IDG ILLUMINATING the DRUGGABLE GENOME

Pre-application Webinar
May 26, 2021 11:00 EST

RFA-RM-21-020

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

NOT-RM-21-019

Notice of Special Interest (NOSI) for Illuminating the Druggable Genome (IDG) Initiative: Request for Administrative Supplements to Existing Grants for incorporating single cell data into the IDG Knowledgebase

We will be taking questions at the end of the webinar.
This presentation is being recorded and a transcript will be available.

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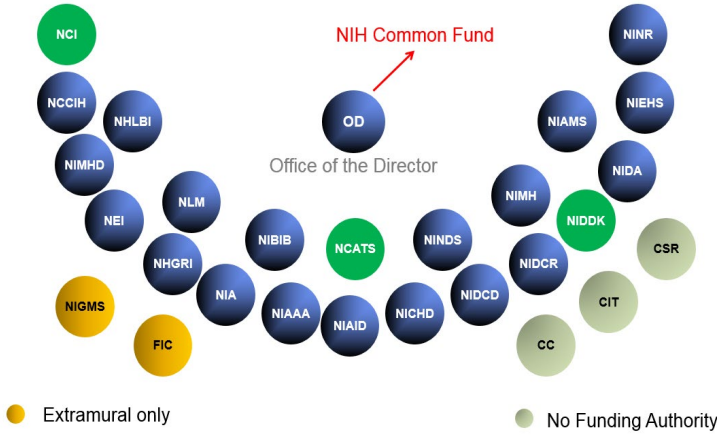
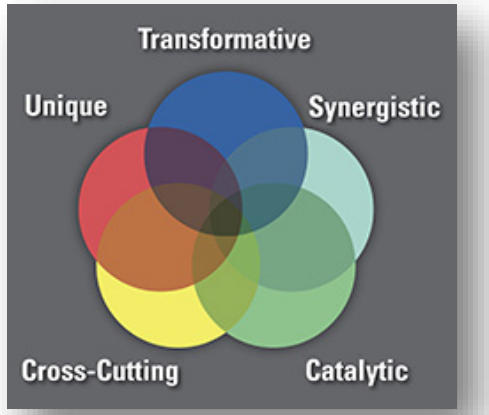
Criteria for Common Fund Programs





Program Expectations

Transformative: Exceptionally high and broadly applicable impact

Catalytic, Short Term and Goal-driven: Achieve goals within 5-10 years.

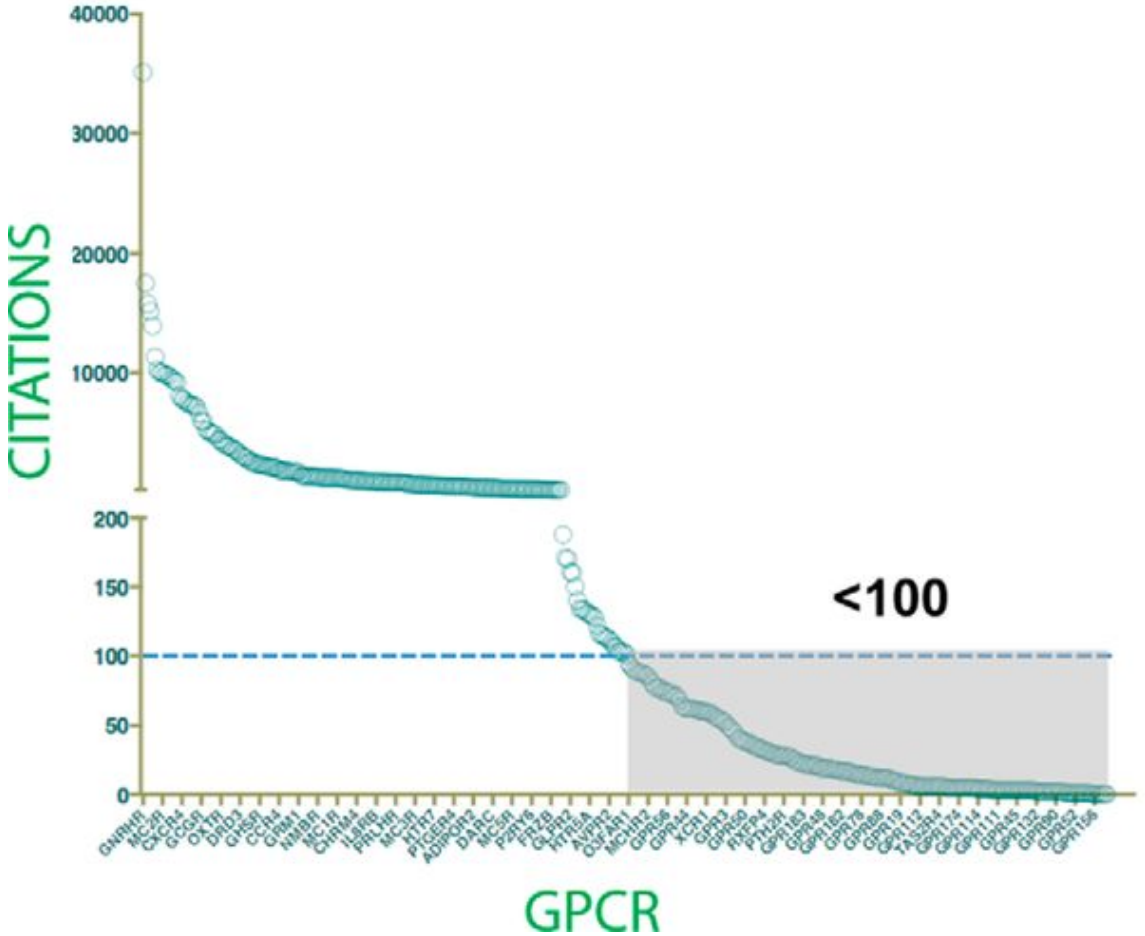
Synergistic /Enabling: Advance the missions of multiple NIH ICs

