Boris V Nikonenko et al., J Bacteriol Parasitol 2017, 8:6(Suppl)
DOI: 10.4172/2155-9597-C1-040

Activity of new indole derivatives against *Mycobacterium tuberculosis* and *Mycobacterium avium* in HIV combined mycobacteriosis

Boris V Nikonenko[1], **Alex S Apt**[1] and **Valeria S Velezheva**[2]
[1]Central Institute for Tuberculosis, Russia
[2]A N Nesmeyanov Institute of Organoelement Compounds, Russia

Given the data of high-level activities of original lead compounds, obtained earlier at All-Union Scientific Research Chemical-Pharmaceutical Institute (does not exist now) and A N Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences (INEOS RAS), we designed now about 300 multi-target compounds in which electron donor (indole and and ferrocene) and electron acceptor pyridine scaffolds, including INH, are linked via N-N-containing pharmacophore groups, either linear or within the heterocyclic structure. Compounds were tested at the Central Institute for Tuberculosis (CNIIT). Results demonstrated that about 40 agents exhibited proven high activity *in vitro* and *ex vivo* against both drug-sensitive *M. tuberculosis* H37Rv (MIC = 0.05-2 μg/mL) and the isoniazid (INH)-resistant clinical isolates of *M. tuberculosis* CN-40 (MIC = 0.018-4.44 μg/mL), as well as against *M. avium* (MIC = 0.05-1.5 μg/mL for 15 compounds) and other non-tuberculosis HIV co-infections. Thus, these agents were virtually as active as INH against *M. tuberculosis* H37Rv; however, unlike INH, those showed remarkable activity against the INH-resistant *M. tuberculosis* strain and *M. avium*. 3-triazeneindole TU112 demonstrated high level activity against dormant non-culturable *M. tuberculosis*. In addition, about 80 compounds among the tested ones show MIC values in the range of ≥2 and ≤ 10 μg/mL, thus ~40% of the compounds exhibited appreciable anti-TB activity. The compounds are hybrid molecules designed on a basis of privileged scaffolds – 3-indolyl (substituted at positions 1,2,5) and 2-4-pyridines including isoniazid one. The strategy of designing new agents based on a concept of molecular hybridization, as well as a recently emerging concept of development membrane-active (redox-mediated) agents as a strategy for treating persistent infections.

Biography

Boris V Nikonenko MD, PhD, Doctor of Medical Sciences is a leading Researcher at Central Research Institute for Tuberculosis in Moscow. He is an expert in immunology and genetics of experimental tuberculosis and other mycobacterial infections, as well as testing of TB vaccines and drugs. Along with colleagues, he mapped three loci in the mouse genome that regulates the course of TB infection and immunity and revealed the role of other (known) genes in mouse ant-TB resistance and immunity. For 12 years, he worked in biopharm company Sequella, Inc. (Rockville, USA) testing the activity of established drugs against *M. tuberculosis, M. avium, M. abscessus, Candida* in the mouse models.

b.nikonenko@mail.ru

Notes: