MDM2 splice variants in oral cancer

Type: Meeting Abstract

Content:

Introduction: MDM2 is a negative regulator of the p53 tumor suppressor protein. The presence of a variety of MDM2 splice variants have been reported in many different types of tumor and some have been shown to be associated with patient prognosis. Materials and methods: In this study, we demonstrated the occurrence of MDM2 splice variants in OSCC tissues. RNA was extracted from 45 OSCC tissues and 17 normal oral mucosa tissues and reverse transcribed into cDNA. Nested PCR was performed to amplify the MDM2 transcripts and the PCR amplicons were cloned into cloning vector pTZ57R/T and sequenced. Results: We demonstrated that 37/45 OSCC and 14/17 normal oral mucosa tissues contained MDM2 splice variants and a total of 34 transcript variants were found. Comparing with the reported splice variants in GenBank, four known variants, MDM2B, MDM2C, MDM2-EU2 and MDM2-PM2 were found in tumor samples with MDM2B being the most common variants found in our samples. None of these known variants were found in normal oral mucosa tissues. The other 30 transcript variants were novel, where 3 of these were present in both tumor and normal tissues, 23 were found only in tumor tissues and 4 were exclusive to normal oral mucosa tissue. Discussion: The common loss among the variants was sequences coding for the p53 binding domain, acidic domain, nuclear localization and nuclear export domains. In general, all 30 novel transcript variants were aberrantly spliced, however, interestingly, 9/23 aberrantly spliced variants in OSCC codes for an in-frame putative protein, suggesting that despite the aberrant splicing, these transcripts may still result in a functional protein and therefore further work to study how these splice variants affect MDM2 function directly or how they may affect other binding partners is needed.

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