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

Info

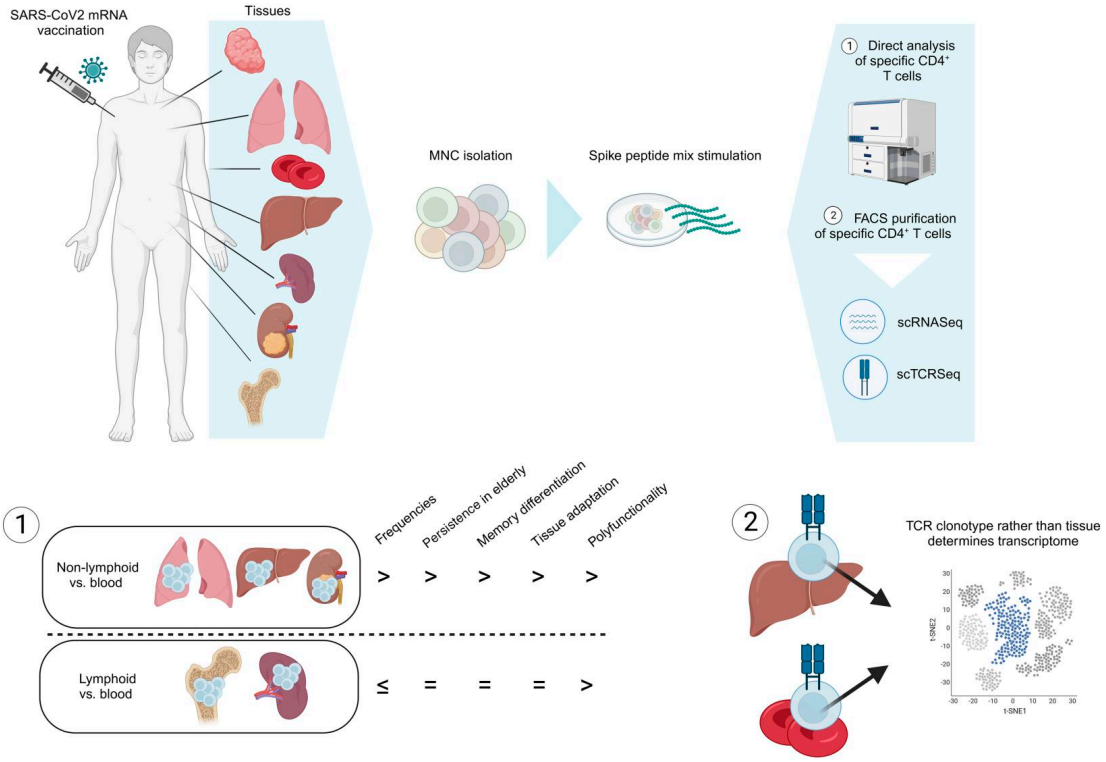
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Authors

Vanessa Proß Arne Sattler Sören Lukassen Laura Tóth Linda Marie Laura Thole Janine Siegle Carolin Stahl An He **Georg Damm** **Daniel Seehofer** **Christina Götz** Christian Bayerl Pia Jäger Alexander Macke Stephan Eggeling Bernadette Kirzinger Thomas Mayr Hermann Herbst Katharina Beyer Dominik Laue Jan Krönke Jan Braune Friederike Rosseck Beatrice Kittner Frank Friedersdorff Mandy Hubatsch Sarah Weinberger Nils Lachmann Veit Maria Hofmann Eva Schrezenmeier Carolin Ludwig Hubert Schrezenmeier Katharina Jechow Christian Conrad Katja Kotsch



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.