

## Genome-wide Analysis Identifies a Tumor Suppressor Role for Aminoacylase 1 in Iron-induced Rat Renal Cell Carcinoma

Onuki J.<sup>2,4</sup>, Zhong Y.<sup>2</sup>, Yamasaki T.<sup>3</sup>, Ogawa O.<sup>3</sup>, Akatsuka S.<sup>1,2</sup>, Toyokuni S.<sup>1,2</sup>

<sup>1</sup> Department of Pathology and Biological Responses, Graduate School of Medicine, Nagoya University, Nagoya, Japan. <sup>2</sup> Department of Pathology and Biology of Diseases; <sup>3</sup> Department of Urology, Graduate School of Medicine, Kyoto University, Kyoto, Japan. <sup>4</sup> Laboratory of Biochemistry and Biophysics, Butantan Institute, São Paulo, Brazil. Email: onuki@butantan.gov.br

A number of studies indicate a link between oxidative stress and cancer. Here we performed a genome-wide analysis to study characteristics of genomic alteration and identify putative genes involved in the development of ferric nitrilotriacetate (Fe-NTA)-induced rat renal cell carcinoma (RCCs). Array-based comparative genomic hybridization (aCGH) analyses revealed a chromosomal loss spanning chromosome 8 in most of the RCCs studied, with a common deletion at 8q31-32, which was confirmed by loss of heterozygosity (LOH) analysis. Studies of gene expression in RCCs or following Fe-NTA treatment revealed globally decreased transcription levels of 34 genes derived from chromosome 8 that are expressed in the kidney. Among them, the aminoacylase 1 (Acy1) gene, which maps to 8q32 and is highly expressed in the kidney, displayed a significantly decreased level of expression in RCCs. Significant amounts of the Acy1 protein were detected in the cytoplasm as well as in the nuclei of renal proximal tubular cells of untreated rats. Transfection of Acy1 into RCC cell lines inhibited proliferation and colony formation on soft agar. An increased number of apoptotic cells were observed following Acy1 transfection. The rat 8q31-32 chromosomal region corresponds to human 3p21.31-24.1, a hot spot where LOH is frequently found in various human cancers. Our data demonstrate that Acy1 functions as a tumor suppressor in this rat RCC model. *Financial support: MEXT, JSPS, FAPESP.*