

»»» 2023 NEWSLETTER «««

ALANA DOWN SYNDROME CENTER



**BUILDING RESEARCH, TRAINING, AND
TECHNOLOGY FOR A WORLD OF GREATER
INCLUSION, POSSIBILITY, AND ACCESSIBILITY
FOR PEOPLE WITH DOWN SYNDROME.**

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BRAIN CIRCUITS AND STIMULATION

➤➤➤ GAMMA FREQUENCY OSCILLATIONS

Foundational studies in the Tsai lab have demonstrated that manipulating specific brain oscillations in the gamma frequency range of 40Hz, using sensory stimulation such as light and sound, can decrease Alzheimer's disease (AD) pathology and improve cognition in AD mouse models. Preliminary Phase 2 clinical results suggest the therapy may be effective in patients with early Alzheimer's as well. **Now we've been able to extend these studies to Down syndrome models as well as tests in humans.**

BIG DATA APPROACHES

Down syndrome changes how a person's body and brain develop, causing both mental and physical challenges. But outcomes vary greatly across individuals and cognitive, behavioral and social interactions. The molecular underpinnings of this variability aren't well known and could significantly impact therapeutic interventions to improve outcomes for people with Down syndrome. Our goal is to explore these molecular underpinnings using big data approaches.

➤➤➤ CREATING A CELL ATLAS FOR DOWN SYNDROME

Understanding the molecular basis of Down syndrome variables requires systematic mapping of the molecular pathways, biological processes, regulators, individual cells and brain regions in multiple DS individuals. And because the cognitive decline and amyloid plaque formation characteristic of Alzheimer's disease significantly increase in people with Down syndrome, AD provides an important setting for studying biological variability. **We are comparing gene expression differences in each single cell and chromatin regulatory areas across cells from brains of people with DS and/or AD.**

A LETTER FROM THE DIRECTOR

As the director of the ADSC, I want to emphasize the vital role research plays in understanding and improving the lives of those with Down syndrome. Our commitment to investigating the consequences of trisomy 21 is not just a scientific pursuit; it's a humanitarian necessity. Through focused research, we strive to uncover breakthroughs, and aim to foster a society where every individual, regardless of their genetic makeup, can flourish and contribute meaningfully.

Li-Huei Tsai
Director, ADSC



UNDERSTANDING BODY SYSTEMS DYSFUNCTION

»»» BUILDING BETTER HEARTS FOR BABIES WITH DOWN SYNDROME

We are seeking to build better hearts by identifying the gene control mechanisms that drive development and disease. Down syndrome is a particular focus: of the 6,000 babies born with DS every year in the US, half have heart defects. The most common defect is a hole in the center of the heart, which can be repaired with surgery, but the repair itself can cause scar tissue and cardiovascular complications. **Our goal is to elucidate how Trisomy 21 leads to this increased incidence of congenital heart defects.**

»»» THE CONNECTION BETWEEN DS AND CHILDHOOD LEUKEMIA

We know that the extra chromosome 21 carried by people with Down syndrome reduces fitness in normal cells and is implicated in cancers suffered by DS patients. People with DS are much more susceptible to pediatric blood cancers: the risk of acute myeloid leukemia is more than a hundred-fold higher in children with DS. **Our aim is to investigate the relationship between T21 and the leukemia predisposition in hematopoiesis, the process of forming blood cells.**

NEUROTECHNOLOGY DEVELOPMENT

Our research has focused on developing and applying technologies to map how the structure and dynamics of the brain change in Down syndrome. The goal is to find new mechanisms underlying Down syndrome and to provide targets that, when modulated, can improve the cognitive abilities of people with DS.

IMAGING AND MAPPING <<<

We've been developing two technologies to study the brain. The first is a technology for mapping the structure of cells of people with Down syndrome with great enough precision to see the fundamental building blocks of life. The second is a technology for imaging the dynamics of the brain in mouse models with enough precision to see individual neural codes.



