Keynote: Perspectives on Extramural Research in the Era of COVID-19

Michael Lauer, MD
Deputy Director for Extramural Research; Director, Office of Extramural Research
National Institutes of Health (NIH)

NIH Virtual Seminar
November 1, 2021
Virtual Meeting
Disclosures: None
Peer-reviewed report on Moderna COVID-19 vaccine publishes

Data from Phase 3 clinical trial confirm vaccine is effective.

What

The investigational vaccine known as mRNA-1273 was 94.1% efficacious in preventing symptomatic coronavirus disease 2019 (COVID-19), according to preliminary results from a Phase 3 clinical trial reported in the New England Journal of Medicine. The vaccine also demonstrated efficacy in preventing severe COVID-19. Investigators identified no safety concerns and no evidence of vaccine-associated enhanced respiratory disease (VAERD).

The vaccine was co-developed by Moderna, Inc., a biotechnology company based in Cambridge, Massachusetts, and the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.


Francis Collins to step down as director of the National Institutes of Health

Francis S. Collins, M.D., Ph.D., today announced his decision to end his tenure as the director of the National Institutes of Health by the end of the year. Dr. Collins is the longest serving presidentially appointed NIH director, having served three U.S. presidents over more than 12 years.

"It has been an incredible privilege to lead this great agency for more than a decade," said Dr. Collins. "I love this agency and its people so deeply that the decision to step down was a difficult one, done in close counsel with my wife, Diane Baker, and my family. I am proud of all we've accomplished. I fundamentally believe, however, that no single person should serve in the position too long, and that it's time to bring in a new scientist to lead the NIH into the future. I'm most grateful and proud of the NIH staff and the scientific community, whose extraordinary commitment to lifesaving research delivers hope to the American people and the world every day."

A physician-geneticist, Dr. Collins took office as the 16th NIH director on August 17, 2009, after being appointed by President Barack Obama and confirmed by the U.S. Senate. In 2017, he was asked to continue in his role by President Donald Trump, and in 2021, by President Joe Biden. Prior to becoming the NIH director, Dr. Collins served as the director of the National Human Genome Research Institute (NHGRI) from 1993-2008, where he led the International Human Genome Project, which culminated in April 2003 with the publication of the human genome.

• Consensus
  • Community and expertise
  • Empirically-informed dissent
• Diversity
  • Overcome shared biases
  • Multiple perspectives
• Methodological openness, flexibility
NIH INTRAMURAL RESEARCH
NIH is an institution

Supports:
• Over 6,000 scientists
• 11% of NIH budget
• Primary location: Bethesda, MD
• A few labs throughout U.S.

NIH EXTRAMURAL RESEARCH

Supports:
• Over 2,600 institutions worldwide
• Over 300,000 scientists & research personnel
• Awards issued to over 100 countries
• Clinical, Basic, & Translational Research
• Over 80% of the NIH budget

*All figures are estimates.
## Supporting a Growing Community: FY2021 Budget

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Amount ($B)</th>
<th>Percent NIH Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Projects (RPG)</td>
<td>23.1</td>
<td>54.0</td>
</tr>
<tr>
<td>SBIR/STTR</td>
<td>1.17</td>
<td>2.7</td>
</tr>
<tr>
<td>Research Centers</td>
<td>2.75</td>
<td>6.4</td>
</tr>
<tr>
<td>Other Research</td>
<td>2.95</td>
<td>6.9</td>
</tr>
<tr>
<td>Training</td>
<td>0.95</td>
<td>2.2</td>
</tr>
<tr>
<td>Research Contracts</td>
<td>3.36</td>
<td>7.8</td>
</tr>
<tr>
<td>Intramural Research</td>
<td>4.54</td>
<td>10.6</td>
</tr>
<tr>
<td>RMS</td>
<td>2.07</td>
<td>4.8</td>
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</tbody>
</table>
R01-equivalent Numbers

Number of R01 Awards (Thousands)

Fiscal Year

Summary of Trends: Growing Community

• Increased number of awards and awardees
• Increased number of Early-Stage Investigators
• Increased proportion of women (but well below parity)
• Persistent low proportion of Black investigators
• Increased success, funding rates despite more applications / applicants
Medical Research Is Locked Down, Too

Clinical trials grind to a halt as patients are told to stay home and research personnel are redeployed.

