

Association of the G/G-SNP309 variant in the mdm2 gene with earlier tumor onset in female renal cell carcinoma patients

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Abstract

Mdm2 (Human mouse double minute 2) is an important opponent of the tumor suppressor p53. The G/G variant of SNP309 in the MDM2 promoter can increase Mdm2 mRNA/protein expression and is associated with an increased risk and earlier onset of different cancers especially in Asian populations. But the frequency and impact of the G/G variant has not been studied in Caucasian renal cell carcinoma (RCC) patients. Therefore, we analyzed an unselected German cohort of 197 consecutive RCC patients and detected the G/G variant in 18 (9.1%) patients, the G/T variant in 116 (58.9%) patients and the T/T variant in 63 (32.0%) patients. Studying the association between age at tumor onset and SNP309 genotypes, no correlation was detected in the entire RCC cohort or among the male RCC patients. However, the female G/G patients (median age 59.5 years) were diagnosed 13.5 years earlier than the T/T females (median age 73 years). Next, when separating all females into two groups at their median age (68 years), 7 patients and 1 patient with the G/G variant and 9 patients and 13 patients with the T/T variant were noted in these age groups ($P = 0.024$). To study the age dependency of tumor onset further, a second, age-selected cohort of 205 RCC patients was analyzed, which comprised especially young and old patients. Interestingly, the G/G type occurred more often at lower tumor stages and tumor grades compared with higher stages ($P = 0.039$ and $P = 0.004$, respectively). In females, the percentage of the G/G variant was only slightly higher in the younger age group, whereas in males, the percentage of the G/G variant was remarkably higher in the younger age group (19.4% vs. 8.0%). In summary, female Caucasian RCC patients with the MDM2 SNP 309 G/G variant showed a significantly earlier tumor onset than patients with the wildtype T/T genotype.