

The NIH Common Fund High-Risk High-Reward Research Program

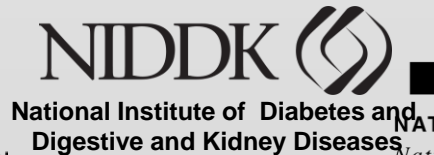
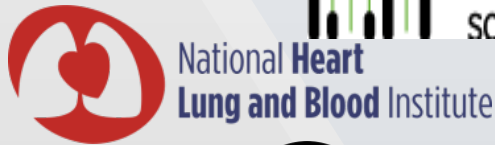
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Office of the Director
NIH

July 16, 2015

The National Institutes of Health



27 NIH Institutes and Centers



NIH Reauthorization Bill (2006) provides broad language:

- Establishes the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)
- Establishes the CF to support cross-cutting, trans-NIH programs that require at least two NIH Institutes or Centers (ICs) or would benefit from strategic planning and coordination
- Office of Strategic Coordination (OSC) within DPCPSI to manage CF

Vision for the Common Fund :

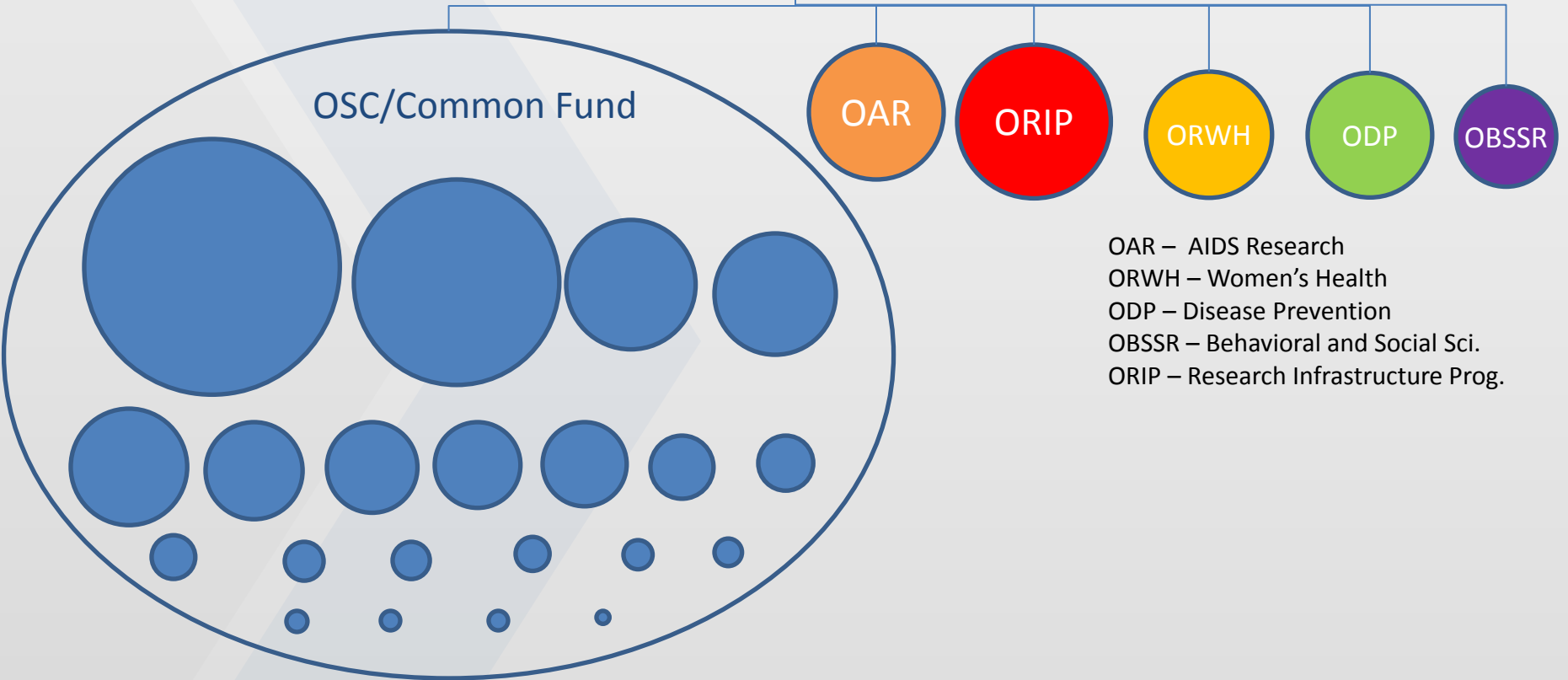
- Serve as a “test bed” for high-risk, enabling programs to overcome significant obstacles to scientific progress and capitalize on emerging scientific opportunities
- Limited-term investment to accelerate the pace of discovery and improve the translation of research findings into medical and health interventions

