Research Down Syndrome

LuMind™

FOUNDATION

RESEARCH SPOTLIGHTS

Our vision is to enable independence and enrich community engagement for all individuals with Down syndrome.

14 years ago

families founded LuMind RDS, supporting 15 clinical studies with 1300 participants since.

In 5 years

novel treatments for Alzheimer's, cognition, speech and sleep will be in clinical trials.

In 10 years

the first gene therapy clinical trials to restore gene balance will be ongoing.

LUMINDRDS.ORG

LUMIND RDS VALUES

FOCUS

We are laser-focused on four research categories in which we fund groundbreaking, high impact research and we evaluate every grant dollar through the lens of translation

FOLLOW THE SCIENCE

We constantly revisit our views on what is groundbreaking research and of where to spend the next dollar raised. We use Translational Key Opinion Leader Meetings to help define the next development steps and frontiers to overcome for the most promising research targets

PIONEERS

Since 2004, we have a history of being at the forefront of research and we continue to pioneer innovations

SPEED

We leverage relationships, collaborate and draw on our network to accelerate research in Down syndrome

COLLABORATION

We collaborate whenever possible to access knowledge, speed up research and save costs

NETWORK

We have a close-knit, passionate community of families, researchers and advocates, and a deep biotech and pharma industry network

TRANSPARENT

We share our goals with internal and external stakeholders

ALZHEIMER'S 2020 VISION

Promising Alzheimer's treatments are in clinical trials in the general population now. By 2020, we hope to collaboratively put in place

- ☑ the necessary infrastructure to rapidly enroll large (~500 participants) Alzheimer's clincial trials in Down syndrome,
- ☑ rally the Down syndrome community behind these trials, develop the necessary clincial trials outcome measures, and
- ☑ engage with pharma companies to initiate clinical trials in Down syndrome with their most promising amyoid beta and tau targeting molecules.

KEY ACCOMPLISHMENTS

- ☑ Defined multiple mechanisms involved in cognitive impairment
- ☑ Identified 10 new potential therapeutic drug targets
- ☑ Developed Down syndrome-specific cognitive test batteries across life-span (ACTB, A-MAP)
- ☑ Established early clinical testing network
- ☑ Stimulated several large NIH initiatives (registry, biomarkers, AC Immune & A-MAP)
- ☑ Supported 14 clinical trials on 1,300 participants, including:

  Roche Roc, Basmisanil (RG1662):
  Developmental Intellectual Disability in Down syndrome

  AC Immune (ACI-24):
  Alzheimer's Disease in Down syndrome

  Balance Therapeutics (BTD-001):
  Developmental Intellectual Disability in Down syndrome

  Transition Therapeutics (ELND-005):
  Alzheimer's Disease & Cognition in Down syndrome

- ☑ Founding sponsor of the first international research consortium, the Trisomy 21 Research Society

LUMIND RDS SCIENTIFIC RESEARCH CATEGORIES FOR DOWN SYNDROME

PREVENT ALZHEIMER ONSET

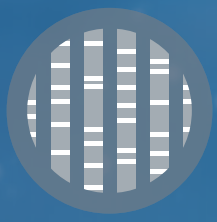
- Encourage industry-led clinical trials of therapeutic approaches
- Develop necessary resources: assessment scales, registry, etc.

DEVELOP GENE THERAPIES

- Silence genes of concern or extra chromosome
- Restore the right level of specific gene(s)

IMPROVE COGNITION

- Translate Down syndrome-specific approaches to clinical trials
- Validate Down syndrome-specific cognition targets



ADVANCE UNDERSTANDING

- Discover novel targets (stem cells, sequencing/phenotyping)
- Improve mouse models to better test novel targets

PARTNER INSTITUTIONS FUNDED BY LUMIND RDS

Funded $17M in research, including $1.8M in grants in FY2017, which has led to significant concurrent funding from NIH and industry partners.

SPOTLIGHT #1 — Johns Hopkins University School of Medicine

A Down Syndrome Center for Fundamental Research-Cognition

RESEARCH CATEGORY / IMPROVE COGNITION

One component of this work 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. A second 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.

