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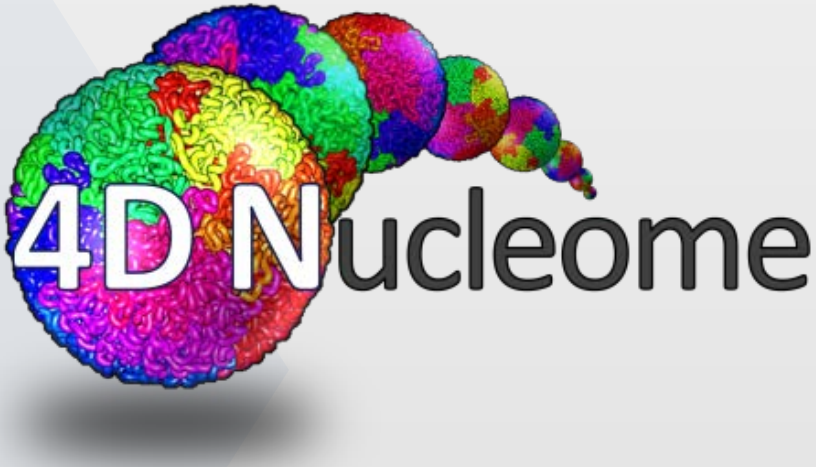

November 10, 2014, Noon-2:00pm Eastern Time

To submit questions to be answered during the webinar, please email questions to: 4DNucleome@mail.nih.gov.

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Origins of the Common Fund

One Hundred Ninth Congress
of the
United States of America

AT THE SECOND SESSION

Begun and held at the City of Washington on Tuesday, the third day of January, two thousand and six

An Act

To amend title IV of the Public Health Service Act to revise and extend the authorities of the National Institutes of Health, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "National Institutes of Health Reform Act of 2006".

TITLE I—NIH REFORM

2004: NIH Roadmap is launched

December 9, 2006: Congress unanimously passes a reauthorization bill affirming importance of NIH and its vital role in advancing biomedical research to improve the health of the Nation

Established the **Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)** within Office of the Director and the **NIH Common Fund** to provide a dedicated source of funding to enable **goal-driven trans-NIH research**

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Common Fund Enables a Different Approach to Science and Science Management

Transformative: Programs are expected to have **exceptionally high and broadly applicable impact.** They should be relevant to many diseases. They should set new standards for research or clinical practice, create entirely new approaches to research or clinical care, or establish new biological paradigms.

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 NIH Institutes and Centers, with the output enabling the mission of NIH.

Requires a High Level of Trans-NIH Coordination: CF programs should address complex issues requiring trans-NIH teams, insights, and perspectives to design and manage. There must be a reason why strategic coordination is required.

Novel: Programs should provide new solutions to specific challenges.

Designed to accomplish goals and deliverables within 5-10 years
Evaluation of program outputs/outcomes is essential

