THE UCLA CENTER FOR AUTISM RESEARCH AND TREATMENT (CART)



from CART

SPRING 2012

UCLA CART

VOLUME 2, ISSUE I

DID YOU KNOW?

- Autism spectrum disorder (ASD) now affects 1 in 88 US children.
- UCLA CART is both an NIH Autism Center of Excellence (ACE) Center and the lead site of an ACE Network.

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New Faculty at CART

Scientific Advances
* Participate in
CART Research *

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Message from the CART Director

Welcome! Much has happened since our first CART Newsletter last spring. This issue, released during Autism Awareness Month, continues our goal to communicate new developments at the UCLA CART and in the field of autism research in general. CART scientists continue to make great strides in research aimed at improving the diagnosis and treatment of children and adults with an Autism Spectrum Disorder (ASD). This is critically important as estimates of ASD continue to rise with recent US reports of a prevalence of I in every 88 children.

Using rigorous scientific methods, Dr. Connie Kasari aims to understand the optimal methods for working within the school environment to improve the learning and social skills of ASD children. On a related front, Dr. Jeffrey Wood recently received a prestigious NIH grant to support his work to develop and scientifically test unique programs to reduce anxiety in children and adolescents with ASD. Drs. Mirella Dapretto and Susan Bookheimer continue to make progress in understanding how the brain circuitry of ASD children differs from their neurotypical peers. Dr. Ted Hutman is defining the early predictors of autism in infancy and contributed to a very important paper published this last year, showing the recurrence risk for siblings of children with autism is greater than previously thought, between 15 to 20%.

On the genetics front, the Geschwind laboratory developed an autistic mouse model that can serve to help develop and screen new pharmacotherapies (see p.3). Recently, our work with Yale University researchers made headlines, including the New York Times front page, by performing the most comprehensive genetic analysis of autism yet using Next Generation Sequencing. Our group and two others used this new technology to identify several new autism risk genes, which allows us to predict how many genes are likely to actually cause autism for the first time. Genome sequencing has become so cost effective that partial genome sequencing for developmental and other disorders including autism is now a clinical test available at UCLA. **Genetic testing can identify**



causal mutations in up to 1/5 of children with an ASD. Current recommendations are that all children with autism should have an array-CGH as a first-line clinical test.

These new findings mentioned here, and others, make our understanding of ASD one of the most rapidly evolving areas in medicine today. As such, we remain very optimistic about the future.

We are grateful for the generous contributions from our donors, for all the families who have participated in CART research and those in the community who are involved in autism advocacy and treatment. Please visit our website (<u>www.autism.ucla.edu</u>) to stay informed about our research projects, clinical programs, lecture series, annual symposium and other events. All CART lectures are open to the community. As always, we invite your feedback so that we can best provide you with what we hope will be interesting and useful information and updates about our work. With best wishes, and many thanks for your support,

Daniel H. Geschwind, M.D., Ph.D.

Gordon and Virginia MacDonald Distinguished Chair in Human Genetics; UCLA Professor of Neurology, Psychiatry & Human Genetics

CART Mission Statement

The mission of the UCLA Center for Autism Research and Treatment is to continue to play a leading role, both nationally and internationally, in efforts to develop an improved understanding of the biological basis of autism, so as to improve diagnosis, and develop and disseminate new, more effective, treatments for autism spectrum disorders across the lifespan. We hope to achieve these goals by fostering a strong collaborative environment for basic and applied research, as well as a challenging, but supportive, environment for trainees.

NEWS FROM CART

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"Now that we have identified patterns of behavior that indicate heightened risk for Autism Spectrum Disorder (ASD) in 12-month olds, the next challenge is to identify mechanisms during the first year that give rise to these behavior patterns."

— Dr. Hutman



Dr. Hutman speaking at CART annual symposium

Introducing CART Faculty Member – Ted Hutman, Ph.D.

Ted Hutman, Ph.D., a developmental psychologist, became an Adjunct Assistant Professor in the UCLA Department of Psychiatry in July 2011.

