Letter from the Program Director

Dear Colleagues,

Welcome to the Summer 2022 edition of the PET-RTRC newsletter. The PET-RTRC Workshops and Scientific Session held in January were highly successful despite the pandemic forcing a change to a fully virtual format from the originally planned hybrid format. The Workshop focused on preclinical and clinical imaging, while the Scientific Session had outstanding plenary lectures from Dr. Frank Bengel, who spoke on “Molecular imaging guided repair of the heart” and Dr. Charles Manning, who discussed “Targeting cancer metabolism for molecular imaging and therapy”. The sessions attracted more than 220 registered attendees from fifteen countries and six continents. Post workshop survey indicated that more than 95% of the attendees felt that the workshop met their objectives. This past month, in conjunction with the World Molecular Imaging Society, Dr. Georges El Fakhri gave a webinar entitled “In vivo quantitative mapping of cardiac membrane potential”. In addition, we were a sponsor for the annual Dan Biello lecture given by Dr. Umar Mahmood. His talk, entitled “Precision imaging to guide targeted cancer therapy”, was in a hybrid format and well-received by all. This summer, we are back to attending conferences in person with our booths at both iSRS in Nantes, France, and at SNMMI in Vancouver, BC. Come see us at Booth 406 at WMIC in Miami, Florida this September!

In this issue, the Spotlight section focuses on the exciting work of Dr. Robyn Klein, MD, PhD, and Co-Leader of TR&D 1. This project investigates the use of radiotracers targeting inflammatory StP receptors in the context of multiple sclerosis and other inflammatory diseases and has been successful in the clinical translation of these radiotracers. Please visit our website to learn more about the PET-RTRC and our upcoming activities. Our 2023 Workshop and Scientific Session are set for February. Be on the lookout for registration information this fall. To stay up to date with our most recent developments or to be added to our mailing list, please contact Michelle Hoelscher at michellehoelscher@wustl.edu

Best Regards,

Robert J Gropler, MD
PET-RTRC Program Director
Spotlight

The NIBIB funded P41 PET-RTRC program at WUSTL and MIR aims to develop new PET radiotracers to deliver accurate diagnosis and personalized treatment of human disease. During the current funding cycle, the PET-RTRC programmatic mission is focused upon developing PET radiotracers for imaging inflammation. Among the three Translational Research and Development (TR&D) projects, TR&D 1 (Led by Dr. Zhude (Will) Tu, Professor of Radiology and Co-leader Dr. Robyn Klein, Professor of Medicine, Pathology & Immunology, and Neurosciences) has been working on the development and evaluation of imaging agents targeting S1PR receptors, which are of clinical significance in Multiple Sclerosis (MS) and cancer.

Our collaborative project is focused on the use of PET radioligands to measure sphingosine phosphate-1 (S1P) receptor 2 (S1PR2) levels in the brains of patients with MS to identify patients that may benefit from treatment with S1PR2 antagonists. MS is a chronic autoimmune disease of the central nervous system (CNS) that displays a strong sex bias with a prevalence of 3:1 in females: males. Most patients present with relapsing-remitting MS (RRMS), and later progress to secondary progressive MS (SPMS), with fewer remissions and increasing clinical deterioration.

The sphingosine–1 phosphate receptor (S1PR) is a family of G-protein coupled receptors involved in many immunologic processes, particularly in innate immune cell function, immune cell trafficking, and germinal center niche confinement. There are five members of the receptor family, S1PR1-5, that share a common ligand, sphingosine-1 phosphate (S1P). S1PR2 is expressed by brain endothelial cells and has been shown to modulate microglial activation. In published studies, we demonstrated that vessel associated expression of S1PR2 was significantly increased in the hindbrains of MS patients compared to non-MS patients, with female MS patients exhibiting higher S1PR2 protein levels compared to males. This sexually dimorphic expression pattern also occurs in SJL animals, which display a relapsing-remitting phenotype during EAE; female SJLs display increased S1PR2 expression at baseline and during EAE compared to males. S1PR2 antagonism improves EAE disease course in SJL animals by reducing relapse severity, diminishing numbers of white matter lesions, and preserving axonal integrity. In collaboration with Dr. Zhude (Will) Tu, we demonstrated that PET radioligands of S1PR2 detect sexually dimorphic expression within the hindbrains of SJL mice. In ongoing studies, we are working to improve the blood-brain barrier penetrance of these ligands and use them to define the central nervous system (CNS) regions where S1PR2 is upregulated in Swiss Jim Lambert (SJL) mice, including non-parenchymal CNS compartments such as the meninges.

