**Abstract: Modeling the Cleavage Potential of Cross-Species TMPRSS2 Variants to Subunits of SARS-CoV-19**

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a positive-stranded RNA virus, has caused >100,000 infections and >50,000 deaths during the 2020 pandemic. The spike (S) glycoprotein mediates cell entry by recognizing the angiotensin converting enzyme II (ACE2) receptor, which initializes cleavage of the protein to induce cell membrane fusion. However, in previous studies transmembrane protease/serine subfamily member 2 (TMPRSS2) has increased the bonding affinity for SARS-CoV-2 to ACE2. This study aims to characterize cross-species variants of TMPRSS2 and its potential to cleave deviates of S proteins in silico. We hypothesize that TMPRSS2-like endoprotease aids in the spillover of SARS-CoV-19 to alternate host by cleavage of structurally similar ACE2. We will design a phylogenic construct of S proteins and TMPRSS2 amongst species to assess their similarity to human strains. We will utilize protein databanks to characterize the amino acid changes that would suppress TMPRSS2’s cleavage of SARS-CoV-19 S protein and ACE2. Additionally, databanks on the variation of TMPRSS2 within human populations will be used to gain insight on genetic drift. This will be used to create a model that scores the susceptibility/severity of various species to SARS-CoV-19 based off phylogenetic changes within TMPRSS2. This study will provide insight on possible spillover into alternate host with structurally similar TMPRSS2 strains compared to humans. While tracking the infectivity of SARS-CoV-19 by means of mutation in TMPRSS2 within human populations.

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