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Abstract

SA-β-galactosidase activity in effector and regulatory T cells †

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Abstract: The aging of the immune system is accompanied by a significant increase in the risk of developing age-related pathologies, including inflammatory, autoimmune diseases and oncology. Age-dependent decline in immune function is accompanied by a gradual accumulation of senescent (aged) cells that are the source of chronic inflammation. The main producers of proinflammatory cytokines in the body are activated effector T cells. With age, along with an increase in chronic inflammation (InflammAging), the ability of the immune system to suppress and/or remove activated and senescent effector cells decreases. With age, there is also a decrease in the function of $CD3^+CD4^+CD25^{hi}CD127^{lo/-}$ T-regulatory cells (Treg), which unbalances the immune system and increases the risk of autoimmune pathologies.

In *ex vivo* analysis, senescence status of activated ($CD25^+$ and $HLA\text{-}DR^+$) and non-activated ($CD25^-$ and $HLA\text{-}DR^-$) $CD4^+$ and $CD8^+$ T cells, as well as Tregs with phenotypes $CD3^+CD4^+CD25^{hi}CD127^{lo/-}$ and $CD3^+CD8^+CD127^{lo/-}HLA\text{-}DR^+$ ($CD4^+$Treg and $CD8^+$Treg respectively) were assessed by using SA-β-galactosidase activity assay.

Among donors in activated ($CD25^+$ and $HLA\text{-}DR^+$) both $CD4^+$ and $CD8^+$ lymphocytes, SA-β-Gal activity was higher compared to non-activated lymphocytes. Whereas, SA-β-Gal activity was lowest in Tregs, suggesting their specific metabolic patterns. There were no significant differences between the populations of $CD3^+CD4^+$ and $CD3^+CD8^+$ lymphocytes in SA-β-Gal activity. Thus, the activity of SA-β-Gal marker of senescent and activated effector T cells can be used to analyze the aging of the immune system in further functional tests.

Using this approach, the phenotypic features and functional activity of senescent T cells among young (< 30 years old) and older (> 60 years old) donors will be studied in detail. The development of this model in non-human primates of different age groups will facilitate future preclinical trials for senolytic and senomorphic drugs, and substances that enhance the repair of double-strand breaks.

Keywords: SA-β-Gal; senescence; lymphocytes; regulatory T cells; Treg.

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