Did you know?

Even though autism spectrum disorder (ASD) is diagnosed between ages 2 and 3, symptoms and signs emerge much earlier. Research in high-risk infants (with risk defined by having an older sibling with autism) has shown that between 12 and 18 months of age, infants who develop autism may show the following signs: reduced eye contact, failure to point, poor visual attention, and motor delays. Studies in brain imaging have found differences in the development of brain connections as early as the first few months of life. The earlier we detect risk markers, the earlier we can start interventions to try and improve developmental outcomes!

- Centers for Disease Control and Prevention

UCLA CART Awarded Autism Center of Excellence

The National Institutes of Health has renewed its support of the UCLA Center for Autism Research and Treatment (CART) with a five-year, $9.7 million grant. This is the third consecutive time UCLA CART has received the Autism Center of Excellence (ACE) grant. ACE awards support innovative, multidisciplinary research aimed at developing interventions and services for people with ASD. ASD is one of the fastest growing neurodevelopmental disorders in the United States, affecting one in 68 children. The increase in awareness and diagnosis of ASD along with the limitations in current therapies has necessitated more research for better clinical care, better treatment, and greater dissemination of educational programs.

The ACE grant is directed by Dr. Susan Bookheimer, co-director of UCLA CART and director of the Intellectual and Developmental Disabilities Research Center at UCLA. The ACE grant supports three projects led by autism experts Drs. Daniel Geschwind, Jim McCracken, and Connie Kasari.

From left to right: Drs. Mirella Dapretto, Shafali Jeste, James McCracken, Susan Bookheimer, Daniel Geschwind, Amanda Gulsrud, and Connie Kasari. Not pictured: Dr. Elizabeth Laugeson.

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CART scientists are taking a multidisciplinary, integrative approach to study the relationship between genetic, brain, and symptom heterogeneity among individuals with ASD. Using this approach, investigators will determine if we can explain individual differences between individuals with ASD using biological mechanisms. CART scientists are looking for clues that may help determine which children will develop autism, which genetic factors contribute to autism, and which treatments are most effective for different children. Research will focus on (1) sensorimotor processing, or how people process information from their senses; (2) social communication, the ability to use language and gestures for interactions with others; and (3) social motivation, the need to interact with others and be accepted by them and if social motivation can be changed using medication.

Project 1: Beyond Infant Siblings: Early Trajectories and Biomarkers of Risk for ASD
(PI: Dr. Shafali Jeste)

Identification of the earliest markers of risk for ASD holds tremendous clinical relevance. Determining risk for ASD informs selection of early interventions that may reduce symptoms and even prevent the development of the disorder. Studying infants at heightened genetic risk for ASD affords us a valuable opportunity to examine both distinct and shared neurobiological pathways to the core features that define autism symptoms. Such investigations not only shed light on mechanisms underlying atypical development in high-risk infants, but they can also clarify the ideal timing and target of early interventions that may modulate developmental trajectories. In this study, we take a genetics-first approach and investigate biomarkers of risk for ASD and predictors of outcome in early infancy in three genetically defined groups with elevated risk: infants with an older sibling with ASD (familial risk), infants with Tuberous Sclerosis Complex (TSC), and infants with 22q11.2 deletion syndrome (22q11). Studying these three groups allows us to examine ASD as it emerges in the context of genetics and biomarkers. We combine electroencephalography (EEG) with magnetic resonance imaging (MRI) to examine neurodevelopmental processes in the first year of life that may underlie the impairments that define ASD: (1) resting state/baseline neural synchrony and connectivity, (2) low level sensory processing and (3) brain activity and connectivity in language and salience networks. We study infants at 1.5, 3, 6, 9, and 12 months with MRI (1.5 and 9 months), EEG (3-12 months), and behavioral assessments (3-12 months), and then...
sequence of intervention delivery and specific parent and child characteristics that may influence the effect of treatment. This study involves three stages of intervention. During the first stage of the study (4 weeks), parents and children will either participate in a parent education group (parent support and education on social communication development), or a behavioral intervention program in which either a therapist or the parent (with training and support) will implement the strategies. In stage 2 of the study (8 weeks), parents will either stay in their current placement or begin receiving either parent education or behavioral intervention (whichever they did not previously have). In the final stage (8 weeks), all participants will receive support in maintaining the skills they have learned through either video chat/text check-ins or in-home visits from an expert therapist.

The goal of this study is to test the optimal sequence of intervention delivery and specific parent and child characteristics that may impact treatment success. The study will be conducted by two expert researchers: Dr. Connie Kasari and Dr. Amanda Gulsrud.

Eligibility:
- Children 12-36 months old with an existing diagnosis or clinical concern for autism
- Child must not have active seizure activity (or is stable on medication)
- Parent available for sessions two times per week at UCLA

For more information, contact:
Consuelo Garcia, (310) 825-4775

Project 3: Proof of Mechanism Study for Early Childhood Autism Research

Infants less than six weeks of age (pregnant mothers are also encouraged to contact us) who have either:
- A sibling diagnosed with autism
- A clinically confirmed diagnosis of Tuberous Sclerosis Complex
- A clinically confirmed diagnosis of 22q11.2 deletion or duplication syndrome
- No family history of autism

For more information, contact:
Lisa Jackson, (310) 825-3478
www.babybibs.org

Project 2: Parent-mediated Interventions for Toddlers with ASD: Heterogeneity in Timing and Responses to Treatment
(Pi: Dr. Connie Kasari)

Parent-mediated interventions are commonly used to target social communication skills in young children with ASD. Thus far, these approaches have been shown to have mixed effectiveness in impacting social communication skills. This is likely due to the fact that every parent, child, and family are different and need an intervention that is tailored to their unique needs. Each parent may experience stress associated with their child's diagnosis differently. Additionally, parents may have different expectations for the intervention and each have unique ways of interacting with their child. For children, factors that can impact the effect of intervention include their current language level, communication style, and sensory needs. In seeking optimal outcomes for each family, it is imperative that we better understand how to tailor early intervention approaches to fit each parent and child. One way to do this is to use an adaptive intervention approach that seeks to capitalize on the differences among children and parents. Utilizing an adaptive treatment design, the current study tests the optimal

ACE, continued from page 2
Question: My child just got diagnosed with ASD. What kind of medical work up does he need? I am wondering specifically about an MRI and EEG.

Answer: Your child has been diagnosed with Autism Spectrum Disorder (ASD), and you are left with wondering what the next steps are for the evaluation of your child. This time can be filled with feelings of uncertainty because it may seem like there are many tests that can be performed for ASD. However, very few medical tests are necessary to help guide your child’s care. There are guidelines regarding medical evaluation that have been created by the American Academy of Neurology (AAN), American Academy of Pediatrics (AAP), and American Academy of Child and Adolescent Psychiatry. It is recommended that your physician perform a thorough evaluation of your child to determine if there are any medical or developmental concerns that require testing or referrals to specialists (neurologist, psychiatrist, or geneticist).

Genetic testing is routinely recommended as medical workup for all individuals with ASD. All children should undergo a Chromosomal Microarray (CMA), but other specific genetic testing will depend on associated signs and symptoms and a detailed family history. If your child has already been diagnosed with a genetic syndrome it is important that you receive the appropriate counseling on the genetic results and guidance on potential medical screening that might be indicated. All children with ASD should be screened for sleep disturbances (such as insomnia, difficulty falling asleep, and difficulty staying asleep) and be evaluated for any medical concerns that might be leading to these disturbances. There are behavioral interventions and medical treatments for sleep disturbances and a pediatrician, neurologist, or psychiatrist can aid in identifying these treatments after an evaluation.

Testing such as Magnetic Resonance Imaging (MRI), which is a picture of the structure of the brain, or an electroencephalography (EEG), which is a test of brain waves, are not routinely recommended in children with ASD. An MRI should only be obtained if there is concern for an abnormal neurologic exam or a genetic condition that is associated with structural abnormalities of the brain. An EEG is only recommended if there are concerns for seizures or if there has been a significant regression in development such as loss of language or loss of motor skills. If any of these concerns are identified, it is important that your child is evaluated by a neurologist to determine the appropriate course of action.
Introducing the CARING Clinic (formerly DNG): Care and Research in Neurogenetics

With rapid advances in genetic testing and its routine use in the medical evaluation of children with a neurodevelopmental disorder (NDD), an increasing number of children and adults are being diagnosed with genetic causes for their developmental disability, with up to 25% of children being diagnosed with a genetic condition. There is a tremendous gap in the counseling and care of patients with neurogenetic syndromes, and families are left with questions about the implications of the genetic diagnosis and confusion around next steps in care. To fill these gaps, two years ago we developed a clinical program through CART called the Developmental Neurogenetics Clinic (DNG), which brought together genetics, neurology, and psychiatry to evaluate and treat patients with genetic conditions associated with NDDs. Over the last two years we have evaluated more than 150 patients, and we identified further gaps in care, including intervention, school based services, medication management, and advocacy. Last month, to meet these greater needs, we rebranded and expanded our clinic. We now introduce the UCLA CARING Clinic (Care and Research in Neurogenetics) directed by Dr. Shafali Jeste. Our monthly multidisciplinary clinic now evaluates and treats children and adults with suspected or identified genetic etiologies for their neurodevelopmental conditions, with the goal of building a platform for clinical trials. Specialists include the original disciplines of pediatric neurology, genetics, and psychiatry and now introduce social work, educational consulting, and speech/language consultation. The CARING Clinic also directly integrates with research studies in neurogenetics at CART, with families given opportunities to participate in several ongoing studies on biomarkers, clinical characterization, and treatment.

For more information about the clinic:
Please contact the coordinator:
Careese Stephens
cmstephens@mednet.ucla.edu
(310) 206-7404

EXPERT, continued from page 4
the need for an EEG and MRI and the type (duration) of EEG and MRI.

Resources: At UCLA, we have two multidisciplinary clinics (neurology, psychiatry, genetics, psychology, and social work), The Child and Adult Neurodevelopmental Clinic (CAN) and the CARING Clinic (Care and Research in Neurogenetics; formerly the Developmental Neurogenetics) to aid in the appropriate evaluation, diagnosis, and treatment for children with ASD. If you would like to make an appointment for the CAN Clinic, please call (310) 794-4008. If you would like to make an appointment for the CARING Clinic, please call (310) 206-7404.

The CARING Clinic (from left to right): Dr. Benjamin Schneider, Careese Stephens, Dr. Shafali Jeste, Dr. Charlotte DiStefano, Dr. Julian Martinez-Agosto, Dr. Rujuta Bhatt Wilson, and Dr. Aaron Besterman
The UCLA CAN Research, Education, Awareness, and Community Help (REACH) Training Program is a new multifaceted training program created for community professionals and parents to improve access to cutting edge, empirically-driven information, training, and resources regarding individuals with autism spectrum disorder (ASD). The program was in partnership with Dr. Tanya Paparella and Dr. Stephanny Freeman and is directed by Dr. Amanda Gulsrud. It is generously supported by donations from the Kaplan and Rothstein families and friends and is a partnership between the UCLA Child and Adult Neurodevelopmental (CAN) Clinic and the UCLA Early Childhood Partial Hospitalization Program (ECPHP). The training program aims to build partnerships with local community providers, including behaviorists (e.g., BCBA providers) and teachers, by providing free clinical workshops, educational lectures, and teacher trainings on evidence-based practices for individuals with ASD. It also serves as a resource for parents to obtain up-to-date information on empirically supported interventions for their children.

