

Supplementary information, Fig. S1. I-R-F induces more robust neutralization antibodies than RBD. **(a)** BALB/c mice (n=6/group) were i.m vaccinated with 10 μ g of I-P-F or equimolar of RBD, RBD-dimer, and R-F protein or PBS control with a single vaccination regimen. The levels of RBD-specific IgG in serum on day 28 after immunization were determined by ELISA. **(b)** BALB/c Mice (n=6/group) were intramuscularly vaccinated with 1 μ g of I-R-F or equimolar R-F plus IFN α protein without adjuvant and boosted with the same dose at a 14-day interval. Serum samples were collected on day 14 after the second immunization to evaluate the levels of RBD-specific IgG. **(c)** BALB/c mice (n=8/group) were immunized intramuscularly or subcutaneously with alum-adsorbed 10 μ g of I-R-F and boosted on day 14 after initial immunization with equivalent dose. Serum samples were collected every week to determine the SARS-CoV-2-specific IgG antibody titers by ELISA. **(d)** BALB/c mice (n=8/group) were immunized intramuscularly with alum-adsorbed 10 μ g of I-R-F by using a single dose (day 0), two-dose (day 0/14), and three-dose (day 0/14/28) immunization procedures, respectively. Sera were collected on days 7, 14, 21, 28, 35, and 42 after the initial immunization and analyzed by ELISA to determine the IgG titer. **(e)** The neutralization antibody titers in serum described in Fig (2d-2f) on day 28 were determined by SARS-CoV-2 pseudovirus neutralization assay. The dashed line indicates the limit of detection. Data are shown as mean \pm SEM. *P*-values were calculated by one-way ANOVA with multiple comparison tests. ns (not significant), **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.

