PMedIC

Pacific Northwest bioMedical Innovation Co-laboratory (PMedIC):

An OHSU/PNNL Collaboration

OHSU

Pacific Northwest NATIONAL LABORATORY

PMEDIC SUMMER 2024 NEWSLETTER

Interviews with PMedIC Innovation Award Winners

The PMedIC Innovation Grant funds collaborative research projects between OHSU and PNNL scientists, with the goal of generating preliminary data that will lead to larger joint grant applications. OHSU faculty in the professorial or research series are eligible to apply for up to $50,000 in funding. Daniel Streblow and John Melchior, recent PMedIC Innovation grant awardees, were interviewed about their research projects.

DANIEL STREBLOW

Give us a little history about the idea behind the project, how did it get started?

We have two antivirals that show broad activity against RNA and DNA viruses, but we have found it difficult to identify the targets for these small molecules. By reviewing the literature, I learned about a new technique called Protein Integration Solubility Assay (PISA) that uses less material, has increased throughput and a relatively straightforward data analysis that could be used to identify molecular interactions. It is based on a thermal stability assay. I approached the co-leaders of PMedIC, Dr. Jamie Lo (OHSU) and Dr. Josh Adkins (PNNL) to determine whether this could be a collaborative effort with PNNL. They introduced me to Dr. John Melchior, who has been using thermal proteome profiling (TPP) to characterize

PMedIC was launched in 2018. This partnership between Oregon Health and Science University (OHSU) and Pacific Northwest National Laboratory (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.

Visit pmedic.labworks.org for projects, highlights, and seminars.

molecular interactions. John and I realized quickly that PISA would offer many advantages to conventional TPP assays including the ability to multiplex and perform experiments in a more high-throughput manner, which saves time, materials, and money. Our groups have been working together since last September to discuss and optimize the assay, and the PMedIC Pilot Project seed money is going to help us launch PISA and perform the necessary control experiments to show selectivity and demonstrate feasibility and hopefully identify the targets to our orphan antivirals.

Why are you motivated to do this project?

The project is perfect for promoting OHSU/PNNL interactions, develop a shared technology that benefits both institutions, and promotes the discovery of new molecular interactions.

If this project is successful, how will it impact our understanding?

We have performed small molecule library screens against alphaviruses and have identified countless inhibitors that block virus replication but have yet unknown targets. The PISA assay can be used to identify the targets, which is critical for chemical optimization of the inhibitors using structural information, identifying target interactions and potential toxic liabilities, and for understanding the mechanism of action of the small molecule. Other researchers at OHSU could tap into this technique in collaboration with PNNL to help with their drug development studies.

What is the role of each of you in this project? How are you dividing up the work?

The Streblow lab will perform the tissue culture experiments and thermal treatments.

Dr. Melchior's group, including Drs. Victoria Prozapas and Kwame Attah at PNNL, will perform the sample preparation and mass spectrometry.

A graduate student in the Streblow lab, Samuel Medica, did an internship (see article about other internships) at PNNL during April and May of this year to learn how to process the PISA proteomics data and statistical analysis. Sam will work directly with Dr. Tong Zhang at PNNL to analyze the data from our study and to help establish the analysis pipeline for the group.

JOHN MELCHIOR

Give me a little history about the idea behind the project, how did it get started?

The technology development started with the Predictive Phenomics Initiative. Our team started implementing high-throughput workflows that measure biophysical properties of a protein rather than protein abundance. Independent of that, Dan had stumbled upon this novel assay published by another group and reached out to PNNL to see if we had those capabilities. Well, it just so happened we were developing this assay, and it was a perfect fit. The PMedIC leadership team introduced us and we have been exchanging ideas and collaborating ever since.

Why are you motivated to do this project?

I'm motivated because I believe our workflow can meet a major need in the field. Novel pathogens will continue to emerge, and I imagine a future in which we can essentially search a catalog of existing chemicals that are readily available to combat that pathogen before it spreads and causes another pandemic. Dan and I discussed this much bigger idea, and this is a first step in that direction. Most science is incremental in nature. This is a big idea and a real chance to have a major, positive impact on the world.

If this project is successful, how will it impact our understanding of target compounds?

It will not only tell us the target of the compounds, but it will also provide an understanding of off-target impact. Meaning, we can also evaluate the unintended consequences of the drugs for more precision treatments.

What is the role of each of you in this project? How are you dividing up the work?

Dan's laboratory will perform all of the infection studies and supply the samples and compounds, while my team will perform the assays and data analysis.

