

Abstract

There is an increasing evidence that alterations in chromatin remodeling play an important role in tumorigenesis. The SWI/SNF chromatin remodeling complexes contribute to the regulation of gene expression by altering the local chromatin structure. Depending on the context, they can act as either transcriptional activators or repressors. All SWI/SNF subcomplexes contain one of two ATPase subunits, Brm (Brahma) or Brg1 (Brahma related gene 1), which provide the energy for remodeling. Malignant melanoma is an aggressive cancer and is known for its notorious resistance to conventional anticancer therapies. MITF (microphthalmia-associated transcription factor) plays an essential role in melanoma biology and is placed on the central crossroad in the regulation of melanocyte development, differentiation, maintenance of lineage identity, and survival of both normal and malignant melanocytes. Our results show that the active SWI/SNF complex is strictly required for the expression of MITF. This complex is also required for expression of some transcriptional MITF targets. The survival of melanoma cells is absolutely dependent on functional SWI/SNF complex and all subunits of this complex are expressed at high levels in melanoma cell lines. Primarily, Brg1-containing subcomplexes are more important for MITF expression and melanoma cells proliferation, but after Brg1 loss its function could be compensated by Brm. Anyway, at least one ATPase must be expressed in order for melanoma cells to express MITF and proliferate. The study of Brg1-knockdowned melanoma cells has revealed the importance of SWI/SNF subcomplexes resulted from the manipulation of level of MITF. Furthermore, proliferation and survival of melanoma cells is increased by other SWI/SNF-dependent prosurvival and pro-oncogenic factors independently of the MITF axis. Although SWI/SNF complex is mostly regarded as a tumor suppressor, it is presented here its crucial positive role in melanoma proliferation and survival. Similarly as in the case of some other cancer types (prostate cancer, gastric and colorectal cancer), SWI/SNF complex, or at least some of its components (mostly Brg1) seems to be a tumor promoter for melanoma. Thus, inactivation of its activity may be a promising target in melanoma therapy.