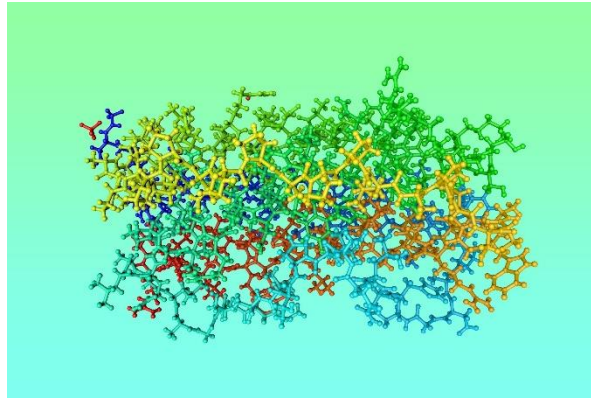


In Mice Blocking IL-11 Extends Lifespan and Improves Health

A team of researchers used [murine models](#) and various pharmacological and genetic approaches to examine whether pro-inflammatory signaling involving interleukin (IL)-11, which activates signaling molecules such as extracellular signal-regulated kinase (ERK) and mammalian target of rapamycin complex 1 (mTORC1), was negatively associated with health- and lifespan.



Study

In the present study, the researchers hypothesized that IL-11, a pro-fibrotic and pro-inflammatory cytokine belonging to the [IL-6 family](#) of cytokines, could be involved in pathologies related to aging and lifespan reduction. They based this hypothesis on the role of IL-11 in activating the ERK-mTORC1 and Janus kinase-signal transducers and activators of transcription-3 (JAK-STAT3) pathways.

For this study, the researchers used mouse models and [human hepatocyte](#) cultures. Primary human hepatocytes were cultured and then stimulated with IL-11 for varying durations. The supernatants from these stimulated cells were then used for proximity extension assays using an inflammation panel consisting of 92 proteins.

Additionally, human cardiac fibroblasts treated with immunoglobulin G (IgG) or X209, the neutralizing antibody that targets the [IL-11 receptor alpha subunit](#) (IL11RA), were used for high throughput phenotyping assay. Serum-starved human cardiac fibroblasts were also used to measure the mitochondrial oxygen consumption rate and fatty acid oxidation rate.

Three strains of mice were used for the animal model experiments — mice with deleted interleukin 11 receptor subunit alpha 1 (IL11RA1) gene, mice with deleted IL11 gene, and mice with the gene for [enhanced green fluorescent protein](#) (EGFP) inserted into the IL11 gene. These mice were subjected to various treatments, such as IL-11 deletion and administration of anti-IL11 antibodies, and used to assess metabolic parameters, physiological traits, and lifespan.

Lifespan and [tumor progression](#) were monitored after the mice were intraperitoneally injected with IgG or anti-IL-11 antibodies. The animals were also subjected to glucose and insulin tolerance tests, and echo magnetic resonance imaging was used to analyze their body composition.

Grip strength assessments were also conducted, and indirect and [bomb calorimetry](#) was performed to measure the body's metabolic parameters and energy content from stool samples.

Additionally, various assays, including colorimetry, were used to assess biomarkers such as cholesterol, collagen, and various interleukin levels and liver function parameters such as alanine transaminase and aspartate aminotransferase activities.

The researchers also conducted quantitative polymerase chain reaction and sequencing of ribonucleic acid (RNA) extracted from the cells and immunoblotting using protein extracted from various tissues such as the liver, visceral gonadal white adipose tissue, and [skeletal muscle](#). Histological and immunofluorescence-based examinations were also performed.

Findings

The study found that in aging mice, the expression of IL-11 was upregulated in various types of cells and tissues and that the deletion of either the [gene coding](#) for IL-11 or the IL-11 receptor's alpha 1 subunit protected the mice against metabolic decline, frailty, and multimorbidity as they aged.

Furthermore, administering antibodies against IL-11 in mice aged 75 weeks and older for both sexes for 25 weeks improved muscle function, boosted metabolism, lowered [aging biomarkers'](#) levels, and reduced frailty. The deletion of the IL11 gene was found to extend the lifespan of the mice by an average of 24.9%, and treatment of 75-week-old mice with anti-IL-11 antibodies increased the median lifespan of male and female mice by 22.5% and 25%, respectively.

Additionally, given that mortality in mice due to old age is often cancer-related, it was observed that IL-11 inhibition significantly lowered the incidence of age-related [cancers](#) and tumorigenesis.

Conclusion

To conclude, the results highlighted the detrimental role of the pro-inflammatory cytokine IL-11 in mammals' health span and lifespan. The study found that anti-IL-11 antibodies improved metabolic parameters and muscle function and lowered cancer incidence in mouse models. These findings indicate that therapeutic targeting of IL-11 might be valuable in cancer therapy and treating fibrotic [lung disease](#).

Source:

<https://www.news-medical.net/news/20240718/Breakthrough-in-aging-research-Blocking-IL-11-extends-lifespan-and-improves-health-in-mice.aspx>