Scott Roy
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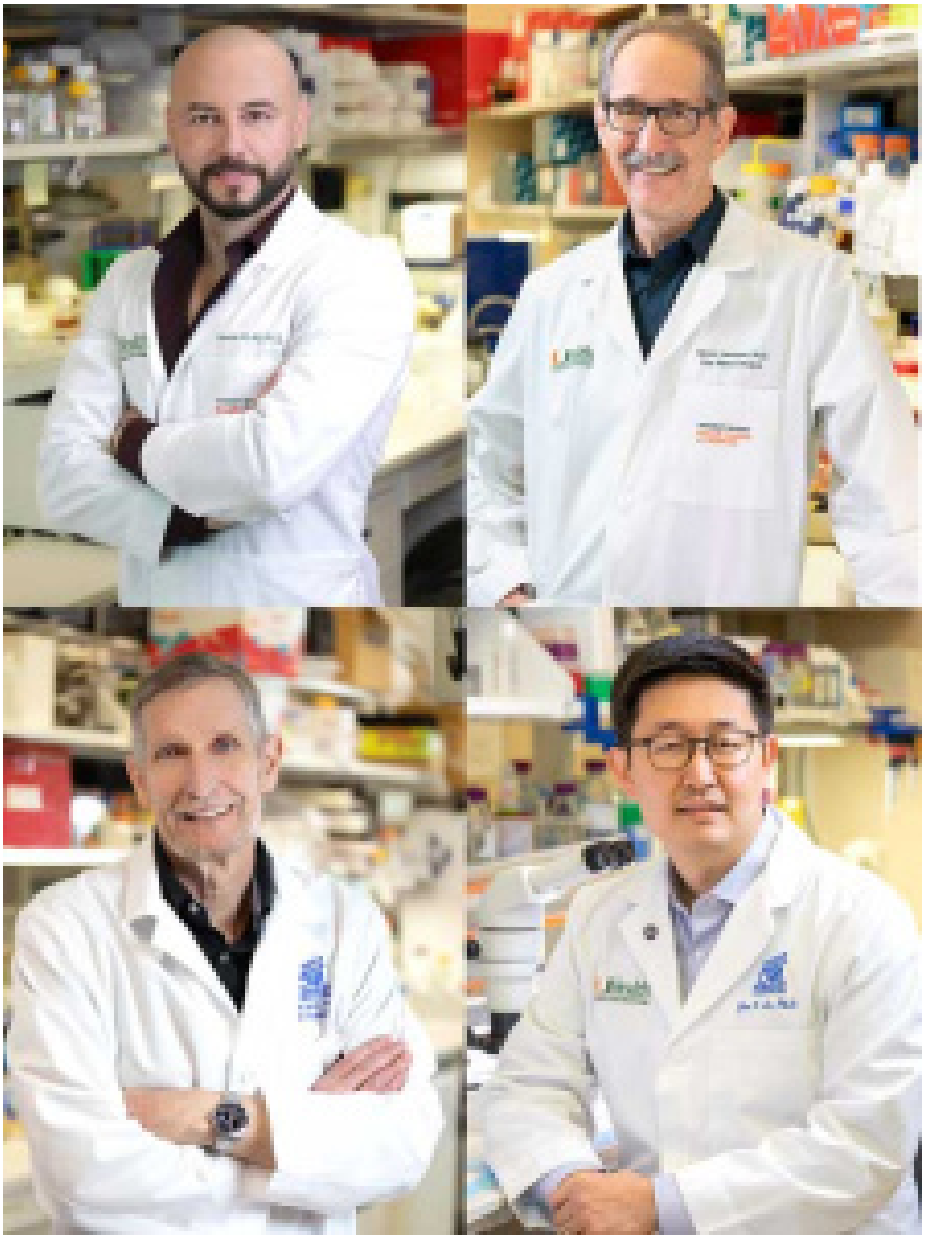
Miami Project Research Team Receives Blueprint Neurotherapeutics Network Grant

A group of researchers from The Miami Project to Cure Paralysis at the University of Miami Miller School of Medicine has received a grant from the NIH/NINDS Blueprint Neurotherapeutics Network to fund investigation of a treatment for spinal cord injury (SCI).

