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Macrophage NOS1 -derived nitric oxide controls foam cell formation and endothelial dysfunction in atherosclerosis

Anjali Roy

Indian Institute of Technology Indore, India

Abstract

Atherosclerosis, the cause of coronary artery disease, myocardial infraction, stroke, and peripheral artery disease, is an inflammatory disease. It involves the formation of lesions in the arteries that are characterized by inflammation, foam cell formation, cell death, and fibrosis. Macrophages, the major immune cell population in lesions, have been shown to play critical roles in all stages, including the initiation and progression of advanced atherosclerosis. The mechanisms that drive initial atherosclerotic lesion/ plaque building remain largely unknown. An increased understanding of the process of macrophage foam cell formation will help to develop novel therapeutic interventions for atherosclerosis.

We studied the role of nitric oxide synthase 1 (NOS1) -derived nitric oxide (NO) on Oxidized low-density lipoprotein (OxLDL) uptake by bone marrow-derived macrophages (BMDMs). Pharmacological inhibition of NOS1 significantly reduces the OxLDL uptake by BMDMs. Also, the proinflammatory cytokine expression was significantly reduced in the presence of specific NOS1 inhibitors. One of the important observations revealed that OxLDL stimulation resulted in an increase of CD36 expression in macrophages, implying a feed-forward loop for foam cell formation. Further, we demonstrate that macrophage NOS1-derived NO has a role in endothelial junction permeability.

Thus, this is a novel study involving NOS1 as critical players of foam cell formation and would reveal much about the critical molecular proteins involved in atherosclerosis. Therefore, targeting macrophage NOS1 and its regulated signaling proteins would be a useful strategy in reducing foam cell formation and dampening the atherosclerosis progression.

Biography:

Anjali Roy is pursuing her Ph.D. from the Indian Institute of Technology (IIT) Indore, a premier educational organization. She has published 8 papers in reputed peer-reviewed journals and has been serving as an active member of the International Academy of Cardiovascular Science and Indian society of Atherosclerosis research. She is an awardee of many best poster presentation awards including prestigious N S Dhalla Best Poster Award. During Ph. D., her work mainly focused on understanding the role of NOS1 derived nitric oxide in macrophage polarization and macrophage foam cell formation. She also studies inflammatory mediators in regulating endothelial junction and permeability, leading to endothelial dysfunctioning. Using computational techniques, she screened various drugs to be repurposed as anti-inflammatory molecules and checked the efficacy of drug employing in-vivo mice models in the study. She believes that her research interest focuses on improving global health and discovering novel therapeutics against cardiovascular disease and sepsis.

Speaker Publications:

1. "Potential therapeutic targets for inflammation in toll-like receptor 4 (TLR4)-mediated signaling pathways"; International Immunopharmacology / 2016 / Vol 40, Pages: 79-89.

2. "Heterotrimeric complex of p38 MAPK, PKCδ, and TIRAP is required for AP1 mediated inflammatory response"; International Immunopharmacology/ 2017/Vol 48/Page: 211-218.

3. "Repurposing Thioridazine (TDZ) as an anti-inflammatory agent"; Scientific Reports/ 2018.

4. "Macrophage neuronal nitric oxide synthase (NOS1) controls the inflammatory response and foam cell formation in atherosclerosis"; International Immunopharmacology/2020/ Vol 83/106382.

5. "Tumor-derived exosomes in the regulation of macrophage polarization"; Inflammation Research / 2020, Vol 69/ Pages 435-451.

3rd International Conference on Cardiovascular Diseases and Therapeutics; Paris, France- April 01-02, 2020.

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