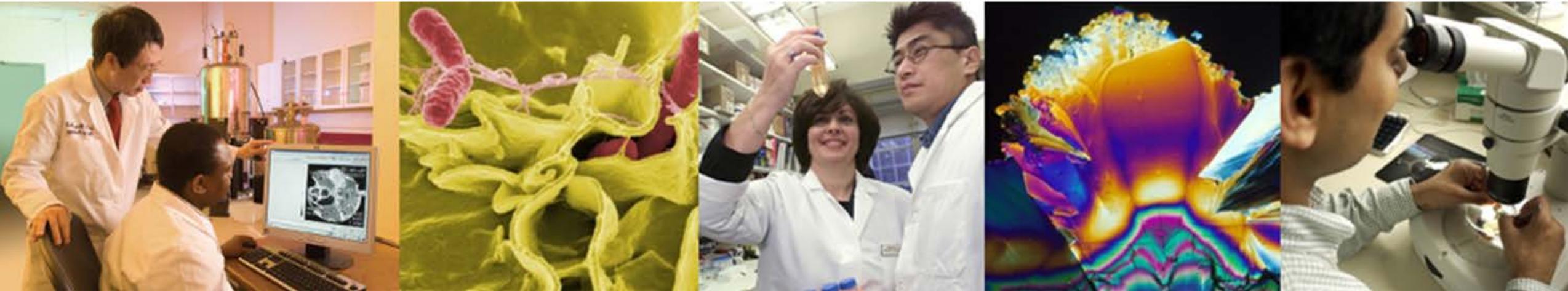


ACD High-Risk, High-Reward: Working Group Interim Recommendations

*ACD Meeting
June 13, 2019*



Brendan Lee, MD, PhD
Chairman and Professor, Department of Molecular and Human Genetics
Baylor College of Medicine

Lawrence A. Tabak, DDS, PhD
Principal Deputy Director, NIH
Department of Health and Human Services



High-Risk, High-Reward – Unique Common Fund Programs

- Investigator-initiated scientific goals
- Enable investigators to launch a potentially transformative project without preliminary data
 - *Risk involved is mitigated by emphasizing past accomplishments during review and by allowing changes of course during the funding period*
- Individual awards are 5 years
- Piloting novel application and review processes



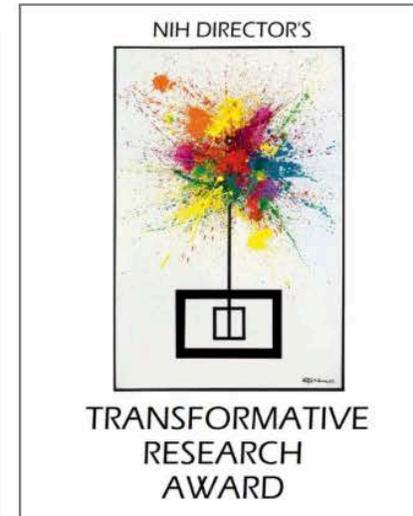
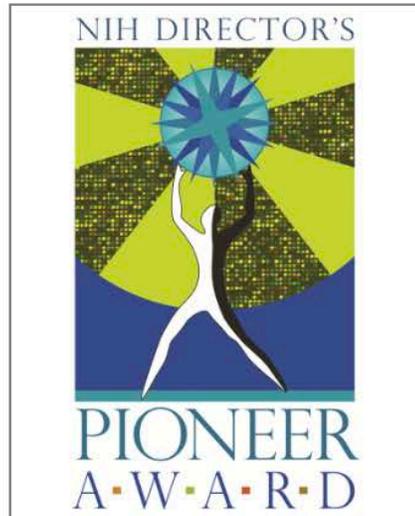
National Institutes of Health

Office of Strategic Coordination - The Common Fund

High-Risk, High-Reward – Unique Common Fund Programs

Funding opportunities for outstanding scientists at all career stages

The High-Risk, High-Reward Research program supports **exceptionally creative scientists** pursuing **highly innovative research with the potential for broad impact** in biomedical or behavioral science. The program's four constituent NIH Director's awards provide a diverse set of funding opportunities.



