A novel naturally occurring PKC-inhibitor with Anti-tumorigenic activity

Dr. Barak Akabayov, the Department of Chemistry, Ben-Gurion University of the Negev, Beer- Sheva, Israel

Technology

We have developed a novel approach, combining fragment-based screening with NMR and virtual screening (FBVS) to select small molecules new chemical entities (NCE) that target the bacterial DNaG primase. A proof-of-concept (POC) study on T7 primase, serves as the basis for the approach for the development of other anti-bacterial agents. Following this methodology, we have isolated several compounds that inhibited DnaG primase within the mycobacterium tuberculosis (Mtb) replisome, leading to the inhibition of bacterial growth. The study graduated a Kamin project with the Israel Innovation Authority.

Application

There are very few antibiotics are in the pipeline to tackle the global crisis of drug resistance, which is responsible for the rise of almost untreatable infections around the world, the World Health Organisation warns. Among the alarming diseases that are increasing and spreading is bacterial multi-drug resistant is Mtb, which requires treatment lasting between nine and 24 months. There are 250,000 deaths a year from drug-resistant Mtb and only 52% of patients globally are successfully treated. Yet, only 2 new Mtb antibiotics have reached the market in 70 years. Among of the major challenges in reaching this goal are the long and expensive drug discovery processes.

Advantages

- The FBVS approach combines tools from different disciplines in drug development that bypasses many of the limitations of current drug discovery high-throughput screening (HTS) in terms of costs and time.
- FBVS enable the isolation of inhibitors against targeted pathways that cannot be adapted for HTS and therefore considered as “undruggable” targets.
- This platform serves as the basis for the development of inhibitors targeting any biochemical pathway.

Patent

WO 2018/073828