

M.I.N.D. Matters



SPRING 2007

Post-doctoral trainees forge new directions in autism research

The M.I.N.D. Institute is committed to ensuring that autism science continuously benefits from new thinking, new approaches, new perspectives and the insights that come from interdisciplinary studies. This is why the Autism Research Training Program (ARTP) was launched two years ago. A select group of six postdoctoral researchers is currently participating in the program, funded by a \$1.5 million grant from the National Institute of Mental Health and with the goal of creating a new wave of talented experts in autism research.

“It’s not enough for a researcher to simply have laboratory expertise or clinical experiences in working with autism,” said Sally Rogers, professor of psychiatry and behavioral sciences and the program’s director. “Finding

a cause, a new treatment or a cure demands integration of a variety of vantage points – from the molecular to the behavioral. Our goal is to make sure that the next generation of autism scientists is fully prepared to work with scientists from a range of disciplines.”

Through the program,

up-and-coming scientists with backgrounds in diverse aspects of the behavioral or biological sciences develop specialized knowledge in particular areas of autism, while also growing comfortable and knowledgeable in other areas – genetics, epidemiology, child development, clinical diagnosis and neuroanatomy. Faculty from different disciplines are paired with the students during the course of a two-year training period that involves a specific research project, weekly classes and continuous interaction with mentors who are recognized leaders in the field.

All trainees are expected to make strong contributions to the field of autism science. In this article, we introduce you to three of these rising stars.

“Thanks to this program, I will be well prepared to do the work that really needs to be done.”

– ARTP trainee Jane Weru



Susan Swanberg (right) and Janine LaSalle discuss progress on research related to hindbrain development in autism.

Bridging scientific fields

Susan Swanberg’s research into the genetic roots of autism illustrates well the complexity of the disorder – and why it is necessary in autism science to understand genetics.

Swanberg explains that what emerges in a child with autism – characterized by poor verbal and communication skills, repetitive behaviors and an inability to form social connections – is likely the end result of a variety of different events, depending on the child.

“There may be up to 20 genes involved in autism spectrum disorders, with many different combinations of an unknown number of these 20 genes involved in each person,” she said.

Swanberg’s background includes research on cellular

(continued page 2)

Inside

IMFAR and the future generation of autism scientists	3
How probing mind and brain builds understanding of a genetic disorder	4
A lifelong fascination with the developing mind.....	5
New community lecture series	6
Meet the “Lucy and Ethel” duo propelling the annual gala.....	6
Executive director’s message	8

Autism research *(from page 1)*

aging in animals. Her research now focuses on where she thinks some of the answers to autism are – the cerebellum, pons and medulla oblongata, which are parts of the hindbrain.

“There is evidence that the serotonergic neuronal network may be dysfunctional in at least a subset of autism cases,” Swanberg said. She hypothesizes that, since this network develops from neurons in the hindbrain, it is possible that something may go awry very early in development that causes defects in serotonin production or regulation.

As part of the ARTP, Swanberg developed a project in which she will explore expression of the MeCP2 gene in the brains of children with autism. This gene is involved in defects in cortical function and in Rett syndrome, the only autism spectrum disorder with a known genetic cause. Swanberg is considering the role of MeCP2 in other forms of autism and other parts of the brain. “I want to know if it is more broadly implicated in autism and specifically in hindbrain dysgenesis,” she said.

For Swanberg, the ARTP has initiated a career shift. “The program has helped accomplish my goal of becoming a human geneticist,” she said.

“Susan is a great example of how a Ph.D. trained in another scientific field can make the transition to autism research through this program,” said Janine LaSalle, an associate professor of medical microbiology and immunology and Swanberg’s primary mentor. “She is already getting very promising results.”

Making MRIs fun

ARTP trainee Christine Nordahl is particularly interested in linking behavior with specific brain structures

and functions. Doing so starts with an important tool – MRI, or magnetic resonance imaging, which creates a series of detailed three-dimensional images of the brain.

