The mechanisms of septic acute kidney injury：
focus on mitochondrial genome

Yang Yi Kidney Disease Center, the First Affiliated Hospital, College of Medicine, ZhejiangUniversity

Sepsis induced acute kidney injury (AKI), also called septic AKI, is a global health issue associated with high morbidity and mortality. Clinical data indicated that even a small increase in serum creatinine level is associated with worse outcomes and higher mortality in both short- and long-term follow-up. However, the mechanism of septic AKI is not very clear so far. Lots of studies showed that mitochondria, especially mitochondrial genome (mtDNA), play crucial role in the pathological procedure of septic AKI.

Mitochondrion is the miraculous organelle of mammal which contains its own DNA. Human mitochondrion contains multiple copies of a small circular genome of approximately 17,000 nucleotide base pairs, and this mtDNA encodes for 13 peptides, 2 ribosomal ribonucleic acids, and 22 transfer RNAs.

Human mtDNA is maternally inherited and the population can be divided into several mtDNA haplogroups on the basis of specific single nucleotide polymorphisms (SNPs) scattered throughout the mitochondrial genome. A body of evidences suggested that mtDNA haplogroups had functional importance, being associated with respiratory-chain activity and diseases susceptibility. Our preliminary study indicated mtDNA haplotypes associated with severe sepsis and septic organ dysfunction, and some special haplotypes would predict different outcome of the diseases. In the next stage we will utilize the bio-coding technique and high-throughput sequencing technique to establish new strategy for facilitating the mDNA research.

mtDNA has been indentified as the important damage associated molecules (DAMPs) of human beings, which might due to the mitochondrial derivation. The circulating serum mtDNA may play important role in the amplification of the inflammatory cascade. Our study also found that high circulating mtDNA copies associated with poor outcome of the critically ill patients, including individuals

suffering peritoneal dialysis associated peritonitis. Meanwhile, the serum or urine mtDNA content might serve as the diagnostic or prognostic predictor of AKI, as well as septic AKI.

mtDNA instability caused by stress factors inducing renal tubular cell (RTC) injury, which serves as a basis of the pathological change of AKI and its regulating mechanism is unclear. And maintaining mtDNA stability is also crucial for the mitochondrial biogenesis and dynamic balance. Therefore, it is necessary to carry out the studies for mtDNA protection and repair. Such works might apply new and promising therapeutic strategies of the septic AKI prevention and treatment.