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Redox Biology in the 21st Century: A New Scientific Discipline

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The role of interleukin-6 in redox homeostasis and migration capacity in human trophoblast cells JEG-3 under condition of chemically induced hypoxia

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Highly regulated processes of proliferation, invasion and survival of extrovillous trophoblasts on endometrium and spiral arteries of uterus are crucial elements for successful establishment of placenta. Elevated plasma levels of interleukin-6 (IL-6), the main inflammatory cytokine, during certain stages of gestation has been implicated as a potential risk factor in the development of some pathological forms of pregnancy. The aim of the study was to investigate the possible contribution of increasing elevated concentrations of interleukin-6 in chemically induced hypoxia on physiological dysfunctioning of trophoblasts, and in elucidation of its pathological potential in placental disorders associated with inadequate trophoblastic invasion and survival. Throughout the study, cell viability, migration capacity and the parameters of oxidative metabolism (such as superoxide anion radical and nitrites), were evaluated. IL-6 slightly elevated trophoblast migration capacity in hypoxic condition, while provoking an excessive migration boost in normoxia. The results show that treatment with interleukin-6 maintained cell proliferation ratio, compared to non-treated cells. IL-6 treatment in hypoxic conditions has not induced statistically significant changes in production of superoxide anion radical, in contrast to the reduced values in normoxic cells, implying its potential significant contribution in maintaining of optimal levels of oxidative metabolism in conditions of reduced oxygen availability. The reduction of nitrite levels may also be of physiological significance in reducing of excessive mobility of trophoblasts and inadequate colonization of the endometrium. In condition of chemically induced hypoxia, IL-6 exerted beneficial role on maintenance of cell viability, redox metabolism and migration potential, in contrast to the effects obtained in normoxia where it may affect trophoblast migration and redox balance. Our results suggest that in normoxic, later stages of pregnancy, the elevated levels of IL-6 may have disturbing effects on redox balance and trophoblast migration capacity, making it a possible risk factor in the pathogenesis of certain placental disorders.

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