CLINICAL STUDIES

➤➤➤ NON-INVASIVE GENUS IN PEOPLE WITH DS

The Tsai lab's GENUS therapy began as a potential therapy for AD. GENUS – or Gamma ENtrainment Using Sensory stimulation — doesn't involve drugs or implants but uses non-invasive stimulation of the senses to improve the brain's defense against disease. Our Phase I studies in healthy adults and patients with mild Alzheimer's disease demonstrated that GENUS is safe, well-tolerated and effective for evoking responses in brain networks to oscillate at 40Hz during stimulation.

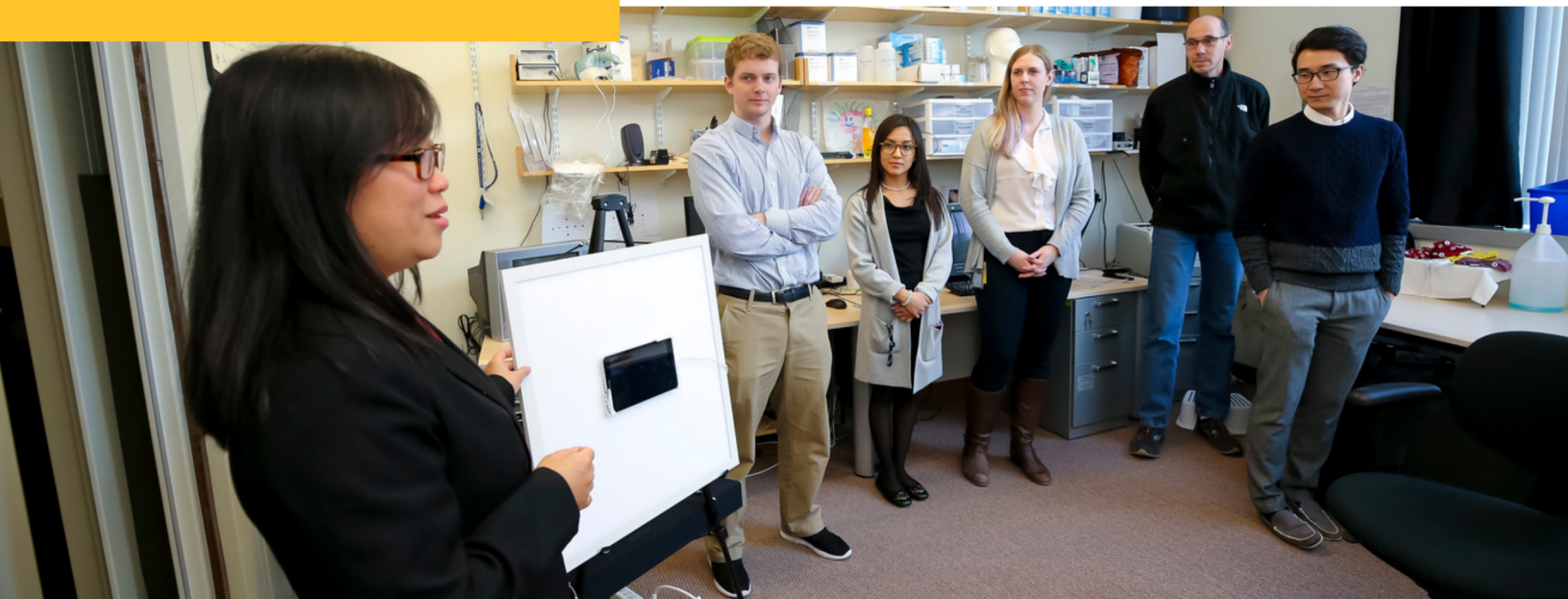
Based on these results and the launch of the Alana Center, labs at MIT initiated a study to determine whether GENUS therapy could benefit people with Down syndrome. A key question is whether Down syndrome participants are equally responsive to GENUS stimulation. Past studies have shown that greater responsiveness to stimulus correlates with greater reduction of pathology and greater cognitive improvements.

FROM BENCH TO BEDSIDE

In the four short years of the Alana Center's existence, we have moved from lab bench to human clinical trials in two different areas: 1) testing the GENUS 40 Hz therapy for Down syndrome and 2) testing an improved device for obstructive sleep apnea, including in Down syndrome.