Cross-Cutting: Address complex issues that require trans-NIH teams

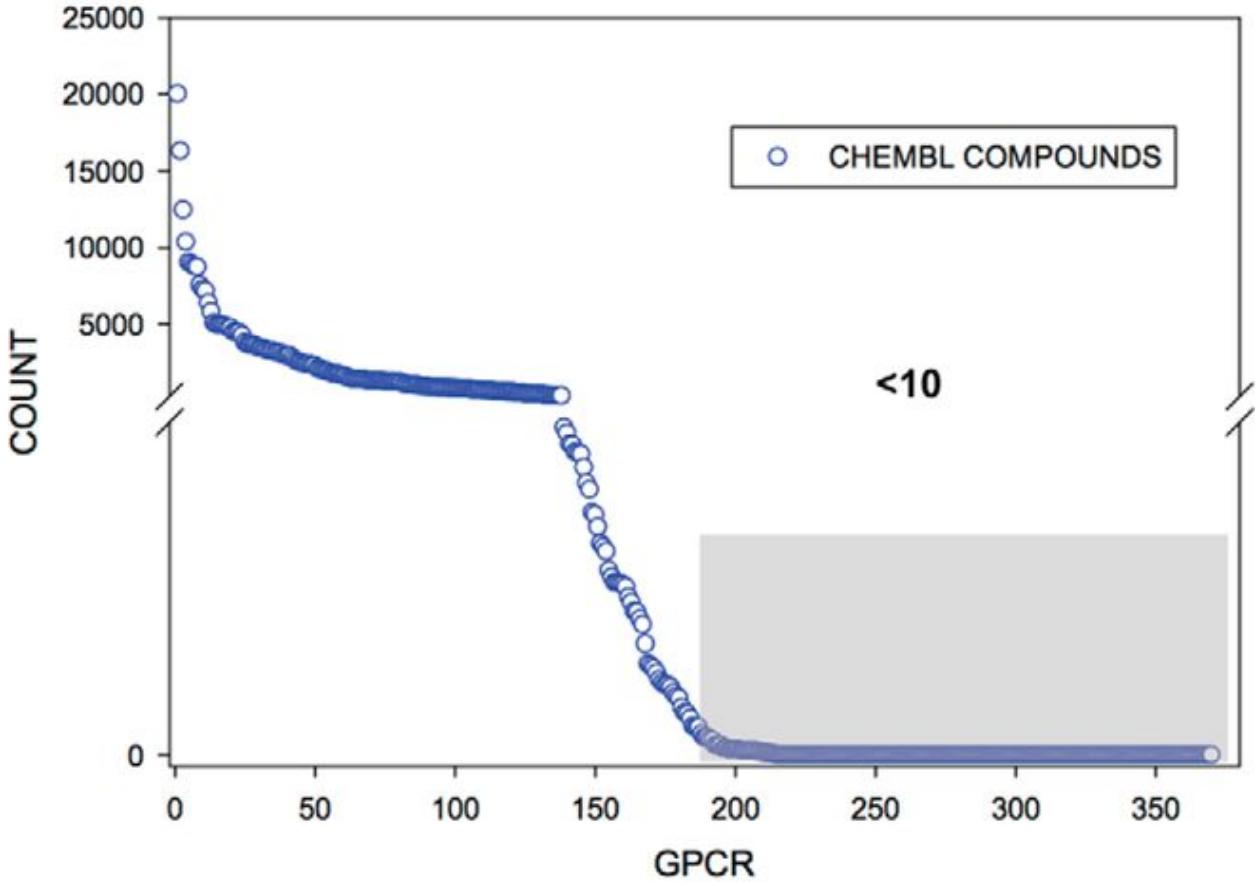
Novel: Provide new solutions to specific challenges

Many Members of the GPCR, Ion Channel and Kinase Protein Families are Understudied

PubMed Publications for GPCRs (1980-2013)

