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Spotlight

New partners for old friends: Plant SWI/SNF complexes

The physical accessibility of specific genomic regions is a chromatin property that regulates gene expression and allows the establishment of an appropriate transcriptional landscape in response to environmental and developmental signals. In eukaryotes, ATP-dependent chromatin remodeling complexes use the energy produced via ATP hydrolysis by an ATPase subunit to perform DNA translocation. These complexes are classified into four subfamilies, based on the domain organization of their catalytic ATPases (Clapier et al., 2017).

Within the different remodeling complex subfamilies, SWI/SNF (Switch defective/sucrose non-fermentable) remodelers have been the most exhaustively characterized in organisms from different taxa, including plants (Reyes, 2014). SWI/SNFs are typically associated with increasing chromatin accessibility, since they have been reported to slide and eject nucleosome from their target regions (Clapier et al., 2017). The *Arabidopsis* genome encodes multiple homologs of several SWI/SNF subunits: two canonical ATPase subunits, SPLAYED (SYD) and BRAHMA (BRM); four SWI3 subunits (SWI3A–SWI3D); two actin-related proteins (ARP4 and ARP7); two BRM-associated factors (SWP73A and SWP73B); and BUSHY (BSH, an ortholog of SNF5/INI1) (Thouly et al., 2020). Their combinational assembly has been associated with the formation of complexes with different functions, some of which have been elucidated in the last two decades.

Plant SWI/SNF complexes have been shown to be involved in the regulation of a wide range of developmental processes, including embryo and leaf development, cotyledon separation, juvenile-to-adult transition, flowering time, and flower organ development. They are also crucial for photomorphogenesis, responses to plant hormones, and abiotic stresses (Reyes, 2014). Part of their specificity for their target genomic regions has been attributed to the physical interaction of their subunits with DNA-binding proteins, which have been proposed to recruit them to specific loci. Several examples of these regulatory mechanisms have been described since the beginning of the study of the plant SWI/SNFs (e.g., AN3, REF6 [Thouly et al., 2020]), highlighting their importance in the regulation of well-studied genes and molecular pathways. Despite these, the general mechanisms by which SWI/SNF complexes bind and regulate the expression of their genomic targets remain elusive.

TWO NOVEL BRM-INTERACTING PROTEINS CONTROL BRM BINDING AND SWI/SNF SUBUNIT ABUNDANCE

In recent years, various studies with new insights have contributed to the understanding of the composition and mode of action of the *Arabidopsis* SWI/SNF complexes. By combining classic protein biology approaches with genetics and -omic technologies, Li's group identified and characterized two novel SWI/SNF subunits, BRIP1 and BRIP2 (BRAHMA-interacting proteins 1/2), containing a GLTSCR (glioma tumor suppressor candidate region) domain (Yu et al., 2020) (Figure 1). In agreement with their name, these proteins were found to physically interact with BRM. Due to their high degree of sequence similarity and expression patterns, the authors generated and studied the *brip1 brip2* double mutant, which they found to display transcriptome and phenotypes similar to those of the *brm-3* mutant (*BRM* lacking its bromodomain), including short roots, downward-curled leaves, early flowering, and reduced fertility. Furthermore, BRIP1 and BRIP2 were found to be required for BRM binding to its genomic targets, indicating that this is a BRIP1/2-dependent process. Remarkably, the loss of BRIP1 and BRIP2 not only affected BRM binding to chromatin but also decreased its abundance. The chemical inhibition of the proteasome in *brip1 brip2* partially complemented BRM levels, suggesting that BRIP1/2 post-translationally contribute to BRM stability. Similarly, the relative abundance of other known SWI/SNF subunits was also altered in the *brip1 brip2* background, highlighting the role of these two novel proteins in the maintenance of SWI/SNF complexes.

THE FUNCTION OF BROMODOMAINS IN PLANT SWI/SNF COMPLEXES

Bromodomains are highly conserved eukaryotic protein domains that recognize and bind to acetylated lysines on histones. In animals and yeast, some SWI/SNF subunits contain bromodomains, which have been associated with the SWI/SNF binding to acetylated nucleosomes in these organisms (Awad and Hassan, 2008). An association between SWI/SNF subunit binding and histone acetylation has been observed in *Arabidopsis* (Jégu et al., 2017). However, BRM, the—until recently—only known plant SWI/SNF subunit containing a bromodomain, did not show any preferential binding for their acetylated histones, raising the question of whether other bromodomain-containing proteins are involved in the SWI/SNF recruitment to chromatin.

