

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

**Program Evaluation Special Interest Group Meeting**  
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National Institutes of Health  
Office of Strategic Coordination - The Common Fund

# 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.

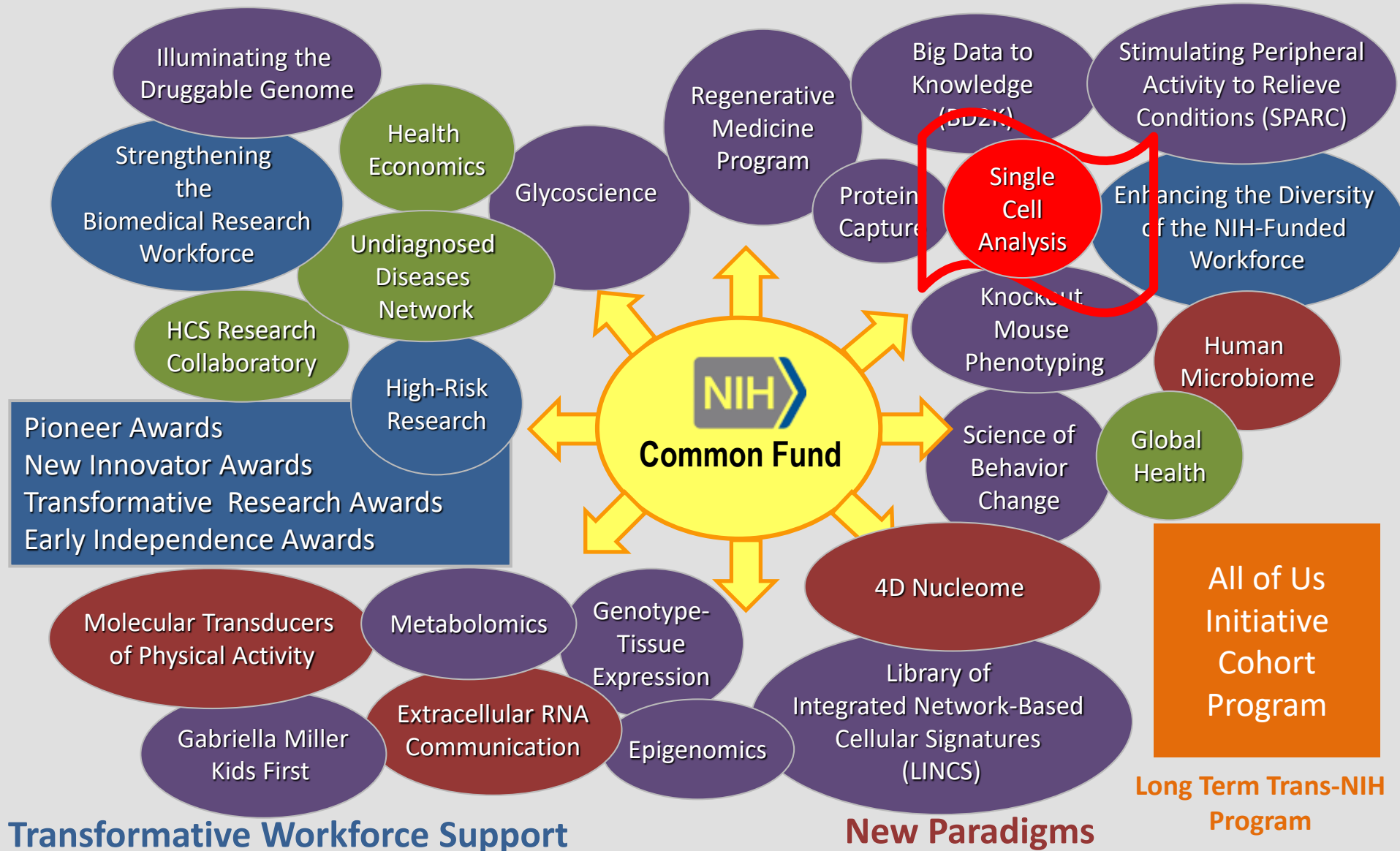


**Common Fund programs are intended to benefit the entire biomedical research community**

# Common Fund Programs

## New Types of Clinical Partnerships

## Data/Tools/Methods



# Getting to Outcomes: SCAP Closeout Assessment

Program Proposal,  
Detailed Plan

Annual Progress Reports

Program  
Close Out

FY2011

FY2012

FY2013

FY2014

FY2015

FY2016

FY2017

- NIH Big Think
- Workshop on Single Cell Analysis
- Innovation Brainstorm: Transforming Discovery into Impact
- Request for Information
- Portfolio Analysis

