LUMIND RDS VISION: To be the global leader in funding a comprehensive portfolio of research to meaningfully improve memory, cognition, and independence in individuals with Down syndrome.

LUMIND RDS VALUE:
- Dedicated focus, prioritizing a comprehensive portfolio of cognition research for Down syndrome
- Close-knit, passionate community of families, researchers and advocates
- World-renowned Scientific Advisory Board
- Strategic relationships and promotional avenues.

LUMIND RDS SCIENTIFIC RESEARCH CATEGORIES
- PREVENT
  - Alzheimer onset
- IMPROVE
  - cognition
- DEVELOP
  - gene therapies
- ADVANCE
  - understanding

KEY ACCOMPLISHMENTS
- Established a Scientific Advisory Board dedicated exclusively to cognition research for Ds
- Defined multiple mechanisms involved in cognitive impairment
- Identified 10 new potential therapeutic drug targets
- Developed Ds-specific cognitive test batteries across life-span (ACTB, A-MAP)
- Established clinical testing network
- Nearly $17M provided to research to date
- Supported 4 major clinical trials:
  - Roche Roc, Basimisanil (RG1662): Developmental Intellectual Disability in Ds
  - AC Immune (ACI-24): Alzheimer’s Disease in Ds
  - Balance Therapeutics (BTD-001): Developmental Intellectual Disability in Ds
  - Transition Therapeutics (ELND-005): Alzheimer’s Disease & Cognition in Ds
- Stimulated several large NIH initiatives (registry, biomarkers, AC Immune & A-MAP)

We’ve made great progress and are realizing unprecedented results since our founding in 2004. However, more funding, both public and private, is needed to maintain and accelerate the current momentum. Whether you are a parent, a sibling, a friend, an individual with Down syndrome, or just someone who wants to support a cause that has the potential to change the lives of over 206,000 individuals in the U.S. and millions worldwide living with Down syndrome, there are many ways to help.

- Sign up to Receive our Newflash and Spread the Word
  https://events.lumindrds.org/newsflash
- Donate a one-time or recurring gift or fundraise with the LuMind RDS Runners and #Race4eXtraordinary — https://www.lumindrds.org/get-involved/

Ds remains one of the lowest funded conditions by the NIH.
Defining Genes, Mechanisms and Treatments for Neurodevelopment and Neurodegenerative Causes of Cognitive Dysfunction in Down Syndrome

This research will explore the mechanisms responsible for amyloid-precursor-protein (APP), which is linked to degeneration in Down syndrome, and to further evaluate APP-directed treatments. This will advance the characterization and development of new potential drugs to decrease APP, prevent or reverse the disruption of age-related cognitive dysfunction and Alzheimer’s disease pathology associated with Down syndrome. **Funded to date: $2.7M**

University of California San Diego has long been at the forefront of “bench-to-bedside” research, transforming patient care through discovery and innovation leading to new drugs and technologies. **Principal Investigator:** Dr. William Mobley, MD, PhD

A Phase 1B Multi-Center, Double-blind, Randomized, Placebo-Controlled Dose Escalation Study of the Safety, Tolerability, and Immunogenicity of AC1-24 in Adults with Down Syndrome

This landmark study represents the first major clinical trial by a pharmaceutical company for Alzheimer’s Disease (AD) in Down syndrome (Ds) using a novel, mechanism: an anti-Ab therapeutic agent targeting the consequences of amyloid precursor protein over-expression and early-onset AD dementia in Ds. It also represents the first ever private-public partnership in Ds (NIH, LuMind RDS, and AC Immune) with the potential for the development of a Ds clinical trials network by leveraging Alzheimer’s Disease Cooperative Study (ADCS) consortium clinical trial sites to conduct further trials addressing AD in Ds. **Funded to date: $0.6 M**

AC Immune is passionate about making a difference in the lives of people affected by Alzheimer’s and other neurodegenerative diseases. Their goal is to become the global leader in personalized treatment of neurodegenerative diseases, one of the biggest challenges facing society today and future generations. **AC Immune and UC San Diego School of Medicine, Principal Investigators:** Wolfgang Barth, PhD, Dr. Andrea Pfeiffer, PhD, Dr. William Mobley, MD, PhD, and Michael Rafii, MD, PhD
Learning Through Objects in Infants and Toddlers with Down Syndrome

Early motor training in infants may result in positive long-term effects in other areas of development, according to a collaborative study by researchers at Vanderbilt University, the University of Pittsburgh and Seton Hall University.