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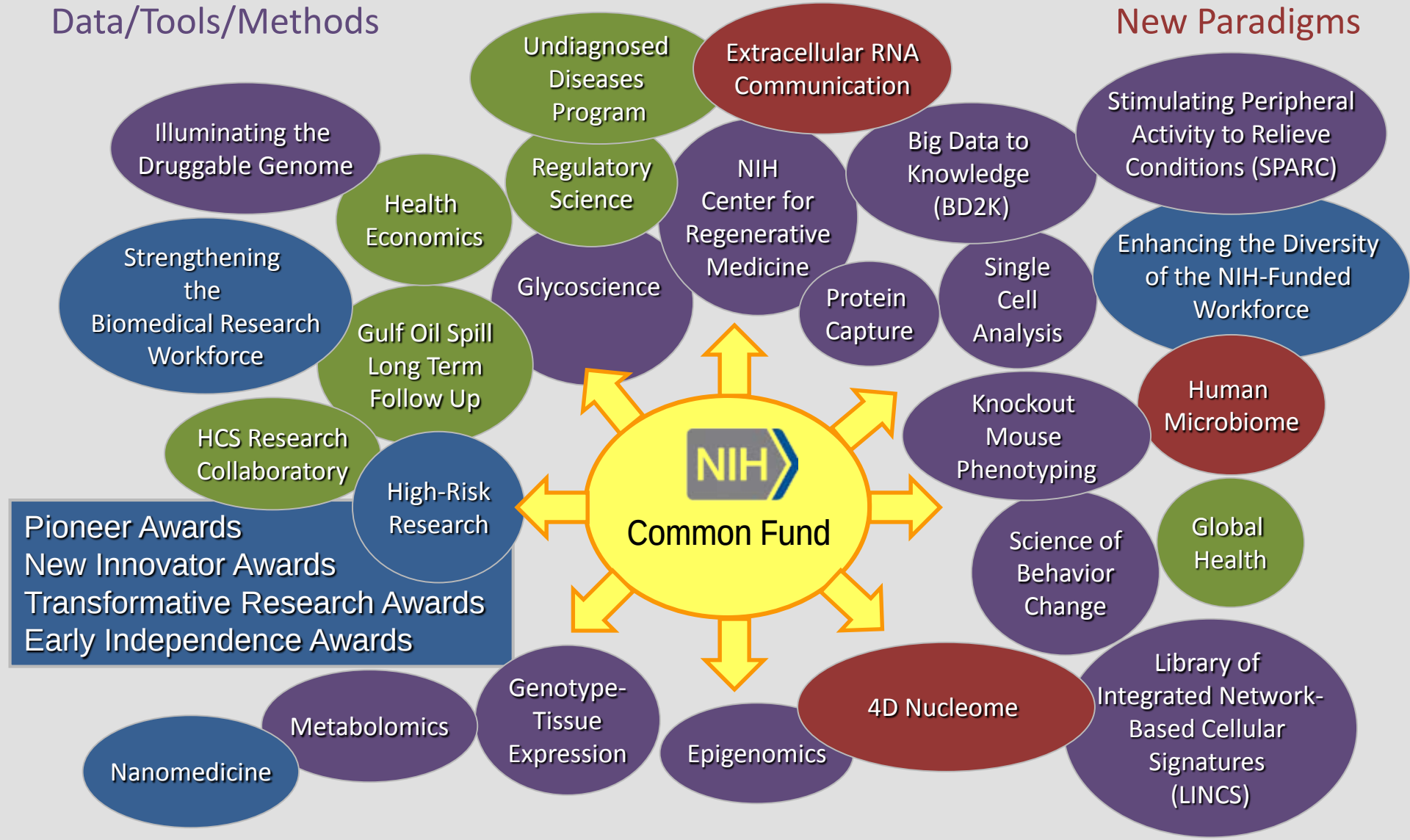
Current Common Fund Programs (FY15)



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CF Programs Build "Foundations" to Catalyze Research

- **New Approaches to Foster Innovation and Build Multi-Disciplinary Research Teams**
  - High-Risk High-Reward (Pioneer, New Innovator, Transformative Research, Early Independence Awards)
  - Nanomedicine
  - ExRNA Communication
- **New Tools, Infrastructure, and Data to Support or Establish New Fields of Study**
  - Human Microbiome Project
  - Epigenomics
  - Knockout Mouse Phenotyping
- **New Technologies and Approaches to Overcome Barriers to Progress in a Field**
  - Structural Biology
  - Regulatory Science – Tissue Chip for Drug Screening
  - Strengthening the Biomedical Research Workforce – New training approaches

CF Programs Emphasize Clear Goals, Milestones, and Deliverables

- To achieve maximum impact within a limited (5-10 year) time frame, Common Fund programs are driven by well-defined quantitative goals and milestones, and aim to produce concrete deliverables that will catalyze research beyond the lifetime of the program.
- All initiatives will have clear goals and milestones, and progress towards these goals and milestones will be used to evaluate the success of the program.
- An External Scientific Panel (ESP) of experts will assess progress towards goals and milestones on a regular basis.
- **Deliverables are KEY!** The 4DN program will produce data sets, tools, technologies, and other resources that will be widely disseminated to the scientific community

