a 3-d render of the merged lung [18F]F-FDG volume at baseline, O_3-0, 24 and 28 h.

The 3-d volume rendered view shows color-coded sequential frames (F0 in blue, F1 in green, F2 in red and F3 in magenta).

Please note that in the 3-d pooled FDG view, yellow indicates a merge of green (F1 frame) and red (F2 frame) and white indicates a merge of all the colors (i.e. frames).

The yellow arrow-heads indicate regions of high lung [18F]F-FDG uptake.

Pre-clinical testing of novel lung molecular targets: The third phase of Dr. Aulakh's research is focused on pre-clinical testing of novel lung molecular targets, such as nesfatin-1, CD34, angiostatin, integrin β3 and ATP synthase complex V in acute lung injury. Dr. Aulakh's team has made progress in their current understanding of CD34 protein in neutrophil and platelet biology.[8] She has also carried out parallel studies in order to better understand the immunomodulatory role of angiostatin, vitronectin, integrin β3 and ATP synthase complex V in acute lung injury. The pre-clinical findings were presented at 102nd Canadian Chemistry Conference and Exhibition, June 3-7, 2019, Quebec, Canada.

Nuclear Tagging of Proteins: Dr. Aulakh is also interested in nuclear tagging of proteins in her research work. This requires strong collaborations with established principal investigators in nuclear research as well as specialized equipment. A Gallium-68 generator was procured to carry out this collaborative research, and Dr. Aulakh is pursuing additional research funding and personnel to advance this specialized work.

Growth of WCVM Medical Imaging Infrastructure: Since Dr. Aulakh's appointment to the Fedoruk Chair, medical imaging infrastructure at the WCVM has expanded significantly. With the 2019 opening of the Allard Rozen Imaging Centre, the WCVM became the first veterinary college in Canada to have a PET-CT suite for animal and human research. The presence of the SCCS just meters away has created new opportunities to design and test novel radiopharmaceuticals for clinical applications in veterinary patients and companion animal models of human diseases. The WCVM team of clinicians and researchers of which Dr. Aulakh is a member have successfully obtained funding from the Fedoruk Centre to optimize PET-CT diagnostic procedures for companion animals and to evaluate the benefits of PET-CT imaging in two companion animal models involving cancer and a life-threatening infectious disease. This research has One Health interdisciplinary aspects that could benefit animals and humans.

Additional Impacts

As an early career investigator, Dr. Aulakh has leveraged over $500,000 in new research grants and had a few "firsts." She secured a CIHR COVID-19 operating grant, with Dr. Alice Mui (UBC) as the principal and herself as the co-applicant, and is actively collaborating with Drs. Shelley Kirychuk and Dean Chapman (USask) in exploring synchrotron imaging schemes to characterize the response of lungs to chronic insecticide and LPS exposures. She has supported Drs. Petros and Silvana Papagerakis (USask College of Medicine) in submitting CFI and CIHR funded project applications for COVID-19 related research grants.

Dr. Aulakh has supervised two undergraduate students, four Master students and one research associate. She has three published peer-reviewed journal articles, several peer-reviewed papers and 2 book chapters, as well as one report, one broadcast interview, four text interviews, six published conference abstracts and seven presentations. Her research findings have been shared with public audiences as well as with scientists at nuclear forums. Dr. Aulakh is an active member of several committees within the College and serves as an editorial reviewer for 4 different journals.

With the guidance of Dr. Monique Mayer, lead veterinary clinician in the Department of Radiology at the WCVM, Dr. Aulakh has designed an undergraduate course to provide a basic introduction to the field of radiation, radiobiology, nuclear imaging and radioisotope research. An advanced level course for graduate students aims to develop a line of study in nuclear/radiation toxicology. The course was first offered in 2019 and is being offered for a consecutive year, due to the demand.

OTHER CORE RESEARCHERS

The groundwork for building Saskatchewan's nuclear imaging research capacity has been laid, in part, through strategic hires of world-class researchers and emerging new investigators. The following are scientific highlights from these other core researchers.

HUMPHREY FONGE

Production, Processing and Evaluation of Pharmaceutical-Grade ^{225}Ac and ^{67}Cu for Cancer Theranostics

Dr. Fonge is a radiopharmacist at the Saskatoon Health Authority and Associate Professor of Medical Imaging at the USask College of Medicine, where he is active in nuclear medicine teaching and research. He has authored many scientific publications and has been principal investigator and/or co-investigator of research grants in excess of $9 million over the last seven years.