- Meetings with External Program Consultants
- Monthly meetings of U01 awardees
- Program Annual Meetings
- Working Group meetings with NIH Program Staff
- Bibliometrics

- Bibliometrics
- Patents and Inventions
- NIH Staff Survey and Focus Group
- External Consultants and Industry Focus Groups
- Grantee Focus Groups
- 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

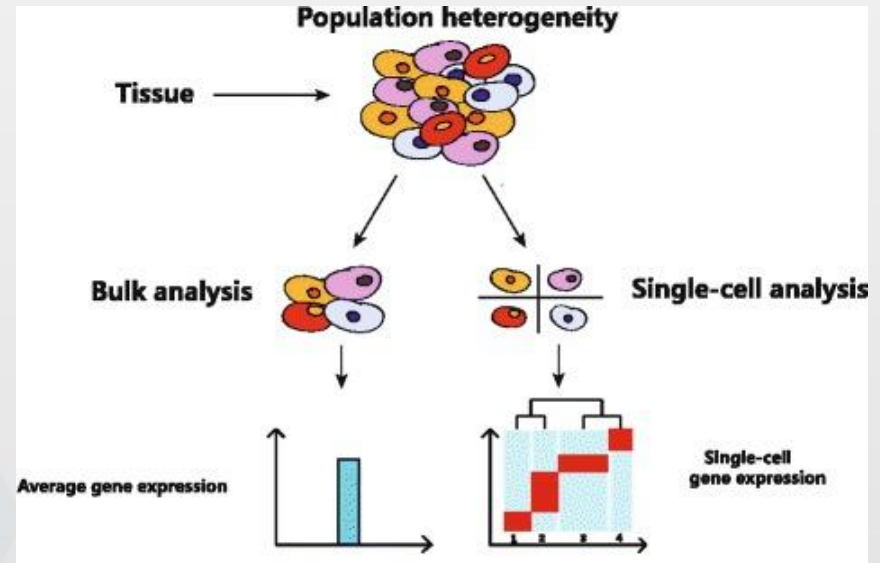
- Effective strategies used to ensure progress
- Adequacy of type and level of support to awardees to attain goals
- Communication and coordination effectiveness

