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骨髓瘤细胞表达APE1促进THP-1细胞破骨样分化

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Title: APE1 expression in multiple myeloma cells promotes differentiation of THP-1 cells into osteoclast-like cells

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关键词: APE1; 骨髓瘤骨病; 共培养; THP-1; RNA干扰

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摘要: 目的 研究在非接触式共培养体系下，RNA干扰多发性骨髓瘤细胞株U266 APE1表达对与其共培养的THP-1细胞破骨样分化的影响。 方法 ①将构建的APE1 siRNA表达载体导入U266细胞中。②Western blot法检测U266细胞中APE1及破骨细胞分化因子（RANKL）蛋白表达。③建立非接触式共培养体系：THP-1+U266共培养组、THP-1+U266$^{APE1\ siRNA}$共培养组和THP-1细胞单培养组。④抗酒石酸酸性磷酸酶（TRAP）染色鉴定破骨样细胞，RT-PCR法检测THP-1细胞Cathepsin K和V-ATPase mRNA表达水平。⑤光镜下观察骨切片陷窝形成。 结果 APE1 siRNA能明显抑制U266细胞中APE1及RANKL蛋白表达（P<0.01）。THP-1细胞与U266细胞共培养后，THP-1细胞可分化为TRAP阳性的破骨样细胞，Cathepsin K和V-ATPase基因表达显著升高（P<0.05）；U266细胞经APE1 siRNA处理后，共培养体系中THP-1细胞诱导分化的OCLs数量减少，Cathepsin K和V-ATPase基因水平降低，差异均有统计学意义（P<0.05）。 结论 APE1 siRNA能明显抑制U266细胞诱导的THP-1细胞的破骨样分化，其机制可能与APE1下调U266细胞RANKL有关。

Abstract: Objective To determine the effect of RNA interference (RNAi) of apurinic/apyrimidinic endonuclease (APE1) in multiple myeloma cell line U266 on the differentiation of a human monocytic cell line THP-1 into osteoclast-like cells in a contactless co-culture system. Methods Constructed APE1 siRNA expression vector Ad5v2 APE1 siRNA was used to transfect the U266 cells. The protein levels of APE1 and RANKL were detected by Western blotting. A co-culture system of THP-1 cells and U266 cells was established with Transwell insert culture dish. The co-culture system were divided into 3 groups:THP-1+U266 group,THP-1+U266$^{APE1\ siRNA}$

group and the control group (THP-1 cells). Osteoclast-like cells were identified through tartrate-resistant acid phosphatase (TRAP) staining. The mRNA levels of Cathepsin K and V-ATPase were examined by RT-PCR. Osteoclast bone resorption was measured by pit assay. Results U266 cells transfected with Ad5v2 APE1 siRNA had significantly lower protein expression of APE1 and RANKL than the untransfected cells.THP-1 cells differentiated into the osteoclast-like cells with the elevated mRNA expression of Cathepsin K and V-ATPase（P<0.05）. The number of osteoclast-like cells was decreased significantly in the THP-1+U266$^{APE1\ siRNA}$ group, as well as the mRNA levels of Cathepsin K and V-ATPase（P<0.05）. Conclusion Inhibiting APE1 expression in U266 cells in a co-culture system suppresses the differentiation of THP-1 cells into osteoclast-like cells, which may be related to APE1 down-regulating RANKL in U266 cells.

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