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Design of small synthetic molecules that mimic IL-4 binding to IL-4Rα, which therefore promotes alternate macrophage differentiation (M2) with minimal effect on the endothelial and vascular IL-4Rα

Murad H Al-Salamat
Jordan University of Science and Technology, Jordan

An essential step in atherosclerosis progression is the infiltration of monocytes to the sub-endothelial space of arteries where they differentiate into M1 phenotype (the classical pathway) or M2 phenotype (the alternative pathway), where polarization depends mainly on the environmental cytokines. Macrophages play an imperative role in foam cell formation that ends up with plaque rapture and thrombosis, which are all mediated by secreted inflammatory factors, proteolytic enzymes, and other factors produced mainly by M1 phenotype. M2 or known as the Anti-inflammatory pathway driven by IL-4, and IL-13; shows great ability to suppress the progression of atherosclerosis. However, IL-4 displays pro-atherogenic action that may account for its effects on the endothelial cells by increasing the expression of P-selectin, 15-lipoxygenase, VCAM-1, and matrix metalloproteinase 1 (MMP-1). We have designed small synthetic molecules that mimic IL-4, where it binds to IL-4Rα specifically to induce M2 macrophage polarization and M1 transformation into M2, meanwhile with minimal active endothelial and vascular smooth muscle IL-4Rα. We rely on a series of amino-acids to induce this expected activation on the macrophage, and on lipophilicity as well to enhance the targeting macrophage IL-4Rα and M1 transformation, as the M1 phenotype is predominately found in the lipid core of the atherosclerotic plaque.

Biography

Murad Al-Salamat is a Pharm D. at Jordan University of Science and Technology/King Abdullah University Hospital. He has received a royal award for his bachelors with various awards and funds for his researches and projects from different organization, such as King Abdullah II Fund and Development (KAFD). He has worked in Jordan Hospital as clinical pharmacist and then at the Princesses Haya Biotechnology Center (PHBC) on signal transduction and molecular genetics. He has also worked with a research team in the Pharmaceutics Research Unit (PRU). Murad has participated in several local, regional, and international conferences, as well as having publications on signal transduction, and molecular pharmacology.

mhms_just@yahoo.com