DPCPSI Scientific Org Chart

5-10 Year efforts to address specific challenges and catalyze IC-funded work



Sustained efforts to stimulate and coordinate research in the ICS

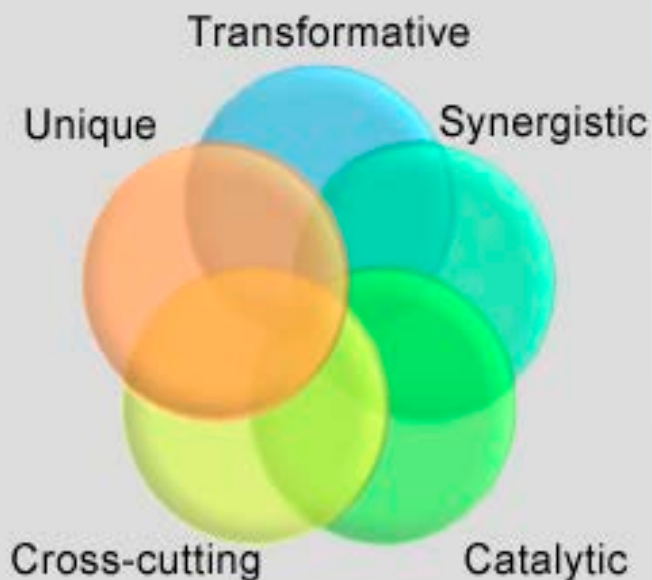


- OAR – AIDS Research
- ORWH – Women’s Health
- ODP – Disease Prevention
- OBSSR – Behavioral and Social Sci.
- ORIP – Research Infrastructure Prog.

Common Fund Enables a Different Approach to Science and Science Management

Transformative: Programs are expected to have exceptionally high and broadly applicable impact.

Catalytic, Short Term and Goal-driven: Programs must achieve - not just work toward - a goal. They have deliverables - data sets, tools, technologies, approaches, or fundamental principles of biology, etc – that can be achieved within 5-10 years.

