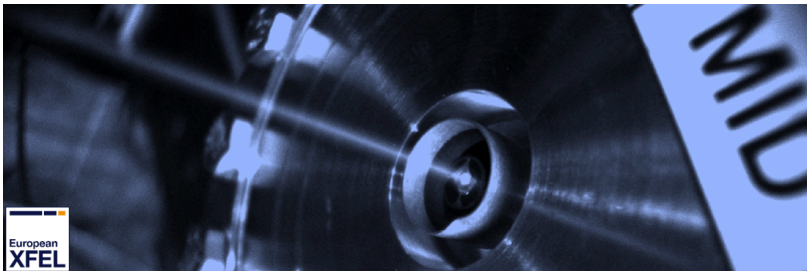

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Structural insight into the binding mode of sisomicin derivatives and gentamicin C2b to the decoding center of the 30S ribosomal subunit

Thursday 19 January 2023 19:23 (7 minutes)

Aminoglycosides are antibiotics that cause translational misreading of mRNA by binding to the A-site in the 30S ribosomal subunit. Together with the importance of antibiotics in the clinic, there are still missing details about their binding mode and structural dynamics on the decoding center of the 30S ribosomal subunit. Sisomicin is a precursor of structurally similar aminoglycoside antibiotic gentamicin and gentamicin involves five subtypes (C1, C1a, C2, C2a, C2b). Each subtype displayed differences in ototoxicity in vitro. Within them, gentamicin C2b is detected as less ototoxic compared to sisomicin. Although sisomicin is a highly effective broad-spectrum antibiotic for the treatment of bacterial infections, the side effects in terms of oto- and nephro- toxicity play a critical role during the treatment. Previously, it was determined that modifications on the sisomicin lowered ototoxicity with variable effects on antimicrobial activity. Here, revealing the crystal structure of 30S ribosomal subunit in complex with sisomicin derivatives and assessing ribosomal interaction at atomic-level of resolution will provide invaluable information for future studies. Additionally, comparison of binding modes with 30S ribosomal subunit in complex with gentamicin C2b will highlight the structural dynamics of the decoding region.

Primary author: DESTAN, Ebru

Co-author: DEMIRCI, Hasan (Koc University)

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