It is estimated that the total value of the award could reach $10 million if all project milestones are met as planned. The University of Miami will retain intellectual property rights for any drugs developed through the Blueprint Network. The grant is in response to the team's proposal, entitled "Developing a kinase inhibitor drug to treat spinal cord injury," and will allow for the optimization of a lead compound, complete pre-clinical development, filing of an Investigational New Drug (IND) application with the FDA, and the execution of a Phase 1 clinical trial.



Clockwise from top left, Hassan Ali, Ph.D., M.S.M.; Vance Lemmon, Ph.D.; Jae K. Lee, Ph.D.; and John Bixby, Ph.D.

“Given pharma’s current reluctance around early-stage drug development for neurological indications in general, and spinal cord injury specifically, this funding program constitutes a lifeline that will allow us to de-risk our therapeutic candidate, creating a viable path toward

regulatory approval that may not exist," said principal investigator Hassan Ali, Ph.D., M.S.M., research assistant professor in the Departments of Neurological Surgery and Medicine, and The Miami Project.

Promoting CNS Axon Regeneration

The research is based on the use of novel phenotypic screening and machine learning approaches that have identified a series of compounds that strongly promote CNS axon regeneration. The other researchers include John Bixby, Ph.D., professor in the Departments of Molecular and Cellular Pharmacology and Neurological Surgery; Vance Lemmon, Ph.D., the Walter G. Ross Distinguished Chair in Developmental Neuroscience, and professor in the Department of Neurological Surgery; Jae K. Lee, Ph.D., professor in the Department of Neurological Surgery; and Alberto Martinez-Arizala, M.D., clinical associate professor in the Departments of Neurology, Neurological Surgery, and Orthopedics and Rehabilitation Medicine, all of whom are also affiliated with The Miami Project.

"I'm immensely grateful to the talented team at The Miami Project who make all of this possible – especially Drs. Lemmon and Bixby, who have laid the scientific foundation for us to build upon," Dr. Ali said.

The researchers have validated the in vivo efficacy of these compounds using multiple animal models of SCI, where the compounds consistently promoted axon regeneration as well as behavioral recovery.

Potential Benefit to Millions

"This support is so very important for the translation of a

novel treatment that could potentially benefit millions of individuals living with disabilities associated with SCI and other neurological disorders. Congratulations to Drs. Ali, Bixby, and Lemmon, and their collaborators on this most exciting development," said W. Dalton Dietrich III, Ph.D., the scientific director of The Miami Project.

This application addresses the critical need for a therapeutic to promote axon growth after spinal cord injury. Axon regeneration in the central nervous system (CNS) is limited due to both the absence of intrinsic regenerative capacity in adult CNS neurons, and the extrinsic inhibitory microenvironment confronting damaged axons. The team has shown that a small molecule kinase inhibitor can promote robust neurite outgrowth in vitro and axon regeneration in SCI rodent models, as well as functional recovery. The axon growth is due primarily to the kinase inhibitor's ability to inhibit both pathways, which target intrinsic and extrinsic axon growth repression.

The project will use the Blueprint Neurotherapeutics Network program to design and screen molecules for improved potency, stability and safety profiles, confirm target engagement in vitro and in vivo, and demonstrate efficacy in two rat injury models as part of the IND preparation.

The Time Is Right

"Dr. Lemmon and I participated in this innovative NINDS translational program way back at its inception in 2011, but we did not have the right therapeutic candidate in our pipeline," Dr. Bixby said. "More important, we did not have Dr. Ali leading our team. We believe that the strength of our current scientific program, combined with the wonderful team

that has been assembled, gives us an excellent chance to move this candidate forward."

Added Dr. Lemmon, "Third time's the charm. Our team submitted a proposal to the Blueprint Neurotherapeutics Network program three times over three years. Our persistence allowed us to cross the threshold into the funding range. This gives us the opportunity to take our kinase inhibitor with remarkable polypharmacology into a program to develop a drug for CNS injury. It's a dream scenario for any scientist and a wonderful example of team science. Thanks to all members of our lab, past and present, whose rigorous science enabled this."

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