Dr. Fonge's research expertise lies in the area of precision diagnostics and therapeutics using different antibody and peptide platforms and radionuclides. Developments in molecular medicine are changing the approach to cancer diagnosis and treatment. Many cancers have been fully characterized by their underlying molecular and genomic aberrations rather than by clinical signs and symptoms. Nuclear medicine offers a powerful combination of diagnostic and therapeutic medicine, called theranostics. Engineered antibodies and peptides are integral to the development of theranostic agents. Identification of cancer cell-surface biomarkers and advances in antibody engineering have led to increases in the development of therapeutic antibodies and peptides. These same advances are leading to the development of a promising new generation of radiolabeled agents, making theranostics. one of the fastest growing classes of molecules in the biotech industry. In addition to providing specific diagnosis and therapeutic potential, these agents can be used to study target availability, drug occupancy, pharmacokinetics, pharmacodynamics, metabolism and dosing, thereby helping streamline the drug development process.

Dr. Fonge's project involves producing, processing and testing pharmaceutical grade ^{225}Ac and ^{67}Cu. ^{67}Cu (t1/2 2.58 days) offers pharmacokinetic and logistical advantage over ^{177}Lu as a beta-emitting theranostic isotope. It emits β- (beta) particles and γ (gamma) rays (93 keV, 35% and 185 keV 45%) making it suitable for radiotherapy and SPECT imaging. Successful pilot production of ^{67}Cu has occurred with Canadian Isotope Innovations Inc. and further improvements and automation of processing is ongoing. Quality control (QC) processes and preparation of pharmaceutical-grade ^{67}Cu will soon follow.

In vitro and in vivo studies of prostate-specific membrane antigens (PSMA) and other peptides synthesized in the lab using ^{67}Cu as a radionuclide will also be completed in the near future. If successful in pre-clinical studies, this work will be taken to clinical trials.

Dr. Fonge is also collaborating with Canadian Nuclear Labs (CNL) and TRIUMF to process pharmaceutical-grade ^{225}Ac. ^{225}Ac is an ideal isotope for radiotherapy of cancers and is up to 1000-fold more potent than beta-emitting therapeutic isotopes. Dr. Fonge's lab is developing ^{225}Ac-labeled therapeutics against many biomarkers/receptors overexpressed on cancer cells. These therapeutics are being evaluated in different solid tumors, including breast, colorectal, prostate, pancreatic, brain, ovarian, neuroendocrine tumors, and osteosarcoma. The availability of clinical-grade ^{225}Ac will facilitate the translation of these novel therapeutic agents in phase I clinical trials that will benefit Canadian cancer patients.

STEVE SICILIANO

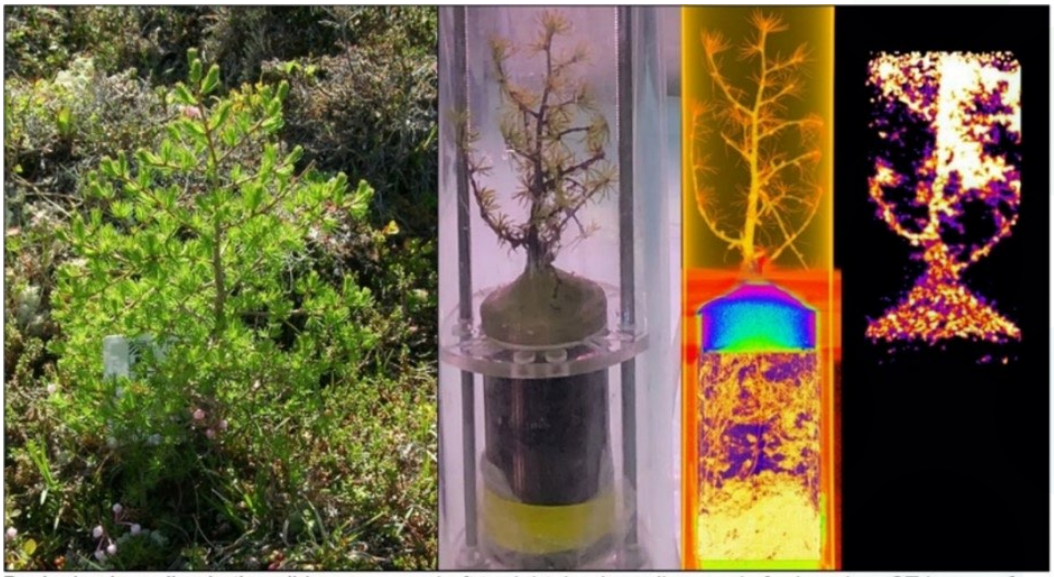
Understanding Biochemical Processes In Soils

Dr. Steven Siciliano is the NSERC/FCL Industrial Research Chair in In Situ Remediation and Risk Assessment, Director of CREATE Human and Ecological Risk Assessment Program, and professor in the Department of Soil Science at USask. His lab focuses on incidental soil ingestion and the soil nitrogen cycle to understand how human activities impact ecosystems and how these ecosystems impact human health. This work contributes to our understanding of the biochemical processes in soil sciences through insight into plant metabolisms and root uptake. It also allows scientists to comprehend the effects of climate change on the environment.

