EuroSciCon

EuroSciCon Conference on

Bacteriology and Mycology

June 18-19, 2018
Paris, France

Arch Clin Microbiol 2018, Volume: 9
DOI: 10.4172/1989-8436-C1-006

IDENTIFICATION OF NOVEL SECONDARY METABOLITE GENE CLUSTERS (SMGC) TO PRIORITIZE ANTIBIOTIC DISCOVERY STUDIES ON RARE ACTINOMYCETES

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The evolution of drug-resistance and the decrease in the discovery rate of novel antibiotics pose significant threats to current antimicrobial chemotherapy. The most problematic bacterial pathogens are the ESCAPE microorganisms (*Enterococcus faecium, Staphylococcus aureus, Clostridium difficile, Acinetobacter baumannii, Pseudomonas aeruginosa* and members of the Enterobacteriaceae), but also Mycobacterium tuberculosis, which is currently the leading cause of death from a single infectious agent. The portfolio of useful antibiotics is shrinking because of drug-resistance proliferation. It is not clear if there are enough leads entering the antimicrobial drug pipeline to assure novel therapeutics in the coming decade, and thus new sources are urgently needed. Rare actinomycetes (Actinomadura, Actinoplanes, Amycolatopsis, Kibdelosporangium, Kitasatospora, Planobispora, Planomonospora, Microbispora, Micromonospora, Salinispora, Streptosporangium and Verrucosispora) have recently been attractive for the discovery of novel antibiotics. Whole-genome sequencing capabilities have increased in the last years and significant genomic data is available at the molecular databases such as the National Center for Biotechnology Information (NCBI). There are currently around 150 genomes of the rare actinomycetes published; however there is a void on secondary metabolite gene cluster analysis across species, a procedure essential to select important strains for fermentative studies which will ultimately lead to novel antibiotics. A preliminary bioinformatic approach enabled to survey the rare actinomycetes and coupled to chemical antibiotic structure literature, some strains species were prioritized for fermentative culture studies, as they have novel cryptic biosynthetic genes enshrined in their genome. The results from this study will save time and resources as the experimental research will focus on the activation of silent genes of selected strains by altering growth conditions for stimulating the excretion of novel bioactive molecules.

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