AN ESSENTIAL ROLE FOR THE 5' NON-CODING *VAR* REGION IN CHROMATIN-MEDIATED IMPRINTING OF MONO-ALLELIC EXPRESSION OF ANTIGENIC VARIATION GENES IN MALARIA PARASITES

Jose Juan Lopez-Rubio[1], Alisson M. Gontijo[1], Marta Nunes[1], Neha Issar[1], Rosaura Hernandez Rivas[2] & Artur Scherf[1]

[1]Institut Pasteur-CNRS, 25 rue du Dr. Roux, 75724 Paris, France
[2]Department of Molecular Biomedicine, CINVESTAV, 7360,Mexico D.F., Mexico

Antigenic variation in protozoan parasites facilitates long-term chronic infection of the host. In the human malaria parasite *Plasmodium falciparum* this is achieved by mutually exclusive transcription of a single member of the 60-member *var* family. The active mode of a *var* gene alternates between transcribed and non-transcribed (poised) phases during the 48 hour asexual life cycle. *var* promoters are key DNA elements in this process because they are able to nucleate epigenetic factors that control mono allelic expression. We show that tri-methylation of histone H3 lysine 4 peaks in the 5´ upstream region of transcribed *var* regions, whereas a shift to di-methylation occurs in the poised state, 'bookmarking' this *var* for re-activation at the onset of the next cycle. In stably repressed *var* loci high levels of histone H3 lysine 9 tri-methylation define an antagonist to lysine 4 methylation. Our data demonstrate an essential role for the 5' non-coding *var* region in chromatin-mediated imprinting of mono-allelic expression during blood stage cycles.