Contribution ID: **8** Type: **not specified**

New therapeutic targets against Non-Tubercolulous Mycobacteria: Salycilate Synthase from M. abscessus

Wednesday, 21 June 2023 15:00 (15 minutes)

Non-tubercolous mycobacteria (NTM) encompass a diverse group of 172 species with distinct virulence features, that differentiate from the M. tuberculosis complex. NTM are widely distributed in the environment and affect individuals with chronic pulmonary diseases like cystic fibrosis (CF), leading to severe infections. Among NTM, M. abscessus is emerging as one of the most virulent pathogens, contributing to increased morbidity and mortality in CF patients. Complex M. abscessus infections are extremely difficult to treat due to their high drug and disinfectant resistance. Novel therapeutic strategies are essential to enhance clinical outcomes in CF patients with M. abscessus infections, and targeting iron intake, essential for many virulence factors, appears promising for inhibiting M. abscessus proliferation pathogenicity.
In this study, we employed a Structure-Based Drug Discovery approach to identify potential inhibitors with a furan-based scaffold against M. abscessus Salycilate Synthase (Mab-SAS), an enzyme involved in siderophore biosynthesis and iron intake. We conducted Grating Coupled Interferometry measurements on repurposed Mab SAS inhibitors and newly developed compounds. Additionally, the crystal structure of Mab-SAS was determined to serve as a structural foundation to virtual screening.
These findings hold implications for the discovery of novel therapeutic candidates against M. abscessus infections in CF patients. Targeting Mab-SAS to inhibit iron intake could provide an effective approach to limit the proliferation and pathogenicity of M. abscessus.

Faria S., et al. J. Pathog. 2015, 2015,809014
To K., et al. J Clin. Med. 2020, 9,2541
Mori M. et al. Pharmaceutics, 2023, 15, 502

Presenter: Dr CASSETTA, Alberto (IC-CNR)

Session Classification: Session