Docket #: S19-283

Enhancing the Antiviral Efficacy of RNA-Dependent RNA Polymerase Inhibition by Combination with Modulators of Pyrimidine Metabolism

Stanford researchers in the Khosla lab have identified a host-targeting antiviral strategy by modulating the host's pyrimidine metabolism. This combination therapy markedly increased the potency of R1479, an RNA-dependent RNA polymerase (RdRp) inhibitor, against dengue virus replication. At efficacious drug doses, the effect on the growth rates of uninfected cells was minimal. With increasing interest in RdRp inhibitors as antiviral agents, this research offers a promising way to enhance their clinical utility by combining them with modulators of mammalian pyrimidine metabolism.

Related technology: S15-464

Applications

- Lead molecules are known to be safe in mice and do not show appreciable toxicity.
- This research suggests a potential therapy against RNA viruses with a combination strategy that targets both host pyrimidine biosynthesis and viral RdRp.

Advantages

- Potentially improves the therapeutic index of R1479, lowering the EC50 of the well-characterized RdRp inhibtior R1479 by more than four fold.

- Focusing on devising host targets (instead of virus targets) may serve the next-generation broadspectrum antiviral therapeutics development.

Patents

- Published Application: WO2021011572
- Published Application: 20220280513

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