Work in Prof Carmen Melendez's lab on Myelin regeneration was recently featured in an article on MS (Multiple Sclerosis) from the Department of Defense..

The article is included below. For the entire DOD brouchure **click here**



Carmen Melendez-Vasquez, Ph.D.

## Promoting Myelin Formation via Manipulation of Oligodendrocyte Cytoskeleton

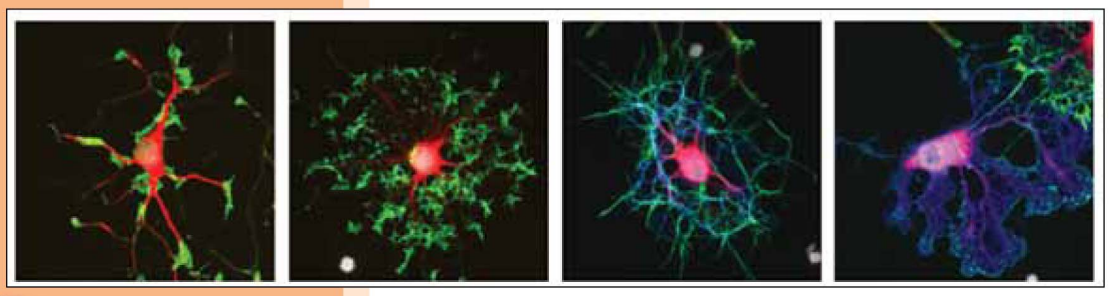
**Carmen Melendez-Vasquez, Ph.D., City University of New York, Hunter College**

MS is characterized by an autoimmune attack on myelin sheaths, causing demyelination of the axons and subsequent disruptions in nerve transmission. Myelin repair is mediated by oligodendrocytes, which are cells responsible for myelin production. Oligodendrocyte progenitor cells (OLPs) are recruited into areas of MS lesions and differentiate into mature oligodendrocytes, which remyelinate the axons and restore nerve function. However, oligodendrocyte differentiation and remyelination become less efficient over the course of the disease, leading to cumulative damage to the central nervous system. The underlying mechanisms of myelin repair inhibition are largely unknown.

Previously, Dr. Carmen Melendez-Vasquez found that myosin II (a key regulator of cellular actin assembly and contractility) activity of OLPs inversely correlated with the ability to differentiate and produce myelin. While differentiating into mature oligodendrocytes, OLPs' actin cytoskeleton undergoes extensive remodeling, including extension of multiple branches that eventually give rise to myelin-producing structures. Myosin II is largely responsible for controlling this cytoskeleton remodeling and does so by responding to the mechanical properties of the cell's microenvironment (i.e., the extracellular matrix [ECM]). Due to scar tissue formation, ECM of MS lesions tends to be stiffer and less elastic than that found in normal brain tissue. Dr. Melendez-Vasquez hypothesizes that the stiffness of the ECM in MS lesions may be inhibiting OLP differentiation and remyelination in a myosin II-dependent manner.

With support from an FY10 MSRP Concept Award, Dr. Melendez-Vasquez first assessed whether ECM stiffness affects the cytoskeletal changes required for OLP differentiation in vitro. Results demonstrated that OLPs grown in soft (i.e., normal brain-like) ECM more readily formed cytoskeletal branches and produced more myelin basic protein than OLPs grown in stiff (i.e., MS lesion-like) ECM, indicating that ECM stiffness indeed plays a significant role in OLP differentiation and myelin repair.

Next, Dr. Melendez-Vasquez assessed whether myosin II inhibition can promote OLP differentiation and remyelination of induced focal demyelinating lesions in mice engineered to lack myosin II in their oligodendrocytes. Interestingly, evidence of remyelination was observed as early as 7 days after injury. Encouraged by these results, Dr. Melendez-Vasquez is extending her studies into inflammatory models that more closely resemble MS pathology. Results of her work may lead to novel therapeutic strategies for promoting neuroregeneration and myelin repair in MS patients.



A composite showing the development of oligodendrocyte progenitors in culture from less mature (left panel) to mature (right panel). This sequence shows very nicely the changes in the cytoskeleton of the cells. Red: tubulin, green: actin, blue: myelin basic protein, and white/grey: nuclei.

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