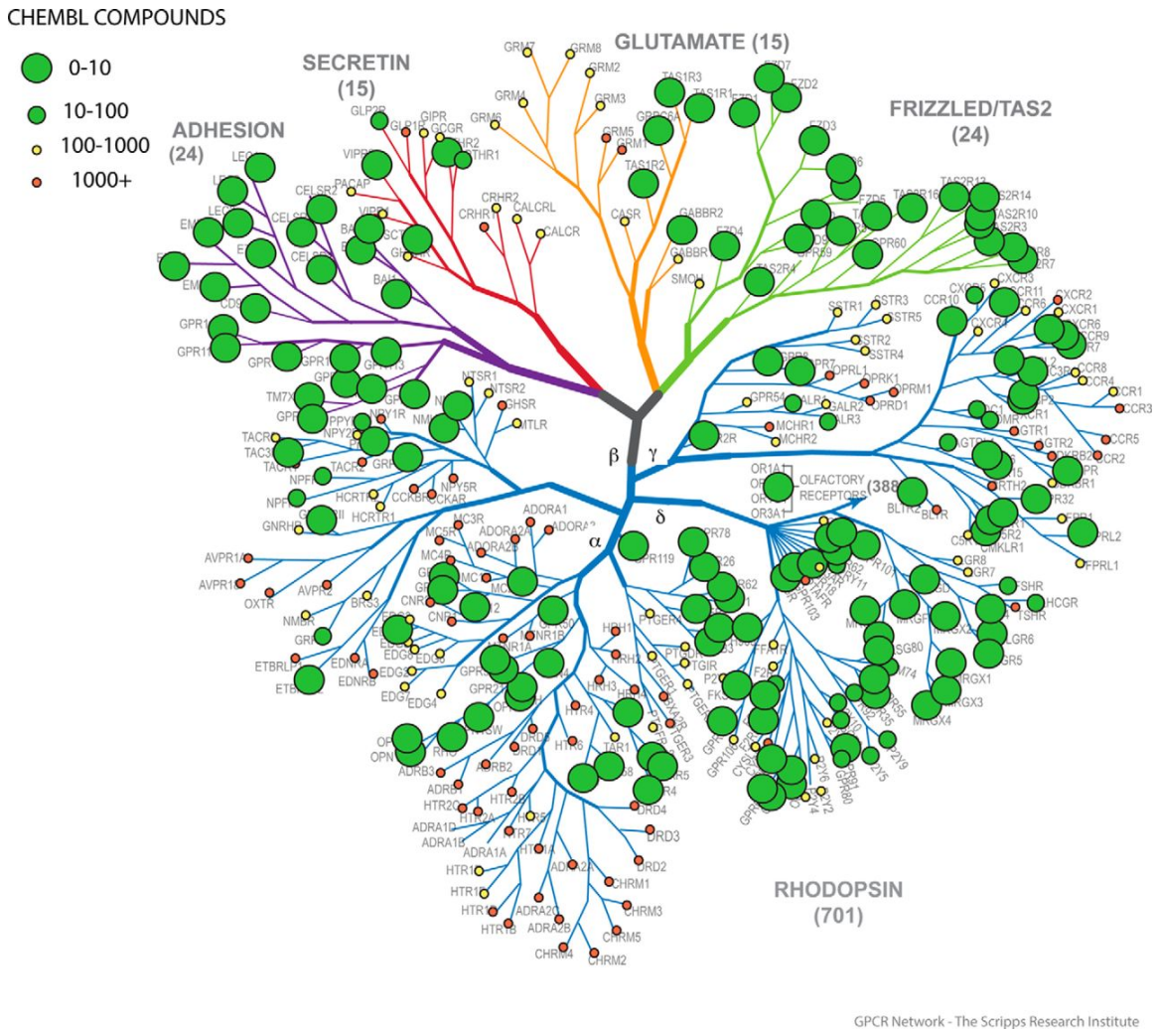


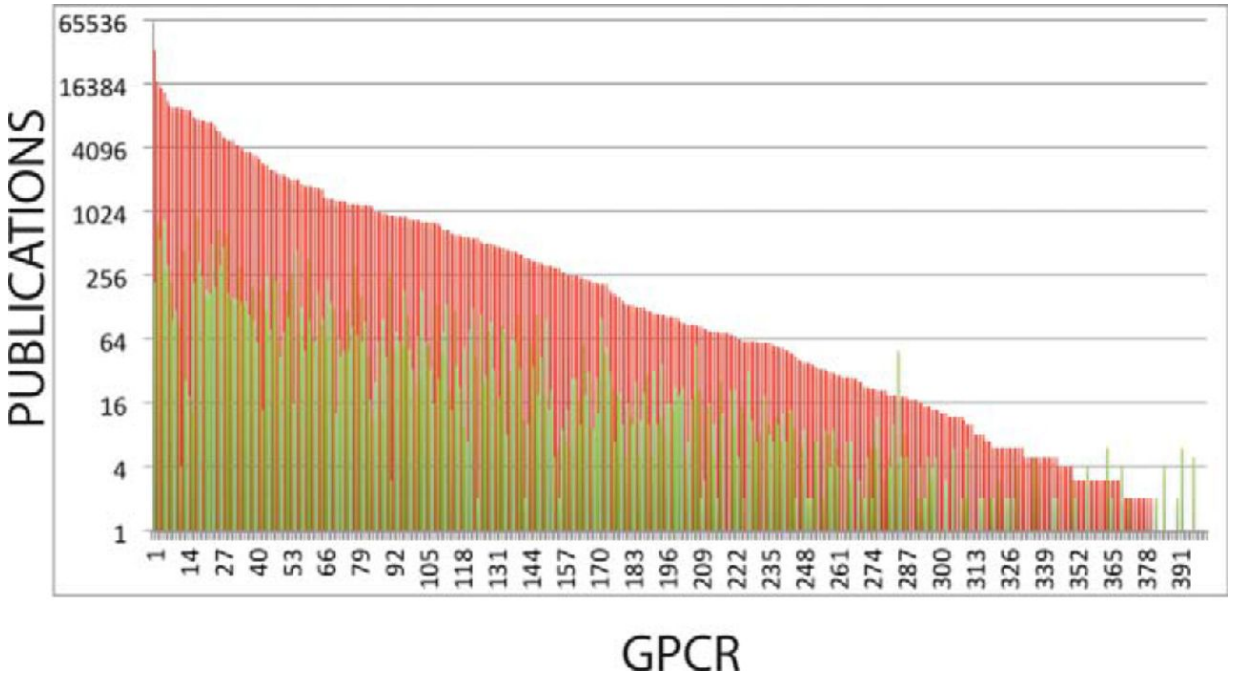
GPCRs with Known Chemical Modulators



Roth and Kroeze, JBC 2015

Most Scientific Work Continues to Focus on Well Studied Proteins





Green – Publications in 2014
Red – Publications predating 2013

Roth and Kroeze, JBC 2015

Illuminating the Druggable Genome (IDG) Program

- Druggable Genome - the subset of the ~20,000 genes in the human genome that express proteins potentially able to bind drug-like compounds.
