Molecular diagnosis of drug resistance of tuberculosis by a DNA array

Tuberculosis (TB) is caused by Mycobacterium tuberculosis complex (MTBC) and is one of the world's most important infectious diseases. According to World Health Organization, the annual incidences of new TB cases were 8.7 million and 1.4 million people died from TB. An alarming increase in the global incidence of drug-resistant TB has threatened the control and treatment of TB. Drug susceptibility of MTBC takes 3 weeks, resulting in deferred and inadequate treatment. Drug-resistant TB is associated with mutations in several genes, including \( \text{rpoB} \) for rifampin (RIF), \( \text{katG} \) and \( \text{inhA} \) regulatory region for isoniazid (INH), \( \text{embB} \) for ethambutol (EMB), \( \text{gyrA} \) and \( \text{gyrB} \) for fluoroquinolones [such as ofloxacin (OFX)], \( \text{rrs, rpsL} \), and the promoter of \( \text{eis} \) for second-line injectable drugs [streptomycin (SM), kanamycin (KM), amikacin (AM), and capreomycin (CAP)]. An oligonucleotide array used to detect mutations of the aforementioned genes was developed. Specific oligonucleotide probes were designed to detect mutations in these genes. The assay consisted of multiplex PCR amplification, followed by hybridization of the amplicons with probes on a nylon membrane. A total of 204 patients were analyzed. The performance of the array were: sensitivities, 98.7% (RIF), 91.9% (INH), 84.6% (EMB), 85.3% (SM), 93.8% (OFX), 80% (KM), 60% (CAP), and 75% (AM), respectively; specificities, 100% (RIF), 99.0% (INH), 99.3% (EMB), 98.9% (SM), 100% (OFX), 100% (KM), 97.9% (CAP), and 100% (AM), respectively; positive predictive values, 100% (RIF), 99.0% (INH), 97.8% (EMB), 98.9% (SM), 100% (OFX), 100% (KM), 60% (CAP), and 100% (AM), respectively; negative predictive values, 99.2% (RIF), 92.9% (INH), 95.0% (EMB), 98.9% (OFX), 98.4% (KM), 97.9% (CAP), and 99.3% (AM), respectively. In conclusion, the array can effectively detect drug resistance of TB in a working day.

Biography

Tsung Chain Chang currently is a Professor at National Cheng Kung University, Tainan, Taiwan. His research focuses on developing chips for rapid diagnoses of human pathogens and drug resistance (tuberculosis). He has published about 90 SCI papers and obtained more than 40 patents issued from Taiwan, USA, the United Kingdom, France, Germany, and Australia. He also transferred several molecular diagnostic technologies to the biotechnology companies.

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