In silico prediction of immune-escaping hot spots for future COVID-19 vaccine design

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February 14, 2023

Abstract

The COVID-19 pandemic has had a widespread impact on a global scale, and the evolution of considerable dominants has already taken place. Some variants contained certain key mutations located on the receptor binding domain (RBD) of spike protein, such as E484K and N501Y. It is increasingly worrying that these variants could impair the efficacy of current vaccines or therapies. Therefore, how to design future vaccines to prevent the different variants remains urgent. In this work, we proposed an in silico approach, in which we combined binding free energy measured by computational mutagenesis of spike-antibody complexes and mutation frequency calculated from viral genome sequencing data, to estimate an immune-escaping score (*IES*) and predict immune-escaping hot spots. We identified 23 immune-escaping mutations on the RBD, nine of which occurred in omicron variants (R346K, K417N, N440K, L452Q, L452R, S477N, T478K, F490S, and N501Y), despite our dataset being curated before the omicron first appeared. The highest immune-escaping score (*IES*=1) was found for E484K, which agrees with recent studies stating that the mutation significantly reduced the efficacy of neutralization antibodies. Furthermore, our predicted binding free energy and *IES* show a high correlation with high-throughput deep mutational scanning (Pearson's r = 0.70) and experimentally measured neutralization titers data (mean Pearson's r = -0.80). In summary, our work provides valuable insights and will help design future COVID-19 vaccines.