Available online at www.sciencedirect.com
ScienceDirect
Mutation Research 618 (2007) 3–17
Fundamental and Molecular Mechanisms of Mutagenesis
www.elsevier.com/locate/molmut
Community address: www.elsevier.com/locate/mutres

Mechanisms of ATP dependent chromatin remodeling

Vamsi K. Gangaraju [1], Blaine Bartholomew *

Department of Biochemistry and Molecular Biology, Southern Illinois University School of Medicine, Carbondale, IL. 62901-4413, USA

Received 4 August 2006; accepted 14 August 2006
Available online 21 January 2007

Abstract

The inter-relationship between DNA repair and ATP dependent chromatin remodeling has begun to become very apparent with recent discoveries. ATP dependent remodeling complexes mobilize nucleosomes along DNA, promote the exchange of histones, or completely displace nucleosomes from DNA. These remodeling complexes are often categorized based on the domain organization of their catalytic subunit. The biochemical properties and structural information of several of these remodeling complexes are reviewed. The different models for how these complexes are able to mobilize nucleosomes and alter nucleosome structure are presented incorporating several recent findings. Finally the role of histone tails and their respective modifications in ATP-dependent remodeling are discussed.

Keywords: Chromatin remodeling; Nucleosome; SWI/SNF; ISWI; CHD; INO80; SWR1; Twist diffusion; Bulge propagation; Nucleosome spacing

1. Introduction

Nucleosomes are the fundamental unit of chromatin that are a highly compact and yet dynamic nucleoprotein complex. Nucleosomes are formed by wrapping ~147 bp of DNA around a histone octamer [1]. All DNA related processes in eukaryotes have to overcome the compaction of DNA by chromatin. Histone octamers which were long considered to be just a structural backbone or molecular spools have recently been found to be more dynamic and to have a regulatory role. The dynamic nature of chromatin is caused by two distinct mechanisms. The first kind involves covalent modifications of the histone N-terminal tails and occurs without the hydrolysis of ATP [2]. The second mode requires the hydrolysis of ATP and involves the movement of histone octamers relative to DNA in order to make the DNA accessible [3]. Even though these mechanisms are distinct, they are functionally interconnected inside the cell. In certain cases these two functions co-exist in the same complex or they exist in separate complexes that are both required for maximum opening of chromatin and activation of transcription, DNA replication and repair.

Movement of nucleosomes along DNA has to overcome at least 100 contacts between the histone octamer and DNA [4]. A wide variety of nucleosome remodeling complexes exists inside the cell and hence it is possible to have a wide variety of mechanisms for nucleosome mobilization. Recent discoveries have shown that different chromatin remodeling complexes share a common mechanism for remodeling chromatin. First, we review

* Corresponding author at: Department of Biochemistry and Molecular Biology, Southern Illinois University School of Medicine, 1245 Lincoln Dr., Room 229, Carbondale, IL 62901-4413, USA.
Tel.: +1 618 453 6437; fax: +1 618 453 6440.
E-mail address: bbartholomew@siumed.edu (B. Bartholomew).
[1] Present address: Department of Cell Biology, Yale University School of Medicine, 333 Cedar Street, NS287, New Haven, CT 06520, USA.

0027-5107/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.mrfmmm.2006.08.015

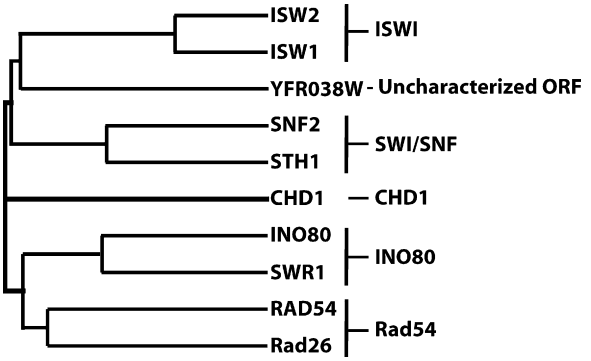

Fig. 1. Similarity of different ATP dependent remodeling complexes in *S. cerevisiae*. Clustering of complexes into different subfamilies is dependent on the sequence homology between the members of the subfamily.

the general properties of several of the different ATP remodeling families and second, examine the emerging view of the underlying mechanism of remodeling that is in common with these different remodelers.

