Relationship between plasma IGF-I levels, in vitro correlates of immunity, and human senescence.

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Insulin-like growth factor-I (IGF-I) is a polypeptide mitogen which is regulated by growth hormone (GH). IGF-I mediates many of the biological functions of GH, including the maintenance of lymphoid mass and functions. Since GH secretion declines with age, we asked whether changes in the availability of IGF-I might contribute to age-associated alterations in immune functions. As a first step, we examined relationships between plasma levels of IGF-I and in vitro correlates of immunity in young and elderly subjects. Heparinized plasma and lymphocytes were collected from the peripheral blood of 34 healthy young (aged 27 +/- 0.9 years, mean +/- SEM) and 41 elderly (79 +/- 1.3 years) volunteers (31 males and 44 females in total). Plasma levels of IGF-I, measured by radioimmunoassay after the removal of IGF-I-binding proteins, were reduced among elders compared to young controls (138 +/- 8.7 ng/mL vs 80.2 +/- 4.7 ng/mL, $P < 0.001$). The number of circulating lymphocytes did not change with age. The proliferative response ([3H]thymidine uptake into DNA) of T-cells to concanavalin A and B-cells to pokeweed mitogen were reduced among elders ($P < 0.05$). An increased spontaneous antitumor natural killer (NK) activity ($P < 0.001$) was accompanied by a higher percentage of CD16(+) NK cells among lymphocytes in older subjects ($P < 0.001$). The NK cell number was positively related to IGF-I levels in young volunteers but not among elders. Correlation analysis demonstrated a highly significant relationship between plasma IGF-I levels and T-cell (but not B-cell) proliferative response during aging ($r = 0.492$, $P < 0.001$). Our results imply that reduced immunocompetence may be one of the consequences of reduced IGF-I levels in human aging. Among the three types of immune cells tested, the T-cells were most sensitive to fluctuations in IGF-I levels. Reduced IGF-I availability may be one of the determinants of the decline in T-cell-mediated immune function in the elderly. To our knowledge, this is the first report presenting correlative data on concurrent changes in IGF-I levels and immune parameters in human aging.

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