

Abstract Type : Poster

Abstract Submission No. : 1453

Impact of NAMPT on acute kidney injury following regeneration in adult zebrafish model

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Objectives: Nicotinamide phosphoribosyltransferase (NAMPT, which is also known as visfatin or pre-B cell colony-enhancing factor (PBEF)) is preferentially produced by visceral adipose tissue and its enzymatic basis and structure has been established as a ubiquitous intracellular protein. In this study, we investigated the effect of NAMPT on puromycin-induced kidney injury following regeneration in adult zebrafish model.

Methods: We injected 100ug of puromycin or/and 500ng of NAMPT via intraperitoneal injection into adult wild zebrafish, which were sacrificed at 1, 3, 5, 7, and 14 dpi. Then, NAMPT expressions was evaluated in zebrafish kidney. We used *in situ* hybridization, western blot analysis, immunohistochemistry, and immunofluorescent staining.

Results: First, the synthesis of NAMPT was demonstrated in the kidney of zebrafish model by *in situ* hybridization, RT-PCR, and IF staining. Second, we observed that kidney injuries began immediately after puromycin injection in adult zebrafish and NAMPT expression was dramatically increased immediately after puromycin treatment and decreased during a recovery of injured kidney. Next, we saw that the pathological changes of kidney after puromycin treatment through H&E stain showed severe tubular necrosis and atrophy were observed and inflammatory cells were infiltrated in the interstitium of kidney. On the other hand, we observed the recovery of kidney injury at 7dpi and 14 dpi after puromycin treatment. NAMPT administration promoted this recovery after puromycin-induced renal injury. As a renal progenitor marker, *lhx1a* production during the recovery after acute kidney injury was increased by NAMPT. Finally, through the genetic effect of NAMPT on puromycin-induced renal regeneration, NFkb-NAMPT pathway was demonstrated to be activated during regeneration after kidney injury.

Conclusions: Our results showed that NAMPT promoted regeneration after acute nephron injury induced by puromycin administration and provided therapeutic potential after kidney injury induced by nephrotoxic drugs.