

## BIOFILM FORMATION AS A KEY FACTOR OF ANTIBIOTIC RESISTANCE IN *MYCOBACTERIUM TUBERCULOSIS*

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**Relevance:** Biofilm formation is identified as a key factor of antibiotic resistance (ABR) in *Mycobacterium tuberculosis* due to slow or incomplete penetration of antibiotics into the biofilm. Current treatment for tuberculosis (TB) entails the use of isoniazid, rifampicin, pyrazinamide, streptomycin, and ethambutol, for a minimum of 6 to 9 months, leading to multidrug-resistant TB (MDR-TB). Ukraine is a country with a high burden of MDR-TB and war only aggravates the world's most serious MDR-TB epidemic.

**Objective:** Comparative analysis of the incidence of TB in Ukraine, the EU/EEA, and the US for 2010-2020 and the search for scientific articles on *M. tuberculosis* biofilm-specific genes concerning ABR.

**Methods:** Statistics on TB incidence, mortality, and MDR-TB from 2010 to 2020 in Ukraine, the EU/EEA, and the US were obtained from official reports and open sources. Statistical processing of information was carried out using the Microsoft Office Excel 2010 program. Polynomial regression (PR) was used to forecast trends in the incidence of MDR-TB in Ukraine for the years 2021-2023.

**Results:** A decrease in the incidence of TB was established in Ukraine, the EU/EEA, and the USA, respectively – in 2020, 73/9.2/2.7 new cases per 100,000 population were registered, against 110/15/3.6 in 2010. But the rate of MDR-TB in Ukraine increased – in 2020, 23.8 cases per 100,000 population were registered, against 18.3 in 2010. PR showed that MDR-TB in Ukraine may exceed 23.8 and approach 24.7, 25.8, and 27.0 within the years 2021-2023. The incidence rate of MDR-TB in the EU/EEA and the US remained stable.

Biofilm-specific genes, in particular *Ppib* (codes for *Ppib*), *Rv1284*, *Rv3588c*, and *Rv3273* (code for carbonic anhydrase (CA)  $\beta$ -1,  $\beta$ -2, and  $\beta$ -3), are important for drug repurposing. *Ppib* inhibitors, including cyclosporine-A, acarbose, and gallium nanoparticle, inhibited biofilm formation and caused a 2-4 fold decrease in the dosage of isoniazid and ethambutol. CA inhibitors include sulfonamides, mono- and dithiocarbamates, phenolic natural products, and phenolic and carboxylic acids.

**Conclusions:** The incidence of MDR-TB in Ukraine is increasing, which prompts doctors and pharmacists to look for new or alternative drugs. Biofilm-specific protein inhibitors, namely CA inhibitors and *Ppib* inhibitors, are a valuable source of drug repurposing targets.