Global climate change due to rising greenhouse gas concentrations is projected to result in unprecedented increases in temperatures worldwide by the end of the 21st century, particularly in the Arctic, which makes up 40% of Canada's territory. This suggests Arctic ecosystems may be particularly vulnerable to future climate changes. Adding to this concern is the expected increase in permafrost thaw, converting previously frozen soil carbon to greenhouse gases, such as dioxide (CO_2) and methane (CH_4). This could lead to further warming through greater greenhouse gas emissions, increased permafrost thaw and release of greenhouse gases, effectively triggering a feedback loop. The extent to which these feedbacks may influence future climate scenarios in the Arctic remains unclear, as they are controlled by a delicate interplay of plant and microbial activities that modulate atmospheric carbon cycling in Arctic soils.

A major thrust of Dr. Siciliano's research program at the SCCS is to use radionuclide tracers combined with PET and radiographic imaging strategies to develop a novel perspective on the plant and microbial-driven biogeochemistry of carbon in Arctic soils. Traditional soil science approaches for probing these processes lack spatial definition and/or are destructive. Key spatial relationships between activity and soil biogeochemistry are, therefore, unattainable using established methodologies. Use of appropriate positron-emitting radionuclide labelled tracers, such as the $^{11}CO_2$ and $^{11}CH_4$ produced at the SCCS (and non-destructive imaging strategies allows for spatial visualization of carbon fluxes while maintaining soil structure. This in turn allows for a more informed analysis of soil processes in relation to the localized soil environments that foster them.

At the SCCS, Drs. Schmidt, Mamet and Siciliano are engaged in visualization of $^{11}CO_2$ fixation and distribution within a larch sapling from the Canadian Subarctic. Larch and other photosynthetically active plants fix atmospheric CO_2 in Arctic ecosystems, typically moving carbon into soils through root systems. Using PET and computerized x-ray tomography, they were able to visualize the uptake and distribution of $^{11}CO_2$ within the sapling. PET imaging showed that fixed $^{11}CO_2$ largely remained in aboveground plant tissues, with little observed in roots. Future work will focus on growing larch under different projected climate scenarios to visualize how CO_2 fixation may respond to a changing climate.

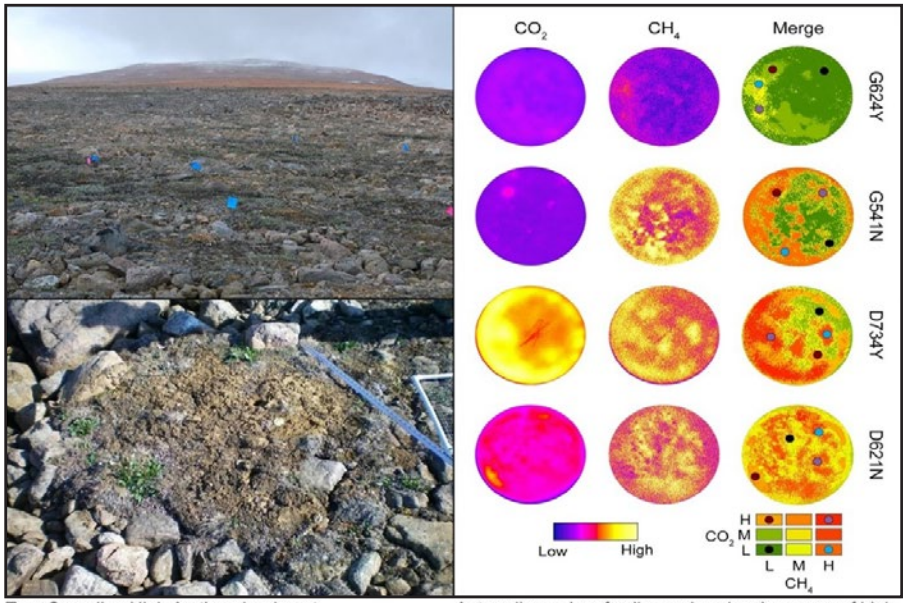


Bushy larch sapling in the wild

Left to right: larch sapling ready for imaging, CT image of larch morphology, PET image of fixed $^{11}CO_2$.

