분류번호	Ⅲ-P-61

Autocrine mechanism for viability enhancement of BAL eosinophils after segmental antigen challenge in allergic asthmatics.

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Eosinophils are known to be important effector cells in pathogenesis of asthma. The elucidation of mechanism by which eosinophil survival is regulated in vivo at sites of inflammation is critical to our understanding of asthma pathogenesis. The maintenance of these cells at site of inflammation depends upon the balance between its tendency to undergo apoptosis and the local eosinophil-viability enhancing activity. Qualitative and quantative phenotypic differences have been observed between bronchoalveolar lavage (BAL) and peripheral blood (PB) eosinophils (EOS). We hypothesize that BAL EOS possess altered functional feature compared to PB EOS. BAL and PB EOS were obtained from ragweed allergic asthmatics after segmental antigen challenge (SAC) at 24 hour or one week, and purified over percoll and CD16 negative selection. Cells were cultured in duplicate in RPMI, 15% FCS and 1% penicillin/streptomycin without exogenous cytokines. Eosinophil purity and viability was >92%. BAL EOS viability was 69±4.4% versus 39±1.6% for PB EOS ($p<0.005$) at 48 hour time point, and this difference was maintained through day 5 (32±7.6% vs. 3.0±1.4%, $p<0.05$). Among BAL EOS, those harvested one week after SAC appeared to have an prolonged survival compared to those harvested at 24 hour. Coculture of BAL and PB EOS resulted in significant viability enhancement than expected. Direct neutralization of GM-CSF activity, not IL-3 and IL-5, markedly decreased the survival of BAL EOS in culture, and abrogated the viability enhancing activity of their culture supernatants in a dose dependent manner. We conclude that BAL EOS activated in vivo possess enhanced viability compared to PB EOS. Mixing and neutralization experiments suggest a role for autocrine production of GM-CSF.