- 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)

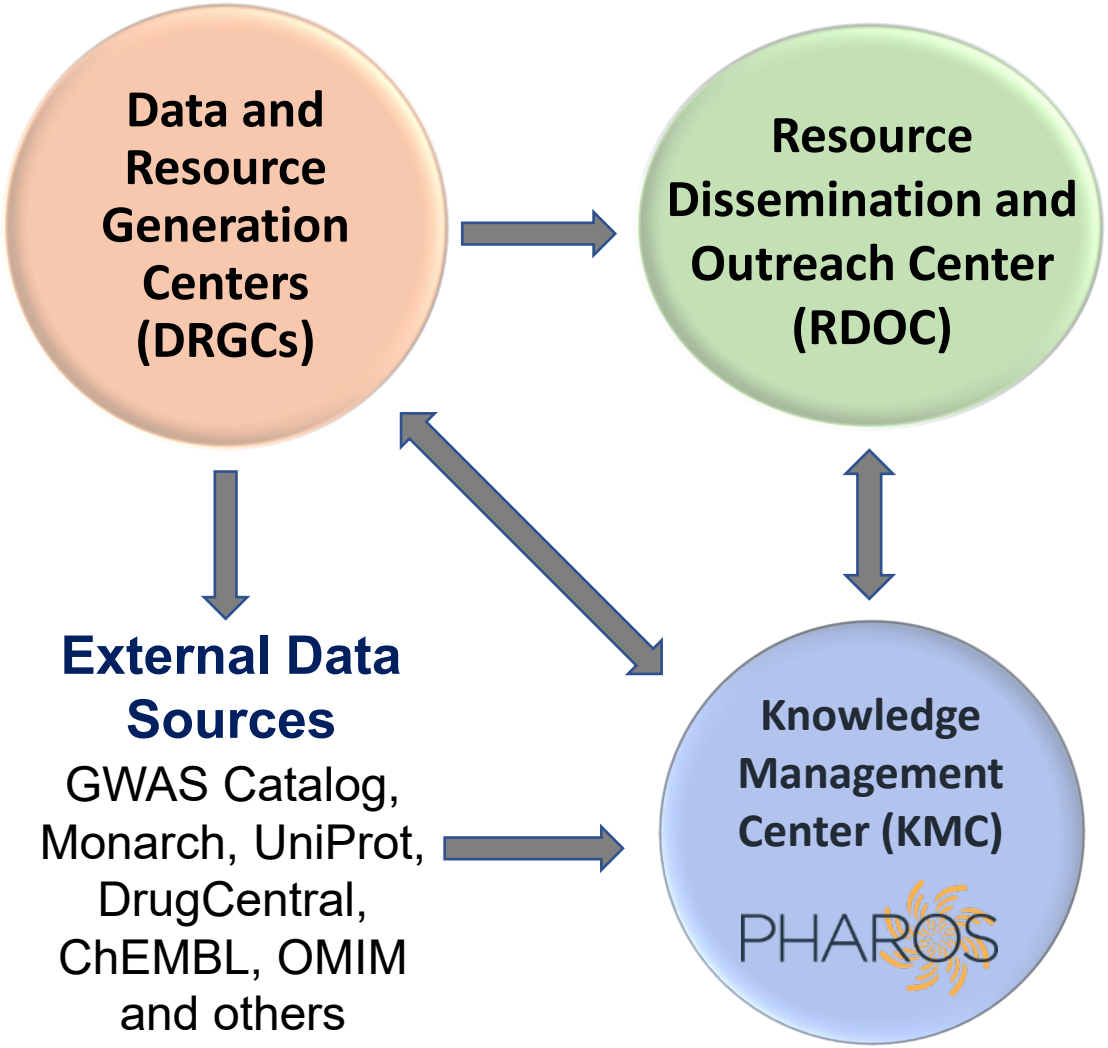
1. To integrate information about understudied druggable proteins from disparate sources into a single informatics site.
2. To foster technology development to enable the determination of function and therapeutic potential of understudied druggable proteins at sufficient scale.

