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REDUCED LEVELS AND FUNCTIONAL ABILITY OF NAÏVE T-LYMPHOCYTES IN ELDERLY PEOPLE MIGHT INFLUENCE THE DEVELOPMENT OF IMMUNOLOGICAL MEMORY AGAINST NEOANTIGENS

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We wanted to study age's influence in the development of immunological memory against neoantigens using the SARS-CoV-2 vaccination as model of a first encounter with an antigen. For this, we analysed 35 elderly donors (ED; age:75.5, IR:6) and 35 young donors (YD; age:40, IR:10). We performed immunophenotypes by flow cytometry, analysed activation (CD25, CD69, HLA-DR) and proliferation (Ki-67) ability of naïve T-lymphocytes in response to anti-CD3 and studied the development of immunological memory against a neoantigen a month after receiving SARS-CoV-2 vaccine. Specific memory T-lymphocytes to SARS-CoV-2 were quantified using IFN-g-Enzyme-Linked ImmunoSpot Assay (ELISpot) after their stimulation with viral peptide pools.

As expected, ED presented higher percentages of highly-differentiated subpopulations effector memory (EM) and EMRA and lower naïve than YD in both, $CD4^+$ and $CD8^+$ T-lymphocytes ($p<0.05$ and $p<0.001$). CD31 expression in naïve $CD4^+$ T-lymphocytes was lower in ED ($p<0.001$). We also found lower absolute numbers of naïve B-lymphocytes in ED ($p<0.05$). Activation and proliferation ability of naïve T-lymphocytes was studied. Naïve $CD4^+$ T-lymphocytes expressed lower CD25 and CD69 ($p<0.05$) and naïve $CD8^+$ T-lymphocytes expressed lower CD25 ($p<0.05$) in ED. Reduced percentages of $Ki\text{-}67^+$ cells were found in both, naïve $CD4^+$ and $CD8^+$ T-lymphocytes, in ED ($p<0.001$). We observed that naïve $CD8^+$/EMRA $CD8^+$ ratio, but not naïve $CD4^+$/EMRA $CD4^+$ ratio, was positively correlated with the $Ki\text{-}67^+$ cells percentage in $CD4^+$, naïve $CD4^+$, $CD8^+$ and naïve $CD8^+$ T-lymphocytes ($p<0.01$, $p<0.05$, $p<0.001$ and $p<0.001$, respectively).

ED presented more SARS-CoV-2 non-responders than YD (29/35 vs 34/35) and lower number of specific IFN-g-producing T-lymphocytes/10^6PBMC ($p<0.05$). No relationship was found between lymphocyte subpopulations and response to vaccination.

In summary, ED had a highly-differentiated immune system and a defective functionality of naïve T-lymphocytes, with lower level of activation and proliferation compared to YD, and this might negatively influence in the development of immunological memory against neoantigens.