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Genomic instability and characteristic DNA methylation pattern in chordoma

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Chordomas are rare mesenchymal tumors occurring exclusively in the midline from clivus to sacrum. Early tumor detection is extremely important as these tumors are resistant to chemotherapy and irradiation. Despite continuous research efforts surgical excision remains the main treatment option. Because of the often challenging anatomic location early detection is important to enable complete tumor resection and to reduce the high incidence of local recurrences. The aim of this study was to explore whether DNA methylation, a well-known epigenetic marker, may play a role in chordoma development and if hypermethylation of specific CpG islands may serve as potential biomarkers correlated with SNP analyses in chordoma. The study was performed on tumor samples from ten chordoma patients. We found significant genomic instability, it was interesting to see that all chordomas showed a loss of 3q26.32 (PIK 3CA) and 3q27.3 (BCL6) thus underlining the potential importance of the PI3K pathway in chordoma development. By using the AITCpG360 methylation assay we elucidated 20 genes which were hyper/hypomethylated compared to normal blood. The most promising candidates were nine hyper/hypomethylated genes C3, XIST, TACSTD2, FMR1, HIC1, RARB, DLEC1, KL, and RASSF1. In summary, we have shown that chordomas are characterized by a significant genomic instability and furthermore we demonstrated a characteristic DNA methylation pattern. These findings add new insights into chordoma development, diagnosis and potential new treatment options.

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