From the director
This year, we are celebrating the 20th anniversary of the MIND Institute, which officially launched with a bill passed by the California legislature in 1998. Recruitment of faculty and staff, funding of innovative seed grants, and securing key financial gifts from generous donors followed – and, in 2003, the MIND Institute’s two-building complex opened on the UC Davis Health campus.

Today, the MIND Institute is home to 57 faculty members, nearly 70 graduate students and postdocs, and 250 staff. The institute is truly interdisciplinary, with the faculty drawn from five colleges and 16 academic departments across UC Davis. The breadth of our research extends from “cells to communities.” Moreover, activities are no longer confined to our buildings – more than one-third of our faculty members are located on the Davis campus, evidence of the growing interest in autism and neurodevelopmental disorders at UC Davis. The MIND Institute is no longer a physical space but rather the focal point and catalyst for research, clinical care, and education in neurodevelopmental disorders for the entire UC Davis campus.

The MIND Institute continues to thrive because of donors who believe and invest in our mission. In this issue, you will read about a number of recent achievements, some involving senior faculty, such as David Amaral and his new Autism Center of Excellence, and others involving early-career scholars, such as Lauren Libero and Annie Vogel Ciernia, who promise to continue bringing us closer to new ways of helping families. You also will read about our expansion of partnerships around the world. Each of these achievements depended in one way or another on donor support. On behalf of everyone at the MIND Institute, thank you.

Leonard Abbeduto
Director, UC Davis MIND Institute

MIND Institute wins ACE grant

The UC Davis MIND Institute has been awarded a 5-year, $12 million Autism Centers of Excellence (ACE) grant, one of five in the nation, to create a “Center for the Development of Phenotype-based Treatments of Autism Spectrum Disorder.”

The UC Davis ACE will be administered by the National Institute of Child Health and Development, one of the National Institutes of Health.

The center will take a personalized medicine approach to addressing autism spectrum disorder (ASD) treatment based on a child’s behavioral and biological characteristics with the goal of identifying and tailoring treatments that improve quality of life.

“Autism is a truly heterogeneous disorder; no two individuals with ASD have exactly the same characteristics, and so it is unlikely that a single drug or treatment will be the answer,” said David Amaral, Beneto Foundation Chair, MIND Institute researcher, professor of psychiatry and behavioral sciences and director of the ACE.

“We plan to home in on specific ASD subtypes to ultimately enable development of more effective therapies for each one.”

The center will initially focus on two subgroups: children with ASD who also have troublesome anxiety, and those with ASD and also have enlarged brains.

An estimated 40-80 percent of children with ASD experience clinically significant anxiety, a condition often missed in children who are nonverbal or have intellectual disability. Even children who have pervasive anxiety symptoms are rarely treated for the condition.

Marjorie Solomon, Marvin “Buzz” Oates and Family Endowed Chair in Lifespan Development in Autism, MIND Institute faculty member, and professor in the Department of Psychiatry and Behavioral Sciences, will lead an effort to identify children with ASD who have anxiety, even if they have intellectual disability, and treat them with cognitive behavioral therapy and a medication called sertraline, a type of serotonin reuptake inhibitor, or SSRI. The team also will conduct brain scans in participants before and after these interventions to investigate potential neural signatures of anxiety and of responses to treatment.

ACE continued on back page
Results of parallel studies conducted at the MIND Institute and at the Massachusetts Institute of Technology Picower Institute for Learning and Memory appeared in the journal Neuropsychopharmacology.

“Our collaborative teams found that treatment with the drug R-baclofen improved scores on several learning and memory tasks, and on a standard assay of social behavior, in 16p11.2 mutant mice,” said MIND Institute researcher Jacqueline Crawley, Robert E. Chason endowed chair in translational research, professor in the Department of Psychiatry and Behavioral Sciences and co-senior author of the paper along with MIT’s Mark Bear.

“This corroboration of findings by two independent labs, using two distinct lines of mice with the same mutation, increases confidence that R-baclofen may be an effective pharmacological treatment for some of the symptoms of human 16p11.2 deletion syndrome, including intellectual impairment and autism.”