PMedIC Empowers Students in Biomedicine

Leveraging a PNNL and OHSU joint research collaboration for student success and impact

Pacific Northwest National Laboratory (PNNL) Computational Scientist Jason McDermott received his PhD in microbiology and immunology from Oregon Health and Science University (OHSU). Today he remains connected to his alma mater through the PNNL and OHSU joint research collaboration Pacific northwest bioMedical Innovation

Pacific Northwest National Laboratory (PNNL) Computational Scientist Jason McDermott (top left), Oregon Health and Science University (OHSU) PhD candidate and former PNNL intern Justine Nguyen (top right), OHSU Associate Professor of Molecular Microbiology Fikadu Tafesse (bottom left), and PNNL Biomedical Scientist Jennifer Kyle

Co-laboratory (PMedIC). McDermott has a joint appointment with OHSU as an adjunct professor, and he is the education outreach coordinator on the PMedIC Core team.

"Building stronger connections with an institution that I'm very familiar with and exposing graduate students to the national laboratory system has been really rewarding," said McDermott.

PMedIC is working to improve human health and treatment of diseases by generating, interpreting, and integrating multi-dimensional data, imaging, and clinical results to understand diseases better and develop innovative therapies.

"I started out my career in the biomedical sciences area working in infectious diseases and cancer and have since moved into the Department of Energy space where I'm looking at soil microbiomes to enhance crop growth and for bioenergy applications," said McDermott. "I use computational methods to address biological problems, whether that's development of new algorithms, data analysis, or interpretation of large data that comes from our mass-spectrometry capabilities."

OHSU students often take on internships at PNNL to learn and complete research for PMedIC projects.

Justine Nguyen, an OHSU PhD candidate in informatics, interned with McDermott during her master's program exploring computational methods for prediction protein function.

"I'm really interested in pushing our biological knowledge and understanding basic biological questions, like why proteins interact with each other."

Research from the internship transferred to her graduate work and dissertation.

"The computational biomedicine research that Jason and I were working on during my internship was really interesting," said Nguyen. "My thesis stems from that collaboration and is focused on applying computer science to model proteins to better understand how they're behaving and predict how they're functioning."

McDermott remains connected to Nguyen as a mentor and member of her thesis committee.

"It's difficult to encapsulate how integral he's been in my scientific journey," said Nguyen. "He is someone I go to for advice and mentorship."

McDermott is also serving on the thesis committee of another OHSU student.

"At PMedIC, we get to combine PNNL's fundamental science and biomedical research with OHSU faculty and clinicians' resources and skills to potentially translate the work we do to clinics," said McDermott. "We also get to introduce bright and excited students to the national lab system, many of whom don't know that exists for biomedical research and expose them to careers as a research scientist. Together, this can be really impactful."

Along with McDermott, PNNL Biomedical Scientist Jennifer Kyle, a joint appointee with OHSU, has been works to create opportunities for students to collaborate with national laboratories. Since 2018, Kyle has worked closely with OHSU Associate Professor of Molecular Microbiology Fikadu Tafesse and his graduate students on different virus-related research.

Read the full story here: https://www.pnnl.gov/publications/pmedic-empowers-students-biomedicine

Grant Collaborations for Accelerating Scientific Discovery

FY24

Vladislav Petyuk, PhD (PNNL) and Vivek Unni, MD, PhD (OHSU)
Exploring the role of alpha-synuclein in the DNA damage response in Parkinson's Disease and melanoma
Jon Jacobs (PNNL) and Afam Okoye (OHSU)
Defining proteomic markers of therapeutic mRNA/SIV vaccine efficacy.
Sneha Couvillion, PhD (PNNL) and Lisa Vrooman, PhD (OHSU)
Determination of rhesus macaque oviductal fluid composition (Macaca mulatta)
Lisa Bramer, PhD (PNNL) and Leslie Myatt, PhD (OHSU)
Placental Health Signature Discovery via Multi-omics Image Integration

Ways to Connect and Learn

Quarterly Seminar Series

View all upcoming seminars and previous recordings here: https://pmedic.labworks.org/events.stm

Departmental Seminars

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

Focus Forums

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

Bi-Annual Newsletter

Our PMedIC Newsletter provides regular communication about successful collaborations and ongoing initiatives and events. If you'd like to share this newsletter with a colleague, they are able to sign up by contacting your institutional co-director.

How to Acknowledge PMedIC

Acknowledging partnership in publications, posters, and talks:

> "This research has been facilitated, in part, by the PMedIC joint research collaboration between OHSU and PNNL."

Add PMedIC Pilot Funding Acknowledgments as Appropriate (publications, posters, talks):

> **Annual OHSU PMedIC Innovation Grant:** "Supported by an Innovation Grant from the OHSU School of Medicine."
>
> **Exploratory Research Seed Grant:** "Supported by an Exploratory Research Seed Grant from the OHSU School of Medicine."
>
> **PNNL Laboratory Directed Research and Development:** "Supported by the Laboratory Directed Research and Development Program at Pacific Northwest National Laboratory, a multiprogram national laboratory operated by Battelle for the Department of Energy."
>
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