MIND Institute researcher Sally Rogers among clinicians charged with revising autism criteria

Sally J. Rogers, professor of psychiatry and behavioral sciences and internationally renowned researcher with the UC Davis MIND Institute, is one of 13 members of the Neurodevelopmental Disorders Work Group of the American Psychiatric Association, charged with developing proposed revisions to the Diagnostic and Statistical Manual V (DSM-5). The committee proposes that the next edition of the DSM-5 make some changes regarding diagnosis of autism from the current manual, the Diagnostic and Statistical Manual IV (DSM-IV).

In DSM-5 the overall umbrella term is changed from “pervasive developmental disorder” to “autism spectrum disorder.” It also recommends that various aspects of the disorder, such as intellectual disability, symptom severity, and presence of co-occurring biological conditions be described as specifiers rather than as separate diagnoses that were previously captured by the use of a variety of diagnoses.

Continued on page 4

Groundbreaking research

Internationally renowned neuroscientist joins the MIND Institute

Jacqueline N. Crawley, one of the world’s foremost researchers in behavioral neuroscience and a leading investigator using mouse models to develop novel, targeted treatments for individuals with autism spectrum disorder, recently joined the faculty of the UC Davis School of Medicine and UC Davis MIND Institute as the Robert E. Chason Chair in Translational Research.

MIND Institute researchers show new medication for fragile X is effective

A study by MIND Institute Medical Director Randi Hagerman and colleagues around the country has found that an investigational drug is effective for addressing the social withdrawal and challenging behaviors characteristic of the fragile X syndrome, making it the first such discovery for fragile X syndrome and, potentially, the first for autism spectrum disorder. The study was published in September in the journal Science Translational Medicine.

Continued on page 5
Bauman receives coveted NARSAD Young Investigator Grant

MIND Institute research Melissa Bauman has received one of the most prestigious mental-health grants in the world to investigate one of the least understood and devastating psychiatric disorders: schizophrenia.

Bauman is one of only 200 researchers worldwide selected from more than 1,000 applicants for the NARSAD Young Investigator Grants. The grants are distributed by the Brain & Behavior Research Foundation, formerly known as the National Alliance for Research on Schizophrenia and Depression (NARSAD), the world’s leading private philanthropy devoted to funding research on psychiatric disorders.

“This is a well-deserved honor,” said MIND Institute Director Leonard Abbeduto. “Dr. Bauman uses multiple model systems and methodologies to understand the ways in which the trajectory of brain development can be altered by genetic and environmental risk factors. She is emerging as a leader in our field.”

Also an assistant adjunct professor in the Department of Psychiatry and Behavioral Sciences, Bauman is examining prenatal risk factors for schizophrenia, particularly how the mother’s immune system may impact fetal brain development. She will use an animal model to compare human and animal neuropathology as a potential pathway to identifying preventive or therapeutic strategies.

Bauman’s research is examining an emerging hypothesis in schizophrenia: that it is actually a neurodevelopmental disorder with origins in fetal development.

“It’s a great honor to receive a NARSAD Young Investigator Award,” Bauman said. “I think this is really an important area of research, and the support that’s available through the young investigator program will allow us to make some important steps toward identifying prenatal risk factors for schizophrenia and other neurodevelopmental disorders,” she said.

Schizophrenia is a chronic, severe and disabling brain disorder affecting about 1 percent of Americans today, according to the National Institutes of Mental Health. People with schizophrenia may hear voices other people don’t hear, believe that people are reading their minds, controlling their thoughts, or plotting to harm them. People with schizophrenia are at high risk for suicide. Approximately one-third will attempt it and 1 in 10 eventually will take their lives.

The NARSAD Young Investigator Grants support early career investigators with grants of $60,000 over two years to pursue brain and behavior research in four main categories: basic research, new technologies, diagnostic tools/early intervention and next-generation therapies. The grants are among the most competitive in biomedical research, because of the great ability and career success of the applicants.
## 2012-2013 Distinguished Lecturer Series

Now in its eleventh season, the MIND Institute’s Distinguished Lecturer Series annually features nine presentations, October through June, by internationally recognized scientists known for their contributions to the understanding and treatment of neurodevelopmental disorders.

