ACD High-Risk, High-Reward: Working Group Update

ACD Meeting
June 14, 2018

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

Brendan Lee, MD, PhD
Chairman and Professor, Department of Molecular and Human Genetics
Baylor College of Medicine
High-Risk, High-Reward – Unique Common Fund Programs

- Investigator-initiated scientific goals
- Enable investigators to launch a potentially transformative project on any topic 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
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.
FY17 Pioneer Awards

Only 1 of the 12 Awardees is a woman

- *What factors contributed to this outcome?*
- *How can we promote gender diversity in this program?*
- *What about other HRHR programs?*

ACD working group assembled to explore these and related questions for HRHR programs
ACD High-Risk, High-Reward Working Group

Lawrence Tabak, D.D.S., Ph.D. (Co-Chair)
Office of the Director, NIH

Molly Carnes, M.D.
University of Wisconsin

John Carpten, Ph.D.
Keck School of Medicine, USC

Griffin Rodgers, M.D.
NIDDK

Amy Palin, Ph.D.
Eunice Kennedy Shriver NICHD

Nicole Perry
Vanderbilt University

Brendan Lee, M.D., Ph.D. (Co-Chair)
Baylor College of Medicine

Sandra Schmid, Ph.D.
UT Southwestern Medical Center

Scout, Ph.D.
The Torvus Group

Jason Sheltzer, Ph.D.
CSHL

Shirley Tilghman, Ph.D.
Princeton University

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

All 4 Common Fund HRHR programs will be evaluated

- Pioneer Award, New Innovator, Early Independence, Transformative Research Award (has lowest percent women among awardees)

Metrics for evaluation of success of HRHR awards:

- Productivity (in proportion to resources)
  - RCR data (bibliometric analysis), patents and licenses
- Impact
  - Translation to clinic, network analyses of topics, appearance of new terms in papers published by HRHR awardees
  - Number of editorial or perspectives pieces written on papers published by HRHR grantees

For Early Independence Awards “success” may include:

- Awardees career position; ability to obtain and maintain tenure-track position
- Securing additional (R01-level) NIH funding
- Compare recipients to finalists and Early Stage Investigators
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 is
  - More impactful than similar and random R01s and about as impactful 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

<table>
<thead>
<tr>
<th>Bibliometric indicator</th>
<th>NI Awardees compared with ESI R01 Awardees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Citations per Publication</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>IPP (Journal impact factor)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>RCR (Relative Citation Ratio)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>SNIP (Journal Source-Normalized Impact per Paper)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>SJR (Scimago Journal Rank)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>H - Index</td>
<td>No statistically significant difference</td>
</tr>
<tr>
<td>Number of publications</td>
<td>ESI R01 awardees &gt; NI awardees</td>
</tr>
<tr>
<td>Average annual publications</td>
<td>ESI R01 awardees &gt; NI awardees</td>
</tr>
<tr>
<td>Time to first publication (Faster is greater)</td>
<td>ESI R01 awardees &gt; NI awardees</td>
</tr>
</tbody>
</table>

Evaluated outcomes of NI awardees in first 3 cohorts

- NI-funded research is more innovative, risky, and impactful 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)
Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

Fewer women apply for HRHR awards compared to traditional R01s... Why?

Is additional bias introduced during review processes?
Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

- Fewer women applying to HRHR program awards – Why?
  - Analyze FOA language
  - Analyze outreach efforts

### Gender

<table>
<thead>
<tr>
<th>Grant/Program and Cohort year</th>
<th>Cohort Year</th>
<th>Applicants</th>
<th>Finalists</th>
<th>Awardees</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Withheld/Unknown</td>
</tr>
<tr>
<td>Pioneer Award, 2004-2017</td>
<td>TOTAL</td>
<td>3257</td>
<td>987</td>
<td>61</td>
</tr>
<tr>
<td>New Innovator, 2007 - 2017</td>
<td>TOTAL</td>
<td>5126</td>
<td>2293</td>
<td>161</td>
</tr>
<tr>
<td>Transformative Research, 2009-2017</td>
<td>TOTAL</td>
<td>4304</td>
<td>1127</td>
<td>179</td>
</tr>
<tr>
<td>Early Independence Award, 2011-2017</td>
<td>TOTAL</td>
<td>305</td>
<td>207</td>
<td>77</td>
</tr>
</tbody>
</table>
Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