CAN REACH provides bi-monthly clinical workshops, an intensive teacher training in the summer, and several parent lectures throughout the year. To learn more about upcoming events and to view past events please visit: www.uclacanreach.com

In its introductory year, CAN REACH provided five clinical training workshops, three teacher trainings, and two educational lectures for parents. These training workshops and educational lectures were attended by over 70 educators, 75 parents, and 250 professionals (e.g., psychologists, BCBAs, social workers, teachers) working with children with ASD. Dr. Catherine Lord from Columbia University, Dr. Nathan Call from the Marcus Autism Center at Emory University, and Dr. Elizabeth Laugeson from the UCLA Center for Autism Research

Speaker Dr. Catherine Lord and CART faculty Dr. Connie Kasari
The Geschwind Lab at UCLA and Dennis Wall at Stanford University continue to study the genetic basis of ASD as part of the Hartwell Autism Research and Technology Initiative (iHART). Recent studies of patients diagnosed with ASD have resulted in the identification of several dozen risk genes but also uncovered the fact that there are many more risk genes to discover. These studies estimated that there are at least 1,000 risk genes in the human genome (total >18,000 genes) that contribute to autism risk when mutated. The majority of these genetic studies focused on small families with a single child with an ASD diagnosis. The use of these families facilitated the identification of new (de novo) mutations found in the child, but not found in the parent (these mutations arise in the sperm or egg of the parents). In contrast, the iHART study leverages the Autism Genetic Resource Exchange (AGRE) cohort, which collected families with two or more children with an ASD diagnosis. Using blood samples donated by each of our 2,308 study participants, the labs performed whole-genome sequencing (WGS) to look for changes in DNA that affect ASD risk.

In this study, a set of new inherited mutations contributing to autism risk – a total of 16 novel ASD-risk genes have been identified. Many of these are genes for which mutations that remove protein function are transmitted from the parents to the affected children. Also, these genes are not random, but are working together in specific pathways that are identifiable, including those involved in development of the brain. The data is provided as the Hartwell Autism Research and Technology Initiative (iHART), an open access cloud-computing repository to further empower ASD genetics research.

The iHART Team at UCLA:
Importance of Gene Expression

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder with many diverse genetic and environmental causal influences. This diversity makes identifying causal biological processes in ASD challenging since it complicates the search for ‘starting points’ (such as a single causal gene) that can guide ASD research. Therefore, to begin understanding how ASD is caused, it is first necessary to identify biological processes that are active in all forms of ASD as starting points for research. One method that can help find these biological processes is gene expression analysis. Gene expression provides a ‘snapshot’ of which biological processes are active in a certain tissue sample. Studying gene expression in samples from the ASD brain allows for identification of active disorder-relevant biological processes.

Previous work has already discovered that neuronal processes are disrupted and immune processes are overly active in the ASD brain through gene expression analysis. Although these are important findings, they are limited to only a few brain regions where gene expression was measured. It is necessary to determine if the neuronal and immune processes that are disrupted in the few previously studied brain regions are similarly disrupted (or not) across the entire brain.

Additionally, it is necessary to identify any currently unknown brain region-specific biological mechanisms that may be disrupted in ASD. Because of these needs, current research measures ASD gene expression across eleven distinct regions in the brain. This research will determine if the neuronal and immune dysregulation previously observed in just a few brain regions is present across the entire brain, and it will also elucidate region-specific dysregulation in the ASD brain. The whole-brain gene expression analysis will allow for enhanced spatial understanding of disorder-relevant biological processes and will be essential in guiding future ASD research.

Members of the research team from the Geschwind Lab (from left to right): Dr. Elizabeth Ruzzo, Dr. Vivek Swarup, Dr. Michael Gandal, Jillian Haney, Dr. Gokul Ramaswami, Jing Ou, Chris Hartl, Sepideh Parhami. Not pictured: Dr. Laura Perez-Cano, and Dr. Daniel Geschwind
The Geschwind lab and collaborators recently completed a five-year study funded by NIH to elucidate the genetic basis of autism in families of African-American descent through our Autism Centers for Excellence (ACE) Network. Together with collaborators at Albert Einstein/Yeshiva University, Emory University, and Washington University, researchers examined nearly 600 African-American children with autism and their family members, and we have had approval that our study will receive funding for an additional five years.