Dr. Hutman's pathway to CART was not a traditional one. He studied economics at the Wharton School of Business, and philosophy and literature at Stanford where he received bachelor's and master's degrees. Before his academic training in psychology, he spent 14 years at the Los Angeles Philharmonic in a variety of positions including Orchestra Personnel Manager and Orchestra Manager. Seeking to build on this intensive experience with a rarefied population of highly talented people, in 2001 Dr. Hutman left the Philharmonic to work with Marian Sigman, Ph.D. in the UCLA Psychology Department.

With Dr. Sigman, Hutman studied autism, social-emotional development, and socialcognitive development. He was a study coordinator and interventionist in a parentmediated treatment study designed to improve the quality of play interactions and to boost communication skills in lowfunctioning preschoolers with autism.

As a postdoctoral scholar in the Department of Psychiatry, he directed the UCLA CART study of infant siblings of children with autism, a primary project of consecutive NIH-funded Center grants. These studies involved longitudinal assessment of infants whose older sibling(s) had been diagnosed with autistic disorder. The importance of infant research is that little is known about early development of children with autism because most are not diagnosed before their third birthday. Additionally, early identification allows children to access treatment during a period in development when the brain is growing rapidly and critical skills such as language and social cognition are emerging. As Dr. Hutman explains:

"Now that we have identified patterns of be-

havior that indicate heightened risk for Autism Spectrum Disorder (ASD) in 12-month olds, the next challenge is to identify mechanisms during the first year that give rise to these behavior patterns. We can do this by studying gaze, learning, and brain activity during social tasks. This work will shed light on processes affected by ASD at the earliest stages of development. It will also improve screening and treatment for ASD during infancy."

Under Dr. Hutman's supervision, the UCLA CART infant sibling study contributed to a collaborative report indicating that nearly 20% of infant siblings are diagnosed with ASD. The percentage is even higher for male infants and those with more than one older sibling with ASD. In collaboration with UC Davis researchers, Sally Ozonoff, Ph.D. and Sally Rogers, Ph.D., the UCLA CART infant study has identified a variety of behavioral characteristics that distinguish high-risk 12-month olds who go on to be diagnosed with ASD from those who did not. Infants later diagnosed with ASD demonstrate less looking to faces, smiling and vocalizing to others, pointing, showing, imitating, and responding to social information.

Dr. Hutman's current and future projects aim to identify early signs of ASD in infants. He is pursuing funding to translate findings about infants later diagnosed with ASD into treatment protocols geared toward infants in order to boost social and language development. He has close collaborations with other CART faculty including Drs. Jeste, Dapretto, Kasari, and Geschwind. Dr. Hutman's work has been supported with grants and fellowships from the National Institutes of Health (NIMH and NICHD), the UCLA CART and the UCLA Intellectual and Developmental Disabilities Research Center, the Friends of the Semel Institute, the FPR/ UCLA Center for Culture, Brain & Development, the UCLA Graduate Division, Autism Speaks, and the Mattel Foundation.

SPRING 2012



What is Autism Spectrum Disorder?

Autism spectrum disorder (ASD) is a developmental disorder with neurobiological origins that affects the child's ability to use imagination, express feelings and ideas and his ability to establish relationships with others. The three core impairments in ASD are:

• **Communication problems** can be seen in a significant developmental delay, in language ability or no language use at all, robotic, formal speech or repetitive use of language.

• **Socialization Issues** are evident through a difficulty in developing peer relationships, lack of spontaneous engagement for enjoyment, and difficulty in the "give and take" of social interactions.

• **Restricted/Repetitive behaviors** include preoccupations that are atypical in intensity or focus, inflexibility in routines, and rituals, stereotyped movements, and preoccupations.



Recent Scientific Advances

New Mouse Model May Facilitate Autism Research and Treatment —

Last September, Daniel Geschwind, M.D., Ph.D., Director of the UCLA

CART, postdoctoral researcher Olga Peñagarikano,

Ph.D. (shown at right), and UCLA colleagues reported on a new mouse model that may represent a more useful animal model for studying autism spectrum disorder (ASD) and testing potential treatments. The new mouse model lacks the autism risk gene CNTNAP2, a gene which inherited



mutations cause a genetic syndrome known as cortical dysplasia-focal epilepsy, whose symptoms include seizures, loss of language and hyperactivity. And nearly two-thirds of those affected by this rare disorder are also diagnosed with ASD.