Figure 18 – Visualization of $^{11}CO_2$ fixation in larch sapling.

In a series of studies on the distribution of microorganisms that fix atmospheric CO_2 (autotrophic microorganisms) and CH_4 oxidation (methanotrophic microorganisms) in Arctic soils, Schmidt, Mamet and Siciliano demonstrated for the first time the utility of gaseous radiotracers to spatially define microbiological activity in soil with autoradiographic imaging. Results suggest that both CO_2 fixation and CH_4 oxidation are localized in discreet active areas across soil samples. Collaborative work is underway with the Canadian Light Source to relate biological CO_2 and CH_4 uptake with local soil chemical environments. Future work includes genomic analysis to identify and quantify the microorganisms present in active areas and better link carbon fluxes in Arctic soils with specific microbial groups.



Top: Canadian High Arctic polar desert.
Bottom: frost-churned soil.

Autoradiography of soil samples showing areas of high and low activity and their overlap between CO_2-fixing and CH_4-oxidizing communities.

Figure 19 -Use of gaseous radiotracers to spatially define microbiological activity in soil with autoradiographic imaging.

ERIC PRICE

Innovative Chemistry at the Forefront of Molecular Imaging and Targeted Radionuclide Therapy

A Canada Research Chair in Radiochemistry and an Assistant Professor in Chemistry, Dr. Price runs an interdisciplinary, collaborative research group. His lab performs synthetic organic and inorganic chemistry to produce new chemical tools as well as to enhance and improve existing tools. Projects funded by the Fedoruk Centre include the cyclotron production of radionuclides and the application of new chelators and linkers towards imaging pancreatic cancer.

New Chelators, Linkers and Vector Conjugates for Imaging and Treating Cancer: To generate radiopharmaceuticals, radiometals are attached to biological probes by using selective chelators that "grab" the radiometal ions and hold them tightly. Excellent chelators will prevent the release of the radiometal in the body, which would lead to "free" radiometal being taken up by healthy tissues, causing damage to healthy tissues and decreasing image quality. For example, the current gold standard ^{89}Zr-chelator, desferrioxamine (DFO), releases [^{89}Zr]Zr4+ in the body, which is substantially retained in bone. Dr. Price and his team are developing a new family of chelators that improve upon DFO and should allow other therapeutic radionuclides to be chelated.

Dr. Price and his team are also making new "linker" groups, which are essential short molecular "chains" that link a chelator to a peptide, antibody, nanoparticle or any other desirable molecular scaffold. The linkers being designed and studied in the Price lab are unique in that they are designed to imbue their attached drug with new functionality or properties such as fluorescence, retention in certain tumours, enzyme-cleavability, and reduction in healthy tissue uptake (e.g. lower kidney uptake).

With the help of SCCS facility manager Dale Schick-Martin and funding from the Fedoruk Centre, Dr. Price has been developing the complete workflow of cyclotron target production (electroplating), cyclotron irradiation, target dissolution and finally purification and characterization. This work includes 3D printing and custom fabrication of electroplating, dissolution and purification apparatus.