In this study, researchers continue to observe that African-American children with autism tend to be diagnosed later in life than Caucasian children. Detailed behavioral assessments are used to ask: do autism symptoms differ between African-Americans and Caucasians? Are there biases in the healthcare system that interfere with accurate diagnosis? How can these differences be addressed to improve each patient's access to high-quality care?

Using blood samples donated by each of our study participants, genomic techniques such as whole-genome sequencing are used to look for changes in DNA that affect autism risk. It is likely that most of the genetic risk is shared with other groups, but it is also very possible, similar to studies in cardiovascular disease risk, that there may be genetic factors that are specific to African-Americans. One thing that genetic studies are teaching us is that an individual's genetic risk for disease may be different in those with different ancestries, such as European, African, etc. To be able to interpret the risk of particular disorder, such as autism in an individual patient, it is important to have information from affected and unaffected individuals sharing similar ancestry. So, this research will allow for a greater understanding of what genes and biological processes contribute to autism.

For more information on the Autism Genetics and Human Diversity Study, contact the study coordinator:
Dr. Erin Graham
egraham@mednet.ucla.edu
(310) 794-4090
Research at CART

Are you interested in participating in a research study? CART’s goal is to improve the lives of families impacted by ASD, by understanding the causes, improving the diagnosis, and developing transformative therapies. Our team is full of brilliant minds pursuing groundbreaking investigations for ASD. Research studies at CART focus on early markers for high-risk infants, early intervention, treatment, genetics, brain imaging, EEG, and clinical trials.

To learn more, go to www.autism.ucla.edu, contact the study coordinator directly, or call (310) 825-9041.

<table>
<thead>
<tr>
<th>AGE RANGE</th>
<th>STUDY NAME</th>
<th>CONTACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>SPARK</td>
<td>(310) 206-7478</td>
</tr>
<tr>
<td>Infants under 6 weeks</td>
<td>Baby BIBS</td>
<td>(310) 825-3478</td>
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<td>0 - 7 years</td>
<td>AIMS</td>
<td>(310) 825-4475</td>
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<td>1 - 18 years</td>
<td>Brain and Behavior in Genetic Syndromes (B-BiGS)</td>
<td>(310) 825-8738</td>
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<td>12 - 36 months</td>
<td>Baby BEARS</td>
<td>(310) 206-1268</td>
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<tr>
<td>12 - 36 months</td>
<td>Early intervention for infants with Tuberous Sclerosis Complex</td>
<td>(310) 825-8738</td>
</tr>
<tr>
<td>2 - 10 years</td>
<td>Technology and ASD (Latino/a/Hispanic Families)</td>
<td>(310) 794-6633</td>
</tr>
<tr>
<td>1st - 6th grade</td>
<td>Autism Diagnosis and Service Access for Latino Immigrant Parents</td>
<td>(310) 206-1268</td>
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<tr>
<td>Pre-K/5th grade/8th grade</td>
<td>AIR-B III: Building Better Bridges, Mind the Gap</td>
<td>(310) 206-1268</td>
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<td>3 - 21 years</td>
<td>Autism Genetics and Human Diversity Study</td>
<td>(310) 794-4090</td>
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<td>4 - 11 years</td>
<td>Autism Biomarkers for Clinical Trials</td>
<td>(310) 825-0180</td>
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<td>5 - 11 years</td>
<td>Treatment with Aripiprazole and Behavior Intervention for Children with Autism who have Low Language Ability</td>
<td>(310) 825-6170</td>
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<tr>
<td>7 - 17 years</td>
<td>Brain Imaging in Children with Autism or Typical Developing Children</td>
<td>(310) 206-4482</td>
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<tr>
<td>8 - 17 years</td>
<td>Brain Imaging Study for Verbally Fluent Children with ASD</td>
<td>(310) 825-5326</td>
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<tr>
<td>8 - 17 years</td>
<td>Sensory Over-responsivity in Children with Anxiety, ASD or in Typically Developing Children</td>
<td>(310) 825-5326</td>
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<tr>
<td>15 - 20 years</td>
<td>Brain Wave Study of Autism Spectrum Disorders</td>
<td>(310) 206-9012</td>
</tr>
<tr>
<td>18 - 35 years</td>
<td>Measuring Brain Inflammation in Autism</td>
<td>(310) 267-4798</td>
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Treatment Services at CART

