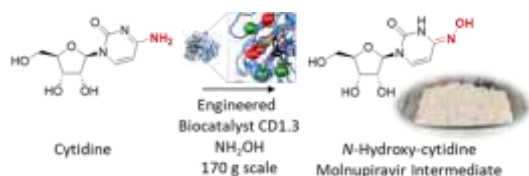


AN ENGINEERED CYTIDINE DEAMINASE FOR BIOCATALYTIC PRODUCTION OF A KEY INTERMEDIATE OF THE COVID-19 ANTIVIRAL MOLNUPIRAVIR

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The Covid-19 pandemic highlights the urgent need for cost-effective processes to rapidly manufacture antiviral drugs at scale. Here we present a concise biocatalytic process for Molnupiravir, a nucleoside analogue recently approved as an orally available treatment for SARS-CoV-2. Key to the success of this process was the development of an efficient biocatalyst for

the production of *N*-hydroxy-cytidine through evolutionary adaption of the hydrolytic enzyme cytidine deaminase. This engineered biocatalyst performs >85 000 turnovers in less than 3 h, operates at 180 g/L substrate loading, and benefits from *in situ* crystallization of the *N*-hydroxy-cytidine product (85% yield), which can be converted to Molnupiravir by a selective 5'-acylation using Novozym® 435.