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Trained immunity in monocytes from atherosclerotic patients is associated with increased mitochondrial activity and intracellular cholesterol level

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Abstract

Training of circulating monocytes could be responsible for the formation of chronic inflammation in arterial wall. We evaluated the ability of circulating monocytes isolated from the blood of atherosclerotic patients to activation and tried to find responsible factors.

The study involved healthy donors (N=36) and patients with subclinical atherosclerosis (N=40) diagnosed by ultrasonographic measurement of intima-media thickness of common carotid arteries (cIMT). Monocytes were isolated by magnetic CD14+ separation and incubated with 1 ug/ml of LPS for 24h followed by TNF secretion measuring by ELISA. In parallel, intracellular cholesterol level of circulating monocytes was evaluated using AmplexRedCholesterol Kit. Monocytes were also incubated with 100 ug/ml of 5-aminolevulinic acid for 4h to induce protoporphyrin IX (PpIX) accumulation. Fluorescence of PpIX and potential-dependent Mitotracker dye were visualized by confocal microscopy and analyzed with ilastic Software.

The secretion of TNF was significantly increased in LPS-stimulated monocytes isolated from the blood of atherosclerotic patients compared to healthy participants. The strong correlations of TNF secretion and intracellular total cholesterol level with cIMT were observed indicating that monocytes from atherosclerotic patients have increased inflammatory state as well as increased total cholesterol content. Surprisingly, secretion of TNF by LPS-stimulated cells and cIMT had significant correlation with monocyte Mitotracker/PpIX ratio indicating that trained monocytes of atherosclerotic patients are characterized by higher mitochondrial activity.

We've demonstrated that immunologically trained monocytes circulating in atherosclerotic patients with increased cIMT are characterized by increased intracellular total cholesterol level and mitochondrial activity.

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Biography

Nikita Nikiforov is as a PostDoc working in Institute of General Pathology and Pathophysiology, Laboratory of Angiopathology, Moscow, Russian Federation.

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