DCX (a potent microtubule stabilizer) can also invade the actin-rich regions of the growth cone once it has been phosphorylated by JNK[17]. Thus, it is likely that several pathways converge to control the complex navigation of neurons to their proper cortical destination. Together, these findings highlight the importance of cytoskeletal regulation during neuronal migration and shed light on the signalling pathways that impinge on this developmental process. □

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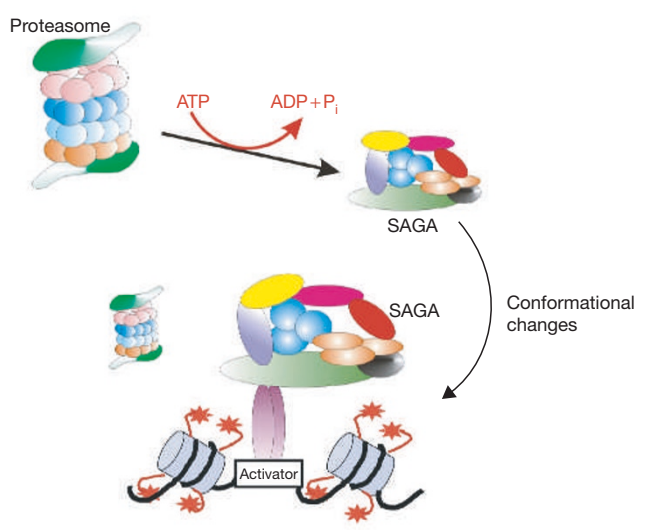
A SAGA of proteasomal ATPases

In the November 4 issue of *Cell* (**123,** 423–436; 2005), Jerry Workman and colleagues report on a novel non-proteolytic function for proteasomal ATPases in transcription.

Degrading ubiquitinated proteins is probably the most well known function of the proteasome — a complex containing a catalytic core capped by a regulatory particle at either end. However, it is now evident that the regulatory particle has functions beyond protein degradation, particularly in transcription. Each regulatory cap consists of discrete sub-particles called the base and the lid. The base contains six ATPases, and previous work has implicated two of these ATPases in histone methylation. The Workman group now establish a link between the ATPase Rpt6/Sug1 and the SAGA complex, an essential transcriptional coactivator that facilitates formation of the transcriptional pre-initation complex.

The authors showed that the purified regulatory particle can stimulate interactions between SAGA and transcriptional activators, and increase SAGA recruitment to DNA. Enhanced recruitment of SAGA was dependent on ATP hydrolysis by the regulatory particle and, in fact, the base sub-particle alone was sufficient for enhanced SAGA recruitment.The regulatory particle was unable to enhance targeting of NuA4, another coactivator complex that (like SAGA) is targeted to promoters by activators through a common subunit. These findings lead the authors to propose that the regulatory particle must be directly modifying SAGA's properties. Consistent with this view, the regulatory particle also stimulated the histone acetylase activity of SAGA.

The authors then focused on determining which ATPases were important for the enhanced recruitment and found that the ATPase Rpt6 associated with SAGA subunits *in vivo* and *in vitro*. SAGA contains



The proteasome regulatory particle facilitates interaction between SAGA and promoter-bound activator in an ATP-dependent manner.

the Gcn5 histone acetylase and defects in Gcn5 are known to result in reduced global histone H3 acetylation. Extending their *in vitro* analysis, the authors found that yeast mutants with point mutations in the Rpt6-ATPase domain had reduced global H3 acetylation of, decreased Gcn5 targeting to, and reduced Gcn5-dependent H3 acetylation of target promoters *in vivo*. These findings demonstrate that Rpt6 is essential for the effects of the regulatory particle on SAGA.

Determining exactly how proteasomal ATPases enhance SAGA recruitment and activity — for example, by inducing conformational alterations in SAGA subunits or refashioning the composition of the complex — will be the next challenge. Whether proteasomal ATPases have additional functions in other DNA-dependent processes, such as repair, has yet to be determined.

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