PET-RTRC

The latest news from the PET Radiotracer Translation and Resource Center

Washington University in St. Louis
School of Medicine

Fall/Winter 2023

A Look Inside

Letter from the Program Director

Dear Colleagues,

Welcome to the Fall/Winter 2023 edition of the PET-RTRC newsletter. First and foremost, the Center was renewed for an additional five years starting this past September! After a rigorous Site Visit review in April and followup with the NIBIB program office it was determined that the Center was a valued national resource that should be continued into the next cycle. We would like to thank everyone involved in the Center, including the Collaborative Projects, Service Projects, and External Advisory and Tracer Review Committees. The Center is such a valuable resource due to everyone's involvement.

Over the summer, we had booths at SNMMI in Chicago and WMIC in Prague. Thanks to everyone who stopped by to learn more about the Center. In addition, a P41 Symposium was held at the WMIC meeting in Prague. This symposium was well attended and presentations were given by Dr. Tatjana Atanasijevic of NIBIB who described the P41 funding mechanism as well as by Drs. El Fakhri (MGH), Pomper (Johns Hopkins), and Gropler who discussed the resources and science around their P41 Centers. Dr. Zahi Fayad from the Icahn School of Medicine gave an outstanding seminar in October entitled "Whole Person Care: Toward Data Driven Medicine". In December, the PET-RTRC will co-sponsor the Michael Welch lecture given by Dr. Robert Mach from UPenn.

In this issue, the Spotlight section focuses on the exciting work of Zhude (Will) Tu, PhD, PI of TR&D 1. This project investigates the development and evaulation of imaging agents targeting S1PR receptors, which are of clinical significane in Multiple Sclerosis and cancer. Our 2024 Workshops and Scientific Session are set for February 20-22. Registration is now open. The Workshops will focus on Imaging of Immunotherapy, Neuroimaging, and FDA regulatory updates. The Scientific Session will feature Kory Lavine, MD, PhD and Steven Brody, MD. These sessions will be conducted in a hybrid manner and those that can attend in person can tour our facilities on the morning of February 22.

Please visit our website to learn more about the PET-RTRC and our upcoming activities. 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

The PET-RTRC is the U.S. innovation hub for the development of novel PET radiotracers. Leading the way for a nationwide network of collaborators, the center seeks to expand the understanding of diseases and advance the mission of precision imaging.

MIR Mallinckrodt Institute of Radiology

NIH National Institute of Biomedical Imaging and Bioengineering

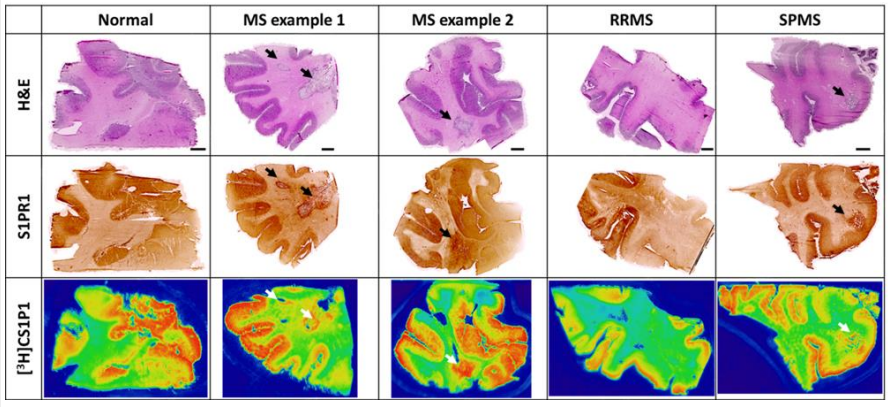
The PET-RTRC is supported by the NIH NIBIB Grant # P41 EB025815

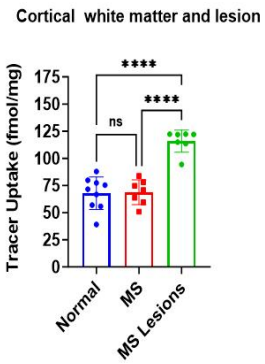
Spotlight

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.

