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

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Abstract

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 β_2 integrin and ICAM-1, respectively. We show that binding of EDP to the ERC leads to desialylation of monocyte β_2 integrin and endothelial ICAM-1 through membrane NEU1. Importantly, desialylation of either monocyte β_2 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 β_2 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.

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Biochemistry is both life science and a chemical science - it explores the chemistry of living organisms and the molecular basis for the changes occurring in living cells. It uses the methods of chemistry,

"Biochemistry has become the foundation for understanding all biological processes. It has provided explanations for the causes of many diseases in humans, animals and plants."

physics, molecular biology, and immunology to study the structure and behaviour of the complex molecules found in biological material and the ways these molecules interact to form cells, tissues, and whole organisms.

Biochemists are interested, for example, in mechanisms of brain function, cellular multiplication and differentiation, communication within and between cells and organs, and the chemical bases of inheritance and disease. The biochemist seeks to determine how specific molecules such as proteins, nucleic acids, lipids, vitamins, and hormones function in such processes. Particular emphasis is placed on the regulation of chemical reactions in living cells.

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