Clinical Summary

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Sharma R, Padwad Y. Nutraceuticals-Based Immunotherapeutic Concepts and Opportunities for the Mitigation of Cellular Senescence and Aging: A Narrative Review. Ageing Res Rev 2020;63:101141.

The Big Three in Nutritional Modulation of Immunosenescence

Cellular senescence is increasingly linked to biological aging of immune cells, which regulate the accumulation of senescent cells within tissues. This review examines aging processes that affect specific populations of immune cells from both adaptive and innate aspects of immunity. The authors propose three classes of nutraceuticals—phytonutrients, probiotics, and omega-3 fatty acids—for slowing and potentially reversing the progress of senescence in immune cells and, ultimately, reducing senescent cell burden.

Immunosenescence is broadly considered the aging-related alterations in the targeting accuracy of the immune system targeting and the overall efficiency of the immune response. These functional changes are associated with:

- Accumulation of aged, damaged, or dysfunctional immune cells due to insufficient cell and tissue rejuvenation as well as resistance to normal cellular apoptosis
- Shifts in the overall balance among the many adaptive and innate immune cell types, due in part to altered regulation of cell replication and clonal expansion
- Changes in the signaling behaviors and cytokine secretion of aging immune cells—their senescence-associated secretory phenotype (SASP)

While heightened propensity towards inflammation is often thought of as the hallmark of immunosenescence, it can also result in other syndromes of immune imbalance such as autoimmunity, immunosuppression, cancer, and hypersensitivity.

Dietary makeup has long been linked to mortality, frailty, and physical and mental disease burden, but recent research alludes to the value of particular dietary components that may

impact immunosenescence via multiple mechanisms of action. This review article focuses on recent research into the immunomodulatory effects of phytonutrients (mainly polyphenols), probiotic bacteria, and omega-3 fatty acids.

According to the authors:

"The ageing immune system can accelerate the accumulation of [senescent cells]."

"Impairment in immune function is emerging as a critical regulator of known age-associated accumulation of [senescent cells]. Immune cells dysfunction with age are multi-faceted and are uniquely attributed in the independent processes of immunosenescence and cellular senescence which may collectively impair immune system mediated clearance of [senescent cells]."

Review Summary

Among the research findings related to immunosenescence and dietary immunomodulation cited by the authors, we highlight the following:

- Results from recent studies into immune-specific effects of quercetin, oleuropein (from olives), epigallocatechin gallate (EGCG), resveratrol, and fisetin suggest that polyphenols like these possess capacity for reducing senescent cell burden and inhibiting the development of the senescence-associated secretory phenotype (SASP)
- Carotenoids and grape polyphenols have been seen to aid the function and targeting of neutrophils taken from young as well as old human study participants
- In individuals at cardiovascular risk, high consumption of cocoa rich in polyphenols (40 grams/day) resulted in downregulation of genetic expression of immune factors related to proinflammatory monocyte activity
- In aging mice, the green tea polyphenol EGCG improve organ aging, antibody profiles, and expression of T cell surface markers
- In mice with accelerated senescence, Pu-erh tea extract improved balance among T cell populations and increased natural killer cell levels, yet lowered levels of interleukin-6
- The authors note correlations between inflamm-aging and dysbiosis, and propose that application of targeted probiotic organisms may ameliorate gut microbiota composition and alter the course of immunosenescence and SASP development
- Older subjects given L. delbrueckii ssp. bulgaricus 8481 demonstrated enhancements in naïve T cell and natural killer cell populations as well as lower cytokine levels
- In elderly individuals, consumption of a beverage containing Lactobacillus casei Shirota enhanced natural killer cell function after 4 weeks
- In older persons, L. gasseri supplementation improved T cell balance as well as T cell surface marker expression
- Aging animals given L. acidophilus and Bifidobacterium bifidum displayed a reversal in age-related loss of macrophage and lymphocyte activity

- Supplementation with L. paracasei NCC2461 improved aged animals' adaptive immune response to antigenic challenge without altering the innate immune response
- Aged and malnourished animals given L. johnsonii La1 showed greater intestinal immunoglobulin A (IgA) production, better nutritional status, and an improved immune response
- Fish oil supplementation ameliorated T cell balance and phagocyte activity in aged persons while also reducing cytokine levels, diverse effects that allude to improvement in overall immune balance and function
- Overweight middle-aged and older individuals given omega-3 fatty acids displayed reductions in markers of inflamm-aging after 4 months' supplementation
- Clinical studies have repeatedly associated omega-3 fatty acid intake with greater telomere length in white blood cells, suggesting a positive impact on immune cell senescence.

Crucial aging-related changes seen in immune cell populations include alterations in T-helper cell balance, reductions in naïve T cell numbers, expansion of memory T cells, and changes in macrophage M1/M2 polarization. Because older people tend to display more distinct signs of immunosenescence, research into the manifestations and modulation of cell and tissue aging are frequently conducted in those populations.

NUTRITION CONCLUSION

Evidence increasingly suggests that organismic aging and increased senescent cell burden are related to aging and imbalanced immune function. Particular types of food components are emerging as mediators of cellular autophagy, immune expression, cells' resistance to aging processes, the senescence-associated secretory phenotype (SASP), and of cell and tissue rejuvenation. Especially promising nutritional factors include phytonutrient polyphenols (like EGCG and quercetin), probiotic bacteria (with many Lactobacillus species represented in research), and omega-3 fatty acids.