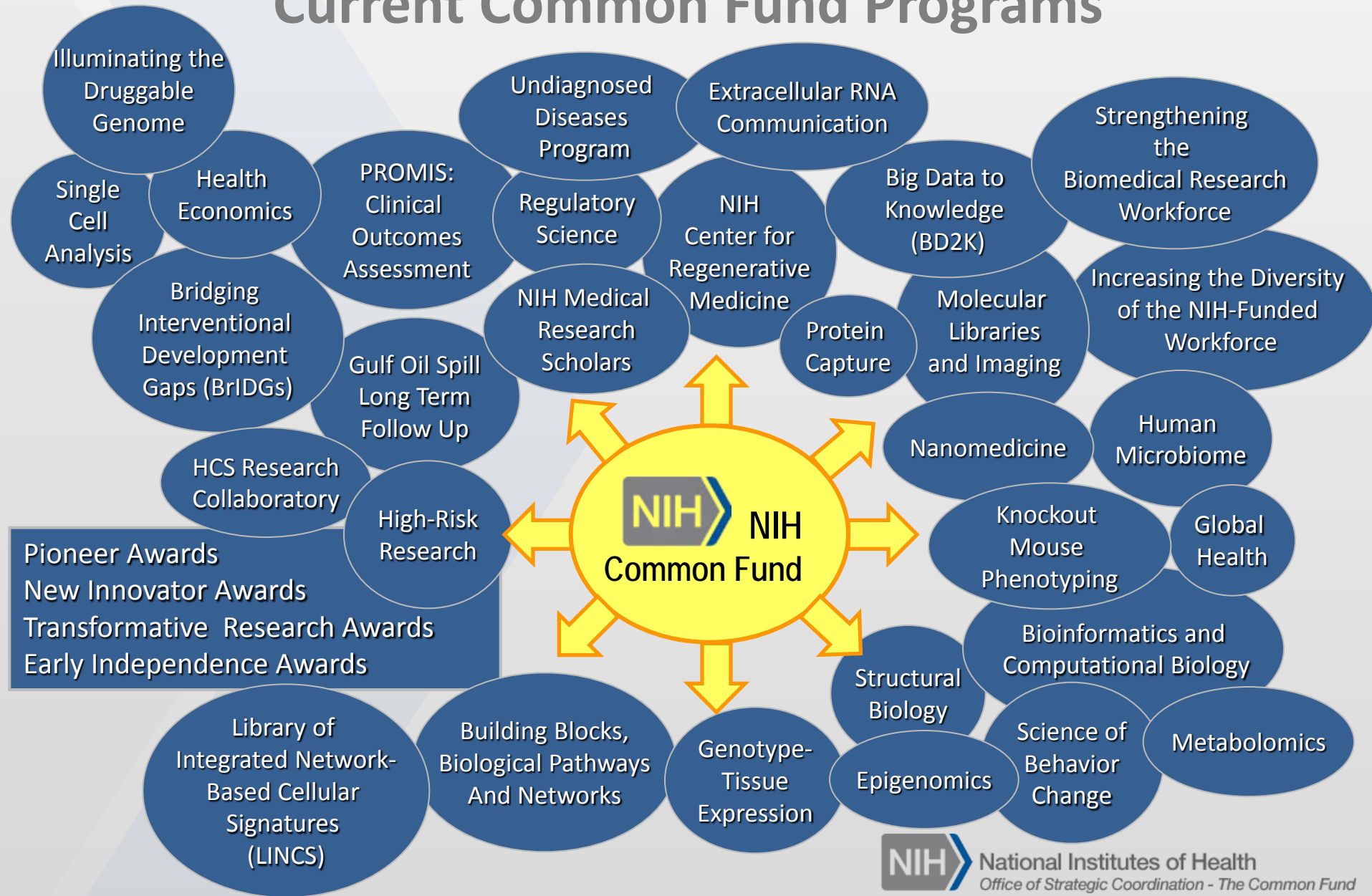


Synergistic /Enabling: Programs should be valued-added to the ICs, with the output enabling the mission of multiple ICs.

Cross-cutting: CF programs should address complex issues that require trans-NIH teams, insights and perspectives to design and manage.