4:30 – 6 p.m.  
MIND Institute Auditorium  
2825 50th Street  
Sacramento, CA 95817

For additional information, including directions and videos of prior presentations, please visit our Web site mindinstitute.ucdavis.edu or call 916-703-0280

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### Minds Behind the MIND

#### Understanding Down Syndrome Program

Recent estimates place the prevalence of Down syndrome at 1 in 691 births, making it the leading known genetic cause of intellectual disability. The January Minds Behind the MIND presentation will provide an update on what is known about Down syndrome, its impact on the individual and their family, and possible treatments.

The discussion will be held from 5:30 p.m. to 7 p.m. on Wednesday, Jan. 16, and panelists will include Leonard Abbeduto, director of the MIND Institute, and Heather Green, president, the Down Syndrome Information Alliance. The program will be moderated by Robin Hansen, director of MIND Institute Clinical Programs and the Center for Excellence in Developmental Disabilities.

Research information focused on Down syndrome will be available prior to the presentation from 4:30 p.m. to 5:30 p.m. Attendees will have the opportunity to learn more about research studies specific to the evening’s subject. There also will be an extended “ask the experts” session with the panelists.
Sally Rogers from page 1

included in prior versions of the Diagnostic and Statistical Manual, including the diagnoses ‘autistic disorder,’ ‘pervasive developmental disorder not otherwise specified (PDD-NOS),’ ‘Asperger’s disorder’ ‘Rett Disorder,’ and ‘childhood disintegrative disorder,’ and that the former disorders be removed or collapsed into fewer categories.

The Diagnostic and Statistical Manual is the guide that psychiatrists use to diagnose all psychiatric conditions, including neurodevelopmental disorders. The rationale for the proposed changes is in part that because autism spectrum disorder is defined by a common set of behaviors, it is best represented as a single diagnostic category that is adapted to the individual’s clinical presentation by inclusion of clinical specifiers (e.g., severity, verbal abilities and others) and associated features (e.g., known genetic disorders, epilepsy, intellectual disability and others). Consolidating the various umbrella diagnoses of DSM-IV into a single spectrum disorder in DSM-5 was considered by the committee to better reflect of the state of knowledge about pathology and clinical presentation.

If approved, the proposed criteria for diagnosing the condition ‘autism spectrum disorder’ will include three levels of severity for the condition. Each level will include descriptions of the extent to which persons of various ages have deficits in social communication and restricted interests and repetitive behaviors, the core features of autism spectrum disorder.

These revisions are not final; however, the American Psychiatric Association closed comment on proposed revisions to all sections of the DSM-5 in June. The DSM-5 is slated for publication in May of 2013.

Jacqueline N. Crawley from page 1

Crawley came to UC Davis from the National Institute of Mental Health (NIMH) Intramural Research Program, where she led a large behavioral neuroscience laboratory. She is the recipient of numerous national and international awards and honors. She said she chose to join the faculty of the MIND Institute because of the opportunity to work with other outstanding researchers.

“The MIND Institute is internationally famous for its groundbreaking clinical research into early diagnosis and behavioral interventions for very young children with autism, basic science research into the biological causes of autism, and clinical trials of novel therapeutics for autism and fragile X syndrome,” Crawley said. “I look forward to many productive collaborations with clinical experts at the MIND Institute. Opportunities at the MIND Institute to observe the specific and diverse features of autism and other neurodevelopmental disorders will enhance our development of the most analogous mouse behavioral assays. In addition, I anticipate synergistic interactions with MIND Institute investigators pursuing clinical trials with pharmacological interventions.”

Crawley currently is engaged in translational research that uses mice genetically engineered to have mutations associated with autism spectrum disorder. Her laboratory at the NIMH developed mouse-behavioral assays that mirror the diagnostic symptoms of autism in humans. These behavioral measures are employed to test investigational medications for reversal of social abnormalities, communication deficits, repetitive behaviors and motor stereotypies in the mouse models that are relevant to the core features of autism.

“\textit{I anticipate synergistic interactions with MIND Institute investigators...}”

– Jacqueline N. Crawley

Continued on page 5
**Crawley from page 4**

Breakthrough research by Crawley and her colleagues published recently in the journal *Science Translational Medicine* found that an investigational compound reversed behaviors in two mouse models with behavioral traits that resemble two of the three core symptoms of autism spectrum disorder. The drug successfully increased social interactions and decreased repetitive behaviors in the mouse models.

The study by Crawley and her colleagues suggested that a single compound could effectively target multiple diagnostic symptoms in human subjects with autism.

