



# ON THE ROAD TO PREVENTION

2019 Annual Report

**LIBD**

LIEBER INSTITUTE *for*  
BRAIN DEVELOPMENT  
MALTZ RESEARCH LABORATORIES



Dear Friends,

Two of the most frequent questions I'm asked by families are, "How close are we to finding cures, and, why is it taking so long?" My first response is nearly always the same, "We've never been closer."

Because of the genomic revolution in science, we have learned more about the basic causes of schizophrenia, bipolar disorder, depression, PTSD in the past decade than in all of past history, and this has encouraged expectations that we can find new treatments and approaches to prevention based on the underlying causes and not just effects.

The Lieber Institute for Brain Development & Maltz Research Laboratories were created with a vision expressed by the founders, Connie and Steve Lieber and Tamar and Milton Maltz, to plot a new course in biomedical research that would change the lives of individuals affected with these developmental brain disorders. We are one of the only research institutions in the world focused specifically on understanding how genes and the environment influence the way our brains develop that lead to conditions such as schizophrenia, autism, bipolar disorder and related developmental brain disorders. Through our cutting-edge research, answers are emerging and being translated into a robust pipeline of new drugs in development. And, by focusing on genes and their dynamic interplay with the environment, we are getting even closer to the "holy grail" in medical research, the discovery of strategies for primary prevention.

As we enter the second decade of this new era of genomic medicine, we have identified more risk factors for major psychiatric illness than we might have imagined possible, and the challenge is no longer to find the genes; it is to understand how these genes impact the development and function of brain circuits that cause illness at the level of an individual person.

The study of human brain samples donated by more than 3,000 committed families around the country, is the single most important Institute resource enabling all of our cutting-edge research. Our brain repository now stands as one of the largest and most extensively characterized human brain repository devoted to psychiatric illness in the world. Because of this tremendous resource, Lieber researchers are able to build human cell models of illness, including three dimensional organoids "mini-brain" models, leading to the discovery of potentially breakthrough insights into the underlying mechanisms of disease.

We remain dedicated to changing the landscape of brain research and deliver on the promise of new treatments. Already we have five new drug targets that have emerged from this work, with our most advanced treatment starting clinical trials in 2020. And, while we have accomplished a great deal in a very short time, we are impatient for the answers.

We invite you to partner with us as we push the scientific frontier to do better, faster!

## Daniel R. Weinberger, M.D.

Director and CEO, Lieber Institute for  
Brain Development

Professor, Departments of Psychiatry,  
Neurology, Neuroscience and The  
McKusick Nathans Institute of Genetic  
Medicine, Johns Hopkins University  
School of Medicine



Dear Supporter,

I understand how challenging it is for a parent to accept that their child suffers from a mental illness handicap. It is something we dealt with as parents in early childhood and then with the greater difficulty of early adulthood. We recognized that our knowledge of these disorders was inadequate. Impatient with the pace of scientific research, we became determined to find answers leading to cures.

Over the past 30 years, Connie and I dedicated our lives and resources to finding those answers by supporting researchers around the world who are unraveling the origins of these brain disorders.

With the advent of the genomic era and new discoveries on the horizon, we took a giant leap of faith with the Maltz family and founded the Lieber Institute for Brain Development, under the remarkable leadership of Dr. Daniel Weinberger and the scientific team he assembled. Our mission is tenacious and simple; discover ways to prevent, treat and ultimately cure conditions like schizophrenia, which have robbed so many children like ours from living to their greatest potential.

I am proud to introduce you to our work. Since we founded the Institute nine years ago, we have made tremendous progress, with exciting discoveries that may ultimately prevent developmental brain disorders, such as schizophrenia, autism, ADHD and bipolar disorder. We have also developed a promising pipeline of new treatments in development that are approaching clinical trials.

I want you to know that at the Lieber Institute for Brain Development we are dedicated to doing everything we can, with all of our resources, to speed up the process of finding cures and ways for prevention. We are getting closer every day. As Connie liked to say, 'Hope is on the horizon!'

As you explore our work, I invite you to partner with us, as a fellow impatient optimist, on this heroic journey.



**Steve Lieber**  
*Founder*



THE LIEBER INSTITUTE FOR BRAIN DEVELOPMENT  
AND THE MALTZ RESEARCH LABORATORIES

# We live in an era of hope

The genomic revolution is uncovering more about the basic causes of schizophrenia, bipolar disorder, depression, and PTSD in the past decade than in all of past history. It is a matter of time before we find new treatments and approaches to prevention, and ultimately cures.

We know that every one of us have either experienced first hand, or had a close friend or family member struggle with a mental illness. With 1 in 5 people experiencing a major mental health issue in any given year, it's more common than the flu and the leading cause of disability worldwide.

# MISSION

We relentlessly push the scientific frontier to discover ways to treat, cure and ultimately prevent neuropsychiatric disorders.

1

## What We Do

The Lieber Institute for Brain Development is one of the only research institutions in the world focused specifically on understanding how genes and the environment influence human brain development in ways that lead to schizophrenia and other related developmental brain disorders.

2

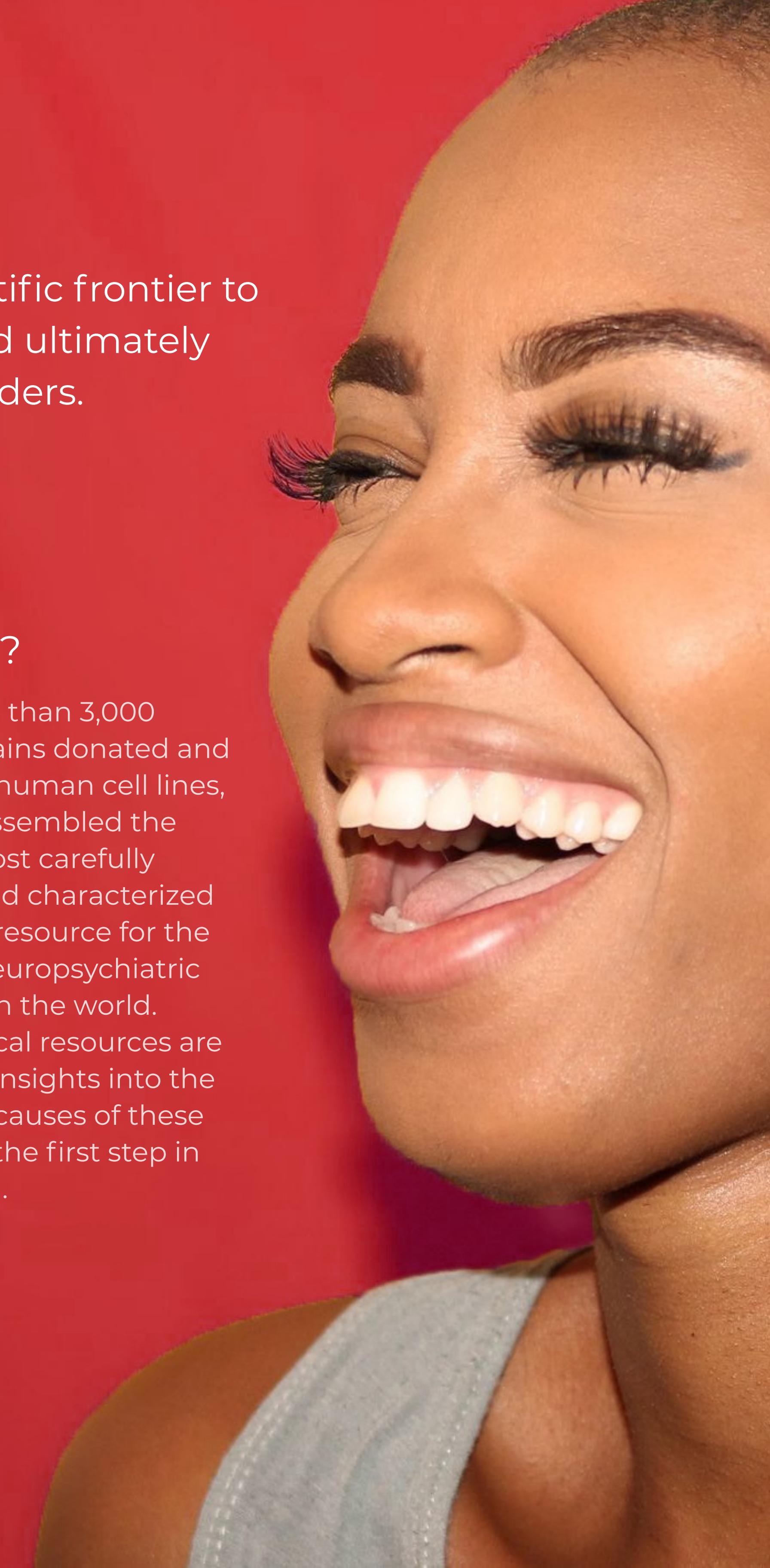
## Who We Are

We are a group of impatient, multi-disciplinary and optimistic researchers, working at the cutting edge of science, utilizing state-of-the-art tools to unlock the mystery of the brain and transform the way we approach the development of new treatments, and ultimately cures.

3

## Why Us?

With more than 3,000 human brains donated and over 1,200 human cell lines, we have assembled the largest, most carefully curated and characterized biological resource for the study of neuropsychiatric disorders in the world. These critical resources are providing insights into the biological causes of these disorders, the first step in prevention.



