Rational Approaches For Better Tuberculosis Therapies

Dr. Martin Gengenbacher
Department of Immunology
Max Planck Institute for Infection Biology
Berlin, Germany

Abstract
The approved tuberculosis vaccine, Bacillus Calmette–Guérin (BCG), provides insufficient protection and can cause adverse effects in immunocompromised individuals. We previously reported improved pre-clinical efficacy and safety of the recombinant vaccine candidate BCG ΔureC::hly, secreting pore-forming listeriolysin O of Listeria monocytogenes. Here we evaluate a second-generation derivative, BCG ΔureC::hly Δpdx1, deficient in pyridoxine synthase, an enzyme required for biosynthesis of the essential cofactor vitamin B6. Our data demonstrate for the first time that efficacy of a profoundly attenuated recombinant BCG vaccine construct can be controlled by a small molecule. This principle will foster development of safer tuberculosis vaccines required for immunocompromised individuals, notably HIV+ infants.

List of key references