NICHD Director’s Report

Diana W. Bianchi, M.D.

June 7, 2021
Talk Outline

• NIH Budget
• COVID-19 Research Updates
• Human Placenta Project
• NICHD Staff Updates
FY 2022 Appropriations

- Congress is interested in NICHD-supported science!
- Testified at both House and Senate Appropriations subcommittee hearings for the FY 2022 budget
- Questions on:
  - COVID in children (including long-term effects of the pandemic)
  - Maternal health
  - Medications taken by breastfeeding women
  - Trans-NIH Pediatric Research Consortium (N-PeRC)
  - Artificial intelligence
  - Environmental influences on Child Health Outcomes (ECHO)
FY 2022 Appropriations

- President’s Budget released May 28, 2021
- NIH - $51 billion, increase of $9 billion
  - Includes $6.5 billion to establish an Advanced Research Projects Agency for Health (ARPA-H)
- NICHD –
  - $1.94 billion, which includes:
    - $30 M for the IMPROVE initiative (Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone)
    - $15 M for research on effects of SARS-CoV-2 infection in children
  - Proposes to move two programs (and their budgets) from NIH OD to NICHD
    - Environmental influences on Child Health Outcomes (ECHO)
    - INCLUDE project (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome)
Environmental influences on Child Health Outcomes (ECHO)

- Understanding the effects of environmental exposures on child health and development through existing cohort studies

- Two major components
  - Cohorts — observational research
    - Share standardized core data elements
    - Current data includes >90,000 participants (>57,000 children)
  - IDeA States Pediatric Clinical Trials Network — intervention research

- Focuses on 5 key pediatric outcomes with high public health impact
  - Pre-, peri-, and postnatal outcomes
  - Upper and lower airway disorders
  - Obesity
  - Neurodevelopment
  - Positive health
ECHO Research and Opportunities

- ECHO staff will add expertise to NICHD: pediatric epidemiology, longitudinal studies, clinical trials, building networks/consortia, data science, toxicology, team science
- We are already close collaborators (e.g., DIPHR)
- Opioid epidemic - ECHO partners with NICHD on the Advancing Clinical Trials in Neonatal Opioid Withdrawal (ACT NOW) as part of the HEAL initiative
  - Pharmacologic and non-pharmacologic trials to build evidence for best practices to care for newborns with opioid withdrawal syndrome
- Recent ECHO research headlines
  - Development of new asthma differs by age, sex, and race for children
  - Identified a chromosomal variant associated with wheezing phenotypes in childhood
  - Understanding childhood obesity in the US: Leverages data from 37,000 children across 70 cohorts
  - Influence of sleep on children’s well-being
- Upcoming workshop: Pre-conceptional Origins of Child Health Outcomes (June 17-18)
COVID-19 Vaccination and Menstruation

• 56 letters of interest responding to initial outreach

• NICHD issued a Notice of Special Interest (NOT-HD-21-035) seeking projects that would include:
  • Validated measures
  • Participants from diverse/understudied populations
  • Existing large cohorts or data sets

• High priority projects include studies that:
  • Include baseline (pre-vaccination) menstrual health data
  • Address mechanism for vaccine-related menstrual changes, if found
  • Account for effects of non-vaccine variables of the current environment (e.g., stress) on menstrual health

• Applications due June 17; awards anticipated late July 2021
Intramural Research: COVID-19 and the Placenta

• This study, which included NICHD DIR staff, demonstrated that the placenta does express receptors, such as ACE2, at term
• The expression level of these receptors varies over gestation
• The study suggests a mechanism for why SARS-CoV-2 does not cross the placenta

https://msphere.asm.org/content/6/2/e00250-21
Rouault Lab: Section on Human Iron Metabolism

A new proposed medicinal therapy for COVID-19 based on the discovery that its RNA dependent replicase (RdRp) requires iron sulfur (FeS) cofactors for in vivo function

- The Rouault Lab is studying ways to prevent early SARS-CoV-2 infection from spreading to neighboring cells.

- SARS-CoV-2 uses an enzyme, RNA replicase, to replicate its genome and transcribe its genes. Targeting this enzyme can cripple the virus’ ability to replicate and infect cells.

- The lab has found that the SARS-CoV-2 RNA replicase requires iron sulfur clusters as cofactors. Targeting these cofactors can potentially serve as a therapeutic for people with COVID-19.

- Published online in Science
TEMPOL inhibits the activity of the RdRp complex of SARS-CoV-2 and kills live virus in cell cultures

- The drug TEMPOL is a membrane-permeable radical scavenger that can degrade accessible iron sulfur clusters
- The experiment in the middle shows that TEMPOL can block the activity of the SARS-CoV-2 RNA replicase. The experiment on the right shows that TEMPOL can kill live virus in cell cultures
- The doses that kill the virus are comparable to doses used in previous mouse and human studies for other conditions
- The lab is working with collaborators to potentially test TEMPOL in a clinical study for COVID-19
- Published online in *Science*
NIH Rapid Acceleration of Diagnostics (RADx)℠

<table>
<thead>
<tr>
<th>Project</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RADx Tech</td>
<td>Highly competitive, rapid three-phase challenge to identify the best candidates for at-home or point-of-care tests for COVID-19</td>
</tr>
<tr>
<td>RADx-Advanced Testing Program (RADx-ATP)</td>
<td>Rapid scale-up of advanced POC technologies to accelerate and enhance and validate throughput – and support of ultra-high throughput machines and facilities</td>
</tr>
<tr>
<td>RADx-Radical (RADx-rad)</td>
<td>Develop and advance novel, non-traditional approaches or new applications of existing approaches for testing</td>
</tr>
<tr>
<td>RADx-Underserved Populations (RADx-UP)</td>
<td>Interlinked community-engaged projects focused on implementation strategies to enable and enhance testing of COVID-19 in underserved and/or vulnerable populations</td>
</tr>
</tbody>
</table>
RADx-UP Return to School Diagnostic Testing Approaches