# Institute Accomplishments

1  
**3,000+**

BRAINS  
COLLECTED

6  
5  
NEW DRUGS  
3 IN DEVELOPMENT  
2 OUT-LICENSED

2  
**1,200**

HUMAN CELL  
LINES

7  
**\$191M**

INVESTED  
TO DATE

3  
**160+**

PAPERS

8  
**\$42M**

IN GRANTS  
& CONTRACTS

4  
**115**

TEAM  
MEMBERS

9  
**51**

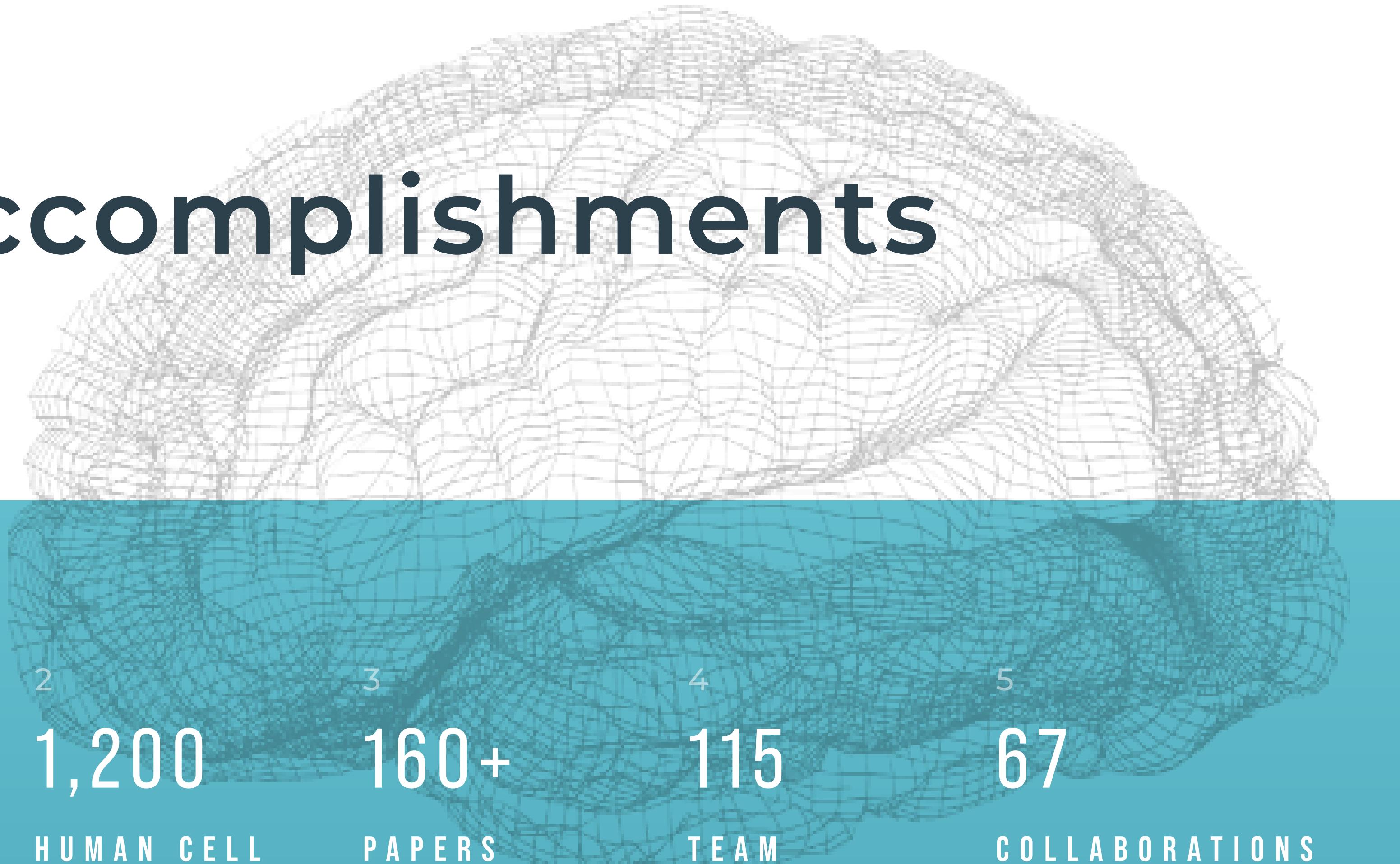
MEDIA  
PIECES

5  
**67**

COLLABORATIONS

10  
**2**

NEW FEDERAL  
LAWS ENACTED



## LIBD in the News

The  
New York  
Times

The  
Washington  
Post

 PBS NEWSHOUR

THE  
BALTIMORE  
SUN

BBC  
WORLD

THE CONVERSATION

 NATIONAL  
GEOGRAPHIC

STAT

“

Lieber's goal is to unravel what happens biologically in the brain to make these conditions occur and then to develop therapies to treat these conditions at their root cause, or even prevent them from happening in the first place.

Emily Mullin  
**WASHINGTON POST**

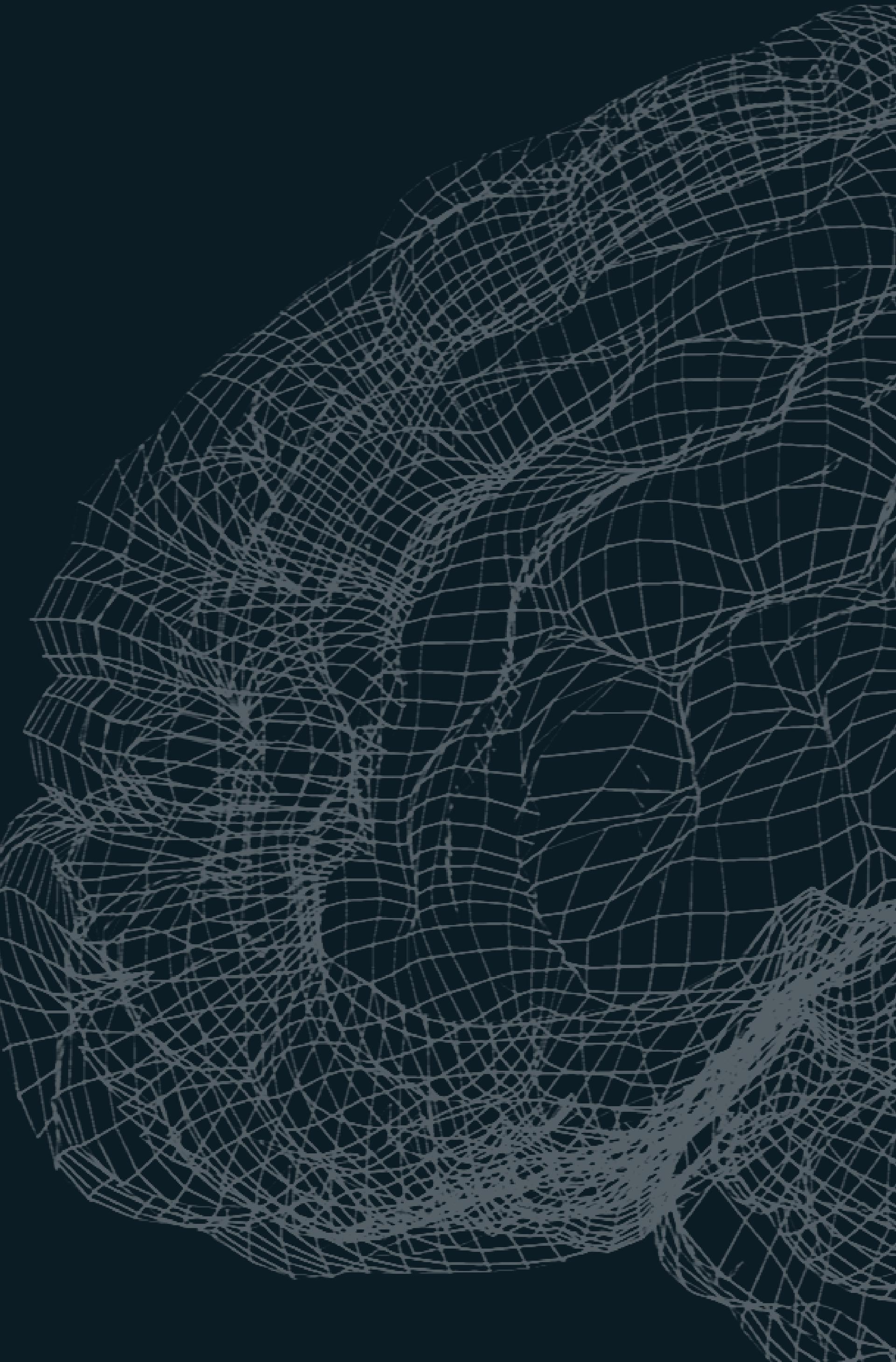




## PROGRESS

# Building One of the Most Extensive Brain Repositories in the World

With 3,000+ human brains collected, the Lieber Institute has assembled one of the largest, most carefully curated and characterized collections of human postmortem brains for the study of neuropsychiatric disorders in the world.