Implementation Phase – (2017-2023)

1. Identify biochemical, cellular, or animal model phenotypes for understudied proteins from druggable gene families.
2. Enable further investigation of these proteins by providing reagents and tools
3. Generate, maintain and facilitate the use of a minable knowledgebase.

Existing Program Structure

IDG Consortium Structure



IDG Program – Other Initiatives

•Cutting Edge Informatics Tools (CEIT) Awards - FOA issued in 2018 and **2021** 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, 2020 & **2021** to support the generation of preliminary data and tools around eligible understudied protein(s) with the intent of elucidating the function of these proteins in the context of human disease and to obtain sufficient preliminary data for subsequent R01 applications and/or drug discovery projects.

•**ACTIVE:** Commercializing Understudied Proteins from the Illuminating the Druggable Genome Project (SBIR and STTR) - To initiate early research ultimately leading to the commercialization of assays or products focused on understudied proteins identified by the IDG Program.

https://commonfund.nih.gov/idg/grants#current

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Data and Resource Generation Centers

GPCRs

Bryan Roth, M.D., Ph.D
University of North Carolina

Brian Shoichet, Ph.D.
University of California, San Francisco

Protein Kinases

Gary Johnson, Ph.D
University of North Carolina

Ion Channels

Lily Jan, Ph.D
Michael McManus, Ph.D.
University of California, San Francisco

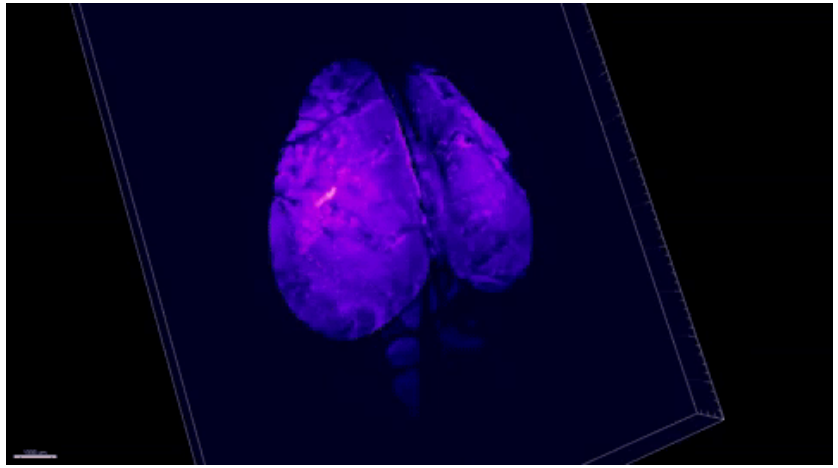
IDG Approach – Generate data and modulatory tools:

26 NOVEMBER 2015 | VOL 527 | NATURE | 477

Allosteric ligands for the pharmacologically dark receptors GPR68 and GPR65

Xi-Ping Huang[1,2]*, Joel Karpiak[3]*, Wesley K. Kroeze[1]*, Hu Zhu[1]†, Xin Chen[4,5]†, Sheryl S. Moy[6], Kara A. Saddoris[6]†, Viktoriya D. Nikolova[6], Martilias S. Farrell[1]†, Sheng Wang[1], Thomas J. Mangano[1,2], Deepak A. Deshpande[7], Alice Jiang[1,2]†, Raymond B. Penn[7], Jian Jin[4,5]†, Beverly H. Koller[8], Terry Kenakin[1], Brian K. Shoichet[3] & Bryan L. Roth[1,2,5]