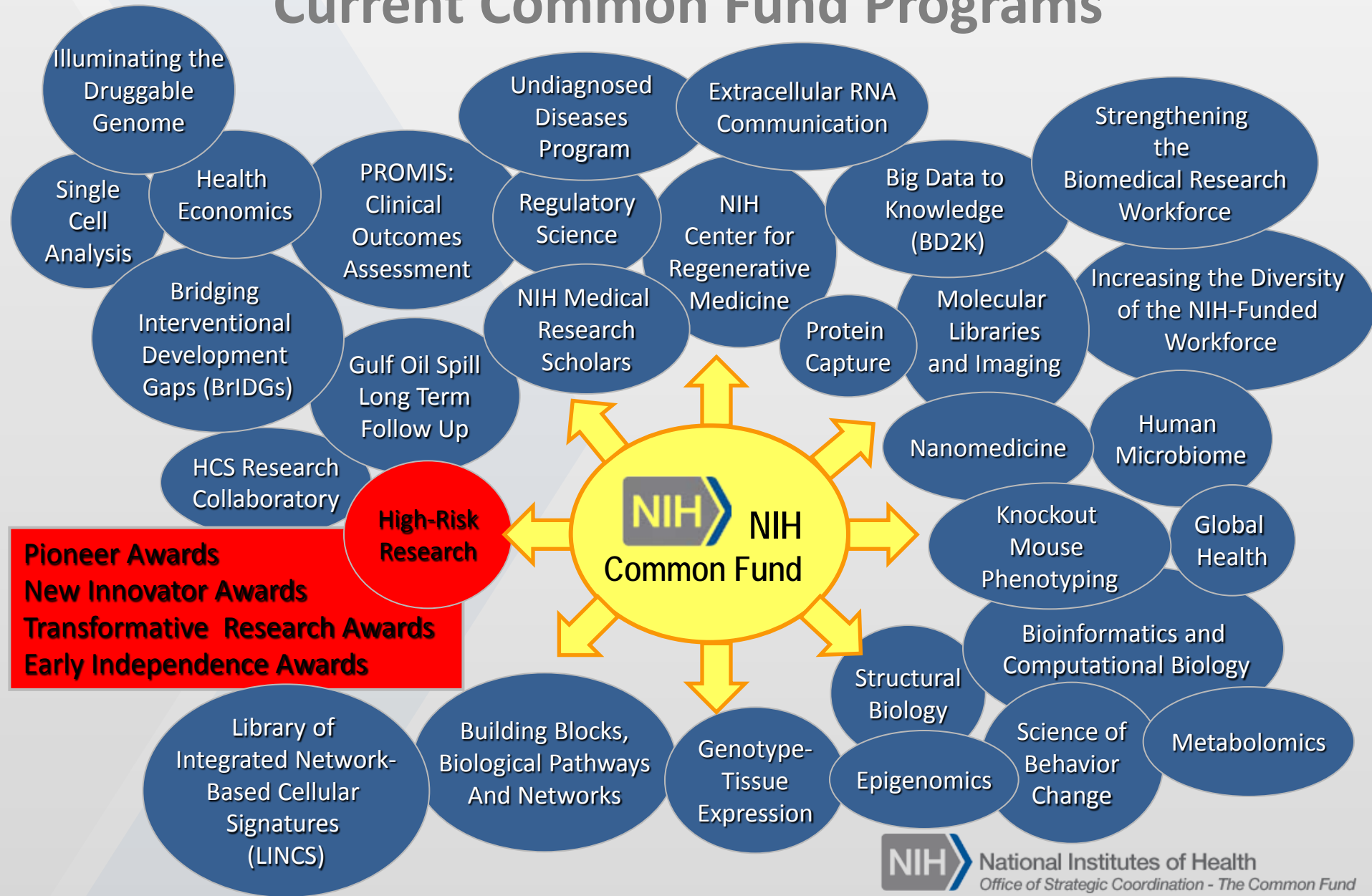
Novel: Programs should provide new solutions to specific challenges.

Current Common Fund Programs



<http://commonfund.nih.gov/>

Current Common Fund Programs



High-Risk High-Reward Initiatives of the NIH Common Fund

(Common Fund program for “investigator-initiated” HRHR research)



Pioneer Award



New Innovator Award



Early Independence Award



Transformative Research Award

NIH Common Fund High-Risk High-Reward Working Group

Chair:

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Director
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director

Common Fund Program Leader:

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Pioneer Award Initiative



- Started in 2004
- Any qualified investigator
- \$500K DC/year for five years
- Individual scientists of exceptional creativity who propose pioneering and possibly transforming approaches to addressing major biomedical or behavioral challenges



Origins of the NIH Director's Pioneer Awards

- Dr. Zerhouni becomes NIH Director in 2002
- Surveys biomedical research committee about research funding and NIH
In responses, sometimes too conservative nature of review is prominent theme
- Because of the conservative nature, opportunities for making leaps in sciences are lost
- Assembles trans-NIH “High-Risk Research Working Group”
- Dr. Zerhouni initiates Pioneer Award program, part of the NIH Roadmap
- First awards made in 2004, awards made annually since then



Fundamental characteristics of the Pioneer Award program

- Person-focused
- Allow unusual flexibility
(Pioneer awardee may change direction of research)
- Provide generous resources
(\$500k direct costs per year for 5 years)



To implement the Pioneer Award program, wanted to make it very distinctive from the major NIH grant Program (R01):

Application format:

Review:

Program administration:



Pioneer Award Application format:

R01: 25 pages research strategy including detailed experimental plan and preliminary data

- **Pioneer:** 3-5 page essay
 - Scientific problem, significance, and pioneering approach
 - Evidence for innovativeness
 - How is research direction different from ongoing?
 - Why Pioneer Award mechanism?

