Granted projects from the first JPIAMR transnational call
InnovaResistance: Innovative approaches to address antibacterial resistance

Non-conventional approaches for peptidoglycan cross-linking inhibition

Peptidoglycan (PG) is an attractive and validated target for antibacterial drug development for two main reasons. First, it is an essential and unique bacterial cell wall polymer with no counterpart in human cells, minimizing the risk of drug toxicity. Second, the essential PG synthases are exposed at the outer surface of the cytoplasmic membrane, making them highly accessible for antibiotic inhibition. Formation of the PG network requires glycosyltransferases for glycan chain elongation and transpeptidases for peptide cross-linking. Transpeptidation involves two stem peptides that act as acyl donor and acceptor substrates, respectively. Read more

Keywords: B-lactam; Peptidoglycan; transpeptidase, Penicillin-bindning protein (PBP); glycosyltransferase

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Sensiting Preudomonas aeruginosa biofilms to antibiotic and reducing virulence through novel target inhibition

The traditional approach to combating bacterial infections has been based on the use of antibiotics which kill bacteria or inhibit their growth. There has also been a strong emphasis on the identification of essential gene targets for drug intervention. A major problem with therapeutic approaches targeting viability is that they induce strong selective pressures resulting in the rapid emergence of antimicrobial resistance. An alternate approach is to inhibit virulence rather than bacterial viability and this will be explored in the SENBIOTAR project. Read more

Keywords: Novel targets, inhibition of virulence, drug delivery, combination therapy, sensitising biofilms to antibiotics

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Repotentiating Beta Lactam antibiotics

The most common form of resistance to B-lactam antibiotics is the expression of B-lactamase enzymes. These bacterial enzymes are capable of inactivating B-lactam drugs by hydrolyzing their B-lactam ring, rendering them ineffective. Co-administration of a B-lactam antibiotic with a B-lactamase inhibitor is a recognized strategy to circumvent this type of bacterial resistance, yet the number of compounds that have actually made it to clinical application so far is extremely limited. The aim of this project is to discover and characterize new molecules of botanical origin that selectively inhibit B-lactamases, yielding new lead compounds. Read more

Keywords: beta-lactamases, inhibitors, PECKISH library

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Structure-guided design of pan inhibitors of metallo-p-lactamases

The fight against infectious diseases is one of the greatest public health challenges, especially with the emergence of pan-drug resiββstant carbapenemase-producing Gram-negative bacteria. In particular, the pandemic NDM1 and other plasmid-borne-metallo-β-lactamases (MBLs) disseminating worldwide in Gram-negative organisms threaten to take medicine back to thepre-antibiotic era as the treatment options remaining for infections caused by these “superbugs" are very limited. Read more

Keywords: Class B carhapenemases ,metallo-beta-lactamases, X-ray crystallography, biochemistry, mutagenesis, pan inhibitors design, docking, pharmacophore models, focused virtual ligand libraries, organic synthesis, mechanistic enzymology

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New intervention strategy for tuberculosis: blocking multiple essential targets

Mycobacter tubercolosis is the causative agent of tuberculosis (TB), a disease responsible for almost 1.3 million deaths per year. In recent years, different classes of drug resistant M. *tubercolosis* strains have emerged, making the discovery of novel anti-TB drugs a major global priority. This awareness has resulted in several new initiatives to find new (classes of) antimicrobial compounds. One of these initiative is NM4TB, a consortium containing two no TBsec members which discovered the benzothiazinones as promising new antimycobacterial compounds. Read more

Keywords: tuberculosis, secretion, ESX, multi-target, synergistic

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Capturing the natural antibiotic'ome: Developing Nature's EVOlved AntiBIOTIC Collective

Naturally evolved antibiotics are our primary mode of treating drug-resistant pathogens. Although individual antibiotics do succumb to resistance via pressures they place on organisms, the producers of these agents innovate through modular antibiotic drug (bio) synthesis programs to naturally thwart drug resistance mechanisms. Moreover these same antibiotic drug biosynthesis programs are now revealed to construct other agents that perturb microbial physiology apart from killing (i.e. blocking resistance). Read more

Keywords: natural products, antibiotic biosynthesis, evolved antibiotic pathways, metagenomics, metabolomics

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Investigating the Mechanism of Eradication of Multi Drug Resistant Bacteria by Inorganic (mixed metal oxides), Organic (antibiotic), and PROJECT is RELATED TO Protein-based Nanoparticles

The increase in nosocomial infections is adding a substantial burden to the medical system as they result in extended periods of hospitalization. This increase is strongly associated with the emergence of antimicrobial-resistant bacterial strains over the last two decades. The widespread use of antibiotics has resulted in the evolution and spread of these resistant genetic determinants: multidrug resistant (MDR) and extremely drug resistant (XDR) bacteria. There is an urgent need to develop novel antimicrobial agents. Read more

Keywords: Nanoparticles; Quarum sensing; biofilm; metal oxides; Sonochemistry

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