

## CYP141 gene: A New approach for Mycobacterium Tuberculosis Identification

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To the Editor,

Tuberculosis is one of the dangerous infectious diseases in the world; annually, two million people die of the disease. Right now, there are a number of phenomena such as the emergence of extensively drug resistant *Mycobacterium tuberculosis* (XDR-TB), multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB) and Human Immuno deficiency Virus(HIV) which have also exacerbated the existing situation<sup>(1, 2)</sup>. Furthermore, Non-tuberculosis mycobacteria (NTM) species which live in the environmental resources can cause pulmonary infections in human which are symptoms, clinical manifestations of the patient and the results of radiological pictures similar to the tuberculosis and potential to misdiagnose with tuberculosis disease<sup>(3)</sup>.

In many developing countries, given that Tuberculosis disease is usually epidemic in these regions clinically isolates of *Mycobacterium*

species are not diagnosed at the species level<sup>(3)</sup>; moreover, according to the isolation methods of mycobacterium spp. are similar and opportunistic species of Non-tuberculosis mycobacteria analogous to *Mycobacterium tuberculosis* complex (MTBC) are acid-fast bacilli in Ziehl-Neelsen (ZN) staining; therefore, it is probable that both groups of mycobacteria (NTM and MTBC) are misdiagnosed. Unfortunately, NTM species are resistance to anti-tuberculosis antibiotics and the treatment regimen of Non-tuberculosis mycobacterium infections are different from *Mycobacterium tuberculosis*; accordingly, many drug-resistant tuberculosis (DR-TB) reports from developing countries are actually misreports<sup>(3, 4)</sup>. Given that *Mycobacterium* species in these laboratories have not been identified at the species level and these species reported as *Mycobacterium tuberculosis* (limited to the results of ZN-staining and microscopic evaluation), according to NTM species anti-tuberculosis drugs are resistant to these antibiotics; therefore, the patients have not been cured and reported as drug-resistant tuberculosis (DR-TB)<sup>(3, 4)</sup>. There are two methods for *Mycobacterium* species identification to the species level: 1) Conventional methods including acid-fast staining, growth at different temperatures, growth rate, pigment construction, Tween 80 hydrolysis, growth on MacConkey agar, nitrate reduction, iron uptake, urease activity, pyrazinamidase, Arylsulfatase (3 days), niacin accumulation, Heat labile catalase and Heat stable catalase tests and 2) molecular test such as direct sequencing, Polymerase Chain Reaction-restriction fragment length polymorphism (PCR-RFLP), DNA probes and DNA hybridization techniques. *Mycobacteria* identification according to the

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phenotypic methods are laborious, time-consuming, difficult and need to expertise technicians, however, molecular tests are rapid, efficient, accurate and reliable to *Mycobacterium* identification spp. to the species level<sup>(5, 6)</sup>.

The popular markers that are applied in NTM species detection and differentiation to species level are 16S rRNA, *hsp65*, *rpoB*, *gyrB* and *recA1*<sup>(5)</sup>. Furthermore there are several genes for *Mycobacterium tuberculosis* identification such as Insertion sequence especially *IS6110*, *mtb-4*, *dnaJ*, and heat shock proteins (HSP gene). Based on the literatures, *IS6110* (Insertion Sequence) is the most important option that is reported as a selective marker in *Mycobacterium tuberculosis* identification<sup>(2, 7)</sup>. However, the use of this gene is limited in some cases for example in Beijing strains detection; these strains of *Mycobacterium tuberculosis* are of the high prevalence *Mycobacterium tuberculosis* families in the Asia which are associated with drug-resistance TB, or *Mycobacterium bovis* which are consisted of few copies of this gene<sup>(7, 8)</sup>. Therefore, it is essential to compare selective identification marker of *Mycobacterium tuberculosis* strains in order to determine which gene has a better performance. Recent reports have indicated that *CYP 141* gene is an appropriate candidate for *Mycobacterium tuberculosis* strains<sup>(2, 7, 9)</sup>.