ACD High-Risk, High-Reward Working Group



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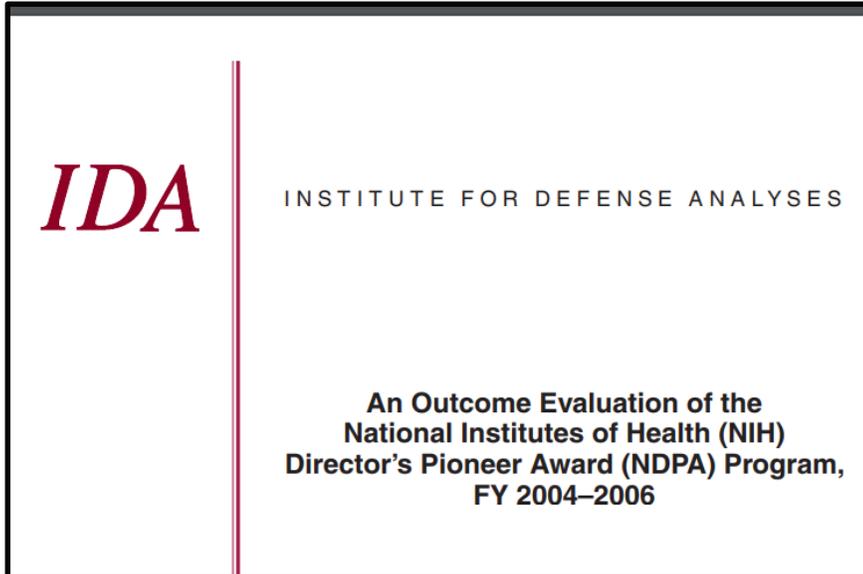


Hannah Valantine, M.D.
OD Scientific Workforce
Diversity, NIH

Charge to the Working Group

- Review effectiveness of NIH HRHR research programs
- Analyze participation of women and other underrepresented groups in the applicant, finalist, and awardee pools of HRHR grants to identify possible causes for their underrepresentation
- Examine institutional diversity and diversity of scientific topics in the applicant and awardee pools
- Propose steps that NIH might take to enhance the diversity of applicants and awardees in HRHR programs, while supporting the best science

Review effectiveness of NIH HRHR research programs



- Compared research outcomes of the 33 Pioneers in first 3 cohorts to similarly qualified R01 investigators, random R01 sets, and HHMI investigators
- Assessed scientific impact and innovation through bibliometrics and expert analysis
- Found Pioneer-funded research has
 - More impact than similar and random R01s and about as much impact as HHMI
 - More innovative than similarly qualified R01 investigators' research and similar to HHMI

Review effectiveness of NIH HRHR research programs

Table 1. Comparison of bibliometric indicators

Bibliometric indicator	NI Awardees compared with ESI R01 Awardees
Average Citations per Publication	NI awardees > ESI R01
IPP (Journal impact factor)	NI awardees > ESI R01
RCR (Relative Citation Ratio)	NI awardees > ESI R01
SNIP (Journal Source-Normalized Impact per Paper)	NI awardees > ESI R01
SJR (SciImago Journal Rank)	NI awardees > ESI R01
H - Index	No statistically significant difference
Number of publications	ESI R01 awardees > NI awardees
Average annual publications	ESI R01 awardees > NI awardees
Time to first publication (Faster is greater)	ESI R01 awardees > NI awardees

New Innovator Award
Outcomes Evaluation
Report by the Science &
Technology Policy Institute