Compounds commercially available
Ogerin - SML1482
Ogerin control - SML1483



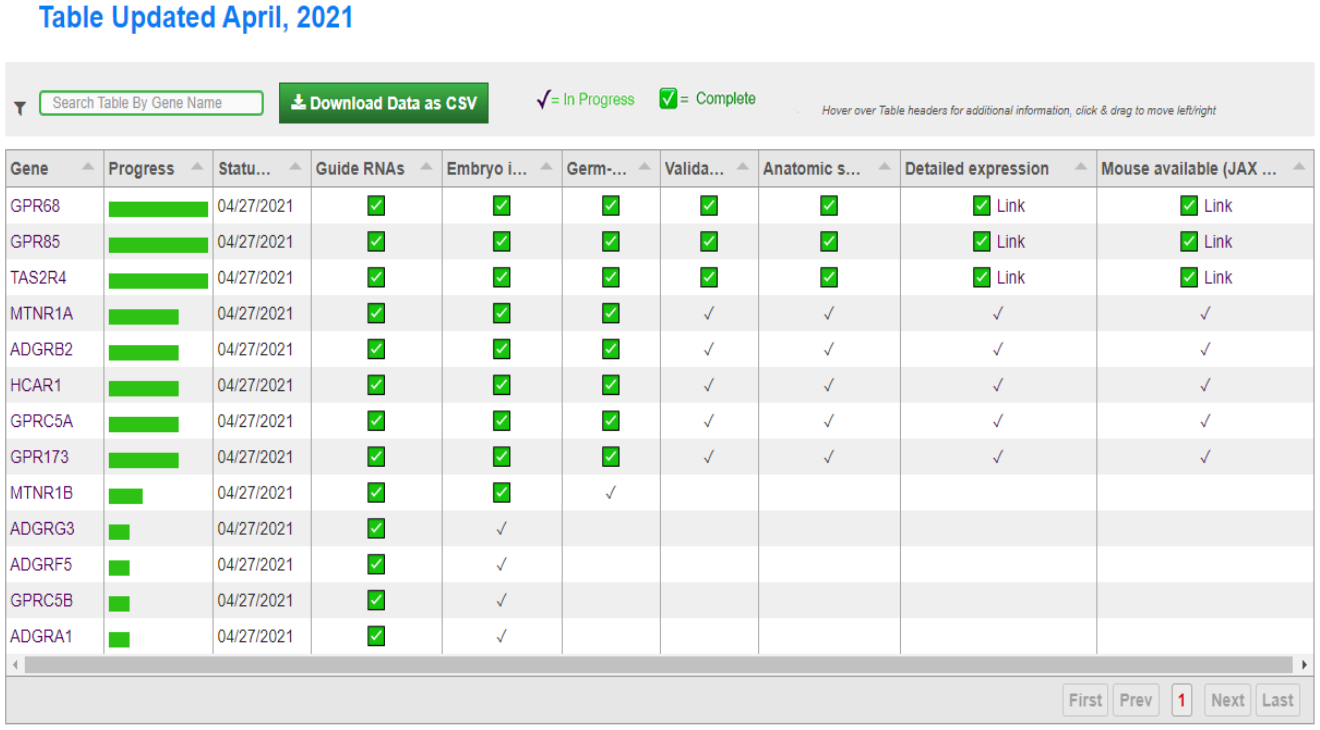
tomato-GPR68 µDISCO light sheet microscopyRoth IDG award, unpublished video; whole body imaging underway

Resource Dissemination and Outreach Center

Stephan Schürer, Ph.D.
University of Miami

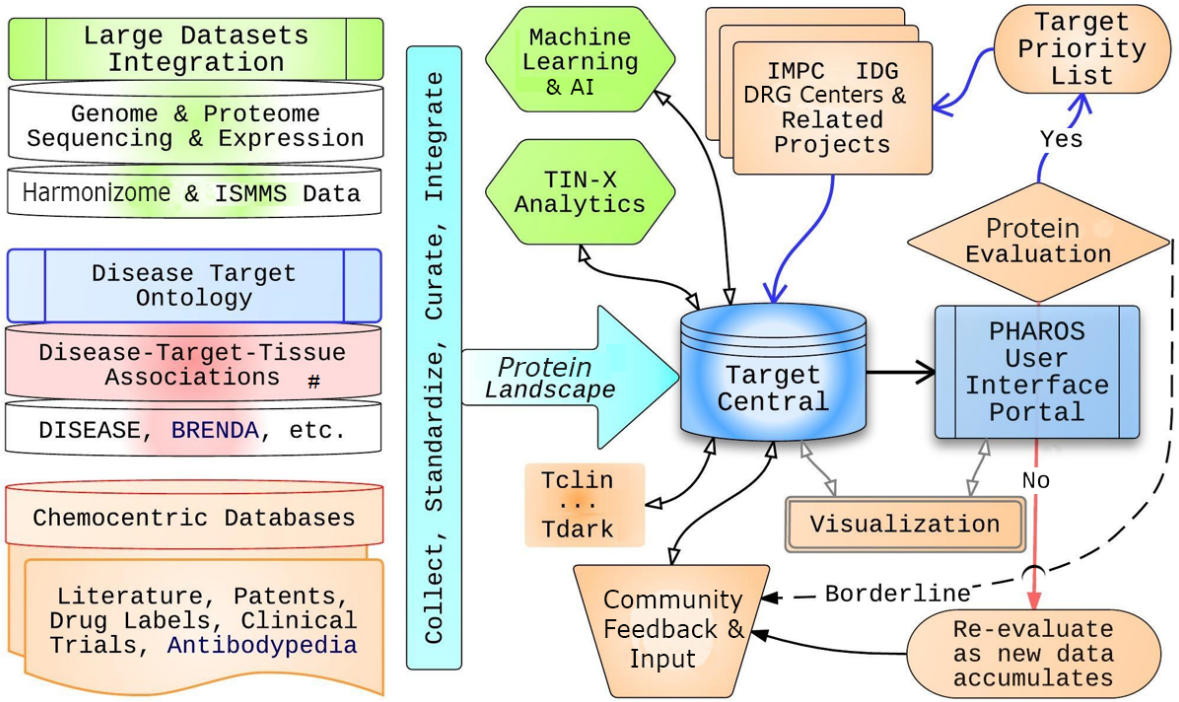
Tudor Oprea, Ph.D., M.D.
Larry Sklar, Ph.D.
University of New Mexico

