The SWI/SNF complex and its Role as a Chromatin Remodeler

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Introduction

- The EMT, or epithelial to mesenchymal transition is a phenomenon where cells became able to travel from their original location to other places in an organism.
- The SWI/SNF complex is an ATP dependent chromatin remodeling complex that has been linked to cancer.
- The PROTAC ACBI1 can target and degrade the catalytic subunits (SMARCA2/4) of the SWI/SNF complex.
- TGF (Transforming Growth Factor)-beta induces the EMT process.
- The links between the SWI/SNF complex and the EMT are not well studied. Further research should investigate the potential role of the SWI/SNF complex as a promoter of TGF-Beta-induced EMT.

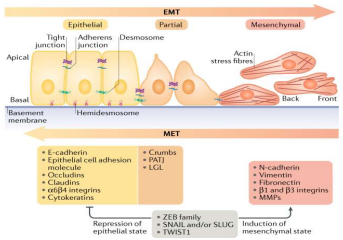


Figure 1: Outline of a typical EMT program

Methods

- To investigate the temporal effect of SWI/SNF in TGF-β-induced EMT, we treated near normal MCF10A cells with ACBI1 for 8 hours, followed by TGF-β treatment for 0, 2, 4, 8, 24, and 48 hours.
- Imaging was conducted at each timepoint to observe how the absence of SMARCA4/2 affects the cellular morphology.
- The Wound healing Assay conducted at each timepoint to evaluate the acquisition of migratory characteristics.
- RNA extraction was done using a MN Nucleospin® kit.
- The harvested RNA was run on a 1% gel for integrity
- A PCR was done to identify possible contamination
- To evaluate the cellular transition to mesenchymal state, qPCR was conducted to compare the relative expression of EMT transcription factors (TFs) and mesenchymal markers between the treated and control groups.

Fig. 2: Function of SWI/SNF chromatin-remodeling complexes

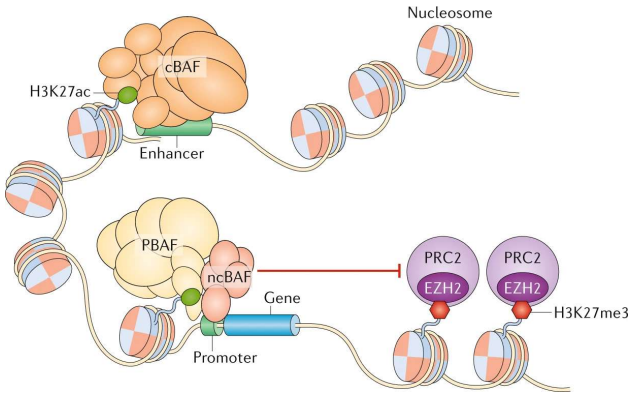
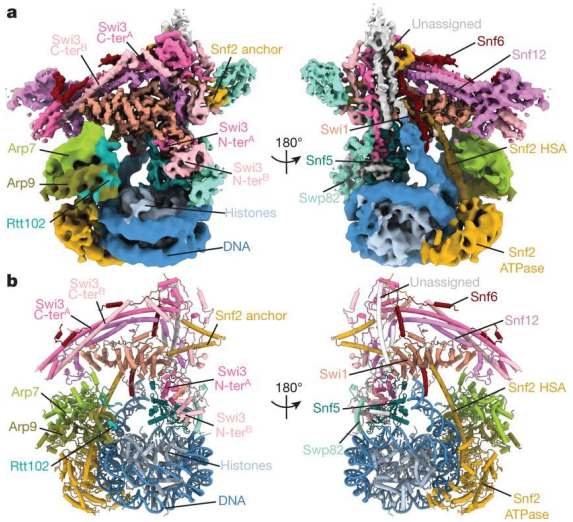


Figure 3:Cryo-EM structure of the SWI/SNF–nucleosome complex



Results/Conclusions

- Our results are preliminary and require further testing and analysis
- TGF-Beta treatment can shift the morphological characteristics and the expression of molecular markers of the MCF10A cell line toward mesenchymal state.
- We observed that in the absence of SMARCA 2/4, the expression of EMT-TF's are delayed.
- These results suggest that the SWI/SNF complex plays a role in TGF-Beta induced EMT.

Significance

- Our observation introduced the SWI/SNF complex as a chromatin remodeler that is involved in TGF-B-induced EMT.
- We showed that SWI/SNF complex can promote the transition into mesenchymal state.
- Given the function of SWI/SNF in EMT process induced by TGF-B, SMARCA4/SMARCA2 could be potential targets for tumor treatment.
- Future studies should investigate the direct function of SMARCA4/SMARCA2 in tumor metastasis.

References

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