# SCAP Background and Context

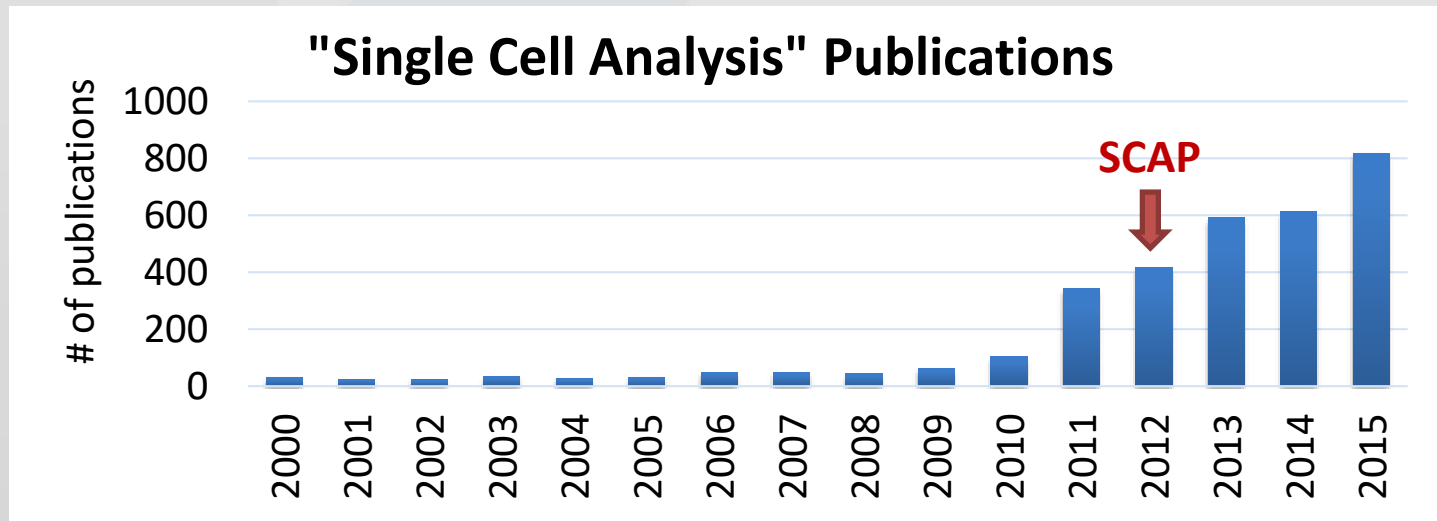


# Why Single Cell Analysis?

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



Ye F, et al. J Hematol Oncol. 2017



# Single Cell Analysis Program (SCAP)

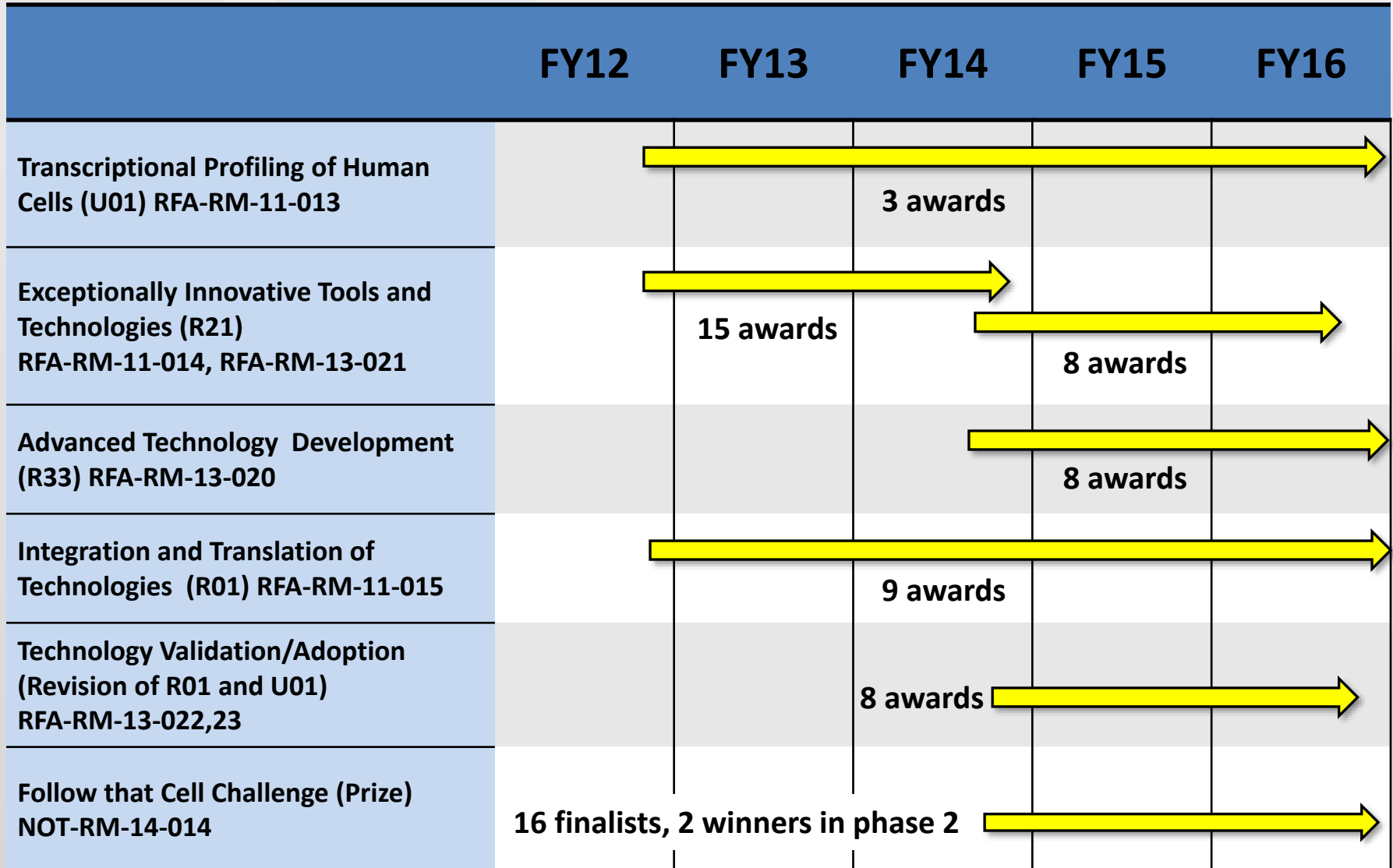
## Major Goals

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

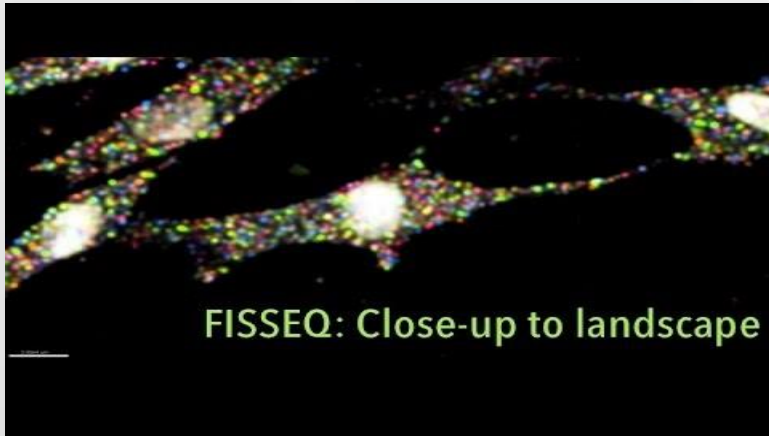
- Address key roadblocks in analyzing single cells
- Catalyze the emerging field by building a synergistic program of unique initiatives
