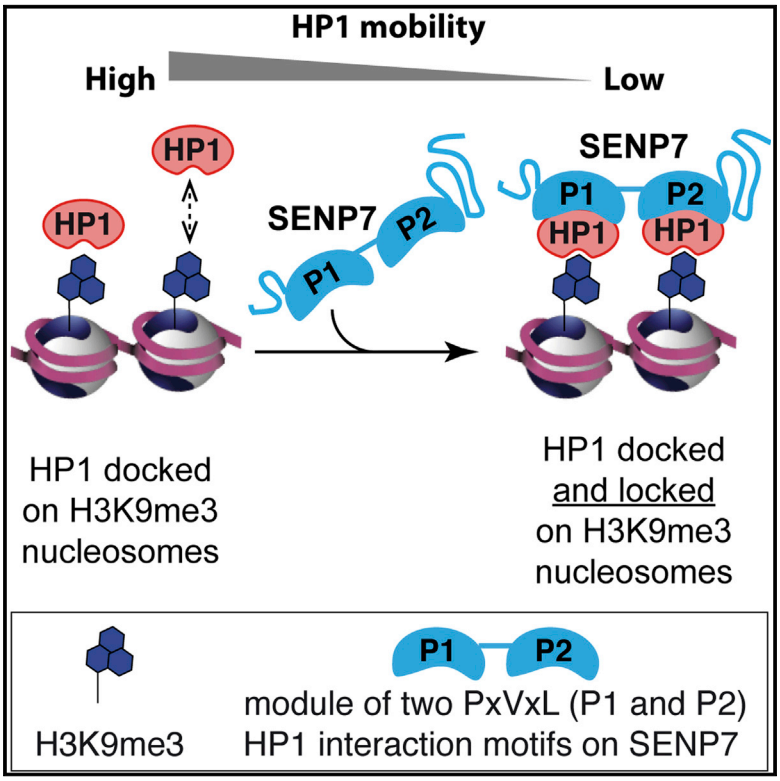
Article

Cell Reports

The SENP7 SUMO-Protease Presents a Module of Two HP1 Interaction Motifs that Locks HP1 Protein at Pericentric Heterochromatin

Graphical Abstract



Highlights

- Loss of the SENP7 SUMO-protease impacts mitosis
- SENP7 interacts with HP1α via a module of two PxVxL HP1 interaction motifs
- In mouse 3T3 cells, HP1α enrichment at pericentric domains requires this module
- HP1α mobility at pericentric heterochromatin is restricted by this module

Authors

Kelly Romeo, Yann Louault, ..., Geneviève Almouzni, Jean-Pierre Quivy

Correspondence

genevieve.almouzni@curie.fr (G.A.), jpquivy@curie.fr (J.-P.Q.)

In Brief

HP1 enrichment at pericentric domains is essential for mitosis. Romeo et al. show in mouse cells that SENP7 contains a module, comprising two HP1 interaction motifs, that restricts HP1 mobility at pericentric domains. They propose that this module locks HP1 molecules docked on H3K9me3-modified nucleosomes to promote stable HP1 accumulation.

Romeo et al., 2015, Cell Reports *10*, 771–782
February 10, 2015
http://dx.doi.org/10.1016/j.celrep.2015.01.004

Cell Reports
Article

The SENP7 SUMO-Protease Presents a Module of Two HP1 Interaction Motifs that Locks HP1 Protein at Pericentric Heterochromatin

Kelly Romeo,[1,2,3,4,5] Yann Louault,[1,2,3,4,5] Sylvain Cantaloube,[1,2,3,4,5] Isabelle Loiodice,[1,2,3,4,5] Geneviève Almouzni,[1,2,3,4,5,*] and Jean-Pierre Quivy[1,2,3,4,5,*]
[1]Institut Curie, Centre de Recherche, Paris 75248, France
[2]Centre National de la Recherche Scientifique (CNRS), UMR3664, Paris 75248, France
[3]Equipe Labellisée Ligue contre le Cancer, UMR3664, Paris 75248, France
[4]Université Pierre et Marie Curie (UPMC), UMR3664, Paris 75248, France
[5]Sorbonne University, PSL, Paris 75005, France
*Correspondence: genevieve.almouzni@curie.fr (G.A.), jpquivy@curie.fr (J.-P.Q.)
http://dx.doi.org/10.1016/j.celrep.2015.01.004

