proceedings

Abstract

A Cross-Reactive Mouse Monoclonal Antibody against Rhinovirus Mediates Phagocytosis In Vitro †

Mohammad Amin Behzadi [1], James Duehr [1,2], Angela Choi [1,3], Michael Schotsaert [1,3], Adolfo García-Sastre [1,3,4], Peter Palese [1,4] and Raffael Nachbagauer [1,*]

[1] Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA; ma.behzadi@mssm.edu (M.A.B.); james.duehr@icahn.mssm.edu (J.D.); angela.choi@icahn.mssm.edu (A.C.); michael.schotsaert@mssm.edu (M.S.); Adolfo.Garcia-Sastre@mssm.edu (A.G.-S.); peter.palese@mssm.edu (P.P.); raffael.nachbagauer@gmail.com (R.N.)
[2] School of Medicine, University of Pittsburgh, Pittsburgh, PA 15213, USA
[3] Global Health and Emerging Pathogens Institute, Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA
[4] Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA
* Correspondence: raffael.nachbagauer@gmail.com
† Presented at Viruses 2020—Novel Concepts in Virology, Barcelona, Spain, 5–7 February 2020.

Published: 15 July 2020

Abstract: Human rhinoviruses (RVs) are the main cause of the common cold worldwide. To date, more than 160 serotypes of the virus have been recognized. These viruses are categorized into three major groups: A, B, and C. There are currently no approved vaccines available to prevent infection with RVs. We designed a mouse immunization strategy that aimed to elicit a humoral response against conserved regions of capsid proteins of RV-A viruses. To this end, recombinant DNA plasmids expressing the capsid proteins (VP1-4) and two proteases (2A and 3C) of RV1A, 16, 49, 68, and 71 were engineered. Mice were sequentially vaccinated with these DNA plasmids at three-week intervals. After a final boost with purified whole virus using the RV15 strain, mice spleens were extracted and cells expressing monoclonal antibodies (mAbs) were generated by hybridoma fusion. A total of 98 mAbs with reactivity to different strains of RV-A were isolated. After isotyping, 22 mAbs expressing an IgG Fc-domain were selected for further expansion and purification. Three mAbs showed cross-reactivity against multiple strains of RV-A viruses by ELISA, including 1A, 1B, 15, 16, and 49. Additional mAbs had strain-specific binding patterns, with a surprising number of mAbs showing reactivity to RV15, the strain used for the final vaccination. Using a microneutralization assay, we found that the RV15-specific mAbs, but not the cross-reactive mAbs, were highly neutralizing. Additional testing in a flow cytometry-based antibody-dependent cellular phagocytosis (ADCP) assay revealed a high degree of ADCP activity for one of the cross-reactive mAbs. Epitope mapping of the neutralizing mAbs via escape mutant viruses revealed binding sites with a shared epitope on VP1 of RV15. The epitope of the ADCP-active, non-neutralizing mAb was determined by the microarray analysis of cyclic constrained peptides generated from the VP1 capsid protein. This study identified a cross-reactive mAb that mediates phagocytosis. These findings could be used toward the development of vaccines against RV. The full study results have since been published (https://doi.org/10.1038/s41598-020-66600-x).

Keywords: rhinovirus; monoclonal antibody; phagocytosis; neutralization; cross-reactive