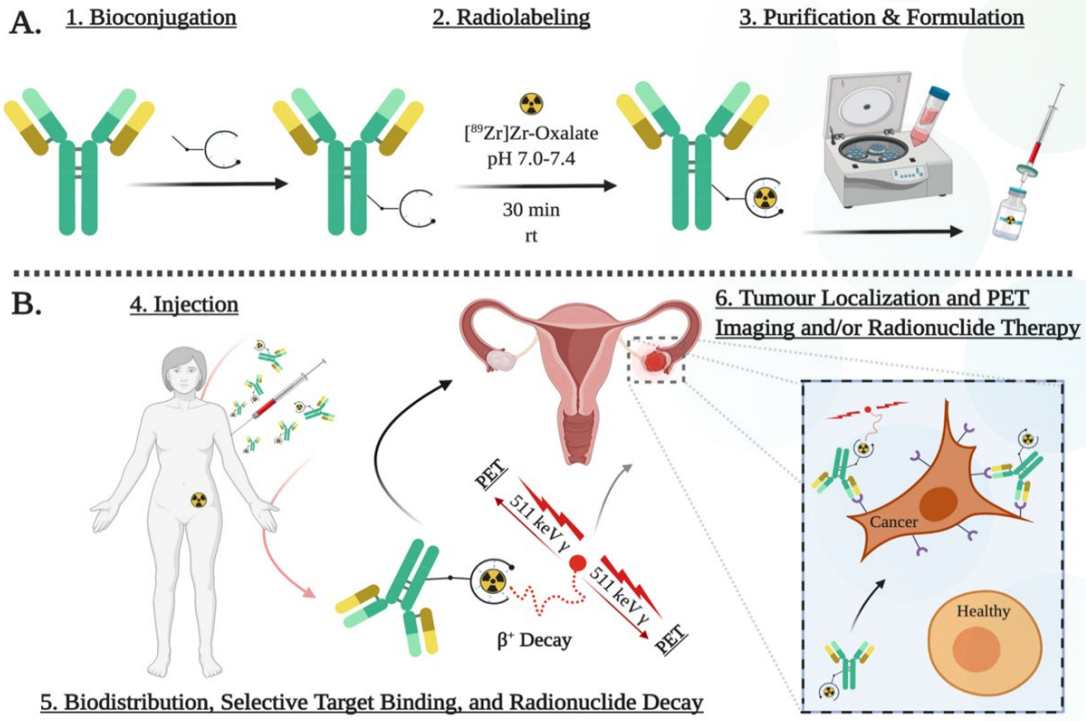
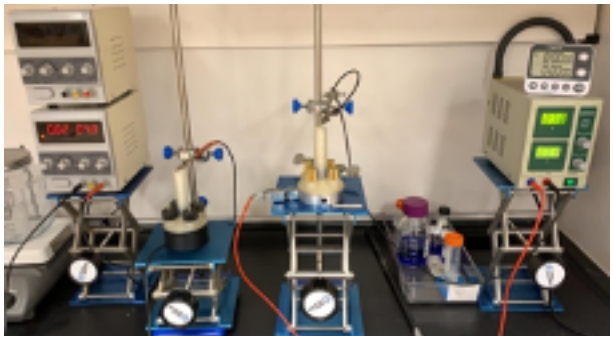


Figure 20 - Depiction of 1) antibody modification via bioconjugation of chelators or other reporter groups, 2) radiolabeling with a radionuclide for imaging or therapy, 3) purification and quality control, 4) injection in patients, 5) biological distribution and localization of radiolabeled antibody into target tissue (ovarian cancer depicted, e.g. AR20.5 MUC1-targeting antibody) and 6) PET imaging or radionuclide therapy (depending on which radionuclide is chelated, e.g. zirconium-89 for PET imaging, actinium-225 for therapy).

Scientific Highlights: A new set of DFO2-based chelators are being synthesized to improve the initial DFO2 work. A small library of 10 different DOTA-linker-TATE derivatives (NetSpot) is now available for gallium-68 radiolabeling and PET imaging studies. Saskatchewan's capability to produce clinically significant isotopes has been enhanced with the production of copper-64 and cobalt-55 isotopes. The development of a small targetry laboratory for design, 3D printing, fabrication and electroplating of primary materials used in isotope production establishes a new capability for radionuclide production in Saskatchewan. The new capacity developed by Dr. Price's lab creates highly qualified personnel and trainee resources specialized in radioisotope production, separation, and radiochemical synthesis.

Dr. Price and his team are also preparing to perform extensive zirconium-89 (^{89}Zr) experiments with a new generation of chelators.

As a result of the contributions made by Dr. Price and his team, the SCCS has integrated a new radioisotope (^{68}Ga) in the production cycle. The in-house production of ^{68}Ga (currently very expensive and not readily available) will be a cost-effective resource that will further support the development of new imaging agents in Saskatchewan.



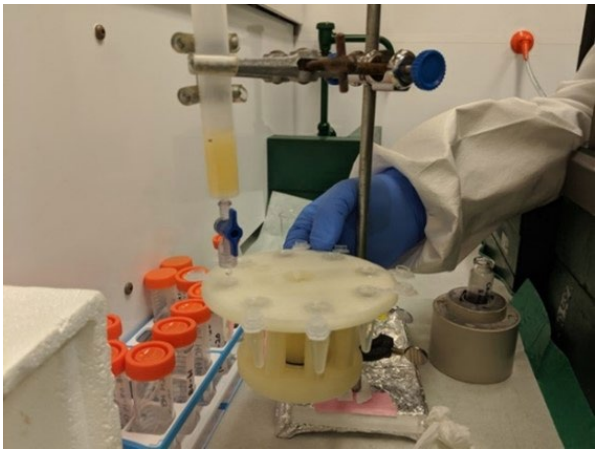


Figure 21 - (Top left) 3D printers in the Price lab used for designing and fabricating items for the production and purification of radionuclides. (Top right) Custom 3D-printed electroplating cells being used to plate high-purity (99.99%) natural nickel onto pure silver disks. (Bottom) Dissolution and purification of a mixture of copper-61/64 and cobalt-55 produced at the SCCS from custom Price-lab targets and house-made apparatus, including a 3D-printed fraction collector (which is now fully hands-free).