List-serv: idg.rdoc@gmail.com
Website: http://druggablegenome.net/
Twitter: @DruggableGenome,@IDG_Pharos



Knowledge Management Center

Target Central Resource Database



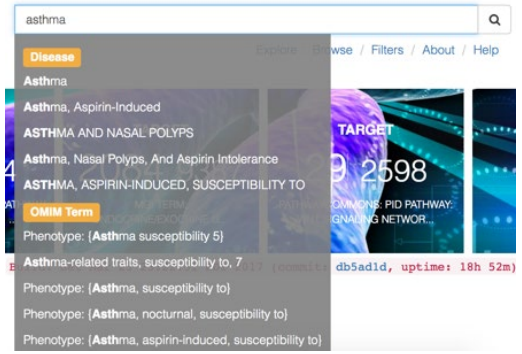
Tudor Oprea, Ph.D., M.D.
University of New Mexico

Avi Ma'ayan
Mt. Sinai

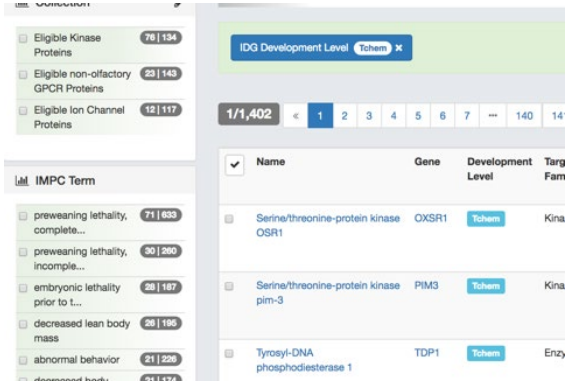
PHAROS

https://pharos.nih.gov/

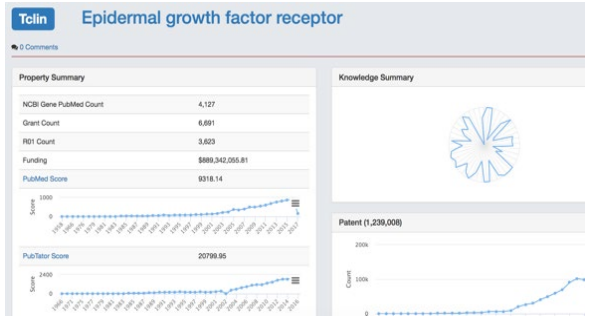
Searchable



Browsable - filters



Detailed protein views



Robust REST API


```
{
  created: 1427039469970,
  modified: 1427039469978,
  etag: "e10325daa1f99e6f",
  uri: "https://pharos.nih.gov/api/targets",
  path: "/api/targets",
  method: "GET",
  sha1: "85e4d4a23ba0f98fbb08fa5449d75493f6f78e1a",
  total: 1789,
  count: 10,
  skip: 0,
  top: 10,
  status: null,
  query: "",
  filter: null,
- content: [
  - {
      id: 6365,
      name: "Lysophosphatidic acid receptor 3",
      description: null,
      idgFamily: "GPCR",
      idgClass: "Tmacro",
      self: "https://pharos.nih.gov/api/targets(63
      _organism: "https://pharos.nih.gov/api/keywc
    - _links: {
        count: 5,
```

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

Program Contact: Jerry Li, MD, PhD; NCI
DruggableGenome@mail.nih.gov

Grants Management Contact: Crystal Wolfrey, NCI
wolfreyc@mail.nih.gov

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Key Dates

Open Date (Earliest Submission Date)	June 15, 2021
Letter of Intent Due Date	June 15, 2021
Application Due Date	July 15, 2021

(by 5:00 PM local time of applicant organization)

We strongly suggest applications are submitted a week in advance

Scientific Merit Review	Nov 2021
Advisory Council Review	January 2022
Earliest Start Date	April 2022

Administrative Details

Read all directions carefully

- Resource Sharing Plan will be considered carefully
- Authentication Plan, if applicable, is now required
  - See: http://grants.nih.gov/reproducibility/faqs.htm
- Consideration of Sex as a Biological Variable in NIH-funded Research
  - http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102.html
- Research Plan
  - There is a 12-page limit
  - Data Sharing Plan does not count towards this limit
  - Do not use the appendix to circumvent the page limit

