# 生体侵襲時におけるヘムオキシゲナーゼ-1を介する血栓形成制御機構め解明

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## 生体侵襲時におけるヘムオキシゲナーゼ-1を介する血栓形成制御機構め解明

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| **研究概要** | 【目的】ヘムオキシゲナーゼ(HO)はヘム分解の律速酵素であると同時に、細胞を酸化ストレスかによる傷害から守る細胞保護蛋白である。われわれが経験した世界第一例のHO-1欠損症患者は、持続する発熱、肝腫大、血管内皮傷害による溶血性貧血、DIC様の著明な凝固・線溶系の充進を認め、さらには単球系の機能異常も認めた。そこで、今回の研究は、HO-1が血栓形成阻害に果たす役割を末梢血単球、血管内皮細胞(HUVEC)を用いて、明らかにすることを目的とした。【方法】1)ヘミン単独刺激の影響:HUVECにHO-1誘導剤であるヘミン(100μM)を添加し、2〜8時間培養後HO-1、組織因子(TF)、PAI-1、トロンボモジュリン(TM)の各mRNA量を測定した。2)TNF-α刺激に対するHO-1の効果:HUVECにヘミンを添加した群と添加しない群を作製し6時間培養後洗浄、その後さらにTNF-α(10ng/ml)を添加し0.5〜3時間培養後、HO-1、TF、PAI-1、TMの各mRNA量を測定した。それぞれのmRNAは細胞からtotal RNAを抽出後、リアルタイムPCR法を用いて測定した。【結果】1)ヘミン単独刺激により、HO-1、TF、TM mRNA発現は増加し、PAI-1 mRNA発現は低下した。2)ヘミン刺激群では、非刺激群と比べてHO-1、TM mRNA発現は増加し、TF、PAI-1 mRNA発現は低下した。【考察】ヘミン刺激でHO-1を誘導した後、炎症性サイトカインであるTNF-α刺激を加えたところ、HO-1を誘導していない群に比べてTM mRNA発現は増加し、TF、PAI-1 mRNA発現は低下した。以上の結果より、炎症性ストレス下において血管内皮細胞でHO-1が高発現していると、TF、PAI-1 mRNAの発現が抑制され、またTM mRNAの発現も促進され、結果として血栓形成抑制作用を示す可能性が示唆された。 |

## 研究成果 (73件)

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