# Brain Repository Overview



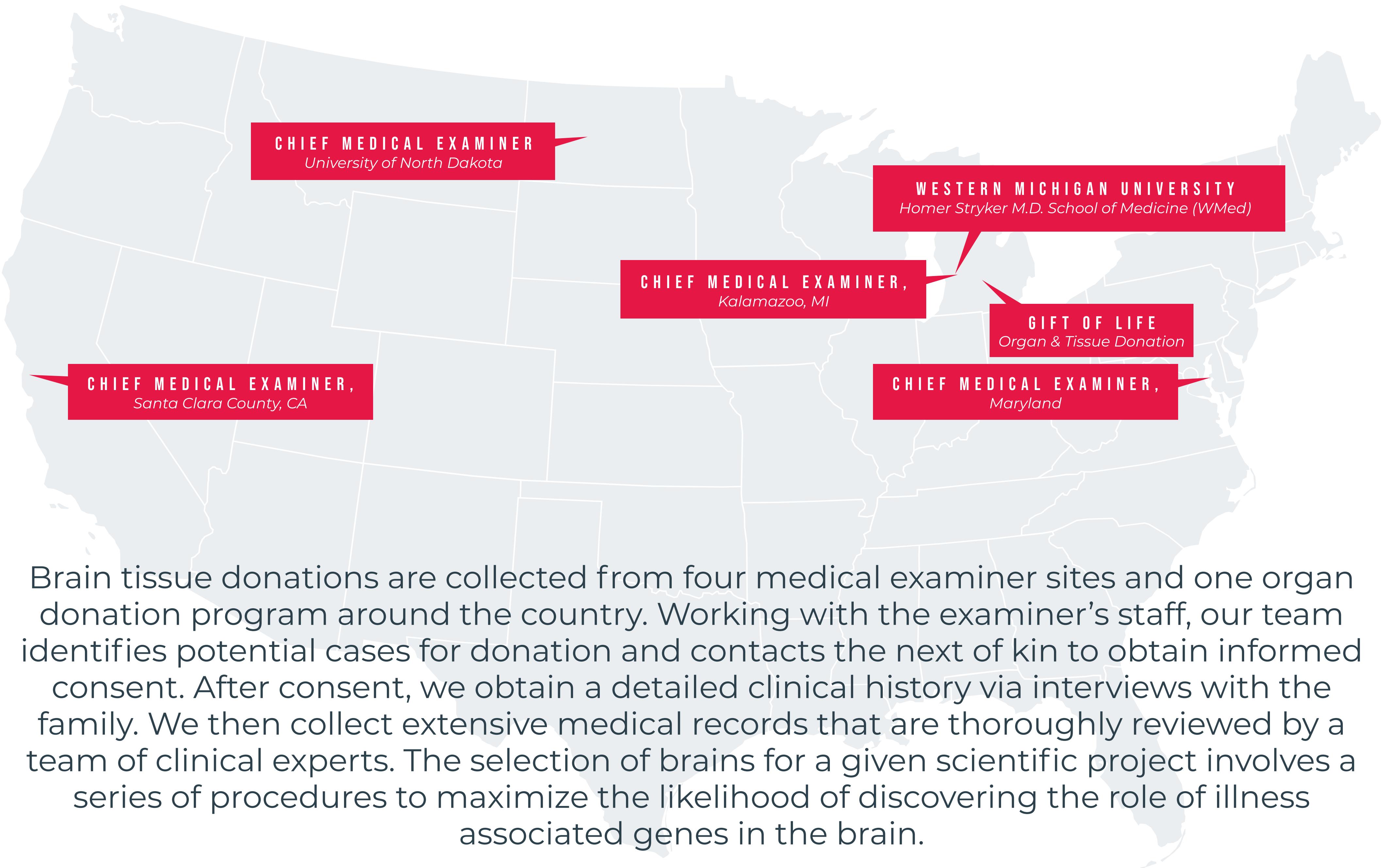
COLLECTION



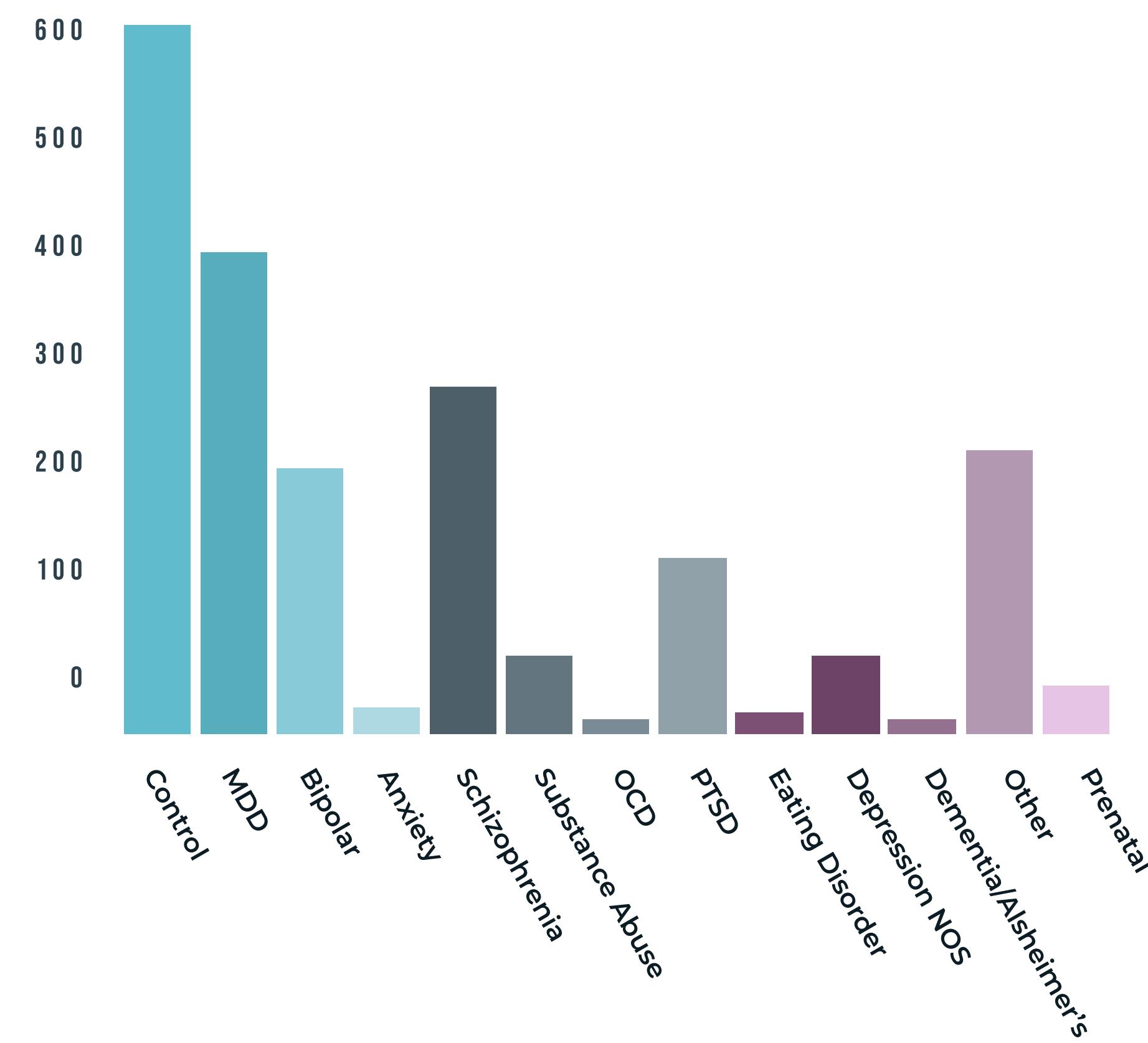
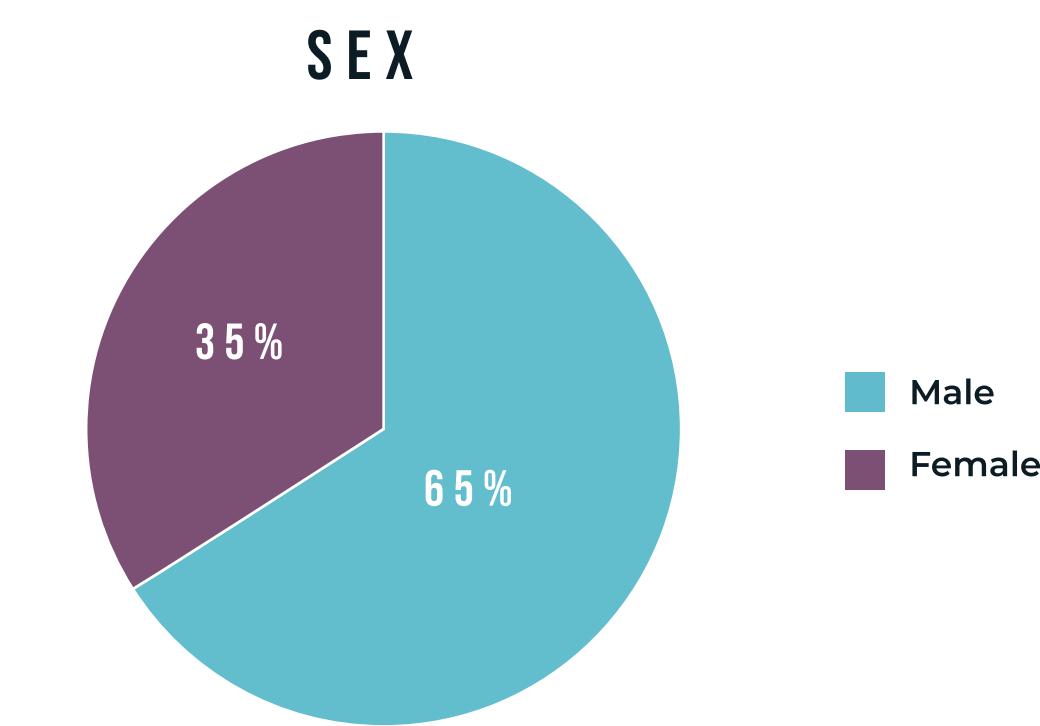
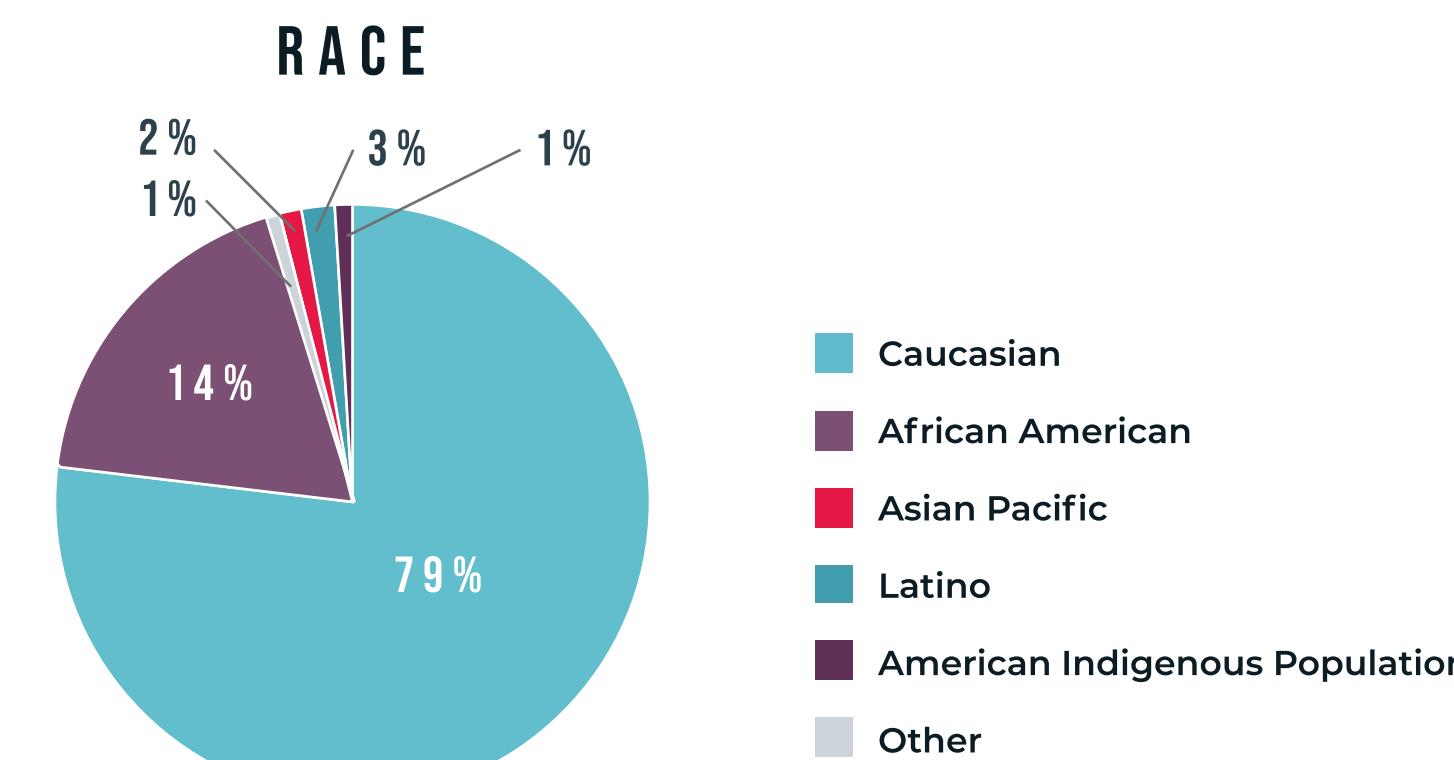
INVENTORY



RESEARCH



The brain repository is a catalytic resource that drives discovery of the mechanisms of diseases. Our brain repository covers lifespan, sex, and race. The mean age in our repository is 45 years. This allows us to conduct innovative research along all stages of life and including many brain disorders.



## The Lieber Institute has produced the largest genomic data set on the human brain in the world.



Now in its 4th year, BrainSEQ™ is a landmark, pre-competitive collaboration that started with seven leading pharmaceutical companies to uncover the genetic origins of brain disorders in order to identify novel therapeutic targets. BrainSEQ™ also works to make data freely available to scientists worldwide and all data sets produced are publicly available for future research.



For the past two years, the Lieber Institute has partnered with 23andMe, a consumer genomic data company working to revolutionize health, wellness and biomedical research. Through this novel collaboration, we have identified four new potential targets for anxiety and depression therapies. We are poised to advance these discoveries in the coming year.

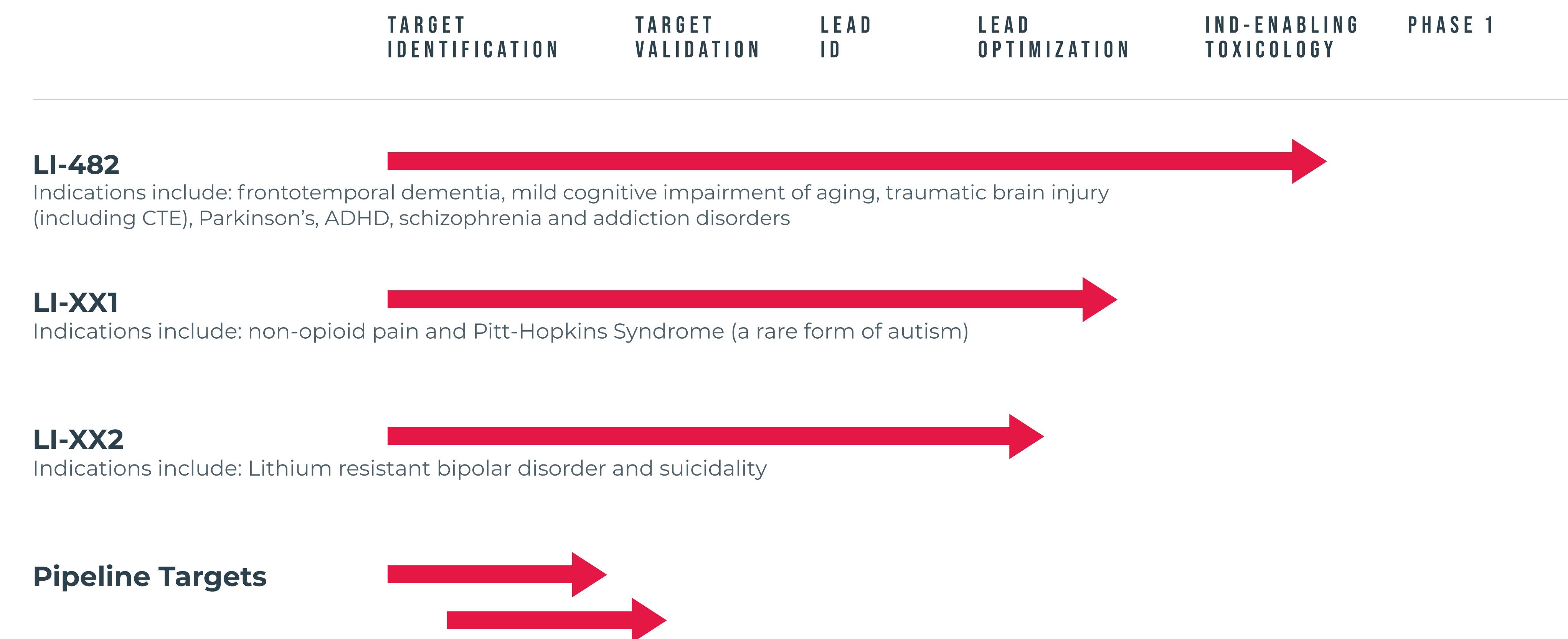


Collaborating with the VA and distinguished researchers from around the country, the Lieber Institute is producing the world's largest PTSD data set on the human brain. These data will be a public resource for researchers at institutions around the world. This work not only explores the role of genetic risk, but also uncovers how traumatic experiences alter gene function through a process called epigenetics. Understanding the genetic and epigenetic mechanisms of PTSD will identify biological targets for new diagnostics and drug therapies to improve the lives of our Veterans, and their families.