- Coordinate NIH efforts to improve our ability to characterize cells and understand the biological significance of heterogeneity



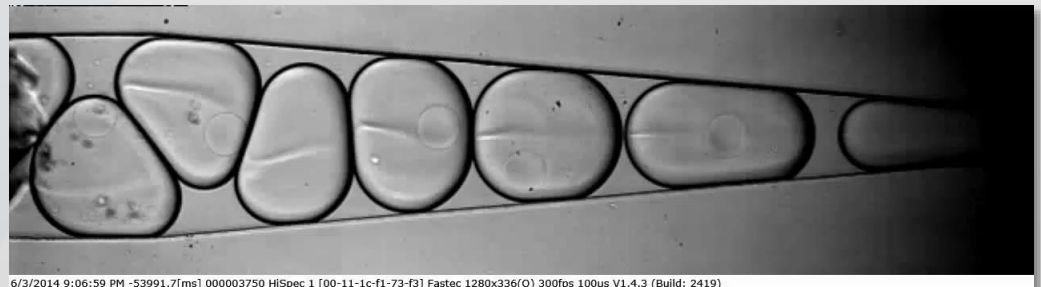
# Timeline



# 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

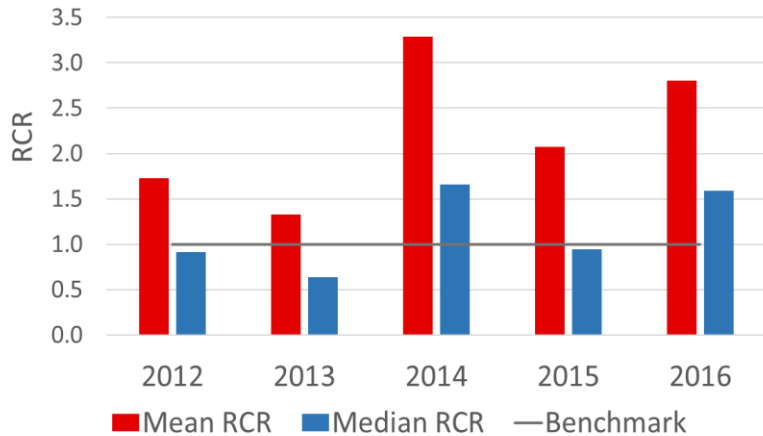
# Methods and Results

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



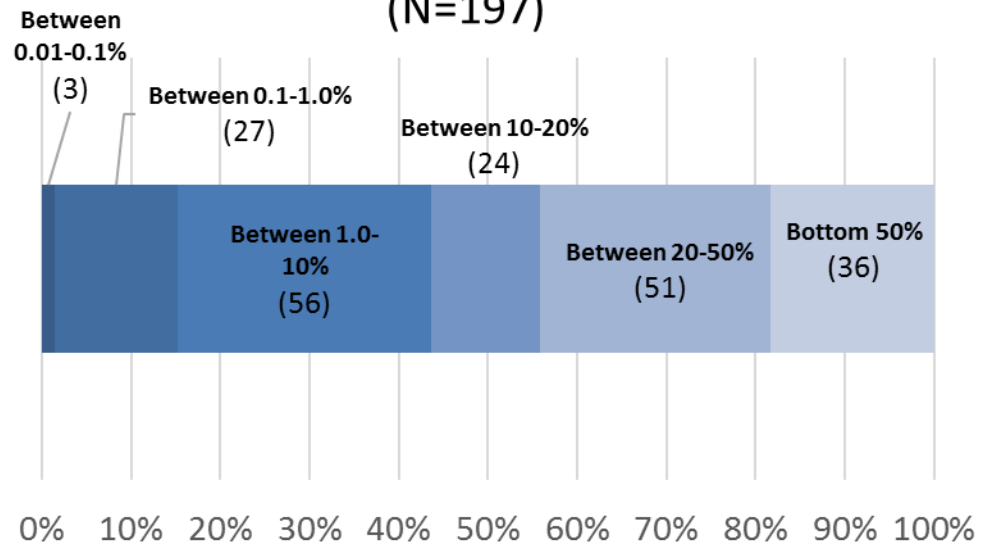
# Bibliometrics

Single Cell Analysis Program Publications  
2012-2016 (N=176)