2. Nucleosome remodeling complexes

2.1. SWI/SNF family

The discovery of chromatin remodeling factors started with that of SWI/SNF which is a ~11-subunit complex. It was originally identified as a regulator of mating type switching (SWI) or as a requirement for growth on energy sources other than sucrose (SNF – sucrose nonfermenting) [5–7]. In *S. cerevisiae*, as in *Drosophila* and humans, there appears to be two versions (SWI/SNF and RSC) of the SWI/SNF complex (Figs. 1 and 2). RSC is more abundant in the cell than SWI/SNF and RSC is essential for cell growth while SWI/SNF is not. SWI/SNF and RSC have been shown to have distinct, non-overlapping roles. The catalytic subunit of yeast SWI/SNF is the Swi2 or Snf2 protein and its paralog in RSC is the Sth1 subunit [8]. RSC has also been shown to exist in two functionally distinct complexes that differ by containing either

SWI/SNF Subfamily -

S.cerevisiae		*D.melanogaster*		*H.sapiens*	
SWI/SNF	RSC	BAP	PBAP	BAF	PBAF
Swi2/Snf2	Sth1*	Brahma*	Brahma*	Brg1 or hBrm*	BRG1*
Swi1/Adr6		OSA	BAF250		
	Rsc 1,2&4		Polybromo		Polybromo/BAF 180
	Rsc9		BAP170		
Swi3	Rsc8	Moira	Moira	BAF170&155	BAF170&155
Snf5	Sfh1	Snr1	Snr1	hSNF5/INI1	hSNF5/INI1
Swp82/Yfl049w	Rsc7/ Npl6p				
Swp73/Snf12	Rsc6	BAP60	BAP60	BAF60a	BAF60aorb
Arp7/Swp61	Arp7/Rsc11	BAP55	BAP55	BAF53	BAF53
Arp9/Swp59	Arp9/Rsc12				
		Actin	Actin	Actin	Actin
Snf6					
Swp29/Tfg3/Taf14/Anc					
Rtt102	Rtt102				
Snf11					
	Rsc 5,10,13-15				

INO80 Subfamily -

S.cerevisae		*H.sapiens*
yINO80	ySWR1	hINO80
Ino80*	Swr1*	hIno80*
Arp8		Arp8
Arp5		Arp5
Arp4	Arp4	BAF53a/Arp4
Rvb1	Rvb1	Tip49a
Rvb2	Rvb2	Tip49b
Ies2		hIes2/PAPA-1
Ies6		hIes6/C18orf37
Act1	Act1	Amida
Taf14	Arp6	FLJ90652
Nhp10	Aor1/Swc5	NFRKB
Ies1	Vps71/Swc6	MCRS1
Ies3	Vps72/Swc2	FJL20309
Ies4	Yaf9	
Ies5	Bdf1	
	Swc1/Swc3	
	Swc4/God1	

ISWI Subfamily -

S.cerevisae			*D.melanogaster*		*H.sapiens*				*M.musculus*	
ISW1a	ISW1b	ISW2	ACF	CHRAC	NURF	WCRF/hACF	WICH	hCHRAC	RSF	SNF2h/Cohesin	NoRC	mWICH
Isw1*	Isw1*	Isw2*	ISWI*	ISWI*	ISWI*	hSNF2h*	hSNF2h*	hSNF2h*	hSNF2h*	hSNF2h*	mSNF2h*	mSNF2h*
Ioc3	Ioc2	Itc1	Acf1	Acf1		hAcf1		hAcf1		Mi2	Tip5/Baz2a	
	Ioc4						Wstf					mWstf
		Dpb4		Chrac16				hChrac17		Mta1 & 2	p50	
		Dls1		Chrac14				hChrac15		HDAC1 & 2	p80	
					Nurf301				p325	RbAp46		
					Nurf55					RbAp48		
					Nurf38					MBD2 & 3		
										Rad21		
										SA1 & 2		
										Smc1 & 3		

CHD Subfamily -

S.cerevisae	*D.melanogaster*		*M.musculus*		*H.sapiens*	
CHD1	Mi2	CHD1	CHD1	Mi2	NuRD	ATRX
Chd1*	Chd4*	Chd1*	Chd1*	Chd4/Chd3*	Chd3/Chd4*	ATRX*
	Rpd3			HDAC1 & 2	HDAC1 & 2	
				RbAp48	RbAp48	
				Icaros 1,2 & 7	RbAp46	
				Aiolos	MBD3	
					MTA2	

CHD Subfamily is the least characterized and can have uncharacterized proteins

Fig. 2. Subunit composition of members of each subfamily of remodeling complexes. The catalytic subunit is marked by an asterisk on the side. Subunits which are shared by multiple complexes in the same organism are underlined. Subunits which are homologous in different organisms by virtue of their sequence are shadowed in grey.