

## 조영제 신독성에서 NRF2 발현에 관한 연구

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### The Role of NRF2 Expression in Radiocontrast Induced Nephropathy

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**Introduction:** Radiocontrast induced nephropathy (CIN) is the third common cause of acute renal failure among in-patients. Although the number of patients taken the exams using radiocontrast is increasing, little has been progressed in the treatment for CIN. The pathophysiology of CIN was known as tubular injury by oxidative stress. Nuclear factor-erythroid-2-related factor 2 (NRF2) has been known as a key player to coordinate intracellular antioxidative process. We investigated the role of NRF2 in CIN.

**Methods:** CIN was induced with intraperitoneal injection of iohexol (Omnipaque, 5 g iodine/kg) in male C57BL/6J mice according to previous study. Tubular injury caused by iohexol was also examined in vitro model using rat tubular cells (NRK-52E, 100 mg/dL). To determine the role of NRF2 in CIN, reduction of NRF2 expression was induced by SiRNA treatment in vitro study, and genetic engineered deletion of function was introduced in vivo study.

**Results:** Increased expression of NRF2 was noted after iohexol treatment both in mice kidneys and rat tubular cells. Serum creatinine at 24hrs after iohexol injection was significantly increased in NRF2 KO mice compared to controls (control vs KO:  $1.41 \pm 0.28$  vs  $2.11 \pm 0.44$ ,  $p < 0.05$ ). NRF2 inhibition with SiRNA also induced the decrease of cell viability measured by MTT assay (vehicle vs SiRNA:  $0.480 \pm 0.05$  vs  $0.346 \pm 0.05$ ,  $p < 0.05$ ) and increased caspase 3 expression. Increased reactive oxygen species measured by CM-DCFDA assay and decreased expression of HO-1 were associated with aggravated renal injury with iohexol treatment after NRF2 inhibition.

**Conclusion:** It was demonstrated that proper function of NRF2 was implicated in the pathogenesis of CIN. Targeted therapy with control of NRF2 expression to mitigate CIN should be studied further.

**Key Words:** 조영제 신독성, 급성신부전, 산화 스트레스

Radiocontrast induced nephropathy, NRF2, Oxidative stress