Clinical Immunology 229 (2021) 108765

Contents lists available at ScienceDirect

Clinical Immunology

journal homepage: www.elsevier.com/locate/yclim

Full Length Article

Effective DNA damage response after acute but not chronic immune challenge: SARS-CoV-2 vaccine *versus* Systemic Lupus Erythematosus

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ARTICLE INFO

Keywords:
SARS-CoV-2
Influenza
Vaccination
Acute immune activation
Chronic immune activation
Type I interferon
Oxidative stress
DNA damage response

ABSTRACT

Whether and how an acute immune challenge may affect DNA Damage Response (DDR) is unknown. By studying vaccinations against Influenza and SARS-CoV-2 (mRNA-based) we found acute increases of type-I interferon-inducible gene expression, oxidative stress and DNA damage accumulation in blood mononuclear cells of 9 healthy controls, coupled with effective anti-SARS-CoV-2 neutralizing antibody production in all. Increased DNA damage after SARS-CoV-2 vaccine, partly due to increased oxidative stress, was transient, whereas the inherent DNA repair capacity was found intact. In contrast, in 26 patients with Systemic Lupus Erythematosus, who served as controls in the context of chronic immune activation, we validated increased DNA damage accumulation, increased type-I interferon-inducible gene expression and induction of oxidative stress, however aberrant DDR was associated with deficiencies in nucleotide excision repair pathways. These results indicate that acute immune challenge can indeed activate DDR pathways, whereas, contrary to chronic immune challenge, successful repair of DNA lesions occurs.

1. Introduction

Vaccination constitutes an essential way to restrain the spread of severe infectious diseases, which impose a potentially serious threat to public health. Life-threatening diseases like smallpox have been eradicated, while others like polio, tetanus, diphtheria, and measles have been significantly restricted, since vaccination implementation [1]. Especially, in the case of influenza, annual vaccination is the most effective protection. When the circulating strain matches the strains included in the Influenza vaccine, vaccination can reduce serious illness probability by 40–60% [2].

At the end of 2019, a new pathogen imposed a major threat to public health [3]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused an outbreak of viral pneumonia, a disease known as Corona Virus Disease-2019 (COVID-19). COVID-19 was declared a pandemic in March 2020 causing more than 2.5 million deaths worldwide and a major socio-economic impact [4,5]. To confront this critical need, a plethora of vaccination technologies are being tested against SARS-CoV-2. The newer mRNA (Pfizer/BioNTech, Moderna) and adenovirus-based (AstraZeneca/Oxford) vaccine platforms have been licensed for use in humans, while other technologies, *i.e.* inactivated viruses and recombinant protein-based vaccines (Sanofi, Novavax, Sinovac and GSK), are currently being tested [6,7].

Vaccination effectiveness is significantly influenced by the immunological cellular response to vaccine antigens. After vaccination, innate immune response is temporarily activated. Type I interferons (IFN), which are key mediators of antiviral innate immune response, have been shown to be transiently increased after vaccination against viruses like Influenza [8,9]. This acute innate immune activation is thought to be of great importance, since type I interferon induction can activate the adaptive immune response and influence the neutralizing antibody production [10].

Oxidative stress, an imbalance between the oxidant and antioxidant mechanisms after exposure to deleterious stimuli, plays a pivotal role in the pathogenesis of viral infections. Acute immune activation following a viral infection is associated with increased oxidative stress, as a result

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https://doi.org/10.1016/j.clim.2021.108765
Received 2 April 2021; Received in revised form 29 May 2021; Accepted 31 May 2021
Available online 2 June 2021