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

Publications per Citation Percentile Rank  
(N=197)



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

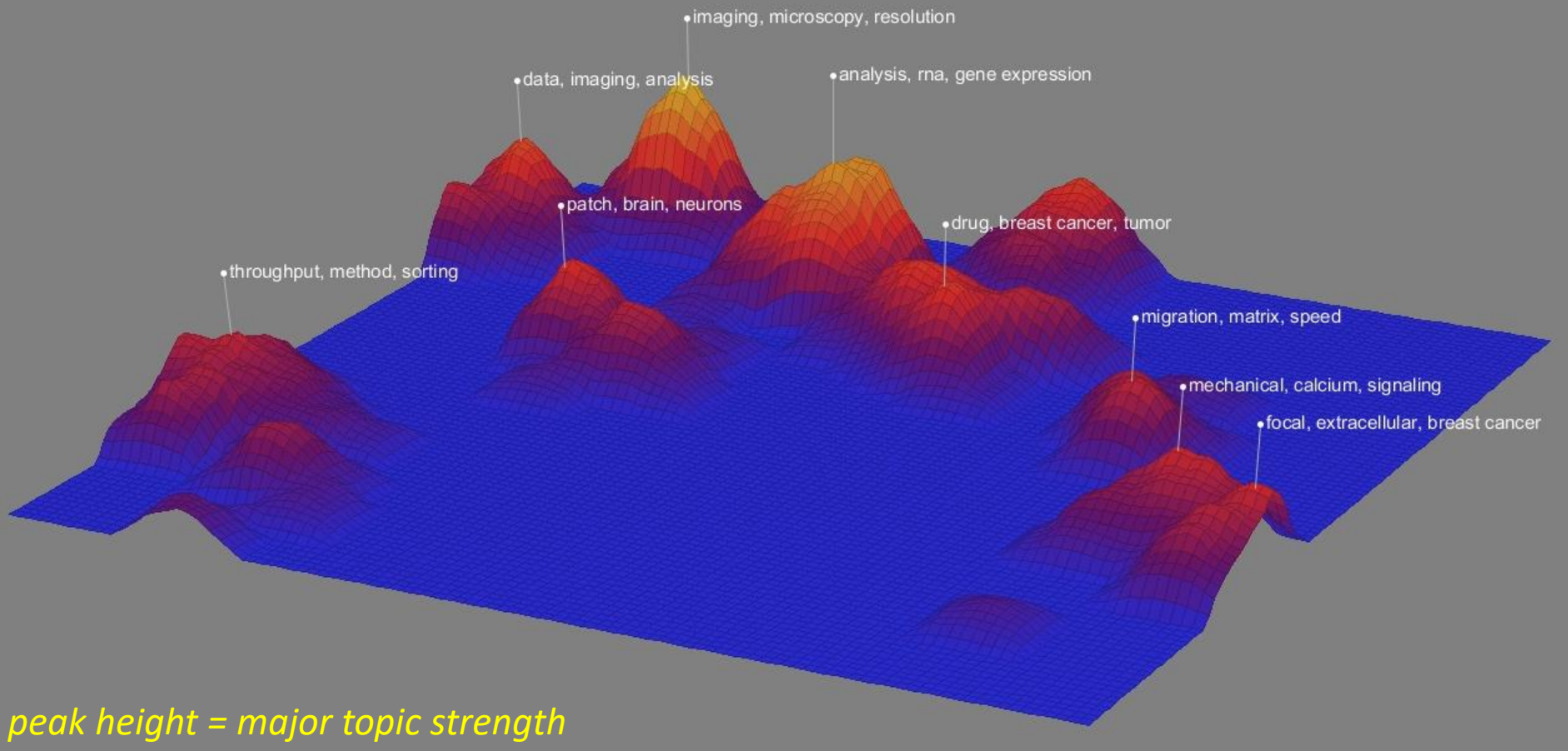
*Relative Citation Ratio (RCR): A New Metric That Uses Citation Rates to Measure Influence at the Article Level. PLoS Sept. 2017.*

*Percentile Ranking of Your Publication using Web of Science and Essential Science Indicators – NIH Library*