As one of the three TR&D projects in the previous P41 cycle, we successfully developed, validated, and transferred a C-11 labeled sphingosine phosphate-1 receptor 1 (S1PR1) radiotracer into clinical imaging for neurological diseases such as multiple sclerosis (MS), AD/PD, cerebrovascular cognitive dementia, schizophrenia, and other diseases. Our proof of mechanism study in MS demonstrated that S1PR1 could serve as a biomarker for neuroinflammation in MS, thus PET with a S1PR1 radiotracer can quantitively assess the status of neuroinflammation in the brain. Our autoradiography study and immunohistochemistry analysis showed that MS white matter lesion regions have 1.7-fold high S1PR1 expression compared to MS white matter non-lesion regions and normal brain white matter. We are now in the process of transferring an F-18 labeled S1PR1 specific radiotracer to clinical use. This F-18 radiotracer will facilitate multiple clinical trials to explore S1PR1 PET in neurological diseases and in other peripheral system disorders.

In addition, we are also developing S1PR2 radiotracers for MS and bladder cancer. PET with a S1PR2-specific radiotracer will help identify MS or bladder cancer patients that may benefit from treatment with S1PR2 antagonists, or with S1PR2-targeted radiotherapies. Both S1PR1 and S1PR2 belong to a five members family (S1PR1-5) that are G-protein coupled receptors. They play critical roles in the central nervous system, immune system, metabolite system, diabetes, and cancers. S1PR2 is particularly involved in innate immune cell function, immune cell trafficking, and germinal center niche confinement. S1PR2 is expressed by brain endothelial cells and has been shown to modulate microglial activation. In published studies, we reported the synthesis of > 60 new molecules as candidate S1PR2 ligands including some that have high potency and high selectivity for S1PR2. We are evaluating the lead candidates in animal model of diseases to identify the most promising S1PR2 radiotracer for translational clinical investigation.





In the white matter, the uptake of [^{3}H]CS1P1 in MS lesions was ~1.7-fold versus the normal non-lesion MS brain.

ACS Chem Neurosci. 2023 Nov 15;14(22):4039-4050.

Collaborative Projects

ALABAMA

University of Alabama at Birmingham
Cancer Inflammation

ARIZONA

BNI Phoenix
Multiple Sclerosis

CALIFORNIA

Stanford University
Multiple Sclerosis
Pancreatic Cancer

CONNECTICUT

Yale University
Abdominal Aortic Aneurysm
Acute Respiratory Distress Syndrome

GEORGIA

Emory University
Bacterial Infection

LOUISIANA

Louisiana State University
Ischemic Vascular Remodeling

MISSOURI

Washington University School of Medicine
Abdominal Aortic Aneurysm
Cardiac Inflammation
Neuroinflammation
Neuroinflammation in Nigrostriatal Injury

NEW YORK

Memorial Sloan Kettering Cancer Center
Cancer Biology

NORTH CAROLINA

University of North Carolina at Chapel Hill
Bladder Cancer

Service Projects

CALIFORNIA

University of California San Diego
Metastatic Cancer

University of Southern California
Myeloma Bone Disease

CONNECTICUT

Yale University
Mitochondrial Diseases
Neuroinflammation

MISSOURI

Saint Louis University
Cardiac Inflammation

Washington University School of Medicine
Multiple Sclerosis
Osteoarthritis
Pulmonary Fibrosis

NEW YORK

Icahn School of Medicine at Mount Sinai
Myocardial Infarction

PENNSYLVANIA

University of Pittsburgh Medical Center
Atherosclerosis

TEXAS

University of Texas Southwestern
Kidney Injury

UTAH

University of Utah
Atherosclerosis

WASHINGTON DC

Howard University
Traumatic Brain Injury

GERMANY

Hannover University
Cardiac Inflammation and Fibrosis

Interested in becoming a member of the Center?

Please fill out the Collaborative Project or Service Project application and send to michellehoelscher@wustl.edu

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P-41 Symposium @ WMIC | September 9, 2023

Robert Gropler, MD | Georges El Fakhri, PhD | Martin Pomper, MD, PhD | Tatjana Atanasijevic, PhD

The Directors of the 3 Centers that comprise the faction of Molecular Imaging Technology P-41 Centers were invited to speak along with NCBIB P41 Scientific Program Manager, Dr. Tatjana Atanasijevic, at WMIC in Prague, Czech Republic in September.

Seminar Speaker | October 10, 2023

Zahi Fayad, PhD- Icahn School of Medicine at Mount Sinai

In October, we welcomed Dr. Zahi Fayad from the Icahn School of Medicine at Mount Sinai to give a Seminar titled "*Whole Person Care: Toward Data Driven Medicine*". This lecture was offered both in person and via Zoom.


