IS HEME A NEW PHYSIOLOGICAL INDUCTOR OF MATRIX METALLOPROTEINASE-2 ? A POSSIBLE LINK BETWEEN THE INFLAMMATORY RESPONSE AND TISSUE REMODELING.

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Matrix metalloproteinases (MMPs) are zinc-dependent proteases that have the capacity to degrade extracellular matrix components. Physiological process such as inflammatory cell migration, wound healing and angiogenesis depend on their activity. Free radicals could affect the activity of MMPs and modulate its expression. Heme is a potent pro-inflammatory molecule, able to induce the activation of human neutrophils and macrophages. Since heme is involved in the generation of oxidative stress by promoting reactive oxygen species (ROS) production in these cells, we sought to investigate whether it would be involved in the secretion and/or expression of MMPs in RAW and DU145 cells. We first treated the different cell lines with heme and then measured the activity of MMPs by zymography. MMP-2 mRNA expression was evaluated by RT-PCR. Heme induced the secretion and synthesis of pro-MMP-2 in a dose- and time-dependent fashion. This induction was blocked by NAC and apocynin suggesting the potential involvement of ROS. To determine whether the heme-induced MMP-2 secretion was associated with activation of NFkB pathway, cells were pre-treated with PDTC and the stimulatory effect of heme was no longer observed. Our results suggest that release of heme due to an injury can increase the expression of MMPs by different cell types, which could in turn, play an important role by promoting tissue remodeling.

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