Evaluated outcomes of NI awardees in first 3 cohorts

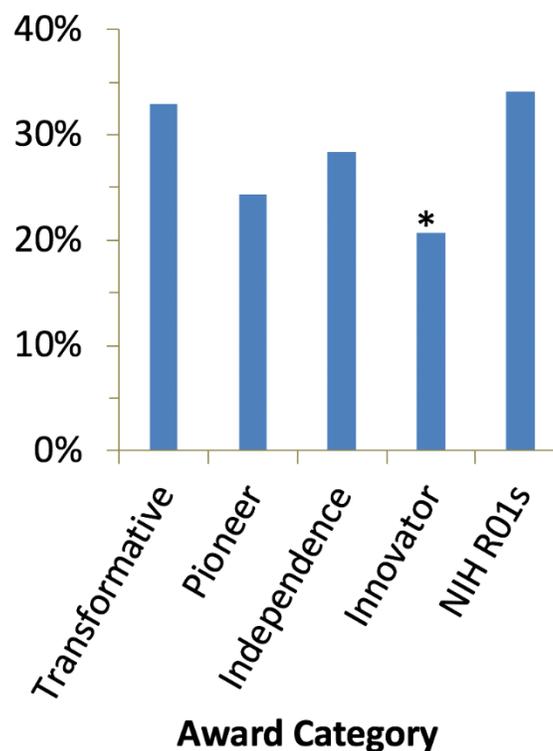
- NI-funded research is more innovative, risky, and has more impact than ESI R01 research
- Awards did not have significantly more positive or negative impact on the careers of its awardees than did ESI R01s (risk of research project did not put careers at risk)

Clinical and technological impact: HRHR vs. NIH R01 awards

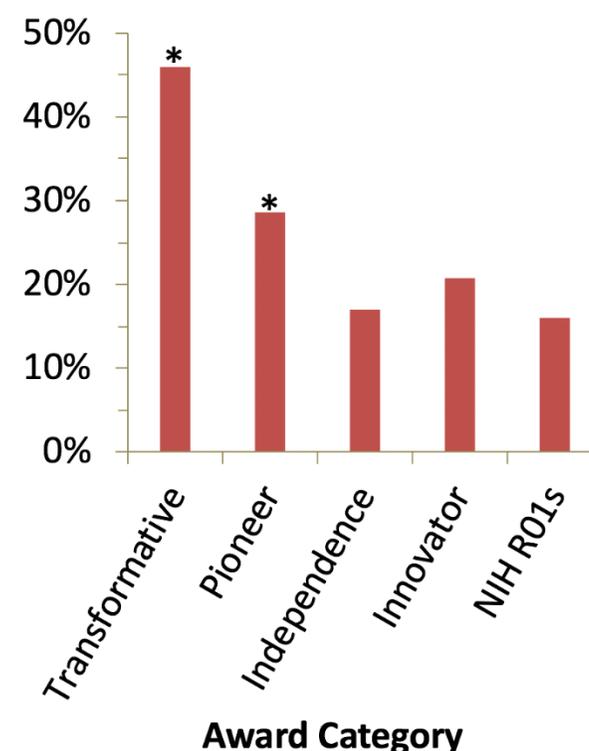
Type 1 HRHR and NIH R01 awards, FY2011-FY2016

Award Type	Number of awards	Awards with clinical impact	Awards with technological impact
Transformative	76	25 (32.9%)	35 (46.1%*)
Pioneer	70	17 (24.3%)	20 (28.6%*)
Independence	88	25 (28.4%)	15 (17.0%)
Innovator	280	58 (20.7%*)	58 (20.7%)
NIH R01s	22,559	7708 (34.2%)	3617 (16.0%)

