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 (1, 2). 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 (3).

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 (3); 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 ZihelNeelson (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 mycobacteria infections are different from Mycobacterium tuberculosis; accordingly, many drug-resistant tuberculosis (DR-TB) reports from developing countries are actually misreports (3, 4). 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 ad 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) (3, 4). There are two methods for Mycobacterium specie 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
CYP141 gene ...

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\(^5\).\(^6\)

The popular markers that are applied in NTM species detection and differentiation to species level are 16S rRNA, hsp65, rpoB, gyrB and recA\(^1\). 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\(^2\).\(^7\). 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\(^7\).\(^8\). 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\(^2\).\(^7\).\(^9\).

CYP 141 (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 exist 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\(^7\).\(^10\).

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\(^7\).\(^9\).

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