When performing immunoprecipitation followed by mass spectrometry of BRM-GFP, Li's team also identified three bromodomain-containing proteins—BRD1, BRD2, and BRD13—that interact with BRM and other core subunits of the *Arabidopsis* SWI/SNF complexes (Yu et al., 2021) (Figure 1). The transcriptomic and phenotypic characterization of the triple

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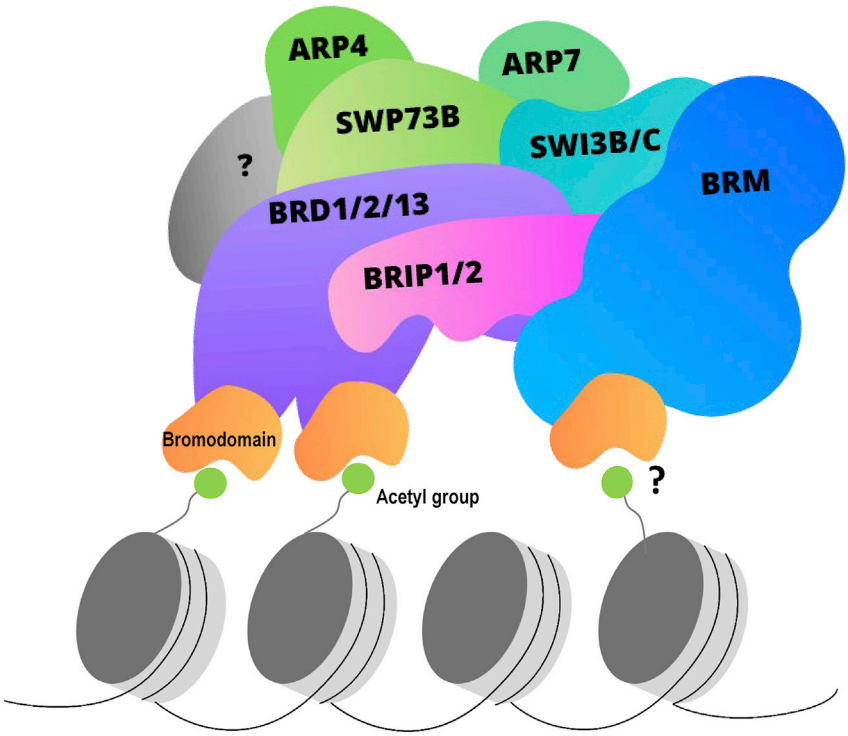

Figure 1. A simplified model illustrating the action mechanisms of the BRD- and BRIP-containing SWI/SNF complexes in *Arabidopsis thaliana*.
According to this model, two BRD1, BRD2, and/or BRD13 proteins are recruited by SWP73B and SWI3B/C into a BRM-containing SWI/SNF complex. BRD1/2/13 also interact with BRM and BRIP1/2. BRD bromodomains may bind acetylated nucleosomes to direct the SWI/SNF complex to specific genomic regions. The role of the BRM bromodomain in directing the SWI/SNF toward chromatin remains unknown (question mark). Unidentified SWI/SNF subunits are represented in gray.

brd1/2/13 mutant suggested that these BRDs act redundantly to control the expression of a common gene set with BRM, since the *brd1/2/13* mutant phenocopied the *brm-3* mutant. Furthermore, through chromatin immunoprecipitation sequencing analyses, the authors showed that the BRDs co-localize with BRM on H4K5ac- and H4K8ac-rich chromatin, suggesting that they are bona fide SWI/SNF subunits. Additionally, the disruption of the bromodomain in BRD2 was found to significantly reduce its genomic occupancy and the absence of BRDs to negatively influence BRM recruitment, indicating that BRD bromodomains are essential for the recruitment of SWI/SNF complexes to chromatin (Figure 1). Interestingly, and similar to *brip1 brip2*, the loss of function of *brd1/2/13* leads to a dramatic decrease of BRM at the protein level, suggesting that BRDs contribute to maintaining the physiological abundance of BRM (Yu et al., 2021).