Collaborators: The Price lab has a diverse network of collaborators—local, national and international. Dr Price and his team are currently collaborating with Dr. Phenix (Chemistry, USask); Dr. Michael Moser (Surgeon, RUH, NanoKnife); Drs. Graham George and Ingrid Pickering (Geological Sciences, USask, chelator spectroscopy and computations); Dr. Siciliano (Soil Sciences, USask); Dr. Greg Adams (Veterinary Medicine, USask, Llama imaging); Dr. Behzad Toosi (Veterinary Medicine, USask, pancreatic cancer imaging); Dr. Steven Machtaler (Medical Imaging, USask, microbubble imaging); Dr. Andrew Freywald (Medicine, USask, antibody PET imaging); Dr. Franco Vizeacoumar (Saskatchewan Cancer Agency, antibody imaging); Dr. Fonge (Medicine, USask and Saskatchewan Health Region, antibody imaging and radionuclide therapy); Dr. Valery Radchenko (TRIUMF, radiochemistry); Dr. Jon Engle (University of Wisconsin-Maddison, radionuclide production); Dr. Brian M. Zeglis (Hunter College, NYC, antibody conjugation and imaging); Dr. David Palmer (Chemistry, USask) and Dr. Jason S. Lewis (Memorial Sloan Kettering Cancer Center, NYC, radiochemistry).

CHRIS PHENIX

New Chemical Tools to Study Biological Processes in Plants, Animals and Humans

Dr. Chris Phenix, an Assistant Professor in the Department of Chemistry at USask, joined the group of core researchers in Nuclear Imaging Program 2016. Since then, he has contributed to the establishment of radiochemical sciences at USask. The main focus of the Phenix lab is to develop molecular imaging probes and radiotracers for imaging enzymatic and other biological processes.

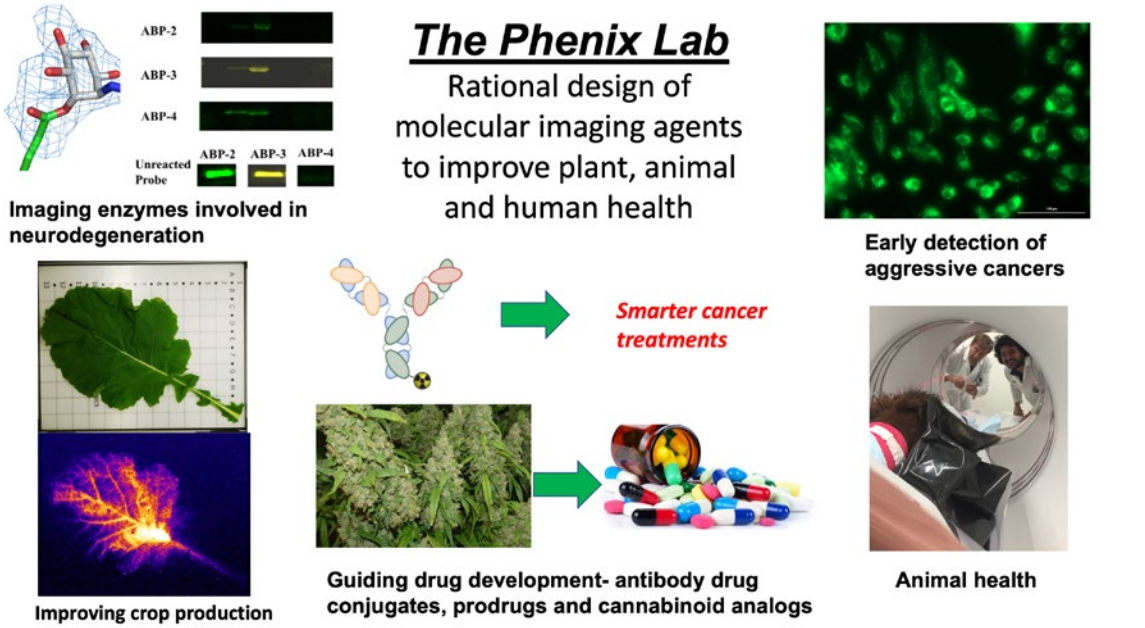


Figure 22 – Summary of research underway in the Phenix lab.

