Mycobacterium tuberculosis (Mtbc), the causative agent of tuberculosis (TB), is an extraordinary human pathogen that has latently infected one-third of the world population and causes 9 million new cases and about 1.5-2 million deaths each year globally. Comparing the complete genome sequences of an avirulent Mtbc strain H37Ra versus the typical virulent strain H37Rv and a clinical isolate, CDC1551, multiple H37Ra-specific variations were identified (PLoS ONE 3:e2375, 2008). Among them, the A219E variation of the mycobacterial (d)NTP pyrophosphohydrolyase MazG was identified as a loss-of-function mutation and its function in cell surviving under oxidative stress was impaired (Journal of Biological Chemistry 285:28076, 2010). We have been cooperating with researchers in Shanghai to further evaluate the virulence role of mycobacterial MazG in vitro and in vivo. The mazG null mutant of Mtbc H37Rv was constructed and used to infect C57BL6 mice. In the acute infection phase, i.e., the 1st and the 14th day post-infection, the mazG mutant did not show any difference in growth defect from that of the wild type H37Rv. However, after 5 weeks of post-infection, reduced bacterium survival in the spleen and pulmacy histopathologic damage was observed in the mazG mutant infected mice, when compared to that of H37Rv infection. Indicated by these results, mycobacterial MazG is likely a virulence factor affecting the
survival/dormancy of the bacteria in lymphocytes. The molecular mechanisms underlying mazG as a virulence factor has also been studied with respect to its potential housecleaning function by degrading oxidised dNTPs.

Besides, as a result of the collaboration with Professor Stephen Tsui of the School of Biomedical Sciences of CUHK, Professor Wan Kanglin of the Centres for Disease Control and Prevention (CDC) of the United States and Professor Wang Shengyue of the Chinese National Human Genome Centre at Shanghai for sequencing and annotating the Mtb Beijing family strains, the genetic basis of its microevolution prone for population expansion and drug resistance are revealed through comparative genomic analysis of three multiple or total drug resistant strains versus two drug sensitive strains (manuscript submitted).

RECOGNITIONS:

GRANTS AND CONSULTANCY

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<th>Details</th>
<th>Member’s Name</th>
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<td>Health and Medical Research Fund (1/4/2012 - 31/3/2014)</td>
<td>Guoping Zhao</td>
<td>973,840</td>
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<tr>
<td>Title: Mechanisms of virulence attenuation in Mycobacterium tuberculosis mazG mutant—a cellular level study.</td>
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PUBLICATIONS:


