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Inducing Robust Humoral and Mucosal Immunity against SARS-CoV-2 using Yeast Surface Display System

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Abstract

The SARS-CoV-2 virus, the causative agent of the COVID-19 pandemic, has become a serious global health threat. The receptor-binding domain (RBD) of the spike protein is a critical component of the virus, essential for its entry into human cells, and a prime target for vaccine development. In this study, we aimed to enhance humoral and mucosal immunity by developing recombinant *P. pastoris* yeast displaying the RBD on its surface using the SEDI anchor. The RBD gene was synthesized and electroporated into competent *P. pastoris* cells. After screening positive clones on PAD plates, *P. pastoris*/pPink-αHC-RBD-SEDI was cultivated in BMGY medium and subsequently induced in BMMY medium. The surface expression of the RBD protein was confirmed using ELISA, flow cytometry, and immunofluorescence assays. Oral immunization was administered to mice on days 1 and 2 for primary immunization and on days 14 and 15 for booster immunization. Blood and fecal samples were collected on day 28. ELISA results indicated that the absorbance at 450 nm for yeast expressing RBD was twice as high as that of the control yeast. Mice administered with RBD-expressing yeast exhibited higher serum IgG levels compared to those receiving control yeast. Fecal IgA levels were also elevated in mice treated with RBD yeast compared to the control group, indicating enhanced mucosal immunity. Our findings underscore the significance of the RBD as a key target for SARS-CoV-2 vaccine design and provide evidence for the efficacy of an orally administered yeast based SARS-CoV-2 vaccine in inducing robust immune responses. Importantly, the yeast surface display system could serve as a universal technological platform for the development of other oral vaccines.

Key words: *p. pastoris*, SARS-CoV-2, receptor-binding domain (RBD), Immune response, yeast surface display.

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