Dr. Phenix's research can be broken down into three major categories. The first is focused on inhibitors, fluorescent activity-based probes and PET radiotracers for beta-Glucocerebrosidase, an important enzyme in human health. Beta-Glucocerebrosidase (GCase) is an enzyme responsible for degrading glycolipid molecules in many human cell types, most notably neurons in the brain, immune cells and liver.

Interestingly, GCase activity drops substantially in Gaucher Disease and Parkinson's disease. The exact role that GCase has in Parkinson's disease progression is an area of intense scientific and pharmaceutical interest. As a result, new chemical tools to evaluate GCase activity in cells, animals and humans are urgently needed.

The Phenix lab has developed new chemical tools to help understand the role of GCase in Parkinson's disease progression as well as assist scientists in developing GCase-enhancing therapies for Parkinson's disease. To date, Dr. Phenix and his team have created new chemical scaffolds to generate fluorescent-activity-based probes capable of imaging GCase activity in cells, cell homogenates, tissues and animals. These probes may be useful in a blood test to help identify patients who have Parkinson's disease and would be good candidates for GCase enhancing therapies. At the SCCS, Dr. Phenix and his team have also developed promising lead compounds that for the first time are capable of sensitively imaging GCase activity in brain tissue sections. These novel chemical tools are currently being validated in cells and animals and sent to collaborators investigating the role of GCase in Parkinson's disease.

The second area of research focuses on fluorescent probes and PET radiotracers for Cathepsin B (CTB). Metastasis is a biological process where aggressive cancer spreads from the initial tumour to distant sites. Approximately 90% of cancer deaths result from these metastatic tumours. CTB is a protease enzyme that digests proteins as a natural part of human metabolism. In aggressive cancers, a high amount of CTB is found in tumours and is released into the tumour environment. Once outside the tumour, CTB helps digests proteins in the local tissue, producing a permissive space for cancer cells to invade; the first step in metastasis.

Dr. Phenix and his team have developed probes capable of revealing CTB activity in living cancer cells. The probes are currently being used to study the enzyme's role in metastasis and prodrug therapy.

Given the promising results of these fluorescent probes, Dr. Phenix and his team are currently developing ^{18}F-labeled versions to image aggressive cancers in animal models of disease using PET. Such tracers could be useful in assessing the aggressiveness of tumours and in helping guide therapeutic decision making. Since many new anti-cancer treatments are antibody drug conjugates that rely on CTB to release the drug at the tumour site, a PET method capable of detecting CTB could be useful for predicting patient response to the antibody-drug conjugate.

Dr. Phenix's third area of research focuses on using PET methods to understand abscisic acid trafficking in plants, which could help design drought-resistant crops.

Abscisic acid (ABA) is a plant hormone that signal plants to preserve water in response to drought. It also plays a prominent role in response to microbial diseases attacking plants. However, a plant's ability to release ABA and transport the hormone to various tissues is poorly understood. Dr. Phenix and his team have prepared an ^{18}F-labeled version of ABA to monitor its transport in living plants in order to better understand how crops can resist drought conditions. Studies are currently underway to assess ABA transport in various breeds of canola.

Interestingly, ABA is a signalling molecule in the human immune system and glucose regulation. Further investigation regarding the use of ^{18}F-labeled ABA to detect immune response to cancers and as a tracer to image the biological processes in diabetes are being planned.

RON GEYER

Developing Innovative Cancer Imaging Probes to Transform Cancer Detection

Dr. Geyer is Director of the Centre for Biologic Imaging Research and Development in the Department of Pathology and Laboratory Medicine at and the Nutrien Chair in Clinical Research at USask College of Medicine. His research is focused on developing innovative cancer imaging probes, including novel antibody-based imaging probes for clinical applications in nuclear imaging, surgery and immunotherapy.

Support from the Nutrien Chair is enabling Dr. Geyer's research team to develop a PET imaging probe for diagnosing and monitoring cancers, an optical imaging probe to assist surgeons in resecting tumors, and engineered immune cells to eradicate cancer cells. He is currently undertaking clinical trials to validate a PET imaging probe for detecting lung and colorectal cancers and a fluorescent imaging probe to assist surgeons in resecting lung cancer tumors. His team is also working on a novel strategy to target cells to specific cancers and improve patient outcomes.

Dr. Geyer and his team are also working on the development of a molecular imaging probe that detects responses to anti-cancer therapies by determining if the induction of necrotic death can be imaged. Tumor necrosis is a type of cell death characterized by the swelling and rupturing of mitochondria and lysosomes followed by the disruption of the cell membrane. Tumor necrosis has been shown to be an important prognostic factor for cancer staging and treatment efficacy evaluation in patients.

