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Education:

- Postdoc 1998-2003 New York University School of Medicine
- Postdoc 1997 London University, England
- PhD 1996 London University, England
- MSc 1992 Instituto Venezolano de Investigaciones Cientificas
- BSc 1991 Universidad Central de Venezuela

Research Interest:

Cytoskeletal Regulation of Myelin Formation & Repair

Myelin is a specialized membrane, which wraps around axons in the peripheral (PNS) and central (CNS) nervous systems. In diseases such as multiple sclerosis (CNS) and Guillain-Barre Syndrome (PNS), loss of myelin around the nerve cells results in conduction block and underlies the clinical deficit characteristic of these disorders. Remyelination restores nerve conduction and leads to resolution of symptoms. However, there are currently no treatments designed to directly target the efficiency of myelin repair and the return of nerve function. Our studies focus on the role of cytoskeletal signaling and its impact on myelinating glial cell differentiation, a fundamental knowledge that is currently lacking in the field. There are two types of specialized myelin-forming glial cells: Schwann cells (SC) in the PNS, and oligodendrocytes (OL) in the CNS. We have found that a cytoskeletal protein: non-muscle myosin II (NMII) regulates the development of myelinating glial cells. NMII inhibition impairs myelin formation in the PNS, but enhances CNS myelination. Our laboratory uses in vitro and in vivo models to elucidate the mechanisms behind these observations. The long-term goal of our research is to apply this knowledge to help the development of novel therapeutic tools to treat human demyelinating diseases. Two major research projects are currently active in the lab:

1. Ablation of myosin II in oligodendrocytes as a novel mechanism for neuroprotection

Our laboratory has found that mice missing NMII specifically in OL, exhibit enhanced myelin

repair and lesser nerve damage after chemically-induced demyelination. In addition, we also found that pharmacological inhibition of NMII activity protects OL from damage cause by inflammatory stress in vitro. We seek to characterize the cellular and molecular changes brought about by lack of NMII in OL that are responsible for these beneficial effects. To this end, we have developed novel genetic tools and in vitro models that will allow us to examine both the repair and immunomodulatory effects of myelinating glia in pre-clinical models of multiple sclerosis (MS), and the mechanisms that may relate them to the NMII inhibition. This work will yield invaluable knowledge for designing highly targeted and specific interventions to reverse demyelination in patients with MS.

2. Mechanical properties of the injured CNS and its implications for remyelination and axonal repair

Chronic MS is characterized by lesions in the brain and spinal cord that are stiffer than healthy tissue. Our workhas shown that OL do not develop normally when they are grown in high-stiffness conditions, similar to those they might encounter in chronic MS. However, both the effect of mechanical forces on OL development as well as how the mechanical properties of brain tissue change during MS have not been well-studied. This lack of knowledge means that we may not be able to accurately predict how healthy OL transplanted into the brain of an MS patient will behave when they encounter an area of the brain with abnormal mechanical properties. The primary goal of this project is to use atomic force microscopy (AFM), a technique that allows very accurate and detailed measurements of tissue stiffness, to examine the mechanical properties of MS tissue from human donors as well as brain tissue from animal models of demyelination. This work could help with therapies involving the transplantation of stem-cell derived OL to promote myelin repair, since data on how tissue stiffness changes in MS and how that affects OL differentiation can be used to maximize the success of such transplants.

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