The study, published in the journal Cell, showed that the mouse shows all three core autism traits: communication deficits, social dysfunction and repetitive behaviors (which included motor stereotypies and mental inflexibility/insistence on sameness) as well as hyperactivity and epileptic seizures, paralleling the human symptoms. In addition, brain studies reveal that the mice exhibit atypical patterns of brain activity and connectivity that are similar to those seen in many persons with ASD.

The mouse also responds to a drug (risperidone) already approved by the FDA to treat ASD-associated 'irritability' and shown to reduce repetitive behaviors in humans. In the mice, this drug significantly reduced hyperactivity, repetitive behaviors and insistence on sameness. This suggests the mice may be particularly suited for testing promising new medicines aimed at relieving autism's most disabling symptoms.



Participate in CART Research

Are you interested in learning more about our research projects, including how to enroll in a study? If so, please visit our website:

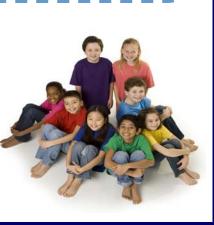
www.autism.ucla.edu

Or email us at: info@autism.ucla.edu



Call JONI, CART





NEWS FROM CART

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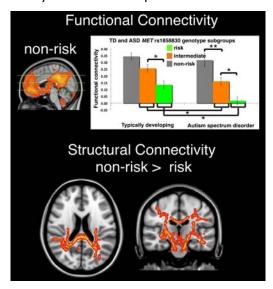


Jeff helping at CART community outreach event

Spotlight on CART Research Trainee

Jeffrey Rudie, Ph.D. Candidate

Recent autism neuroimaging research led by UCLA graduate student Jeffrey Rudie and UCLA CART faculty - Drs. Mirella Dapretto, Susan Bookheimer and Dan Geschwind - has characterized how a genetic risk factor for autism affects brain circuitry. A common risk allele in the Met Receptor Tyrosine Kinase (MET) gene was shown to impact multiple aspects of brain wiring in children and adolescents with and without autism spectrum disorder (ASD). Across both groups, children and adolescents carrying the risk allele were found to display atypical functional activity in response to emotional faces, including hyperactivation of the amygdala (a structure playing a key role in processing emotional information). Additional analyses revealed that this risk allele also disrupts both functional and structural connectivity of brain networks involved in social behavior and previously implicated in autism. The risk allele affected brain networks in both typically developing (TD) children and children with ASD but was shown to have a stronger impact in the ASD individuals. These findings provide new insight into the neurobiological basis of the disorder and may ultimately aid in the development of more effective diagnostic tools and biologically based interventions. This work was presented at the International Meeting for Autism Research and the Society for Neuroscience Meetings in 2011 and is currently under review for publication.



This figure depicts the average functional connectivity map for the non-risk group (top left) and average functional connectivity values for each TD and ASD genotype groups (top right). The bottom images depict regions of diminished structural connectivity for the risk carrier group.

CART in the **NEWS**:

Every year the Autism Speaks staff and the Scientific Advisory Committee compile and vote on the Top 10 most significant advances in autism science from the many scientific papers published over that year. We are proud that **two of the Top 10 exceptional research achievements in 2011 were by UCLA CART researchers in Dr. Dan Geschwind's lab.**

The papers describe how "Different forms of autism share striking brain similarities" (Geschwind & Irina Voineagu; *Nature*) and a "Gene knockout mouse may offer leap forward in autism animal models" (Geschwind & Olga Peñagarikano; *Cell* - see related story on page 3).



Dr. Daniel Geschwind

Summaries of the Top 10 advances are available at www.autismspeaks.org.

