20th Meeting of the Down Syndrome Consortium: A Public-Private Partnership

June 11, 2021; 12:30-2:00pm ET

Agenda

- Roll Call – Rachel Goldman, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), National Institutes of Health (NIH)
- Welcome and Office of the Director (OD) Updates– Melissa Parisi, NICHD, and Erica Landis, OD, National Institutes of Health (NIH)
- NIH and Down Syndrome Research Plan Updates – Melissa Parisi and Rachel Goldman, NICHD
- Summary of Data Coordinating Center (DCC) Listening Tour – Amanda Hill, INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) Project DCC
- Down Syndrome Diversity Group (DS-DG) – Sujata Bardhan, NICHD
- Round Robin – All
- Brief Discussion about recent U.S. Food and Drug Administration (FDA) approval of Aducanumab for Alzheimer's Disease

Meeting Participants

- Adam Apostoli, Leidos
- Sujata Bardhan, NICHD, NIH
- Nicole Baumer, Down Syndrome Medical Interest Group (DSMIG)
- Alicia Bazzano, Special Olympics
- Laura Berkson, Office of Legislation, Public Policy, and Ethics (OLPPE), NICHD
- Marilyn Bull, American Academy of Pediatrics (AAP)
- Sarah DeMaio, Association of University Centers on Disability (AUCD)
- David Egan, Self-Advocate
- Kathleen Egan, Parent
- Joaquin Espinosa, Linda Crnic Institute
- Rachel Goldman, NICHD, NIH
- Heather Harmer, Special Olympics
- Ashley Helsing, National Down Syndrome Society (NDSS)
- Jim Hendrix, Lumind IDSC
- Amanda Hill, INCLUDE DCC
- Hampus Hillerstrom, Lumind IDSC
- Colleen Jackson-Cook, International Mosaic Down Syndrome Association (IMDSA)
- Debbie Jae, Invitae
- Matthew Janicki, National Task Group (NTG)

- Seth Keller, NTG
- Erica Landis, OD, NIH
- Mitchell Levitz, Self-Advocate
- Huiqing Li, National Heart, Lung, and Blood Institute (NHLBI), NIH
- Cara Long, National Institute of Neurological Disorders and Stroke (NINDS), NIH
- Keith Mason, Jerome Lejeune Foundation
- Anna Mazzucco, OD, NIH
- Sarah Mulligan, Down Syndrome Affiliates in Action (DSAIA)
- Brad Newsome, Fogarty International Center (FIC), NIH
- Maggie Nygren, American Association on Intellectual and Developmental Disabilities (AAIDD)
- Melissa Parisi, NICHD, NIH
- Roger Reeves, T21 Research Society (T21RS)
- Adam Resnick, INCLUDE DCC
- Margot Rhondeau, NDSS
- Robert Riddle, NINDS, NIH
- Laurie Ryan, National Institute on Aging (NIA), NIH
- Charlene Schramm, NHLBI, NIH
- Malcolm Smith, National Cancer Institute, NIH
- Heather Snyder, Alzheimer’s Association
- Nathaniel Stinson, National Institute on Minority Health and Health Disparities, NIH
- David Tolleson, National Down Syndrome Congress (NDSC)
- Jessamy Tang, Down Syndrome International (DSI)
- Erika Tarver, NIA, NIH
- Frosso Voulgaropoulou, National Institute of Allergy and Infectious Diseases, NIH
- Chris Weber, Alzheimer’s Association
- Michelle Sie Whitten, GLOBAL

Welcome and OD Updates

Melissa Parisi, NICHD, Chair, and Erica Landis, OD, NIH

- Welcome to Laura Berkson, who is replacing Lisa Kaeser as the Director of OLPPE at NICHD.
- Welcome to Erica Landis, who previously worked with Anna Mazzucco in NIH OD and will continue working on the INCLUDE project as Anna transitions to the Helping to End Addiction Long-term® Initiative. Dr. Landis mentioned she would usually give a budget update at this time, but we are still waiting to hear from Congress about the appropriation for INCLUDE.
- Welcome to Brad Newsome at FIC. Dr. Newsome emphasized the interest in bringing international involvement to the INCLUDE project.

NIH and Down Syndrome Research Plan Updates

Melissa Parisi, NICHD, NIH

- Dr. Parisi discussed the FY2021 appropriation for INCLUDE, which is $65 million.
- Regarding the 2021 NIH INCLUDE Down Syndrome Research Plan, we are working on the bibliography and incorporating feedback from the second request for information (RFI) (NOT-HD-21-014); the finalized Down syndrome research plan is scheduled for release at the end of the summer.

