Technology Overview

Most COVID-19 patients develop mild to moderate symptoms, while 15-20% of patients face hyper-inflammation induced by massive cytokine production, called a “cytokine storm,” ultimately leading to alveolar damage and respiratory failure. A significant challenge in targeting these immune responses is an incomplete understanding of how these cells trigger a cytokine storm. Using a combination of phenotypic screening with machine learning-based modeling, Fred Hutch researchers identified several protein kinases which act as regulators of SARS-CoV-2 spike protein N-terminal domain (NTD) stimulated cytokine and chemokine release. Specifically, they experimentally validated multikinase inhibitors, including the FDA-approved ponatinib, cobimetinib, sunitinib, and bosutinib, as potent inhibitors of S1 protein-mediated cytokine storm in PBMCs from healthy donors and COVID-19 patients. Treatment with ponatinib or cobimetinib outperformed other drugs, including dexamethasone and baricitinib, inhibiting all cytokines in response to NTD from SARS-CoV-2 and emerging variants. Therefore, these inhibitors could represent strong candidates for drug repurposing efforts aimed at providing an alternative and timely treatment for COVID-19 patients exhibiting major, life-threatening symptoms.

Applications

- Therapeutic treatment for COVID-19

Potential Advantages

- Experimental results suggest that specific multikinase inhibitors outperform other currently utilized therapeutic drugs.
- Identified compounds are FDA approved with known safety profiles.