R01: Biographical sketch limit 4 pages

- **Pioneer:** Biographical Sketch - 2 pages

R01: Budget, animal, human subject information – details required

- **Pioneer:** No detailed budget, other information brief

R01: letters of collaboration encouraged

- **Pioneer:** letters of collaboration not allowed



Pioneer Award Application format (continued):

Components of Pioneer application not present for R01 application

- **Most significant research accomplishment (one page max.)**
- **Statement of suitability of proposal for Pioneer - research must be different from established research projects in the applicant's laboratory**
- **Statement of commitment of at least 51% research effort to project**
- **Three letters of references**

Pioneer application format designed to focus on person and scientific vision



Pioneer Award Review process:

R01 review:

Review by a single panel

Review by topic experts

Asked to consider: significance/impact, innovation, approach, investigator, and environment

Focus tends to be on approach and feasibility

➤ Pioneer review:

Review through 2 phase review (2 panels)

Reviewers not assigned by specific topic expertise

Asked to consider: innovation/impact, investigator, and suitability for award

Involves in-person interviews



Overall Pioneer Review Process

Phase I
(electronic
panel)

Electronic review of
all
applications

Identify 25
for
interview

Phase II
(interview
panel)

Interview
25

Provide scores



Pioneer Award Review – 1st phase

Phase I
(electronic panel)

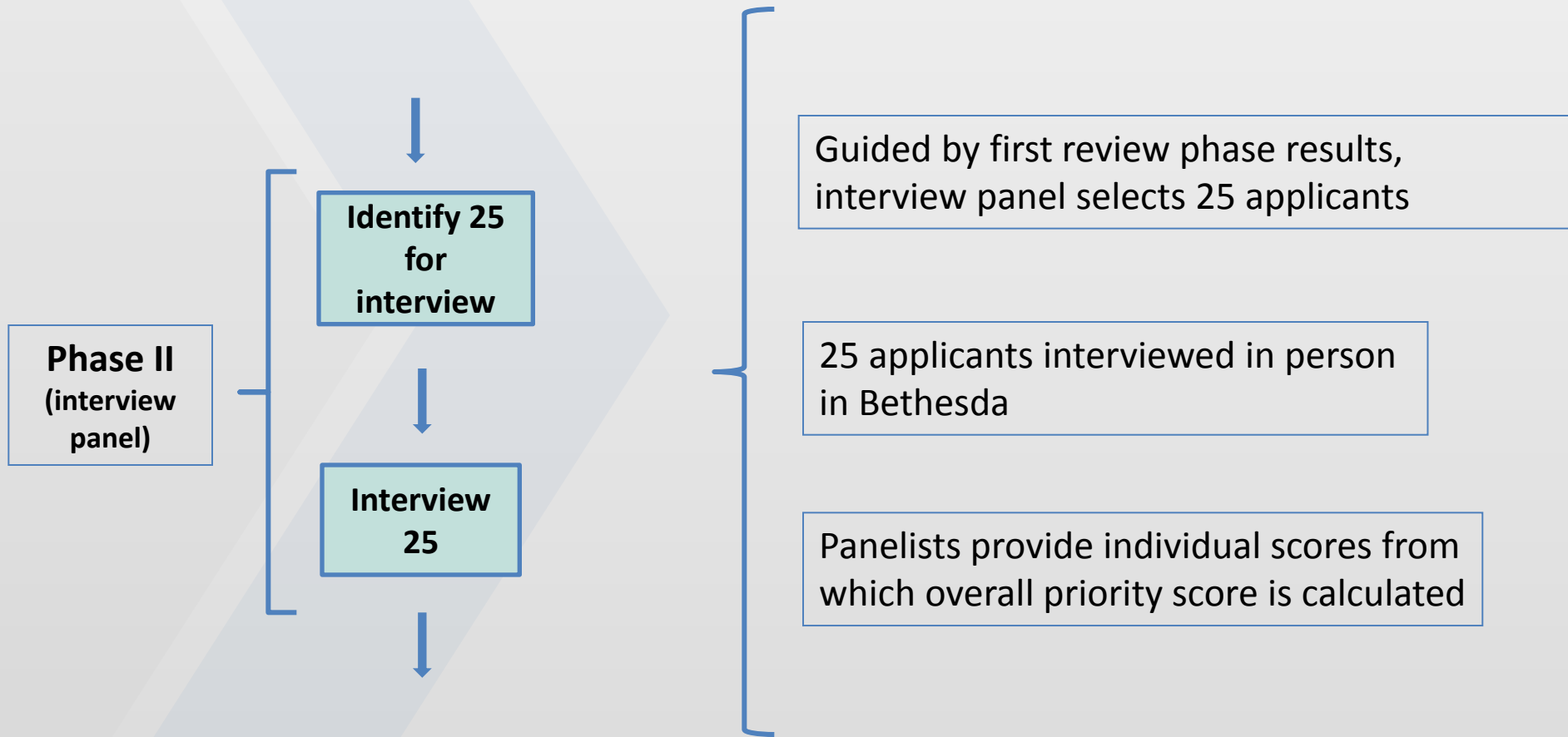
**Electronic review of
all
applications**