INCLUDE DCC Listening Tour Update

Amanda Hill, Strategic Coordinator, Administrative and Outreach Core, INCLUDE DCC, Linda Crnic Institute for Down Syndrome, University of Colorado

- Held community listening tours to share the mission and activities of the INCLUDE DCC and gather feedback from community members. Spoke with most of the organizations represented in the NIH DS Consortium and more than 36 community members and clinical/scientific professionals. Reviewed summary of tours and emergent themes; created collaborative draft of internal response and plans; and finalized reports for internal use/reference to share with community organizations.
- Emerging themes in listening tours:
    - Educating the community on the research process and research opportunities
    - Empowering health providers to engage their practices and patients in research
    - Communicating results and discoveries to the community in an understandable manner
    - Communicating results and discoveries to clinicians and their implications for clinical care
    - Structuring the hub and communications to support advocacy and policy development
    - Increasing diversity and inclusion in data and dissemination
    - Creating bi-directional information flows for interactions with users
    - Leveraging community partnerships to ensure continued success

- Plans and actions in response:
    - Create a Communications and Outreach Strategy to educate and engage with key audiences, including the Down syndrome community and health providers
    - Define user personas and use cases for the Down syndrome community and researchers
    - Develop and broadly disseminate requirements for a minimal common dataset
    - Create a “Down Syndrome Diversity Group” to address diversity, equity and inclusion
    - Create a formal structure for Down syndrome community organizations to partner with the DCC → supporting mission and activities

Down Syndrome Diversity Group (DS-DG)

Sujata Bardhan, NICHD, NIH

- The NIH UNITE initiative was established to identify and address structural racism within the NIH-supported and the greater scientific community; to establish an equitable and civil culture within the biomedical research enterprise and reduce barriers to racial equity in the biomedical research workforce; and to identify opportunities, make recommendations, and develop and implement strategies to increase inclusivity and diversity in science. A recent RFI was issued to gather stakeholder input. NICHD has also committed to doing more to address underlying causes of health disparities through the STRIVE (Strategies to EnRich Inclusion and AchieVe Equity) Initiative. NICHD is especially interested in supporting the pipeline of new investigators, starting as early as undergraduate students. The DS Consortium can assist with community engagement, increasing diversity in the pipeline, increasing our investment in low-resourced communities, and increasing diversity in our communities.

- Members of the DS Consortium commented that we also need to increase the number of families in clinical studies with individuals severely affected by Down syndrome. Members also suggested reaching out to genetic counselors at historically Black colleges and universities and focusing on families from low-income communities. Dr. Bardhan mentioned that the NIH definition of diversity includes people from low-resourced communities and discussed the possibility of forming a subgroup within the consortium to discuss these issues. An NIH member of the consortium will send out an email asking for nominations, including family members and self-advocates, to join the subgroup.

Round Robin

All

- Maggie Nygren, AAIDD – no updates and gave time to group.

- Heather Snyder, Alzheimer's Association – Alzheimer's Association International conference is this summer in Denver and will be offered in-person and virtually. There will be several sessions looking at AD-related changes. The iSTAART webinar series will be held every other month.
    - More information on Alzheimer's Association International Conference: alz.org/AAIC
    - More information on iSTAART webinars (you may need to click on Archived discussions): https://www.alz.org/research/for_researchers/grants/research-webinars

- Marilyn Bull, AAP – AAP is in the process of revising the Child Healthcare guidelines for Down syndrome and is hoping to publish within the next few months. AAP has a strong diversity initiative and is excited about the diversity discussion taking place within the consortium.

- Sarah DeMaio, AUCD – The annual conference will take virtually on Nov 15-17, 2021. The theme is "Learning Together: Connecting Research and Lived Experience," and the call for proposals ended 6/11/21. There will be a focus on translation of scientific materials to plain language for persons with intellectual and developmental disabilities (IDDs). Please reach out to Sarah DeMaio for partnerships about plain language and standards.
  - Link to AUCD's conference website and proposal submission page: https://www.aucd.org/conference/template/page.cfm?id=50268

