MAIN FIELDS OF RESEARCH

Searching for new antitubercular drugs and novel targets

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. We have identified the target of the benzothiazinones (BTZ), that is DprE1, an enzyme involved in the biosynthesis of arabinogalactan, a cell wall component. One BTZ derivative is in clinical human trials in Russia and in Europe. Recently, we identified a new druggable cellular target, the CTP synthetase PyrG, and new interesting inhibitors. 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 drugs against *Mycobacterium abscessus* and other nontuberculous mycobacteria

Nontuberculous mycobacteria (NTM) are emerging as important pathogens in cystic fybrosis (CF) lung disease worldwide with an estimated prevalence of about 9-24%; the *Mycobacterium abscessus* strains are the most spread in Europe. The *M. abscessus* treatments are further complicated by the diffusion of strains with inducible macrolide resistance. In these cases, the surgical resection of infected lung tissue could be beneficial in selected patients. Moreover, unsuccessful *M. abscessus* eradication is considered a contraindication for lung transplantation, being associated with treatment failure and increased mortality.

Consequently, new more active drugs are urgently needed, in particular against *M. abscessus*. In this project, taking advantage of our experience in tuberculosis research, we would like to move all our knowledge in the new challenging NTM field, by pursuing the following goals:

- Screening of a several compounds (more than 500) synthesized by our collaborator Dr. V. Makarov against *M. abscessus* growth.
- Evaluation of the sensitivity of other NTM species and clinical isolates to selected compounds.
- Characterization of the mechanism of action/resistance of the selected compounds.

Collaboration: Makarov V (Bakh Institute of Biochemistry, Russian Academy of Science, Moscow, Russia).