Linked to Variant Neutralisation Nasal COVID Vaccine Boost Increases IgA Responses

Current intramuscular vaccines excel at eliciting blood-based immunity but sometimes fail to prevent SARS-CoV-2 transmission, a discrepancy attributed to their inability to induce a response in the upper respiratory mucosa. However, the present study evaluated immune responses rather than clinical transmission outcomes.

In a recent study published, researchers investigated whether intranasal (IN) boosters could augment the efficacy of prior intramuscular COVID vaccines (inactivated whole-virus) in a small human cohort, with paired antibody analyses in six volunteers, cytokine analyses in eight volunteers, and detailed monoclonal antibody and multi-omics analyses largely derived from a single donor.

Study findings demonstrated that two-dose INs (Ad5-S-Omicron vaccine) "reprogrammed" existing immune memory from previous injections, triggering a specialized "class switch" to Secretory IgA (sIgA) antibodies.

Encouragingly, these novel nasal antibodies were observed to be substantially, in some cases hundreds-fold, more effective at neutralizing Omicron variants than standard blood antibodies. By identifying molecular features consistent with mucosal homing rather than directly tracking cell migration, this study provides preliminary mechanistic insight relevant to next-generation mucosal vaccines.

Study

The present study aimed to address this knowledge gap by investigating whether nasal booster vaccinations could augment the efficacy of intramuscular vaccinations in protecting individuals against future infections, and the mechanisms underpinning the recruitment of sIgA into the nasal cavity, while recognising that clinical protection outcomes were not directly measured.

The study sample comprised multiple small subgroups: six participants for paired antibody potency analyses, eight for cytokine profiling, and intensive monoclonal antibody discovery largely from a single donor, which limits generalizability. Study participants received a two-dose intranasal booster with the Ad5-S-Omicron vaccine, an adenovirus-based platform encoding the spike protein of the Omicron BA.1 variant.

The study leveraged next-generation "multi-omics" methodologies to monitor participants' immune responses. These included:

- Mass Spectrometry of Immunoglobulin sequencing (MS Ig-seq), a liquid chromatography-tandem mass spectrometry-based approach used to identify specific antibody proteins in nasal washes.
- Single-cell B Cell Receptor sequencing (scBCR-seq) is a high-throughput method that enables genetic characterization of B cells responsible for the antibodies identified in MS Ig-seq.
- Single-cell RNA sequencing (scRNA-seq), high-throughput gene expression profiles of B cells at multiple time points (Day 10 and Day 30) to observe how and when they migrate to the nasal cavity, inferred primarily from receptor expression patterns rather than direct in vivo tracking.
- Using cytokine assays, the study measured the concentrations of 15 signaling proteins in nasal swabs to characterize the chemical environment that recruits immune cells to the respiratory lining.

Findings

Study findings revealed a significant disparity between nasal and blood immunity. Purified nasal sIgA was observed to be significantly (many fold) more potent than the serum IgG found in the same individuals.

Specifically, nasal sIgA was 17-fold more potent against the Wild-Type virus, 30-fold against BA.1, 125-fold against BA.5, and 813-fold against the XBB.1.5 variant.

The analyses of multi-omics data successfully tracked the "reprogramming" of participants' immune systems. Key findings included:

- Memory restimulation: The intranasal booster was observed to not only stimulate the creation of new immune cells, but it also restimulated "memory" B cells created by the original needle injections to secrete antibodies.
- Antibody class switch: Notably, these restimulated B cells underwent Class Switch Recombination (CSR), shifting from IgG to IgA production. The probability of this switch increased to approximately 70.8% in clonotype-level analyses, rather than the cohort-wide estimate, after the nasal booster.
- Gene upregulation: Following nasal booster administration, B-cell homing receptors, specifically CCR10 (Chemokine Receptor 10) and α4β1 (Integrin alpha-4 beta-1), were found to be significantly upregulated.
- Cytokine upregulation: The study observed a transient rise in cytokines like CCL27 and CCL28 ($p < 0.05$ or $p < 0.01$), which served as the target for the homing receptors on the surface of the IgA-secreting cells, thereby signaling these B cells to congregate in the nose, although the causal migration pathway remains incompletely defined.

Conclusion

The present study provides preliminary human evidence, albeit from small and partly single-donor analyses, that a "prime-boost" strategy, augmenting a previous intramuscular vaccine with a nasally administered adenovirus-based platform, allows for a multi-system defense from entry

point (sIgA-based mucosal protection) to the lungs (IgG-based blood protection), but clinical effectiveness and durability require confirmation in larger trials.

The study observed a decline in nasal sIgA levels over time (a 65% reduction within 3 months), suggesting that regular mucosal boosters may be necessary to maintain immunity. However, the implications for real-world protection remain uncertain.

Source:

https://www.news-medical.net/news/20260215/Nasal-COVID-vaccine-boost-increases-IgA-responses-linked-to-variant-neutralisation.aspx