PRIMARY INVESTIGATOR

Dr. Roger Reeves, PhD

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.

FUNDED TO DATE

$3.6M

SPOTLIGHT #2 — Emory University School of Medicine

The Down Syndrome Cognition Project

RESEARCH CATEGORY / ADVANCE UNDERSTANDING

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.

PRIMARY INVESTIGATORS

Dr. Roger Reeves, PhD

Dr. Stephanie Sherman, PhD

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.

FUNDED TO DATE

$1.1M

SPOTLIGHT #3

University of California San Diego

Defining Genes, Mechanisms and Treatments for Neurodevelopment and Neurodegenerative Causes of Cognitive Dysfunction in Down Syndrome

RESEARCH CATEGORY / **PREVENT ALZHEIMER'S ONSET**

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.

PRIMARY INVESTIGATOR

Dr. William Mobley, MD, PhD

UC San Diego

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.

FUNDED TO DATE

$2.7M

SPOTLIGHT #4

The University of Arizona

Brain Development, Sleep and Learning in Down Syndrome

RESEARCH CATEGORY / **IMPROVE COGNITION**

The Down syndrome Research program at the University of Arizona (PI Edgin) will continue to engage in research designed to best inform treatment efforts in Down syndrome, 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 Down syndrome, 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 Down syndrome.

PRIMARY INVESTIGATOR

Dr. Jamie Edgin, PhD

THE UNIVERSITY OF ARIZONA

Arizona is ranked among the top 25 of public research universities nationwide and is a member of the prestigious Association for American Universities (AAU).

FUNDED TO DATE

$2.1M

SPOTLIGHT #5

Stanford University

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

RESEARCH CATEGORY / IMPROVE COGNITION

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 Down syndrome. We believe this quest will lead to the development of potential therapies that will improve cognitive abilities. Another focus of our research is understanding how certain genes triplicated in Down syndrome influence brain development and the continued renewal of neural stem cells. Identifying downstream targets of those gene products should open new opportunities for therapeutic approaches. The ultimate goal of our research is to improve the abilities of individuals with Down syndrome to learn, remember, and process new information.

PRIMARY INVESTIGATORS

Dr. Maddalena Adorno, PhD

Dr. Craig Heller, PhD

Stanford University

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.

FUNDED TO DATE

$5.0M

SPOTLIGHT #6

VA Palo Alto Health Care System

Improving Beta-Adrenergic Signaling for the Treatment of Cognitive Dysfunction in Down Syndrome

RESEARCH CATEGORY / IMPROVE COGNITION

The proposed research will continue to test whether i) combining physical exercise with adrenergic agonists could induce stronger positive effects on cognitive function than each treatment individually, ii) quantification of metabolites in urine and plasma could be used as predictors for cognitive dysfunction, and iii) investigate whether exercise-induced increases in PGC-1 used in synergy with adrenergic agonists could improve cognitive function in mouse models of Down syndrome. It is expected that this project will advance research and development of potential norepinephrine-ergic — based therapies for cognitive disabilities in children and reduce Alzheimer's disease-related abnormalities in adults with Down syndrome.

PRIMARY INVESTIGATOR

Dr. Ahmad Salehi, MD, PhD

VA PALO ALTO HEALTH CARE SYSTEM

VAPAHCS maintains one of the top three research programs in the VA with extensive research centers in geriatrics, mental health, Alzheimer's disease, spinal cord regeneration, schizophrenia, Rehabilitation Research and Development Center, HIV research, and a Health Economics Resource Center.

FUNDED TO DATE

$0.8M

SPOTLIGHT #7 — AC Immune & University of California San Diego

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

RESEARCH CATEGORY / PREVENT ALZHEIMER'S ONSET

This landmark study represents the first major clinical trial by a pharmaceutical company for Alzheimer's Disease (AD) in Down syndrome using a novel, mechanism: an anti-Ab therapeutic agent targeting the consequences of amyloid-precursor protein over-expression and early-onset AD dementia in Down syndrome. It also represents the first ever private-public partnership in Down syndrome (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 Down syndrome.

