

cisplatin으로 유도한 급성신부전에서의 MRN complex 발현

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Mre11-Rad50-Nbs1 Complex in Cisplatin-acute Kidney Injury

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The cisplatin-induced acute renal failure (ARF) is a major side effect, which limits long-term chemotherapy. Mre11, Rad50 and Nbs1 (MRN) complex play critical roles in the early phase of the cellular response to the DNA double strand breaks and DNA damage repair. The present study was performed to explore whether the MRN complex is associated with DNA repair mechanisms in cisplatin-induced ARF. The rats were randomly allocated into three groups as follows: control, 5D and 10D (sacrificed 5 and 10 days after 5 mg/kg of cisplatin injection, respectively). The 5D group showed disrupted renal function index, together with enhanced apoptotic cells in the kidney. The expression of MRN complex was prominently increased in the 5D group which was confirmed in the both immunohistochemistry and western-blot analysis. In the 10D group, recovered cisplatin-induced damages were observed and the MRN expression was relatively reduced compared to the 5D group, although the expression was still higher than the control group and distinctive in proximal tubular cells. Furthermore, DNA repair related signals were enhanced after cisplatin injection and the increased expressions were persistent in the 10D group. In the *in vitro* study, the mirin, MRN complex inhibitor, pretreated HEK293 cells showed markedly decreased viability after cisplatin treatment than the cisplatin alone treated cells. Co-treatment of mirin suppressed MRN complex as well as proliferating cell nuclear antigen in cisplatin treated HEK293 cells. Taken together, cisplatin treatment could trigger the MRN complex expression in the kidney and the complex might play key role in cisplatin-induced damage recovery process.

Key Words: 급성신부전, 시스플라틴, MRN 복합체

Acute kidney injury, Cisplatin, MRN complex