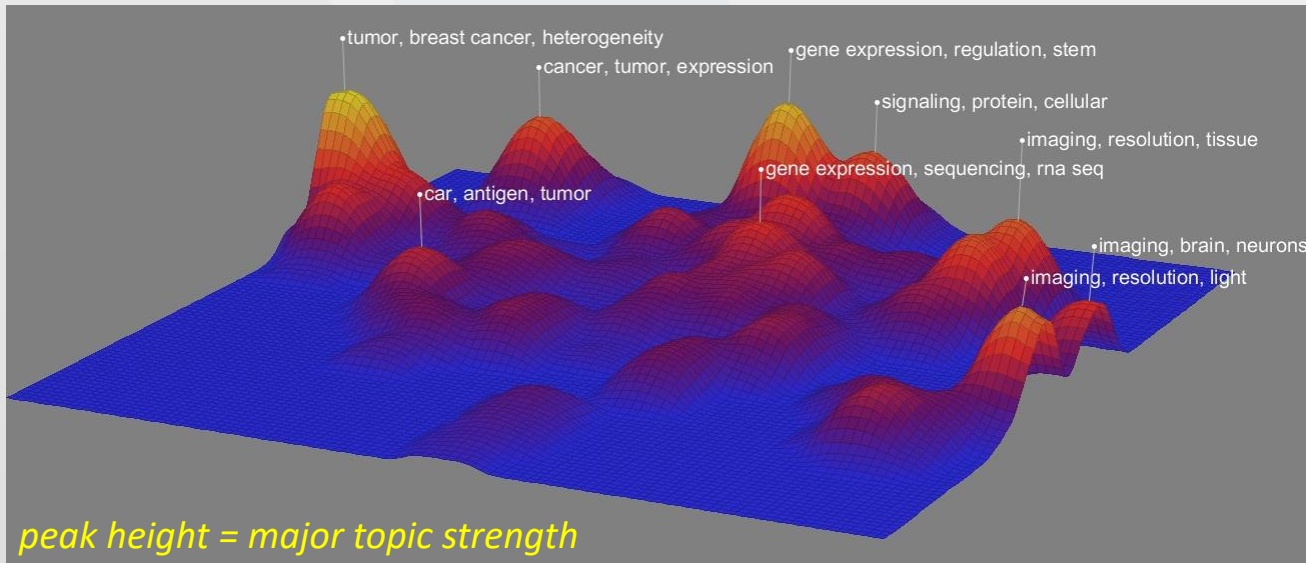
# Bibliometrics – Top 10

Total Citations	RCR	Percentile	Year	Title	Journal
300	28.67	Between 0.01-0.1%	2015	Droplet barcoding for single-cell transcriptomics applied to embryonic stem cells.	Cell
116	23.15		2016	Adult mouse cortical cell taxonomy revealed by single cell transcriptomics.	Nat. Neurosci.
268	17.37		2014	Clonal evolution in breast cancer revealed by single nucleus genome sequencing.	Nature
213	16.09		2014	Single-cell phenotyping within transparent intact tissue through whole-body clearing.	Cell
104	15.65		2015	Acoustic separation of circulating tumor cells.	Proc. Natl. Acad. Sci. U.S.A.
160	12.64		2014	Hypoxia and the extracellular matrix: drivers of tumour metastasis.	Nat. Rev. Cancer
187	11.24		2014	Highly multiplexed subcellular RNA sequencing in situ.	Science
27	9.78		2016	Rotational manipulation of single cells and organisms using acoustic waves.	Nat Commun
59	9.66		2016	Dynamics of epigenetic regulation at the single-cell level.	Science
45	9.25		2016	A shared neural ensemble links distinct contextual memories encoded close in time.	Nature

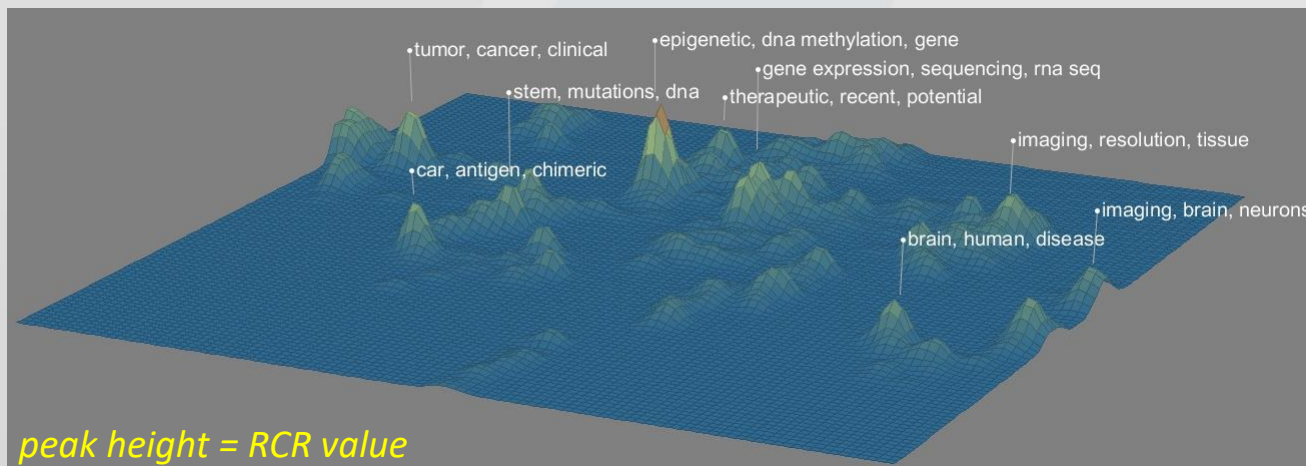
# Topical clustering of SCAP Publications



