

Abstract

Recent studies have demonstrated that the longevity-associated variant (LAV) of bactericidal/permeability-increasing fold-containing family B-member-4 (BPIFB4) protein promotes health and longevity, by enhancing the vascular cell homeostasis, revascularization after ischemic injury, and largely counterbalancing age-related impairments of the immune system and cardiovascular system. These findings helped us to partially explain the health status of Long-Living-Individuals (LLIs) and their homozygous genotype enrichment for LAV-BPIFB4. The levels of circulating BPIFB4 may have an influence on the composition of monocytes and macrophages and may shift the balance toward an anti-inflammatory status. An association was found between non-classical CD14⁺CD16⁺⁺ monocyte counts, which are precursors of M2 macrophages with immunomodulatory functions, and LLIs' state. During the ageing process, systemic aging is driven by the senescent immune system, which could be a key therapeutic target to prevent the pathological consequences of aging and extend longevity. Several data show a new senotherapeutic action of LAV-BPIFB4 that may offer a valuable therapeutic tool to control aging and reduce its pathophysiological disorders, such as CVDs or, in senescent GBM cells, enhancement of their sensitivity to temozolomide and a selective reduction of the T cells' senescence from GBM patients. As a result of its pleiotropic effects on both immune compartments and cellular homeostasis, LAV-BPIFB4 may represent an attractive candidate for developing a new treatment for HD. Indeed, when compared to normal

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STHdh Q7/7 cells, STHdh Q111/111 cells were unable to induce pro-resolving microglia phenotype, but LAV-BPIFB4 transduction promptly restored the central immune control through a mechanism involving the CXCR4 axis. Since platelets are primary mediators in innate immune response and combat infection, it was researched the role of this blood figurative elements in immunomodulatory processes of the BPIFB4 protein.