RV144 VACCINE INDUCED IGA INHIBITS NEUTROPHIL PHAGOCYTOSIS

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Background: Immune correlates analysis of the moderately protective RV144 vaccine trial revealed that Env-specific functional antibodies activating innate immune cells were potentially protective. However, plasma IgA to gp120 was a negative correlate. Neutrophils are highly functional effector cells with the potential to induce both Antibody-Dependent Cellular Cytotoxicity (ADCC) and antibody dependent phagocytosis. Neutrophils are highly abundant at key HIV transmissions sites, however, RV144 vaccine samples have not yet been evaluated for neutrophil Fc mediated responses. We investigated the role of plasma IgA and IgG for mediating Antibody-Dependent Neutrophil Phagocytosis (ADNP) and neutrophil antibody-dependent cellular cytotoxicity (NADCC).

Methods: Plasma samples were obtained from the RV144 vaccine trial (80 Vaccinees and 20 placebo recipients). We developed new methods to assess primary blood neutrophil ADNP and NADCC and assessed whole plasma, IgA-depleted plasma and purified IgG fractions for activity.

Results: Purified IgG from RV144 vaccinees was able to stimulate ADNP and NADCC compared to placebo recipients IgG (both $P < 0.0004$). IgA-depleted plasma induced higher ADNP responses than the whole plasma samples at the same concentration of IgG ($p = <0.0001$), suggesting IgA inhibits ADNP. There was no significant difference between the IgA-depleted plasma and whole plasma in mediating NADCC responses.

Conclusion: The RV144 vaccine induced HIV antibodies capable of mediating ADNP and NADCC responses. IgA inhibited neutrophil mediated phagocytosis, suggesting a possible mechanism behind the negative correlation with IgA and vaccine efficacy. Understanding the mechanisms of why IgA inhibits ADNP and not NADCC responses could lead to improved future HIV vaccine design. Since neutrophils are abundant at key sites of HIV transmission, they are a key effector cell for analysis of Fc mediated effector functions in future vaccine trials.

Disclosure statement:
The authors declare no competing conflicts of interests.