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Titel des Beitrags:
Target gene activation of the Wnt signaling pathway in nuclear beta-catenin accumulating cells of adamantinomatous craniopharyngiomas.

Abstract:
Activating beta-catenin (CTNNB1) mutations can be identified in the majority of adamantinomatous craniopharyngiomas (adaCP), suggesting an aberrant Wnt signaling pathway in this histopathologically peculiar tumor entity. However, there is no proven evidence that nuclear translocation of beta-catenin is associated with CTNNB1 mutations and target gene activation. We performed a laser-microdissection-based study comparing beta-catenin accumulating vs. non-accumulating tumor cells. Mutational analysis and gene expression profiling using real-time polymerase chain reaction were conducted in adamantinomatous and papillary tumor specimens. Target gene activation, that is, over-expression of Axin2 could be detected in adaCP, especially in tumor cells with nuclear beta-catenin accumulation. In addition, increased expression of BMP4 was identified in the accumulating cell population, which supports the hypothesis of an oral ectodermal origin. Interestingly, accumulating and non-accumulating tumor cell populations carried CTNNB1 mutations within exon 3. We extended the analysis, therefore, towards genetic regions encoding for membrane linkage and active/passive nuclear transport mechanisms (exon 4 and exon 8-13), but could not detect any alteration. This is the first report
demonstrating an association between nuclear beta-catenin accumulation and target gene activation in adaCP. The results confirm the Wnt signaling pathway as molecular basis of the distinct and challenging clinical and morphological phenotype of adaCP.