

Review Article (The 89th Annual Meeting Educational Lecture)

SENSORS IN MYCOBACTERIA FOR THE DETECTION OF REDOX STRESS

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Abstract *Mycobacterium* species are exposed to oxidative and nitrosylative stress from environments within and outside the host cells. After the host is infected with the bacilli, macrophages produce superoxide molecules via NADPH oxidase activity and nitric oxide (NO) via inducible NO synthase activity to kill the bacilli. The pathogenic bacilli can successfully survive in host cells via anti-oxidative and anti-nitrosylative mechanisms. In particular, *Mycobacterium tuberculosis* persists pose a great problem for chemotherapy because most anti-mycobacterial drugs are ineffective against mycobacteria that are in the persistent state. In accordance with the changes in redox balance, the bacilli change their metabolic pathways from aerobic to anaerobic ones, thereby leading to a change from an actively growing state to a dormant state. Therefore, *M. tuberculosis* is expected to be equipped with sensors that detect redox stress in the environment such that it can switch to the dormant state and change

its metabolic pathways accordingly. In this review, roles of the mycobacterial O₂, NO, and CO gas sensors, DosS and DosT, consisting of the DosR regulon, and mycobacterial DNA binding proteins WhiBs, which contain iron-sulfur clusters, in latent infection are discussed.

Key words: Redox, DosS, DosT, DosR regulon, WhiBs

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Report and Information

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— (4) Tuberculosis Treatment and Treatment Outcomes —

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Abstract The frequency of re-treatment among patients newly notified with tuberculosis (TB) may indicate inadequate prior treatment. Out of 20,495 new TB patients notified in 2013, 1,262 patients had a previous history of TB treatment. More than half of these patients had received previous TB treatment after 2000. A combination of isoniazid, rifampicin, pyrazinamide, and ethambutol (or streptomycin) has been the standard initial treatment regimen recommended in Japan, and it was used in approximately 90% of all forms of TB patients aged 15–49 years. However, there was a substantial decline in this percentage in the ≥ 80 years age group. Of the 12,660 patients who were initiated on TB treatment regimen with pyrazinamide in 2012, approximately 13% had not completed the 2-month long regimen with pyrazinamide by the end of 2013.

In 2013, 15,972 patients were newly notified with pulmonary TB (PTB). The proportion of hospitalizations at the beginning of TB treatment increased among patients aged ≥ 40 years. As of end-of-year 2012, the median treatment duration for all forms of TB notified in 2012 was 273 days. The corresponding figure for cases with smear-positive pulmonary TB was 276 days.

The treatment success rates for patients with new sputum smear-positive TB ($n=7,694$), re-treatment ($n=579$), sputum

positive for other bacteriological tests ($n=5,656$), and bacteriologically negative sputum and other PTB patients ($n=2,482$) registered in 2012 were 49.4%, 45.1%, 58.0%, and 62.0%, respectively. The rates of patients lost to follow-up among new sputum smear-positive patients and of patients undergoing re-treatment were 3.7% and 3.5%, respectively — both well below 5%. The death rate among the new sputum smear-positive PTB patients was 22.6%, of which more than one-fifth died before the completion of their treatment course. The death rate was relatively high in the 70–79, 80–89 and ≥ 90 years age groups (23.7%, 36.1%, and 47.8%, respectively).

Key words : Tuberculosis, Treatment history, Treatment status, Duration of treatment, Treatment outcomes

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