Jarończyk and collaborators also identified the *Arabidopsis* BRD1, BRD2, and BRD13 as SWI/SNF components (Jarończyk et al., 2021). In addition to showing that BRDs interact with BRM and other SWI/SNF subunits, they provided evidence that SWI3C and SWP73B (BAF60) enable the simultaneous incorporation of two BRDs to the SWI/SNF complexes *in vivo*, contributing to the understanding of the assembly of these complexes in plants (Figure 1). Aside from the developmental characterization of *brd1/2/13*, they found that, as for other previously described SWI/SNF subunit mutants (Sarnowska et al., 2016), *brd1/2/13* displays increased abscisic acid and paclobutrazol (a gibberellin biosynthesis inhibitor) sensitivity. Moreover, the quadruple *brm-3 brd1/2/13* mutant was shown to phenocopy the *brm-1* null mutant. These findings provide strong genetic evidence that the studied BRDs are SWI/SNF components that act in the same complex as BRM for the regulation of previously known SWI/SNF-regulated pathways. Remarkably, the fact that the loss of three BRDs and the BRM bromodomain in *brm-3 brd1/2/13* enhances the *brm-3* phenotype suggests that the BRD subunits act in cooperation with the bromodomain of BRM, whereas the underlying molecular mechanisms remain unclear so far.

Even though these studies represent important milestones in the characterization of plant SWI/SNFs, they also raise numerous fundamental questions about the understanding of the molecular function of these complexes in the green lineage. For instance, although the presence of bromodomain-containing proteins in SWI/SNFs suggests that they direct the complexes to acetylated nucleosomes (Figure 1), this remains to be experimentally validated, as they could also exert their main molecular function via other mechanisms, e.g., interacting with other proteins.

On the other hand, the specific role of SWI/SNF complexes in transcription remains to be deciphered. Unlike SAGA or polycomb complexes, which mediate the deposition of H3K14ac and H3K27me3, respectively, SWI/SNFs are not specifically associated with either active or repressive transcriptional states. In fact, their effect on transcription appears to be context dependent, a phenomenon that could be associated with the combinational assembly of different subunits for the formation of SWI/SNFs with different molecular properties. For instance, previous co-immunoprecipitation of the histone deacetylase HD2C interactors identified various SWI/SNF subunits (BRM, SWI3A, SWI3B, SWP73B, and BSH) (Buszewicz et al., 2016); however, no BRD was detected in this complex, which may suggest the existence of BRD-free SWI/SNFs with affinity for genomic regions different from those of their BRD-containing counterparts. This hypothesis is supported by the fact that from the known four *Arabidopsis* SWI3 and two SWP73 SWI/SNF subunits, only SWI3B, SWI3C, and SWP73B physically interact with the described BRDs (Jarończyk et al., 2021; Yu et al., 2021) (Figure 1). This suggests that the incorporation of different SWI3 and SWP73 isoforms may lead to or inhibit the recruitment of a diverse number of BRDs into SWI/SNF complexes. SWI3B has also been recently reported to interact with the HDA6 histone deacetylase to co-repress a subset of transposable elements

(Yang et al., 2020), suggesting that the differential incorporation of SWI3 and SWP73 isoforms with different interacting partners leads to the formation of SWI/SNFs with dissimilar molecular roles. The further detailed identification of the SWI/SNF subunit interactome, combined with genetic, transcriptomic and epigenomic methods, will allow the identification of a divergent set of plant SWI/SNFs and their specific biological function in the future.

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Juan S. Ramirez-Prado[1] *and Moussa Benhamed*[2,3,4,*]

[1]Centre of Microbial and Plant Genetics, KU Leuven, 3001 Leuven, Belgium
[2]Institute of Plant Sciences Paris-Saclay (IPS2), Université Paris-Saclay, CNRS, INRAE, Univ Evry, Orsay 91405, France
[3]Institute of Plant Sciences Paris Saclay, Université de Paris, CNRS, INRAE, Orsay (IPS2) 91405, France
[4]Institut Universitaire de France (IUF), France
***Correspondence: Moussa Benhamed (moussa.benhamed@u-psud.fr)**
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