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ANALYSIS OF CORONAVIRUS PROTEASE INHIBITORS AS POTENTIAL THERAPEUTICS

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SARS-HCoV, or Severe Acute Respiratory Syndrome, is a novel human coronavirus that appeared within China in 2003. To date there are no vaccines or antiviral drugs able to either halt or prevent an infection by the virus. As part of an ongoing study, experiments were designed to develop and assess broad-spectrum antiviral drugs against several human and murine coronaviruses. The research involved testing antiviral drugs against the mouse coronavirus MHV. These drugs, which were composed of branched organic compounds, targeted the active site of one of the two proteases of the murine coronavirus, 3CLPro, halting the enzymatic activity resulting in viral inhibition. The drugs had already been proven effective in purified protease samples, but had yet to be tested in living cells. Thirty-five drugs were tested, and while twenty-two displayed no viral inhibition and five exhibited cell toxicity, eight drugs were shown to strongly inhibit viral replication. The drugs that were found to be effective at inhibiting the viral replication will continue on to be tested against SARS-HCoV in the Biosafety Level 3 lab at UIC. The effective drugs were also used further in order to screen for drug resistant variants of the virus. These mutants can then be sequenced so that the drugs can be improved and the resistance avoided.