➤➤➤ TREATING SLEEP APNEA

A second series of clinical trials enabled by the Alana Down Syndrome Center activities focused on addressing obstructive sleep apnea in individuals with Down syndrome. This work is funded by the Deshpande Center for Technological Innovation's "Technology to Improve Ability" (TTIA) program (see pg 6), and is supported through the TTIA program to address this common chronic health condition, particularly for people with DS. This program has created an oral device to hold the tongue away from the throat during sleep, potentially replacing the standard treatment, uncomfortable and noisy positive airway pressure machines (CPAPs).



BUILDING THE PIPELINE

ALANA FELLOWS

INVESTING IN THE FUTURE

In scientific research, we teach graduate and postdoctoral students to do something more difficult than merely how to follow our research path. We train them to create their own. Scientific discovery and biomedical innovation depend entirely upon unprecedented thinking and action. No one succeeds in our field by only doing what has already been done. Our charge is to advise and guide them, and to make sure they have all the support they need to make their unique contributions to knowledge.

TRAILBLAZERS

By providing the base from which these explorers can blaze their trails, the Alana Center has built the foundation for Alana Fellows to succeed. We're immensely proud of the accomplishments of the ten Alana Fellows from around the world who have been indispensable to our research. They mentor young trainees, lead their own Down syndrome projects and have become next-generation leaders making significant contributions to DS research. Two Alana Fellows have moved on to become faculty at other institutions, bringing their newfound knowledge of Down syndrome research with them.

CRISTINA BLANCO-DUQUE, PHD



YIXI LIU



MICHAEL GUTBROD, PHD



BEN LENGERICH, PHD



ZEGUAN WANG



HIRUY MEHARENA, PHD



BO ZHAO, PHD



LEAH BORDEN PHD



JIEKUN (JACKIE) YANG, PHD



TIM MULLEN, PHD



ACADEMIC AND COMMUNITY ENGAGEMENT

Keynote Speaker/
Distinguished Lectures

16



Presentations at
Conferences, Seminars and
Grand Rounds

72



Alana Center Conferences
and Symposia, and Webinars

4



Scientific Papers
Published/In Preparation

14



»»» OUTREACH

Outreach, collaboration and engagement with the academic world and the wider Down syndrome community continue to be top priorities for the Alana Center. In just four years, Alana DS Center faculty and fellows have shared their findings in more than 80 venues. They've served as keynote speakers, lectured worldwide at conferences and symposia, contributed to seminars and poster sessions, participated in grand rounds at leading medical centers, and published in widely distributed scientific press. In addition, we've hosted three highly successful conferences and symposia to introduce our findings to the scientific community. We've initiated outreach to multiple Down syndrome support organizations. And we've received extensive media recognition in publications as diverse as STAT and The Economist. Finally, and perhaps most important, **we continue to strengthen our ties with the Down syndrome community** through comprehensive sessions with self-advocates and their families.

“

“I am hopeful that the research being done today will improve medical care and the quality of life of people with Down syndrome,” said Kate Bartlett, at the Translational Research in DS symposium at MIT. “Your work is important for me and my peers. Together we can make a better world for all people to lead active, healthy, fulfilling lives.”

”

KATE BARTLETT, MEMBER, SELF-ADVOCATE ADVISORY COUNCIL, MDSC

TECHNOLOGY TO IMPROVE ABILITY PROGRAM

»»» CATALYST

To generate awareness of unmet needs and generate grant submissions, the TTIA program funded a “Catalyst” course run by MIT Professor Martha Gray. A cohort of 14 students and professionals followed a structured discovery and design process to imagine potential products and solutions to address needs in Down syndrome.

Fellows ranged from MIT undergraduates to clinicians from local hospitals. Faculty included staff from the Deshpande Center and the Alana Center, along with faculty from Harvard, Massachusetts General Hospital and biotech.

The **TTIA Sleep Apnea Project** (see more in Clinical Studies section) was a successful product of the Catalyst students.

