

# REPORT

## Interleukin-6 And Aging

One of the many effects of calorie restriction is the ability to lower blood levels of Interleukin (IL-6) a protein produced by a wide variety of cells, which is one of a class of immune system regulators called cytokines. IL-6 plays a critical role, along with other cytokines such as Interleukin-1 (IL-1) and Tumor Necrosis Factor (TNF), in the acute phase inflammatory response to cellular injury.

Scientists have demonstrated that blood levels of IL-6 rise with advancing age in mice, monkeys, and humans, and that elevated levels of IL-6 are found in a wide variety of aging associated diseases including lymphoma, multiple myeloma, rheumatoid arthritis, osteoporosis, and Alzheimer's disease. As a result it's been suggested that dysregulation of IL-6 may be a cause of aging and a contributing factor to many of the diseases of aging. William B. Ershler and his associates at the University of Wisconsin propose that: "inappropriate IL-6 levels trigger a constellation of changes that may contribute to 'normal aging: Furthermore, these changes may render a host susceptible to certain disease processes. "

Since the regulation of IL-6 expression is tight and complex, little or no IL-6 can be found in the serum of young people. However, with advancing age, there is an apparent relaxation of this tight genetic regulation and increasing amounts of measurable IL-6 can be found in the blood, even in the absence of an inflammatory stimulus.

Furthermore, there is evidence that free radical damage may be responsible for changes in the genetic control of IL-6 regulation, which, in turn, causes elevated levels of IL-6 in the elderly and in diseased patients. Since calorie restriction markedly reduces free radical activity, it may be that its antiaging effects may be due in part to its ability to prevent the dysregulation of IL-6 (and perhaps other cytokines), which influences the growth of tumor cells and other types of abnormal cells within the body.

### PREVENTING THE ONSET OF LYMPHOMAS IN MICE

A recent study at the University of Wisconsin linked the formation of lymphomas in mice to the dysregulation of IL-6 and then showed that calorie restriction can derail this process, thereby preventing the onset of this form of cancer in mice.

**Table 1. IL6 AND AGING RECENT FINDINGS**

<b>Group</b>	<b>Species</b>	<b>Findings</b>
Tang et al.	MRL/lpr mice	Serum levels increase with age.
Effros et al.	C3B1OF1 mice	Endotoxin lipopolysaccharide (LPS) peritoncal macrophage IL-6 levels rose with age, but dropped at 24 months.
Foster et al.	Fischer 344 rats	LPS-stimulated peripheral blood mononuclear cell IL-6 production increased with age. Oldest group (33 months) 10 x higher level than middle-aged.
Daynes et al.	BALBC/c and C3H/HeN	Serum IL-6 levels rise through the life span. Highest levels in the oldest mice and humans subjects. Also, spontaneous and LPS-induced IL-6 production higher in old animals.
Wei et al.	Humans	IL-6 levels higher in healthy older people but no age differences observed for IL-1.
Ershler et al.	Rhesus monkeys	Serum IL-6 levels rise through the life span.
	Humans	Plasma IL-6 levels higher in healthy old people than young.

The scientists observed that serum IL-6 levels were much higher in mice with lymphomas than in healthy young mice, which

correlated with the elevated IL-6 levels found in patients with Hodgkin's lymphoma...with the higher the IL-6 level, the worse the prognosis for the patient.

The Wisconsin study showed a major reduction in lymphoma development in mice subjected to mild-to-moderate calorie restriction, as well as a significant decline in IL-6 levels, which suggests that any therapy that reduces elevated IL-6 levels could produce anti-aging effects such as the prevention of cancer and, perhaps even, the retardation of normal aging.

### **TREATING AUTOIMMUNE DISEASES WITH DHEA**

Scientists have shown that levels of IL-6 in humans may be linked to the age-related decline in levels of dehydroepiandrosterone (DHEA) and there is clinical evidence that DHEA may be an effective treatment for autoimmune diseases such as rheumatoid arthritis.

If the effective treatment of autoimmune disorders can be linked to the ability of DHEA to lower abnormally high levels of IL-6, it will suggest the possibility that DHEA may be an effective treatment for all the diseases associated with high levels of IL-6, including Alzheimer's disease, and perhaps for aging itself.

Some of these questions may be answered at a major conference on DHEA And Aging, which will be held in Washington, D.C. in June.

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