The Lieber Institute's drug discovery program has produced a robust pipeline of potential therapeutics with our leading candidate beginning Phase 1 clinical testing in 2020.

We have successfully developed and out-licensed two compounds for common medical disorders, and continue to optimize the way we identify drug targets. The Institute is looking for partners and support to advance the development of our robust pipeline of promising treatments.

## CURRENT PIPELINE OVERVIEW



## LIEBER INSTITUTE

# Programs

The human brain is the most complex object in the known universe, comprised of some 100 billion neurons, which together form a network of Internet-like complexity. There have been relatively few breakthroughs in the treatment of brain disorders in the past 60 years. Nearly all current treatments for psychiatric conditions were discovered by chance, without understanding the underlying biological causes. New technology, including our ability to decode the human genome, is significantly accelerating our understanding of complex brain disorders.

## Content

- SCHIZOPHRENIA
- MATERNAL/CHILD HEALTH
- AUTISM
- MOOD DISORDERS
- ADDICTION
- SUICIDE
- AGING DISORDERS
- PTSD/TBI/CTE
- HEALTH DISPARITIES





**PROGRAM**

# Can we prevent schizophrenia?

We understand what it's like being a family member of someone who has lost their identity to schizophrenia. It can be a terrifying experience. Schizophrenia is the cancer of mental illness that robs a young person of the opportunities to achieve their full potential, at the threshold of independence.

Experiencing a son or daughter's first serious mental health event is life-altering. It's a heartbreak felt each and every day, and can lead to a lifetime of challenges for families. Constant worry is common, as disease and current treatments may contribute to poor health overall.

The cause of schizophrenia remains a mystery. Recent large-scale genetic studies have identified hundreds of potential risk genes for schizophrenia. The challenge is understanding how a risk gene translates into an at-risk brain. With the availability of brain tissue, like that at the Lieber Institute, researchers can make this translation. These discoveries represent the first objective clues to the basic causes of illness.

Six decades have passed since the discovery of drugs that remain the primary treatment for schizophrenia, and these drugs are known to have many side effects. New treatments are urgently needed.

The Lieber Institute's primary focus is discovering strategies to prevent, better treat and ultimately cure schizophrenia. We conduct cutting-edge research, utilizing state-of-the art technologies, to discover the underlying biological causes. One approach we take starts with living cells collected from the dura, the outer protective barrier for the brain. We reprogram these cells into pluripotent stem cells and then neurons. We examine these lab-grown neurons from individuals with schizophrenia, to see how they vary from neurons derived from people with no known history of mental illness. After studying these differences, we identify potential new targets for drug development. Our researchers are also experimenting with organoids - tiny, self-organized three-dimensional 'mini-brains'. Findings from these models are leading to the discovery and development of new treatments to improve cognition, one of schizophrenia's most disabling features. Our leading drug candidate, LI-482, targets this disability and will begin human safety trials in 2020.



## PROGRAM

# Prioritizing maternal child health & early brain development

Finding out you are an expecting mother can trigger both tremendous joy but also fear. Suddenly, you scrutinize everything you do to optimize your baby's growth and development. Besides receiving good prenatal care, taking your vitamins, eating healthy, avoiding drugs and alcohol and keeping stress to a minimum, the medical community can offer little advice on reducing the risk for autism, schizophrenia and a myriad of other health conditions. This can be a scary time for parents, especially if the family has a history of mental illness or brain disorders. We are often asked, "Will our baby inherit the family illness?" Our founders share these concerns, and it's the reason the Lieber Institute exists - to map out how the brain develops, beginning at the earliest stages in life.

What role do genes play? We know that genes for mental illness are not genes of fate, but genes of risk. Psychiatric illness emerges from a combination of a child's genome interacting with his or her environment. We at the Lieber Institute are gaining critical insights into this dynamic interplay between genes and the environment by identifying strategies that will one day prevent these devastating conditions.

In 2018, the Lieber Institute published a landmark finding in *Nature Medicine*. We analyzed gene expression in placental tissue from complicated and uncomplicated pregnancies and found that the genes associated with schizophrenia risk were "turned on" in the placentas from complicated pregnancies. After extensive analysis, researchers found this occurrence increases risk of schizophrenia by at least five-fold. For the first time, we can connect genetic risk and early life complications to explain how this leads to mental illness later in life. The missing link has been hiding in plain sight: it's the placenta.

You may be wondering what you can do to reduce the risk of pregnancy complications, especially if you have experienced them in the past. We encourage you to talk with your doctor, to ensure you get the best prenatal care possible. It's also important for you to know that the placenta is developed using your baby's genomic data, not yours. In other words, the sensitivity of your placenta is not a factor of your genetics, but your baby's.

How close are we to finding the answers? The Lieber Institute is leading the neuroscience research frontier by developing cell-based model systems utilizing non-embryonic stem cells derived from our brain collection, and programming them to become placenta cells. These placenta cells then organize themselves into placenta organoids, tiny versions of the actual placenta. Researchers mimic the conditions of a complicated pregnancy, such as exposing the organoid to stress hormones or lowering oxygen levels, as happens with preeclampsia and eclampsia. The tissue is then examined to see how genes respond to the stressed environment and seem to increase risk of schizophrenia, autism, attention deficit hyperactivity disorder, and intellectual disability.

This new frontier in neuroscience research, optimizing placental health, is a promising new strategy we are exploring to reduce the probability of developing a mental illness long before someone begins to show signs of disease.



## PROGRAM

# A breakthrough treatment in autism spectrum disorder

If you have a child with autism, you know first-hand that it affects every family member in different ways. You confront a landslide of challenges as you learn to manage complicated therapies, juggle medical visits, raise your other children, and hold down a job.

The financial burden can also be enormous. Insurance seldom covers every treatment and therapy, meaning medical expenses can become substantial. If your son or daughter's autism is severe, they may require your financial support for their entire lifetime.

At the Lieber Institute for Brain Development, we are working hard to uncover the biology of autism, by studying variations in genes that we know contribute to the risk and severity of symptoms. Through our research, we have come to appreciate both similarities and also differences in symptoms of spectrum disorders. People with autism can be college graduates with high IQs who have difficulty socializing and maintaining relationships. Others may be nonverbal and require constant care throughout life, like patients with a rare disorder called Pitt-Hopkins Syndrome.

Researchers at the Lieber Institute are studying Pitt-Hopkins Syndrome as a promising window into other more common forms of autism, which occur due to a series of tiny changes across many genes, most of which are still not understood. Pitt-Hopkins, however, is caused by a mutation to a single gene on the 18th chromosome, leading to distinctive facial features and developmental delay.

Researchers at the Lieber Institute discovered that the Pitt-Hopkins genetic mutation causes a sodium channel on the surface of brain cells to be overly active. After learning how the altered brain cells function, we found a drug that blocks the effects of the sodium channel. In animals, the drug appears to restore more normal brain function. This research is helping scientists better understand other forms of autism as well, how brain function is altered, and what can be done to restore brain cells to perform normally.

Our scientists have also uncovered a previously unappreciated and potentially critical role of the cells in the brain that make myelin, the insulation for neurons. These cells represent a new target for therapeutic intervention.

The Lieber Institute is pursuing the development of LI-XX1, as a treatment for those with Pitt-Hopkins Syndrome. With additional financial support, we could test this new drug in clinical trials within the next two years.



## PROGRAM

# Mood Disorders: 1 in 5

There is a high likelihood that someone you know has experienced the debilitating effects of anxiety, depression or another mood disorder. One in five people experience a mood disorder at some point in their lives.

Many believe depression, anxiety or bipolar disorder is a personal weakness and that these disorders can be cured through force of will. That is not the case! These are complex brain disorders, and just like cancer invades the body, mood disorders invade the psyche. Left untreated, mood disorders likely exacerbate other health problems such as diabetes, heart disease and stroke. Mental health is health.

Surprisingly, the vast majority of mood disorder treatments have been around for a long time, and were actually serendipitous discoveries that were found to be effective, although we are still uncertain why. Unfortunately, many people do not respond well to current treatments, even though they are the best available.

If you or a loved one suffers from bipolar disorder for example, you may have been prescribed lithium. While lithium remains the first-line treatment for preventing manic and depressive recurrences, studies show that this drug only helps a third of people. We desperately need new therapies!

The Lieber Institute has discovered a potential new treatment for bipolar disorder, LI-XX2. It may be an alternative to lithium, or it may improve lithium's effectiveness in patients who have not responded well. We are in the early stages of developing this drug candidate, and with additional support, we hope to advance this into clinical trials.

Our effort to discover new drugs doesn't stop there. In conjunction with researchers at the Johns Hopkins School of Medicine, we are utilizing brain tissue donated to the Lieber Institute to conduct a large study of the genes implicated in bipolar disorder. This research is providing clues to help us identify how currently prescribed pharmaceuticals affect brain function, while better explaining the underlying biology that will lead to novel treatments.



## PROGRAM

# Chemical Hostage: What we are learning about addiction disorders

America is facing its largest addiction crisis of modern times. Nearly one in three people now say they know someone addicted to opioids. Rates of drug overdose deaths jumped in 2017 and the federal government reports that the life expectancy for a baby born in the U.S. has fallen for the second time in three years as a result of this crisis.

We see this devastation everyday through our work with medical examiner's offices around the country. More than 40% of the donated brains in our repository have come from a victim who died with a history of a substance abuse disorder, and the vast majority also suffer from underlying psychiatric illness. Family members regularly reach out to us to learn more about our addiction research, and they are placing their bets on science to find the answers.

Addiction occurs because drugs hijack the same brain circuitry involved in learning and reward. The neurobiology underlying drug abuse has led to the recognition of addiction as a chronic disease of the brain. Mechanisms of action vary by drug.

Nicotine, for example increases activity in certain brain cell receptors, while cannabis causes other receptors to decrease activity. Repeated use of methamphetamine causes brain cells to slow the release of dopamine, the main reward signal in the brain.

The Lieber Institute is looking into how addiction can affect a developing brain and how genes play a role in the addiction and recovery process. Despite well documented concern over cigarettes, 8.4% of women continue to smoke while pregnant in the United States. To get a more precise measure of how this might harm brain development, Lieber Institute scientists have analyzed genetics from human postmortem brain tissue. The results found that while smoking caused changes in expression in very few genes in adults, the children showed changes in many genes, meaning that the brains of developing babies are more sensitive to smoking.

Some of these genes expressed in the developing brain have been implicated in psychiatric disorders, raising concern that mothers who smoke may increase the risk of mental illnesses in their children after birth.

Drug addiction requires access to drugs, but it also includes heritable genetic variations that are passed down through the generations. We know that the liability to develop alcohol use disorder is approximately 50% heritable, meaning based on genetic variations. The addictive drug sets up a cycle of use and abuse by interacting with the genes to modify their function. This effect is based on something called, epigenetics.

Epigenetics does not involve changes to the DNA sequence. Instead small chemical markers can be attached to parts of the sequence to silence certain genes and turn other ones on. The Lieber Institute is delving into these epigenetic processes to understand how epigenetic factors are involved in addiction and recovery.

By understanding the underlying biological mechanisms of addiction, our hope is to discover strategies that both reduce risk and also better treat this brain disorder.

In the case of alcoholism and addiction to stimulants such as amphetamines, studies indicate that genetic variations in the catechol-O-methyl transferase (COMT) gene influence the likelihood of abuse. Our lead molecule LI-482, a drug that inhibits COMT, has potential to reduce the craving that drives the cycle of addiction and abuse and be a potential treatment for individuals struggling with addiction disorders.



## PROGRAM

# Chemistry not Character: Biology of Suicide

Many of you have come to know the Lieber Institute after experiencing a tragic suicide in your family. Unfortunately, suicide has become far too common, and with someone taking their own life every 40 seconds, it is a public health crisis. Shockingly, suicide now accounts for more deaths across the globe every year than war and homicide combined.

More than 350 of the brains donated to the Lieber Institute by families who have had a loved one die from suicide are being used to accelerate research around this complex disorder. We are looking toward science for answers. Researchers at the Lieber Institute have discovered genes that can identify who might be at greater risk, while providing clues that allow us to develop treatments to reduce suicidal thoughts, and ultimately prevent an attempt. We know from prior studies that lithium may be effective at reducing suicide risk, demonstrating the complicated biological mechanisms underpinning suicide.

