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ELDERLY PEOPLE RESPOND TO SARS-COV-2-VACCINATION BUT REQUIRE MORE IMMUNIZATIONS THAN YOUNG DONORS TO GENERATE IMMUNOLOGICAL MEMORY AND DO NOT REACH THE LEVELS ACQUIRED AFTER INFECTION

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Taking advantage of the COVID-19 pandemic and the vaccination campaign against SARS-CoV-2, we have taken this vaccination program as a model to study the development of immunological memory against new antigens.

To study the ability of elderly people to respond to neoantigens, we analysed the immunological memory of 35 elderly donors (ED; age: 75.5, IR:6) and 57 young donors (YD; age: 50, IR:34) a month after receiving the second dose RNA-based SARS-CoV-2 vaccine, and 34 elderly patients who were studied six months after their recovering from SARS-CoV-2 infection in 2020 (EP; age: 71.5, IR:16). In 25 ED we also studied the immunological memory a month after receiving the third dose of the SARS-CoV-2 vaccine.

Specific memory T-lymphocytes to SARS-CoV-2 were quantified using IFN-□-Enzyme-Linked ImmunoSpot Assay (ELISpot) after their stimulation with viral peptide pools (S1, S2, N). We found IFN-□□producing T-lymphocytes in 28/35 and 56/57 patients in ED and YD, respectively. The median number of specific IFN-□□producing T-lymphocytes was 116 (IR:340) and 252 (IR:292) cells/10^6PBMC, respectively ($p<0.05$). ED had also less specific IFN-□□producing T-lymphocytes than EP (median: 526, IR:797) ($p<0.001$).

Although no significative differences were found between the number of specific memory T-lymphocytes in ED after the third dose of the vaccine (median: 168, IR:290) and YD after the second one, levels were still lower than in EP ($p<0.01$).

We compared ED individuals with higher and lower cellular immune responses and we observed a higher percentage of naïve B-lymphocytes and higher absolute number of Th2 and follicular helper memory $CD4^+$ T-lymphocytes in those with higher cellular memory ($p<0.05$).

Our results suggest that, despite their aged immune system, elderly people can respond to SARS-CoV-2-vaccination, although they require more immunizations than young donors to generate the same level of immunological memory and their responses are lower than the ones generated after SARS-CoV-2 infection.