Macrophages extracellular vesicles and immune function: a new crosstalk in metabolic disease and related disorders

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Macrophages are critical effectors in inflammation as they can shifth from a pro-inflammatory M1 phenotype to an anti-inflammatory M2 phenotype in response to microenvironmental changes and external stimuli. In this process, a pivotal role is played by bioactive molecules transported by extracellular vesicles (EVs), including microvesicles (MVs) and exosomes (EXOs). Local or systemic inflammation accompany metabolic diseases progression and pathology, like diabetes, in which induction to M1 phenotype macrophages is observed. We hypothesized that the EVs released by glucose-treated macrophages could activate other M0 macrophages to reprogram the phenotype. This hypothesis was verified using an in vitro model of hyperglycemia, in which human THP-1 PMA-differentiated macrophages (M0) were cultered with 15 (MG15 macrophages) and 30 mM (MG30 macrophages) glucose for 24 hours. The EVs secretion by MG15 and MG30 macrophages increased as well as the levels of pro-inflammatory (CD86, MHCII, TLR4, iNOS, NFkB, IL-1β, IL-6, IFNγ, IFNα, TNFα) but not anti-inflammatory (CD163, STAT6, IL-10, CCL17) markers. MG15 and MG30 derived EVs were isolated by differential centrifugation in fraction 1 (MVs enriched-fraction) and fraction 2 (EXOs enriched-fraction) and characterized by electron microscopy and dynamic light scattering. Fraction 1 and 2 of MG15 and MG30 macrophages added to in vitro M0 macrophage for 24 hours induced polarization of M0 macrophage toward M2b like-phenotype. These results hightlight macrophages as pivotal EVs targets for the regulation of inflammation related to hyperglycemia and hightlights the need to define the molecules and the mechanisms involved.