Finishing the Job:
Understanding Genome Organization

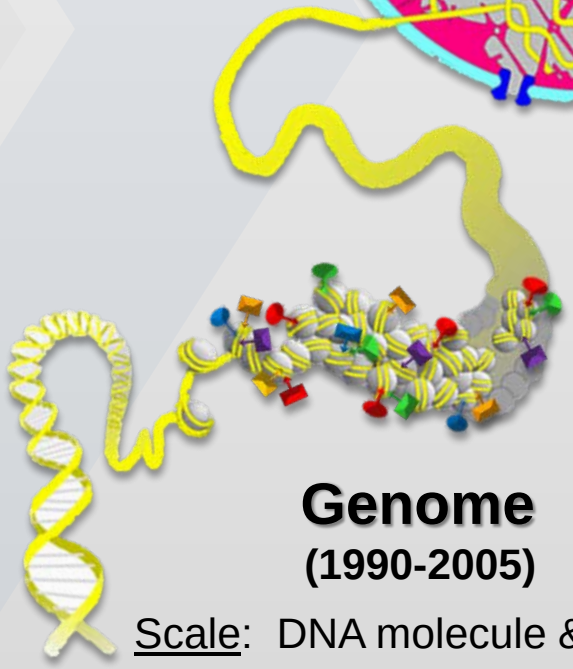
4D Nucleome

3D Nucleome
(2015-2022?)

Scale: cell nucleus & chromatin domains

ENCODE

ROADMAP epigenomics PROJECT



Epigenome
(2005-2015)

Scale: nucleosome & epigenetic marks

Human Genome Project

Genome
(1990-2005)

Scale: DNA molecule & sequence

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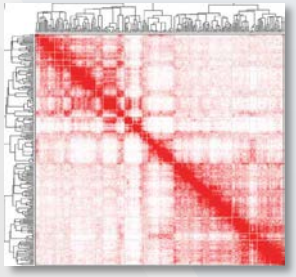
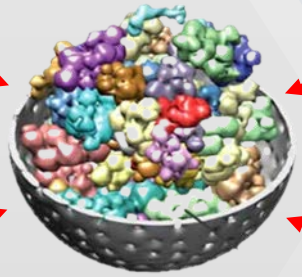
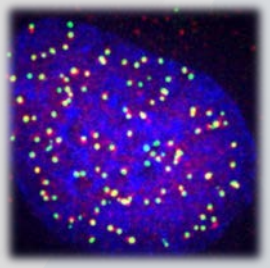
Some Deliverables of the 4DN Program



Global interactions between gene loci and regulatory elements.



Predictive modeling of structure/function relationships.



Imaging dynamics of nuclear interactions in single cells.

- **Development of the next generation tools** to explore relationship between genome organization and function;
- **Reference maps** of the 3D organization of the genome in a variety of human cells/tissues and cell states;
- **Predictive models** of structure/function relationships;
- **Biological validation** through controlled disruption of nuclear architecture and single-cell imaging, and in the context of specific biological paradigms;
- **Development of community standards and metrics;**
- **Greater understanding of poorly-characterized nuclear structures and nuclear bodies** and their contribution to genome organization.

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Six Related Funding Opportunity Announcements

Nuclear Organization and Function Interdisciplinary Consortium (NOFIC) (U54) (RFA-RM-14-006): NOFIC will be composed of multidisciplinary teams that will develop and validate novel approaches and genome-wide mapping technologies that will lead to a deeper understanding of nuclear organization in time and space, and the role of this organization in regulating gene expression programs.

Nucleomics Tools (U01) (RFA-RM-14-007): development and validation of chemical and biochemical approaches for measuring specific aspects of 3D nuclear organization of the mammalian genome.

Study of Nuclear Bodies and Compartments (U01) (RFA-RM-14-008): This initiative will support the development of tools and strategies to study the three dimensional architecture of the nucleus in relationship to the spatial arrangement of nuclear bodies and molecular machinery regulating gene expression, the structure and function of poorly characterized nuclear structures and compartments, and the role of specialized proteins and RNAs in nuclear organization and function.

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Six Related Funding Opportunity Announcements

4D Nucleome Imaging Tools (U01) (RFA-RM-14-009): This initiative will stimulate the development of novel or higher throughput, higher resolution and higher content imaging approaches that can measure changes in nuclear organization in live single cells.