- No attempt to closely match reviewer expertise to proposal topic – 1 reviewer must be outside broad science area
- Use 3 Pioneer-specific review criteria
 - Proposal
 - Investigator
 - Suitability for Pioneer program
- Reviewers provide only scores and brief comments
- No discussion of applications/scores



Pioneer Award Review – 2nd phase





Pioneer Awards – Program Administration

- Pioneer project must represent at least 51% of the awardees research effort (first 3 years, reduced to 33% and 25% in 4th and 5th years, respectively)
- Pioneer Awardee allowed to change course of research direction, to follow most promising path as the science evolves
- Acknowledgment that not all projects will succeed as proposed



Pioneer Awards – Comparison Evaluation

- Evaluation of Pioneer supported research
- Conducted by independent entity (Science and Technology Policy Institute of the Institute for Defense Analysis)
- Compared research outcomes of Pioneers (first three cohorts) to comparison groups (similarly qualified R01 investigators, random R01 sets, and HHMI investigators)
- Used both bibliometric and expert analysis to assess scientific impact and innovation
- Concluded that Pioneers have more impact than similarly qualified R01 investigators and random R01s and about as much impact as HHMI investigators
- Evaluation available at http://commonfund.nih.gov/sites/default/files/P-4899_Final_Redacted.pdf



New Innovator Award Program

- Started in 2007 (in response to concerns that young investigators had difficulty in being funded)
- Must be Early Career Stage Investigator at time of award (<10 years from Ph.D./clinical residency with no significant NIH support as PI)
- Up to \$300K DC/year for five years (MYF at \$1.5M)
- Highly innovative research ideas
- Investigators must have track record of exceptional creativity and have outstanding promise



New Innovator Awards program implementation:

- Very similar in spirit to the Pioneer Awards
- Focuses on the individual
- Limited to Early Career Stage Investigators
- Application is longer (10 page essay, preliminary data allowed but not required)
- Review criteria very similar
- Review process also has two phases but the second does not include interviews

Transformative Research Award Program



- Started in 2009
- Arose from NIH Innovation workshop and Enhancing Peer Review process
- Individuals or teams with a project to overturn or create a fundamental paradigm
- Focus is more on the idea than the individual(s)
- “Outside-the-box” ideas
- “No limit” budget



Transformative Research Award Program - implementation

- Focuses more on the project than the individual(s)
- Encourage teams of investigators to apply
- Application was shorter than standard R01, but now uses standard format
- Application directs individuals to address program specific aspects, such as challenge, impact, innovation, suitability
- Review process uses “Editorial Board” model
 - Editorial Board screens all applications to identify most exciting subset (assignments not made on close topic expertise)
 - Most exciting subset sent forward for technical review by experts
 - Editorial Board uses technical review to discuss and score

Early Independence Award Program



- Started in 2011
- Started because of extraordinary length of time typically taken for an investigator to get first NIH R01 grant (~42 years old)
- Graduate students and clinicians within one year of degree or clinical residency who wish to “skip” the post-doc
- Talented young scientists who have the intellect, scientific creativity, drive and maturity to flourish independently without the need for traditional post-doctoral training
- Up to \$250k DC/year for 5 years

Early Independence Award Program - implementation

- Each institution is allowed to submit up to only 2 applications
- Uses standard R01 application packet, but with applicants focusing on program specific topics

Three to five letters of recommendation required

Review process is similar to that of Pioneer

- All applications sent for technical review
- Panel selects ~30 of these for in-person interview

Site visit first year to awardees' institutions

Since still an experimental program, all awards remain as "OD" awards

Annual NIH Common Fund High-Risk, High-Reward Symposium

2014 High-Risk, High-Reward Research Symposium



December 15-17, 2014 - Bethesda, MD

[Agenda](#) • [Abstracts](#) • Videocasts from [Day 1](#), [Day 2](#), and [Day 3](#)



Save the date for the **2015 High-Risk, High-Reward Research Symposium** on December 7-9 at Natcher Conference Center, NIH, Bethesda, MD!