Infants' early learning experiences have been found to positively affect later development through processes called "developmental cascades." For example, walking and fine motor skills have been associated with vocabulary size and later language development. A new study demonstrates a powerful link between training infants to reach for an object and later heightened interest in objects and focused attention. Because reduced grasping activity and delays in motor skill development have been associated with risk for developmental disorders, a new study is now focused on the implications for individuals Down syndrome. **New Grant: $0.1 M**

Vanderbilt is one of only fourteen universities ranked in the top 25 on each of two key indicators: U.S. News & World Report’s Best Universities and Colleges (ranked 15) and federal obligations for science and engineering (ranked 21). Vanderbilt University and Vanderbilt University Medical Center researchers are at the forefront of discovery, innovation, scholarship, and creative expression. **Principal Investigators: Drs. Amy Needham, PhD and Maninderjit (Mandy) Kaur, PhD**

Brain development, sleep and learning in Down syndrome

The Down syndrome (Ds) Research program at the University of Arizona (PI Edgin) will continue to engage in research designed to best inform treatment efforts in Ds, including the development and validation of a new iPad cognitive battery for use in clinical trials across the lifespan [i.e., the Arizona Memory Assessment for Preschoolers and Special Populations (A-MAP)]. Further, we will continue to examine the links between sleep and learning in young children with Ds, including the investigation of behavioral sleep modifications that may support learning. This project will pinpoint promising targets for intervention, and help to develop a deeper understanding of how to best support learning and cognitive development in those with Ds. **Funded to date: $2.1 M**

Arizona is ranked among the top 25 of public research universities nationwide and is a member of the prestigious Association for American Universities (AAU). **Principal Investigators: Drs. Jamie Edgin, PhD, Stephen Cowan, PhD, and C Clark, PhD**

Sleep, Circadian, and Stem Cell Renewal Factors in the Learning Disability of Down Syndrome

Our research aims at understanding the causes of intellectual disability in individuals with Down syndrome and applying that knowledge to develop therapies that will improve learning and memory in this population. One focus of our work is the roles of sleep and circadian rhythms in learning and memory and how they are altered by Ds. Another focus of our research is understanding how certain genes triplicated in Ds influence brain development and the continued renewal of neural stem cells. The ultimate goal of our research is to improve the abilities of individuals with Ds to learn, remember, and process new information. **Funded to date: $4.85 M**

Stanford University is one of the world’s leading research and teaching institutions in the field of medicine, with over 6,000 ongoing research projects. **Principal Investigators: Dr. Craig Heller, PhD, Dr. Maddalena Adorno, PhD**
The primary research objective in Dr. Pinter’s lab is to learn how chromosome topology, non-coding (nc)RNA and chromatin modifiers orchestrate gene expression. He is an expert on diseases and conditions of the X chromosome, including chromosome silencing using the XIST promoter which is a gene therapy target of big interest in Down syndrome research. We are very happy to attract this investigator to apply his deep expertise to Down syndrome research. Over a decade of genome-wide association studies has revealed a common theme in a wide variety of conditions, namely, that the vast majority of risk/benefit conferring variants reside not in genes, but in non-coding regions of the genome that control gene expression. The X chromosome provides a unique and informative perspective on this problem, in a classic model of epigenetics: X chromosome inactivation (XCI), the process by which one X chromosome in females is silenced to achieve gene dosage parity with males. Sex chromosomal dosage compensation in mammals takes the form of X chromosome inactivation (XCI), driven by the non-coding RNA Xist. This same mechanism could be applied to inactive the extra chromosome 21.

