

# 12<sup>th</sup> European Diabetes Congress

September 15-17, 2016 Berlin, Germany

## DNA methylation, an epigenetic wrestler, links environmental insults to the pathogenesis of autoimmune diabetes

Cong-Yi Wang

Huazhong University of Science & Technology, China

Type 1 diabetes (T1D) is resulted from the interaction of susceptible genes and environmental factors. DNA methylation acts as a footprint to link susceptible genes and environmental factors, and encodes information beyond DNA to record the impact of environmental insults on DNA, which is interpreted by the methyl-CpG binding domain (MBD) proteins in a cell and gene-dependent manner. Particularly, MBD2, one of the MBD proteins, is preferentially induced upon pathological insults, which then deciphers DNA methylome-encoded information to modulate disease susceptibility. MBD2 was found to regulate the homeostasis of CD4 T cell differentiation and functionality, and mice deficient in MBD2 were completely protected from MOG35-55 induced experimental autoimmune encephalomyelitis (EAE). On the other hand, NOD mice deficient in MBD2 showed exacerbated T1D. Mechanistic studies revealed that MBD2 selectively binds to the methylated CpG sites at the T-bet and Hlx promoter, and by which it suppresses the transcription of IFN- $\gamma$ . As a result, loss of MBD2 leads to altered IFN- $\gamma$  expression, which then renders naïve T cells preferentially differentiating to Th1 cells along with impaired Th17 development. Moreover, elevated Hlx transcriptional activity resulted from MBD2 deficiency synergizes with T-bet to mediate IFN- $\gamma$  expression in IL-4 producing Th2 cells. In patients with fulminant T1D, environmental insults in genetic predisposed subjects triggered Foxp3 promoter hypermethylation, which then prevented IRF-7 binding to the Foxp3 promoter, thereby impairing the development and functionality of regulatory T cells (Tregs). Collectively, these discoveries demonstrate how environmental factors trigger autoimmune responses during T1D development.

### Biography

Cong-Yi Wang, MD, PhD, Professor is the Director of the Center for Biomedical Research, Vice Director of Department of Sponsored Program Administration, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. Before 2014, he served as a tenured Associate Professor at the Department of Pathology, and the Director of Georgia Esoteric & Molecular Laboratories, LLC, Georgia Regents University, USA. The major focus for his research is to dissect the role of genetic and epigenetic factors in the pathogenesis of diabetes and diabetic complications. Particularly, he employs animal models and human subjects to address how environmental insults interact with genetic factors to modulate disease susceptibility, and through which to develop effective therapeutic approaches for prevention/intervention of these devastating disorders.

wangcy@tjh.tjmu.edu.cn

### Notes: