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IMMUNOPROTECTIVE ACTION OF IRISIN – STUDY ON MACROPHAGE RAW 264.7

Agnieszka Irena Mazur-Bialy¹; Ewa Pochea²; Marcin Zarawski³

KEYWORDS: irisin, anti-inflammatory activity, exercise, macrophage, immune defense

Irisin, an adipomyokine secreted mainly by skeletal muscles and by adipocytes, is intensively studied since its re-discovery by Boström et al. in 2012 in the new context as ‘an exercise hormone’⁽¹⁾. Due to an increase of circulating irisin level during physical exercise, it is referred to as the mediator of physical activity⁽²⁾. A growing number of studies indicated its potentially protective action in some metabolic disorders, including obesity-related diseases⁽³⁾. The aim of the present study was to determine the impact of irisin on inflammation generated by macrophages. Different concentrations of irisin (0 - 100 nM) were applied to assess the activity of quiescent and lipopolysaccharide (LPS)-activated murine RAW264.7 macrophages in apoptotic and viability tests as well as migration and adhesion assays. The study analyzed also irisins effect on the expression and secretion of oxidative stress mediators and pro-inflammatory cytokines released by macrophages. The results showed that irisin, by reduction of reactive oxygen species (ROS) and enhancement of heme oxygenase 1 (HMOX-1), and catalase 9 (CAT-9) levels, protects against oxidative stress in a dose-dependent manner. The anti-inflammatory potential of irisin includes the ability to impair macrophages migration via regulation of expression and release ratios of matrix metalloproteinase-9 (MMP-9) and its tissue inhibitor (TIMP-1). The biological activity of irisin, mediated through the TLR4/MyD88 signaling pathway, results in attenuation of the mitogen-activated protein kinases (MAPKs) and phosphorylation of nuclear factor kappa B (NFkB) and finally reduction of pro-inflammatory cytokines expression and secretion, including tumor necrosis factor (TNF), interleukin 1 and 6 (IL-1a, IL-6), C-X-C motif chemokine ligand 1 (CXCL1), monocyte chemoattractant protein-1 (MCP-1) and high mobility group

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box-1 protein (HMGB1). Our study clearly demonstrated that irisin is a promising molecule for the anti-inflammatory treatment of macrophages. In addition to obvious health benefits of regular physical activity, also by modulation of the immune system, we showed that irisin is involved in the reduction of macrophage pro-inflammatory activity and protection from oxidative stress generated by these immune cells.

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