Human chromosome 16p11.2 deletion syndrome is caused by the absence of about 27 genes on chromosome 16 at position p11.2. The prevalence in the general population is estimated at three in 10,000. People with 16p11.2 deletion syndrome may have impaired communication and social skills, as well as delayed development of speech and language and intellectual impairments, recurrent seizures, and an increased risk for obesity. Some with the deletion have no identified physical, intellectual or behavioral abnormalities.

Growing knowledge about genetic mutations in people with autism is enabling researchers to evaluate hypothesis-driven pharmacological interventions for their ability to alter the biological and behavioral consequence of specific mutations that cause autism. One of the genes in the 16p11.2 deletion region regulates the inhibitory neurotransmitter GABA. Crawley and her colleagues decided to test the hypothesis that increasing GABA neurotransmission using R-baclofen, which binds to GABA-B receptors, could reverse analogous behavioral symptoms in a mouse model of 16p11.2 deletion syndrome.

In the current paper, researchers reported the results of animal model studies using two independently derived lines of mutant mice, each missing a chromosomal region analogous to human 16p11.2. Normal and mutant mice at both labs were tested after receiving R-baclofen in their drinking water on three tasks: novel object recognition, object location memory and contextual recognition learning and memory. Mice of each genotype that received no R-baclofen in their drinking water were used as controls in the experiments. Drug-treated mutant mice scored better after treatment on each cognitive task than the untreated mutant mice.

“Remarkably, R-baclofen also increased some scores on a standard assay of mouse social behaviors – male-female reciprocal social interactions — in the 16p11.2 mutant mice,” Crawley said.

Crawley, along with investigators at three other universities, is currently conducting a replication study to determine the robustness of the R-baclofen reversal of behavioral symptoms in mutant mice.

“If the preclinical mouse data prove consistently promising, our translational studies may encourage a new clinical trial with the human Arbaclofen compound in people with 16p11.2 deletion syndrome,” said Crawley.

The consortium’s research project is supported by the Simons Foundation, which leads a major research initiative focused on people with 16p11.2 deletion syndrome.
MIND Institute faculty to educate Filipino scholars in neurodevelopmental disorders

The MIND Institute will host four scholars from the Philippines thanks to a grant from the Philippine-California Advanced Research Institutes (PCARI), a government-run organization that aims to strengthen scientific, technological and institutional capabilities and promote cooperation.

The scholars will each spend at least three months at the MIND over the next two years, as part of the MIND Institute’s International Training Program in Neurodevelopmental Disorders (ITPND), created to educate scholars and providers from around the world to better address the needs of people with neurodevelopmental disorders.

Robert Miller, manager of the ITPND program at the MIND, said the collaboration will begin in late February when a MIND Institute team will travel to Manila for a conference with their Filipino colleagues. The MIND Institute team will address diagnostic techniques such as molecular DNA testing, population screening for fragile X syndrome, evaluation tools such as the Autism Diagnostic Observation Schedule, and interventions, including the Early Start Denver Model for children with autism spectrum disorder (ASD).

“In addition, a data gathering component of this project is to better understand the prevalence of ASD in the Philippines, including fragile X,” Miller said. “Our hope is to help professionals develop multidisciplinary centers for diagnosis and treatment and plant the seeds to develop research programs that will advance treatments for neurodevelopmental disorders.”

In addition to Miller, the MIND Institute team going to the Philippines includes Randi Hagerman, Flora Tassone, Melissa Mello, Aubyn Stahmer, Sarah Dufek and Hazel Maridith Barlahan Biag.

MIND scientist creates startup

Tony Simon, MIND Institute faculty member and professor of psychiatry and behavioral sciences, is developing video games that act as “digital medicine” to treat children with cognitive impairments, as well as people with cognitive limitations resulting from brain injury or aging. He created Cognivive, a company built on research, funded in part by donors, by Simon and others, showing that playing action video games can enhance players’ spatiotemporal cognitive abilities. Cognivive is one of 22 startups selected by the Association of Public and Land-grant Universities and the Association of American Universities for an Innovation and Entrepreneurship Showcase in Washington, D.C., in November 2017. The company was also recently awarded a Small Business Innovation Research grant from the National Institute of Aging, part of the National Institutes of Health, for feasibility studies.
UC Davis MIND Institute researchers have shown in a mouse model that an elevated maternal immune response changes the epigenetic landscape in offspring’s microglia, immune cells found in the brain and spinal cord. These changes affect genes associated with immune signaling and neural development, some of which have been implicated in autism spectrum disorder (ASD). The study was published in the journal *Glia*.

