The human metapneumovirus (hMPV) is the second leading cause globally of acute infection of the respiratory tract in children, infecting the upper and lower airways. The hMPV may induce an inappropriate Th2-type immune response, which causes severe pulmonary inflammation, leading to the obstruction of airways. Despite its severe epidemiological relevance, no vaccines are currently available for the prevention of hMPV-induced illness. In this investigation, we demonstrated that immunization of mice with the recombinant hMPV nucleoprotein (hMPV-N) mixed with the AbiSCO-100 adjuvant reduced viral replication in lungs following challenge with the virus. We found that immunized mice had reduced weight loss, decreased granulocytes in the lung, an increased level of specific nucleoprotein antibodies of IgG1 and IgG2a-isotypes, and a local profile of Th1/Th17-type cytokines. Our results suggest that immunization with the hMPV-N and the AbiSCO-100 adjuvant induces a reduction of viral infection and could be considered for the development of an hMPV vaccine.