By Kevin Sheth
May 4, 2020 5:58 pm ET

I lead clinical trials for medications to treat crippling disorders such as stroke and brain hemorrhages. During the past few months, every one of these studies has come to a grind halt. The pandemic has thrown clinical trials, the lifeblood of new treatments, into disar

STAT

Covid-19 has shuttered scientific labs. It could put a generation of researchers at risk

By Justin Chen
May 4, 2020
“To those individuals in the biomedical research enterprise who have endured disadvantages due to structural racism, I am truly sorry. NIH is committed to instituting new ways to support diversity, equity, and inclusion, and identifying and dismantling any policies and practices at our own agency that may harm our workforce and our science.”

— Francis S. Collins, M.D., Ph.D., NIH Director
2020 NIH Extramural Surveys: The Impact of COVID-19 on the Research Community

In October of 2020, 45,348 researchers at domestic, NIH-funded institutions and 224 research leaders from the top 1,000 NIH-funded domestic institutions responded to an NIH COVID-19 Impact on Extramural Research Survey, which aimed to gauge the impact of COVID-19 on the research community.
At a high-level, survey findings emphasized the impact of COVID-19 on the career trajectory, mental health, and research productivity of extramural researchers:

- 55% of respondents said the pandemic will have a negative impact on their career trajectory.
- 68% of respondents said societal/political events negatively affected their mental health, more than other factors.
- 78% of respondents reported lower levels of productivity since the pandemic began.

Source: NIH COVID-19 Impact Infographic
Impact on Career Trajectory by Career Stage

- Postdoctoral fellow/Resident: 69%
- Faculty (0-6 years): 67%
- Faculty (7-14 years): 61%
- Student: 56%
- Researcher (0-6 years): 54%
- Researcher (7-14 years): 49%
- Faculty (15+ years): 43%
- Researcher (15+ years): 34%
Impact on Career Trajectory by Type of Research

- Laboratory: 61%
- Computational: 52%
- Clinical: 49%
- Sociological / Community-based: 46%
- Epidemiologic / Public Health: 45%
# Impact on Career Trajectory by Race & Gender

<table>
<thead>
<tr>
<th>Race by Gender</th>
<th>% Impacted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian, Men</td>
<td>67%</td>
</tr>
<tr>
<td>Asian, Other Gender</td>
<td>64%</td>
</tr>
<tr>
<td>Asian, Women</td>
<td>62%</td>
</tr>
<tr>
<td>White, Other Gender</td>
<td>61%</td>
</tr>
<tr>
<td>Two or More Races, All Genders</td>
<td>59%</td>
</tr>
<tr>
<td><strong>All Respondents</strong></td>
<td>55%</td>
</tr>
<tr>
<td>AIAN, Women</td>
<td>41%</td>
</tr>
<tr>
<td>African American, Men</td>
<td>40%</td>
</tr>
<tr>
<td>African American, Women</td>
<td>39%</td>
</tr>
<tr>
<td>NHPI, Men</td>
<td>31%</td>
</tr>
<tr>
<td>African American, Other Gender</td>
<td>22%</td>
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</table>
Most Important Predictors of Career Trajectory Concerns

