

VAC_01 - Second-generation Vaccines: Adjuvants and Booster Doses

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Introduction: The second generation of vaccine preparations is really important to trigger a humoral/cellular immune response and to induce a Th1/Th2 type immune response. The outer membrane vesicles (OMV) are viable/suitable for both mucosal and parenteral immunization, so their use as an adjuvant should be studied.

Objective: We proposed a new vaccine platform with the recombinant receptor-binding domain (rRBD) of the Spike protein of SARS-CoV-2 (antigen), *Neisseria meningitidis* OMVs and aluminum hydroxide (AH) as adjuvants. Along with this, we analyzed the cellular and humoral response immunization following 2 intramuscular (IM) and 2 intranasal (IN) doses.

Methodology: Swiss mice (n=5 each group) were immunized with 3µg of rRBD complexed to 0.1mM AH plus 10µg/mL of *meningococcus* OMV B:8:P1.6 (prep.1) or C:2a.P1.5 (prep.2) or rRBD alone (control). We immunized them with 2 IM doses 15 days apart and 2 IN doses 7 days apart. IN inoculation was performed without AH. IgA and IgG production was assessed 15, 30, 37, and 45 days after the 1st dose by ELISA. Avidity and neutralization were studied as well. 45 days after immunization, the spleens were collected for ELISpot assay (cytokines - IFN- γ /IL-17) under rRBD stimuli. The significance of the results was evaluated by One-way ANOVA followed by Tukey post-test. P values were considered significant when $p \leq 0.05$.

Results: We observed an increase in IgG production when rRBD was mixed to OMV plus AH, in both prep1 and prep2. IgA was detected in sera collected at days 37 and 45, only after IN doses. Adjuvanted groups presented IgG of intermediate avidity and higher neutralizing indexes. We found an increase of cytokines producing cells in splenocyte culture from animals immunized with prep1/prep2. The results suggest a good immunostimulatory, using rRBD plus OMV, showing a promising platform for the second generation of COVID-19 vaccine.

Conclusion: Future COVID-19 vaccines, which will be used as boosters, should be effective in eliciting neutralizing antibodies and cellular immune responses. Therefore, new adjuvants should be tested, using new variants, along with the use of other OMVs to develop new vaccine platforms and allow more countries to expand their immunization programs.

Keywords: SARS-CoV-2 vaccines; Outer membrane vesicles (OMV); Aluminum hydroxide (AH)