Imaging the degree of tumor necrosis has the potential to impact cancer patient treatment and management. Dr. Geyer and his team are assessing ^{18}F-labeled GLA (^{18}F-FGA) as a more sensitive PET probe to monitor treatment efficacy by measuring different degree of necrosis in lung cancer-bearing mice induced by chemotherapy drug.

Dr. Geyer's research in the Centre for Biologic Imaging and Research and Development (C-BIRD), where he is pursuing the development of the next generation of targeted molecular imaging agents for cancer treatment, bridges research at the SCCS) with pathologists at the USask-led Advanced Diagnostic Research Laboratory, oncologists at the Saskatchewan Cancer Agency, and surgeons at the Saskatchewan Health Authority. Dr. Geyer's research is at the forefront of the burgeoning field of precision medicine, where therapies and monitoring strategies are customized to individual patient's cancer.

ENDNOTES

1 The Saskatchewan Program for Nuclear Imaging (SPNI) - Proposal – The Application of Nuclear Imaging to Life Sciences in Human, Animals, and Plants
Submitted by: Paul Babyn, Beth Horsburgh, Karen Chad, Mark de Jong, Emil Lloyd Hallin, David Palmer, Zisis Papandreou, Chary Rangacharyulu, Ildiko Badea, Humphrey Fonge, Ron Geyer, Ed Krol, Baljit Singh, John Stavrinides, Kishor Wasan, Sue Abrams, Sina Adl, Paul Arnison, Christopher Yost.
Submitted to: Fedoruk Centre on September 2, 2014

2 Development of a Novel High-quantum-efficiency MV x-ray Detector for Image-guided Radiotherapy: A Feasibility Study
Liu J, Teymurazyan A, Papandreou Z, Xu Y, Pang G.
Medical Physics 47(1) (2020)
https://doi.org/10.1002/mp.13900

3 Sask. home to new phytoPET device for monitoring crops, plants
Albert Couillard/Radio-Canada
CBC News
Posted: Jun 12, 2017 2:16 PM CT | Last Updated: June 12, 2017
https://www.cbc.ca/news/canada/saskatoon/phytopet-imaging-plant-scienceuniversity saskatchewan-1.4157264

4 University of Saskatchewan tests Canada's First PhytoPET Imaging System
Julie Mintenko & Thomas Piller, Global News
Posted June 13, 2017 8:51 am | Updated June 13, 2017 8:52 am
https://globalnews.ca/news/3522527/phytopet-imaging-system-fedoruk-centreuniversity saskatchewan-crop/

5 Characterization of low-dose ozone-induced murine acute lung injury
Gurpreet Kaur Aulakh, Jessica Andrea Brocos Duda, Claudia Marcela Guerrero Soler, Elisabeth Snead, Jaswant Singh
Physiological Reports 8: e14463 (2020)
https://doi.org/10.1021/acs.bioconjchem.0c00087

6 Quantification of Regional Murine Ozone-Induced Lung Inflammation Using [18F]FDG MicroPET/CT Imaging Gurpreet Kaur Aulakh, Manpreet Kaur, Vanessa Brown, Samantha Ekanayake, Behlol Khan, Humphrey Fonge
Research Square - May 6, 2020
https://www.researchsquare.com/article/rs-24914/v1
DOI: 10.21203/rs.3.rs-24914/v1

7 Quantification of regional murine ozone-induced lung inflammation using [18F]F-FDG microPET/CT imaging
Gurpreet Kaur Aulakh, Manpreet Kaur, Vanessa Brown, Samantha Ekanayake, Behlol Khan, Humphrey Fonge
National Library of Medicine, National Centre for Biotechnology Information - Sept. 24, 2020
https://pubmed.ncbi.nlm.nih.gov/32973318/
DOI 10.6084/m9.figshare.12233576

8 Lack of CD34 produces defects in platelets, microparticles, and lung inflammation
Gurpreet Kaur Aulakh
National Library of Medicine, National Centre for Biotechnology Information - July 22, 2020
https://pubmed.ncbi.nlm.nih.gov/32700121/ DOI: 10.1007/s00441-020-03243-4

SASKATCHEWAN'S NUCLEAR IMAGING PROGRAM

Fedoruk Centre
SYLVIA FEDORUK CANADIAN CENTRE FOR NUCLEAR INNOVATION

303-111 RESEARCH DRIVE, SASKATOON SK S7N 3R2
www.fedorukcentre.ca