“Dr. Crawley is one of the leading neuroscientists studying autism, and we are incredibly proud that she has chosen to join the faculty of the UC Davis MIND Institute,” said Leonard Abbeduto, director of the MIND Institute. “She has created behavioral assays for documenting social impairment in mouse models of human disorders that are being used in laboratories around the world.”

“Her research provides the critical link between researchers working to discover the causes of autism and those working to develop biomedical treatments,” Abbeduto continued. “We fully expect that Dr. Crawley will help to accelerate the pace of translating the findings of MIND Institute scientists into efficacious treatments for the core symptoms of autism and related neurodevelopmental disorders.”

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**Randi Hagerman from page 1**

“This study shows that STX 209 could become an important part of the treatment for fragile X syndrome, because it appeared to improve symptoms in those with significant social deficits or autism as well as fragile X syndrome,” Hagerman said. “Additional studies also are suggesting that STX 209 could be helpful for autism without fragile X syndrome. Until now, there have been no targeted treatments available for autism. This appears to be the first.”

Fragile X syndrome is the most common, known cause of inherited intellectual disability, formerly referred to as mental retardation, and the leading known single-gene cause of autism. Social impairment is one of the core deficits in both fragile X and autism. The U.S. Centers for Disease Control and Prevention (CDC) estimates that about 1 in 4,000 males and 1 in 6,000 to 8,000 females have fragile X syndrome. An estimated 1 in 88 children born today will be diagnosed with autism, according to the CDC.

The medication trial included patients from 6 to 39 years of age who participated in two six-week-long treatments. The effects of the medication were scored on variables of the Aberrant Behavior Checklist (ABC), a behavior-rating scale for the assessment of drug-treatment effects. The checklist includes variables for irritability, lethargy/withdrawal, stereotypic (repetitive) behavior and hyperactivity, among other factors.

The study found improvement for the full study population on the social-avoidance subscale, an analysis validated by secondary ratings from parent observation of improvement in subjects’ three most problematic behaviors. It found that the medication was the same as placebo, however, on the subscale for irritability.

“We are looking forward to further studies utilizing STX 209 in both autism and fragile X syndrome because the fragile X mouse studies demonstrate long-term strengthening of synaptic connections with continued use of this medication,” Hagerman said.

The study is one of several at the MIND Institute aiming to help improve behavior and cognition for individuals with fragile X syndrome or autism spectrum disorder. Hagerman currently is leading larger controlled trials of STX 209 at UC Davis that also are being carried out at multiple centers and are enrolling individuals with fragile X syndrome from ages 5 to 50. Individuals interested in enrolling may contact Lindsey Partington at 916-703-0471 or via e-mail at lindsey.partington@ucdmc.ucdavis.edu. Details of the study also can be found at ClinicalTrials.gov, an online resource for people interested in learning more about advanced clinical studies in a variety of different therapeutic areas.

“Fragile X syndrome is the most common, known cause of inherited intellectual disability...”

– Randi Hagerman
Eric Everson, a Pleasanton, Calif., philanthropist, businessman and the father of two sons with autism spectrum disorders, in July was named the new chair of the MIND Institute Advisory Council.

“Being selected as the chair of the MIND Advisory Council is an honor,” Everson said. “I have an intense passion to help the kids and their families currently affected, as well as stopping the epidemic of these disorders.”

I have two main goals as the chair,” Everson continued. “The first will be to help increase the visibility of the MIND. The second will be to help increase donations and grants to the MIND, so that their experts will find a cause and a cure for an array of neurodevelopmental disorders as soon as possible.”

Everson and his wife Cindy have donated more than $1 million to various recipients with the majority going to the MIND Institute through a non-profit organization they founded, PAR (Providing Autism Research) 4 Kid’s Sake. PAR 4 Kid’s Sake also has supported the Exceptional Needs Network, School of Imagination, cash grants to special education teachers in the San Francisco Bay area and camps for special needs kids. In 2008, when Everson joined the council, the Eversons and PAR 4 Kid’s Sake were recognized for their philanthropic activities by the U.S. Congress.

Everson has also been involved with the not-for-profit Happy Talkers Autism Screening Events. The free, public events provide concerned families with the first steps toward obtaining answers about their children’s development through free developmental screenings.