PRIMARY INVESTIGATORS

Dr. Wolfgang Barth, PhD
AC IMMUNE

Dr. Andrea Pfeiffer, PhD
AC IMMUNE

Dr. Michael Rafii, MD
UCSD

AC Immune

UC San Diego

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.

FUNDED TO DATE

$0.6M

SPOTLIGHT #8 — Vanderbilt University

Learning Through Objects in Infants and Toddlers with Down Syndrome

RESEARCH CATEGORY / IMPROVE COGNITION

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. This 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, this study is now focused on the implications for individuals Down syndrome.

PRIMARY INVESTIGATORS

Dr. Maninderjit (Mandy) Kaur, PhD

Dr. Amy Needham, PhD

VANDERBILT UNIVERSITY

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 and federal obligations for science and engineering. Vanderbilt University and Vanderbilt University Medical Center researchers are at the forefront of discovery, innovation, scholarship, and creative expression.

FUNDED TO DATE

$125K

SPOTLIGHT #9

University of Connecticut

Trisomy 21 Dosage Correction and Mapping Resource (T21DoCoMap) and XIST Silencing in Mature Neurons

RESEARCH CATEGORY / DEVELOP GENE THERAPIES / ADVANCE UNDERSTANDING

The primary research objective is to learn how chromosome topology, non-coding (nc)RNA and chromatin modifiers orchestrate 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.

PRIMARY INVESTIGATOR

Dr. Stefan Pinter, PhD

UCONN UNIVERSITY OF CONNECTICUT

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 knowledge of the basic life sciences to propel the development of new and innovative drugs and treatments.

FUNDED TO DATE

$270K

SPOTLIGHT #10

Massachusetts Institute of Technology

Disomic and Trisomic Pluripotent Stem Cell (iPSC) to Study Pharmacologic Intervention Affecting Gene Expression Patterns in Other Chromosomes

RESEARCH CATEGORY / IMPROVE COGNITION

The Picower Institute for Learning and Memory 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 patients exhibit a spectrum of pathologies which include heart disease, cancer, craniofacial abnormalities and most predominantly ~99% of Down syndrome patients have deficits in memory and learning. This project will utilize patient derived iPSCs to generate specific cell types of the brain to capture the epigenetic and transcriptomic signatures unique to Down syndrome. Ultimately, the goal is that these techniques will facilitate and expedite drug screening and discovery to screen engineered human brain organoids for compounds and therapies likely to work in the human brain.

PRIMARY INVESTIGATOR

Dr. Hiruy Meharena, PhD

Massachusetts Institute of Technology

The Picower Institute for Learning and Memory's is one of three neuroscience groups at the Massachusetts Institute of Technology. It'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.

FUNDED TO DATE

$220K

Systematic Analysis of 21ST Chromosome Genes Using C. Elegant (2010–2013)

RESEARCH CATEGORY / IMPROVE COGNITION

This work investigated the development of new animal models for Down syndrome using C. elegans, a major, long-standing experimental laboratory organism, together with a novel high-throughput screening system to discover the function of novel genes on the 21st chromosome and to identify potential drugs to prevent neurodegeneration in Down syndrome-related Alzheimer's disease.

PRIMARY INVESTIGATOR

Dr. Jon Pierce-Shimomura, PhD

TEXAS
The University of Texas at Austin

Ranked among the biggest and best research universities in the country by *U.S. News & World Report*, UT Austin is home to more than 51,000 students and 3,000 teaching faculty. Together they are working to change the world through groundbreaking research and cutting-edge teaching and learning techniques.

FUNDED TO DATE

$176K

Research Down Syndrome LuMind FOUNDATION

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CONTACT LUMIND RDS

To learn more about LuMind RDS' work in down syndrome research, or to explore how you can get involved, please contact Jill Reslock at the LuMind RDS office: **jreslock@lumindrds.org** / **508.630.2177**.

lumindrds.org