Characterization of novel interactions with plasma membrane NEU1 reveals new biological functions for the Elastin Receptor Complex in vascular diseases

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Remodeling of elastin during pathophysiological vascular aging leads to the production of elastin-derived peptides (EDP), also known as elastokines. These peptides trigger biological effects through the elastin receptor complex (ERC). Data from the last decade have brought significant insights on the critical role played by its catalytic subunit, Neuraminidase-1 (NEU1), in the biological effects mediated by EDP in vascular and metabolic diseases. We recently developed a proteomic approach dedicated to the purification and identification of membrane NEU1-associated protein complexes in human macrophages and identified several promising candidates (Kawecki et al, CMLS. 2019). Here, we validated and characterized two novel interactions with NEU1 in human monocytes and endothelial cells involving the β2 integrin and ICAM-1, respectively. We show that binding of EDP to the ERC leads to desialylation of monocyte β2 integrin and endothelial ICAM-1 through membrane NEU1. Importantly, desialylation of either monocyte β2 integrin or endothelial ICAM-1 by EDP is sufficient to potentiate monocyte adhesion to a monolayer of endothelial cells.

In conclusion, these results demonstrate, for the first time, that binding of EDP to the ERC modulates the sialylation levels of monocyte β2 integrin and endothelial ICAM-1 through NEU1, and highlight that EDP and the ERC may be important regulators of circulating monocytes recruitment to inflamed vascular sites through this sialidase. By its ability to interact with and to modulate the sialylation of key membrane glycoproteins through NEU1, new biological functions are anticipated for EDP and the ERC in vascular diseases involving elastic fibers and elastin degradation.

Biography

Dr Pascal MAURICE, 44 years old, is Senior Scientist at the UMR CNRS/URCA 7369 MEDyC located at Reims, France. He is working in Team 2 "Matrix Aging and Vascular Remodeling". After a PhD in the field of vascular biology and thrombosis, he performed a post-doc training in the field of GPCR and GPCR interactomics. To date, his track-record is 50 publications (ORCID ID:0000-0003-2167-4808). At present, he is working on extracellular matrix remodeling during pathophysiological vascular aging and the role of sialidases.