Strategies to encourage women and URM to apply for HRHR grants:

- Mentoring programs
- Publicize Early Independence Awards with training/career offices, like K awards
Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

- Are numbers reduced as review process proceeds?
  - Group is considering gender, ethnicity, and URM data

### Gender

<table>
<thead>
<tr>
<th>Grant/Program and Cohort year</th>
<th>Cohort Year</th>
<th>Male</th>
<th>Female</th>
<th>Withheld/Unknown</th>
<th>Total</th>
<th>% Female</th>
<th>Male</th>
<th>Female</th>
<th>Withheld/Unknown</th>
<th>Total</th>
<th>% Female</th>
<th>Male</th>
<th>Female</th>
<th>Withheld/Unknown</th>
<th>Total</th>
<th>% Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pioneer Award, 2004-2017</td>
<td>TOTAL</td>
<td>3257</td>
<td>987</td>
<td>61</td>
<td>4305</td>
<td>23%</td>
<td>231</td>
<td>73</td>
<td>5</td>
<td>309</td>
<td>24%</td>
<td>130</td>
<td>50</td>
<td>0</td>
<td>180</td>
<td>28%</td>
</tr>
<tr>
<td>New Innovator, 2007 - 2017</td>
<td>TOTAL</td>
<td>5126</td>
<td>2293</td>
<td>161</td>
<td>7580</td>
<td>31%</td>
<td>734</td>
<td>290</td>
<td>15</td>
<td>1039</td>
<td>28%</td>
<td>323</td>
<td>174</td>
<td>5</td>
<td>502</td>
<td>35%</td>
</tr>
<tr>
<td>Transformative Research, 2009-2017</td>
<td>TOTAL</td>
<td>4304</td>
<td>1127</td>
<td>179</td>
<td>5610</td>
<td>21%</td>
<td>661</td>
<td>150</td>
<td>17</td>
<td>828</td>
<td>18%</td>
<td>181</td>
<td>40</td>
<td>4</td>
<td>225</td>
<td>18%</td>
</tr>
<tr>
<td>Early Independence Award, 2011-2017</td>
<td>TOTAL</td>
<td>305</td>
<td>207</td>
<td>77</td>
<td>589</td>
<td>40%</td>
<td>115</td>
<td>55</td>
<td>18</td>
<td>188</td>
<td>32%</td>
<td>73</td>
<td>25</td>
<td>1</td>
<td>99</td>
<td>26%</td>
</tr>
</tbody>
</table>
Analyze participation of women and other underrepresented groups … to identify possible causes for their underrepresentation

- Evaluate male and female applicants. Are the starting applicant pools equivalent (look at number and evaluation metrics)?
  - Metrics: Funding received (R grants; NSF, F awards and T32 support for Early Independence; private/foundation awards)
- Aggregate analyses of letters of recommendation using text mining
  - Make comparisons between language used for letters for men, women, URM, awardees, and non-awardees
Pioneer Award Review Process

- Early Independence Award review process looks similar
- Pioneer Award, Early Independence Award, New Innovator Award ask for letters of recommendation

Slide Credit: Betsy Wilder
Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

- Evaluate review processes for the Common Fund HRHR programs
  - Also look at National Institute of Arthritis and Musculoskeletal and Skin Disease X02 applications, which are anonymized for review

- Metrics for reviewer analyses
  - Reviewer gender, race/ethnicity, institutions, field of research
  - Reviewer expertise related to topics of the research proposals

- What might an ideal review panel look like for various stages of review?
Examine institutional diversity and diversity of scientific topics in the applicant and awardee pools

- **Institutions** of applicants and awardees
  - Why do certain institutions have higher frequencies of applicants and awardees?

