The NIH Common Fund
Single Cell Analysis Program:
An Early Outcomes Assessment

Program Evaluation Special Interest Group Meeting
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What is the NIH Common Fund?

- Supports a set of trans-NIH scientific programs
- “Venture capital” space for high-risk, innovative endeavors with potential for extraordinary impact
- Short-term (5-10 year), goal-driven programs focused on developing specific deliverables (data, tools, technologies, etc.) to catalyze research
- Managed by the Office of Strategic Coordination within the NIH Office of the Director, in partnership with the NIH Institutes and Centers.

Common Fund programs are intended to benefit the entire biomedical research community
Common Fund Programs

New Types of Clinical Partnerships

- Illuminating the Druggable Genome
- Strengthening the Biomedical Research Workforce
- Health Economics
- HCS Research Collaboratory
- Undiagnosed Diseases Network
- High-Risk Research
- Pioneer Awards
- New Innovator Awards
- Transformative Research Awards
- Early Independence Awards

Data/Tools/Methods

- Big Data to Knowledge (BD2K)
- Stimulating Peripheral Activity to Relieve Conditions (SPARC)
- Enhancing the Diversity of the NIH-Funded Workforce
- Knockout Mouse Phenotyping
- Science of Behavior Change
- Human Microbiome
- Global Health

Common Fund

- Single Cell Analysis
- Regenerative Medicine Program
- Protein Capture
- Epigenomics
- Extracellular RNA Communication
- Extracellular RNA Expression
- Metabolomics
- Genotype-Tissue Expression
- Epigenomics
- Library of Integrated Network-Based Cellular Signatures (LINCS)
- 4D Nucleome

Transformative Workforce Support

- Molecular Transducers of Physical Activity
- Gabriella Miller Kids First

All of Us Initiative Cohort Program

Long Term Trans-NIH Program

New Paradigms

https://commonfund.nih.gov
Getting to Outcomes: SCAP Closeout Assessment

**Program Proposal, Detailed Plan**
- FY2011: NIH Big Think
- FY2012: Workshop on Single Cell Analysis
- FY2013: Innovation Brainstorm: Transforming Discovery into Impact
- FY2014: Request for Information
- FY2015: Portfolio Analysis

**Annual Progress Reports**
- FY2013: Meetings with External Program Consultants
- FY2014: Monthly meetings of U01 awardees
- FY2015: Program Annual Meetings
- FY2016: Working Group meetings with NIH Program Staff
- FY2017: Bibliometrics

**Program Close Out**
- FY2017: Patents and Inventions
- FY2017: NIH Staff Survey and Focus Group
- FY2017: External Consultants and Industry Focus Groups
- FY2017: Grantee Focus Groups
- FY2017: Close Out Meeting & Survey
Close Out Topics

State of the Science
• Evolution and attainment of program goals
• Products of research
• Significant contributions to the field of science
• Utilization of knowledge generated, research products

Management
• Effective strategies used to ensure progress
• Adequacy of type and level of support to awardees to attain goals
• Communication and coordination effectiveness
SCAP Background and Context
Why Single Cell Analysis?

Approaches that only examine population-level characteristics can obscure crucial differences between individual cells.


https://commonfund.nih.gov/singlecell
Single Cell Analysis Program (SCAP)

Major Goals

**Overall Goal:** approaches to analyze heterogeneity of biologically relevant populations of cells *in situ*

- Address key roadblocks in analyzing single cells
- Catalyze the emerging field by building a synergistic program of unique initiatives
- Coordinate NIH efforts to improve our ability to characterize cells and understand the biological significance of heterogeneity
## Transcriptional Profiling of Human Cells (U01) RFA-RM-11-013
- FY12: 3 awards
- FY13: 15 awards
- FY14: 8 awards
- FY15: 8 awards
- FY16: 8 awards

## Exceptionally Innovative Tools and Technologies (R21) RFA-RM-11-014, RFA-RM-13-021
- FY12: 3 awards
- FY13: 15 awards
- FY14: 8 awards
- FY15: 8 awards
- FY16: 8 awards

## Advanced Technology Development (R33) RFA-RM-13-020
- FY12: 3 awards
- FY13: 15 awards
- FY14: 8 awards
- FY15: 8 awards
- FY16: 8 awards

## Integration and Translation of Technologies (R01) RFA-RM-11-015
- FY12: 3 awards
- FY13: 15 awards
- FY14: 9 awards
- FY15: 8 awards
- FY16: 8 awards

## Technology Validation/Adoption (Revision of R01 and U01) RFA-RM-13-022,23
- FY12: 3 awards
- FY13: 15 awards
- FY14: 9 awards
- FY15: 8 awards
- FY16: 8 awards

## Follow that Cell Challenge (Prize) NOT-RM-14-014
- FY12: 3 awards
- FY13: 15 awards
- FY14: 9 awards
- FY15: 8 awards
- FY16: 8 awards