Ultimately, better answers that might lead to prevention will come when we treat suicide like every other brain disorder and mainstream it into the rest of medical science. For example, we know genetics determines 43% of the likelihood of committing suicide, and that many of the genes implicated involve other mental illnesses such as addiction, schizophrenia, bipolar disorder, and depression.

Researchers at the Lieber Institute are studying genes linked to impulsivity and aggression, which are passed down through generations within families. People considering suicide often struggle with impulse control and aggression—behaviors caused by disorders in brain physiology and circuitry. Because suicide attempts often happen in a hasty, unplanned manner, we are working to better understand the genetic and biological mechanisms associated with impulsive and aggressive behavior.

The Lieber Institute is developing a potential new treatment, LI-XX2, to reduce suicidal thoughts and to prevent attempts. This new drug may be an alternative to lithium or may improve the effectiveness of lithium in those that did not respond before. Our leading drug candidate is early in development. With additional support, we hope to accelerate efforts to advance this drug into clinical trials.

We are committed to pushing the scientific frontier to better understand the complicated biology of suicide. Our wish for you and for your family is that you appreciate the critical role of chemistry, not character, when it comes to suicide. We invite you to join us in our pursuit of scientific answers.



## PROGRAM

# Turning the aging hypothesis on its head

Every 67 seconds, with monotonous cruelty, Alzheimer's takes up residence in another American. More than five million of us are believed to have it, two-thirds are women. And for each one of us affected, two, three or more family members must be available for care.

Age-related disorders, such as Alzheimer's and other forms of dementia, are some of the most feared of all diseases. They rob you of memories collected over a lifetime, memories that define you as a person—how you feel and think, your desires and needs. It slowly robs your ability to perform everyday tasks, and eventually, it takes your life.

While the elderly population is most affected, few realize that brain changes linked with Alzheimer's disease begin 20 or more years before symptoms appear. And, medical experts do not consider dementia part of the normal aging process. Unfortunately, even though genetics contributes about 60% heritability for Alzheimer's, creating opportunities for biological targets, ongoing research has so far failed to provide meaningful treatments.

Utilizing our robust brain repository, the Lieber Institute is taking novel approaches to address age-related brain diseases. Our researchers found that when patients had a larger number of mutations, they had decreased function in a brain region important for memory, called the hippocampus. This held true even in people who appeared outwardly healthy. Building on this study, we hope to identify those most at risk and discover strategies to prevent and better treat the disease.

The Lieber Institute is studying “resilience” genes. These are mutations that do not prevent Alzheimer’s but seem to protect people if they get signs of the disease. Physicians first recognized these genes after examining healthy donors whose brain showed all pathological signs of Alzheimer’s, but who had gone their entire lives without any memory loss or other dementia symptoms. We are now seeking to decipher how these genes operate to find new treatments to protect brains from the effects of aging.

We are also conducting the first human brain cell-specific study in dopamine neurons. Utilizing state-of-the-art technology, we isolate single dopamine neurons, the principal cells affected in Parkinson’s Disease and linked with schizophrenia. We compare cells from young and old, diseased and not diseased individuals, to discover why some of these brain cells die early, while others seem to be resilient to the aging process. From these biological insights we hope to discover new drug therapies, or ways to prevent the premature death of brain cells.

Recent years have seen a series of failures in potential drugs to treat Alzheimer’s, but most of these unsuccessful therapies focused at a point in the disease progression where the brain was already being harmed. At the Lieber Institute, we are turning the field of age-related brain research on its head. New or unprecedented approaches to drug development and prevention therapies are desperately needed.



**PROGRAM**

# Trauma and the brain: A focus on Veterans and Athletes

## Post-traumatic Stress Disorder

The Lieber Institute for Brain Development is deeply committed to reducing rates of veteran suicide and improving quality of life by advancing our knowledge of the biology of post-traumatic stress disorder (PTSD) and traumatic brain injury. Nobody who has served, or is serving our country, should struggle with these conditions.

Current treatments for PTSD are woefully inadequate, pointing to the urgent need to better understand the biology of psychological trauma. At the Lieber Institute, we have acquired the world's largest collection of human postmortem brains with a confirmed diagnosis of PTSD.

We have endeavored to ensure funding is available to speed up research on the brains donated by family members who have lost a loved one with PTSD. And Congress has heard and acted. As a result of our outreach to legislative offices and federal agencies, Congress has appropriated nearly \$40M in new funding to support the Veteran Administration's National Center for PTSD. We are working in partnership with the Veteran Administration to produce the largest data set in the world on PTSD to gain insights into the biology of this complex brain disorder.

We are devastated by the fact that more Veterans die of suicide than in combat—a staggering 20 death-by-suicides per day. We understand that the consequences of PTSD and brain injury can fracture relationships and tear apart families. We are with you on the front lines to ensure that the scientific frontier leads the way to better outcomes.

## Traumatic Brain Injury & Chronic Traumatic Encephalopathy

Many parents, spouses and fellow athletes have approached us to better understand the consequences of concussion and traumatic brain injury. We know that the scientific pursuit has been too slow to explain who is at risk. Even worse, we lack the knowledge to treat those enduring long-term effects related to these brain injuries.

We also know that incurring repeat concussive injury, or a single traumatic brain injury, contributes to higher rates of suicide and drug abuse. Symptoms related to concussive head injuries can contribute to challenges with mood, sleep, the ability to maintain focus and often can result in impulsive and self-destructive behavior. It's not imagined or 'just in your head'; these symptoms are the result of injury that disrupt the circuits in your brain. Unfortunately, there are no FDA-approved treatments for the long-term effects of traumatic brain injury and resulting chronic traumatic encephalopathy. We are working to change that paradigm.

The Lieber Institute's most advanced drug candidate, LI-482, is a novel therapeutic targeting the long-term effects of brain injury. This new treatment aims to improve focus and memory and reduce aggressive and impulsive behavior, in addition to addiction tendencies. We plan to test this promising new drug in clinical trials beginning in 2020.



## PROGRAM

# Reducing Health Disparities in Genomic Research

Have you ever wondered how genes related to your ancestry may put you at greater risk for disease? While humans are 99.9% genetically identical, the 0.01% of difference account for all human diversity! Little variations can make a big difference.

The genomic revolution in medicine has the potential to provide the most personalized and effective medical treatments in history. Having access to large-scale genomic data from all ethnic groups is crucial to comprehending human diseases and ultimately ensure that the promise of personalized medicine is for all.

However, minority groups, like African Americans, are poorly represented in these large-scale genomic studies.



<16%

OF THE WORLD IS OF  
EUROPEAN DESCENT, BUT

81%

OF LARGE-SCALE GENOMIC DATASETS  
ARE OF PEOPLE OF EUROPEAN DESCENT.



"My clergy colleagues and I believe that precision medicine has the potential for finding cures and treatments for diseases that uniquely affect African Americans. This revolution in medicine has largely left behind ethnic minority groups like African Americans, and it is time to change this."

REV. DR. ALVIN C. HATHAWAY, SR.

A 2019 landmark study of 910 individuals of African descent revealed that the human reference genome, used universally in genetic research, omits almost 10% of the African genome. This means that a vast majority of scientific advancements in precision medicine apply exclusively to individuals of European ancestry. In neuroscience studies, underrepresented minority groups, including African Americans, make up less than 5% of all the ethnic groups studied.

The Lieber Institute is dedicated to ensuring that ethnic minority groups are not left behind. We've invested over \$20 million to expand our brain collection sites around the country and improve ethnic diversity in our brain repository. To date, we now have more than 500+ brains of individuals of recent African Ancestry, which is the largest, most carefully characterized repository in the world.

Together with community leaders in Baltimore, MD, we've launched the nation's first African American Neuroscience Research Initiative, aimed at ensuring that genomic research and neuroscience studies are representative of individuals across all populations including African ancestry.

This year, 1 in 4 African Americans will experience a serious mental health disorder. Suicide rates for African American children under the age of 13 are twice as high as children of European ancestry. And minor genetic differences between ethnic groups is incredibly important. In Alzheimer's, an important gene for predicting risk in individuals with European ancestry is much less important in predicting this disease in the African American population. And Alzheimer's disease is about twice as common in African Americans.

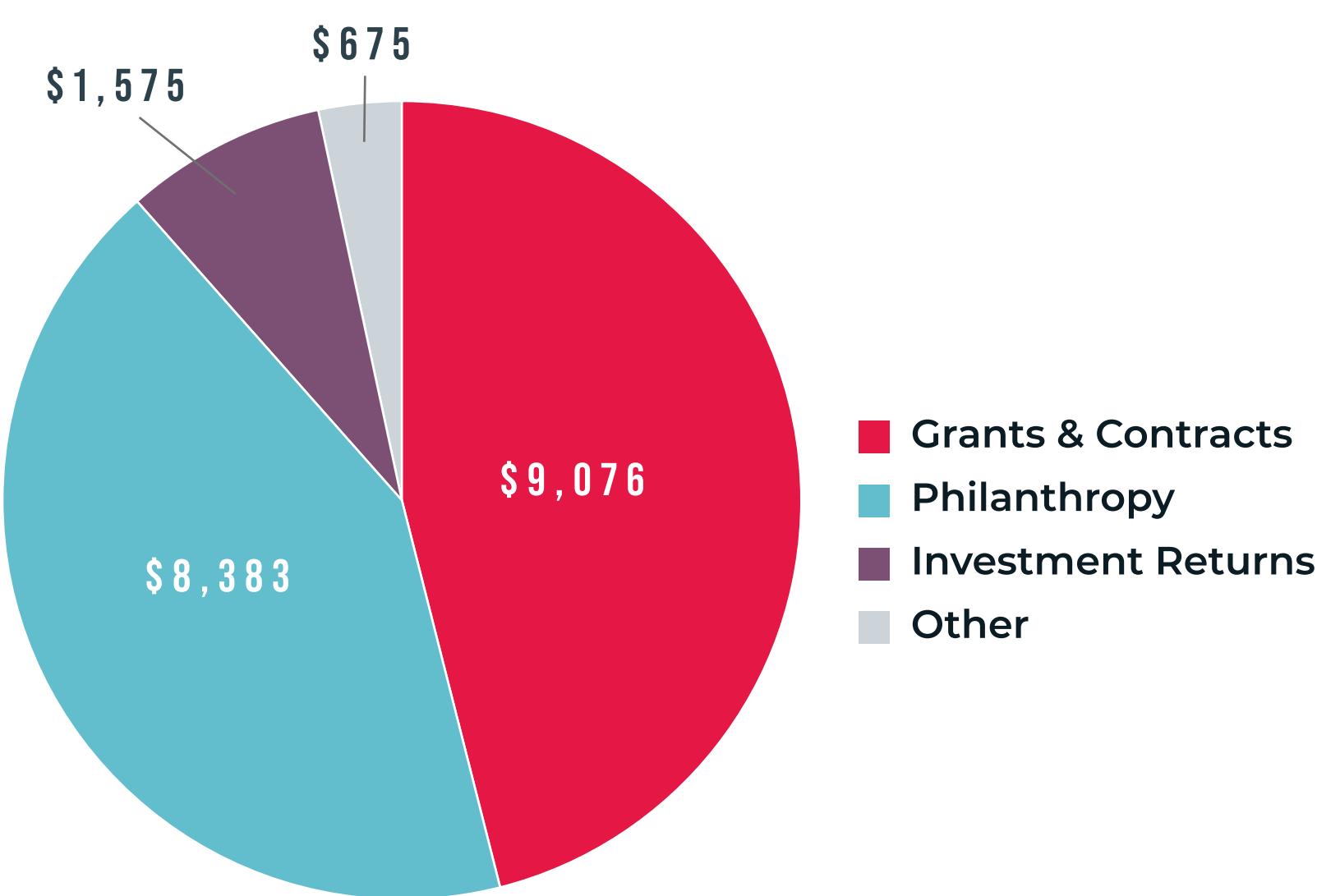
There has never been a more urgent time than now to ensure African Americans and other ethnic minority groups are involved with scientific discoveries.

Join us to ensure all people can benefit from advances in personalized medicine.

