CONCEPT CLEARANCE

Illuminating the Druggable Genome, an NIH Common Fund Program

Proposed action: Reissue **RFA-RM-18-011**: *Cutting Edge Informatics Tools for Illuminating the Druggable Genome (U01 Clinical Trial Not Allowed)*

Planned Funding: $1.4M/yr (2-3 2-yr awards at ~$450K/yr, currently budgeted in FY2022 & 2023)

Overview of the IDG Program: The goal of the Illuminating the Druggable Genome (IDG) program is to identify and provide information on proteins that are currently not well studied within commonly drug-targeted protein families (kinases, GPCRs, and ion channels) using experimental and informatics approaches. Demonstration of this approach's effectiveness should facilitate its application to a broader array of protein families beyond the three families of proteins in the Program. The program supports three Data and Resource Generation Centers (DRGCs), a Knowledge Management Center (KMC), and a Resource Dissemination and Outreach Center (RDOC).

The Goals of the Cutting Edge Informatics Tools (CEIT) initiative: The purpose of the FOA was to augment the capability of the KMC as well as the broader IDG Consortium by developing and deploying tools to: (1) process, analyze, and visualize IDG data, (2) enable new data resources and methods to be incorporated into Pharos https://pharos.nih.gov/idg/index that will strengthen predictions about physiological and disease associations, and (3) prioritize understudied IDG families for deeper experimental study.

Impact of the first cohort of awards: The three currently funded teams have contributed significantly to the enhancement of the Pharos target pages (CEIT PIs: Wu and Kannan) and Pharos disease pages (CEIT PI Robinson), including ways to summarize sequence (and phylogenetic relationships) among the kinases, and creating effective summaries of pathway-based information, leveraging deep expertise with relevant ontologies. The groups are building predictive models that are in the process of experimental validation by the investigators.

Award No.	Principal Investigators	Institution	Title
U01-CA239106	**Kannan** & Kochut	UGA	A Data Analytics Framework for Mining the Dark Kinome
U01-CA239108	**Robinson**, Mungall, & Oprea	Jackson Lab	Illuminating the Druggable Genome by Knowledge Graphs
U01-CA239069	**Wu**, Deustachio, & Stein	OHSU	Reactome IDG Portal: Pathway-based Analysis and Visualization…

Rationale for Continued Investment: We continue to need a larger diversity of informatics expertise than currently exists in the IDG program in order to effectively use the breadth and depth of data available in Pharos to build models for elucidating the biological roles of the understudied proteins. These are complex and difficult questions to model, and we need groups that will leverage specialized expertise to address this problem. This will also establish a means to attract the research community to fundamental questions of how best to deploy predictive (AI, ML and causal) models for determining the functions of understudied proteins, and how to update such models as additional data arrive.

To address these needs, we plan to reissue the CEIT FOA in FY2022. The goal of the new FOA will be to attract the larger community of informaticians to the task of building predictive models for establishing the roles of understudied kinases, GPCRs, and ion-channels in normal and diseased states.

Complementary Activities: The program will also issue a NOSI (approved internally at OSC/DPCPSI) offering administrative supplements to funded investigators outside the IDG program to support the incorporation of single-cell data into Pharos. There is currently no expertise for the incorporation of single cell data into Pharos within the IDG program, and this has been identified as a priority by the community and our External Program Consultants. This administrative supplement opportunity will be modeled after NOT-RM-19-009 and adapted for the purposes of the IDG program.