<table>
<thead>
<tr>
<th></th>
<th>Top 10 Variables (Negative Class Predictors)</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ability to apply for grants</td>
<td>0.1634</td>
</tr>
<tr>
<td>2</td>
<td>Progress towards promotion/tenure</td>
<td>0.0627</td>
</tr>
<tr>
<td>3</td>
<td>Reduced access to on-site laboratories</td>
<td>0.0604</td>
</tr>
<tr>
<td>4</td>
<td>Reduced access to core facilities</td>
<td>0.0573</td>
</tr>
<tr>
<td>5</td>
<td>Concern for the health of family and friends</td>
<td>0.0510</td>
</tr>
<tr>
<td>6</td>
<td>Reduced access to colleagues</td>
<td>0.0479</td>
</tr>
<tr>
<td>7</td>
<td><strong>Caretaking responsibilities</strong></td>
<td>0.0402</td>
</tr>
<tr>
<td>8</td>
<td>Lost access to expertise</td>
<td>0.0321</td>
</tr>
<tr>
<td>9</td>
<td>Timeline uncertainty for returning to work</td>
<td>0.0277</td>
</tr>
<tr>
<td>10</td>
<td>Personal mental/physical health has impacted productivity</td>
<td>0.0258</td>
</tr>
</tbody>
</table>

AUC = 79.3
NIH’s Priorities for Early Career Investigators

Thanks to Francis Collins
Flexibilities

• No-cost extensions (2nd no-cost extensions)
• Funded extensions for select F and K awards
• Eligibility extensions:
  • Early-Stage Investigator status: ~500 to ~1000
  • K99/R00
• Leniency on late applications
• Preliminary data post-submission
Childcare Allowance

• $2500 / year / Fellow
• Defray child-care costs
  • Children < 13 years, disabled < 18 years
  • Licensed childcare provider
  • Recipient responsible for documentation
• Plan for T awardees in FY2022
This article has been retracted: N Engl J Med. DOI: 10.1056/NEJMc2021225.

Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19

Mandeep R. Mehra, M.D., Sapan S. Desai, M.D., Ph.D., SreyRam Kuy, M.D., M.H.S., Timothy D. Henry, M.D., and Amit N. Patel, M.D.
A Genomic Strategy to Refine Prognosis in Early-Stage Non–Small-Cell Lung Cancer

Anil Potti, M.D., Sayan Mukherjee, Ph.D., Rebecca Petersen, M.D., Holly K. Dressman, Ph.D., Andrea Bild, Ph.D., Jason Koontz, M.D., Robert Kratzke, M.D., Mark A. Watson, M.D., Ph.D., Michael Kelley, M.D., Geoffrey S. Ginsburg, M.D., Ph.D., Mike West, Ph.D., David H. Harpole, Jr., M.D., and Joseph R. Nevins, Ph.D.
“Vincent E. Price, president of Duke University, said … ‘This is a difficult moment for Duke. This case demonstrates the devastating impact of research fraud and reinforces the need for all of us to have a focused commitment on promoting research integrity and accountability.’”

Consequences for Scientists

THE UNITED STATES ATTORNEYS OFFICE
DISTRICT of MASSACHUSETTS

U.S. Attorneys » District of Massachusetts » News

Department of Justice
U.S. Attorney’s Office
District of Massachusetts

FOR IMMEDIATE RELEASE

Former Newton Scientist Agrees to Pay $215,000 to Resolve Allegations of False Statements in Grant Application

BOSTON – A former Newton scientist sponsored by Massachusetts General Hospital (MGH) has agreed to resolve allegations that he submitted false statements on a grant application to the National Institutes of Health (NIH).
University Researcher Sentenced to Prison for Lying on Grant Applications to Develop Scientific Expertise for China

WASHINGTON – An Ohio man and rheumatology professor and researcher with strong ties to China was sentenced to 37 months in prison for making false statements to federal authorities as part of an immunology research fraud scheme. As part of his sentence, Zheng was also ordered to pay more than $3.4 million in restitution to the National Institute of Health (NIH) and approximately $413,000 to The Ohio State University.
Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Baranzewicz, A P Dhillon, M A Thompson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years; range 3–10), 11 boys, were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records, ileocolonoscopy, and biopsy sampling, magnetic resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings One of behavioural symptoms was assessed by the parents, and measures, and no vaccination in eight of the 12 children, with measles, mumps, and rubella in one, and influenza B in one. All children had intestinal abnormalities ranging from lymphoid nodular hyperplasia to severe ileitis. Histology showed patchy chronic inflammation in 11 children and reactive changes in inflammatory cells in seven, but not granulomas. Neurological examination included autism, tic disorder, attention deficit disorder (ADD), or possible postnatal or autistic behaviour. There were no focal neurological abnormalities. EEG in two children and ETS tests were normal. Although neurological symptoms were significantly raised in patients with ASD compared with agematched controls, we were unable to demonstrate a role for ASD in four children, and autism and ADD in four children.

