PARASITOLOGY

# Epigenetic regulation of *VSG* expression

The controversial issue of the chromatin structure at *VSG* expression site loci in African trypanosomes seems to have been resolved with the publication of two papers in *Eukaryotic Cell* showing that nucleosomes are depleted at active *VSG* expression sites.

In the bloodstream of the mammalian host, *Trypanosoma brucei* avoids immune detection by periodically switching its variant surface glycoprotein (VSG) 'coat' by a process known as antigenic variation. In contrast to most of the protein-coding genes, which are transcribed by RNA polymerase II and are regulated post-transcriptionally, *VSG* genes are transcribed by RNA polymerase I and are regulated at the transcriptional level.

Although there are hundreds of *VSG* genes in the *T. brucei* genome, only a single gene is transcribed at any one time in 1 of approximately 15 telomeric bloodstream form expression sites (BESs). The role of chromatin organization in this monoallelic exclusion has been the subject of some debate, but resolving this issue was complicated by the fact that telomeric expression sites in *T. brucei* are highly conserved. Tara Stanne and Gloria Rudenko and, in a complementary study, Luisa Figueiredo and George Cross were able to overcome this obstacle by using some of the latest chromatin analysis techniques to look at nucleosome distribution in isogenic bloodstream form *T. brucei* cell lines that contained different antibiotic-resistance markers downstream of active and silent BES promoters. Both groups used chromatin immunoprecipitation (ChIP) assays to compare nucleosome occupancy at active and silent BESs, and they found that nucleosomes are dramatically depleted at active loci. Each group confirmed these observations using micrococcal nuclease assays, with Figueiredo and Cross detecting the reaction products using Southern blotting, and Stanne and Rudenko using a modified protocol that involved quantitative PCR. Figueiredo and Cross also used formaldehyde-assisted isolation of regulatory elements (FAIRE) analysis, which can detect nucleosome-depleted regions, and again confirmed that the chromatin at active BESs is more open than that at silent BESs.

Taken together, these data provide evidence that chromatin remodelling has a key role in the monoallelic expression of *VSG* loci in *T. brucei*. Further work is required to determine the molecular mechanisms involved, but these results lend further credence to the idea that *VSG* expression in African trypanosomes is under epigenetic control.

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**ORIGINAL RESEARCH PAPERS** Stanne, T. M. & Rudenko, G. Active *VSG* expression sites in *Trypanosoma brucei* are depleted of nucleosomes. *Eukaryot. Cell* **9**, 136–147 (2010) | Figueiredo, L. M. & Cross, G. A. M. Nucleosomes are depleted at the *VSG* expression site transcribed by RNA polymerase I in African trypanosomes. *Eukaryot. Cell* **9**, 148–154 (2010)
**FURTHER READING** Figueiredo, L. M., Cross, G. A. M. & Janzen, C. J. Epigenetic regulation in African trypanosomes: a new kid on the block. *Nature Rev. Microbiol.* **7**, 504–513 (2009)