

Lowering the Survival Chance of Bacteria

Beamlines: AMX & FMX

P. aeruginosa



wt

wt+NL1

cbs/cse

The left shows a normal bacterial colony with a tight-knit biofilm matrix that can weather attacks by antibiotics. The middle and the right show colonies in which the enzyme CSE is blocked by the study's compound. These colonies can no longer hold together and begin to spread out, making them more vulnerable.

K. Shatalin, A. Nuthanakanti, A. Kaushik, D. Shishov, A. Peselis, I. Shamovsky, B. Pani, M. Lechpammer, N. Vasilyev, E. Shatalina, D. Rebatchouk, A. Mironov, P. Fedichev, A. Serganov, E. Nudler. *Science* **372** (6547), 1169-1175 (2021).

Scientific Achievement

Scientists discovered that some bacteria rely on the enzyme cystathionine γ -lyase (CSE) to produce hydrogen sulfide (H_2S) as a defense mechanism to increase antibiotic tolerance.

Significance and Impact

X-ray structural studies combined with simulations identified drug-like inhibitors of CSE, which block its action and boost the potency of existing antibiotics.

Research Details

- Showed that H_2S production by the enzyme cystathionine γ -lyase (CSE) causes self-poisoning of bacteria so they go dormant to prevent antibiotics from eradicating them.
- CSE structures were determined using NSLS-II beamlines AMX and FMX & ANL NE-CAT beamlines.
- “Virtual screening” was used to identify drug-like compounds that inhibited CSE, and hence H_2S production, with few side effects.