SEQUENCE VARIANTS OF THE AXIN GENE IN HEPATOBlastoma

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Purpose: The Wnt signaling pathway plays critical roles in embryonic development and tumorigenesis. As a part of the Wnt signal transduction, the function of Axin complex is inhibited, leading to accumulation of β-catenin. In hepatoblastomas (HBs), it is highly speculated that abnormally accumulating β-catenin has an important role in the tumorigenesis. To evaluate implication of Axin in HB development, we investigated mutations of the Axin gene.

Methods: Mutation analysis for the Axin gene was performed in 22 HBs and some paired normal tissues. After DNA was prepared from these samples, the whole coding region of the Axin gene was examined by polymerase chain reaction – single strand conformation polymorphism (PCR-SSCP) method. Samples revealing aberrant band patterns in SSCP were subjected to sequencing analysis and details of alterations were determined.

Results: On SSCP and sequencing analyses, a total of twelve sequence variants were identified in the investigated region of the Axin gene. Eight of these were found in the exons, whereas other four were in the introns and regarded as intronic polymorphisms. Of the variants in the exons, seven were silent mutations resulting in no amino acid change, however, the remaining variant at codon 95 (ACG -> ATG) predicted to result in an amino acid change from threonine to methionine. This missense mutation was found in only one HB sample. In the paired peripheral blood DNA from the corresponding patient, the same genetic change was detected.

Conclusions: Although eleven of 12 Axin variants identified in our HB series were regarded as non-pathogenic polymorphisms or silent mutations, detection of the missense mutation at codon 95 in one sample suggests possible implication of Axin abnormalities in a small subset of HB cases. Further investigations with increased sample numbers may help to confirm our results.