

PMedIC Fall 2021 Newsletter

PMedIC by the Numbers



PMedIC:

AN OHSU/PNNL COLLABORATION

PMedIC was launched in 2018, this partnership between Oregon Health and Science University (OHSU) and Pacific Northwest National Lab (PNNL) offers collaborative research and educational experiences for staff, faculty, clinicians, and students at the campuses of both institutions.

Vision:

Improve human health and disease treatment through collaborations that integrate cutting-edge research and education with clinical practice.

Mission:

Generate, interpret, and integrate multi-dimensional panomics data, imaging and clinical results to gain mechanistic understanding of disease and develop innovative therapies.

2020 Collaboration Highlights

Mechanistic Studies of AAP and Capsid Assembly of AAV Vector

By comprehensively studying interactions between assembly-activating protein (AAP), viral capsid protein and host cell proteins, we seek to elucidate mechanism of virion assembly of adeno-associated virus (AAV) vectors in much greater depth, and explore novel strategies that can potentially improve AAV vector production.



Hiroyuki Nakai & Ljiljana Pasa-Tolic
(OHSU) (PNNL)



Jon Jacobs & Holly Hinson
(PNNL) (OHSU)



Predictors of Low-Risk Phenotypes after Traumatic Brain Injury (TBI) Incorporating Proteomic Biomarker Signatures

We propose to develop and assess a series of models incorporating proteomic signatures to classify: acute progressive intracranial hemorrhage, acute neurologic deterioration, and long-term outcomes measured by the 6-month Glasgow Outcome Scale. The project employs highly-sensitive methods to detect immunoregulatory proteins complemented with an unbiased proteomic approach utilizing global discovery mass spectrometry.

Evaluating the role of L,D-Transpeptidases in Mycobacterial Pathogenesis

We propose to develop new molecular probes to identify and validate β -lactam drug susceptibility in mycobacteria. Our approach facilitates monitoring multiple penicillin-binding proteins and L,D-transpeptidases at once, enabling a comprehensive examination of these enzymes. We will detect enzymes in protein gel-resolved lysates using activity-based probes derived from major classes of β -lactam drugs.



Kimberly Beatty & Aaron Wright
(OHSU) (PNNL)



Defining Mechanisms of Viral Persistence in situ at the Single-cell Level

Comprehensive Characterization of Tissue Reservoirs

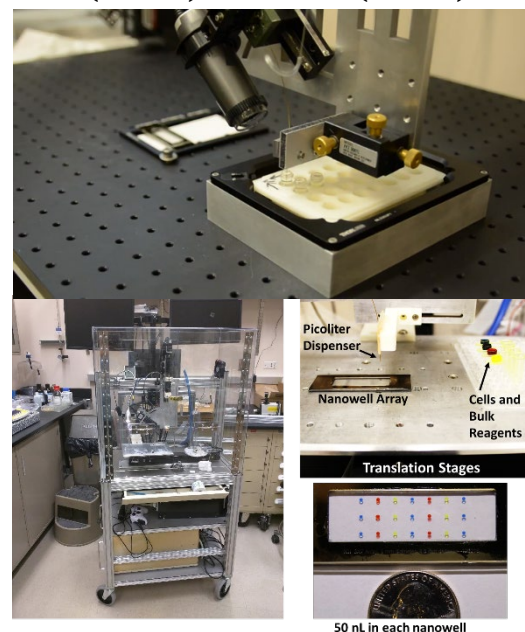
The major obstacle to eradicating HIV is the persistence of cellular viral reservoirs (VR) harboring replication competent viral genomes that have the capacity to produce infectious virus when anti-retroviral therapy (ART) is stopped. Using novel next-generation in situ hybridization platforms (RNAscope, DNAscope and BASEscope) to quantify and generate latent & active VR atlases longitudinally during ART, in-depth phenotypic analysis of VR using multiplexed ion beam imaging (MIBI) proteomic analysis as well as unbiased SNaPP and **nanodroplet** processing in **one-pot** for **trace** samples (nanoPOTs) mass spectrometry approaches for spatiotemporal molecular analyses will help us to identify and characterize novel cellular pathways and factors, phenotypic characteristics and inflammatory immune pathways involved in viral persistence.



