

Common Fund Concept Clearance: Illuminating the Druggable Genome (IDG) Cutting Edge Informatics Tools FOA (reissue)

Council of Councils January 29, 2021

Douglas Sheeley, Sc.D.



Concept Clearance: Reissue (RFA-RM-18-011)

Cutting Edge Informatics Tools for Illuminating the Druggable Genome (U01 Clinical Trial Not Allowed)

Objective: Draw expertise into the IDG program to support development and deployment of models to help the community predict biological role of understudied proteins.

Funds Available and Anticipated Number of Awards: \$1.4M per year in FY22 and FY23; 2-3 awards

Award Project Period: 2 years

Council Action: Vote on continued support of Cutting-Edge Informatics Tools for Illuminating the Druggable Genome

OSC (Common Fund) Illuminating the Druggable Genome (IDG)



- Goal of the IDG Program catalyze research to improve our understanding of the properties and functions of proteins that are currently not well studied within commonly drug-targeted protein families.
- Three protein families identified to contain adequate numbers of understudied members (few or no
 publications, lack of R01 funding) and are well-established druggable families with high potential to impact
 human health once disease associations are made ion channels, GPCRs and kinases

Timelines

Pilot Phase - (2014-2017)

- 1. integrate information into a single informatics site
- 2. technology development to enable determination of protein function and therapeutic potential at scale Implementation Phase – (2017-2023)
- 1. Identify biochemical, cellular, or animal model phenotypes
- 2. Enable further investigation of these proteins by providing reagents and tools
- 3. Generate, maintain, and facilitate the use of, a minable knowledgebase.

OSC (Common Fund) Illuminating the Druggable Genome (IDG)



Data and Resource Generation Centers (DRGCs)



External Data Sources

GWAS Catalog, Monarch, UniProt, DrugCentral, ChEMBL, OMIM and others •Cutting Edge Informatics Tools (CEIT) Awards - FOA issued in 2018 to deploy tools to enhance the community's ability to process, analyze, and visualize data around the understudied proteins.

•**R03 Pilot Projects** – FOA issued in 2018, 2019 and 2020 to support the generation of <u>preliminary data</u> and <u>tools</u> around eligible understudied protein(s) to:

elucidate function in the context of human diseasesupport R01 applications and/or drug discovery projects

•Commercializing Understudied Proteins from the Illuminating the Druggable Genome Project (SBIR and STTR) – Current FOA to initiate early research leading to the commercialization of assays or products.



RFA-RM-18-011: support for development and deployment of tools to better process, analyze, and visualize data around understudied proteins.

Three 2-year awards in FY2019 – significant enhancements to Pharos, the IDG target knowledgebase and associated query tools

- <u>A Data Analytics Framework For Mining The Dark Kinome</u>
 - Kannan and Kochut (UGA)
 - organizing and presenting sequence and phylogenetic relationships of kinases
- Illuminating the Druggable Genome by Knowledge Graphs
 - Robinson (Jackson Lab), Mungall (UC Berkeley) and Oprea (UNM)
 - leveraging deep expertise in relevant ontologies to build knowledge graphs for computations
- <u>Reactome IDG Portal: Pathway-based Analysis And Visualization Of Understudied Human Proteins</u>
 - Wu, (OHSU), D'Eustachio (NYU), and Stein (Ontario Institute for Cancer Research)
 - creating effective summaries of pathway-based information



Cutting-Edge Informatics Tools for Illuminating the Druggable Genome

Rationale for Reissue:

Draw expertise into the IDG program to support development and deployment of models to help the community predict biological role of understudied proteins.

a. need for larger diversity of informatics expertise

b. more effectively use current Pharos data

c. deployment of AI, ML, and causal models to determine protein function

Complementary Activity:

NOSI - administrative supplements for non-IDG investigators to support the incorporation of single-cell data into Pharos.

a. expertise for the incorporation of single cell data into Pharos within the IDG program

b. identified as a priority by the community and our External Program Consultants



Concept Clearance: Reissue (RFA-RM-18-011)

Cutting Edge Informatics Tools for Illuminating the Druggable Genome (U01 Clinical Trial Not Allowed)

Objective: Draw expertise into the IDG program to support development and deployment of models to help the community predict biological role of understudied proteins.

Funds Available and Anticipated Number of Awards: \$1.4M per year in FY22 and FY23; 2-3 awards

Award Project Period: 2 years

Council Action: Vote on continued support of Cutting-Edge Informatics Tools for Illuminating the Druggable Genome