Abstract

TGCTs are tumors of male germ cells. They comprise of seminomas and non-seminomas (embryonal carcinoma, yolk sac tumor, choriocarcinoma, and teratoma). GCT types differ in the stage of differentiation, from undifferentiated seminoma to more differentiated non-seminomas. In our studies, we aimed to characterize specific epigenetic features of GCT types that enable transcription derepression of the human endogenous retrovirus *ERVWE1* in these tumors. We detected upregulated mRNA expression of *TET1-3* dioxygenases in GCTs, especially of *TET1* in seminomas. Moreover, seminomas showed low global levels of 5mC and 5hmC. TET1 knock-down in a seminoma-derived cell line resulted in a decreased amount of 5hmC and unchanged 5mC level. These results stress the dynamics of cytosine modifications, which has not been precisely described yet. Further, we observed high level of *ERVWE1* transcript together with efficient RNA splicing in seminomas. Detected *ERVWE1* transcription is independent of the expression of other examined endogenous retroviruses. *ERVWE1* transcription derepression corresponds with the low global level of 5mC detected in seminomas, which involves extensive DNA hypomethylation of the *ERVWE1* promoter. We propose the high TET1 dioxygenase expression as s marker of undifferentiated GCTs. Furthermore, we propound the high *ERVWE1* RNA expression and its efficient splicing as a marker of seminomas and the seminoma component of mixed GCT.

Key words: TET1, 5-hydroxymethylcytosine, 5-methylcytosine, seminoma, germ cell tumor, human endogenous retrovirus, ERVWE1, promoter DNA methylation, RNA transcription, RNA splicing