Everson is a co-founder of Matchpoint Solutions, a technology and business consulting company with operations in the United States, India and the United Kingdom. He currently manages the profit and loss and oversees business development, sales, marketing, legal and employee development of Matchpoint Solutions.
Higher anxiety is associated with poorer functioning in children with chromosome 22q11.2 deletion syndrome

Targeted interventions may improve future outcomes in this developmental disorder

UC Davis researchers have found that for children with the genetic disorder known as chromosome 22q11.2 deletion syndrome, anxiety—but not intelligence—is linked to poorer adaptive behaviors, such as self-care and communication skills, that affect daily life. The developmental syndrome, which is associated with a constellation of physical, cognitive and psychiatric problems, usually is apparent at birth or early childhood, and leads to lifelong challenges.

The study findings suggest that helping children cope with fear-based symptoms may be the best strategy for increasing independence and protecting against psychiatric problems later in life. The article, titled, “An examination of the relationship of anxiety and intelligence to adaptive functioning in children with chromosome 22q11.2 deletion syndrome,” is published in the Journal of Developmental and Behavioral Pediatrics.

“Our study confirmed our impressions from seeing patients with 22q11.2 deletion syndrome that those with more severe anxiety symptoms tend to be most impaired in their everyday functioning,” said Kathleen Angkustsiri, lead study author and assistant professor of developmental-behavioral pediatrics with the UC Davis MIND Institute. “It highlights the critical importance of recognizing and treating anxiety in these very vulnerable children.”

The disorder also is known as velocardiofacial syndrome as well as DiGeorge syndrome. The currently preferred name of chromosome 22q11.2 deletion syndrome identifies the location on the twenty-second chromosome where a small piece of DNA is missing. The syndrome is estimated to affect about 1 in 2,000-4,000 people, making it the second most common genetic condition after Down syndrome, another genetically based developmental disorder.

Children with 22q11.2 deletion syndrome have a high prevalence of mental-health disorders such as anxiety and attention deficit hyperactivity disorder (ADHD), and IQs usually are in the borderline-to-low range. In early adulthood, about 30 percent may develop a psychiatric disorder such as schizophrenia.

The study evaluated 78 children with the syndrome, ages seven to 15 years, with a battery of standardized tests related to behavior, anxiety, adaptive functioning and intelligence. Thirty-six typically developing children with no known genetic syndromes were also evaluated for comparison.

Mean anxiety scores were found to be significantly higher in children with 22q11.2 deletion syndrome than in typically developing children. Fifty-eight percent of children with the syndrome were found to have at least one elevated anxiety score compared to 14 percent in typically developing children. Only 19 percent of children with 22q11.2DS had previously been diagnosed with an anxiety disorder. In addition, higher anxiety scores correlated with lower adaptive function among children with the syndrome.

“The good news is that we have many effective interventions to treat anxiety, such as medications and counseling, while cognitive impairments are not as amenable to treatment,” said Angkustsiri. “We are hopeful that targeting anxiety can make a difference for children with this disorder, as well as in other vulnerable children.”
From the Director

In the year that I have been director of the UC Davis MIND Institute, I have felt increasingly proud to be part of the phenomenal work of this amazing organization, as our investigators’ pioneering inquiries push the boundaries of research on autism and other neurodevelopmental disorders. Notably, the translational studies of internationally respected researcher and MIND Institute medical director Randi Hagerman are making meaningful, tangible differences in the lives of people with fragile X syndrome, helping them grow and develop in ways that, decades ago, were not considered possible. Her clinical research into new, investigational compounds also offers hope for some children with autism, who one day also may be helped by the drugs she is testing. And MIND Institute researcher and Professor of Psychiatry and Behavioral Sciences Sally Rogers’ ongoing scientific leadership is evidenced by her participation in the rewriting of the definition of autism that will be used by clinicians and diagnosticians for decades to come in the DSM-5. Their accomplishments, and those of other MIND Institute faculty, are described in this new issue of a revitalized MIND Matters. The newsletter also introduces the appointment of Professor of Psychiatry and Behavioral Sciences Jacqueline Crawley, formerly of the National Institute of Health, to our team of neuroscience leaders. I am also pleased to welcome Eric Everson, a philanthropist and tireless advocate for people with autism, to the role of MIND Institute Advisory Committee chair. As we move into the coming year, I look forward with anticipation to working with MIND Institute faculty and staff, the advisory committee and particularly our patients, research study participants and their families, who are the inspiration for everything we do as we continue to advance the understanding and treatment of neurodevelopmental science.

Leonard Abbeduto, Ph.D., a nationally recognized researcher and a leader in improving the lives of children and adults with neurodevelopmental disabilities

– Leonard Abbeduto, Ph.D., Director
UC Davis MIND Institute