“The genes we identified that had differences in methylation and changes in expression showed an overlap or enrichment for genes that had been identified as genetic risk factors for autism, as well as genes that were differentially expressed in autism human brain samples,” said Annie Vogel Ciernia, Autism Research Training Program (ARTP) fellow, senior postdoctoral researcher in the LaSalle lab at UC Davis and first author on the paper.

Epidemiological studies have shown that women who experience asthma, infections and other immune reactions during pregnancy have children who are at higher risk for ASD. However, the science has been murky on how these maternal immune responses translate into neurodevelopmental disorders.

“We wanted to identify some of the mechanisms underlying the epidemiology findings that maternal allergic asthma increases the risk of having a child with ASD,” Vogel Ciernia said.

Epigenetic processes, such as methylation, are one possible mechanism. Epigenetic changes act as intermediaries between the mother’s environment and the child’s DNA, adjusting gene activity without actually altering the genome.

To learn more, the researchers studied a mouse model of maternal allergic asthma developed by Paul Ashwood, MIND Institute faculty member and professor in the Department of Medical Microbiology and Immunology and senior author on the paper. The model exhibits repetitive and other behaviors similar to ASD.

“You have this maternal allergic asthma event during pregnancy, and then you have these very long-lasting effects on the offspring’s behavior,” said Vogel Ciernia. “We wanted to figure out what some of these long-term effects might be driven by. We looked at immune cells in brain, which we thought might be contributing to these effects.”

The team analyzed methylation and gene expression changes in microglia and found significant variations, affecting immune signaling, inflammation and microglial development. In addition, genes associated with synaptic development also were affected. Variations in these genes are sometimes found in people who develop ASD.

“This is an environmental model, but we’re coming back to the same genes that can be genetically mutated and cause autism in rare cases,” said Janine LaSalle, professor in the Department of Medical Microbiology and Immunology, MIND Institute researcher and corresponding author. “That overlap with some of the genes was pretty striking.”

By exposing the role microglial epigenetics may play in ASD, the paper provides a potential therapeutic strategy. However, the researchers warn that these epigenetic mechanisms must be better understood before pursuing treatments.

This research was funded by grants from the National Institutes of Health, International Rett Syndrome Foundation, Autism Speaks Foundation (7567), NARSAD Foundation, The Emch Foundation and the Jane Botsford Johnson Foundation.
Upcoming events

Distinguished Lecturer Series

**MARCH 14**
Early intervention and brain plasticity in autism
PRESENTER: Geraldine Dawson, Ph.D.

**APRIL 11**
The human amygdala and social behavior
PRESENTER: Ralph Adolphs, Ph.D.

**MAY 16**
Can We Improve Treatments for ADHD?
PRESENTER: James McCracken, M.D.

**JUNE 13**
Why study the mind if genes cause autism?
PRESENTER: Francesca Happe, Ph.D.

All distinguished lectures are free in the MIND Institute auditorium and start at 4:30 p.m. and end by 6 p.m.

For details, ucdmc.ucdavis.edu/mindinstitute/events/dls/index.html.

Minds Behind the MIND

**APRIL 25**
Successful transitions for young adults with neurodevelopmental disorders
Presenters: Lauren Lindstrom, Ph.D., Steve Ruder, B.A., Marjorie Solomon, Ph.D.

**APRIL 19**
En español: Estrategias Individuales y Familiares y Apoyos Comunitarios
Como enfrentar retos de los trastornos del espectro autista y otras discapacidades del neurodesarrollo.
PRESENTER: Sergio Aguilar-Gaxiola, M.D., Ph.D.

All Minds Behind the MIND lectures are free in the MIND Institute auditorium and start at 5:30pm and end by 7pm. For details, mindinstitute.ucdavis.edu/events/mindsbehindmind.html.

