Research from the laboratory of Dr. Muro has led to a significant advancement in understanding the delivery of nanomedicines

Research from the laboratory of Dr. Silvia Muro (UM IBBR/BIOE) has led to a significant advancement in understanding the delivery of nanomedicines via a specific endothelial cell pathway. The group recently published the findings, titled “Intercellular Adhesion Molecule 1 (ICAM-1) Engagement Modulates Sphingomyelinase and Ceramide, Supporting Uptake of Drug Carriers by the Vascular Endothelium”, in the journal *Arteriosclerosis, Thrombosis, and Vascular Biology*, an internationally renowned, peer-reviewed scientific journal that has the one of the highest impact factor values for a Peripheral Vascular Disease category journal that publishes original research. The research described in this publication is lauded in an editorial published in the same issue by Dr. Gregory Lanza of Washington University Medical School. Lanza suggests the significance of the findings in the title of his article as “Nature’s Doorway to the Extravascular Tissue Realm”. Daniel Serrano, who is the first author on this publication and a graduate student in Dr. Muro’s lab, is a PhD candidate the Molecular and Cellular Biology Concentration Area of the Biological Sciences Graduate Program at the University of Maryland.

This publication focuses on the regulatory link between specific elements that are involved in endocytosis through ICAM-1. One of the greatest challenges to success of nanomedicine technologies has been that the transport of nanomedicines injected in the circulation across endothelial cells in the vasculature, so that they can be efficiently transported into tissues. Dr. Muro’s group has achieved this using cell adhesion molecule (CAM)-mediated endocytosis, a transport pathway that is reminiscent of the mechanism by which leukocytes travel from the bloodstream into tissues, which remains relatively uncharacterized. In fact, the development of approaches to achieve targeted drug delivery from the circulation into tissues represents one of the “Holy Grails” of modern medicine. In order to achieve the goal to develop more effective treatments, there is the imminent need to expand our understanding of the regulatory pathways essential to the uptake and transport of therapeutics. The research published by Dr. Muro’s group revealed a novel role for a specific lysosomal enzyme, acid
sphingomyelinase (ASM) and the sphingomyelin/ceramide pathway in this process. These data suggest that endothelial cells can internalize and transport relatively large drug carriers that are targeted to ICAM-1. These results will advance current knowledge on the regulation of CAM-mediated endocytosis related to leukocyte extravasation and in the long term, may provide new tools for modulation of drug delivery therapies.

In addition to this research on ICAM-mediated endocytosis, the research in Dr. Muro’s laboratory focuses on other mechanisms of endocytic vesicular transport, including their role in physiology and disease and their translational application for the controlled delivery of nano-scale therapeutics. The research in Dr. Muro’s lab is sponsored by grants from the National Institutes of Health and the American Heart Association.