»»» DHIVE

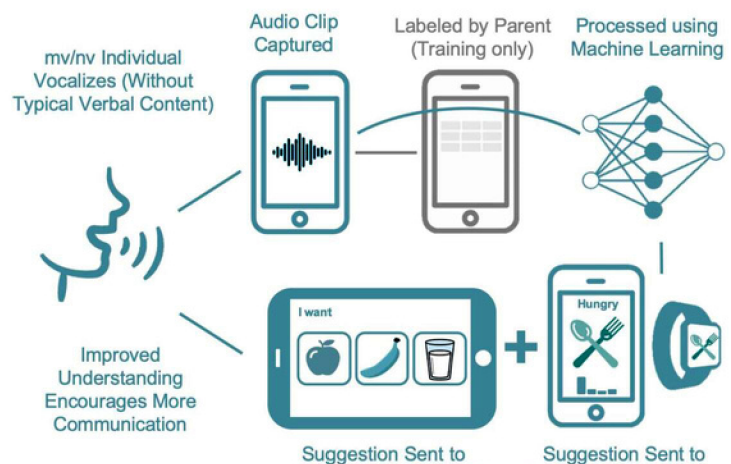
The TTIA program has teamed with a sister organization, the MIT Sandbox Innovation Program, to implement a program encouraging student-led entrepreneurship and focused on healthcare challenges in several areas, including the Down syndrome community.

Through MIT DHIVE – or Dive into Healthcare Innovation and Venture Exploration -- students learn about entrepreneurship and unmet healthcare needs and then brainstorm ways to address those needs.



»»» AUGMENTED COMMUNICATION TECHNOLOGY

Many people with Down syndrome experience stress, frustration and isolation when communicating in a society largely constructed around verbal speech. This project sought to develop a full-feedback augmentative communication system to “translate” non-speech sounds to speech using machine learning algorithms based on vocalizations from nonverbal and minimally verbal people. The goal was to enhance communication between nonverbal or minimally verbal people, parents and caregivers, and the wider community.



LEADERSHIP



Li-Huei Tsai, Director

Dr. Tsai is is Picower Professor of Neuroscience in the Department of Brain and Cognitive Sciences at MIT, Director of The Picower Institute, Director of the Alana Down Syndrome Center and co-founder of the Aging Brain Initiative at MIT.

Ed Boyden, Core Member

Dr. Boyden is the Y. Eva Tan Professor in Neurotechnology in the Departments of Biological Engineering and Brain and Cognitive Sciences at MIT and McGovern Institute.



Manolis Kellis, Core Member

Dr. Kellis is Professor of Computer Science in Computational Biology at MIT and an associate member of the Broad Institute. He's head of the Computational Biology Group at MIT and a Principal Investigator in the MIT Computer Science and Artificial Intelligence Lab.

Laurie Boyer, Core Member

Dr. Boyer is Professor of Biology and Biological Engineering at MIT and an associate member of the Koch Institute for Integrative Cancer Research.



Leon Sandler, Deshpande Center

is Executive Director of the Deshpande Center for Technological Innovation, which empowers MIT researchers to develop innovative technologies in the lab and bring them to the marketplace.



PUBLICATIONS

Johnson, K.T., Narain, J., Quatieri, T., Maes, P., Picard, R.W. (2023) ReCANVo: A database of real-world communicative and affective nonverbal vocalizations. *Scientific Data*.

Meharena, H. S., .., & Tsai, L. H. (2022) Down-syndrome-induced senescence disrupts the nuclear architecture of neural progenitors. *Cell Stem Cell*

Santoro, S. L., Hendrix, J., White, N., & Chandan, P. (2022). Caregivers evaluate independence in individuals with Down syndrome. *American Journal of Medical Genetics Part A*

Yoon, Y-G.*, **Wang, Z.***, ..., and **Boyden, E. S.** (2020). Sparse decomposition light-field microscopy for high-speed imaging of neuronal activity. *Optica*, 7(10):1457-1468.

Hendrix, J. A., **Amon, A.,...** & Yi, J. S. (2020). Opportunities, barriers, and recommendations in Down syndrome research. *Translational science of rare diseases*

Thank you for investing in our research: The Alana Down Syndrome Center Gift Fund #3965164

The Alana Down Syndrome Center's mission is to improve health, ability, inclusion and quality of life for people with Down syndrome. We hope you will consider supporting us in the next year. A gift to the ADSC can be made online at <https://giving.mit.edu> by entering fund number 3965164. For more information, or to make a named or transformational gift, please contact Director of Development Dr. Asha Bhakar- abhakar@mit.edu