Summer Institute

**AUG. 3**
A day-long conference for professionals, consumers, family, caregivers, and students to explore the latest advances and best practices in the field of neurodevelopmental research and treatment. This year’s conference will include a family participation resource fair. Location: UC Davis Conference Center. Registration required. For more information, mindinstitute.ucdavis.edu/events/si_event_index.html

Open House

**APRIL 7**
Celebrating our 20th year with tours, talks and other activities for the public
11 a.m. – 1 p.m., UC Davis MIND Institute, 2825 50th Street Sacramento

Best charitable gifts to make in 2018

With the introduction of tax reform this year, you may wonder how you can continue to be charitable. There are many ways you can make a difference at the MIND Institute while enjoying financial benefits for yourself.

Here are some smart ways to give in 2018:

- Donate appreciated stock: Gift your appreciated stocks to a nonprofit like UC Davis and eliminate capital gains tax.
- Name us as a beneficiary of retirement plan assets: These assets remain taxable when distributed to a loved one but are tax-free when given to a nonprofit.
- Give from your IRA (if age 70½ or older): Regardless of whether you itemize your taxes, this gift helps you fulfill your required minimum distribution and is not considered taxable income.
- Gifts of real estate: Many real estate markets are enjoying gains. Appreciated real estate may be subject to capital gains tax unless donated to charity or transferred to a charitable trust.

Talk with your tax professional

Please consult with your tax or financial advisors to determine the best charitable giving strategies for you.

We are grateful for your generosity. Please contact Elizabeth McBride, Director of Development, MIND Institute, at ekmcbride@ucdavis.edu or 916-703-0221 to discuss how your gift can help advance the MIND Institute’s mission.

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- Name us as a beneficiary of retirement plan assets: These assets remain taxable when distributed to a loved one but are tax-free when given to a nonprofit.
- Give from your IRA (if age 70½ or older): Regardless of whether you itemize your taxes, this gift helps you fulfill your required minimum distribution and is not considered taxable income.
- Gifts of real estate: Many real estate markets are enjoying gains. Appreciated real estate may be subject to capital gains tax unless donated to charity or transferred to a charitable trust.

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Leave a legacy and make a difference through a planned gift

Helen Zaccari of West Sacramento learned about the MIND Institute years ago when seeking information about ADHD that could help her son, who is now in his 20s.

Today, she is a donor, having included the MIND Institute in her living trust to establish the Sean Henry Research & Clinical Care Fund to support ADHD research and clinical services at the MIND Institute, and she has recently joined the institute’s National Council of Visitors.

Gayle Hutchinson of Eugene, OR cared for her father, Bill Hutchinson, as his Fragile X-associated tremor/ataxia syndrome (FXTAS) progressed and he became increasingly debilitated. Herself a FXTAS premutation carrier and research participant, Gayle wants to advance FXTAS research. So in addition to making annual gifts to the MIND Institute, she established the Bill E. Hutchinson Endowment for FXTAS Research and Family Support by including the MIND Institute in her will.

“Making this estate gift and these annual gifts is so very rewarding,” Gayle says. “I feel like I’m doing something positive to change the course of this disorder.”

Helen and Gayle are just two of the many individuals and families who share their passion for our mission and support our efforts to improve the quality of life for people living with neurodevelopmental disorders. These families make a difference by participating in research, becoming community advocates, volunteering and making charitable donations.

Planned Giving is one way to make a substantial difference, strengthening and protecting the MIND Institute today and in the future. A Planned Gift, often called a legacy or estate gift, enables people to make donations now, during their lifetime, or later. Planning an estate gift, as Helen and Gayle have done, allows the donor to accomplish more through their giving than they may have imagined possible.

Ways to make a gift

- **Give Now**
  - Outright gift or five-year pledge
  - Real estate, art, securities, cash, etc.
- **Give Later**
  - Bequest or beneficiary designation
- **Give the Asset, Keep the Income**
  - Life income gift: Gift annuity or charitable remainder trust
- **Give the Income, Keep the Asset**
  - Wealth transfer strategy: Charitable lead trust

It’s easy to make a planned gift. The MIND Institute has planned giving specialists available to assist you in determining how best to achieve your financial, family and philanthropic goals.

There are many different types of planned gifts. Some of the more common are including the charity in your will or living trust, naming the charity as the beneficiary of a retirement plan or life insurance policy, and funding a Charitable Gift Annuity or Charitable Remainder Trust.