4D Nucleome Network Organizational Hub (U01) (RFA-RM-14-010): The 4DN-OH will develop a community website to facilitate sharing of data, reagents, standards, and protocols; foster collaborations; organize yearly scientific meetings; and oversee administrative aspects of the program. 4DN-OH will also administer the Opportunity Pool, a fund to support new projects, initiatives and collaborations.

4D Nucleome Network Data Coordination and Integration Center (U01) (RFA-RM-14-011): 4DN-DCIC will track, store, and display all data generated by 4D Nucleome investigators; provide a Data Analysis Center to assist with integrated analyses; develop metrics and standards to be adopted by the community at large; and provide visualization tools to facilitate access and understanding of complex datasets.

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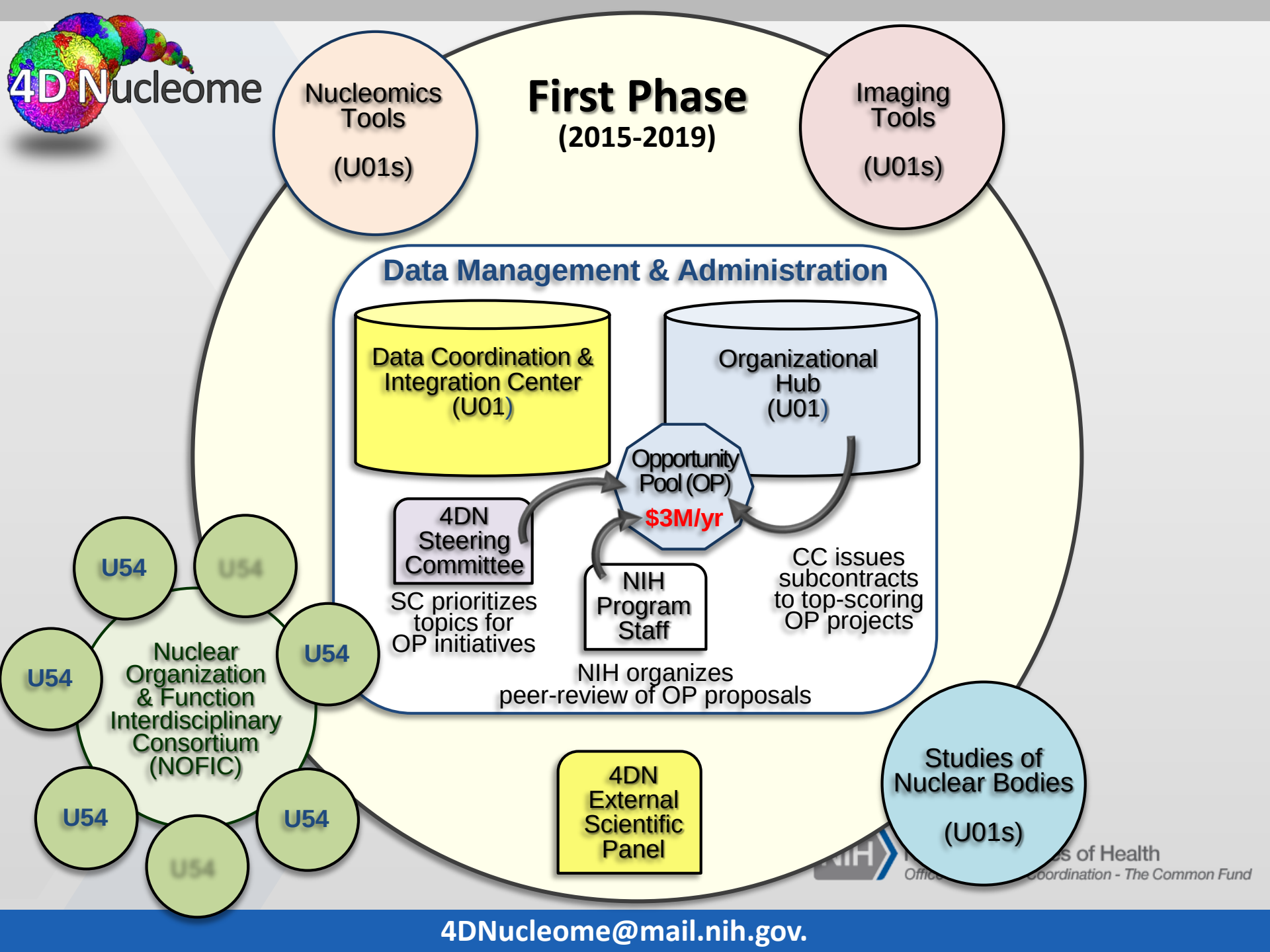
4D Nucleome
First Phase
(2015-2019)
Nucleomics Tools
(U01s)
Imaging Tools
(U01s)
Data Management & Administration
Data Coordination & Integration Center (U01)
Organizational Hub (U01)
Opportunity Pool (OP)
$3M/yr
4DN Steering Committee
SC prioritizes topics for OP initiatives
NIH Program Staff
NIH organizes peer-review of OP proposals
CC issues subcontracts to top-scoring OP projects
U54
U54
U54
U54
U54
U54
Nuclear Organization & Function Interdisciplinary Consortium (NOFIC)
4DN External Scientific Panel
Studies of Nuclear Bodies
(U01s)
s of Health
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Important Dates

