Mycobacterium tuberculosis
“hybrid warfare”: virulence, pathogenicity, persistence and drug resistance. New counteraction concept.

Dmitry Maslov
Valery Danilenko, Prof., PhD, Dr. of Sci.
Vavilov Institute of General Genetics, RAS, Moscow, Russia
maslov_da@vigg.ru; valerid@vigg.ru
http://vigg.ru

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TB situation in the world

- 9 million new TB cases and 1.5 million deaths in 2013
- 360,000 HIV-associated deaths in 2013 – leading killer of HIV/AIDS patients
- Constantly growing number of MDR, XDR and TDR strains
- 1/3 of the world’s population infected with *M. tuberculosis*
TB in Russia

- The fall of Soviet Union and its healthcare system lead to the spread of TB
- The lack of personalized medicine and common drug regimens lead to the emergence and spread of MDR and XDR TB
  - 20% of new-TB cases and 50% of re-treated TB in Russia are MDR
- Recent international and Russian scientific papers state the emergence of new “dangerous” groups of strains with enhanced virulence and pathogenicity, and more likely to develop drug resistance, not detected earlier
M. tuberculosis
“hybrid warfare”

• Virulence and pathogenicity
• Persistence
• Drug resistance
Virulence and pathogenicity

- New strains of “dangerous” genotypes
  - strains with enhanced virulence/pathogenicity (B0/W Beijing lineage and others)
  - strains targeting HIV-positive people (KZN strains)
- The spread of “dangerous” genotypes with migration
  - Especially severe in former Soviet Union countries
Persistence

• Dormant bacilli
• Phenotypic drug resistance
• Latent TB infection (LTBI, 2 billion people infected with *M. tuberculosis*) – a time bomb
TB as a co-infection

• HIV
• Hepatitis
• Diabetis
• Influenza
Global challenges

• **Fundamental**
  - Search for new genes and genetic networks responsible for drug resistance and virulence/pathogenicity
  - Search for new anti-TB drugs with novel mechanisms of action

• **Epidemiologic control**
  - Analysis of epidemiologic situation on different levels:
    - regional
    - national
    - international
  - Search for new “dangerous” genotypes
  - Evaluation of the migration impact on the spread of dangerous genotypes
  - Prevention of TB spread
• Data mining
• Data analysis
TBResist consortium

• A joint international effort to unite competencies in collecting and analyzing data using state of the art technology
  • Whole-genome sequencing
  • Super-computers for genomic analysis
• An opportunity to unite efforts within a country
• An opportunity to unify the methods of clinical and laboratory research
• Experience, samples and data exchange
Russian research group

- Vavilov Institute of General Genetics, RAS, Moscow
- Central TB Research Institute, RAMS, Moscow
- Ural Research Institute of Phtysiopulmunology, Ministry of Health, Ekaterinburg
- Central Research Institute of Epidemiology, Rospotrebnadzor, Moscow
- SRI of Physical-Chemical Medicine, FMBA, Moscow
Expectations and proposals

• Workshops and masterclasses with world-wide known specialists in the area
• Genetic, genomic and proteomic databases of fully characterized (using a standardized questionnaire) TB strains from different regions, including those of “dangerous” genotypes
• Functional analysis of genes and mutations involved in virulence/pathogenicity, persistence and drug resistance
• A diagnostic catalogue of SNPs involved in virulence/pathogenicity and drug resistance
• Evaluation of cross-border spread of TB strains
• International interaction between non-government specialized organizations
A complex and international clinical/microbiological/genetic/bioinformatic approach against the “hybrid warfare” of *M. tuberculosis*
Thank you