The UC Davis Office of Planned Giving is a free resource for donors. Please contact Elizabeth McBride, Director of Development, MIND Institute, at ekmcbride@ucdavis.edu or 916-703-0221 for information about developing a philanthropic plan.

Elizabeth McBride
Director of Development
UC Davis MIND Institute
Lauren Libero, postdoctoral researcher with the MIND Institute, was recently honored with two prestigious awards: the University of California President’s Postdoctoral Fellowship (PPFP) and the UC Davis Chancellor’s Achievement Award for Diversity and Community.

Offered Libero a position in his lab working with the Autism Phenome Project – a longitudinal analysis of children diagnosed with autism spectrum disorder and age-matched typically developing children.

“This was a career-changing move that I am so grateful for,” she said. “I was thrilled to join this lab and learn techniques for collecting brain images from very young children and children with cognitive challenges.”

It’s no surprise Libero’s resume is filled with awards and other achievements – but it doesn’t stop there. Community service holds a significant place on her CV. She is a co-leader for social skills programs at the MIND Institute and created the MIND’s first-ever all-female discussion group, Women on the Spectrum. She believes outreach provides a positive and lasting impression on people who need help.

Libero also serves on the board of the Fly Brave Foundation, an organization dedicated to empowering adults with autism to obtain employment, improve their health, and develop social support networks. Through the foundation, she helped organize Autism Prom for young individuals with autism who didn’t attend their own high school proms because they didn’t have many friends or didn’t go to school in traditional settings.

The event outgrew its original space, and in 2017 the prom was hosted at the MIND Institute.

“This event gave our community an opportunity for everyone to experience real prom – with dancing, a photo booth, karaoke and food. It was a beautiful event that I am proud I was a part of,” Libero said.

What’s next for this inspiring researcher? She’s currently in the fourth of five years as a postdoctoral researcher and is looking for a faculty position. Her UC PPFP award offers a hiring incentive, which could lead to an independent research program and assistant professorship with the University of California.

“The UC Davis MIND Institute has been an amazing home to me for almost four years,” said Libero, “I feel at home working with people who truly care about our research participants and their future, like I do.”
More than 1,250 people attended the MIND Institute’s 15th annual “thank-you party” in December for the families who participate in research at the MIND. Children and their families enjoyed entertainment, crafts and games – all based on favorite children's books and their characters.

Thank you party!

National Council of Visitors welcomes new members and chair

The UC Davis MIND Institute is pleased to welcome two new members, Linette Gill and Helen Zaccari, and a new chair, Gail Heyman to the National Council of Visitors (NCOV). Each member brings a unique perspective and supports the mission to advance the research and treatment of neurodevelopmental disorders.

Linette Gill of Elk Grove, Calif., is a mother of three, realtor and special needs advocate. She and her husband, Ed, have a personal connection to the MIND Institute — their two sons were diagnosed with autism at age 3 thanks to early intervention. She is dedicated to helping the MIND Institute achieve its philanthropic goals to advance research and support services.

Helen Zaccari of Sacramento, Calif., is an associate university librarian and director of administrative services with UC Davis. Her son, Sean, was diagnosed with ADHD in the first grade. Zacarri made it her mission to collaborate with her son’s schools to improve staff and faculty understanding of ADHD. Zacarri’s experience solidified her commitment to the development of effective treatments, programs and services for those with ADHD.

After serving as a member for several years, Gail Heyman accepted a three-year term as chair of the NCOV. Heyman is a dental hygienist in Atlanta, GA, where she lives with her husband, Lyons. The Heymans have three children, Jared, Carly and Scott, who was diagnosed with fragile X syndrome. Carly was diagnosed with fragile X-primary ovarian insufficiency (FXPOI) and other members of the family have Fragile X-associated tremor/ataxia syndrome (FXTAS).

In support of their brother, Carly and Jared focused on careers that include helping others. Carly wrote a book called My eXtra Special Brother and is now a pediatric occupational therapist in Denver, CO. Jared founded CrowdMed, an online tool that connects patients with difficult-to-diagnose cases and “medical detectives” from around the world. Heyman is the president of the Fragile X Association of Georgia, which she co-founded in 1992.

