In molecular biology, SWI/SNF (SWItch/Sucrose NonFermentable) is a nucleosome remodeling complex found in both eukaryotes and prokaryotes. In simpler terms, it is a group of proteins that associate to remodel the way DNA is packaged. It is composed of several proteins – products of the SWI and SNF genes (SWI1, SWI2/SNF2, SWI3, SWI5, SWI6) as well as other
polypeptides. It possesses a DNA-stimulated ATPase activity and can destabilise histone-DNA interactions in reconstituted nucleosomes in an ATP-dependent manner, though the exact nature of this structural change is unknown.

The human analogs of SWI/SNF are BAF (SWI/SNF-A) and PBAF (SWI/SNF-B). BAF in turn stands for "BRG1- or HRBM-associated factors", and PBAF is for "polybromo-associated BAF".

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Mechanism of action

It has been found that the SWI/SNF complex (in yeast) is capable of altering the position of nucleosomes along DNA. Two mechanisms for nucleosome remodeling by SWI/SNF have been proposed. The first model contends that a unidirectional diffusion of a twist defect within the nucleosomal DNA results in a corkscrew-like propagation of DNA over the octamer surface that initiates at the DNA entry site of the nucleosome. The other is known as the "bulge" or "loop-recapture" mechanism and it involves the dissociation of DNA at the edge of the nucleosome with reassociation of DNA inside the nucleosome, forming a DNA bulge on the octamer surface. The DNA loop would then propagate across the surface of the histone octamer in a wave-like manner, resulting in the repositioning of DNA without changes in the total number of histone-DNA contacts. A recent study has provided strong evidence against the twist diffusion mechanism and has further strengthened the loop-recapture model.

Role as a tumor suppressor

The mammalian SWI/SNF (mSWI/SNF) complex functions as a tumor suppressor in many human malignancies. It was first identified in 1998 as a tumor suppressor in rhabdoid tumors, a rare pediatric malignancy. As DNA sequencing costs diminished, many tumors were sequenced for the first time around 2010. Several of these studies revealed SWI/SNF to be a tumor suppressor in a number of diverse malignancies. A meta-analysis of many sequencing studies demonstrated SWI/SNF to be mutated in approximately 20% of human malignancies.
SWIB/MDM2 protein domain

Main article: Mdm2

The protein domain, SWIB/MDM2, short for SWI/SNF complex B/MDM2 is an important domain. This protein domain has been found in both SWI/SNF complex B and in the negative regulator of the p53 tumor suppressor MDM2. It has been shown that MDM2 is homologous to the SWIB complex.[15]

Function

The primary function of the SWIB protein domain is to aid gene expression. In yeast, it expresses certain genes, in particular BADH2, GAL1, GAL4, and SUC2. It works by increasing transcription. It has ATPase activity, which means it breaks down ATP, the basic unit of energy currency. This destabilises the interaction between DNA and histones. This disrupts chromatin and opens up the transcription-binding domains. Transcription factors can bind to this site, leading to an increase in transcription.[16]

Protein interaction

The protein interactions of the SWI/SNF complex with the chromatin allows binding of transcription factors and therefore increase in transcription.[16]

Structure

This protein domain is known to contain one short alpha helix.

Family members

Below is a list of yeast SWI/SNF family members and human orthologs:[17]

<table>
<thead>
<tr>
<th>yeast</th>
<th>human</th>
<th>function</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWI1</td>
<td>ARID1A, ARID1B</td>
<td>contains LXXLL nuclear receptor binding motifs</td>
</tr>
<tr>
<td>SWI2/SNF2</td>
<td>SMARCA4</td>
<td>ATP dependent chromatin remodeling</td>
</tr>
<tr>
<td>SWI3</td>
<td>SMARCC1, SMARCC2</td>
<td>similar sequence, function unknown</td>
</tr>
<tr>
<td>SWP73</td>
<td>SMARCD1, SMARCD2, SMARCD3</td>
<td>similar sequence, function unknown</td>
</tr>
<tr>
<td>SWP61</td>
<td>ACTL6A, ACTL6B</td>
<td>actin-like protein</td>
</tr>
</tbody>
</table>

History
The SWI/SNF complex was first discovered in the yeast, *Saccharomyces cerevisiae*. It was named after yeast mating types switching (SWI) and sucrose nonfermenting (SNF).[^16]

See also

- Mdm2
- Chromatin Structure Remodeling (RSC) Complex
- Transcription coregulator

References