% of awards w/ clinical impact

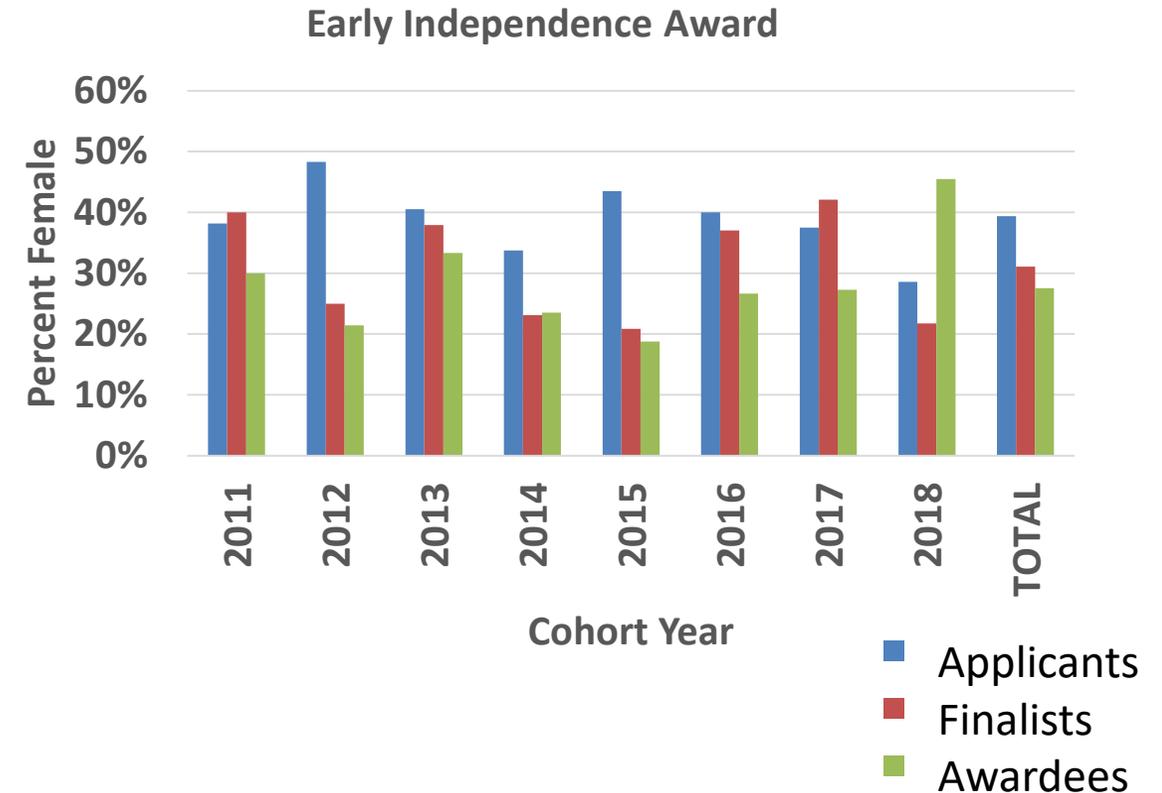
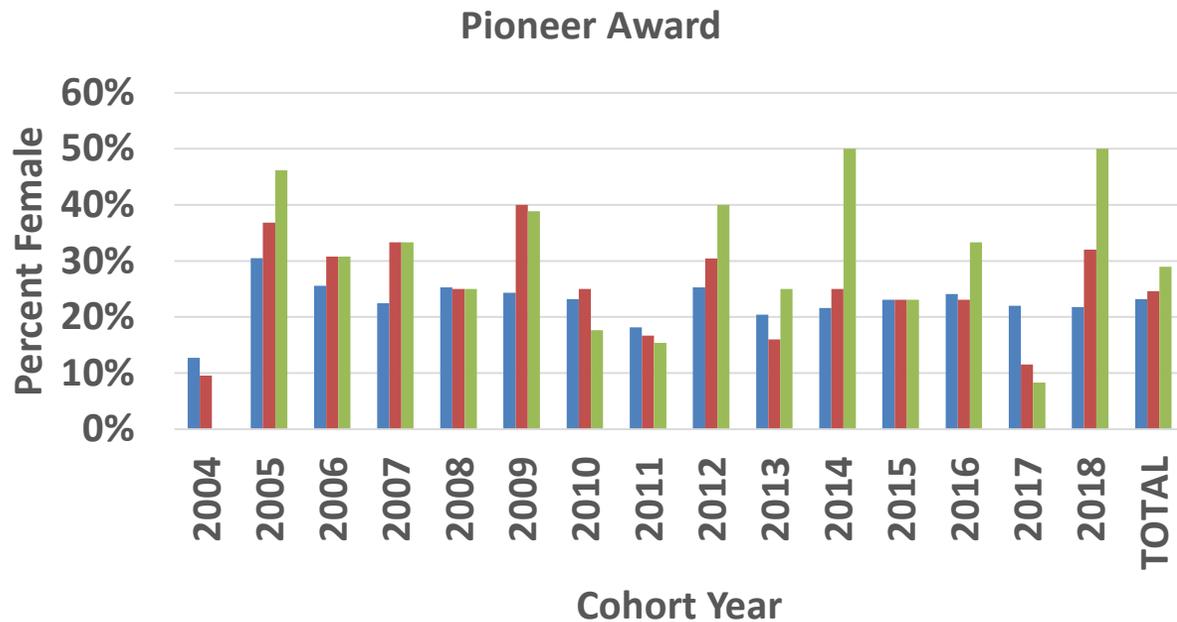


