Faculty Spotlight:
Karen J. Parker, PhD

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Associate Professor, Psychiatry and Behavioral Sciences

"We are transforming health outcomes by developing novel tools to detect and treat social impairments in autism and other brain-based disorders."

Humans are Inherently Social. Human social behavior – behavior that influences, or is influenced by, others – is as equally complex as it is important for our health and survival. Disruption of normal social behavior is a hallmark of most brain-based disorders, and in several disorders like autism, abnormal social functioning is the central symptom. Yet, despite the importance of social functioning in humans, our understanding of the neural mechanisms that control social functioning is limited.

The Parker Lab. As director of the Social Neurosciences Research Program, Dr. Karen Parker's principal goal is to better understand the biology of social functioning using an integrative, translational approach. Her lab's behavioral research spans studies of primate social development to studies of social cognition impairments in various clinical populations (e.g., in children with autism; in survivors of hypothalamic-pituitary tumors; in adults with post-traumatic stress disorder.)

Autism: A Core Research Direction in the Parker Lab. Autism is a brain disorder of early childhood onset characterized by pronounced social impairments which can include diminished eye gaze, abnormal facial and emotional processing, lack of perspective taking, and impaired social judgment. These social impairments jeopardize the development of appropriate social skills and the formation of close personal relationships. Despite the growing prevelance of autism (1 in 68 US children) and its societal impact ($236B expended in the US annually), there are currently no laboratory-based diagnostic tests to detect, or effective medications to treat autism's core social challenges.

To address these barriers to scientific progress, Dr. Parker and her multidisciplinary team are pioneering the development of novel primate models that have behavioral and biological features with direct relevance to human autism. In patients, her research aims to identify novel biological "signatures" of autism in human tissues, test promising new medications that improve social abilities, and identify biological predictors of treatment response to determine which children will benefit most from a given medication. Dr. Parker's research program has high potential to rapidly advance scientific knowledge and transform clinical practice. Findings from her research may lead to the development of clinical diagnostic tools and the first effective and personalized therapeutics to treat autism, thereby enhancing quality of life for people with autism and reducing the emotional and financial burden of autism on patients, their family members, and society. Dr. Parker's current research projects include:

Developing the First Valid Animal Models of Autism. It costs at least $1B to bring a new drug to market. One of the reasons for this exorbitant expense is that most "preclinical" research uses rodent species to test the efficacy of new medications. For brain disorders, over 90% of the compounds that appear to be effective in rodent studies fail in human clinical trials. These challenges underscore the tremendous value in developing novel animal models with more reliable biological and behavioral correlates to human disease. To address this issue for autism, Dr. Parker and her team are pioneering the development of several novel monkey models. These efforts include studies of monkeys that exhibit naturally occurring social impairments and those that are genetically engineered to do so. Her team has also created a sophisticated test battery which measures monkey behaviors that have direct relevance to core autism symptoms. This battery is also allowing her team to test which biological measurements most robustly predict monkey test performance to identify the most promising targets for therapeutic intervention. She and her team are optimistic that further development of these monkey models will facilitate the discovery of novel "drugable" targets, provide biological predictors of treatment response, and support creation of a robust therapeutic testing pipeline. Given the genetic relatedness between monkeys and humans, Dr. Parker's monkey findings stand to enhance the success of

subsequent human clinical trials, thereby accelerating development of the first effective medications to improve social functioning in people with autism.

Developing Novel Diagnostic Tools to Detect Autism. Autism is currently diagnosed using behavioral criteria because no robust biomarkers have been identified. Biomarkers are molecules in the body that indicate a disease state, and they improve our ability to more objectively diagnose a disease. Progress in developing accurate laboratory-based diagnostic tests for autism has been hindered by studying biomarkers in blood, which have thus far met with poor results. Because autism is a brain disorder, it stands to reason that studying brain-related tissue samples [e.g., cerebrospinal fluid (CSF) - a fluid that bathes the brain and spine] would enhance the probability of a scientific breakthrough. Indeed, similar approaches to investigating biomarkers in CSF are already being employed with great success in brain diseases such as Alzheimer's and multiple sclerosis. Although opportunities to collect CSF samples are rare, Dr. Parker is leading a multi-site research team that is capitalizing on clinician ordered collection of CSF samples from children with and without autism during medical evaluations. Her team is studying the neuropeptides arginine vasopressin and oxytocin, which are critical for normal social functioning in animals and people, and which are thought to be deficient in some patients with autism. Her team is also employing "hypothesis-independent" assessments of CSF biomarkers using liquid chromatography with tandem mass spectrometry (LC-MS/MS), the most comprehensive method available to quantitatively characterize hundreds of potential protein and peptide biomarkers simultaneously. By combining these two lines of investigation, Dr. Parker hopes to identify a biological "signature" of autism, which would lead to implementation of earlier and more accurate biologically-based diagnostic tests and provide new biological targets for therapeutic development.

Testing Novel Medications to Improve Social Abilities in Children with Autism. There are currently only two medications approved by the Federal Drug Administration to treat autism. However, these medications, both antipsychotics, target only associated symptoms such as irritability, have unfavorable side-effects, and do not treat autism's core social deficits. New medications that improve social abilities in people with autism are therefore urgently needed. For many years, Dr. Parker's laboratory has studied how the neuropeptides arginine vasopressin and oxytocin support normal social behavior. Experimentally reducing the levels of either neuropeptide or their receptors likewise produces social deficits in animal models. In parallel to these animal studies, Dr. Parker's research team has shown that lower oxytocin and vasopressin levels are associated with social impairments in children with autism. Dr. Parker and her team have recently extended this research to human clinical trials which are testing whether intranasal administration of oxytocin and/or vasopressin improve social abilities in children with autism. Dr. Parker and her team are also studying whether they can identify biomarkers that

predict which patients will have a higher likelihood of responding to a certain drug, and therefore identify who will best benefit from treatment.

Brain Tumors: New Research Direction to Identify Drug Targets and Novel Therapeutics. Survivors of hypothalamic-pituitary brain tumors often exhibit pronounced social impairments that adversely impact quality of life. No systematic research, however, has characterized social impairments in these patients or investigated the biological underpinnings of these impairments. Her team of basic scientists and clinicians is performing comprehensive behavioral phenotyping on these patients and testing whether disease-induced disruption to hypothalamic-pituitary signaling pathways implicated in social functioning (i.e., the neuropeptides oxytocin and vasopressin) underlie these impairments. The ultimate goal of this project is to identify "drugable" targets and develop novel therapeutics to enhance social abilities in this patient population.

Biography

Karen J. Parker, PhD is an associate professor in the Department of Psychiatry and Behavioral Sciences and is the director of the Social Neurosciences Research Program. Dr. Parker received her undergraduate degree in Psychology and her PhD in Biological Psychiatry from the University of Michigan and completed her postdoctoral training in Psychiatry Neuroscience at Stanford University. Dr. Parker is also an affiliate scientist at the California National Primate Research Center. She is a recipient of the American Psychological Association's George A. Miller Award, the NARSAD Young Investigator Award, the University of Michigan's Distinguished Dissertation Award, and is a U.S. National Academy of Sciences Kavli Fellow.

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