MRIs are safe and non-invasive, however getting a young child through the process can be tough. Little ones tend to be antsy and parents prefer not to sedate their children for the process. As a result, most MRI-based autism research has been carried out in older individuals.

“The MRI machine is large and can be daunting. The imaging process is loud. And children have to lie still for a long time,” Nordahl said. “It can be very difficult for any 2-to-4 year old.”

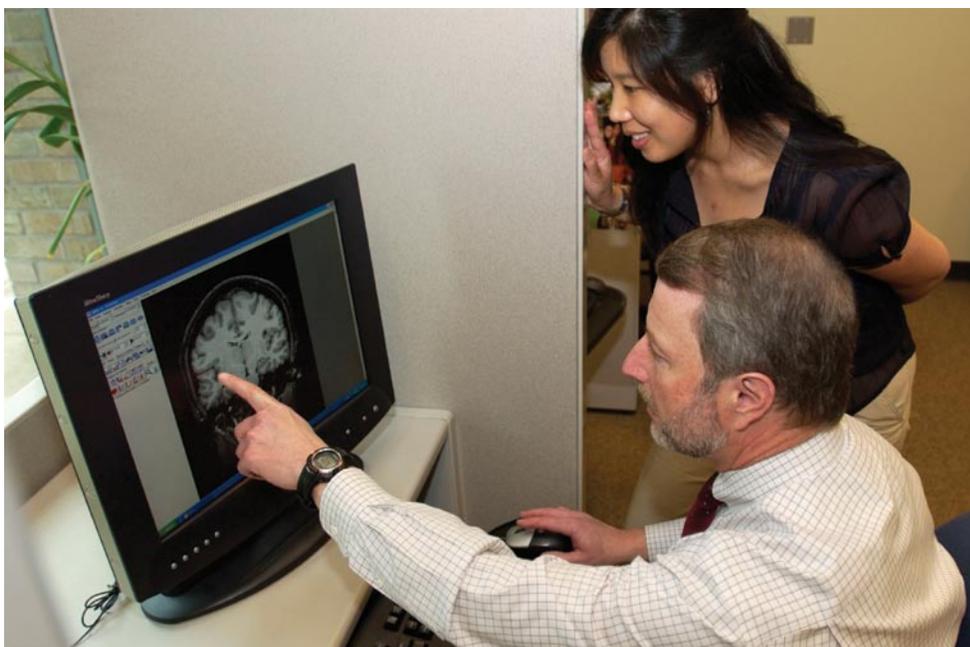
Nordahl has implemented a unique program to ease children into the MRI machine and help them relax while images are being taken. She starts two weeks in advance by talking with parents on the phone, giving them guidance on how to prepare their child. The family also attends a mock MRI session, which is

presented as semi-structured play. The child first watches a researcher or parent “ride” the MRI bed into the “tunnel” and talk about how much fun it is. Pretty soon, the child is asking to do it too.

The actual MRI session, which takes one-to-two hours, is typically done in the evening, when the child is tired and more likely to sleep. The external surroundings of the machine are disguised with child-friendly wall hangings and screens. The MRI bed is widened so that a parent can lie down with the child to help him or her fall asleep.

“It’s amazing what these kids and parents are able to do. The process is not always easy, but it’s an extremely important step in building a complete picture of autism,” she said.

Nordahl will use MRI results to assess how the brains of young children with autism differ from the brains of typically developing children in terms of volume and growth patterns. Different from other



Christine Nordahl tracks changes in brain structure in children with autism. Here, she discusses MRI outcomes with David Amaral.

IMFAR and the future generation of autism scientists

The annual International Meeting for Autism Research (IMFAR), which began in 2002 with just over 200 participants, now attracts an international audience of more than 800 scientists, educators, advocacy groups, parents and others interested in promising avenues in autism research.