“We work selflessly because we are empowered to tell the great story of the MIND and how it has helped not only our families but many others around the world,” Heyman said. “In my experience, it really does take a village and the UC Davis MIND Institute embraces that concept.”
$3.7 million grant to study youth impulsivity

Julie Schweitzer, a professor in the Department of Psychiatry and Behavioral Sciences and MIND Institute researcher, has received a $3.7 million grant from the National Institute of Mental Health (NIMH) to track impulsivity and self-control in teens and young adults over time.

The grant, “Developmental Changes in Neural Processes Underlying Inattention, Impulsivity and Regulation,” represents a five-year renewal and expansion of a prior NIMH grant that is tracking teens and young adults as their brains develop and behavior and function change in an effort to find more precise interventions to prevent or improve functioning.

“We are looking at how impulsivity changes with development, particularly during adolescence and young adulthood, because that’s the time of life most associated with risk taking and impulsive behavior that can have long-term negative consequences,” said Schweitzer, who directs the MIND Institute’s Attention, Impulsivity and Regulation Program. “These years are also recognized as a period of exploration and opportunity with long-term benefits for some teens.”

Impulsive behavior is associated with substance-use disorders, self-harm or suicide attempts, poor physical health, high accident rates and poor performance in school. The project also will assess how one’s irritability and ability to regulate emotions further impacts functioning. Children with ADHD are especially at risk for poor outcomes due to impulsive decision-making.

The new research project will include about 200 young people who were part of the initial study and an additional 50 participants. The study will include people aged 12 to 30 diagnosed with ADHD and others with elevated impulsivity, as well as those with neither. Each study participant will get a thorough clinical evaluation and two MRI brain scans a couple of years apart, as well as complete a self-assessment. Parents of all participants will complete questionnaires about their child’s functioning as a teenager and young adult, as well.

In addition to impulsivity (such as texting while driving, drug use and risky sexual activity) and ability to exercise self-control, participants will be evaluated on their academic, occupational, executive, emotional and psychiatric functioning.

“We want to identify on a neural and behavioral basis those people who are likely to do well and have resiliency and those who are at risk for worse outcomes so that we can develop interventions specific to their challenges,” Schweitzer said.

For example, researchers will use functional MRI and other techniques including diffusion tensor imaging to identify potential problems with connectivity between brain regions to help inform future research to determine what specific intervention for a certain type of impulsivity might work, such as cognitive therapy, meditation, medication or even neuro-stimulation, to prevent a poor outcome for a specific adolescent or young adult.
"If anxiety can be identified and effectively treated, the quality of life of those affected will be enhanced, and this may enable behavioral therapies to better address other symptoms of autism," Solomon said. "The neuroimaging component of the study also may help reveal the neural mechanisms of anxiety and allow us to select psychosocial and medications treatments tailored for affected individuals."

An enlarged brain, also called megalencephaly, is found in approximately 15 percent of boys with ASD, but is less common in girls. Early research data indicate that boys with ASD who have megalencephaly are less verbal at age 3 and make fewer gains in their IQ by age 5. The study aims to determine which cognitive processes and brain systems are most affected children with ASD and megalencephaly.

"These are children who get just as much behavioral therapy as other children with autism but in general don’t seem to benefit as much,” said Christine Wu Nordahl, MIND Institute researcher and associate professor in the Department of Psychiatry and Behavioral Sciences who will spearhead this project. “Our goal is to find new targets for treatment to help these children.”

In addition, collaborators at Stanford University will produce induced pluripotent stem cells (iPSCs) from a subset of the children evaluated in the megalencephaly study. These iPSCs will then be reprogrammed to produce neurons, the primary cell types of the brain, and glial cells, a secondary cell type that has supportive functions such as immune response. The investigators will then study whether these brain cells have alterations of genetic pathways or control mechanisms that may lead to the enlarged brain. Analysis of these cells may provide additional insights into potential treatment targets.

The study will include approximately 390 families already participating in the MIND Institute’s Autism Phenome Project, and plan to recruit an additional 80 young children with ASD, as well as children with both autism and enlarged brains, along with typically developing children who will serve as controls. By the end of five years, the study group will comprise 700 families — the largest such cohort in the world.

Other UC Davis investigators include Susan Rivera, David Hessl, Breanna Winder-Patel, Robin Hansen, Len Abebduto, Clifford Saron and Gregory Young.