### Timeline
[https://commonfund.nih.gov/singlecell](https://commonfund.nih.gov/singlecell)
Next-gen tools and technologies

**Fluorescent in situ sequencing (FISSEQ)** of endogenous RNAs on a confocal microscope, directly within tissue.

**inDrop**: high throughput, inexpensive technique that gives every cell in a sample a unique genetic barcode

[link](https://commonfund.nih.gov/singlecell)
Methods and Results

• Bibliometrics
• Patents and Inventions
• NIH Program Staff Survey and Focus Group
• External Consultants and Industry Focus Groups
• Grantee Focus Groups
• Close Out Meeting & Survey
**Bibliometrics**

Mean Relative Citation Ratio (RCR) = 2.50
Weighted RCR ~522

44% of SCAP publications are in the Top 10% - based on ESI Category and year of publication

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Relative Citation Ratio (RCR): A New Metric That Uses Citation Rates to Measure Influence at the Article Level. PLoS Sept. 2017.
Percentile Ranking of Your Publication using Web of Science and Essential Science Indicators – NIH Library
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<th>Total Citations</th>
<th>RCR</th>
<th>Percentile</th>
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<td>2015</td>
<td>Droplet barcoding for single-cell transcriptomics applied to embryonic stem cells.</td>
<td>Cell</td>
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<td>268</td>
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<td>Nature</td>
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<td>213</td>
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<td>2014</td>
<td>Single-cell phenotyping within transparent intact tissue through whole-body clearing.</td>
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<td>59</td>
<td>9.66</td>
<td></td>
<td>2016</td>
<td>Dynamics of epigenetic regulation at the single-cell level.</td>
<td>Science</td>
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</table>
Topical clustering of SCAP Publications

peak height = major topic strength
Bibliometrics – Citations

peak height = major topic strength

peak height = RCR value

total pubs = 2,830
total pubs with RCR = 1,169
mean RCR = 1.89
median RCR = 0.92
Inventions and Patents

Number of projects that reported inventions and/or patents in RPPR

- **High throughput methods for neuronal phenotyping**
- **T cell immunity signatures, biomarkers of single T cells**
- **Live animal imaging**
- **Microfluidics platforms**
- **Single molecule proteomics, transcriptomics**
- **Laser lysis & mRNA expression method**

<table>
<thead>
<tr>
<th># of projects</th>
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<tr>
<td>R21</td>
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Survey of the SCAP Working Group

**Purpose:** Evaluate effectiveness in reaching goals and provide lessons learned for future programs, as well as shape the discussion of an in-person, focus group

- **How successful was the program in achieving the major goals?**
  - Major goals achieved (95% of respondents*)
  - U mechanism contributed to achieving (100%)
  - Divided about the Challenge (57% agreed, 43% were neutral)

- **Obstacles to achieving major goals:**
  - Changes in the field (33%)
  - Overlap with efforts outside the program (29%)
  - Goals and milestones not realistic (24%)

- **Management Strategies:**
  - Effective – NIH working group meetings (86%), grantee meetings (71%), and the use of external advisers/consultants (71%)
  - Improvement needed – milestone tracking (71%)

*21% response rate (7/33)
SCAP Working Group, Focus Group

• Evolution of the field of single cell analysis was catalyzed by the Common Fund SCAP

• Why was there 100% agreement in the survey that the U01 initiative contributed to achieving the program goals?
  o Goal was to understand cellular heterogeneity and glean fundamental principles
  o Network of U01 grants accelerated the field, as well as thinking of the NIH internally - valuable information for other programs (e.g. BRAIN, HuBMAP)

• In the survey, why was the group divided about Challenge contributing to achieving the program goals?
  o Scientific question or problem being addressed needs to be very carefully considered. For future Challenges, the group suggested a data challenge, computational and number based metrics are easier to measure.

• Recommendations from the Focus Group:
  o Break out sessions for the U01 grant recipients, separate sessions for grantees & external experts at the Close Out meeting in June 2017
Focus Groups at Close Out Meeting

- **Overwhelming agreement from all groups:**
  - Most significant contributions are cutting edge technologies, approaches, and researchers in the field
  - SCAP investment was needed to rapidly advance the field
  - Having a Common Fund program legitimized the field
  - A milestone driven plan for technology development and cutting edge research is difficult due to the unpredictability of the research
Close Out Survey

• Most significant contributions of this program to the field?
  o single cell sequencing
  o in situ imaging
  o live cell imaging
  o computational approaches
  o collaboration and integration
  o understanding and acceptance

*16% response rate (50/318)
In Closing

State of the Science

- SCAP catalyzed techniques, commercial solutions, and insights into biological heterogeneity in cancer, immunology and neuroscience
- Acceptance and interest of single cell analysis at the NIH due to SCAP, which has facilitated funding of single cell analysis projects
- Evaluation in 5 years time needed to measure impact

Management

- Use of R mechanism, challenging to promote strong collaborative community
- SCAP led to wider use of single cell analysis techniques at the NIH
Acknowledgements

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