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## The physiological role of interleukin-6 in placenta and its pathological potential in pregnancy

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Interleukin-6 (IL-6) is pleiotrophic cytokine that has both pro-inflammatory and anti-inflammatory functions. Placentation and pregnancy progression depend on adequate interaction between the processes of proliferation, apoptosis and invasion of trophoblast cells into the endometrium. Various cytokines and growth factors play an important roles in the regulation of these processes, where IL-6 represents one of the major regulatory molecules influencing the trophoblast phenotype. In physiological circumstances, IL-6 is involved in angiogenesis and remodeling of endometrial blood flow, stimulates the production of placental hormones, and is one of the main regulators of inflammation response and immune homeostasis in placenta. Elevated levels of IL-6 are indicated in women with infertility, preeclampsia and placental neoplastic processes. Hypoxic conditions in placenta play a pivotal role in modulating differentiation, invasion and redox homeostasis of trophoblast and also seems to have a significant contribution to IL-6 effects, while IL-6 itself affect oxidative state of trophoblasts, although the mechanisms of these outcomes are yet to be fully understood. Our experiments suggest importance of hypoxic conditions in determining the effects of IL-6 in trophoblasts and differential reactivity of JEG-3 cells in response to this cytokine. Additionally, increased levels of IL-6 in different systemic pathological states induce various disturbances of trophoblast cell homeostasis and could be one of risk factors in development of pregnancy disorders. Recently, increased IL-6 levels are detected in COVID-19 cases, as one of the major actors of the cytokine storm, raising the concerns of infection regarding the effects on placenta and the offspring.