![Autoradiography and PET/CT images](image)

Autoradiography and PET/CT images (A) and quantification of cerebellar uptake (B) of $^{[11}C\)5a in the brains of female and male SJL mice (n=5) upon CsA pre-treatment.
Collaborative Projects

**GERMANY**
Hannover Medical School
The Inflammatory-Fibrosis Axis in Adverse LV Remodeling: Translating Mechanisms into New Diagnostics and Therapeutics (Immu-NoFib HF)

**IOWA**
The University of Iowa
CCR2 Imaging in Cystic Fibrosis

**MASSACHUSETTS**
Massachusetts General Hospital
PET Imaging of Sphingosine 1-Phosphate Receptor 1 (SIP1) in Liver Fibrosis

**MISSOURI**
Washington University School of Medicine
Lymphatic Remodeling and Transport of Dietary Fats in Short Gut Syndrome

**NEW YORK**
Memorial Sloan Kettering Cancer Center
Annotating Cancer Biology Through Non-Invasive Molecular Imaging

**OREGON**
Oregon Health & Science University
Molecular Imaging of Platelets and Oxidative Stress in Atherosclerosis

**CALIFORNIA**
University of Southern California
Development of an in vivo Cell Proliferation Marker for PET Assessment of Chemotherapeutic Response in Cancer

University of California San Francisco
Study of MS

**CONNECTICUT**
Yale University
Multimodal Neuroimaging of Alcohol Withdrawal: the Role of Glutamate in Neural Reorganization

**MISSOURI**
Washington University School of Medicine
Multimodality Imaging and Molecular Targeting of Tolerogenic Macrophages and Dendritic Cells in Lung and Heart Allografts

**NETHERLANDS**
Eindhoven University of Technology
Translational Imaging and Nanomedicine in Inflammatory Atherosclerosis

**NORTH CAROLINA**
University of North Carolina at Chapel Hill
Novel Catalytic Methods for Efficient Radiolabeling of Unactivated Arene Compounds

**PENNSYLVANIA**
University of Pennsylvania
PENN PET Addiction Center of Excellence (PENN PACE)

**TEXAS**
The University of Texas Southwestern Medical Center
Imaging of Liver Cancer

Interested in becoming a member of the Center?

Please fill out the Collaborative Project or Service Project application and send to michellehoelscher@wustl.edu
The Inaugural Sally W. Schwarz Award

T&D Co-Investigator, Sally Schwarz, was recognized by SNMMI for her outstanding contributions to the field of radiopharmacy with a namesake award. The first recipient was Neil A. Petry, director of the Duke Medical Center Radiopharmacy.

Seminar Speaker Georges El Fakhri, PhD
Harvard Medical School | August 12, 2022

Dr. El Fakhri presented virtually “In vivo quantitative mapping of cardiac membrane potential.”
## Publications

**TR&D 1:**


**TR&D 2:**


TR&D 3:


QI2R:
Upcoming Events

SAVE THE DATE | **February 21-23, 2023**

**PET-RTRC Annual Workshop | Scientific Session**

More information and registration link to come on our [website](#).

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**Look for Us**

PET-RTRC BOOTH 406 @ **WMIC Sept 28-Oct 1, 2022** | Miami, Florida, USA
Leadership

Executive Committee Members
Robert Gropler, MD | Chair, Program Director, TR&D 2 Co-Leader
Will Tu, PhD | TR&D 1 Leader, Training & Dissemination Co-Leader-Training
Yongjian Liu, PhD | TR&D 2 Leader
Vijay Sharma, PhD | TR&D 3 Leader
Kooresh Shoghi, PhD | TR&D 3 Co-Leader, QI2R Co-Leader
Dan Marcus, PhD | QI2R Co-Leader
Sally Schwarz, RPh, MS, BCNP | Training & Dissemination Co-Investigator
Buck Rogers, PhD | Training & Dissemination Project Leader
Richard Laforest, PhD | QI2R Co-Investigator
Farrokh Dehdashti, MD | TR&D 2 Co-Investigator
Michael Nickels, PhD | Training & Dissemination Co-Leader-Dissemination
Michelle Hoelscher, CNMT | Program Manager

How to find us...
mir.wustl.edu/pet-rtrc

#PETRTRC

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