Targeting RNA Viruses Using Inhibitors of METTL3

New and effective treatments for COVID-19 and other viral infections caused by RNA viruses.

Technology

NYU Langone Health researchers have found a novel way to suppress viral replication, which can be used against coronaviruses and is also likely effective against many other RNA viruses. The investigators have demonstrated how virus replication is dependent upon the host N6 adenosine methylation (m6A) pathway. Specifically, coronavirus replication can be inhibited by blocking METTL3, the catalytic subunit of an enzyme that methylates adenosine residues at the N6 positions on some RNAs. This replication suppression was achieved both by using chemical inhibitors and by genetic approaches e.g., siRNA. In addition, inhibiting one or more of the YTHDF family of proteins—which are N6 methyladenosine readers that can affect RNA degradation and translation—also inhibits virus replication.

Background

The human coronavirus COVID-19 virus (also called SARS-CoV-2) has triggered a worldwide pandemic that has killed more than 3M people as of April 2021. This RNA virus causes a harsh type of pneumonia and symptoms vary but may include: fever, cough, chills, severe fatigue and trouble breathing. COVID-19 has had major economic and social impacts on life worldwide as many people were forced to quarantine, reduce travel and limit daily activities.Recently, effective vaccines against the COVID-19 virus have been authorized and administered to large parts of the population. However, with large parts of the worldwide population not fully-vaccinated and infection cases rising in many parts of the world, new ways to treat COVID-19 are still very much in demand.

Applications

- Inhibition of one or more of the targets described here as reducing viral replication by a small molecule.
  - METTL3
  - YTHDF1
  - YTHDF2
  - YTHDF3
- Inhibition of the above targets with siRNA-based approaches.
- RNA chemical modifications, such as m6A, are very common and affect gene expression in various cellular processes. Better understanding of these processes and how they modulate virus reproduction can assist in alleviating these disease states.

Advantages

Technology ID

MOH02-08

Category

Life Sciences/Biochemicals & Small Molecules
Life Sciences/Therapeutics/Infectious Disease/Coronavirus
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- This is the first report demonstrating that:
  - SARS-CoV-2 replication can be suppressed by interfering with the cellular m6A modification pathway.
  - A small molecule METTL3 inhibitor displays anti-viral activity.
- Targeting the m6A machinery is specific to viral replication and data from other studies suggest that because METTL3 inhibition does not affect global RNA production and does not diminish anti-viral mRNA levels in the cell, it lacks general toxicity and will be well-tolerated in cells
- Given that replication of other RNA viruses is also dependent upon METTL3, inhibiting the host m6A modification machinery may be an effective strategy to antagonize replication of many viruses.

IP Status

Non-provisional patent application pending