IL-10 expression in macrophages from neonates born from obese mothers is suppressed by IL-4 and LPS-INFγ

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Abstract

Obese women offspring have a higher risk of developing chronic diseases associated with an altered immune function. We aim to determine, in neonatal monocyte■derived macrophages, whether maternal obesity is associated with an altered expression and DNA methylation of pro■ and anti■inflammatory genes, along with a higher pro■inflammatory response. Cord blood from newborns of obese (Ob) and lean (control) women were obtained at delivery. Monocytes were isolated and differentiated into macrophages, in which M1 (LPS/IFNγ) and M2 (IL■4) polarization were assayed. The mRNA levels for TNFα, IL■1β, IL■12A, IL■12B, IL■10, and IL■4R were quantified by qPCR and the DNA methylation of candidate genes determined by pyrosequencing. Results: Ob■monocytes had decreased levels of mRNA for pro■inflammatory cytokines IL■1β, IL■10, and IL■12B compared with controls. Conversely, Ob■macrophages showed increased levels of mRNA for TNFα, IL■4R, and IL■10 compared with controls. M1 response was comparable between both groups, characterized by an important induction of TNFα and IL■1β. In response to an M2 stimulus, control macrophages showed a decreased expression of inflammatory mediators while Ob■macrophages had an additional suppression of the anti■inflammatory mediator IL■10. Changes in IL■1β (monocytes) and IL■10 (macrophages) in Ob■monocytes were paralleled by changes in their promoter DNA methylation in fetal monocytes. These results suggest that monocyte■derived macrophages from obese newborns show a basal anti■inflammatory phenotype with an unbalanced response to M1 and M2 polarization stimuli. The presence of changes in DNA methylation of key inflammatory genes in neonatal monocytes suggests an intrauterine programing of immune function by maternal obesity..

Keywords

DNA methylation, Fetal programming, Macrophages, Maternal obesity, Neonatal monocytes.