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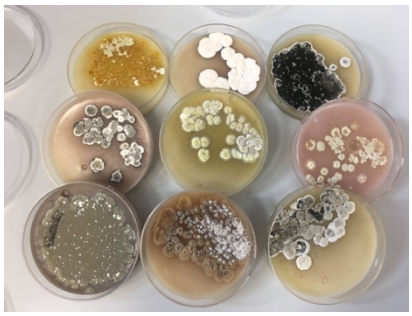
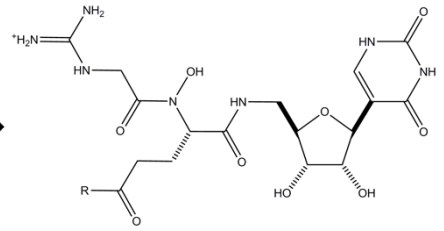
New Antibiotics: Efficient Microbial Extract Screening and Mutational De-Replication



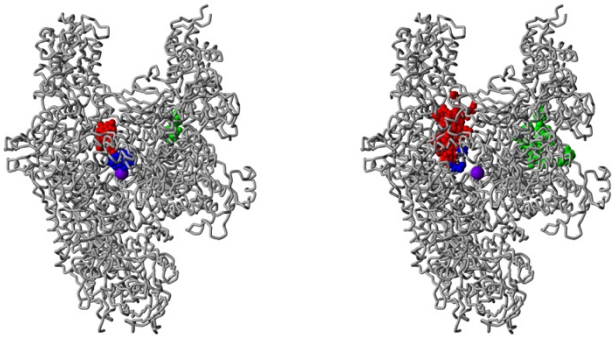


pseudouridimycin

Richard H. Ebright, Ph.D. is Board of Governors Professor of Chemistry and Chemical Biology at Rutgers University and Laboratory Director at the Waksman Institute of Microbiology. His laboratory seeks to understand structures, mechanisms, and regulation of bacterial transcription complexes, and to identify, characterize, and develop small-molecule inhibitors of bacterial transcription for application as antituberculosis agents and broad-spectrum antibacterial agents.

Co-Inventor: Stefano Donadio, Ph.D.

Intellectual Property: US provisional patent application filed on September 27, 2017



Structure of bacterial RNA polymerase, showing the binding sites (left panel) and resistance targets (right panel) for the current antibacterial drug rifampin (red) and the investigational antibacterial compounds pseudouridimycin (blue) and myxopyronin (green).

Innovation Summary: Rutgers University researchers have developed a new platform technology that enables discovery of new antibiotics that function by inhibiting bacterial RNA polymerase.

The new platform technology overcomes two obstacles to discovering and prioritizing new antibacterial compounds by use of microbial-extract screening: (1) microbial extracts can contain previously known antibacterial compounds (resulting in effort wasted on re-isolation of previously known antibacterial compounds), and (2) microbial extracts can contain antibacterial compounds at concentrations that differ by multiple orders of magnitude (invalidating use of rankings of antibacterial activities of extracts to infer antibacterial activities of antibacterial compounds therein).

The new platform technology overcomes these obstacles by using mutational de-replication to eliminate extracts that contain previously identified compounds and by quantifying compounds before assaying antibacterial activities.

Using the new platform technology, the researchers have identified 10 new inhibitors of RNA polymerase, most of which function through new binding sites on RNA polymerase.

Advantage:

- The new platform technology enables discovery of new antibacterial compounds even in microbial-extract collections that previously were screened without success using competing technologies.

Market Applications:

- New antibacterial drug discovery platform.
- Pipeline of new antibacterial lead compounds.

Potential Economic and Social Impact:

- The global market for antibacterial drugs was $42 bn in 2016 and is estimated to be at least $45 bn in 2021.
- Bacterial infectious diseases kill 100,000 persons each year in the US and 11 million persons each year worldwide, representing nearly a fifth of deaths each year worldwide.

Next R&D Steps:

- Structure determination of the identified 10 novel inhibitors.
- Lead validation of the identified 10 novel inhibitors.
- Identification, structure determination, and lead validation of additional novel inhibitors.