SARS-CoV-2 mRNA vaccination–induced immunological memory in human nonlymphoid and lymphoid tissues

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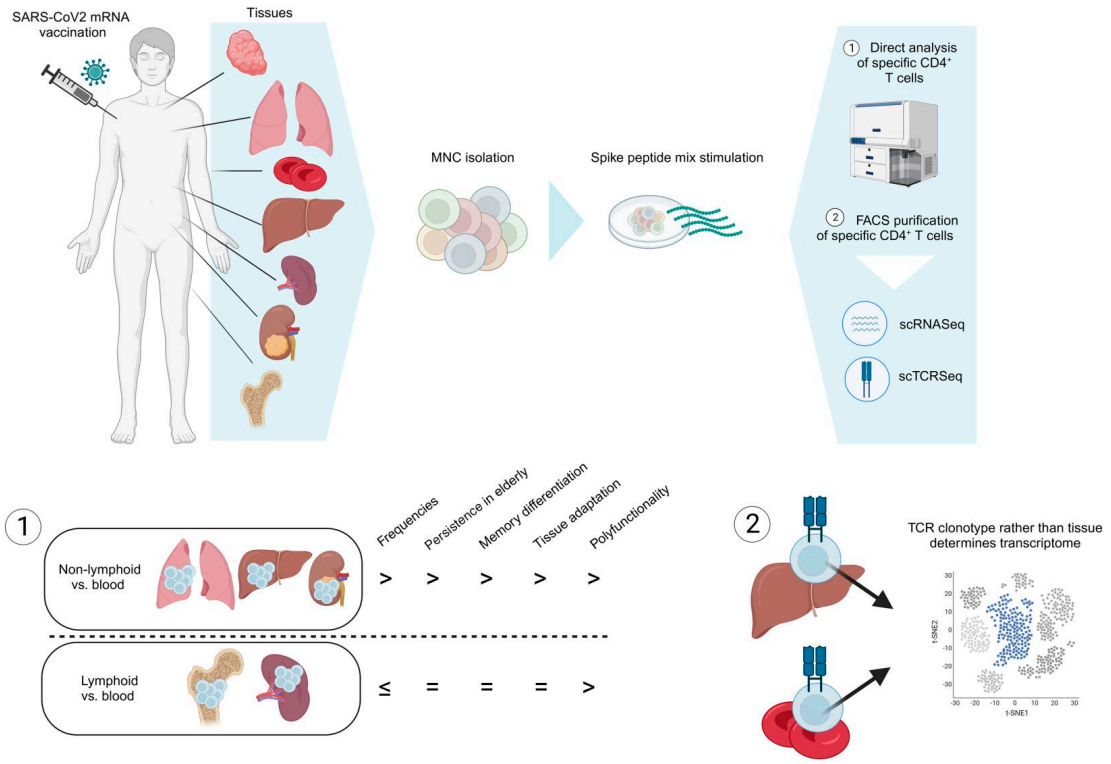

Abstract

Tissue-resident lymphocytes provide organ-adapted protection against invading pathogens. Whereas their biology has been examined in great detail in various infection models, their generation and functionality in response to vaccination have not been comprehensively analyzed in humans. We therefore studied SARS-CoV-2 mRNA vaccine–specific T cells in surgery specimens of kidney, liver, lung, bone marrow, and spleen compared with paired blood samples from largely virus-naive individuals. As opposed to lymphoid tissues, nonlymphoid organs harbored significantly elevated frequencies of spike-specific CD4+ T cells compared with blood showing hallmarks of tissue residency and an expanded memory pool. Organ-derived CD4+ T cells further exhibited increased polyfunctionality over those detected in blood. Single-cell RNA-Seq together with T cell receptor repertoire analysis indicated that the clonotype rather than organ origin is a major determinant of transcriptomic state in vaccine-specific CD4+ T cells. In summary, our data demonstrate that SARS-CoV-2 vaccination entails acquisition of tissue memory and residency features in organs distant from the inoculation site, thereby contributing to our understanding of how local tissue protection might be accomplished.