Chemistry Departmental Colloquium

Integrating Real and Artificial Intelligence to Accelerate Immunomodulatory Drug Discovery

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Artificial Intelligence (AI) and automation has the potential to accelerate several stages of the drug discovery process. I will provide an overview of our journey with examples in the area Molecular Artificial Intelligence and Neuroimmunology that has been the focus of our work. Over the years, we have integrated several aspects of machine learning methods and automation for different areas in chemical sciences leading to the development of AI agents as a 'virtual scientist' for laboratory automation and drug discovery to mimic 'real intelligence'. Although the use of AI can clearly result in enhancing human productivity for automating, analyzing and interpreting chemical experiments, there are limitations related to serendipitous discoveries in the lab, where real intelligence plays a role. I will present one such example where our group identified the role of lipid accumulation and how lipids modulate immune cells in the brain, which has now become one of the major directions in the field of neuroimmunology. Developing molecules to target lipid accumulation as a neuro-immunotherapeutic to combat Alzheimer's disease will be presented which was accelerated by use of machine learning tools and AI agents from our group.

Thursday, September 12, 2024 **4:30pm** **WTHR 104**

PURDUE UNIVERSITY | James Tarpo Jr. and Margaret Tarpo Department of Chemistry

Chopra Bio

Gaurav Chopra is a tenured Associate Professor in the Department of Chemistry and Computer Science at Purdue University. As the Director of the Merck-Purdue Center, an initiative supported by Merck & Co, Chopra oversees research projects spanning across Purdue University. Chopra is also a Scialog Fellow and AnalytiXIN (Analytics Indiana) Fellow in Life Sciences, a core member of the Regenstrief Institute for Healthcare Engineering, Purdue Institutes for Drug Discovery, Neuroscience, Immunology and Physical Artificial Intelligence. His research program in Molecular Artificial Intelligence (AI) and Immunology focuses on identifying and then targeting immuno-metabolic "brakes" of the immune system by targeting immune and glial cell lipid landscapes. Chopra is interested in understanding glial and immune cell dysfunction in response to lipids and lipid accumulation during chronic neuroinflammation, such as neurodegeneration by developing new bioanalytical and mass spectrometry methods for deep and single-cell lipidomics profiling and using AI for chemical synthesis and targeted drug discovery to develop neurological and immune tolerance therapies. Chopra received his undergraduate degree in Mechanical Engineering from the Indian Institute of Technology (IIT), Delhi, India and his M.S. in Mechanical Engineering from the University of California, Irvine. Chopra received his PhD with Professor Michael Levitt (2013 Nobel Laureate in Chemistry) at Stanford University School of Engineering and Medicine. Chopra was selected as a JDRF Fellow at the University of California – San Francisco (UCSF), School of Medicine with Professor Jeffrey Bluestone to develop immune tolerance therapies. Chopra's independent research program at Purdue University has secured over $16M in total funding from several federal agencies and companies, such as National Institutes of Health (NIH), Department of Defense (DoD), Defense Threat Research Agency (DTRA), National Science Foundation (NSF), Merck & Co, Agilent Technologies, to name a few. Chopra has extensive publication record including articles in journals like Nature, Immunity, J. Clinical Investigation, PNAS, to name a few. He has given over 120 invited lectures nationally and internationally to universities and pharmaceutical companies, invited workshops in AI to big Pharma executive team and leadership and to regulatory agencies such as FDA in digital health, immunology, AI-based automation and drug discovery. Recently, Chopra led a team that won the ASPIRE Grand Prize worldwide by the National Center for Advancing Translational Science (NCATS) for developing AI-guided drug discovery and automation platform. His current work with NCATS includes developing large language model (LLM)-based AI infrastructure to plan, execute, analyze and automate chemical and biological experiments to accelerate neurological drug discovery and development. Outside of academia, Chopra has co-founded two companies – Meditati Inc. and BrainGnosis Inc. merging AI, immunology and drug discovery. Chopra is dedicated to fostering diversity in academia to support students from underrepresented minority in STEM at Purdue University funded by NSF. To this end, Chopra lab has also developed a virtual reality-based drug discovery game, MINT, and organized outreach events for K-12 and university students, promoting a love for science and inclusivity in scientific endeavors.

Vision Statement

Chopra laboratory is a leading center for *Molecular Artificial Intelligence and Immunology* that combines chemistry, immunology and artificial intelligence (AI) with basic science guided translational focus to improve human health. Chopra's research program is focused on **identifying and then targeting metabolic "brakes" of the immune system for neuro-immunotherapy with an overarching question – "How do lipids/metabolites modulate immune and glial cells in chronic inflammation"**. The initial focus is to translate novel immunological therapies for neurodegeneration by developing bioanalytical methods (eg. **single-cell lipidomics**), chemical tools (eg. **targeted fluorescent dyes**), targeted drugs (**immune and metabolic checkpoint inhibitors and degraders**) using AI architectures and molecular modeling infrastructure and then validating with *in vitro* and *in vivo* experiments. Chopra has also developed an "AI agent" infrastructure integrated with large language models for automating biological and chemical experiments to accelerate drug discovery with NCATS (National Center for Advancing Translation Science). Chopra's **long-term goal is to harness the immune system for therapy for neurological diseases** (such as Alzheimer's disease) **by targeting the functional lipid/metabolic landscape of immune and glial cells**. Harnessing the immune response for therapy has already demonstrated to provide durable long-term therapeutic responses with impact on disease progression and enhancing quality of life. However, **integration of immuno-metabolome has remained unexplored to develop new immunotherapies**.

Chopra would like to establish a ***Center for Molecular Artificial Intelligence and Immunology*** with both basic science and translational focus to enhance human health in neuroscience and beyond, eventually affecting other areas of medicine. Such a Center does not exist in the United States. This world-class program, as the next frontier with Chemical Science being central to Medicine will be done by **bringing together ideas and expertise from Immunology, Neuroscience, Metabolism, Chemistry, Digital Health, AI, Engineering and Medicine**. The initial focus will translate cell-specific functional biomarkers and immunotherapies for neurodegeneration and extend this to **develop new tools and neuro-immunotherapeutics for neurological diseases**. Neuroimmunology is where cancer immunology was ~15 years ago and this is a huge untapped opportunity for the future of medicine. The basic science in chemistry, immunology and engineering in partnership with disease experts and clinical scientists will be essential to translate these discoveries to new medical frontiers beyond small molecules, biologics and cell therapy. Typically, such diverse fields do not deeply interact with each other, and Chopra's research experience and interdisciplinary expertise is well-suited to take on such a leadership role to make this vision into a reality.

Outside of academia, Chopra has co-founded two companies – Meditati Inc. that develops 'smart' drugs for mental health indications and BrainGnosis Inc. that develops AI-guided brain prognosis and diagnosis biomarkers for diseases. Chopra is *committed to diversity in academia* and have been the co-PI of NSF-REU award that selects underrepresented minority undergraduate students in STEM and funds them to do summer research with faculty at Purdue University. To increase diversity and openness in science for all ages, Chopra group has also developed a virtual reality-based AI drug discovery game called MINT and have conducted several outreach events for K-12 and university students to enhance their love for science (https://chopralab.github.io/MINT/index.html). All software from the Chopra group is publicly available on GitHub (https://github.com/chopralab).