Abundance of DNA methyltransferase 3a (Dnmt3a) and its interaction with Fn14 promoter are repressed in denervated skeletal muscle of mice. Overexpression of Dnmt3a inhibits the gene expression of Fn14 and attenuates skeletal muscle atrophy upon denervation. Denervation also causes the activation of ERK1/2, JNK1/2, and ERK5 MAPKs and AP1 and SP1, which stimulate the expression of Fn14 in skeletal muscle. Collectively, our study provides novel evidence that Dnmt3a and MAPK signaling regulate the levels of Fn14 in skeletal muscle on denervation.

Ma et al., from the Zhejiang Sci-Tech University, Hangzhou, Zhejiang, China examined associations between DNMTs expression and clinicopathological features or promoter methylation status of tumor suppressor genes (TSGs).

Overexpression of DNMTs was detected in pituitary neuroendocrine tumors. Frequencies of DNMT1 overexpression were significantly higher in macroadenomas, invasive tumors, and grade III and IV tumors. DNMT3A was frequently detected in invasive tumors and grade IV tumors. In addition, DNMT1 and DNMT3A were frequently detected in high-methylation tumors. Furthermore, in multivariate logistic regression, the significant association between DNMT1 or DNMT3A and high-methylation status persisted after adjusting for clinicopathological features.

The findings suggested that tumor overexpression of DNMT1 and DNMT3A is associated with tumor aggressive behavior and high-methylation status in pituitary neuroendocrine tumors. This data support a possible role of DNMT1 and DNMT3A in TSG promoter methylation leading to pituitary neuroendocrine tumor invasion and suggest that inhibition of DNMTs has the potential to become a new therapeutic approach for invasive pituitary neuroendocrine tumor [1)].

1)
Ma HS, Wang EL, Xu WF, Yamada S, Yoshimoto K, Qian ZR, Shi L, Liu LL, Li XH. Overexpression of DNA (Cytosine-5)-Methyltransferase 1 (DNMT1) And DNA (Cytosine-5)-Methyltransferase 3A (DNMT3A) Is Associated with Aggressive Behavior and Hypermethylation of Tumor Suppressor Genes in Human pituitary neuroendocrine tumors. Med Sci Monit. 2018 Jul 13;24:4841-4850. doi: 10.12659/MSM.910608. PubMed PMID: 30002361.