Immunogenicity and in vivo protective effects of recombinant nucleocapsid-based SARS-CoV-2 vaccine Convacell®

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February 11, 2023

Abstract

Background The vast majority of SARS-CoV-2 vaccines which are licensed or under development focus on the spike (S) protein and its receptor binding domain (RBD). However, S and RBD from SARS-CoV-2 variants of concerns show considerable sequence variations and repeated injections for boosting specific immunity are necessary. Aim of this study was to develop and characterize a SARS-CoV-2 vaccine targeting the highly conserved nucleocapsid (N) protein. **Methods** Recombinant N protein was expressed in *Escherichia coli*, purified to homogeneity by chromatography and characterized by SDS-PAGE, immunoblotting, mass spectrometry, dynamic light scattering and differential scanning calorimetry. The N protein vaccine was obtained by formulation of recombinant N as squalane-based emulsion and used to immunize Balb/c mice, NOD scid gamma (NSG) mice engrafted with human PBMC, rabbits and marmoset monkeys to study safety as well as antibody and cellular immunity using ELISA for antibodies, measurement of N-specific Th1 and Th2 cytokine secretion and carboxyfluorescein succinimidyl ester (CFSE) dilution assays for CD4 $^{+}$ and CD8 $^{+}$ T cell responses. The protective effect of the vaccine was studied in SARS-CoV-2-infected Syrian hamsters. **Results** Immunization of mice, rabbits and Syrian hamsters with the recombinant N protein-based vaccine formulated as squalane-based emulsion (Convacell®) induced sustainable N-specific IgG responses and a N-specific mixed Th1/Th2 cytokine response. In marmoset monkeys a N-specific CD4 $^{+}$ as well as CD8 $^{+}$ T cell response was observed. Vaccinated and then infected Syrian hamsters showed reduced lung histopathology, reduced virus was detected in lung tissue, lung weight relative to the body was not increased after challenge and body weight was regained faster than in non-vaccinated animals. Repeated dose toxicity studies in mice and rabbits showed that Convacell® was well tolerated and safe. **Conclusions** Convacell® induced a SARS-CoV-2-specific protective immune response in Syrian hamsters. It is a new vaccine targeting the nucleocapsid protein of SARS-CoV-2 and thus may augment the armamentarium of vaccines for COVID-19.

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