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Predicting Pangolin Lineage Call Success with Coverage Rates of SARS-CoV-2 Genomic Samples

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Polymerase Chain Reaction (PCR) diagnostic tests for the SARS-CoV-2 virus (COVID) have been commonplace during the global pandemic. PCR tests involve genomic sequencing of saliva samples. Genomic sequencing allows scientists to identify the presence and evolution of COVID. When a sample is run through a sequencer, the sequencer will make a read on each genomic base pair and the number of times a base pair is read is known as the base pair coverage. A sequencer's ability to obtain good coverage rates (i.e. high reads across the entire sequence) for a given sample depends upon sample quality and the type of PCR primers utilized. A primer is a short, single-stranded DNA sequence used in the PCR process that hybridizes with the sample DNA and subsequently defines the region of the DNA that will be amplified. Primer dropouts occur when the nucleotides of the primer are unable to successfully bind with the DNA of a sample. As the virus mutates, primer dropouts occur more frequently, leading to poor, if any, coverage and thus an inability to make a Pangolin-lineage call (i.e. identify the COVID variant type). New PCR primers for COVID testing are released semi-regularly in order to maintain high coverage rates. A natural question is: at what point should laboratories adopt new primers? This presentation aims to answer this question by investigating the probability of a given SARS-CoV-2 sample making a Pangolin-lineage call using statistical modeling. The explanatory variables are taken to be the coverages for each of the COVD base pairs. Variable selection was utilized to identify the most important regions in the sequence for making a Pangolin-lineage call. Using the identified genomic regions, bioinformaticists can monitor each region over time along with the associated probability of making a lineage call. Any downward trends in region coverages and resulting downward trends in the estimated probability of making a call are considered signals that the existing primers need replacing.

Keywords

SARS-CoV-2; genomics; PCR diagnostic testing

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