Jake Estes
(OHSU)



Jon Jacobs
(PNNL)



nanoPOTs platform



Fikadu Tafesse
(OHSU)



Jennifer Kyle
(PNNL)

For more on other joint projects & the latest PMedIC highlights, please visit our website at:
<https://pmedic.labworks.org>

Determining the Role of Sphingolipids in Mycobacterium Tuberculosis (Mtb) Infection

The main goal is to systematically perturb the key sphingolipid biosynthetic pathways of the host to uncover their function in Mtb pathogenesis and antimicrobial cellular processes such as the inflammasome. Individual knockout macrophage cell lines that lack key genes involved in biosynthesis of sphingolipids will be generated using CRISPR/Cas9-technology. We will use multifunctional sphingolipid precursor analogs to define flux, localization and the interactome of sphingolipids during infection in time- and space-dependent manner and study the significance of sphingolipids in the inflammasome.

Past and Upcoming Events

- **September 8th 3-4 pm** PMedIC Seminar Series

Title: “Clinical Proteogenomic Tumor Analysis Consortium”

A joint presentation by Dr. Jeffery Tyner of OHSU and Dr. Karin Rodland of PNNL and Professor Emeritus at OHSU.

[Watch the presentation](#)

- **September 29th 9-10 am** PMedIC Seminar Series-Guest lecture

Title: Epilipidomics Workflow: Analysis and Data Integration to Decipher the Regulatory Potential of Oxidized Complex Lipids

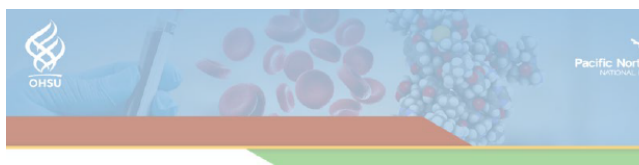
Presented by Maria Fedorova of University Hospital & Faculty of Medicine Carl Gustav Carus of TU Dresden, Germany

[Watch the presentation](#) – Accessible to OHSU internal employees

- **December 8th 3-4pm** PMedIC Seminar Series

Title: TBD

A joint presentation by Dr. Fikadu Tafesse of OHSU and Dr. Jennifer Kyle of PNNL



PMedIC Seminar Series

Clinical Proteogenomic Tumor Analysis Consortium

Wednesday, September 8, 2021
3:00 p.m. – 4:00 p.m. P.T.

[MS Teams meeting link](#)



Dr. Karin Rodland
Laboratory Fellow, Biological Sciences Division,
Pacific Northwest National Laboratory
Professor Emeritus, Developmental & Cancer
Biology, School of Medicine
Oregon Health & Science University



Dr. Jeffery Tyner
Professor, Cell, Developmental, and Cancer
Biology,
Oregon Health & Science University

The Clinical Proteogenomic Tumor Analysis Consortium is focused on the application of cutting-edge mass spectrometry capabilities to compelling problems in cancer biology, and the OHSU-PNNL collaboration to form a Proteogenomic Translational Research Center for Acute Myeloid Leukemia (the AML PTRC) is a perfect example of that objective. The AML PTRC is adding comprehensive, quantitative proteomic and phosphoproteomic analysis to hundreds of patient samples collected through the Beat AML project, with the accompanying genomic, transcriptomic, and ex vivo drug sensitivity data. The objective is to build a proteomic and/or phosphoproteomic predictor of drug response that performs at least as well as the ex vivo drug sensitivity tests. This general approach is also being applied to understand the biological process of drug resistance with the goal of identifying therapeutic targets that will block the emergence of resistant clones.

PNNL-SA-163244 | 6/18/2021



Wednesday
Sep. 29, 2021
9:00 - 10:00 a.m.

OHSU
MS teams
3181 S.W. Sam Jackson
Park Rd.
Portland, OR 97239

PMEDIC SEMINAR SERIES- GUEST LECTURE

Epilipidomics Workflow: Analysis and Data Integration

by **Maria Fedorova, Ph.D.**

University Hospital & Faculty of Medicine Carl Gustav Carus of TU
Dresden, Germany

Epilipidomics Workflow: Analysis and Data Integration to Decipher the
Regulatory Potential of Oxidized Complex Lipids