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Scientific Review

- U01 grants do not use standard R01 review criteria; read RFA.
- Applications deemed to have the highest scientific and technical merit will be discussed and assigned an overall impact score.
- Appeals of initial peer review will not be accepted.
- Recommended applications will receive a second level of review by the NCI Advisory Councils.
- Direct additional peer review questions to:

Vinod Charles, Ph.D.
Center for Scientific Review (CSR)
Email: charlesvi@mail.nih.gov

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Selection Criteria

- The following will be considered in making funding decisions:
  - Scientific and technical merit of the proposed project as determined by scientific peer review.
  - Availability of funds.
  - Relevance of the proposed project to program priorities.
  - Inclusion of **new investigators** and experienced investigators that are **new to IDG consortia**.
  - Evidence that the applicant and investigators are committed to policies as established by the IDG SC including with regard to confidentiality, sharing of information and resources, and cooperative interaction.
  - Evidence of previous productive, cooperative, collaborative interaction.
  - Evidence that the **project will contribute to the diversity of technical and intellectual approaches within the KMC and across the IDG Consortium**.

Resource Sharing Plan

A primary goal of the IDG Program is to make data and resources readily available to the broad scientific community for the improvement of public health.

- Awardees should manage data, resources, protocols, tools, and software in a way that achieves this goal.
- All applications must include a Resource Sharing Plan.
- Applicants should indicate their willingness to abide by all data deposition, quality control metrics, standardization, metadata requirements, data and software release, and public copyright license policies developed by the IDG Steering Committee, including all NIH guidelines.
- Tools need to be made available from Pharos (as appropriate, see https://pharos.nih.gov/idg/faq section Pharos & IDG)

Read the Resource Sharing Instructions Carefully (especially the software sharing plan)
https://grants.nih.gov/grants/guide/rfa-files/RFA-RM-21-020.html#_Section_IV._Application_1

IDG Useful URLs

Webinar URL: https://commonfund.nih.gov/IDG/meetings

Help Email: DruggableGenome@mail.nih.gov

Consortium Homepage: https://druggablegenome.net/

IDG Experimental Resources:
https://druggablegenome.net/IDGResourceTables

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KMC Details: URL Collection

- Pharos: https://pharos.nih.gov/
- Pharos REST API: https://pharos.nih.gov/api
- General Help Page: https://pharos.nih.gov/faq
- Data Sources: https://pharos.nih.gov/about
- Download Pharos data: http://juniper.health.unm.edu/tcrd/download/ (SQL dumps)
- IDG Channel: https://www.youtube.com/channel/UCO71RC4NEvnBPWzj35iqhSg/videos
- IDG Website: https://druggablegenome.net

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Budgets

- Three awards are anticipated under this RFA.
  - Total funds available for this FOA: $1.4 million per annum,
  - Detailed information about NIH Budget preparation is here.
- Application budgets are limited to $300,000 in direct costs (excluding subcontract F&A) per year
  - Need to reflect actual needs of the proposed project
- Maximum project period is 2 years.

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CEIT Goals/Approaches/Strategy

- Predictive Models:
  - Improved ways for associating understudied proteins to biological, disease, or pharmaceutical relevance.
  - Need preliminary/limited experimental data validating the informatics approach (~10% of budget).
  - Make models available to the community via Pharos (see Pharos FAQ: https://pharos.nih.gov/faq)

- Build New Visualizations:
  - Propose new datasets to be incorporated into Pharos and build user-interfaces and visualizations that would enable the community to better utilize and interpret these datasets.

We encourage applications of relevance to Ion Channel Targets

CEIT (Specific/Additional) Review Criteria

- Significance:
  - […] make accurate predictions about the biological roles of an understudied protein?
  - […] is the proposed experimental validation approach suitable and appropriate for generating preliminary (not deep) experimental validation of the method(s)?
- Approach:
  - Are datasets appropriate/justified?
  - Are non-IDG resources proposed to be used freely available?
  - […] containerization, provenances, FAIRness
- Are the plans for making the tools available within Pharos and to the community adequate and appropriate?

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NOT-RM-21-019
Notice of Special Interest (NOSI) for Illuminating the Druggable Genome (IDG) Initiative: Request for Administrative Supplements to Existing Grants for incorporating single cell data into the IDG Knowledgebase

Contact: DruggableGenome@mail.nih.gov

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Key Dates & for NOSI

Application Due Date June 15, 2021
(by 5:00 PM local time of applicant organization)

We strongly suggest applications are submitted a week in advance

Applicants must include "NOT-RM-21-019" (without quotation marks) in the Agency Routing Identifier field (box 4B) of the SF424 R&R form.

Budget: $175K direct cost/yr for 2 years.

Review: Administrative Review

Key Goals NOSI

Applications for supplements to active grants to

- processing,
- query and
- presentation for use by biologists of human single cell data.

Projects submitted to this Notice should enable biologists to prioritize proteins for study based on expression patterns in tissue, systems and cell types.

Create cell x gene matrices

Innovative ideas on how such matrices can be summarized effectively for downstream use by biologists

- following up individual targets and relevance to disease and health

Ease of maintenance of the resulting software

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Questions?

Appendix