



Articles of Significant Interest Selected from This Issue by the Editors

Hydroxyurea, an Old Drug with a Misunderstood Mechanism of Action

Hydroxyurea is commonly suggested to inhibit DNA replication through the inactivation of ribonucleotide reductase and depletion of deoxyribonucleoside triphosphate pools. However, this model is challenged by work from Nazaretyan et al. (e00713-17), who demonstrate that following a brief inhibition, replication rapidly recovers and continues in the presence of this drug. The authors go on to show that hydroxyurea toxicity occurs only after it is processed through a catalase-dependent reaction that generates intermediates that damage DNA directly. The results identify an unexpected mechanism of action for a drug that is widely used in the clinic and laboratory.

Relaxase Requires Unfolding for Efficient Translocation through the Conjugative Type IV Secretion System

Bacterial conjugation is a major mechanism of antibiotic resistance gene spread among bacteria. DNA is transferred from one bacterium to another through a conjugative type IV secretion system (T4SS) while in complex with a protein called a relaxase. Trokter and Waksman (e00615-17) demonstrate that relaxase has to undergo unfolding for efficient translocation through the conjugative T4SS. Additionally, they present several protein substrate modifications that efficiently block substrate translocation and could potentially be used as a tool for trapping the substrate within T4SS channel to elucidate the mechanism of T4SS substrate translocation.