Stanford-affiliated Pioneer Award Recipients

| Recipient | Fiscal Year | Project Title |
|--------------------------|-------------|--|
| DEISSEROTH, KARL A. | 2005 | NIH Director's Pioneer Award (RMI) |
| HARBURY, PEHR A | 2005 | NIH Director's Pioneer Award (RMI) |
| RANDO, THOMAS A. | 2005 | NIH Director's Pioneer Award (RMI) |
| BOAHEN, KWABENA | 2006 | NIH Director's Pioneer Award |
| KIRKEGAARD, KARLA | 2006 | NIH Director's Pioneer Award |
| RELMAN, DAVID A. | 2006 | NIH Director's Pioneer Award |
| CLANDININ, THOMAS ROBERT | 2007 | Dissecting the functional anatomy of the visual system: a new way forward |
| SCHNITZER, MARK J | 2007 | Massively Parallel Brain Imaging |
| CHEN, JAMES K | 2008 | Chemical Embryology: Technologies for Manipulating and Visualizing Development |
| DOLMETSCH, RICARDO E. | 2008 | Using induced pluripotent stem cells to identify cellular phenotypes of autism |
| CHAWLA, AJAY | 2009 | Immune Triggers of Tissue Regeneration |
| CHEN, CHANG-ZHENG | 2009 | The Role of Pre-miRNA Loop in Target Regulation by microRNA Genes |
| COVERT, MARKUS W | 2009 | A Gene-Complete Computational Model of Yeast |
| SHENOY, KRISHNA V | 2009 | Toward an Animal Model of Freely Moving Human |
| SCHNEIDER, DAVID S. | 2011 | Mapping the road to recovery - Does the way we get better differ from the way we |
| BRUNET, ANNE | 2012 | Transgenerational epigenetic inheritance of longevity |
| SMOLKE, CHRISTINA D | 2012 | Synthetic Biology Platforms for Natural Product Discovery and Biosynthesis |
| LIN, MICHAEL Z. | 2013 | Optogenetics for all: A general method for optical control of protein activity |
| WU, SEAN M | 2014 | Enabling Technologies for Human-Machine Hybrid Tissues |



Sean Wu (2014)

Project Title: [Enabling Technologies for Human-Machine Hybrid Tissues](#)

Stanford-affiliated New Innovator Award Recipients

| Recipient | Fiscal Year | Project Title |
|---------------------|-------------|---|
| BRYANT, ZEV | 2008 | Engineering Molecular Motors |
| KESLER, SHELLI R. | 2008 | Assessment and Treatment of Cognitive Deficits in Breast Cancer |
| WU, JOSEPH C. | 2008 | Inducing Pluripotency with MiRNAs: New Paradigm Shift in Cell Reprogramming |
| ASHLEY, EUAN A | 2009 | Nanoscale approaches to allelic silencing in myocardial disease states |
| HEILSHORN, SARAH C | 2009 | Engineering 3D in vitro niches to reveal fundamentals of cellular biomechanics |
| HUANG, KERWYN C | 2009 | Engineering of cell shape and intracellular organization |
| PENN, ANNA A | 2009 | Fetal Brain Damage: A Placental Disorder |
| SONNENBURG, JUSTIN | 2009 | Discovery of gut microbiota-targeted small molecules: new tools and therapies |
| CEGELSKI, LYNETTE S | 2010 | Structure, Function, and Disruption of Microbial Amyloid Assembly and Biofilm |
| DUNN, ALEXANDER R | 2010 | Uncovering New Roles for Mechanical Force in Tissue Development and Remodeling |
| FELDMAN, BRIAN J | 2010 | Using Components of the Circadian Clock to Regulate Stem Cell Fate Decisions |
| FRASER, HUNTER B | 2011 | Systematic functional annotation of human cis-regulatory genetic variation |
| WANG, CHIH-HUNG | 2011 | Healthy Ideas Exchange |
| CARETTE, JAN EDUARD | 2012 | Genetic approaches to discover host factors critical to dengue virus infection |
| CUI, BIANXIAO | 2012 | Engineering external forces for manipulating cargo transport in live neurons |
| ROHATGI, RAJAT | 2012 | Reconstructing Primary Cilia |
| URBAN, ALEXANDER | 2012 | Genomic and epigenomic effects of large CNV in neurons from iPSC |
| BLISH, CATHERINE A | 2013 | Harnessing natural killer cell memory to fight viruses |
| DIEHN, MAXIMILIAN | 2013 | Developing a genomic approach for cancer screening |
| SATTELY, ELIZABETH | 2013 | Liberation of Plant Nutrients by the Gut Microbiota |
| BASSIK, MICHAEL C | 2014 | Accelerating drug development and repurposing using systematic genetic interactions |



