SYNTHESIS OF COMPOUNDS WITH ANTITUBERCULOUS ACTIVITY

Description

A problem of tuberculosis treatment is very difficult because of many factors. The most significant among them is genetically conditioned variability of *Mycobacterium tuberculosis* proteins, which are cellular targets for antitubercular drugs. Therefore, most expedient and perspective is strategy of search and use in clinical practice of new drugs, the targets of which are exactly the most conservative proteins of *Mycobacterium*.
Among potential (and actual) mycobacterial targets the FtsZ-proteins providing bacterial cell division satisfy this requirement best of all on the reason of their highly conservative three-dimensional structures. *In silico* improved tree-dimensional model of micobacterial FtsZ and exact spatial structures of potential drugs can enable a correct docking and subsequent design of new compounds with increased antituberculous activity.

Innovative Aspect and Main Advantages

Basing on our own experience of structural docking of different antimicrotubular drugs and preliminary information concerning a detection of effective inhibitors of bacterial FtsZ polymerisation, we can consider that benzimidazole and phenylcarbamate derivates as the most likely candidates to prevent a polymerisation of FtsZ-proteins. This supposition is based on two arguments. At first, these matters are able to specifically bind by β-tubulins (eukaryotic analogues of FtsZs) from any organic kingdom and share the same interactive site on tubulin surface at that. Secondly, an ability of benzimidazoles/phenylcarbamates to inhibit a prokaryotic cell division was shown earlier for some bacteria species. Application of drugs with increased and more stable activity concerning *Mycobacterium tuberculosis* and characterized less effective doses comparatively with drugs, which are utilized for tuberculosis treatment now (it can weaken a chemical pressure on patient organism), in combination with preventive control (like the improvement of feed of Ukrainian population), can be one from important factors in a fight against tuberculosis epidemics.

Areas of Application

a) Development of technologies rapid screening of known chemical compounds on their biological activity in relation define cell targets.
b) Rational design of antitubercular drugs of new generation.
c) Application of new effective antituberculous compounds with FtsZs depolimerization activity in clinical practice.

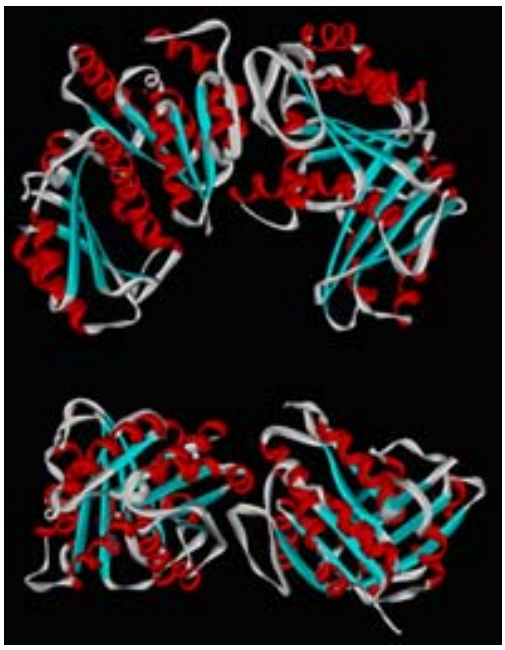

Fig.1. Ribbon diagram of spatial structure of *Mycobacterium tuberculosis* FtsZ.

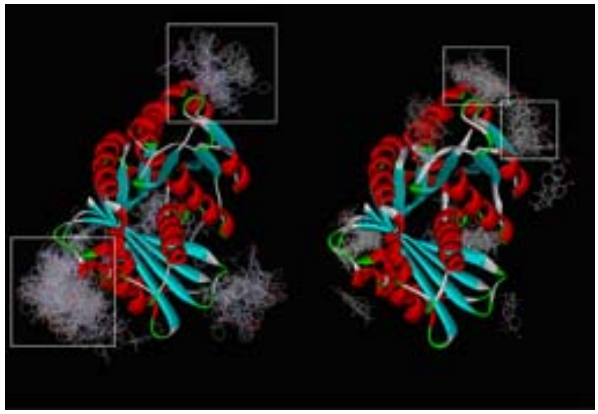

Fig.2. Docking of ethylcarbamate SRI-3072 and totarol with *Mycobacterium tuberculosis* FtsZ.

Stage of Development

Improved model of *Mycobacterium* FtsZ spatial structure are preliminary developed. Docking of benzimidasoles/phenylcarbamates with mycobacterial FtsZ is carrying out.

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