The M.I.N.D. Institute helped launch the first meeting and the influence of its researchers in presentations and poster sessions has been strong ever since. Even relative newcomers to the field, like the ARTP postdoctoral trainees, are poised to make significant contributions.

“The quality of their work and their thinking makes me really excited about the future and the speed of our ability to understand the causes of autism,” said Robert Hendren, executive director of the M.I.N.D. Institute.

One of those newcomers, Tracy DeBoer, an ARTP trainee in the Cognitive Analysis and Brain Imaging Laboratory, appreciates the cross-disciplinary perspective of the conference. “It is easy to be overwhelmed by the complexity of multiple disciplines coming together at one scientific conference. But IMFAR bridges the gaps between the different fields and shows you how all of the pieces fit together,” she said, referencing educational symposia on early detection, genetics, neuroimaging, epidemiology and psychopharmacology.

Seasoned and newer autism researchers will again share their findings at IMFAR 2007, which is May 3-5 in Seattle. They welcome you to join them. The program and registration details are online at www.cevs.ucdavis.edu/imfar.



Jane Weru explores how cultural influences can affect outcomes for children with autism.

studies, she plans to track MRI results on the same children over time.

“It will be really exciting to see how brain growth changes at different points in development,” she said. “I’m helping to answer two of the biggest questions in neuroscience today – where is autism in the brain and when in a child’s life do those changes occur?”

“Structural MRI studies provide important information about the neuropathology of autism,” said David Amaral, research director of the M.I.N.D. Institute, ARTP co-director and Nordahl’s primary mentor. “There is a strong need to evaluate brain structure in very young children with autism, closer to the time of clinical diagnosis and before intensive interventions begin. It’s a significant achievement that Christine has managed to get these kids to a place where we can do this MRI research comfortably and safely.”

Adding a cultural perspective

ARTP trainee Jane Weru is taking yet another approach to autism. She has launched a cross-cultural study comparing the beliefs of African-Americans and Caucasian-Americans about the disorder.

Weru is from Kenya and has first-hand experience with such cross-cultural issues. What led her to study autism was an experience she had in Kenya with a friend’s brother. When she would visit, the brother would hide behind the house and refuse to look at her or to say hello. Later, when earning college degrees in psychology and special education in the United States, Weru recalled that boy. “I remembered everything that boy was doing, and in my mind I diagnosed him as having autism.”

Unfortunately, in Kenya there are no services for children with autism, so the boy never received treatment. “He is about 21 now and his symptoms have not improved,” she said.

As a result, Weru came to the ARTP with a clear goal: “I want to know the cultural factors that can delay diagnosis and intervention.”

For her project, Weru is recruiting African-American and Caucasian-American children ages 5-to-14 years who either have autism or no developmental concerns. Through assessments and parent questionnaires, she will determine if there are cultural differences in beliefs about autism, its symptoms and its causes and how those beliefs affect seeking help for children. Ideally, her work will provide the foundation for culturally appropriate diagnostic tools and programs.

“Jane’s project is important because it explores the influence of culture on the phenotypic expression of autism spectrum disorders, on how people understand autism spectrum disorders, and on the extent to which families access services and cope with the disorder,” said Weru’s primary mentor John Brown, a psychologist and coordinator of outreach and training at the M.I.N.D. Institute.

Weru will eventually study developmental disabilities in developing countries, filling a critical gap in current research. “Thanks to this program, I will be well prepared to do the work that really needs to be done,” she said.

How probing mind and brain builds understanding of a genetic disorder

The genetic disorder known as chromosome 22q11.2 deletion affects an estimated 1 in 4,000 children born in the United States per year. That's more than those born with sickle cell anemia or hemophilia. Although relatively common, scientists do not understand what causes the range of physical and cognitive defects seen in children with 22q11.2 deletion syndrome.

"Right now, we've got a fairly complete description of the syndrome," explained Tony Simon, who directs the Cognitive Analysis and Brain Imaging Laboratory at the UC Davis M.I.N.D. Institute. Simon, a developmental cognitive neuroscientist, is among the few scientists worldwide studying cognitive implications of the syndrome. He is one of even fewer taking an approach that combines the results of experimental tests with those of brain imaging to better understand the neural structures and connective patterns that underlie cognitive functions.

