

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

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# TB situation in the world

- **9 million new TB cases and 1.5 million deaths in 2013**
- **360000 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/geneti  
c/bioinformatic approach  
against the “hybrid warfare”  
of *M. tuberculosis***

Thank you