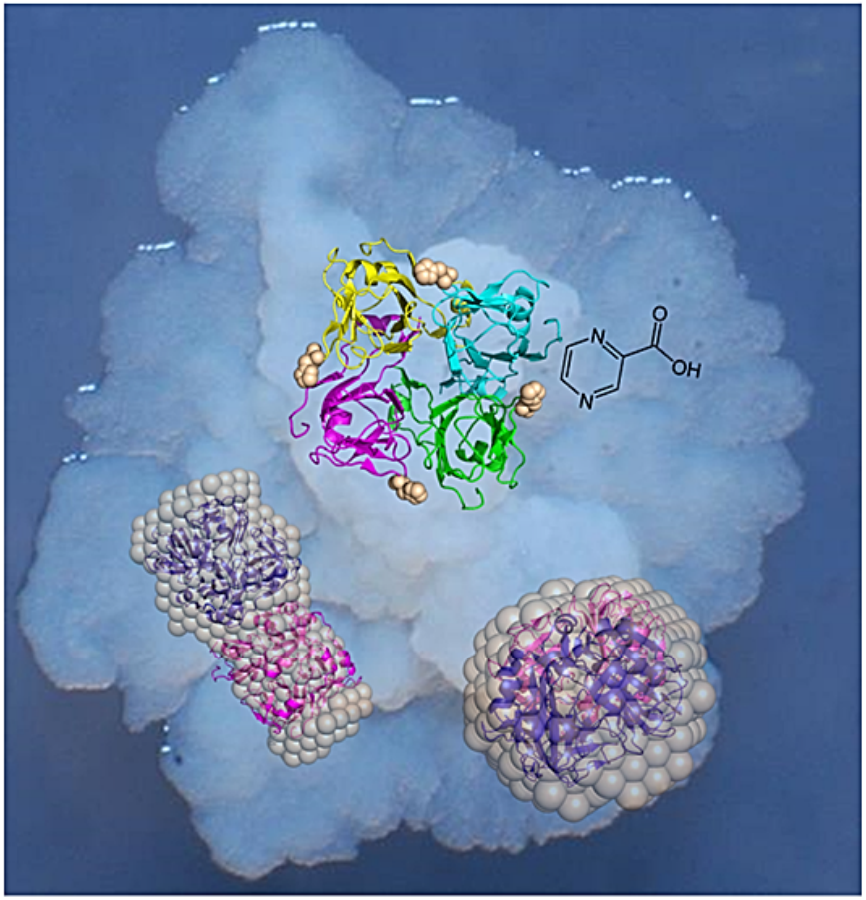
ACS Infectious Diseases

NOVEMBER 2017
VOLUME 3
NUMBER 11
pubs.acs.org/acsinfectious



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Prof Grüber's research team (NTU) and Prof. Dick's (NUS) team uncovered a mechanism of action of the first line TB drug pyrazinamide

The lung disease tuberculosis (TB), caused by *Mycobacterium tuberculosis*, kills more people than any other infectious disease. New and more efficacious drugs are urgently needed. Pyrazinamide is a key first line drug for treatment of TB. However, its bacterial target remained unknown – until recently. In an interdisciplinary research effort the labs of Profs. Dr Gerhard Grüber, NTU and Dr Thomas Dick, NUS and Rutgers, identified inhibition of coenzyme A biosynthesis as the mechanism of action of pyrazinamide. Using a combination of *in vitro* and *in vivo* genetics, metabolomics, biophysics and structural biology the teams showed that the drug inhibits the critical enzyme aspartate decarboxylase. This provides the basis for the rational discovery of next generation pyrazinamide with improved potency.

This research article has been accepted and featured as a cover story in ACS Infectious Diseases (Vol. 3, Pages: 807-819 (2017)).