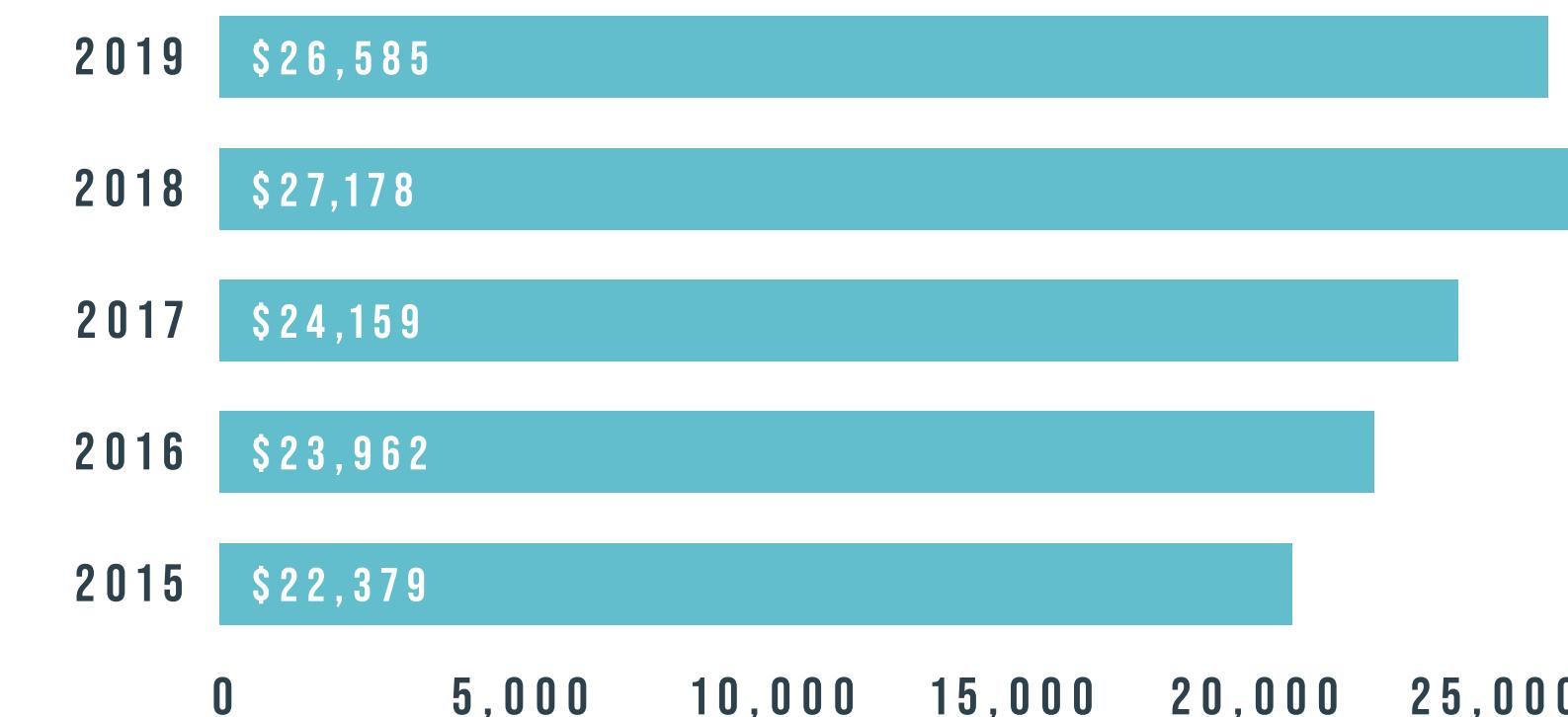
# FUNDING

In 2019, the Institute continued to make significant investments in scientific research to better understand, and ultimately find treatments for, neuropsychiatric disorders such as schizophrenia. The majority of this research was funded through grant and contract revenues and new philanthropic donations.

FY 2019 REVENUE AND OTHER SUPPORT (\$K)



OPERATING EXPENSES (\$K)

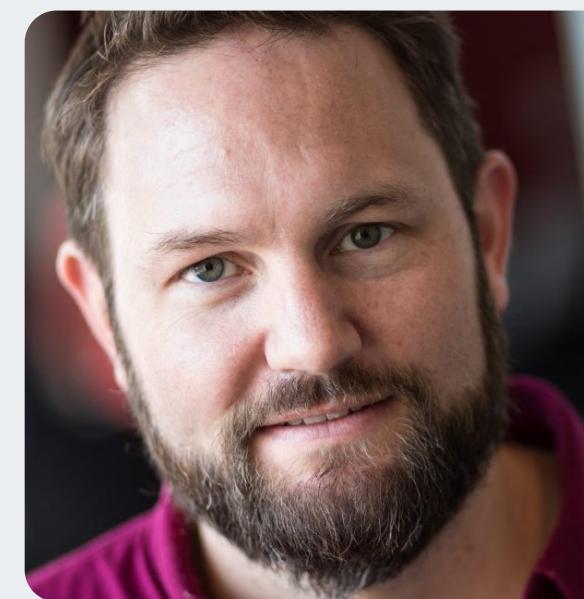


# Featured Researchers



"We are using cutting edge cell-based models to understand the placenta's role in brain development. We test factors that support healthy brain development that may one day lead to discoveries that will prevent conditions such as schizophrenia and autism."

*Maternal/Child Health*  
**JENNIFER ERWIN**  
PH.D.



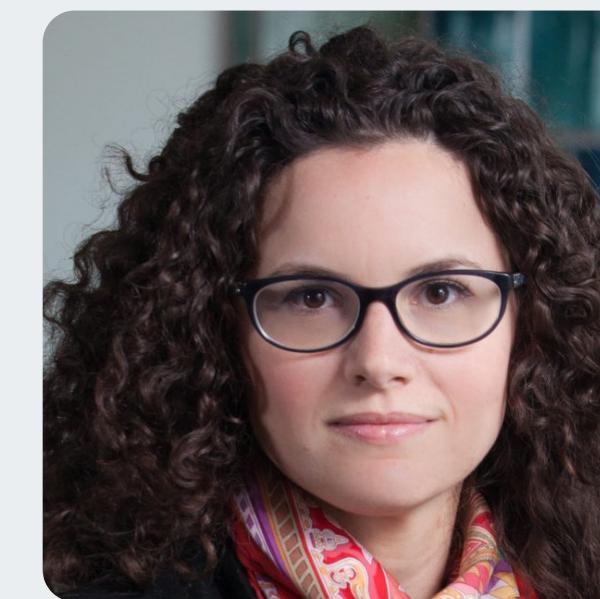
"We've found defects in myelin, the cells that insulate brain neurons, in a rare autism spectrum disorder called Pitt-Hopkins Syndrome (PTHS). We hope this leads to new treatments for PTHS children, but also those suffering from more common forms of autism."

*Autism*  
**BRADY MAHER**  
PH.D.



"We utilize cutting-edge preclinical assays, including touchscreen-based tests of cognitive function, to identify novel compounds with the potential to treat cognitive impairment associated with schizophrenia and related disorders."

*Schizophrenia*  
**GREG CARR**  
PH.D.



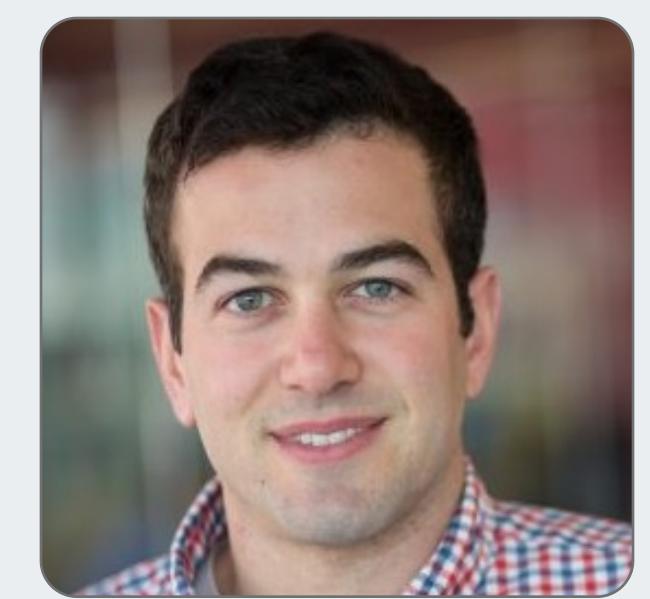
"In studying suicide, we always keep a focus on the individual's experience. We value each case and their stories as we try to relate to them, to how they felt in those critical moments. This is hard, but it's crucial if we want to make sense of the biology underlying the behavior, and ultimately prevent it. And I think we are on the right track."

*Suicide*  
**GIOVANNA PUNZI**  
M.D., PH.D.



"Unlike other organs, the majority of the brain's cells are irreplaceable. So it's critical to understand why some cells age and die faster than others, causing age-related brain disorders. Our brain repository allows us to research new detection, treatment and prevention strategies."

*Aging Disorders*  
**RAHUL BHARADWAJ**  
PH.D.



"We're using big data to better untangle the effects of trauma on the human brain. Utilizing our brain repository, we have produced the largest human brain dataset in the world on Post-traumatic Stress Disorder (PTSD). We are gaining insights that will one day lead to new diagnostics and therapeutics."

*PTSD*  
**ANDREW JAFFE**  
PH.D.

# Leadership



**DANIEL R.  
WEINBERGER**  
M.D. Director, CEO

Regarded worldwide as the preeminent scientist in schizophrenia research. Science magazine highlighted his genetic research as the 2nd biggest scientific breakthrough of 2003, behind the discovery of the origins of the cosmos.



**THOMAS M.  
HYDE**  
M.D., PH.D.  
Chief Medical Officer

Responsible for developing and overseeing the world's largest collection of postmortem human brains dedicated to neuropsychiatric research.



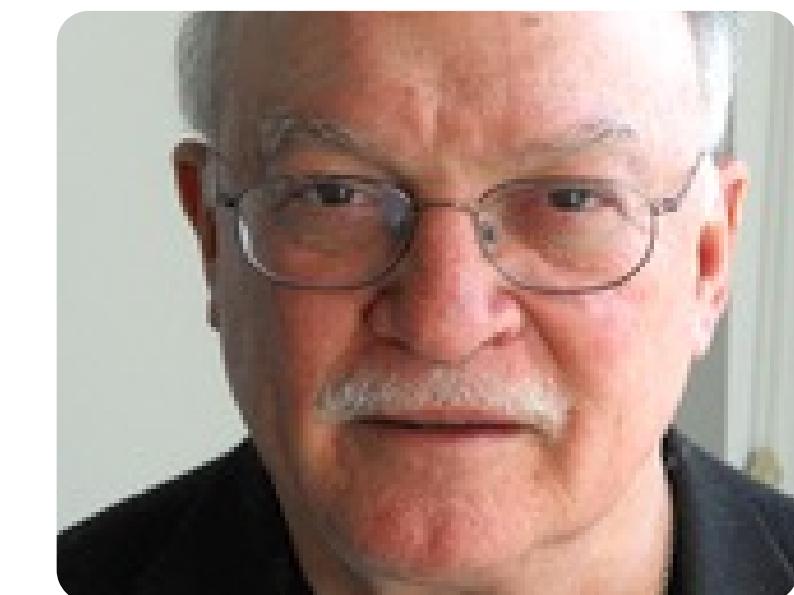
**SOLOMON  
SNYDER**  
M.D. Director of  
Drug Discovery

Distinguished Service Professor at the Johns Hopkins University School of Medicine. Recipient of U.S. National Academy of Science Award in Neuroscience & National Medal of Science.