Lipids are characterized by extremely high structural diversity translated to a wide range of physicochemical properties providing different functions. Moreover, lipids can be enzymatically and non-enzymatically modified via introduction of small chemical groups, including oxidation, nitration, sulfation and halogenation, to compose a new level of lipidome complexity (epilipidome) required to regulate complex biological functions. The main challenges in addressing epilipidome diversity are low natural abundances of modified lipids, and the lack of the knowledge on their chemical diversity in biological matrices. Thus, analysis of epilipidome requires simultaneous application of two different analytical workflows - targeted detection to address their low abundance and untargeted/discovery methods to provide high epilipidome coverage. Over last years, we developed several analytical approaches for detection, identification and relative quantification of complex oxidized lipids in biological context specific manner. By combining mass spectrometry analysis and bioinformatics tools, specific regulatory signature of modified lipids were identified in the context of human metabolic disorders as well as basic cellular processes such as ferroptotic cell death.



For questions, please contact Liz Sturgill, rowland@ohsu.edu

Education & Training

PNNL Internships, an integral addition to several OHSU T32 training grants

In 2020, the PMedIC team worked to develop the 2020 – 2023 PMedIC Strategic Plan. One of our strategic priorities was to “establish educational and professional opportunities.” One of the ways we have implemented this priority was to expand the incorporation of PNNL into OHSU training grants. This included collection of materials and language that supports our continuing efforts to provide exciting opportunities such as internships at PNNL through the Visiting Researchers program. This endeavor included the newly funded T32 training program “Program in Biomedical Sciences” that supports our new graduate program students.

“active learning in real life settings enhances research training. **This “teach science like we do science” approach includes internships such as those provided by the PMedIC collaboration between OHSU and PNNL.”**

- Cheryl Maslen, Professor School of Medicine, OHSU; PBMS T32 PI



BMSC 664 - Research Models and

Research models and Methods is a new course required of all incoming graduate students in the Program in Biomedical Sciences. This fall, Dr. Jennifer Kyle, scientist at PNNL and lipidomics expert will be teaching a class on lipidomics to students. This is Dr. Kyle's second teaching endeavor here at OHSU. Last year, she joined Dr. Fikadu Tafesse to lead an MD/PhD journal club class and co-presented their Nature Communications publication, “A global lipid map defines a network essential for Zika virus replication.”

Methods



[Jennifer Kyle](#)

Biomedical Scientist
Pacific Northwest National Laboratory
Jennifer.kyle@pnnl.gov

New ways to connect and learn

Quarterly seminar series

For all upcoming seminars and previous recordings: <https://pmedic.labworks.org/events.stm>

Departmental Seminars

Schedule an informational talk about PMedIC's opportunities at your next group meeting.

Focus forums to discuss new projects

Have a targeted group meeting with OHSU and PNNL scientists to discuss new research areas.

All-hands PMedIC meeting

We started an annual meeting to be held each winter to bring together scientists from both institutions to showcase their work and to openly discuss their collaborative successes and challenges.

Bi-Annual Newsletter

This newsletter marks the inaugural edition of the PMedIC Newsletter that will provide regular communications about successful collaborations and ongoing initiatives and events.

Contact Information

PMedIC Co-Directors



Beth Habecker, Ph.D.

PMedIC Co-Director

habecker@ohsu.edu

Direct: 503.494.0497



Bobbie-Jo Webb Robertson, Ph.D.

PMedIC Co-Director

bj@pnnl.gov

Direct: 503.375.2292

OHSU Strategic Partnerships



Laura Erker, Ph.D.

Director of Strategic Partnerships

erkerl@ohsu.edu

Direct: 503.494.9904

Cell: 503.250.0524

HOW TO ACKNOWLEDGE PMedIC

Acknowledge partnership in publications, posters and talks:

"This research is affiliated with the PMedIC joint research collaboration between OHSU and PNNL."

Acknowledge Pilot funding (publications, posters, talks):

ERS Grant: Supported by Exploratory Research Seed Grant funding from the OHSU School of Medicine.

LDRD: was conducted under the Laboratory Directed Research and Development Program at Pacific Northwest National Laboratory, a multiprogram national laboratory operated by Battelle for the U.S. Department of Energy
ERS and LDRD: was conducted under the Laboratory Directed Research and Development Program at Pacific Northwest National Laboratory, a multiprogram national laboratory operated by Battelle for the U.S. Department of Energy and Exploratory Research Seed Grant funding from the OHSU School of Medicine.