Tutorial – T2

Keynote-Thursday 9:30 AM EDT
Title: Genomics Enabled Repurposing of Approved Compounds as Countermeasures to SARS-CoV-2 Presenters: Daniel Janies, University of North Carolina-Charlotte, and Samuel Handelman, University of Michigan

Abstract:
Genomics enabled repurposing of approved compounds as countermeasures to SARS-CoV-2

The COVID-19 pandemic is caused by SARS-CoV-2, the most recent in a series of zoonotic lineages of coronaviruses (following SARS-CoV-1 and MERS-CoV) with severe disease outcomes. Rapidly deployable interventions are critically needed to reduce the morbidity and mortality of COVID-19. To recover public health and economic stability, we must identify effective treatments for the current pandemic, prepare for potential of drug resistance, and the emergence of novel pathogens. Genomics is key to all of these challenges.

Genome-wide comparison between SARS-CoV-2 and related coronaviruses informs drug repurposing by identification of areas of the viral genomes that are not easily deleted or modified to confer drug resistance (i.e. evolutionarily conserved regions). Furthermore, if some viral lineages do evolve to render a drug ineffective these can serve as early warning that future drug repurposing and development should be prepared.

The University of Michigan's (U-M) Center for Drug Repurposing (CDR) has established a SARS-CoV-2 infectivity assay that detects pharmacologic antiviral and host-cell protective effects from single agents. The CDR has screened FDA-approved drugs for efficacy against the SARS-CoV-2 viral infection using artificial intelligence enhanced drug discovery techniques. FDA approved drugs can be prescribed off-label immediately and clinical trials are beginning at U-M and other sites. Combinatorial screening is now being used to optimize a cocktail of drugs that can reduce viral infection. With other viral diseases, drug cocktails have demonstrated superior efficacy and dramatically reduced the potential of acquired drug resistance. However, the number of potential cocktails that might be screened is very large. For this reason, genome-wide comparisons will be used to prioritize drugs for inclusion in cocktails when drugs target evolutionarily conserved regions, if the target is known.

Keywords:
SARS, coronavirus, genome, COVID-19, drug repurposing

Bios:

Daniel Janies joined the University of North Carolina at Charlotte in 2012 as The Carol Grotnes Belk Distinguished Professor of Bioinformatics and Genomics. Dr. Janies received a Bachelor of Sciences in Biology from the University of Michigan in 1988 and a Ph.D. in Zoology from the University of Florida in 1995. Dr. Janies worked as a postdoctoral fellow (1996-99) and as a principal investigator (2000-02) at the American Museum of Natural History where he led a team that, using off-the-shelf components, built one of the worlds largest computing clusters in 2001. Dr. Janies originated the field of mapping pathogen genetic data in concert with geography and host animals. Dr. Janies was a tenured faculty member in the College of Medicine at the Ohio State University where he served as a national principal investigator in the Tree of Life program of the NSF. Dr. Janies recent awards include DoD sponsored work to understand the spread of pathogens. Dr. Janies has advised the White House, the Pentagon, and testified to both Houses of Congress.

Samuel Handelman became director of Clinical Informatics in the newly formed Michigan Center for Drug Repurposing in 2020. Dr. Handelman received undergraduate degrees in Biochemistry and Computer Science from UC Santa Cruz in 2001, and a PhD in Biological Sciences from Columbia University in 2010. Dr. Handelman was a postdoctoral fellow at the NSF Mathematical Biosciences Institute, mentored by Dr. Janies.