

ANALYSIS OF TARGET GENES ON CHROMOSOME 8 IN Fe-NTA-INDUCED RAT RENAL CELL CARCINOMA

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Ferric nitrilotriacetate (Fe-NTA) administration in rats induces Fenton-like reaction leading to a high incidence of renal cell carcinoma (RCC) that resembles human RCC of non-clear subtype and it is characterized by high incidence of pulmonary metastasis and peritoneal invasion; tumor-associated mortality; involvement of reactive oxygen species, and increased loss of heterozygosity (LOH). Using PCR with microsatellite polymorphic markers, we detected up to 77 % of LOH in chromosome 8 in RCC. In comparison with gene expression data, aminoacylase 1 (*ACY1*) gene has decreased expression in a region with high incidence of LOH. Real-time PCR analysis of RCC showed a decreased *ACY1* expression in all 19 analyzed tumors. Western blotting and immunohistochemistry of RCC also showed decreased *Acy1* protein expression and *Acy1* seems to be expressed in nucleus and cytoplasm of renal proximal tubules. Reportedly, a decreased expression of *Acy1* is also found in small cell lung cancer and renal cell carcinoma. *Acy1* seems to be involved in the catabolism of acylated proteins and also interacts with other proteins involved in cell growth and apoptosis. This study could contribute to elucidate the genetic mechanisms and biological role of *ACY1* involved in this oxidative stress-induced cancer model.