SUMMARY

HP1 enrichment at pericentric heterochromatin is essential for proper chromosome segregation. While H3K9me3 is thought to be a major contributor to HP1 enrichment at pericentric domains, in mouse cells, the SUMO-protease SENP7 is required in addition to H3K9me3. How this is achieved remains elusive. Here, we find that loss of SENP7 leads to an increased time spent in mitosis. Furthermore, we reveal that a short module comprising two consecutive HP1 interaction motifs on SENP7 is the determinant for HP1 enrichment and acts by restricting HP1 mobility at pericentric domains. We propose a mechanism for maintenance of HP1 enrichment in which this module functions on top of H3K9me3 to lock contiguous HP1 molecules already docked on H3K9me3-modified nucleosomes. H3K9me3 would thus promote HP1 enrichment only if a locking system is in place. This mechanism may apply to other nuclear domains to contribute to the control of genome plasticity and integrity.

INTRODUCTION

A central question in the field of nuclear organization is how a nuclear domain is established at specific chromatin loci during development and then maintained following cellular perturbation, during the cell cycle, or in response to environmental stress (Cavalli and Misteli, 2013). A major role for histone posttranslational modifications, which enable the docking of reader proteins, has been underscored as a means to promote a local stable enrichment-enabling formation and maintenance of specific nuclear domains with dedicated functions. This is exemplified by centromeres, which ensure the delivery of one copy of each chromosome to each daughter cell at every cell division and are, therefore, crucial for genetic stability (Grewal and Jia, 2007; Weaver and Cleveland, 2007). The centromeric organization is conserved in various species and comprises a centric region enriched in centromeric H3 variant (CenH3) and flanking pericentric regions where heterochromatin protein 1 (HP1) proteins accumulate (Maison et al., 2010). Epigenetic marks of the underlying chromatin are believed to contribute to centromere identity and include nuclear RNA, higher-order organization, histone modifications, and histone-binding proteins (Ekwall, 2007; Grewal and Jia, 2007; Karpen and Allshire, 1997; Maison et al., 2010).

Enrichment in HP1 proteins and among mammals of the HP1α isoform at pericentric domains is a hallmark of these regions (Billur et al., 2010; Gilbert et al., 2003; Maison and Almouzni, 2004; Nielsen et al., 2001). Further, enrichment of HP1 at these regions is critical for centromere function since the loss or delocalization of HP1 has been reported to lead to mitotic defects in mammals (De Koning et al., 2009; Obuse et al., 2004; Peters et al., 2001) and in *S. pombe* (Allshire et al., 1995; Ekwall et al., 1995). How maintenance of HP1 enrichment is achieved still remains to be characterized. HP1 features an N-terminal chromodomain, followed by a hinge domain and a C-terminal chromoshadow domain (Maison and Almouzni, 2004). The HP1 chromodomain specifically recognizes methylated H3K9 (Bannister et al., 2001; Jacobs and Khorasanizadeh, 2002) and is critical for the recruitment to heterochromatin regions of the genome (Lachner et al., 2001; Peters et al., 2001). The hinge domain is reported to mediate association with RNA (Maison et al., 2002; Muchardt et al., 2002). The HP1 chromoshadow domain is able to dimerize (Brasher et al., 2000; Cowieson et al., 2000), creating an interface allowing interactions with proteins that contain a PxVxL motif (Murzina et al., 1999; Smothers and Henikoff, 2000; Thiru et al., 2004).

The general view has been that HP1 enrichment at mouse pericentric heterochromatin (PCH) domains is achieved by the recognition of the H3K9me3 modification imposed by Suv39h by the HP1 chromodomain (Bannister et al., 2001; Lachner et al., 2001). However, several results suggest that the H3K9me3 modification on its own is not the only critical parameter for HP1 enrichment. The affinity of HP1 for a histone tail