- Jessamy Tang – The hiring chain video about employment for people with Down syndrome has been very valuable. We will be fielding questions to create employment guidelines. The World Down Syndrome Conference will be November 18-20.
  - Hiring Chain video by CoorDown: https://www.youtube.com/watch?v=SKku4RAWa4M
  - Launch of Education Guidelines: https://www.ds-int.org/blog/launch-of-our-education-guidelines
- Nicole Baumer, DSMIG – the DSMIG conference is June 17-19, 2021. On behalf of David Tolleson who is not available, the NDSC conference is June 21-26, 2021. Both conferences will be held virtually.
- Michelle Sie Whitten, GLOBAL – Will be holding a global research and medical care roundtable at NDSC, which is free to anyone registered. The virtual Leukine trial is going forward, of which GLOBAL and Alzheimer's Association provided seed money for. The Acceptability Gala will be held virtually on July 21, 2021, and costs $25 per person. DSDN will be held in Denver in September. Working on a DEI advisory board with Jamie Foxx family on topics including autism spectrum disorder and mosaicism.
  - Link to the Acceptability Gala: https://www.globaldownsyndrome.org/2021-acceptability-gala/
  - NDSC Convention GLOBAL Research & Medical Care Roundtable - Thursday 6/24/21 from 2pm-5pm MT. https://zoom.us/j/95764722660?pwd=L0R2d2NITzdOQVFzYnIyN0lGTWc4dz09

- Colleen Jackson-Cook, IMDSA – In-person research retreat July 15-18 at Yogi Bear Jellystone Resort in Coryville, PA. The retreat is for everyone with Down syndrome, not just mosaicism. Updated brochure available on website. There will be many socially distanced activities at the retreat.
  - Address for IMDSA retreat weekend: https://www.imdsa.org/R&R2021

- Jim Hendrix and Hampus Hillerstrom, Lumind IDSC – Published first paper from LIFE-DSR study on plasma biomarkers for Alzheimer's disease. Collaboration took place between 50 scientists and 12 working groups to provide recommendations to the NIH Down Syndrome INCLUDE Research Plan. Published an article on that effort as well as a review article. Created Research DS Consortium with Merck and AbbVie and was able to launch four new Down syndrome research studies. Met with FDA in March for DS-AD Clinical Trials; provided debrief meetings with stakeholders. Issues discussed at meeting included how to diagnose AD in Down syndrome, accelerated approval and biomarkers, drug safety, and the Map-Habit digital tool focused on independence. Looking for participants for an open survey for caregivers of adults.

    - Caregiver survey: https://bit.ly/CaregiverChallenges

- NDSC – David Tolleson was not available for the meeting but will be stepping down as director in October.

- Ashley Helsing, NDSS – virtual adult summit finished in April; presentations available on conference website (see below). Working on Capitol Hill. The American Rescue Plan was successful; gave direct funding for IDEA and home-based services and adult dependents. Transition to Competitive Employment Act. Charlotte Woodward Transplant Discrimination Act. Reintroduction of Marriage Act. Always working to ensure that people have more information about ABLE programs and expanding those programs as well.
    - Nondiscrimination in Organ Transplantation Laws & Toolkit: https://www.ndss.org/programs/ndss-legislative-agenda/healthcare-research/nondiscrimination-in-organ-transplantation-laws-toolkit/
    - NDSS Adult Summit materials: https://www.ndss.org/2021-ndss-virtual-adult-summit/

- Matthew Janicki, NTG – Looking at the implications of COVID-19 on people with DS, such as post-COVID mental health issues and the impact on Down syndrome and social isolation, partnering with T21RS on survey regarding this. Concerned that the guidance coming out is lacking specific information about screening individuals with IDDs. Working with NIH and CMS to get this; plan to present at the National Alzheimer's Plan Act meeting in July. Newly approved aducanumab (Aduhelm) medication to treat Alzheimer's disease; created a webpage on NTG site about this for families (below).
    - NTG Aduhelm page: https://www.the-ntg.org/aduhelm-information

- David Egan, Self-Advocate – Remarks read by David:
  Hello, everyone. This is David Egan and I am pleased to give an update. As an advocate for individuals with Down syndrome, I want to thank all of you for caring about the issues that affect the lives of individuals with Down syndrome and working together to improve our lives. As many of you know, I am an eager and enthusiastic supporter of research. It has always been important to me and my family. Since we met last, I have explored further the REACH-UP-DS initiative. Research Education, Advocacy, Core Health You Participate Down syndrome. I started talking about the idea last October with NIH and several national leaders in the Down syndrome community. I also talked about it last February when we all met and told you that the goal is to maximize research participation in the INCLUDE program. I connected a few times with Dr. Espinosa and his team at the National Data Coordinating Center. We are working together to support each other in speaking at conferences to encourage scientists to apply to do research and families with individuals with Down syndrome to participate in studies and clinical trials. I will also join Global at their medical roundtable during the NDSC Convention June 24th. I have worked with many of you within and outside of the Down syndrome associations, like with Special Olympics. Lately I was invited by two Special Olympics groups in Michigan to talk about inclusion and it was a very rewarding experience. I am hoping opportunities may arise with the USA National Games in Florida and later at the World Games in Russia where we can also share