WMIC 2023
WMIC2023
Prague, Czech Republic
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Washington University in St. Louis
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PET Radiotracers
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Publications

TR&D 1:

Luo Z, Han J, Liu H, Rosenberg AJ, Chen DL, Gropler RJ, Perlmutter JS, Tu Z. *Syntheses and in vitro biological evaluation of S1PR1 ligands and PET studies of four F- 18 labeled radiotracers in the brain of nonhuman primates*. Organic & biomolecular chemistry. 2018 December 5;16(47):9171-9184. PubMed PMID: 30462126

Luo Z, Liu H, Klein RS, Tu Z. *Design, synthesis, and in vitro bioactivity evaluation of fluorine-containing analogues for sphingosine-1-phosphate 2 receptor*. Bioorganic & medicinal chemistry. 2019 August 15;27(16):3619-3631. PubMed PMID: 31279524

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Qiu L, Jiang H, Yu Y, Gu J, Wang J, Zhao H, Huang T, Gropler RJ, Klein RS, Perlmutter JS, Tu Z. *Radiosynthesis and evaluation of a fluorine-18 radiotracer ^{18}F-FS1P1 for imaging sphingosine-1-phosphate receptor 1*. Org Biomol Chem. 2022 Feb; 20(5): 1041-1052. PubMed PMID: 35029272

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TR&D 2:

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TR&D 3:

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QI2R:

Zou W, Rohatgi N, Brestoff JR, Moley JR, Li Y, Williams JW, Alippe Y, Pan H, Pietka TA, Mbalaviele G, Newberry EP, Davidson NO, Dey A, Shoghi KI, Head RD, Wickline SA, Randolph GJ, Abumrad NA, Teitelbaum SL. *Myeloid-specific Asxl2 deletion limits diet-induced obesity by regulating energy expenditure*. J Clin Invest. 2020 May1;130(5):2644-2656. PubMed PMID: 32310225

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Upcoming Events

REGISTRATION OPEN | February 20-22, 2024

PET-RTRC Annual Workshop | Scientific Session

More information and registration link on our website.

Look for Us

PET-RTRC BOOTH #206 @ **SNMMI June 8-11, 2024** | Toronto, Canada

The PET-RTRC is supported by the NIH NIBIB Grant # P41 EB025815

Leadership

Executive Committee Members

Robert Gropler, MD | Chair, Program Director, TR&D 2 Co-Leader

Will Tu, PhD | TR&D 1 Leader

Yongjian Liu, PhD | TR&D 2 Leader

Vijay Sharma, PhD | TR&D 3 Leader

Buck Rogers, PhD | Training & Dissemination Project Leader

Michael Nickels, PhD | Training & Dissemination Co-Leader-Dissemination

Richard Laforest, PhD | QI2R Leader

Andrew Gelman, PhD | TR&D 3 Co- Leader

Robyn Klein, MD, PhD | TR&D 1 Co- Leader

Michelle Hoelscher, CNMT | Program Manager

How to find us...

mir.wustl.edu/pet-rtrc

#PETRTRC

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Richard Carson, PhD | Yale University

Peter Caravan, PhD | Harvard University

David Mankoff, MD, PhD | University of Pennsylvania

Sruti Shiva, PhD | University of Pittsburgh

Tracer Review Committee

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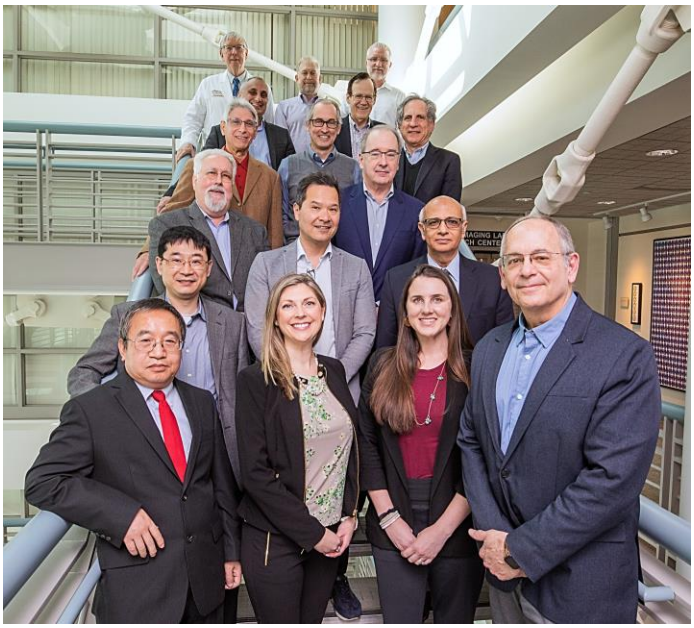
Steven Liang, PhD | Emory University

Julie Sutcliffe, PhD | University of California-Davis

Richard L Wahl, MD | Washington University



For more information about the PET-RTRC contact:

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