- FY17 Pioneer Awards: 12 awards total
  - Broad Institute
  - Harvard (3)
  - Harvard Medical School
  - MIT
  - Rockefeller University
  - Stanford (3)
  - University of Miami School of Medicine
  - Weill Medical College of Cornell University

- Analyze all awards, all years
Examine institutional diversity and diversity of scientific topics in the applicant and awardee pools

- **Scientific topic areas** of applicants and awardees
  - Are there under- or over-represented topics among HRHR awards?
  - Are topics that require heavy collaboration represented in HRHR programs?
    - Examples include population studies, epidemiology, studies looking at health outcomes

- **Types of awards: Person-based versus team-based projects**
  - Include team-based HRHR awards, or build into the applications the option to link to or describe a team
  - Place topics of interest that are underrepresented in funding announcements as topics of interest
Other Considerations

- What strategies can inspire innovation in NIH HRHR programs?
- What are characteristics of an ideal high-risk funding announcement?
- How (when) can one assess conceptual vs technical innovation?
- Are there lessons we can take from other organizations such as DARPA and HHMI to apply to high-risk awards at NIH?
After evaluating and analyzing the HRHR programs, propose steps that NIH might take to enhance the diversity of applicants and awardees in these programs, while supporting the best science

- Initial recommendations: December 2018 ACD meeting
- Final recommendations: June 2019 ACD meeting
NIH...
Turning Discovery Into Health
Lawrence.Tabak@nih.gov
Top 19 applicant institutions for Pioneer Award in years 2013 - 2017

<table>
<thead>
<tr>
<th>Institution</th>
<th># apps</th>
<th>% apps</th>
</tr>
</thead>
<tbody>
<tr>
<td>STANFORD UNIVERSITY</td>
<td>78</td>
<td>7.5</td>
</tr>
<tr>
<td>UNIVERSITY OF CALIFORNIA, SAN FRANCISCO</td>
<td>45</td>
<td>4.3</td>
</tr>
<tr>
<td>UNIVERSITY OF CALIFORNIA SAN DIEGO</td>
<td>35</td>
<td>3.4</td>
</tr>
<tr>
<td>UNIVERSITY OF CALIFORNIA LOS ANGELES</td>
<td>32</td>
<td>3.1</td>
</tr>
<tr>
<td>JOHNS HOPKINS UNIVERSITY</td>
<td>32</td>
<td>3.1</td>
</tr>
<tr>
<td>UNIVERSITY OF PENNSYLVANIA</td>
<td>23</td>
<td>2.2</td>
</tr>
<tr>
<td>COLUMBIA UNIVERSITY HEALTH SCIENCES</td>
<td>22</td>
<td>2.1</td>
</tr>
<tr>
<td>MASSACHUSETTS GENERAL HOSPITAL</td>
<td>22</td>
<td>2.1</td>
</tr>
<tr>
<td>YALE UNIVERSITY</td>
<td>21</td>
<td>2.0</td>
</tr>
<tr>
<td>UNIVERSITY OF MICHIGAN</td>
<td>20</td>
<td>1.9</td>
</tr>
<tr>
<td>HARVARD UNIVERSITY</td>
<td>20</td>
<td>1.9</td>
</tr>
<tr>
<td>BRIGHAM AND WOMEN'S HOSPITAL</td>
<td>19</td>
<td>1.8</td>
</tr>
<tr>
<td>MASSACHUSETTS INSTITUTE OF TECHNOLOGY</td>
<td>17</td>
<td>1.6</td>
</tr>
<tr>
<td>ROCKEFELLER UNIVERSITY</td>
<td>15</td>
<td>1.4</td>
</tr>
<tr>
<td>UT SOUTHWESTERN MEDICAL CENTER</td>
<td>13</td>
<td>1.2</td>
</tr>
<tr>
<td>HARVARD MEDICAL SCHOOL</td>
<td>13</td>
<td>1.2</td>
</tr>
<tr>
<td>UNIVERSITY OF MINNESOTA</td>
<td>13</td>
<td>1.2</td>
</tr>
<tr>
<td>PRINCETON UNIVERSITY</td>
<td>12</td>
<td>1.1</td>
</tr>
<tr>
<td>UNIVERSITY OF WASHINGTON</td>
<td>12</td>
<td>1.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>464</strong></td>
<td><strong>44.4</strong></td>
</tr>
</tbody>
</table>