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The role and mechanism of $K_{Ca}3.1$ channels in human monocyte migration induced by palmitic acid

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Abstract

Monocyte migration into diseased tissues contributes to the pathogenesis of diseases. Intermediate-conductance Ca^{2+}-activated K^+ ($K_{Ca}3.1$) channels play an important role in cell migration. However, the role of $K_{Ca}3.1$ channels in mediating monocyte migration induced by palmitic acid (PA) is still unclear. Using cultured THP-1 cells and peripheral blood mononuclear cells from healthy subjects, we investigated the role and signaling mechanisms of $K_{Ca}3.1$ channels in mediating the migration induced by PA. Using methods of Western blotting analysis, RNA interference, cell migration assay and ELISA, we found that PA-treated monocytes exhibited increment of the protein levels of $K_{Ca}3.1$ channel and monocyte chemoattractant protein-1 (MCP-1), and the effects were reversed by co-incubation of PA with anti-TLR2/4 antibodies or by specific inhibitors of p38-MAPK, or NF-κB. In addition, PA increased monocyte migration, which was abolished by a specific $K_{Ca}3.1$ channel blocker, TRAM-34, or $K_{Ca}3.1$ small interfering RNA (siRNA). The expression and secretion of MCP-1 induced