題名:Apoptosis-dependent and-independent mechanisms mediate the phagocytic recognition/clearance of theHL60-A1 transfectants of prolonged survival.

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上傳時間:2009-08-24T03:31:47Z

摘要:OBJECTIVE: The phagocytic recognition and clearance of the recruited inflammatory cells with prolonged survival play a pivotal role in relieving tissue inflammation and maintaining tissue homeostasis. Transgenic mice expressing Bcl-2 in mature neutrophils demonstrated that Bcl-2 attenuated neutrophil apoptosis, while the homeostasis of the neutrophil population was essentially unaffected. This result suggests that clearance of neutrophils with prolonged survival operates independently from apoptosis. Owing to the constitutive and inducible expression of Bcl-2 homologue, A1 in human neutrophils and the intolerance of preparation for the isolated human neutrophils with prolonged survival, the human promyelocytic HL60-A1 transfectants were established to study the mechanism of phagocytic recognition/clearance of the cells with prolonged survival. MATERIALS AND METHODS: The non-apoptotic cells with prolonged survival were enriched by serum withdrawal for five days and negatively isolated by annexin V-binding beads. Then, the cells were labeled with a fluorogenic marker. Monocyte-derived macrophages (MDM) were co-cultured to perform the phagocytosis assay, and flow cytometry was employed to determine the phagocytic index. RESULTS: In the serum-free condition, the phagocytic index of HL60-A1 transfectants was little different from that of the HL60-EGFP control, despite showing a significantly lower degree of apoptosis. While the phagocytic index of HL60-EGFP control was significantly correlated with the degree of apoptosis,

the index of the HL60-A1 transfectants was less relevant to it. The phagocytic index for the annexin V-positive cells did not distinguish the two cell types. However, the phagocytic index for the annexin V-negative cells from the HL60-A1 transfectants was increased with age in days. Preincubation of MDM with the scavenger receptor inhibitor, Oxi-LDL, and the inhibitory antibodies against alphavbeta3, CD14 and CD36 surface molecules could attenuate the phagocytic recognition of the annexin V-positive HL60 cells but not the annexin V-negative A1 transfectants with prolonged survival. CONCLUSIONS: This study thus suggests that a mechanism unrelated to apoptosis exists, which mediates the phagocytic clearance of the non-apoptotic cells with prolonged survival and may be associated with A1 function in the myeloid cells.