*CYP141* (cytochrome P450) gene is one of these options. *CYP141* gene encodes one of the proteins that plays a mediatory role in the

respiratory chain in redox reactions and energy production in *Mycobacterium tuberculosis*. The genes involved in the biosynthesis of molybdenum are known as *Rv3121*. This gene is not existed in strains of *M. bovis* (pathogenic) and *M. bovis BCG* (non-pathogenic), but *CYP141* (cytochrome P450) gene is present in *Mycobacterium tuberculosis* genome as one of the important virulence factors<sup>(7, 10)</sup>.

Feizabadi and colleagues used *CYP141* gene for the first time in the world, in the study for identifying *Mycobacterium tuberculosis* strains isolated from respiratory samples of 247 patients with suspected tuberculosis. They showed that this target was directly detected in all isolates harboring *M. tuberculosis*. Furthermore, the sensitivity for this target was as low as one pictogram. Moreover, Feizadadi et al, in another study declared that the sensitivity and specificity of *CYP141*-PCR is 85.7% and 97.8%, respectively and this gene can't be distinguished *M. bovis* from patients. Nowadays, there are few studies about this gene (*CYP141* gene); however according to existence literatures, it is found that this gene is a new option for the *Mycobacterium tuberculosis* specific detection in respiratory specimens<sup>(7, 9)</sup>.

In summary, *CYP141* gene is a new approach for rapid and accurate direct *Mycobacterium tuberculosis* identification in clinical specimens.

### Conflict of interest

There is no conflict of interest.

### References

1. Organization WHO. Global tuberculosis report 2013: World Health Organization; 2013.
2. Keikha M, Kamali M, Bakhshi B, et al. Discovery of the new target for identification of *Mycobacterium tuberculosis*. *Avicenna Journal of Clinical Microbiology and Infection*. 2017(In Press).
3. Nasiri MJ, Dabiri H, Darban-Sarokhalil D, et al. Prevalence of non-tuberculosis mycobacterial infections among tuberculosis suspects in Iran: systematic review and meta-analysis. *PloS One*. 2015; 10(6): 1-9.
4. Khaledi A, Bahador A, Esmaeili D, et al. Prevalence of Nontuberculous Mycobacteria (NTM) in Iranian clinical specimens: systematic review and meta-analysis. *Journal of Medical Bacteriology*. 2017; 5(3-4): 29-40.
5. Hashemi-Shahraki A, Bostanabad SZ, Heidarieh P, et al. Species spectrum of nontuberculous mycobacteria isolated from suspected tuberculosis patients, identification by multi locus sequence analysis. *Infection, Genetics and Evolution*. 2013; 20: 312-24.
6. Soini H, Musser JM. Molecular diagnosis of mycobacteria. *Clinical Chemistry*. 2001; 47(5): 809-14.

7. Darban-Sarokhalil D, Fooladi A, Bameri Z, et al. Cytochrome CYP141: a new target for direct detection of *Mycobacterium tuberculosis* from clinical specimens. *Acta Microbiologica et Immunologica Hungarica*. 2011; 58(3): 211-7.
8. Sun Y-J, Bellamy R, Lee AS, et al. Use of mycobacterial interspersed repetitive unit-variable-number tandem repeat typing to examine genetic diversity of *Mycobacterium tuberculosis* in Singapore. *Journal of Clinical Microbiology*. 2004; 42(5): 1986-93.
9. Farzam B, Fooladi AA, Izadi M, et al. Comparison of *cyp141* and IS6110 for detection of *Mycobacterium tuberculosis* from clinical specimens by PCR. *Journal of Infection and Public Health*. 2015; 8(1): 32-6.
10. McLean KJ, Dunford AJ, Neeli R, et al. Structure, function and drug targeting in *Mycobacterium tuberculosis* cytochrome P450 systems. *Archives of Biochemistry and Biophysics*. 2007; 464(2): 228-40.