Séminaire externe

"microRNAs and Nrf2/heme oxygenase-1 system in renal injury ."

Kidney fibrosis is a key determinant of the progression of renal diseases and its development involves many molecular mediators including microRNAs (miRNAs). Recent studies showed that induction of heme oxygenase-1 (HO-1), enzyme with anti-oxidant and anti-inflammatory functions might be protective in acute and chronic renal insults. Therefore, we analyzed the direct consequence of both HO-1 overexpression as well as lack of HO-1 for the fibrosis development. Our *in vitro* and *in vivo* experiments, in a model of ochratoxin A (OTA)–induced fibrosis as well as in cyclosporine A (CsA)-mediated nephropathy indicate that disturbances in not only HO-1, but also in the activity and expression of NF-E2-related factor-2 (Nrf2), the transcription factor regulating the anti-oxidant and inflammatory response contributes to fibrosis development. Significantly, we also found that alterations in the level of microRNAs processing enzymes, microRNA content and in the expression of specific microRNAs are important mechanisms responsible for kidney fibrosis. Understanding the regulation of miRNAs expression during renal fibrosis may not only deepen our knowledge of the pathogenesis of this frequent phenomenon, but also may be a new target for therapeutic interventions.

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References:

1. Boesch-Saadatmandi C, Loboda A, Jozkowicz A, Huebbe P, Blank R, Wolffram S, Dulak J, Rimbach G. Effect of ochratoxin A on redox-regulated transcription factors, antioxidant enzymes and glutathione-S-transferase in cultured kidney tubulus cells. Food Chem Toxicol. 2008;46: 2665-2671

2. Stachurska A, Ciesla M, Kozakowska M, Wolffram S, Boesch-Saadatmandi C, Rimbach G, Jozkowicz A, Dulak J, Loboda A., Cross-talk between microRNAs, nuclear factor E2-related factor 2, and heme oxygenase-1 in ochratoxin A-induced toxic effects in renal proximal tubular epithelial cells. Mol Nutr Food Res. 2013;57: 504-515

3. Ciesla M, Skrzypek K, Kozakowska M, Loboda A, Jozkowicz A, Dulak J. MicroRNAs as biomarkers of disease onset. Anal Bioanal Chem. 2011; 401: 2051-2061

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Salle de conférence du CBM