



PRESS RELEASE

Axial Biotherapeutics Announces the Groundbreaking Discovery of a Biological Link Between the Gut Microbiome and Parkinson's Disease Published in *Cell*

-Caltech researchers and collaborators, led by Axial Scientific Founder Dr. Sarkis Mazmanian, show for the first time that gut bacteria promote hallmark pathology, neuroinflammation and motor dysfunction in a Parkinson's disease mouse model-

BOSTON and Pasadena, CA, December 1, 2016 – Axial Biotherapeutics today announced that researchers from the California Institute of Technology (Caltech) led by Sarkis K. Mazmanian, Ph.D., the company's scientific founder, have discovered a novel biological link between the gut microbiome and Parkinson's disease (PD). In a validated PD mouse model, gut bacteria were shown to promote hallmark disease processes including inflammation of the nervous system and motor dysfunction. The findings suggest that targeting the gut microbiome may provide a new approach for diagnosing and treating Parkinson's disease. The paper titled, "Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease," can be accessed in the current online edition of [Cell](#).

Over the past few years, evidence has accumulated pointing to a critical role of the gut microbiome in human health and disease. In addition, bidirectional communication between the gut and the brain has been implicated in neurological disorders such as anxiety, depression and autism spectrum disorders (ASD). The research published in *Cell* is the first to find that alterations to bacteria in the gut may represent a risk factor for the onset and severity of Parkinson's disease. This finding opens the door for the potential identification of specific gut microbes that may impact PD. In the future, these microbes might be used as a biomarker for disease states, a method to identify patients who might be at-risk for PD and as novel therapeutic targets or microbial-based treatments.

"Our findings provide a completely new paradigm for how environmental factors may contribute to Parkinson's disease and possibly other neurodegenerative disorders. The notion that these diseases may be impacted by pathology in the gut and not only in the brain is a radical departure from conventional research in neuroscience," said Dr. Sarkis Mazmanian, the Louis & Nelly Soux Professor of Microbiology in the Division of Biology and Biological Engineering at the California Institute of Technology and Scientific Founder of Axial Biotherapeutics. "Parkinson's disease is complex and there are several genetic predispositions and environmental risks that play a role,



but we believe our findings shed light on a previously unrecognized and potentially important part of this puzzle.”

Dr. Mazmanian continued, “Gut bacteria in patients with Parkinson’s disease are different from those microbes found in healthy individuals. When we transplanted the microbiome from Parkinson’s patients into mice, we found that symptoms like motor deficits and neuroinflammation were more severe compared to mice harboring gut bacteria from healthy controls. This suggests that there is a fundamental relationship between bacteria in the gut and the disease processes involved in Parkinson’s disease.”

To conduct their experiments, the researchers utilized a mouse model of Parkinson’s disease that overexpresses the human protein, alpha-synuclein. This protein is thought to be central to the disease process of PD. The mice were bred in a germ-free setting, devoid of all microbes. Using the germ-free animals as a platform, the researchers could then investigate how gut bacteria altered disease outcomes in mice. When human gut microbiota from PD patients were introduced into the model system (by fecal microbiota transplants), they were shown to enhance the typical hallmarks of the disease such as motor deficits, inflammation and alpha-synuclein aggregation, compared to microbiota transplants from healthy human donors. The researchers also identified specific microbial metabolites that induce PD-related symptoms in mice. These findings suggest that gut microbes may contribute to, or even cause, PD symptoms in genetically predisposed individuals. The studies were carried out by a multidisciplinary team from Caltech; University of California San Diego; Arizona State University; Chalmers University of Technology, Gothenburg; University of California, Los Angeles; Rush University Medical Center, Chicago and University of Wisconsin-Madison.

“Gut bacteria provide immense physiological benefit, and we do not yet have the data to know which particular species are problematic or beneficial in Parkinson’s disease,” continued Dr. Mazmanian. “It is important to note that there are currently no antibiotic or microbial treatments available for human use that can replicate the effect we observed in mice. However, our next step will be to define the specific gut microbes that may contribute to the development of Parkinson’s disease, as this could translate into novel biomarkers to identify at-risk patients. Additionally, these findings could lead to novel therapeutic approaches that avoid the complications of delivering drugs to the brain and may be safer and more effective.”

“Axial Biotherapeutics will build on these groundbreaking findings and the larger body of work that our scientific founder, Dr. Sarkis Mazmanian, has established in this area. Our goal as a company will be to focus on translating these discoveries into a unique class of microbial-targeted therapeutics that could become breakthrough therapies for a variety of underserved neurological diseases and disorders, including autism spectrum disorder, Parkinson’s and Alzheimer’s disease,” said David Donabedian, Ph.D., Chief Executive Officer of Axial Biotherapeutics.



Axial Biotherapeutics recently launched with a [Series A of \\$19.15 million](#), led by Longwood Fund and Domain Associates, and has executed a license agreement that provides worldwide exclusivity to related intellectual property from Caltech in applications for neurological diseases and disorders.

About Parkinson's Disease

Parkinson's disease is a chronic and progressive movement disorder and a growing medical and social concern, with 1 million in the US affected and more than 10 million people world-wide. Genetic factors do not explain most PD cases, and growing interest in environmental factors has provided some clues as to potential causes or contributors to the disease. Parkinson's involves the malfunction and death of specific nerve cells (neurons) in the brain. As PD progresses, and dopamine-producing neurons die, the amount of dopamine in the brain decreases, leaving a person unable to control movement normally. Primary motor signs of PD include tremor of the hands, arms, legs, jaw and face, bradykinesia or slowness of movement, rigidity or stiffness of the limbs and trunk and postural instability or impaired balance and coordination. Persons with PD often exhibit gastrointestinal symptoms and intestinal pathology that precede motor symptoms by years in some cases, and the idea that disease might originate in the gut was proposed more than a decade ago.

About Axial Biotherapeutics

Axial Biotherapeutics is a biopharmaceutical company harnessing the link between the human gut microbiome and the central nervous system to develop a new class of biotherapeutics to improve the quality of life for people with neurological diseases and disorders www.axialbiotherapeutics.com.

Contacts

MacDougall Biomedical Communications

Kari Watson or Stephanie May, Ph.D.

Direct: +1 781 235 3060 or +49 89 24243494

kwatson@macbiocom.com or smay@macbiocom.com