- **Letter of Intent Due Date**: - November 16, 2014: NOFIC + Data CC + Organiz. Hub
  - January 2, 2015: Nucleomics + Imaging + Nuclear Bodies
- **Application Receipt**: - December 16, 2014: NOFIC + Data CC + Organiz. Hub
  - February 2, 2015: Nucleomics + Imaging + Nuclear Bodies
- **Scientific Merit Review**: - February/March, 2015: NOFIC + Data CC + Organiz. Hub
  - May/June, 2015: Nucleomics + Imaging + Nuclear Bodies
- **Advisory Council**: - May, 2015: NOFIC + Data CC + Organiz. Hub
  - August, 2015: Nucleomics + Imaging + Nuclear Bodies
- **Earliest Start Date**: - July 2015: NOFIC + Data CC + Organiz. Hub
  - September, 2015: Nucleomics + Imaging + Nuclear Bodies

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SCIENTIFIC PEER REVIEW

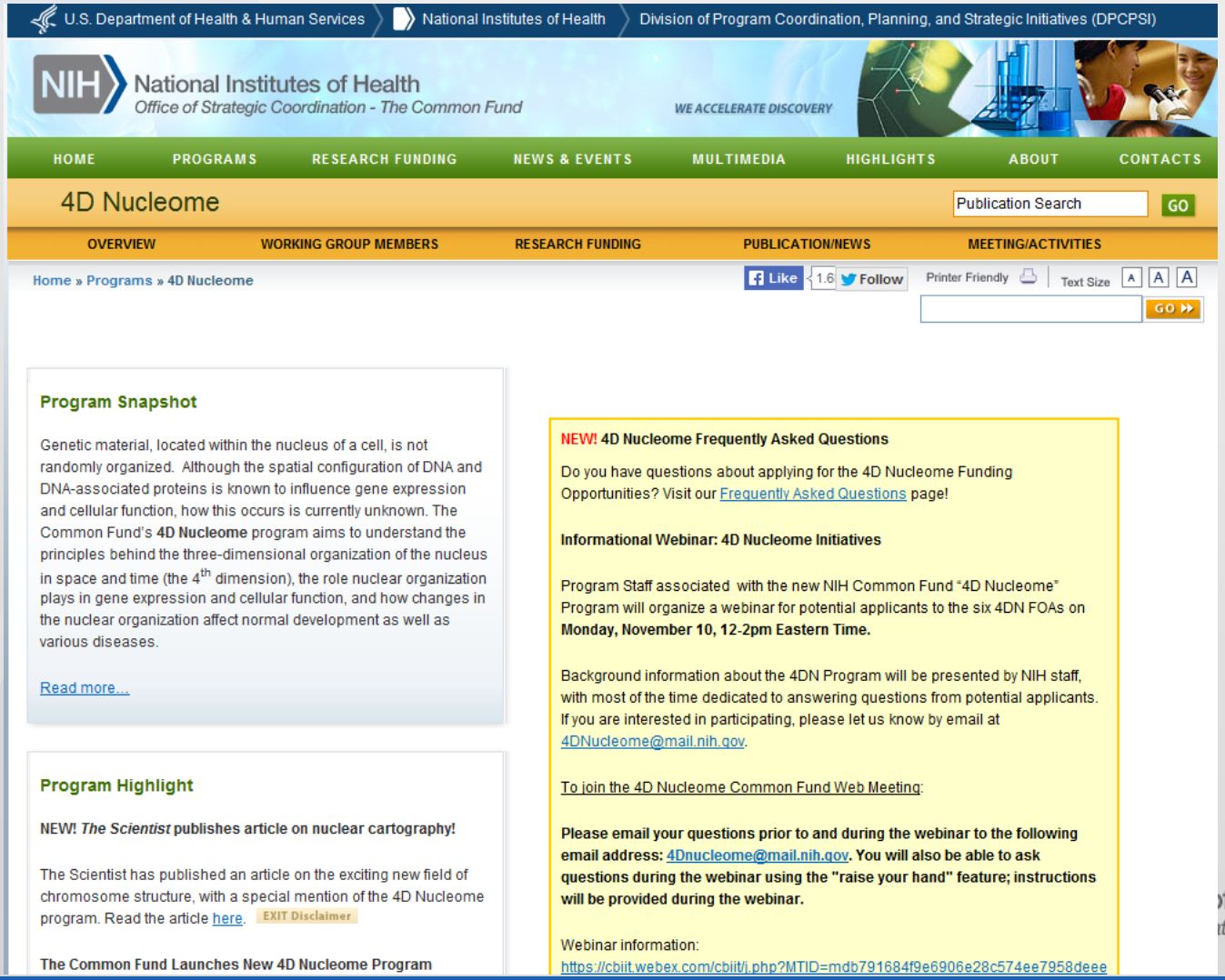
All applications will be reviewed and evaluated:

- For scientific and technical merit by appropriate Scientific Review Groups/Special Emphasis Panels (SEPs) convened by the Center for Scientific Review. Assignment to a Scientific Review Group/SEP will be shown in the eRA Commons.
- During the months of February through June, 2015.
- In accordance with NIH peer review policy and procedures.
- Based on their compliance with the stated Objectives of each RFA.
- Using the stated Review Criteria as indicated under each RFA. Note the "*Specific to this FOA*" section under each Review Criterion.
