Ineffective BCG Vaccination in Mice Depends Upon the Chromosome 17 Locus Distal to the *H2* Complex

Maria Korotetskaya
Laboratory for Immunogenetics, Department of Immunology, Central Tuberculosis Research Institute, Moscow, Russia

Polina Baikuzina
Laboratory for Immunogenetics, Department of Immunology, Central Tuberculosis Research Institute, Moscow, Russia

Alexander Apt
Laboratory for Immunogenetics, Department of Immunology, Central Tuberculosis Research Institute, Moscow, Russia

Abstract

The level of genetic susceptibility to tuberculosis (TB) infection is a polygenic trait regulated by a complex network of interacting genetic loci. Mouse TB models have proved to be an indispensable tool in dissecting the genetic architecture of successful vs. defective responses against mycobacteria in different experimental settings. We are studying genetic reasons for inability of the BCG vaccine to provide immune defense against subsequent TB challenge in a model based upon a pair mouse strains congenic for the H2 complex. B10 (H2b) and B10.M (H2f) strains, that differ exclusively by the alleles of genes occupying the 33.46 Mb segment of the chromosome 17, respond and do not respond to BCG vaccination, respectively. To further dissect the genetic basis of BCG vaccination performance, we applied the cross-intercross-backcross mating system, and established a novel panel of recombinant congenic strains. Comparative analysis of post-vaccination TB-related phenotypes allowed for locating the region responsible for BCG vaccination efficacy within an 11.8 Mb interval distal to the H2 complex. We continue enlargement of our panel of recombinant strains to delineate specific genetic loci responsible for BCG vaccination efficacy – a subject of special interest since these loci do not coincide with those responsible for the level of sensitivity to primary TB infection. This work was supported by the Russian Science Foundation grant 23-14-00030 to AA.

Keywords

BCG vaccination, TB infection, H2-congenic mice, phenotype, recombinant congenic strains.