Child and Adult Neurodevelopmental (CAN) Clinic
Clinic for individuals of all ages offering ASD evaluations and assessments. Treatment focuses on social, behavioral, and developmental problems.
Contact: Maria Shavers
(310) 794-4008

Care and Research in Neurogenetics (CARING) Clinic
Evaluation and care for children and adults with an identified or suspected genetic cause for their developmental disorder.
Contact: Careese Stephens
(310) 206-7404

Early Childhood Partial Hospitalization Program (ECPHP)
Short-term day treatment program for young children (3-5 years old) diagnosed with or may have ASD, ADHD, developmental disabilities, or behavioral disabilities.
Contact: Alice Yokota
(310) 206-2695

Program for the Education and Enrichment of Relationship Skills (PEERS)
16-week social skills training intervention for preschoolers, adolescents, and young adults with ASD, ADHD, anxiety, depression, and other socioemotional problems.
Contact: Nicole Rosen
(310) 267-3377

Upcoming Events

All events are free and open to the public. For more information about these events, contact: (310) 825-9041.

SPARK: Catalyzing Autism Research and Elucidating the Genetic Basis for Autism
Wendy Chung, MD, PhD is a board certified clinical geneticist. She is a co-director of the molecular genetics program at Columbia University, a co-director of the molecular genetics diagnostics lab, and heads a research laboratory in the division of molecular genetics investigating the genetic bases for a variety of Mendelian and complex traits.
Where: Neuroscience Research Building, Auditorium
When: Thursday, May 3, 2018 / 7-8pm
693 Charles E. Young Drive South
Los Angeles, CA 90095

The Changing Faces of Autism
Fred R. Volkmar, MD is Irving B. Harris Professor of Child Psychiatry, Pediatrics, and Psychology and Director of the Yale University Child Study Center, Yale University School of Medicine. He is also the Chief of Child Psychiatry at Yale-New Haven Hospital, New Haven, CT.
Where: Gonda (Goldschmied) Neuroscience & Genetics Research Center, 1st Floor Conference Room
When: Friday, June 22, 2018 / 9 - 10:30am
695 Charles E. Young Drive South
Los Angeles, CA 90095

Program for the Education and Enrichment of Relationship Skills (PEERS)
Wendy Chung, MD, PhD is a board certified clinical geneticist. She is a co-director of the molecular genetics program at Columbia University, a co-director of the molecular genetics diagnostics lab, and heads a research laboratory in the division of molecular genetics investigating the genetic bases for a variety of Mendelian and complex traits.
Where: Neuroscience Research Building, Auditorium
When: Thursday, May 3, 2018 / 7-8pm
693 Charles E. Young Drive South
Los Angeles, CA 90095

SPARKing Partnerships in Autism Research
Wendy Chung, MD, PhD is a board certified clinical geneticist. She is a co-director of the molecular genetics program at Columbia University, a co-director of the molecular genetics diagnostics lab, and heads a research laboratory in the division of molecular genetics investigating the genetic bases for a variety of Mendelian and complex traits.
Where: Gonda (Goldschmied) Neuroscience & Genetics Research Center, 1st Floor Conference Room
When: Friday, May 4, 2018 / 9 - 10:30am
695 Charles E. Young Drive South
Los Angeles, CA 90095