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# 6<sup>th</sup> Clinical Microbiology Conference

October 20-22, 2016 Rome, Italy

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### Turning WGS-based diagnostics into practice for diagnosis of drug resistant tuberculosis

The rapid progresses in M. tuberculosis (MTB) whole genome sequencing (WGS) allow collecting diagnostic information including prompt and accurate identification and prediction of resistance to all anti-mycobacterial drugs with a high gain in term of time to results and cost-containment. Current diagnosis of tuberculosis (TB) is based on culture and commercial molecular based assays. Data obtained by phenotypic sensitivity tests are available with large and do not provide a rapid feedback on response to therapy thus impairing the possibility to implement an appropriate individualized treatment. In addition, for long time MTB has been considered a single pathogen and the association between lineages and drug resistance (DR) was largely underestimated. The major challenge to use SNPs detection for clinical management is the clear understanding of their correlation to the clinical outcome. In order to achieve this goal, a global public-private partnership has been established to develop a Relational Sequencing TB Data Platform (ReSeqTB) to simplify and standardize whole genome sequencing data analysis for interpretation of antimicrobial drug resistance. Based on an exhausting literature review and WGS performed at reference centers worldwide, we have scored the likelihood ratios of each mutation to be associated to drug resistance. A list of 44 mutations to 10 drugs with moderate to high confidence associations with DR phenotypes was identified. Using the PhyResSE web tool, we analyze WGS of early positive liquid cultures and report complete genotypic data (that can overrule phenotypic findings) within 5 working days.

#### **Biography**

Daniela Maria Cirillo is a board certified Clinical Microbiologist, Head of the Emerging Bacterial Pathogens Unit at the San Raffaele Scientific Institute (HSR) in Milan, Italy and Director of the WHO SRL, Collaborating Center ITA98, Italian Reference Centre for Mycobacterial Typing. Her main fields of interest are research on new diagnostic for MDR/XDR-TB, M. tuberculosis pathogenesis, virulence markers, host pathogens interaction, NTMs and nosocomial pathogens. She is the author of more than 130 peer-reviewed original papers. She is currently involved in the WGS Global Surveillance Molecular project coordinated by 'WHO'.

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