Covid-19 mRNA vaccines and autoimmunity.

Federica Marelli-Berg
William Harvey Research Institute, Barts and The London Faculty of Medicine and Dentistry, Queen Mary University of London, UK

The COVID-19 pandemic, caused by severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2), has led to the first approval of mRNA vaccines in humans. By producing full-length SARS-CoV-2 Spike protein, they induce protective anti-viral immunity. Acute myo/pericarditis (AMP) development post-vaccination has repeatedly been reported; however, the pathogenesis of this complication remains elusive. In-depth phenotyping of peripheral blood T-cells was undertaken in cohorts of patients who developed AMP post-mRNA vaccination, patients hospitalized for severe Covid-19 and healthy subject with no cardiac side effect post-mRNA vaccine. Validation studies were carried out using an experimental model of cardiac inflammation, in which a shared epitope elicits functional responses in patients and mice, in which it induces AMP. We show that T-cells from AMP patients recognize vaccine-encoded Spike epitopes homologous to those of cardiac self-proteins. One of these epitopes, mimicking an amino acid sequence from a cardiomyocyte-expressed K+ channel, induced AMP in mice. When functional responses to the Kv2 were analyzed, post-mRNA vaccination AMP patients but not COVID-19 patients displayed an expanded pattern of cytokine production similar to that observed in AMP mice and in autoimmune myocarditis. Crucially, T-cell autoimmunity segregates to cardiotropic cMet-expressing T-cells and is prevented by cMet inhibition, suggesting that heart-homing-imprinting, permitted by the unique mRNA vaccine biodistribution, is required for AMP development.
AMP development post mRNA vaccines is mediated by distinct immune components including molecular mimicry, TCR affinity and – importantly – homing imprinting.