Catherine A. Blish (2013)

Project Title: [Harnessing Natural Killer Cell Memory to Fight Viruses](#)



Maximilian Diehn (2013)

Project Title: [Developing a Genomic Approach for Cancer Screening](#)



Elizabeth Sattely (2013)

Project Title: [Liberation of Plant Nutrients by the Gut Microbiota](#)



Michael C. Bassik (2014)

Project Title: [Accelerating Drug Development and Repurposing Using Systematic Genetic Interactions](#)

Stanford-affiliated Transformative Research Award Recipients

| Recipient | Fiscal Year | Project Title |
|----------------------------------|-------------|--|
| KUO, CALVIN J | 2009 | Three-dimensional Scaffold-based Systems for Primary Human Intestinal Culture |
| PARSONNET, JULIE | 2009 | Childhood infection and prevention of obesity |
| WU, JOSEPH C. | 2009 | Re-Education of the Immune System for hES Cell Tolerance |
| PELTZ, GARY A | 2010 | Human Pharmacogenetics and Human Liver Regeneration |
| WERNIG, MARIUS; SUDHOF, THOMAS C | 2010 | Direct conversion of fibroblasts into neurons: A novel approach to study neuropsychy |
| BOAHEN, KWABENA | 2011 | Fully Implantable and Programmable Spike-based Codecs for Neuroprosthetics |
| PUGLISI, JOSEPH D | 2011 | Single molecule translational profiling |
| BARRES, BEN A | 2012 | An Astrocytic Basis for Humanity |
| BLAU, HELEN M | 2012 | Telomere extension using nucleoside-modified mRNA and exosomes as a novel therapy |
| DEISSEROTH, KARL A. | 2012 | CLARITY: fully-assembled biology |



Ben A. Barres (2012)

Project Title: [*An Astrocytic Basis for Humanity*](#)



Helen M. Blau (2012)

Project Title: [*Telomere extension using nucleoside-modified mRNA and exosomes as a novel therapy*](#)



Karl Deisseroth (2012)

Project Title: [*CLARITY: fully-assembled biology*](#)

Stanford-affiliated Early Independence Award Recipients

| Recipient | Fiscal Year | Project Title |
|------------------------|-------------|---|
| DE LA ZERDA, ADAM | 2012 | Molecular Imaging of Protein Glycosylation in Living Subjects |
| YEH, ELLEN | 2012 | Defining the novel eukaryotic biology of the Apicomplexan plastid |
| ANGELO, ROBERT MICHAEL | 2014 | Predictive signatures in breast cancer using multiplexed ion beam imaging |
| NELSON, ERIC JORGE | 2014 | A novel approach to improve patient care and diarrheal disease research using mobile technology |



Michael Angelo (2014)

Project Title: [Predictive Signatures in Breast Cancer using Multiplexed Ion Beam Imaging](#)



Eric Jorge Nelson (2014)

Project Title: [A Novel Approach to Improve Patient Care and Diarrheal Disease Research using Mobile Technology](#)

Do you have any wild and crazy ideas?

| APPLICATION STATUS | | | | |
|---------------------------|---------------------------------|---|--|--|
| | Early Independence Award | New Innovator Award | Pioneer Award | Transformative Research Award |
| FY 2015 | Applications Under Review | Applications Under Review | Applications Under Review | Applications Under Review |
| FY 2016 | Not Available | RFA-RM-13-007 Due October 16, 2015 | RFA-RM-13-006 Due October 9, 2015 | RFA-RM-15-005 Due October 9, 2015 |

<http://commonfund.nih.gov>