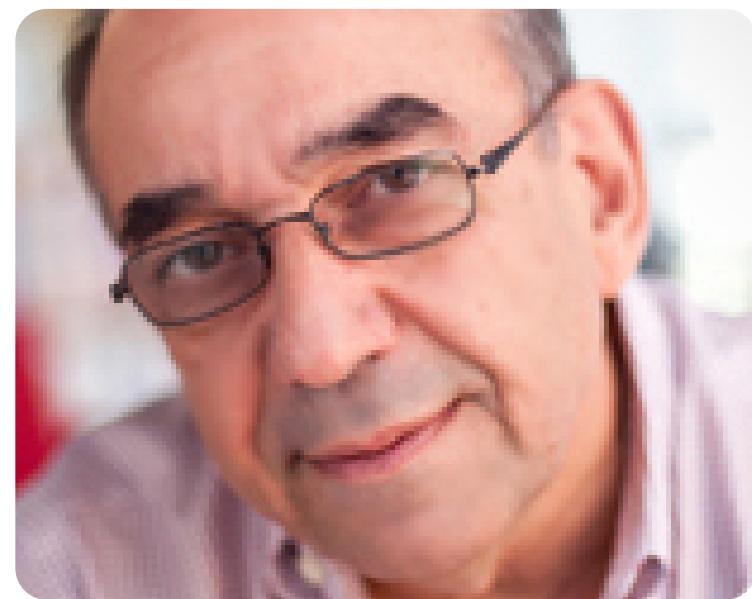
**JAMES  
BARROW**  
Ph.D. Associate Director,  
Drug Discovery

Received his Ph.D. from Harvard before working with Merck Research Laboratories in West Point where his teams advanced several compounds into clinical development.



**JOEL E.  
KLEINMAN**  
M.D., PH.D. Associate  
Director of Clinical  
Sciences

A 36-year veteran of the NIH with over 200 peer-reviewed papers on the postmortem human brain.

**RON  
MCKAY**

PH.D. Adjunct  
Science Advisor

First to show that specific DNA-protein complexes could be analyzed with antibodies. Identified neural stem cells as a tool to study brain.

**ELAINE  
JONES**

Chief Operating Officer

30 years of experience managing major scientific research institutions, including Picower Institute and Allen Institute for Brain Science.

**KARI  
STOEVER**

Chief External  
Relations Officer

Global Health expert with more than 20 years experience in development and innovative finance.

**ANDREW  
MASLAN**

CPA, Chief  
Financial Officer

More than 20 years of comprehensive financial experience, including biotechnology.

**JEAN  
DUBOSE**

Chief of Staff

Over 20 years of experience in non-profit management, resource & program development, & special event planning.

# Board of Directors

**HERBERT  
PARDES**  
M.D., Chair

Executive Vice Chairman  
of the Board of Trustees,  
New York-Presbyterian  
Hospital

**STEPHEN  
LIEBER**  
Founder

**MILTON  
MALTZ**  
Founder

**TAMAR  
MALTZ**  
Founder

**MARY  
RUBIN**  
Founder

**PAUL B.  
ROTHMAN**  
M.D.  
  
Frances Watt Baker,  
M.D., and Lenox D. Baker  
Jr., M.D., Dean of the  
Medical Faculty; vice  
president for medicine  
of The Johns Hopkins  
University; and CEO of  
Johns Hopkins Medicine

**STEVEN S.  
SHARFSTEIN**  
M.D.  
  
Former President and  
CEO of Sheppard Pratt  
Health System

**ROBERT F.  
MUSE**  
Esq.  
  
Partner, Levy, Firestone,  
Muse, LLP

**DANIEL R.  
WEINBERGER**  
M.D.  
  
Director and Chief  
Executive Officer of the  
Lieber Institute for Brain  
Development

# Scientific Advisory Board

**JOSEPH  
COYLE**

M.D., Chair  
Harvard Medical School

Eben S. Draper Professor  
of Psychiatry and  
Neuroscience,  
Chief Scientific Officer of  
McLean Hospital

**MARK  
BEAR**

PH.D. Massachusetts  
Institute of Technology

Picower Professor of  
Neuroscience,  
Professor Department of  
Brain and Cognitive  
Sciences, Investigator,  
Howard Hughes Medical  
Institute

**PAT  
LEVITT**

PH.D. University of  
Southern California

Provost Professor,  
Department of  
Pediatrics, WM Keck  
Chair in Neurogenetics,  
Director-Program in  
Developmental  
Neurogenetics, Institute  
for the Developing Mind

**STEVEN  
SALZBERG**

PH.D. Johns Hopkins  
University School of Medicine

Bloomberg Distinguished  
Professor of Biomedical  
Engineering, Computer  
Science and Biostatistics  
Director of the Center for  
Computational Biology

**TRUDY  
MACKAY**

PH.D. Clemson  
University

William Neal Reynolds  
Distinguished Professor  
of Biological Sciences  
Director, Center for  
Human Genetics

**FLORA  
VACCARINO**

M.D. Yale School of  
Medicine

Harris Professor in the  
Child Study Center,  
Professor in the  
Department of  
Neuroscience

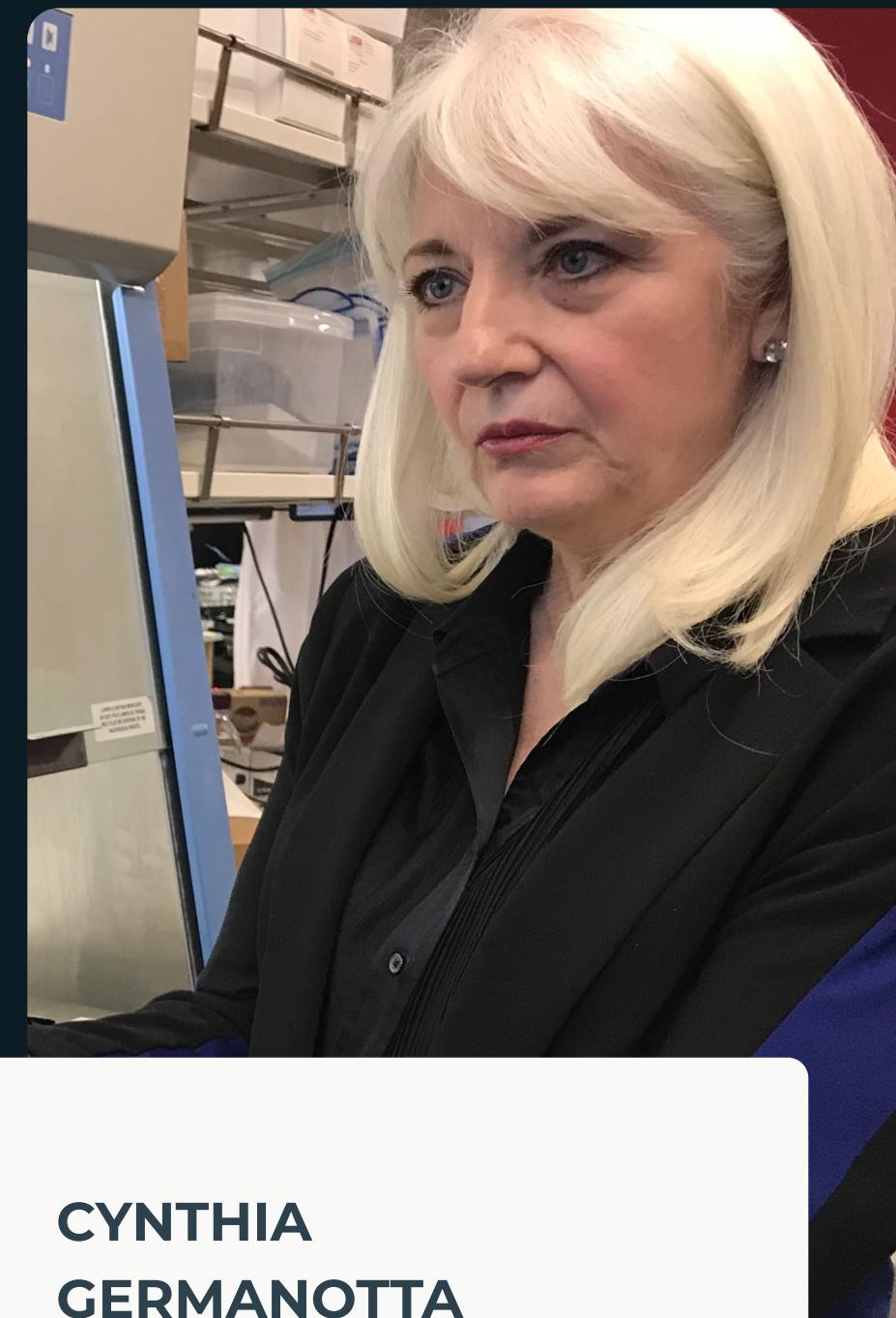
**DARRYLE  
SCHOEPP**

PH.D.

Former Senior VP and  
Head of Neuroscience,  
Merck

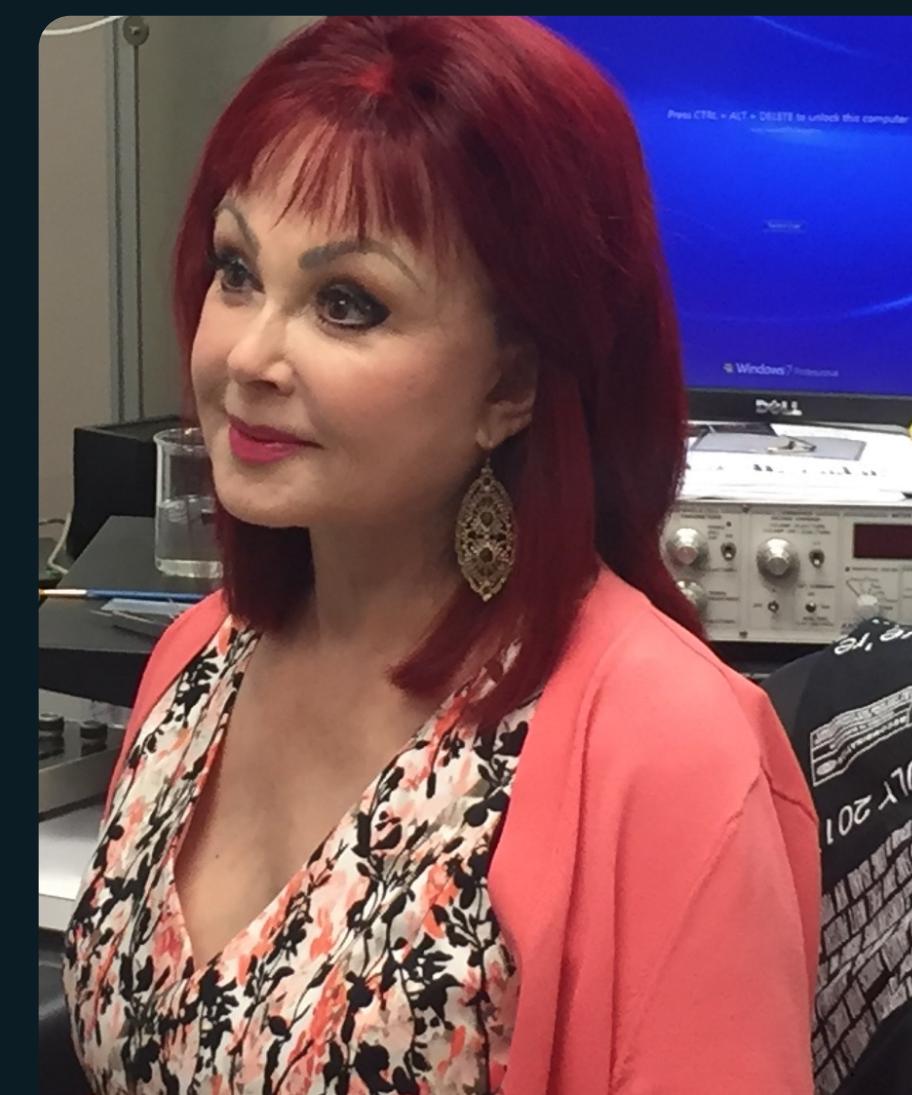
# Champion Council Members

Founding members of the Lieber Institute Champions Council, established to mobilize awareness and support for cutting edge brain research.