New Grant: $0.3 M

The faculty at UConn Health are engaged in a broad range of research activities within the basic, behavioral, and biomedical sciences with the goal of improving the health and well-being of the people of Connecticut and populations across the globe. They seek to expand our knowledge of the basic life sciences in order to propel the development of new and innovative drugs and treatments. The recent addition of Jackson Laboratory (JAX-GM) to our campus has also added strength to the areas of genetics and genomic sciences.

UConn Health views research as a primary path to expanding the successes of modern medicine. It is their goal to continuously identify potentially fruitful areas of research and incorporate them, so we can continually improve and push the boundaries of medical practice. Principal Investigator: Dr. Stefan Pinter, PhD
**Advance understanding**

**Disomic and trisomic pluripotent stem cell (iPSC) to study pharmacologic intervention affecting gene expression patterns in other chromosomes**

Our lab has collected human skin fibroblast lines from healthy individuals as well as Down syndrome patients and reprogrammed them into induced pluripotent stem cells (iPSCs). Down Syndrome (DS) patients exhibit a spectrum of pathologies which include heart disease, cancer, craniofacial abnormalities and most predominantly ~99% of DS patients have deficits in memory and learning. However, the molecular mechanism of how triplication of Chromosome 21 elicits cognitive deficits remains unclear. Here we utilize patient derived iPSCs to generate specific cell types of the brain to capture the epigenetic and transcriptomic signatures unique to DS. Ultimately, we hope that these techniques will facilitate and expedite drug screening and discovery by allowing us to directly screen engineered human brain organoids for compounds and therapies likely to work in the in vivo human brain. *New Grant: $0.2 M*

The Picower Institute for Learning and Memory’s highly collaborative, cross-disciplinary strategy allows them to explore the nature of the brain from the most basic biological interactions of genes and proteins to in-depth explorations of cellular and systemic mechanisms. This comprehensive approach places Picower Institute researchers in the perfect position to study the mechanisms behind developmental disorders such as autism, Down syndrome, psychiatric illnesses such as schizophrenia, and neurodegenerative diseases such as Alzheimer’s disease—conditions that affect millions worldwide. The Picower Institute is seizing every opportunity to focus our broad range of scientific talents on a single goal: improving quality of life through a thorough understanding of our most complex and fascinating organ. *Principal Investigator: Dr. Hiruy Meharena, PhD*

**A next generation mouse model for trisomy 21 that mimics findings from human brain and CSF**

This year's focus is on the characterization of new trisomic mouse model that promises to provide the most accurate genetic model of trisomy 21 to replace the 20+ year old Ts65Dn model for the next 20 years. In his prior work, Dr. Reeves lab has identified a potential approach to restoration of cerebellum structure throughout life after a single injection of a potential drug on the day of birth in mouse models of Down syndrome. This treatment also improves brain functions involved in learning and memory and these efforts are now directed to identification of new therapeutic strategies and targets that will optimize cognition. Another effort has led to the identification of what promises to be a biomarker and possible therapeutic target of Alzheimer’s disease in Down syndrome brains. *Funded to date: $3.6 M*

Johns Hopkins University School of Medicine, headquartered in Baltimore, Maryland, is an integrated global health enterprise and one of the leading health care systems in the United States, it has been ranked number one in the nation by U.S. News & World Report for 22 years. *Principal Investigator: Dr. Roger H. Reeves, PhD*

**The Down Syndrome Cognition Project**

The overarching goal of this project is to identify altered biological pathways as a basis for therapeutic development and precision medicine. To do so, this project has established an infrastructure to collect clinical, neuropsychological, and maternal interview information from individuals with Down syndrome, along with biological samples for genetic studies. These resources are used to discover factors that explain the wide range of severity among Down syndrome-associated conditions, to develop better tests for clinical trials and to build a foundation for a larger DS360 Down syndrome Research Consortium to accelerate research. *Funded to date: $0.9 M*

Emory University School of Medicine & Research Network Consortium has had a remarkable research trajectory over the past 20 years, during which the university has been consistently one of the fastest growing research institutions in terms of total NIH awards awarded. *Principal Investigators: Dr. Stephanie Sherman, PhD, Dr. Roger H. Reeves, PhD*