"What we don't have is an explanation for what causes the cognitive dysfunctions, particularly the learning disabilities associated with the deletion," he added.

Simon explained that a basic neurocognitive understanding of chromosome 22q11.2 deletion syndrome is crucial to developing effective treatments or even cures for the learning difficulties and behavioral problems associated with the deletion.

Before arriving at UC Davis two years ago, Simon had been largely responsible for the view that mathematical and similar types of thinking are constructed from specific attention skills, visuospatial capacity and the representation of objects – all of which are usually developed in early childhood. This led to his interest in chromosome 22q11.2 deletion. The



Tony Simon is one of just a few scientists worldwide studying 22q11.2 deletion syndrome, which is linked to more than 180 behavioral, psychological and physical disorders.

syndrome limits the effectiveness of these competencies in young minds.

Simon has hypothesized that children with this syndrome have what he calls a reduced granularity of mental representa-

"This work is about the hardware of the brain and how it develops in relation to the software of the mind."

– cognitive neuroscientist Tony Simon

tion. "It's not about visual perception," he said. "It's like the low resolution of an inexpensive digital camera. There are fewer pixels, so the picture is not as sharp."

Simon adds that thinking about space, time or quantity requires that humans divide these continuous values into smaller bits – inches, minutes or integers. "The pieces that children with 22q have

are fewer and larger; they get a coarser representation of the world," he said.

Chromosome 22q11.2 deletion occurs when a small segment of the long arm of chromosome 22 is lost during prenatal development. The deletion is linked to over 180 physical, psychological and behavioral anomalies and causes some degree of developmental delay and learning difficulties in all children who have it. Also called velocardiofacial syndrome or DiGeorge syndrome, the deletion can also result in congenital heart defects, cleft palate or other velopharyngeal insufficiencies. Some children may also experience immune deficiencies or neonatal hypocalcemia, a condition that affects the nervous system and has been associated with higher mortality in infants requiring treatment in neonatal intensive care units.

Children with chromosome 22q11.2 deletion syndrome also have increased risks for attention deficit hyperactivity disorder, autism spectrum disorders, oppositional defiant disorder, obsessive-compulsive disorder and, in adulthood, schizophrenia.

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In recent years, physicians have increased their ability to repair congenital heart defects in newborn infants and even in unborn fetuses. “This means more children with chromosome 22q11.2 deletion are surviving to adulthood and facing a range of developmental challenges,” Simon explained. That fact alone gives Simon’s work a sense of urgency. “This is a very important time to be doing this work.”

Since arriving at the M.I.N.D. Institute in 2005, Simon has focused on building a cohort of children and their families who can take part in on-going studies being funded by two National Institutes of Health grants. Along with the genetics team at Elwyn, a nonprofit corporation that provides programs for children and adults with disabilities and disadvantages, the M.I.N.D. Institute co-hosted a two-day conference for families and interested professionals in March. More than 100 families attended and learned practical implications for behavior and learning.

Parents who visit the M.I.N.D. Institute say they appreciate the dedication and expertise Simon’s team offers their children. They often share their gratitude directly with Simon, but also recommend taking part in the studies to other parents through online discussion groups dedicated to children with the syndrome.

Simon and his team have been perfecting the assessment tools and research protocols used to evaluate children. While they do use standardized psychological tests, the lab’s real focus is on the use of specially designed computer games to assess cognitive function.

Brain imaging is also crucial to describing the neuro-biological ramifications of chromosome 22q11.2 deletion. “This work is about the

hardware of the brain and how it develops in relation to the software of the mind,” said Simon.

