TRANSCRIPTION

Stimulating saga

> “...the stimulating ‘saga’ ... has given us insights into a non-proteolytic function of the proteasome.”

The function of the proteasome in ubiquitin-mediated protein degradation is well established, and it has recently been found to ‘moonlight’ in transcriptional regulation. Little is known about the non-proteolytic function of the proteasome at promoters, but, in *Cell*, Tansey, Workman and colleagues now show that the 19S regulatory particle (RP) of the proteasome can alter the SAGA (Spt–Ada–Gcn5 acetyltransferase) coactivator to enhance its interactions with transcriptional activators.

It has previously been shown that the 19S RP can be recruited to promoters in a transcriptional-activator-dependent manner, and the authors observed a direct, but weak, interaction between the 19S RP and DNA-bound activators. They therefore tested whether other factors might be required for its recruitment to promoters, and they focused on the coactivator SAGA — an essential and direct target of several classic yeast activators.

Tansey, Workman and co-workers found that the 19S RP stimulated the targeting of SAGA to a DNA-bound activator in a dose-dependent manner. This stimulatory role was dependent on the ATPase activity of the 19S RP. They extended their study to a promoter in a nucleosome array, and showed that the 19S RP could also stimulate the targeting of SAGA to activators bound to nucleosomes.

SAGA was found to be targeted to DNA in a manner that depends on the activation domain of transcriptional activators. However, the authors showed that the 19S RP doesn’t function by altering activation domains to increase their affinity for SAGA. Instead, they showed that the 19S RP could specifically alter the properties of SAGA, and they subsequently found that the 19S RP and SAGA physically interact.

A loss of the Gcn5 catalytic subunit of SAGA results in a global reduction in the acetylation of histone H3. So, as SAGA and the 19S RP physically interact, does the 19S RP have a role in this global acetylation? This answer is yes, because when they looked *in vivo*, Tansey, Workman and colleagues showed that the presence

URLs

Gcn5 http://db.yeastgenome.org/cgi-bin/locus.pl?locus=Gcn5

of an ATPase-mutant form of the 19S RP resulted in a marked decrease in the level of H3 acetylation. Their data showed that the 19S-RP ATPase activity is important for the targeting and activity of Gcn5 *in vivo*, and that the 19S-RP-stimulated targeting of SAGA to promoters is important for optimal transcription.

So, the stimulating 'saga' described by these authors has given us insights into a non-proteolytic function of the proteasome. It seems that the 19S RP, using its ATPase activity, can modulate the SAGA complex to facilitate its targeting to transcriptional activators at promoters and subsequent transcription events.

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ORIGINAL RESEARCH PAPER Lee, D. *et al.* The proteasome regulatory particle alters the SAGA coactivator to enhance its interactions with transcriptional activators. *Cell* **123**, 423–436 (2005)
FURTHER READING Muratani, M. & Tansey, W. P. How the ubiquitin–proteasome system controls transcription. *Nature Rev. Mol. Cell Biol.* **4**, 192–201 (2003)
WEB SITES
William Tansey's laboratory: http://www.cshl.edu/public/SCIENCE/tansey.html
Jerry Workman's laboratory: http://www.stowers-institute.org/labs/workmanLab.asp