ideas about research and it's impact on our lives. As many of you know, I am an author and my book: "More Alike Than Different: My Life with Down syndrome was distributed to every senator and member of Congress thanks to NDSS who led the initiative after they organized a webinar about the book this past January. The reason I share that with you is that I have a chapter about research in my book and I am thinking that maybe it would be a good idea to have every researcher, physicians and health care provider working with individuals with Down syndrome to have a copy of my book. I think they will enjoy reading it and gaining some insights. In fact, last week, I went for my physical with my doctor and she knew about my book. We talked about the possibility to have a webinar with all of the health care providers at Kaiser Permanente who have patients with Down syndrome. I will keep you posted. So, like I said, I want you to know that I am available to all the entities that belong to this consortium. I want to promote research at your events and in your programs. Feel free to call on me as I am ready to help promote and advocate the needs of individuals with Down syndrome. And as we all know, none of us can do this alone. Collaboration makes us stronger. I welcome feedback and contributions from all of you.
Thank you.
  - David Egan's website: https://davideganadvocacy.com/

- Heather Harmer, Special Olympics – New to this group. Some Special Olympics activities are opening and pairing with vaccination events. Ms. Harmer is co-chairing an aging athlete task force with Dr. Keller. As athletes are getting older, there is less participation in sports, and we want to re-engage these individuals and keep them involved for as long as they would like to be. Collecting data on this.

- Roger Reeves, T21RS – Had a virtual conference this past week. We appreciate everyone's support, including Lumind and GLOBAL, who are founding sponsors. Had representation from every continent in the world except for Antarctica. This is the only regular opportunity for investigators in Down syndrome to get together. Science and Society session for families will be available through T21RS website. Access to recordings of all the sessions on website for T21RS members. Marie-Claude Potier gave a plenary on endosomes as a target for AD. Nice wrap-up of T21RS activities on COVID-19 by Stephanie Sherman.
  - T21RS Science and Society

Aducanumab (Aduhelm) Discussion

- Laurie Ryan, NIA, gave an overview of the Aducanumab drug approved by the FDA this week. It is a monoclonal antibody given by infusion and was approved by the FDA very broadly for the treatment of Alzheimer's disease. There are no exclusionary criteria. Imaging is required to monitor side effect ARIA (Amyloid-Related Imaging Abnormalities), which can lead to swelling and bleeding. NIH cannot endorse or recommend any drug or treatment.

- Members of the consortium engaged in discussion about the approval of the drug and implications for individuals with Down syndrome. Concerns were raised, such as the lack of participation of people with Down syndrome in the studies, so unclear if people with DS will react the same as the neurotypical population. There were also concerns with ARIA because people with Down syndrome have a higher risk of edema. Questions arose about when someone with Down syndrome would be eligible, the association between the amount of plaques and the disease itself, and the increased risk of hemorrhage if drug IV infusion dose is increased too quickly. At least two MRIs are needed to monitor for ARIA, and people with Down syndrome cannot always tolerate imaging. There are some practical challenges associated with the drug, including equity in access due to cost. Other members emphasized that while there are questions about the drug, it is a step forward, but there is still much work to be done. NIH staff invited researchers to apply for funding through the R61/R33 mechanism for phased clinical trials to investigate the drug further.

- Link to INCLUDE R61/R33 FOA: Clinical Trials Development for Co-Occurring Conditions in Individuals with Down syndrome: Phased Awards for INCLUDE (R61/R33 Clinical Trial Required)
- LuMind IDSC statement on Aduhelm and implications for DS: https://www.lumindidsc.org/s/1914/20/interior-share.aspx?sid=1914&gid=2&pgid=1471&cid=3478&ecid=3478&crid=0&calpgid=61&calcid=1176
- Comments on aducanumab approval from some of the scientists involved: https://www.nature.com/articles/d41586-021-01546-2
- NTG Aduhelm Page: https://www.the-ntg.org/aduhelm-information