The team has also developed a comprehensive desensitizing protocol that prepares children for what would otherwise be a challenging MRI session by using a series of “spaceship training” experiences that make the actual scanning procedure seem like a fun and exciting adventure. Without this approach, Simon said, it would be impossible to produce the detailed images of the neural

structures and functions of the brains of children with genetic syndromes such as chromosome 22q11.2 deletion that are so important to his research.

Simon’s work promises to inform the field of neurodevelopmental disorders. “There are many neurodevelopmental disorders, some with no known genetic basis, that have a subset of common symptoms. Neuropsychological tests have identified these similarities, but they don’t tell us why children experience them,” he said.

A lifelong fascination with the developing mind

Many a zoologist has admitted to discovering a passion for science as a child slogging through swamps or creeks, hunting frogs or catching fish. Tony Simon has a similar story of discovering his future career. “I remember looking at babies when I was just a kid and wondering what they were thinking and how they managed to think at all,” said Simon, now a developmental cognitive neuroscientist at the UC Davis M.I.N.D. Institute.

But, Simon did more than just ponder developmental psychology as a kid. A native of England, he took advantage of his country’s free higher-education innovations of the 1960s. “The Open University televised lectures and sent course material through the mail. It was the first ever distance learning university,” he recalled. And, he admitted, “I used to skip high school to watch the lectures on child psychology.”

That childhood passion continues to drive Simon’s interests and his research program at the M.I.N.D. Institute. He considers himself among those lucky enough to get paid for doing something

so incredibly fascinating. “I have no trouble getting out of bed in the morning,” he said.

The potential impact of his current research also motivates Simon. His main research focus involves determining the biological basis for the cognitive impairments associated with chromosome 22q11.2 deletion (see accompanying research profile). “What I’m doing really matters to these children and their families,” he said.

Simon can identify with these families, as he has a young son of his own. And, although being a father and a researcher keeps him busy, he manages to find time to get away for the occasional ski trip to Lake Tahoe.

The nature of Simon’s work as a member of the brain imaging team for the institute’s Autism Phenome Project, however, requires that he often work into the night in order to perform MRI exams on sleeping children. “They have to be completely still for the MRI,” he said. “It demands some late nights, but, because we are doing such exciting work, I don’t feel like sleeping much.”

New community lecture series

You are invited to “The Minds behind the M.I.N.D.” – a new series of discussions with leading M.I.N.D. Institute experts on their research initiatives in autism, Tourette syndrome, fragile X syndrome, attention deficit hyperactivity disorder and more.

April 19

Integrative Medicine: Considering Biomedical Treatments –

Robert Hendren, executive director.

Parents of children with neurodevelopmental disorders often need to consider a bewildering array of possible biomedical treatments for their child. Learn about the benefits that nutrition and medication coupled with conventional medicine can offer to treat a child with these disorders. Also find out more about innovative biomedical research underway at the M.I.N.D. Institute.

July 19

Uncovering the Mysteries of Autism

David Amaral, research director.

Autism is a spectrum disorder, which means that it affects different children in different ways. By identifying the variations on the autism spectrum, better treatment and diagnostic practices will emerge. Discover what the Autism Phenome Project is doing to help define the various types of autism, which will ultimately lead to better understanding of causes, treatments and preventions.

All lectures are free and start at 6 p.m. in the M.I.N.D. Institute auditorium. For more information, call (916) 703-0280. Past lectures are available for viewing via our Web site: www.mindinstitute.org

Meet the “Lucy and Ethel” duo propelling the annual gala

Nancy Brodovsky and Maria Kaufman chuckle about the nicknames they’ve been given. Many at the M.I.N.D. Institute fondly refer to them as “Lucy and Ethel” – a respectful nod to their boundless energy, infectious enthusiasm and strong friendship.

“I’m ‘Ethel,’ said Kaufman, the more reserved and analytical of the two. “And Nancy is ‘Lucy.’ We’re very different from each other, but we have a knack of reading each other’s minds. Our strengths complement each other.”

