

ABSTRACTS

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NOD2 AGONIST PROMOTES THE PRODUCTION OF INFLAMMATORY CYTOKINES IN VSMC IN SYNERGY WITH TLR2 AND TLR4 AGONISTS

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Objectives To investigate the expression of nucleotide-binding oligomerisation domain 2 (NOD2), an intracellular pathogen-pattern recognition receptor, in human vascular smooth muscle cells (VSMC), and the role of NOD2-mediated innate immune signalling pathway in the production of inflammatory cytokines in VSMC. We also explore the possible interaction of NOD2-mediated signalling pathway with those mediated by Toll like receptor 2 and 4 (TLR2 and TLR4) in the production of inflammatory cytokines in VSMC.

Methods Human coronary artery smooth muscle cells were stimulated with NOD2 agonist Muramyl dipeptide (MDP) alone or in combination with either TLR2 agonist Pam3CSK4 (PAM3) or TLR4 agonist lipopolysaccharides (LPS). The mRNA expression of NOD2 and fibroblast growth factor-2 (FGF-2) were measured by RT-PCR assay. The concentration of interleukin-8 (IL-8) and tumour necrosis factor- α (TNF- α) in the culture supernatants was determined by ELISA. VSMC proliferation ability was analysed by the MTT assay.

Results MDP can up-regulate the expression of NOD2 mRNA in VSMC in a time-dependent manner, up-regulate the expression of FGF-2 mRNA in VSMC, induce the production of IL-8 and TNF- α , and increase the proliferation ability of VSMC. Additionally, MDP can synergy with LPS and PAM3 to increase the proliferation ability of VSMC and induce the production of IL-8 and TNF- α .

Conclusions The activation of NOD2 mediated innate immune signalling pathway can increase the proliferation ability of VSMC and induce the production of inflammatory cytokines in VSMC. It is also shown a synergistic effect between TLR2 and TLR4 mediated signalling pathways in this process.



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