MAIN FIELDS OF RESEARCH

European Regimen Accelerator For Tuberculosis (ERA4TB) (funded by EC)

Tuberculosis remains the leading cause of mortality due to a bacterial pathogen, *Mycobacterium tuberculosis*. Moreover, *M. tuberculosis* drug-resistant strains are becoming a threat to public health worldwide. Consequently, there is an urgent necessity of new anti-TB drugs.
This new Project has the aim of developing new combination therapies to treat all forms of TB starting from several drug candidates. ERA4TB project has started on 2020 (1°/01/2020-31/12/2025) and will last six years, at the end of which, the consortium expects to have developed at least two or more new combination regimens with treatment-shortening potential ready for Phase II clinical evaluation. Our group is one of the 31 Partners of this International Consortium and it is involved in the *in vitro* preclinical studies of new anti-TB agents (study of the mechanism of action of the drugs, and of novel drug combinations, etc.). ERA4TB is the biggest european project against tuberculosis disease.
Collaborations: Cole ST (Pasteur Institute, Paris, France); Ramon-Garcia S, Ainsa JA (Department of Microbiology, University of Saragoza, Spain).

Searching for new antitubercular drugs and novel targets

With other collaborators, the study of the mechanism of action and resistance of other new antitubercular drugs is in progress.
Collaborations: Makarov V (Bakh Institute of Biochemistry, Russian Academy of Science, Moscow, Russia); Mikusova K (Comenius University, Bratislava, Slovakia); Baltas M (CNRS, Toulouse, France).

New weapons against *Mycobacterium abscessus* and other nontuberculous mycobacteria

Nontuberculous mycobacteria (NTM) are emerging as important pathogens in cystic fibrosis (CF) lung disease worldwide with an estimated incidence of about 3.3-22.6%. Among NTM subspecies, *Mycobacterium abscessus* is becoming the most spread and the most worrisome pathogen in CF centers worldwide. *M. abscessus* drug therapy is long up to 2 years and its failure causes an accelerated lung function decline. In fact, *M. abscessus* is intrinsically resistant to many drugs, due to its physiology and its acquisition of new mechanisms of drug resistance.
Consequently, there is an urgent need of new drugs against this pathogen with novel mechanisms of action.
Out of 658 compounds tested until now synthesized by Dr. V. Makarov, only 1 molecule, named 11326083, is active against *M. abscessus* growth (CUT-OFF: MIC < 8 μg/ml. It is very active against other NTM species and against *M. abscessus* MDR clinical isolates.
In collaboration with Prof. F. Manetti, the study of the mechanism of action of MmpL3 inhibitors active against *M. abscessus* is in progress.
Collaborations: Makarov V (Bakh Institute of Biochemistry, Russian Academy of Science, Moscow, Russia); Manetti F (Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Italy).