



How to Increase the Immunogenicity of SARS-COV-2 Inactivated Vaccines?

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Seven months after the second dose of SARS-COV-2 Inactivated vaccines (INA), the amount of Spike-specific IgG Memory B cells was very low and the titer of Anti-SARS-COV-2 spike protein neutralizing antibodies (NABs) decreased over time (1, 2).

The T-cells response induced by INA in Mice's Sera is very low or undetectable, and the secretion of Interferon- γ (INF- γ) by T-cells is lower than all other SARS-COV-2 vaccines; only NABs are detectable in Mice's Sera. On the other hand, SARS-COV-2 Ad5-vectored adenovirus vaccines (rAd) have a high ability to stimulate the response of T-cells, but they have low effective NABs. Since the immunogenicity of SARS-COV-2 vaccines depends on NABs level, a heterologous vaccination schedule can be used to increase NABs level and enhance T-cells response (3).

Heterologous vaccination schedule, known as "mix and match", uses different vaccines for the first dose, as a prime dose, and the second dose as a booster dose to increase the stimulus and response of T-cells to SARS-COV-2 but researches on the heterologous vaccination schedule using the INA had only been examined on mice, and human clinical-trials need to be performed to evaluate the safety and immunogenicity (2, 3, 4). With the prime dose of INA, the geometric mean titers (GMTs) of NABs measured in Mice sera after the third dose of INA (3*INA), increased by 3-fold from two dose of INA. In other hand, NABs after the heterologous boost rAd followed by two doses of INA (2*INA+rAd) increased by 25.6-fold compared with 3*INA.

IgG2a titer, significantly higher in 2*INA+rAd than 3*INA. IgG2a/IgG1 ratio of 2*INA and 3*INA had no significant differences between them; but it was higher than IgG2a/IgG1

ratio of 2*INA+ rAd.

There was no significant difference in the response of SFUs/2*10⁵ cells between the 2*INA and 3*INA, But the response of SFUs/2*10⁵ cells were higher in 2*INA+rAd (2). Interleukin-4 levels did not elevate in all vaccinated groups compared to control groups who did not receive any vaccine. The level of Interleukin-2 induced by 2*INA+rAd, 4.16-fold of 2*INA and 2.64-fold of 3*INA. Interleukin-10 level hadn't significant differences in all vaccinated groups (2, 3).

Based on results of animal studies, the boost dose rAd increases the immunogenicity of the INA, although human clinical trials need to be performed to evaluate the safety and immunogenicity (2, 3, 4).

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