We performed repertoire analysis of RSV F-specific antibodies in six DS-Cav1-vaccinated individuals before and after vaccination. Methods: To understand the induced B-cell repertoire at the single-cell level, we evaluated RSV F-specific B-cell responses before and after vaccination in six participants. Using a combination of antigen-specific memory B-cell sorting, paired heavy and light chain sequencing of plasma cells, and unpaired heavy and light chain sequencing of naive and memory B-cell transcripts, we identified and characterized RSV F-specific antibody lineages. Using cryo-electron microscopy, we structurally defined two neutralizing public clonotypes targeting site II and V on pre-F.

Results: DS-Cav1-induced lineages recognized pre-F and were genetically diverse (555 RSV F clonal lineages were identified) from natural infection or whether certain antibody lineages targeting specific epitopes predominate.

Conclusions: Collectively, these findings demonstrate that vaccination with DS-Cav1 generates a diverse polyclonal response targeting all known antigenic sites present on pre-F. In addition, multiple neutralizing public clonotypes were identified, and a predominant prefusion-specific, vaccine-boosted public clonotype was structurally defined.

Abstract

Background: An effective vaccine for RSV is an unrealized public health goal. Recently, a single dose of the prefusion-stabilized fusion (F) glycoprotein subunit vaccine (DS-Cav1) was shown to substantially increase serum neutralizing activity in healthy adults. We sought to determine if vaccination with a stabilized prefusion conformation of F (pre-F) induces a repertoire mirroring the pre-existing diversity from natural infection or whether certain antibody lineages targeting specific epitopes predominate. We performed repertoire analysis of RSV F-specific antibodies in six DS-Cav1-vaccinated individuals before and after vaccination.

Methods: To understand the induced B-cell repertoire at the single-cell level, we evaluated RSV F-specific B-cell responses before and after vaccination in six participants. Using a combination of antigen-specific memory B-cell sorting, paired heavy and light chain sequencing of plasma cells, and unpaired heavy and light chain sequencing of naive and memory B-cell transcripts, we identified and characterized RSV F-specific antibody lineages. Using cryo-electron microscopy, we structurally defined two neutralizing public clonotypes targeting site II and V on pre-F.

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Conclusions: Collectively, these findings demonstrate that vaccination with DS-Cav1 generates a diverse polyclonal response targeting all known antigenic sites present on pre-F. In addition, multiple neutralizing public clonotypes were identified, and a predominant prefusion-specific, vaccine-boosted public clonotype was structurally defined.