

Comparative Study Cell Immunol. 1996 May 1;169(2):185-95. doi: 10.1006/cimm.1996.0109.

Age-related decreases in IL-2 production by human T cells are associated with impaired activation of nuclear transcriptional factors AP-1 and NF-AT

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PMID: 8620546 DOI: 10.1006/cimm.1996.0109

Abstract

Although transcriptional factors AP-1 and nuclear factor of activated T cells (NF-AT) are important for the normal induction of IL-2, ***it is unknown if the age-related decline in IL-2 production by activated human T cells may be associated with aberrancies in transcriptional regulatory proteins.*** In the current studies, IL-2 production by T cells from elderly (mean 78 years) and young (mean 37 years) humans was measured in cultures stimulated with PHA, PHA plus PMA, crosslinked anti-CD3 mAb OKT3 plus PMA, or PMA plus ionomycin. ***Substantial decreases of IL-2 production were observed for cell cultures from 7 of 12 elderly individuals in response to the different stimuli,*** whereas the levels of IL-2 produced by stimulated T cells from other elderly individuals were equivalent to those observed for stimulated T cells of young subjects. Analyses of nuclear extracts by electrophoretic DNA mobility shift assays showed that decreased IL-2 production by stimulated T cells of elderly individuals was closely associated with impairments in the activation of both AP-1 and NF-AT. By contrast, T cells from elderly subjects with normal levels of IL-2 production exhibited normal activation of AP-1 and NF-AT. In addition, the results of competition experiments analyzing the normal components of NF-AT showed that the age-related reductions in stimulus-dependent NF-AT complexes corresponded to the slow migrating complexes that were composed of c-Fos/c-Jun AP-1. The resting and stimulated levels of NF kappa B were reduced in T cells from certain elderly individuals; however, alterations of NF kappa B did not correlate with changes in IL-2 expression. Thus, these results show that age-related impairments in the activation of AP-1 and NF-AT are closely associated with decreased expression of IL-2 and further suggest that aberrancies in the signaling pathways important for the induction of transcriptionally active c-Fos/c-Jun AP-1 may contribute to the impaired activation of NF-AT.