Method of Diagnosing Multidrug Resistant Tuberculosis

Published date: Feb. 1, 2012

Technology description

Summary

The invention relates to the discovery that a putative gene of Mycobacterium tuberculosis (MTb) with no previously identified function is responsible for the ability of the bacteria to activate a class of second line thioamide drugs used for MTb infections. The gene, termed "etaA", codes for the synthesis of a monooxigenase, the enzyme responsible for the oxidative activation of the drugs. Mutation in the etaA gene leads to the expression of mutated, inactivated enzyme, thus resulting in thioamide drug-resistant bacteria. The significance of this discovery is that now, resistance to the class of thioamide drugs in clinical isolates can be identified in a relatively short time, eliminating the need to perform lengthy culturing procedures. The invention claims test methods for determining resistance to thioamide drugs by detecting gene mutation. These include (a) amplifying the etaA gene or a portion of it containing the mutation, with a set of primers which provide amplified product, and sequencing the amplified product to compare the sequence with a known sequence of the wild-type etaA. A difference in sequence patterns indicate mutation, (b) subjecting the amplified gene product to digestion by restriction enzymes and comparing the cleaved DNA gel pattern to the one obtained from digestion of the wild type etaA gene. A difference indicates mutation in etaA, and (c) detecting the mutations by probe hybridization techniques, where the amplified product hybridizes to a nucleic acid of known sequence under stringent conditions, and the hybridized product is detected. In addition to the above, the invention proposes other detection methods such as commonly used for SNPs. Other methods claimed in the invention are immunoassay (i.e. ELISA) for the etaA gene product or mutated versions of it, or immunoassay and chemical analysis of the drug metabolites, whereby the absence of the metabolites indicates gene mutation and impaired activating ability.

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com