% of awards w/ technological impact



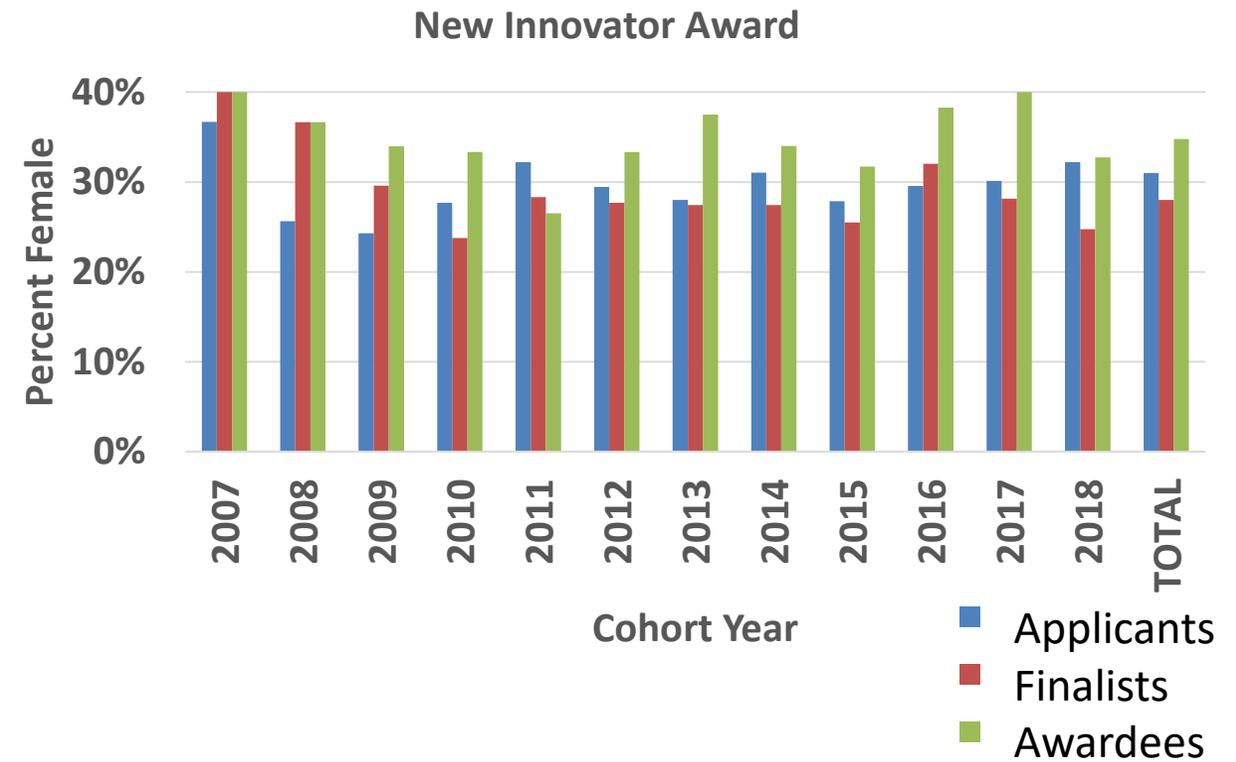
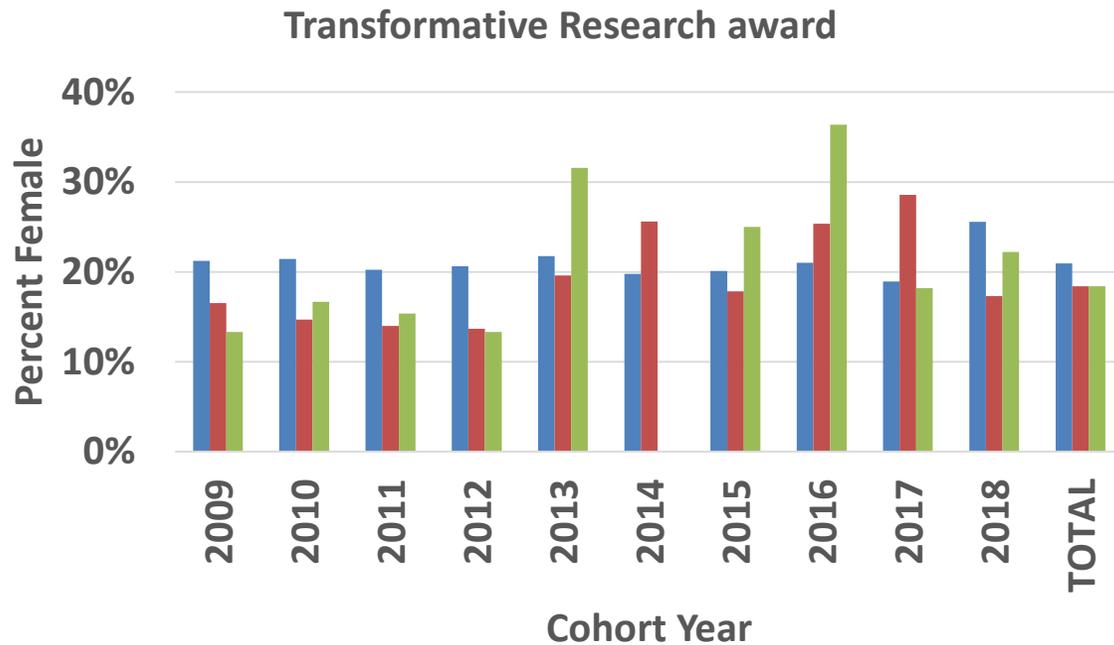
* Statistically significant difference relative to NIH R01s p<0.01

Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation



- Pioneer: no significant difference across review process
- EIA: Significant decrease across review process

Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation



- TRA: variation from year to year, overall no significant increase or decrease
- New innovator: increase is significant from applicant to awardee

Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

- The group concluded that, in general, applications to support female and URM investigators are not being adversely affected by the review process
 - For EIA, the percentage of female applicants was higher than awardees until 2018
 - Across all awards, there is year-to-year variation in percentage of investigators who choose not to identify their gender, ethnicity, and race
- Issue and concern: number of applications to support women and URM investigators is low

Examine diversity of scientific topics in the applicant and awardee pools

HRHR applications and awards map to a narrow range of topics that vary widely in award rates

- For all HRHR programs combined, these 21 clusters (14.2% of the total of 148 clusters) account for over half of the applications
- The range of award rates for these clusters is 1.77% to 14.63%
 - Mean award rate = 6.83%
 - Median cluster award rate = 5.21%