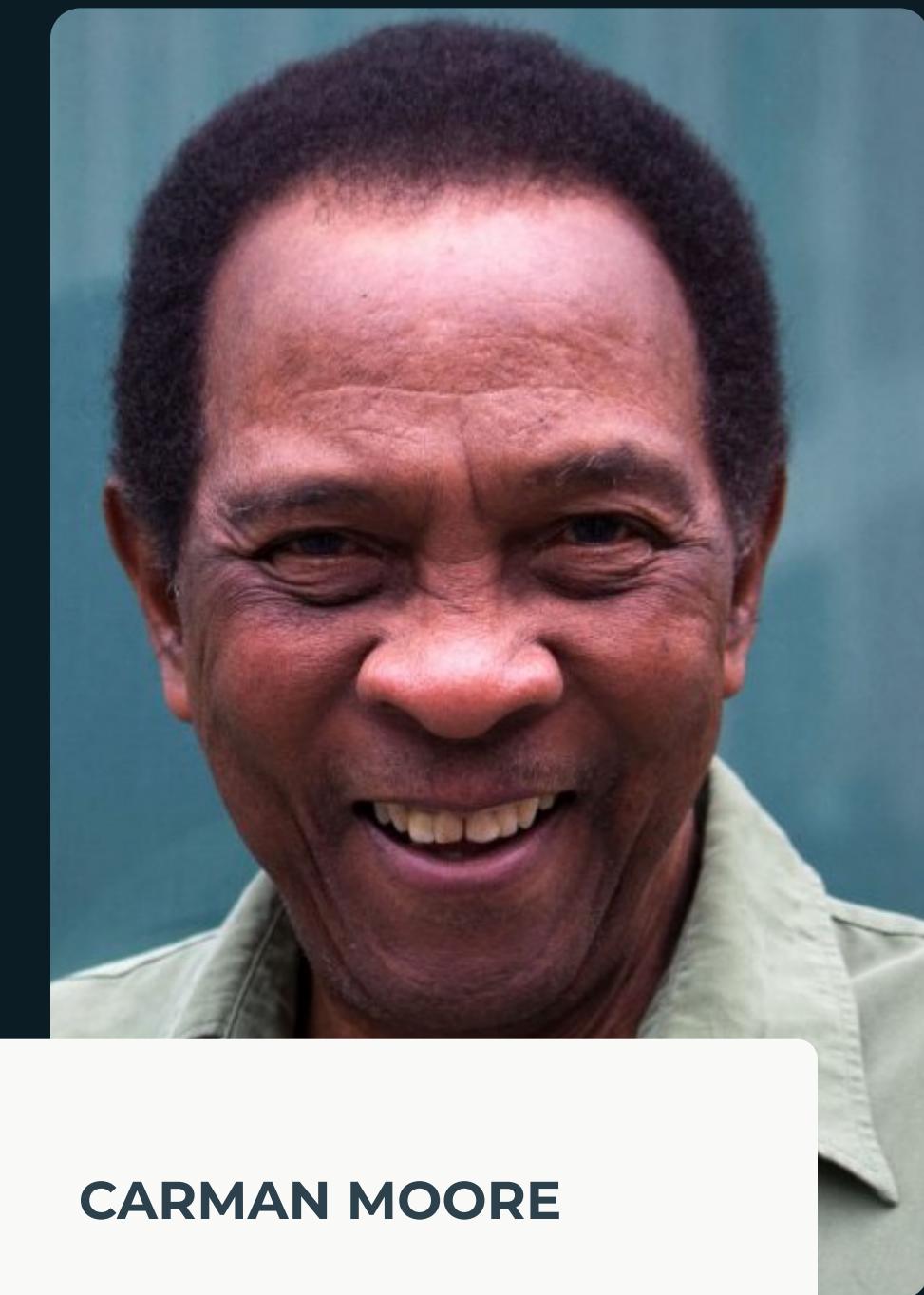
**CYNTHIA  
GERMANOTTA**

Lady Gaga's mother, and Cofounder and Executive Director of Born This Way Foundation.



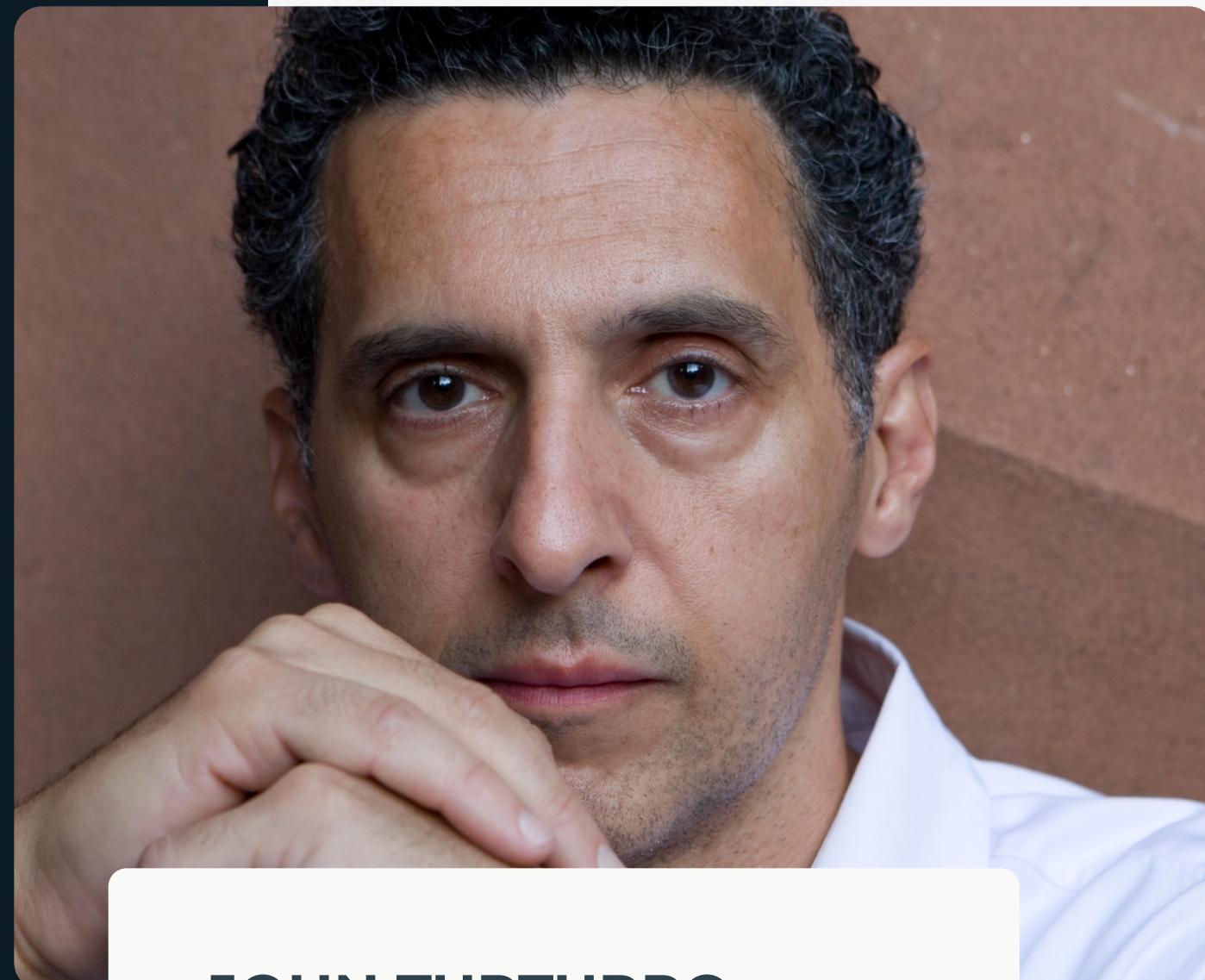
**NAOMI JUDD**

Country music singer, songwriter, actress and activist.



**CARMAN MOORE**

World-renowned composer, conductor, author, and music critic.

**JOHN TURTURRO**

Actor, writer, and filmmaker

LIBD Champions Council

“

Dear Friends,

Growing up with mental illness in my family, my big question for the past fifty years has been, “Why did it happen?” Like you, I’ve been frustrated by the lack of answers. Science has yet to discover what causes mental illness, and even more puzzling is that there have been no major new treatments since my older brother was born 67 years ago.

While it’s been a roller coaster ride for our family, I know we’re not alone. Major mental illness affects one in five people on any given year. I have chosen to speak out to reduce the stigma associated with mental illness, and to advocate for the advancement of science. The more we can understand about the function of the brain and the root causes of these diseases, the closer we are to finding ways to prevent or cure them.

Meeting Dr. Weinberger two years ago and learning about the work of the Lieber Institute gave me hope. I learned that science is on the precipice of discovering not only the root causes, but also new treatments and ultimately, ways to prevent these disorders.

As the guardian of my older brother, I take things day by day. But, as I walk around the streets of NYC, and see men and women living on the streets, I’m reminded that my brother’s disease kills people. Like our families, they need hope as well.

*John Turturro*

# Research Partners



Johnson & Johnson

## ACADEMIA

Case Western Reserve University  
Columbia University  
Duke University  
Harvard University  
University of Colorado  
University of Miami  
University of North Dakota  
Johns Hopkins University  
JHU Applied Physics Lab  
National University of Singapore  
Seoul National University  
Peking University, China  
University of Oxford, United Kingdom  
University of Bari, Italy  
University of Edinburgh  
University of Copenhagen  
University of Sofia

## FOUNDATIONS

Abell Foundation  
American Epilepsy Foundation  
American Suicide Foundation  
Brain & Behavior Research Foundation  
Maryland Stem Cell Research Fund  
Pennington Foundation  
Pitt-Hopkins Foundation

## AGENCIES

National Institutes of Health  
National Institutes of Mental Health  
U.S. Department of Veterans Affairs  
Office of Chief Medical Examiner; Maryland, Kalamazoo, MI, and Santa Clara County, CA  
European Institute of Oncology

## PHARMA

Astella US  
AstraZeneca  
Eli Lilly & Company  
Johnson & Johnson  
Lundbeck  
Pfizer Inc.  
Roche

# Featured Publications

**2019**

NATURE NEUROSCIENCE, 2019

**Genetic regulation of expression in the granule cell layer of the human dentate gyrus.**

Jaffe AE\*, Hoepfner DJ\*, Saito T, Blanpain L, Joy Ukaigwe J, Burke EE, Collado-Torres C, Tao R, Tajinda K, Maynard KR, Tran MN, Martinowich K, Deep-Soboslay A, Shin JH, Kleinman JE, Weinberger DR, Matsumoto M+, Hyde TM+

NATURE COMMUNICATIONS, 2019

**Dissecting transcriptomic signatures of neuronal differentiation and maturation using iPSCs**

Burke EE\*, Chenoweth JG\*, Shin JH, Collado-Torres L, Kim SK, Micali N, Wang Y, Colantuoni C, Straub RE, Hoeppner DJ, Chen H-Y, Lescure A, Shabbani K, Hamersky GR, Phan BN, Ulrich WS, Valencia C, Jaishankar A, Price AJ, Rajpurohit A, Semick SA, Bürli R, Barrow JC, Hiler DJ, Page SC, Martinowich K, Hyde TM, Kleinman JE, Berman KF, Apud JA, Cross AJ, Brandon NJ, Weinberger DR, Maher BJ, McKay RDG+, Jaffe AE+

GENOME BIOL. 2019

**Divergent neuronal DNA methylation patterns across human cortical development reveal critical periods and a unique role of CpH methylation**

Price AJ, Collado-Torres L, Ivanov NA, et al

NEURON. 2019

**Regional heterogeneity in gene expression, regulation, and coherence in the frontal cortex and hippocampus across development and schizophrenia**

Collado-Torres L, Burke EE, Peterson A, et al

AMERICAN JOURNAL OF PSYCHIATRY. 2019

**Thinking About Schizophrenia in an Era of Genomic Medicine**

Weinberger, DR.

**2018**

NAT NEUROSCI. 2018

**Developmental and genetic regulation of the human cortex transcriptome illuminate schizophrenia pathogenesis**

Jaffe AE, Straub RE, Shin JH, et al

NATURE MEDICINE. 2018

**Convergence of placenta biology and genetic risk for schizophrenia**

Ursini G, Punzi G, Chen Q, et al

**2017**

NATURE REVIEWS. NEUROSCIENCE. 2017

**Genetic insights into the neurodevelopmental origins of schizophrenia**

Birnbaum R, Weinberger DR.

**Join us on our journey to prevention.**

Visit [libd.org](http://libd.org) to learn more about becoming an advocate and supporting our mission.