CART OUTREACH

CART Pilot Grant Program



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Purpose: Outreach to UCLA scientific community to stimulate innovative and relevant autism research that attracts new researchers to the autism field, encourages interdisciplinary collaboration, and leads to external funding and future productivity. > 18 Pilot grants funded to date > Basic and clinical research

CART Pilot Grant Funding available for 2012-13: Applications due May 7th. <u>Request for Applications (RFA) is available at CART website.</u>

Autism Affinity Lecture Series

As an ongoing commitment to education and dissemination of scientific research findings, CART hosts monthly Autism Affinity Group Distinguished Guest Lectures in which world-renowned research experts present recent scientific breakthroughs and treatment issues about autism spectrum disorders. To date, CART has hosted over 70 lectures. The remaining speakers for the 2011-12 academic year are:

April 13 – Katarzyna Chawarska, Ph.D. Associate Professor, Psychology Yale School of Medicine "Autism in Infancy: Perceptual, Attentional and Social-Cognitive Features"

April 20 – Roy Grinker, Ph.D. Professor, Anthropology, George Washington University, Washington DC "Three Perspectives on the Autism Epidemic" Dr. Grinker is author of Unstrange Minds: Remapping the World of Autism *Special lecture co-hosted by the FPR-UCLA Center for Culture, Brain & Development

May 4 – Janine LaSalle, Ph.D. Professor, Dept. of Med. Microbiology & Immunology, UC Davis M.I.N.D Institute "Mapping the Neuronal Methylome and its Implications for Autism"

June I – James McPartland, Ph.D. Assistant Professor of Child Psychiatry and Psychology, Yale University "Revisiting the Social Motivation Hypothesis: A Developmental Model of Function & Dysfunction in Autism"

Lectures are held on the first (or 2nd) Friday of the month, from October to June. For more information, please visit the **CART website Calendar page** (www.autism.ucla.edu) for a full list of this year's speakers, lecture titles and map/directions. Lectures are free and open to the public.

CART's 4th Annual Symposium

On February 3rd, CART held its 4th annual symposium -

"Autism 2012" to present the latest scientific findings and evidence-based treatment models for autism spectrum disorders. The all-day symposium offered continuing education credits and was attended by over 200 health-care professionals, including pediatricians, neurologists, psychiatrists, psychologists, nurses, autism practitioners, as well as teachers, advocates, parents, and UCLA trainees, faculty and staff. CART faculty speakers included Drs. Dan Geschwind (genetics), Connie Kasari (behavioral treatments), Shafali Jeste (pediatric neurology and electrophysiology), Elizabeth Laugeson, (social skills training for teens) Mirella Dapretto (neuroimaging), and Ted Hutman (infants at risk). A clinical panel presented case studies and an "Ask the Experts" session concluded the day. <u>Presentations</u> were videotaped and are posted on our website. See following pages for more highlights...



For more information about CART's Scientific Outreach programs, please contact : Candace J. Wilkinson, Ph.D. • Director of Operations & Outreach • 310-825-9041

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SCENES from **CART's 4th Annual Symposium**



CART faculty speaker Connie Kasari, Ph.D. answering questions from attendees at a break.

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CART Director, Dr. Dan Geschwind, discussing research with an attendee.



Dr. Mirella Dapretto presenting a lecture.



(Above, from L to R) at the luncheon: CART symposium co-chairs Dan Geschwind, M.D., Ph.D and Susan Bookheimer, Ph.D., UCLA Director of Development for Neuroscience Alan Han, guest attendee and donor Ed Jones, Ph.D., CART faculty speaker Connie Kasari, Ph.D., and guest attendee and gifted artist Leland Lee who is on the autism spectrum.





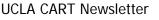
Autism clinic admin. dir. Karin Best. Ph.D. and CART recruitment coordinator Joni Zuckerbrow-Miller, providing information at CART resource table.



Artist

Leland Lee and his mother Karen Lee, an autism advocate from Taipei Taiwan

Attendee Gabriela (L) Simon-Cereijido, Ph.D., CCC-SLP, Assistant Professor at Cal-State Univ. LA and CART Director of Operations & Outreach, Candace J. Wilkinson, Ph.D. who organizes the CART annual symposium.



