

Vitamin B12 may inhibit RNA-dependent-RNA polymerase activity of nsp12 from the SARS-CoV-2 virus

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Abstract

SARS-CoV-2 is the causative agent for the ongoing COVID19 pandemic, and this virus belongs to the Coronaviridae family. Like other members of this family, the virus possesses a positive-sense single-stranded RNA genome. The genome encodes for the nsp12 protein, which houses the RNA-dependent-RNA polymerase (RdRP) activity responsible for the replication of the viral genome. A homology model of nsp12 was prepared using the structure of the SARS nsp12 (6NUR) as a model. The model was used to carry out in silico screening to identify molecules among natural products, or Food and Drug Administration-approved drugs that can potentially inhibit the activity of nsp12. This exercise showed that vitamin B12 (methylcobalamin) may bind to the active site of the nsp12 protein. A model of the nsp12 in complex with substrate RNA and incoming NTP showed that vitamin B12 binding site overlaps with that of the incoming nucleotide. A comparison of the calculated energies of binding for RNA plus NTP and methylcobalamin suggested that the vitamin may bind to the active site of nsp12 with significant affinity. It is, therefore, possible that methylcobalamin binding may prevent association with RNA and NTP and thus inhibit the RdRP activity of nsp12. Overall, our computational studies suggest that methylcobalamin form of vitamin B12 may serve as an effective inhibitor of the nsp12 protein.

Keywords: RNA-dependent-RNA polymerase; SARS-CoV-2; inhibitor; nsp12; vitamin B12.

Figures

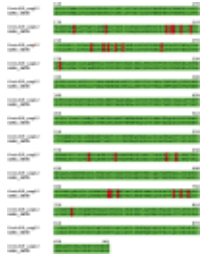


FIGURE 1 Alignment of the sequence of...

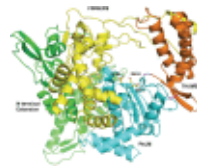


FIGURE 2 Model of the SCV2-nsp12 enzyme...

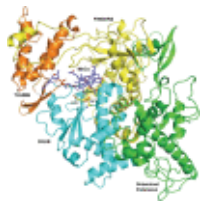


FIGURE 3 Model of the SCV2-nsp12 enzyme...

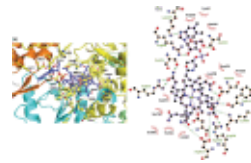


FIGURE 4 Residues of SCV2-nsp12 that interact...

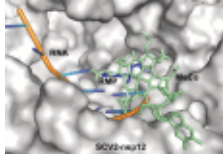


FIGURE 5 Binding site of methylcobalamin (MeCo)...

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