Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis, 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 worldwide.

Studies by Professor Guoping Zhao and his team demonstrated that mycobacterial MazG is a 5-OH-dCTP-specific housecleaning enzyme involved in a pathway preventing the CG to TA mutation and ensuring the persistent infection of Mtb in mouse (PLOS Pathog 9:e1003814. 2013). A recent study showed that mycobacterial MazG is required for Mtb multidrug tolerance through prevention of 5-OH-dCTP-induced double-strand DNA breaks (to be submitted). In addition, the team also found that the human DCTPP1 (MazG homolog) attenuates the sensitivity of human gastric cancer cells to 5-fluorouracil (Oncotarget 7(42): 68623-68637. 2016).

In order to understand the mechanism of persistence infection of Mtb, molybdenum cofactor (MoCo) biosynthesis genes, particularly, the characteristics of the multiple-copy genes, specially found in Mtb but different from that of E. coli or even Mycobacterium smegmatis (Msm), have been under investigation. Interesting and novel discoveries have been observed via site-directed mutation experiments and corresponding biochemical and physiological mechanisms are being analysed.

In addition, aiming at understanding the critical survival mechanism of Mtb under hypoxia dormancy state, nitrate metabolism of both Msm and Mtb are studied via systematic comparison the related Mtb physiology against that of either physiologically phenocopied or genetically manipulated Msm models. Recent progresses were achieved in identification and characterisation of novel nitrate metabolism mechanisms in Msm besides the well-studied NarGHJI-dependent nitrate assimilation system.

Complete genome sequencing of 5 Beijing lineage strains of Mtb revealed the presence of a novel region of difference (RD) of ~4kb, which is absent from other completely sequenced MTBC genomes and designated M-NBjD1. Its potential impact in both physiology/pathology and evolutionary is under investigation. In order to facilitate the molecular manipulation of mycobacterial genomes, which has been the rate-limiting step for the research of the field, development of synthetic biology enabling technology, particularly the CRISPR/Cas9 related techniques, has been a new direction of the laboratory.
Schematic diagram of the Cpf1/crRNA/DNA target complex (top) and the colorful bacterial pigments produced by E. coli harboring constructs assembled in C-Brick standard (bottom a and b).

C-Brick: A New Standard for Assembly of Biological Parts Using Cpf1

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