Brodovsky agrees. “Maria is marvelous at specific ideas and details, whereas I’m a ‘big picture’ concept person. She and I have a wonderful working relationship,” she said.

This “Lucy and Ethel” pair co-chair the M.I.N.D. Institute gala, which they have transformed from “wish-list” item into “A-list” community event. They shepherded the initial sold-out November 2005 gala that generated \$125,000 in proceeds. To date, countless hours have been spent organizing this year’s event, which is scheduled for April 28 to coincide with Autism Awareness Month.

“They are a dynamic force of nature,” said Terri Contenti, M.I.N.D. Institute development officer. “They bring passion, energy and life to everything that they do for us. Their goals are to raise awareness of the M.I.N.D. Institute, raise dollars for important research and create an entertaining and festive event. We are fortunate to have their support and are grateful for their many efforts.”

The two originally met when their husbands’ business interests crossed paths more than 20 years ago. Along



Maria Kaufman (left) and Nancy Brodovsky are leading the “Journey of the M.I.N.D.” gala featuring Montel Williams.

with five friends, they have celebrated birthdays together ever since. Nancy and Maria’s joint venture on the M.I.N.D. gala actually began on a cocktail napkin, when they were attending another organization’s fundraising event. On the napkin, Brodovsky scribbled, “I’ve been asked to create a gala at the M.I.N.D. Institute. Are you interested?” She passed the note to Kaufman, who replied, “Yes!”

Through more notes, Brodovsky said the gala needed a theme to convey the significance of the institute’s research and clinical work. After some thought, Kaufman handed a note to Brodovsky. “It’s a journey to find an answer, like taking a spaceship to Mars, so we should call it ‘Journey of the M.I.N.D. – A Promise for the Future.’”

Within six months, the forces of “Lucy and Ethel” and a committee of community volunteers transformed that idea into an imaginative event that dramatically elevated awareness of the M.I.N.D. Institute.

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Brodovsky and Kaufman are inveterate volunteers with rich experiences serving civic organizations. Both spent countless years at the Crocker Art Museum as board members and volunteers. Brodovsky's countless volunteer activities include the Shalom School, Sacramento Country Day School, River Oak Center for Children, Families First and Mosaic Law Congregation. Currently, she is a M.I.N.D. Institute board member and serves on the UC Davis Health System Leadership Council.

Kaufman dedicated herself to volunteerism after recognizing a dramatic societal shift. "As a result of a significant revolution in the composition of the work force during the past three decades, far fewer women had time for volunteer work," she observed. She and her husband, commercial real estate broker Dan Kaufman, agreed that he would maintain the family business, while Maria maintained the commitment of philanthropy to the community. Her volunteer interests include The Sacramento Opera, St. Francis High School, Jesuit High School, Junior League, Symphony League and the Greek Orthodox Church.

She strayed from that course only after her children were grown. That's when she and a longtime friend launched a popular gardening and home accessories shop called Two Potted Ladies. She drew inspiration for that and other endeavors from a declaration by the late painter Georgia O'Keeffe: "I've been absolutely terrified every moment of my life – and I've never let it keep me from doing a single thing I wanted to do."

Brodovsky's initial career in hotel sales and marketing evolved into expertise in catering sales and management, which led to her involvement with community organizations. She enjoys serving on boards because it gives her a role in shaping and advancing policy.

Her husband, attorney Alan Brodovsky, agreed that is where her talents shine and encouraged her volunteerism.

Brodovsky and Kaufman both felt drawn to support the M.I.N.D. Institute because they both have friends and family members who are affected by neurodevelopmental disorders. They empathize with the difficulties of parents who have children with autism. That's largely the inspiration for making the M.I.N.D. Institute gala fun for attendees, who include many parents of patients and research study participants.

"Our primary goal is to raise awareness about the remarkable work that the M.I.N.D. Institute is doing and to throw a fun party to recognize that." This year will be even better thanks to the involve-

ment of talk show host Montel Williams. Brodovsky and Kaufman were thrilled when he agreed to participate.

"He is a strong advocate for children and health issues and a shining example of community responsibility," said Kaufman. "He'll bring his star quality and motivation to the event."

"We recognize that everybody knows somebody affected with some neurodevelopmental disorder," said Brodovsky. "Whether you are a parent, sibling, student, neighbor, business colleague, employer, teacher or grandparent, each day can pose a challenge. Montel says, 'Success is determined by what you give back to others.' These are words Maria and I live by everyday because that is who we are."

THE JOURNEY OF THE M.I.N.D.
A PROMISE FOR THE FUTURE.

The 2nd annual gala, benefiting the UC DAVIS M.I.N.D. INSTITUTE
April 28

Join us for a gourmet dinner, dancing to the music of Busta-Groove, tours of the M.I.N.D. Institute and inspiration from special guest **Montel Williams**

Contact Terri Contenti at (916) 703-0289 for tickets and more information.

Executive director's message



It's been a great few months for the M.I.N.D. Institute. Randi Hagerman was included in a "Today Show" story about genetics testing and fragile X syndrome, and

Sally Rogers and Sally Ozonoff were featured on "60 Minutes" about early behavioral diagnosis and interventions for autism. We hosted a 22q11.2 deletion syndrome conference where parents continuously spoke about the value of Tony Simon's research and the benefits of his lab to their community of families. The CHARGE (Childhood Autism Risks from Genetics and the Environment) study has been funded for another five years. We will soon launch the MARBLES (Markers of Autism Risk in Babies – Learning Early Signs) study, which will help determine if something occurs during pregnancy that can lead to a child's later diagnosis of autism. And we hit a major milestone in our Autism Phenome Project (APP) – 50 families have now signed up to be part of a comprehensive biomedical-behavioral study that will help

accurately define specific types of the disorder.

But there is still more to be done. And you can help.

One of the ways that all parents can help find causes, treatments and, eventually, cures for neurodevelopmental disorders is to enroll their children in clinical research studies. At the M.I.N.D. Institute, dozens of studies are currently underway on interventions, genomics, brain structure, immunology, learning patterns and more related to autism, fragile X syndrome, developmental delay, Tourette syndrome, attention deficit hyperactivity disorder and other neurodevelopmental disorders. These studies need children who have developmental concerns as well as those who do not. That means that almost any child can be included.

I encourage you to visit our Web site and take a look at the studies enrolling participants or call our clinical research coordinator, Meridith Brandt, at (916) 703-0320. If you enroll your child in a study, your family will be invited to our December party held in honor



The research party is just one of the ways that we say "thank you" to families who support our efforts.

of all research participants. Last year, more than 800 parents and children made candles, painted

T-shirts, decorated cookies, jumped in bounce houses and danced to music in a safe and fun environment. The research party is just one of the ways that we say "thank you" to families who support our efforts.

Between now and our next research party in December, watch for more information about our current work and longer-term goal of establishing a translational research center at the M.I.N.D. Institute where new ideas from basic research will be combined with clinical knowledge to scientifically test new treatments for autism.

More to come.

*Robert L. Hendren, D.O.
Executive Director
UC Davis M.I.N.D. Institute*

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M.I.N.D. Matters is a publication of the UC Davis M.I.N.D. Institute.

Editor: David G. Amaral, Ph.D.

Managing Editor: Kathy Lelevier

Contributing Editor: Laura R. Lacy, Ph.D.

Executive Director: Robert Hendren, D.O.

Research Director: David G. Amaral, Ph.D.

Clinical Programs Director: Robin Hansen, M.D.

Medical Director: Randi Hagerman, M.D.

Chief Administrative Officer: Kathy Lelevier

E-mail questions to: mind@ucdmc.ucdavis.edu

Telephone: (916) 703-0280

Web site: www.mindinstitute.org

UC DAVIS M.I.N.D. INSTITUTE

2825 50th Street
Sacramento, CA 95817

(6463)

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