# Bibliometrics – Citations



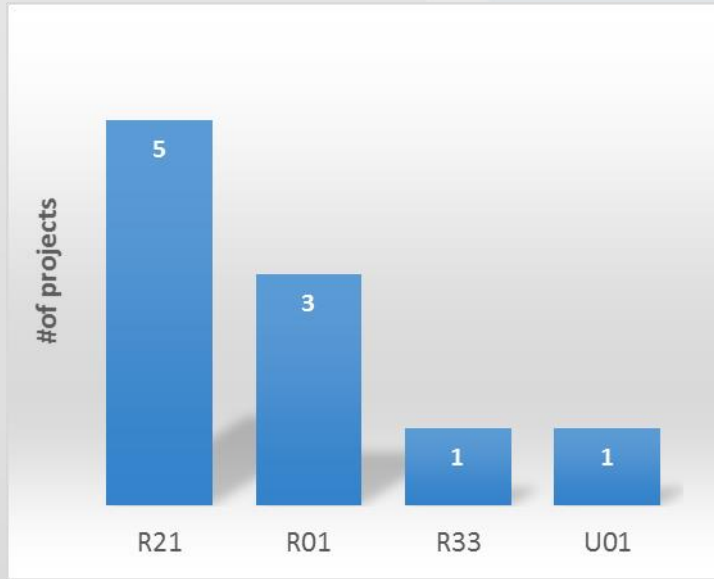
total pubs = 2,830  
total pubs with RCR = 1,169  
mean RCR = 1.89  
median RCR = 0.92



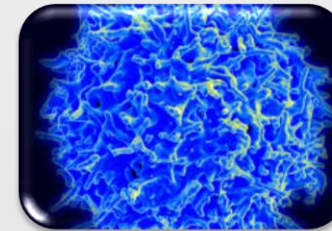


# Inventions and Patents

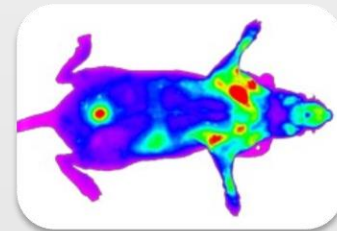
Number of projects that reported inventions and/or patents in RPPR



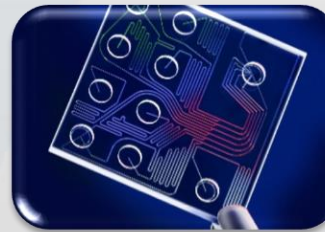
High throughput methods for neuronal phenotyping



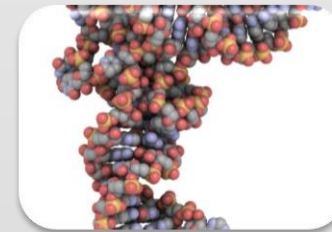
T cell immunity signatures, biomarkers of single T cells



