On Sunday, November 16, 2014, the Seaver Autism Center hosted the 18th Annual Advances in Autism Conference. Attended by researchers, healthcare professionals, educators, and family members, the goals of the conference were to teach participants about recent advances in understanding the causes of autism, brain development in people with autism, and current treatments of autism. There was an energy in the audience as participants gained new knowledge and discussed new ways in which people with autism can be cared for and helped.

“It was a wonderful day and I learned a lot,” remarked one participant. Another participant said, “Thank you to each of the presenters for sharing their wealth of knowledge and expertise.”

Joseph Buxbaum, PhD, Director of the Seaver Autism Center, opened by saying, “As always, it is an honor to host this conference.” He added, “We hope by bringing together researchers, educators, advocates and families, we can advance the field of autism research and treatment.”

In addition to the Scientific Presentations and Keynote Presentation, Hirschell E. Levine, Esq., Co-Trustee of the Seaver Foundation, and Jamie Roitman, sibling of an adult with autism, gave Opening Remarks during the morning and afternoon sessions.

Continued on page 2

18th Annual Advances in Autism Conference Highlights

Autism Spectrum News Leadership Awards

At the 2nd Annual Leadership Awards Reception hosted by Autism Spectrum News on December 4, 2014, Joseph Buxbaum, PhD, and Alison Singer, Chair of the Seaver Autism Center Associates Committee and President of the Autism Science Foundation, received the “Beacon of Hope Award in Scientific Research.” This event celebrates “leaders making a difference in the autism community,” and Dr. Buxbaum was honored for his “vital research in genetics and neurobiology that has led to an increased understanding of the cause and treatment of autism spectrum disorders.” “It was wonderful to see the Seaver Center honored for the huge impact it has on the lives of children with autism and their families,” said Alison Singer, “and a great honor for me to be recognized alongside Dr. Buxbaum.”
Scientific Presentations

▶ “GENETIC ANALYSES AND NOVEL THERAPEUTICS IN ASD”
JOSEPH BUXBAUM, PhD
DIRECTOR, SEAVER AUTISM CENTER
Dr. Buxbaum gave a brief summary of autism genetics, and he explained the benefits to patients, families, and society that can come from discovering the etiology for a neurodevelopmental disorder. He also shared ongoing autism spectrum disorder (ASD) gene discovery in the Autism Sequencing Consortium (See page 4 for more), explaining that, “80% of autism risk is contributed by genes,” and he summarized ongoing work being done by Seaver Autism Center researchers on Phelan-McDermid Syndrome. Participants thoroughly appreciated his overview on the genetics of autism and described his presentation as “brilliant, clear, concise, and interesting.”

▶ “CURRENT TRENDS IN THE PHARMACOLOGICAL TREATMENT OF AUTISM”
ALEX KOLEVZON, MD
CLINICAL DIRECTOR, SEAVER AUTISM CENTER
After summarizing symptom domains and associated features of ASD, Dr. Kolevzon explained how novel therapeutics are developed. He explained the heterogeneous nature of ASD and current treatment trends for fragile X syndrome, Rett Syndrome, and Phelan-McDermid Syndrome. Conference attendees felt his presentation was excellent, and one participant expressed her appreciation for Dr. Kolevzon’s “ability to communicate very complicated concepts in a way that all can understand.”

▶ “DEVELOPMENT OF THE SOCIAL BRAIN: WHAT HAVE WE LEARNED AND WHAT IS ON THE HORIZON?”
BOB SCHULTZ, PhD
DIRECTOR, CENTER FOR AUTISM RESEARCH AT THE CHILDREN’S HOSPITAL OF PHILADELPHIA
Dr. Schultz’s presentation began with an explanation of the social motivation theory of autism, and he described the social communication difficulties present in autism. He also explained the heterogeneity of autism as it applies to brain development. A participant remarked, “When you are involved in research and not client-facing, disorders have a tendency to become about numbers and diagnoses rather than people. The videos Dr. Schultz displayed put faces on the disorder and touched me very profoundly.”

Keynote Presentation

▶ “RAISING CUBBY”
JOHN ELDER ROBISON
NEW YORK TIMES BESTSELLING AUTHOR OF LOOK ME IN THE EYE AND RAISING CUBBY
Described by one participant as, “impactful, honest and forward-thinking,” Mr. Robison’s presentation was very engaging, and one participant stated, “Robison was brilliant, funny, honest, entertaining, touching, inspiring, hopeful. I learned a lot and his lecture made me think differently about my approaches with my family, the arrangement of society and how we educate our children, why vocational skills are frowned upon, and our responsibilities to our children as parents and educators.”

▶ PANEL DISCUSSION

L-R: John Elder Robison; Bob Schultz, PhD; Alex Kolevzon, MD; Joseph D. Buxbaum, PhD
Seaver Foundation Site Visit

At this year’s annual Seaver Foundation Site Visit in November, the trustees of the Seaver Foundation, Hirschell E. Levine, Esq., and John D. Cohen, Esq., graciously contributed $1.16 million in addition to the Foundation’s annual pledge and support of faculty, postdoctoral, and graduate Seaver Fellowships. Kenneth Davis, MD, Chief Executive Officer and President of the Mount Sinai Health System, was present to receive this generous gift, which is earmarked for recruiting additional top faculty for the Seaver Autism Center. “On behalf of everyone here at the Seaver Autism Center,” Joseph Buxbaum, PhD, Director of the Seaver Center, said, “we are beyond grateful to the Foundation for this additional gift, and their ongoing support and generosity.”

If you would like to support active research and programs at the Seaver Autism Center, please visit www.seaverautismcenter.org or call 212-241-0961.

Satellite Event at the Society for Neuroscience Meeting

At the annual Society for Neuroscience Meeting in Washington, DC, Joseph Buxbaum, PhD, co-organized the scientific programming for a satellite event entitled “Synaptopathies in neurodevelopmental disorders: SHANK mutations as a window into synaptic function.” The meeting focused on SHANK3 genetics, model system, and clinical research.

The SHANK3 gene is key to the development of the human nervous system, and loss of SHANK3 can impair how the nervous system develops and functions. Phelan-McDermid syndrome (PMS) is a rare genetic syndrome in which the q13 portion of chromosome 22, which contains the SHANK3 gene, is missing or otherwise mutated. Loss of one copy of SHANK3 is one of the most common monogenic causes of autism, explaining 0.5-2% of ASD cases.

The Phelan-McDermid Syndrome Foundation (PMSF), whose mission is “to improve the quality of life of people affected by PMS worldwide by providing family support, accelerating research and raising awareness,” sponsored and organized the meeting. Geraldine Bliss, Chair of the Research Support Committee for PMSF, said, “We were delighted to have the preeminent scientists in the field discussing topics that spanned the breadth of research related to SHANK3 and PMS. Having scientists come together is an important way of helping to share information and new ideas and of enabling the development of new partnerships that can accelerate the pace of PMS research.” She added, “The symposium also included talks from family members, which set the tone for the meeting and served as a reminder of why we must all work together urgently and diligently.”
Changes in Scores of Genes Contribute to Autism Risk
NEWFOUND GENETIC DIFFERENCES PROVIDE MANY HINTS AT CAUSES

Small differences in as many as a thousand genes contribute to risk for autism, according to a study led by Mount Sinai researchers and the Autism Sequencing Consortium (ASC), and published online in the October 29, 2014 issue of Nature, and in the November 13, 2014 print edition of the journal. The new study examined data on several types of rare, genetic differences in more than 14,000 DNA samples from parents, affected children, and unrelated individuals to dramatically expand the list of genes identified with autism spectrum disorder (ASD).

Assembling by far the largest autism study to date, the international research team collected and analyzed data from 3,871 autism cases and 9,937 controls, including parents or ancestry-matched controls. Founded by Dr. Buxbaum, the ASC was originally funded by the Beatrice and Samuel A. Seaver Foundation and the Seaver Autism Center. The ASC is supported by a cooperative agreement grant to four lead sites funded by the National Institutes of Health (NIH) and the Autism Society of America, together with additional support from the National Human Genome Research Institute (NHGRI). The principal investigators (PIs) are Drs. Joseph D. Buxbaum, Director of the Seaver Autism Center, Mark J. Daly (Broad Institute of MIT and Harvard), Bernie Devlin/Kathryn Roeder (University of Pittsburgh School of Medicine and Carnegie Mellon University), and Matthew State (University of California, San Francisco). Dr. Buxbaum is the communicating PI.

Most of the genes that contribute to autism remain unknown, but the current study increases the number of definitive autism genes almost fourfold to 33, compared to the nine genes most closely tied to risk in recent years by similar studies in several labs. It also identified more than 70 additional, likely ASD genes. These genes are mutated in more than 5% of individuals with autism, signifying a large, relative contribution to risk for a complex genetic disease.

By casting a wider net, the ASC, comprised of researchers from 37 institutions, found that previously unsuspected sets of genes may be involved in ASD risk, including some that control how nerve networks form in the brain.

“The steps we added to our analysis over past studies provide the most complete theoretical picture to date of how many genetic changes pile up to affect the brains of children with autism,” said Dr. Buxbaum, senior author for the Nature study, together with Mark J. Daly, PhD, co-director of the program in Medical and Population Genetics at the Broad Institute of MIT and Harvard. “Beyond autism, we think this work will yield insights into what makes us social beings,” Dr. Buxbaum said.

“While we have very strong findings in these genetic analyses, newfound genetic discoveries must next be moved into molecular, cell and animal studies to realize future benefits for families,” added Dr. Buxbaum. “A study like this creates an industry for years to come, with labs worldwide checking the brain changes linked to each new genetic finding, and searching for drugs to counter them.”

For the first time, the study authors were able to assess the effects of both inherited genetic differences and those that happen spontaneously in the sperm and eggs that go on to form human embryos. While small, rare genetic differences in the top 107 genes were found to confer a relatively large jump in a person’s risk, many more changes in other genes add smaller amounts of risk. According to the authors, the interplay between gene variations, both common and rare, holds the key to understanding autism. Along these lines, the team, by looking at how many times variations occurred in each of the 107 genes, was able to predict that small differences in about 1,000 genes will eventually be found to increase autism risk.

The ASC shares patient data because no single lab has enough to identify obscure genetic patterns scattered across thousands of genomes. The ASC continues to add patients because, so far, the number of risk genes found has steadily increased with the number of patients studied. Its many investigators share samples, data, and ideas before first publishing them in medical journals, a unique level of collaboration that is accelerating discovery.

“The genetics underlying ASD are highly complex and having access to large sample sizes is essential to rooting out the many genetic mutations involved, and the biological mechanisms implicated by those mutations,” said Dr. Daly, also founding chief of the Analytic and Translational Genetics Unit at Massachusetts General Hospital. “This sort of study cannot be done without the collaboration and cooperation we relied on across the consortium.”

The study found that many genetic differences contribute to autism by affecting gene expression (chromatin remodeling and transcription) and the junctions (synapses) that connect nerve cells, as pictured above.