	Topic Awards	Appls	% of all awards	% of all apps	Award rate
Model Organisms and Genetics	24	164	4.67%	2.18%	14.63%
Neuronal Circuits	26	182	5.06%	2.42%	14.29%
RNA Transcription	12	100	2.33%	1.33%	12.00%
Gene Regulation	29	250	5.64%	3.33%	11.60%
Antibiotic Resistance	12	111	2.33%	1.48%	10.81%
Protein Crystallography	19	192	3.70%	2.55%	9.90%
Gut Microbiome	11	119	2.14%	1.58%	9.24%
Systems Biology	25	304	4.86%	4.04%	8.22%
T-Cell Immunotherapy	7	90	1.36%	1.20%	7.78%
Tissue Scaffolding & Engineering	17	229	2.92%	3.05%	7.42%
Stem Cells	15	229	3.31%	3.05%	6.55%
High-throughput Screening	20	306	3.89%	4.07%	6.54%
Imaging Methodology	15	240	2.92%	3.19%	6.25%
Statistics and Modeling	5	96	0.97%	1.28%	5.21%
GWAS Studies	14	270	2.72%	3.59%	5.19%
Drug Discovery	6	148	1.17%	1.97%	4.05%
Software Development	6	148	1.17%	1.97%	4.05%
Brain Cancer	6	185	1.17%	2.46%	3.24%
Nanoparticle Drug Delivery	5	178	0.97%	2.37%	2.81%
Clinical Outcomes	4	156	0.78%	2.08%	2.56%
Clinical Practice	2	113	0.39%	1.50%	1.77%

Examine diversity of scientific topics in the applicant and awardee pools

HRHR awards appear bias toward institutions and organizations with large, well-known biomedical research programs.....

The Office of Portfolio Analysis looked at

- Award distribution and rates using descriptive analysis and multivariate regression
- Productivity trends

Bottom line conclusions:

- Overall, the quality of work resulting from awards directed to institutions and organizations with smaller research programs and “top-tier” institutions was not significantly different
- Similar productivity and quality

Examine Institutional Diversity for HRHR awards

Organization	Annualized R01 \$/applicant	Award rate (FY2011-FY2016)				
		Pioneer	Innovator	EIA	TRA	R01s
Whitehead Institute	\$600,776.86	50.0%	0.0%	60.0%	0.0%	16.7%
Salk Institute For Biological Studies	\$368,047.10	9.1%	30.0%	100.0%	33.3%	20.7%
Gladstone Institutes						
Scripps Research Institute						
Harvard Medical School						
Rockefeller University						
Fred Hutchinson Cancer Research Center						
Massachusetts Institute of Technology						
Dana-Farber Cancer Institute						
California Institute of Technology						
Harvard T.H. Chan School of Public Health						
Stanford University						
Princeton University						
Sanford Burnham Prebys Medical Discovery Institute						
Yale University						
Cold Spring Harbor Laboratory						
Memorial Sloan Kettering Cancer Center						
Harvard University						
University of Pennsylvania						
Washington University	\$226,725.42	15.5%	7.5%	20.0%	8.5%	18.7%
Boston Children's Hospital	\$224,786.90	10.0%	14.8%	0.0%	0.0%	18.2%
University of California, Berkeley	\$224,113.32	0.0%	28.9%	40.0%	0.0%	22.3%
Brigham and Women's Hospital	\$213,383.76	4.5%	5.6%	55.6%	6.9%	14.9%
Boston Medical Center	\$211,295.56	N/A	100.0%	N/A	0.0%	13.1%
Johns Hopkins University	\$210,778.82	6.1%	1.5%	18.2%	5.3%	17.8%

Organizations with the highest funding levels had the highest percentage of awards and the highest award rates.

Considerations:

- Include institutional diversity in HRHR funding announcements, elevating it as programmatic priority
- “Institutional capping” to limit the number of awards each institute can submit

FY2011-
HR-funded
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R grants are
shown next to award rates for
R01 grants for comparison.

Lower award rate and \$/applicant  Higher award rate and \$/applicant

Recommendations

OUTCOMES

The working group agrees there is value in having HRHR programs and that the awards have greater influence on certain scientific areas as compared to traditional R01s.

