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T cell immunosenescence and longevity

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The immunosenescence alterations in the T cell immunity contribute to deficiencies in response to vaccination, in protecting from various infections and increases risk of cancer development and autoimmune diseases. One of the hallmarks of age-related processes is shrinking diversity of TCR repertoire which, on the cellular level, is associated with loss of naive T cells and expansion of the memory and effector T cell populations. Implementing quantitative TCR repertoire profiling, we investigated changes in diversity and architecture of human TCR repertoires starting from umbilical cord blood to centenarian blood samples. Besides the overall reduction in the TCR repertoire diversity with age, we found that TCR diversity and percentage of naive CD4+ cells in males decreases significantly faster by the age of 40 compared to females. This gender difference disappears in more elderly individuals. Remarkably, percentage of naive T cells within CD4 pool stably decreases with age but remains unexpectedly high in the oldest cohort (>75 y.o.) comparing to the ratio in CD8+ compartment. It might indicate a possible association between high percentage of naive CD4+ cells and longevity. Despite the fact that naive CD4+ cells have low survival capacity than naive CD8+, the homeostatic machinery maintains naive CD4+ pool diverse with age. Additionally, our analysis showed that functional TCR repertoires are more similar in the youth, and this similarity gradually decreased with age. These phenomena might be explained by enrichment of public clonotypes among naive T cells, including clones that originate from fetal period. Further analysis of sorted naive CD8 TCR repertoires across different age groups revealed that naive CD8 repertoires were more similar among young compared to aged donors. Identification of mechanisms driving ageing of TCR repertoire might shed light on vulnerability of elderly to infections, autoimmune disease and cancer development.

Biography

Olga Britanova completed her PhD at Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences in 2003. She has been working in Laboratory of Genomics of Adaptive Immunity headed by Prof. D Chudakov, since 2008. Previously, her research was focused on the study of the molecular pathways during embryonic development of the mammalian cerebral cortex. She investigated the role of the transcription factor Satb2 in determination of the cell fate identity of cortical neurons. Her scientific interests are focused on molecular immunology. Particularly, she has developed PCR-based techniques for TCR and BCR profiling analysis.

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