Those who attended the CART Symposium had this to say:

"Learning about the latest findings from CART research projects informs my teaching, clinical work, and research in the field of child language disorders. I am an assistant professor in the Department of Communication Disorders at California State University, Los Angeles, where we train graduate students to become speechlanguage pathologists (SLPs). Many of these future SLPs will work with individuals with autism spectrum disorders (ASD) and, therefore, I want to teach them current research-based knowledge on autism and evidence-based treatment models for this population. The UCLA CART symposium is a great source of information on autism. One of my students who attended last year became inspired and now is pursuing specialized autism training. I feel privileged to know that I, my students, and the families from our clinic can have direct access to such a fantastic autism research center and to its annual symposium in our same city!" — Gabriello Simon-Cereijido, Ph.D., CCC-SLP

"I am truly impressed by all the leading experts in autism at CART with promising scientific findings. Since Leland and I moved back to Taipei 6 years ago, we continue to be involved in promoting the awareness of Autism in Taiwan, Asia. Each year we collaborate with autism researchers and practitioners from various countries to collaborate and exchange methods of interventions. We focus on ability rather than "disability". Leland has autism and he has become a gifted artist with exhibits worldwide. You can learn more about his accomplishments and see his work at www.Lelandlee.com. Attending the CART symposium was a memorable experience and I look forward to collaborations between CART & Taiwan to enhance the breakthroughs for autism."

--- Karen Lee, mother of Leland Lee; Autism Advocate

CART IN THE COMMUNITY

UCLA CART, in partnership with Fiesta Educativa, are working together to provide autism resources for the Latino community in the greater Los Angeles area. On September 29, 2011, Fiesta Educativa, held the 33rd State Wide Annual Conference at The California Endowment Center in Los Angeles. In its continuing efforts to provide the community with information about autism, and to expand its research par-



ticipation opportunities to underrepresented groups, CART was invited to attend the conference and participate as one of the exhibitors. **CART Intern, Alexandra Lopez de Portillo, represented CART at the event**. Alexandra is interning this year with CART's director of operations and outreach, Dr. Candace Wilkinson, and as-

sists with CART research administration and educational outreach programs. Given that the Latino community is the largest minority group in Los Angeles, Ms. Lopez de Portillo's participation in the event as a bilingual (Spanish/ English) speaker opened a window for all monolingual Latino families who attended the event and were seeking more information about autism and CART's programs.

As Alexandra explains:

"There is a great need for autism programs and research opportunities for monolingual Spanish speakers. Many of the attendees at the Fiesta Educativa event expressed their desire to be included in research studies, clinical evaluations and educational events."

Currently, such opportunities are limited for the Latino community, and the ones that exist, are often restricted to bilingual families. Therefore, Dr. Wilkinson has been encouraging CART researchers to develop the necessary translation and validation of key autism assessment tools used in research studies so that, hopefully in the near future, CART can extend its research participation opportunities to monolingual Spanish-speaking families.

(From L to R) Irene Martinez, Fiesta Educativa Executive Director; Alexandra Lopez de Portillo, UCLA CART intern, and Angelica Herrera, Fiesta Educativa Parent Coordinator



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Help us solve the puzzle of autism



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PLEASE VISIT OUR WEBSITE:

ww.autism.ucla.edu

Support Autism Research

You may make an online gift to CART at https://giving.ucla.edu/cart or at the CART website's home page (to access the donation form). If you would like more information about making a gift to CART (Fund #618040), please contact: Alan Han, Director of Development for Neuroscience



CART thanks The Martha J. Weiner Charitable Foundation for its generous support.



The establishment of UCLA CART in 2003 marked an exciting advancement, particularly for the new and upcoming generation of autism researchers. Since then, CART has concentrated its efforts, developing strong collaborations across disciplines and making major scientific breakthroughs to clarify the mechanisms underlying autism and related disorders. CART has also led the field in designing evidence-based treatment interventions. Your support will help UCLA CART continue as well as expand its research, training, and community outreach activities to improve the lives of countless children and their families affected by autism spectrum disorders.





AUTISM Treatment - Clinical Resources at UCLA:

Details and full contact information for the following clinical programs can be found at the websites listed below (with links):

Autism Evaluation Clinic

310-794-4008

Early Childhood Partial Hospitalization Program

310-206-2695

ABC Program for the Enhancement of Achievement,

Behavior, and Cognition

310-825-9989 (ACCESS Center)

Parenting and Children's Friendship Program

310-825-0142

PEERS program for Teens & Young Adults

310 26-PEERS (310-267-3377)

PEERS is generously supported by the Shapell Guerin Family Foundation.



CALL 310-267-CART (267-2278) to see if you are eligible to participate in any of our ongoing research studies

Editor: Candace J. Wilkinson, Ph.D.