Interpretation Developmental and gastrointestinal disorder were associated gastrointestinal disorder and developmental regression in a group of patients with ASD, which was generally associated in time with possible environmental trigger.

Lancet 1998; 351: 537–41
See CONNECTED PDF

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including language. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and vomiting, and, in some cases, food intolerance. We noticed subtle clinical signs, and gastrointestinal features of the illness.

Patients and methods

12 children, 11 boys, referred to the department of paediatric gastroenterology for investigation of a pervasive developmental disorder, with initial complaints of abdominal pain, diarrhea, and constipation, and in some cases, food intolerance. All children were admitted for the investigation and assessment by their parents.

Clinical investigations

Psychometric tests including intelligence and developmental delay tests, and tests for the detection of autism were obtained by the senior clinician (JR-St).

Developmental testing included a review of prospective developmental milestones from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital, all had been assessed previously elsewhere, these assessments were used to the basis for their diagnosis.

After bowel preparation, ileocolonoscopy was performed by SIM or X-ray under sedation with midazolam and pethidine. Pulsed-scan and fluorodeoxyglucose-labeled brain scans were taken from the cervical spine, ascending, descending, and sigmoid colon, and from the rectum. The procedure was repeated by vivo or static images, and were compared with those of the previous seven consecutive pediatric colonoscopies (four normal colonoscopies and three colonoscopy with abnormal colitis), in which the physician reported normal appearances in the terminal bowel. Barium follow-through radiography was possible in some cases.

Alcohol solution, oral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and somatosensory evoked potentials (where compliance made these possible), and lumbar punctures were done.

Laboratory investigations

Thrombocyte function, serum long-chain fatty acids, and cerebrospinal-fluid bacillus were measured to exclude known causes of gastrointestinal, neurological, and psychiatric illness.

In addition, because NIH recipients are expected to provide safe and healthful working conditions for their employees and foster work environments conducive to high-quality research, the request for approval should include mention as to whether change(s) in PD/PI or Senior/Key Personnel is related to concerns about safety and/or work environments (e.g. due to concerns about harassment, bullying, retaliation, or hostile working conditions).
Overarching Themes

1. Transparency and Accountability in Reporting of Professional Misconduct, especially Sexual Harassment
2. Mechanisms for Restorative Justice
3. Safe, Diverse, and Inclusive Environments
4. System-wide Change

Rec 1.1 Create a parallel process to treat professional misconduct, including sexual harassment, as seriously as research misconduct

**Actions:**
- Extramural Integrity Team reviews all professional misconduct allegations
- Complaints involving over 390 individuals received, addressed

Rec 1.3 Establish clear and transparent SOPs to respond to reports/findings of professional misconduct, including sexual harassment, or change in PI status in extramural labs.

- Action: Posted NIH process for handling allegations of sexual harassment on an NIH-funded project at a recipient institution.

Reprise: Perhaps the Current Question

- Consensus
  - Community and expertise
  - Empirically-informed dissent
- Diversity
  - Overcome shared biases
  - Multiple perspectives
- Methodological openness, flexibility

https://press.princeton.edu/books/hardcover/9780691179001/why-trust-science
The extraordinary effort to speed the development of treatments and vaccines in response to the COVID-19 pandemic has put into sharp relief the need for the global science community to share scientific data openly … NIH is addressing this need with a new NIH Policy for Data Management and Sharing. This policy … establishes the baseline expectation that data sharing is a fundamental component of the research process …

• **Growing community**
  – Increasing numbers: awards, awardees (including early career)

• **Stressed community**
  – Ongoing effects of COVID-19
  – Structural racism, opportunities to enhance diversity

• **Assuring trust, transparency, credibility**
  – Integrity above all
  – Enhancing openness through data sharing