A novel factor integrating transcription and repression of surface antigen genes in African trypanosomes

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African trypanosomes express a single variant surface glycoprotein (VSG) from one of 15 sub-telomeric bloodstream expression sites (BESs), requiring coordinated activation of the expressed BES and silencing of all others. Since the discovery of the expression site body (ESB), a specialised extranucleolar compartment for monoallelic VSG transcription, VSG exclusion factors VEX1 and VEX2 have been shown to maintain silencing of inactive BESs, while ESB1 promotes transcriptional activation. How these opposing activities are integrated has remained unclear.

Here, we identify ESBX (Tb927.3.1660), a novel ESB component that cross-connects BES activation and repression. Depletion of ESBX reduces active BES transcription while simultaneously derepressing inactive BESs and causes loss of RNA polymerase I and VEX2 localisation to the ESB. Conversely, ESBX overexpression weakly activates inactive BESs without formation of additional ESBs, indicating that ESBX levels must be finely balanced to maintain monoallelic control.

ESBX is the first factor shown to be required for both active VSG expression and inactive BES silencing. We propose that self-reinforcing recruitment of ESBX and associated factors to a single BES provides a mechanism for how monoallelic exclusion is established and maintained to sustain antigenic variation in African trypanosomes.