- Through a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score. However, all applications will receive a written critique within 30 calendar days from the date of review.

Questions regarding the Peer review Process? Please contact Dr. David Balasundaram at balasundaramd@csr.nih.gov

4DN Website

http://commonfund.nih.gov/4Dnucleome/index



4DN Working Group

Co-Chairs:
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Phil Smith, Ph.D. (NIDDK)

Working Group Coordinators:
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Members:
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Lisa H. Chadwick, Ph.D. (NIEHS)
Richard Conroy, Ph.D. (NIBIB)
Sean Hanlon, Ph.D. (NCI)
Patricia (Trish) Labosky, Ph.D. (NIH OD)
Mike Pazin, Ph.D. (NHGRI)
Lisa Postow, Ph.D. (NHLBI)
Matt Reilly, Ph.D. (NIAAA)
Robert Riddle, Ph.D. (NINDS)
John Satterlee, Ph.D. (NIDA)
Geetha Senthil, Ph.D. (NIMH)
Jose Velazquez, Ph.D. (NIA)

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Frequently Asked Questions

1. What exactly is a U01? A U54? Does it require a group of PIs?

2. Are team projects favored over individual lab projects?

3. How many projects will be funded under each category?

4. What is the cap on awarded funds for each U54? U01?

5. Renewal after 5 years?

6. Are early stage investigators (ESI) encouraged to apply? Will ESI projects be reviewed the same as from senior PIs?

7. Are non-US investigators encouraged to apply?

8. Can I apply to multiple FOAs? What about overlap?