Live animal imaging



Microfluidics platforms



Single molecule proteomics, transcriptomics



Laser lysis & mRNA expression method



# Survey of the SCAP Working Group

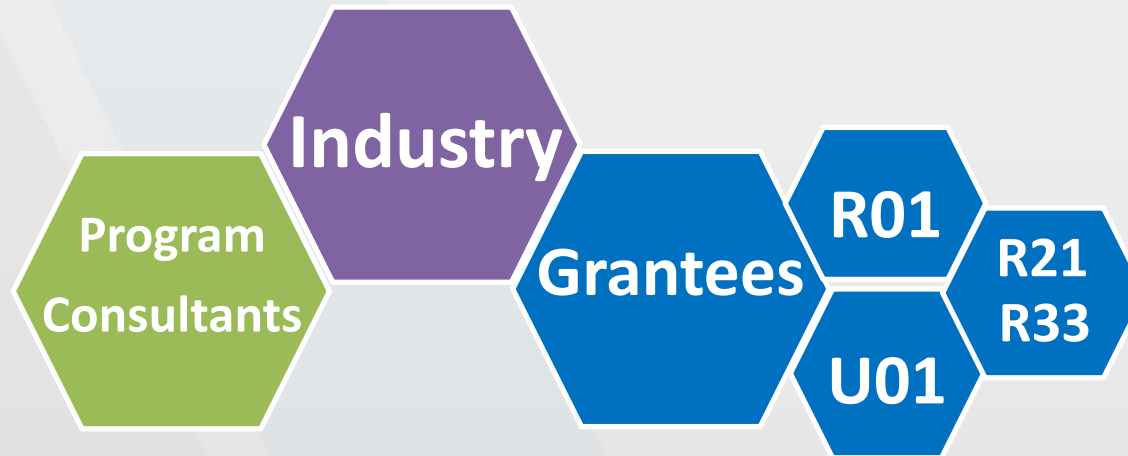
**Purpose:** Evaluate effectiveness in reaching goals and provide lessons learned for future programs, as well as shape the discussion of an in-person, focus group

- **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%)

# SCAP Working Group, Focus Group

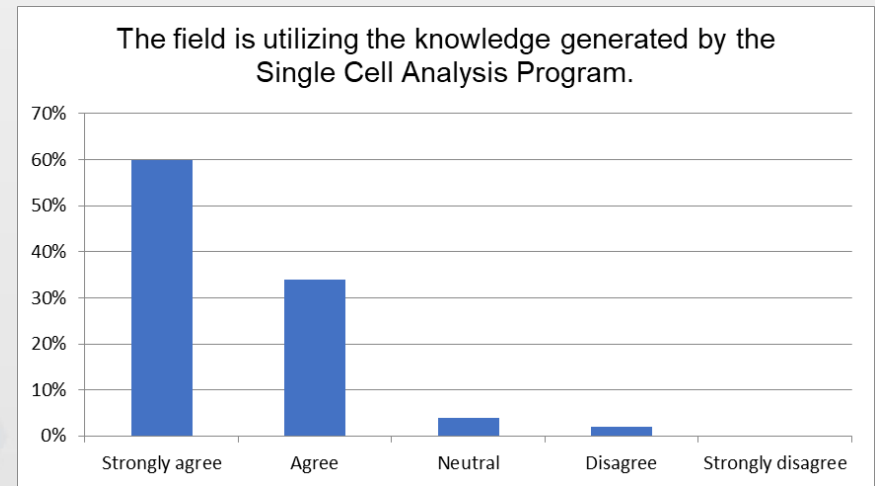
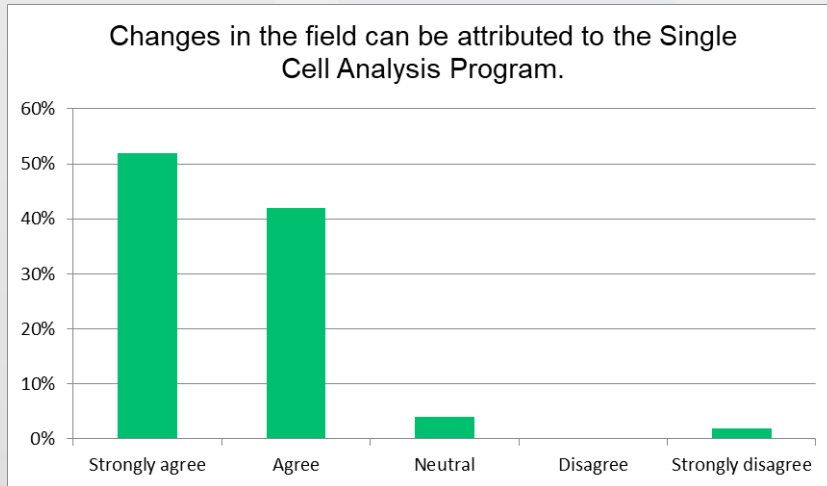
- Evolution of the field of single cell analysis was catalyzed by the Common Fund SCAP
- **Why was there 100% agreement in the survey that the U01 initiative contributed to achieving the program goals?**
  - Goal was to understand cellular heterogeneity and glean fundamental principles
  - Network of 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?**
  - 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:**
  - 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?
  - single cell sequencing
  - in situ imaging
  - live cell imaging
  - computational approaches
  - collaboration and integration
  - understanding and acceptance

# 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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Andrea Beckel-Mitchener, Ph.D. (NIMH)