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Targeting the innate immune response to improve outcomes after CNS injury

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The innate immune response is the first line against infections and damage. Pattern recognition receptors (PRRs) are components of the innate immune response that recognize danger/damage associated molecular patterns (DAMPs) or pathogen associated molecular patterns (PAMPs). Toll-like receptors (TLRs), NOD-like receptors (NLRs), RIG-like receptors (RLRs) and C-type lectin receptors (CLRs) are PRRs involved in the recognition of DAMPs/PAMPs that trigger an inflammatory response. NLRs form inflammasomes that trigger the activation of caspase-1 and the processing of IL-1β. RIG-I is a RLR involved in the production of type-I interferons, and mincle is a CLR involved in the production of tumor necrosis factor (TNF). Following central nervous system (CNS) injury, such as spinal cord injury (SCI), traumatic brain injury (TBI) or stroke, the inflammasome, RIG-I or mincle are activated as part of the inflammatory response. Therefore, these PRRs can be therapeutically targeted to control the inflammatory response in order to improve outcomes after SCI, TBI or stroke. For instance, delivery of an antibody against apoptosis associated speck-like protein containing a CARD (ASC), an inflammasome component, results in decreased inflammation as well as improved histopathological and functional outcomes after cervical contusive SCI in a clinically relevant model in rodents. Similarly, anti-mincle can be used to inhibit TNF production in neurons in culture following stimulation with SAP130. Taken together, our findings indicate that targeting PRRs can be a successful option that can be used to treat the innate immune response after SCI, TBI or stroke.

Biography

Juan Pablo de Rivero Vaccari obtained his PhD in 2007 from the University of Miami for his work on therapeutically targeting the inflammasome to improve outcomes after spinal cord injury. He then continued his studies on innate immune responses after brain trauma as a Post-doctoral fellow at the Miami Project to Cure Paralysis. He became a Research Assistant Professor in the Department of Neurological Surgery at the University of Miami in 2010. Currently, he works on identifying biomarkers and therapeutic targets in the innate immune response to improve outcomes after central nervous system injury and disease.

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