- Overall successful program, continue to expand if possible
- Formally evaluate the Transformative Research Award

Recommendations

OUTREACH

The HRHR working group recognizes that encouraging women and underrepresented minorities to serve as investigators on HRHR awards is of critical importance to increase their representation among the awardees.

- Initiate a special HRHR program that requires a collaboration between an under-resourced institution and resourced institution and addresses diversity in the broadest sense
- Maintain the career development portal that centralizes all NIH training grants and efforts; consider expanding resources to include opportunities along career continuum
 - <https://researchtraining.nih.gov/>
 - <https://researchtraining.nih.gov/programs/other-training-related>
- NIH should host workshops where institutions can send 1-2 students to learn about career advancement opportunity provided by the EIA

Recommendations

OUTREACH

- Provide on the HRHR website prototype example grants similar to the template examples available for R01s and K awards
- Certain HRHR application features can be applied to other NIH grants to enhance broader success of underserved groups
 - New Innovator features should be applied to a special award type for Early Stage Investigators (ESIs)

Recommendations

BIAS – Diversity of Applicant and Awardee Pools

Average representation of females and underrepresented minorities in the applicant pool is reflected in the awardee pool, but there is fluctuation from year to year and the numbers in many cases are small. The group agrees potential for unconscious bias should be mitigated.

- Reviewer education or training
- For the Pioneer and Early Independence awards, withhold the biosketch from the first phase scientific review in an attempt to focus on the approach and more on the person in the second phase of review

Recommendations

BIAS – Diversity of Reviewers

Improve and ensure racial, ethnic, and gender diversity in reviewer panel composition

- Reviewers should also be expert in various backgrounds, as appropriate to evaluate the applications for the HRHR programs
- Reviewers should come from a range of different institutions and organizations, from highly resourced to less well-resourced and from geographically diverse locations
- Continue to track this element and ensure representation on review panels

Recommendations

BIAS - Topics

The group acknowledges that there appears to be bias in the topics that are awarded under HRHR programs. Clinical studies tend to be underrepresented, as do other behavioral, psychological, and sociological topics.

- Special track or separate HRHR program for clinical outcomes; separate review track
- In FOAs for all the HRHR awards, reiterate that all topics are welcome; underrepresented topics can be emphasized
- Continue to ensure reviewer expertise in topics underrepresented in award topic maps and matching of reviewer expertise to applications

Recommendations

BIAS – Institutions

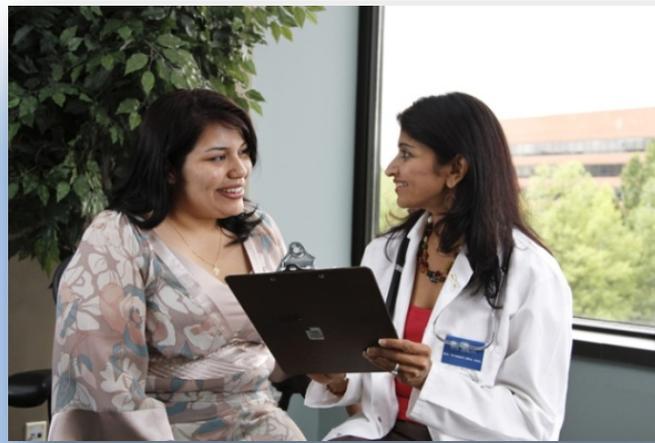
HRHR awardees primarily represent a subset of the top-tier research institutions.

- Elevate institutional diversity as a program priority
- Evaluate the institutional diversity in 10 years to gauge the impact of this modification

Recommendations

HARASSMENT

- Require HRHR grantee organizations to provide assurances that they have effective, fair, and up-to-date policies to preserve a harassment-free environment
- If HRHR grantee institutions become aware of harassment findings related to HRHR grantees, they should alert and work with NIH to arbitrate the situation



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