Review of: "A Review of the Scientific Literature on Experimental Toxicity Studies of COVID-19 Vaccines, with Special Attention to Publications in Specific Toxicology Journals"

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Dr. J.L. Domingo compiled the published nonclinical data on vaccines developed against COVID-19 caused by SARS-CoV-2 at the global level. As the author correctly points out, the Covid-19 pandemic has been one of the most significant events affecting the world in the current century, and its impact was correspondingly immense. The pandemic, which caused millions of deaths worldwide, prompted a major mobilization in the scientific community and the pharmaceutical sector to develop protective vaccines and other treatments. This mobilization quickly bore fruit, and many relatively successful vaccines were made available in a short period. However, the pressure to stop global deaths as soon as possible meant that developing vaccines in such a short time inevitably involved certain risks. This included deferring some of the time-consuming safety studies (such as identifying potential toxicity) typically performed with great care when developing drugs, including vaccines, which could lead to a risk of chronic toxic effects from vaccination while reducing relatively acute deaths caused by SARS-CoV-2. Dr. Domingo reviews the preclinical safety studies that have been published after a period of about five years, albeit in limited numbers, to assess these potential toxic effects and attempt to clarify the situation. Therefore, the rationale for this review is solid, and the timing is quite appropriate. The published studies primarily focus on preclinical animal research, due to the fact that, although adapting results to humans may present significant challenges due to species differences, animal studies are more controllable, standardized, and allow for direct and unequivocal comparison of test group results with control group results compared to human epidemiological studies. The journals where the reviewed studies were published have been categorized into Q1 and Q2 based on their impact factors. Additionally, a review was conducted of journals that are not directly toxicology journals but have published similar studies. The author accurately notes that the number of published preclinical studies is very limited, emphasizes the high likelihood that pharmaceutical companies developing the vaccines possess preclinical study data, and highlights that publishing these data and having them examined by scientists, particularly toxicologists, would be of great benefit for humanity in addressing similar pandemics in the future. The author points out on page 10, in the second paragraph, that Baldrick's (2022) examination of the number and adequacy of preclinical toxicity studies for vaccines and other drugs developed against COVID-19 is intriguing. In this context, it would be appropriate for the author to mention the International Coalition of Medicines Regulatory Authorities (ICMRA), established for the rapid development of COVID-19 vaccines and other drugs, in the Discussion section and to reference an article that raises and discusses this issue (Orhan H, Covid-19 and pharmaceutical strategies (in Turkish). MISED 2021 November; 47-48: 7-16). Although this article is

published in Turkish, it can be easily understood with today's automatic translation tools and is available online. If the author wishes, I can also send it separately. Another suggestion is the recent paper by Gardner et al. (2024), which shows that while an adenoviral Covid-19 vaccine produced by Oxford/AstraZeneca and Janssen elicited a T-cell immune response, this response did not develop with mRNA vaccines. Although this study is based on human rather than animal experiments, it could still be quite important regarding vaccine-related adverse effects and might be worth mentioning in the review article.