**Budget:** $50M Total; $33M recommended for funding in R2S Phase I

**Goal:** Develop and test COVID-19 diagnostic testing approaches to safely return children and staff to the in-person school setting in underserved and vulnerable communities

**Mechanism:** Other Transaction Authority to provide flexibility for changing circumstances and funding of non-traditional partners

- Focus on children and adolescents below the age eligible for vaccination via Emergency Use Authorization; include children through high school based on timing of award and rates of vaccination in the community
- Advance methods to integrate testing in return to or maintenance of in-person instruction
- Identify effective, scalable, and sustainable testing implementation strategies, including in-school testing, in community pediatric primary care clinics, childcare centers, preschool, and school settings serving primarily underserved or disadvantaged children and their families.
Phase I Projects

• Projects cover a range of settings including public, charter, tribal, early education, and special education schools.

• Children range in age from 3-17 years, with the majority of projects covering children from 6-17 years of age.

• Critically, these projects include children with medical complexity or intellectual or developmental disabilities who may not be able to use other mitigation strategies.

<table>
<thead>
<tr>
<th></th>
<th>Number of Projects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blacks/African Americans</td>
<td>6</td>
</tr>
<tr>
<td>Hispanics/Latinos/as</td>
<td>4</td>
</tr>
<tr>
<td>Asian Americans</td>
<td>3</td>
</tr>
<tr>
<td>American Indians/Alaska Natives</td>
<td>2</td>
</tr>
<tr>
<td>Underserved Rural Populations</td>
<td>1</td>
</tr>
</tbody>
</table>
Phase II Scientific Goals

• Address the **impact of vaccine availability** for school personnel and students ages 12 and older; include efforts to increase **vaccine confidence**

• Provide information on circulating **variants** and **breakthrough infections** following vaccination

• Increase the reach of the research in **racial and ethnic groups** not included in applications funded in Phase I

• Ensure coverage of **early education or preschool cohorts** and specific strategies for testing and mitigation in this population

• Focus on increasing the geographic areas covered to understand **regional variation** in mitigation strategies and to increase the number of projects in **dense, urban areas or hard to reach rural areas**
Human Placenta Project
NICHD Science: Human Placenta Project

- The placenta is NICHD’s organ
- NICHD has supported HPP with >$91M over 7 years
- HPP investment is in addition to a large and continued investment in basic placenta research
- Hundreds of publications
- Some advances translate to other areas of research (e.g., rapid COVID-19 testing; novel approaches to isolate extracellular vesicles)
- Placenta is connected to cardiac disease, diabetes, and other conditions later in life
  - “The placenta is the center of the chronic disease universe.” – Kent Thornburg
HPP Imaging Advances: Wave Reflection

• Wave reflection is related to villous tree structure (mouse model)

• Wave reflection measurements are altered in the presence of placental pathology, such as growth restriction in study of 427 patients

• Increased sensitivity compared to Uterine Artery Pulsatility Index

• Potential marker of pregnancies at risk for stillbirth

Lindsay Cahill (Memorial University of Newfoundland) and John Sled (U Toronto)
HPP Advances: Placental Vesicles

- Placental vesicles are a recently appreciated element of the maternal/fetal/placental ecosystem
- Placental vesicle characteristics and cargo (microRNAs, lipids, proteins) may reflect placental health
- Acoustic/microfluidic isolation represents a gentle, high yield approach
- Works for vesicles from any source circulating in blood

Yoel Sadovsky (Magee Women’s) and Tony Huang (Duke)
Welcome to New NICHD Extramural Staff!

Maggie Young
Chief Grants Management Officer
DER

Marianne Galcynski
Grants Management Specialist
GMB

Bob Tamburro, MD, MSc
Senior Advisor for Clinical Research
DER

Jolanta Topczewska, PhD
Scientific Review Officer
SRB

Jagpreet Nanda, PhD
Scientific Review Officer
SRB
Welcome to New NICHD Extramural Staff!

Maria Nurinskaya, PhD
Program Officer
NCMRR

Kimberlea Gibbs, MPH
Nutrition Specialist
PGNB

Alison Harrill, PhD
Program Officer
OPPTB

Molly Minnear, PhD
Program Officer
IDDB
Welcome to New NICHD Intramural Staff!

Laverne Mensah, MD  
Deputy Clinical Director

Bobby Cheon, PhD  
Tenure-track Investigator  
DIPHR

Hiren Karathia, PhD  
Staff Scientist  
DIPHR

James Morton, PhD  
Tenure-track Investigator  
DIPHR
Welcome to NICHD Office of the Director Staff!

Laura Berkson, JD  
Director, Office of Legislation, Public Policy, and Ethics

Kimberly Kober  
Management Analyst

Adam Politis, MA  
Special Assistant to the Deputy Director

Hillary Hoffman, PhD  
Science Writer/Editor
Leadership Positions: Searches Underway

• **NICHD Scientific Director**
  • Readvertising the position
  • Charged the search committee
  • Recruitment open from June 1 - August 1

• **Director, Division of Population Health Research (DIPHR)**

  • We are hiring for multiple other positions
    • Tenure track investigators in basic and translational science
    • Opportunities in Division of Extramural Research
  • More info at [https://www.nichd.nih.gov/about/jobs](https://www.nichd.nih.gov/about/jobs)
Thank You!

Questions?