Lack of functional chromatin dynamics through nuclear motor proteins in aged *Biomphalaria glabrata* snails reveals a mechanism of interest with respect to controlling schistosomiasis.

Daniel Horton[1]; Rita Torres Pereria[1]; Halime Arican-Goktas[1]; Patrick Driguez[2]; Gabriel Rinaldi[2]; Matty Knight[3,4]; Joanna M. Bridger[1]

1) Centre for Genome Engineering and Maintenance (CenGEM), Brunel University London, Kingston Lane, Uxbridge, UB8 3PH. UK
2) Wellcome Sanger Institute, Wellcome Genome Campus, Hinxton, Cambridge, CB10 1SA, UK
3) Division of Science & Mathematics, University of the District of Columbia, 4200 Connecticut Ave. NW Washington, D.C. 20008, USA
4) Department of Microbiology, Immunology & Tropical Medicine, Research Centre for Neglected Diseases of Poverty, School of Medicine & Health Sciences, The George Washington University Ross Hall, 2300 I Street, NW, Washington, DC 20037, USA

We have previously demonstrated that in the interphase nuclei of the intermediate snail host, *Biomphalaria glabrata*, specific genes, such as the (Heat shock protein) *Hsp70* loci are relocated rapidly to new non-random nuclear locations with minutes of the presence of *Schistosoma mansoni* parasites. This relocation is correlated with the subsequent upregulation of the gene in susceptible snails, which is not apparent in resistant snails or in susceptible snails that have been exposed to irradiated attenuated parasites (miracidia).

This active and functional relocation of the *Hsp70* loci can be recapitulated by heat-shocking snails at 32^{o}C. However, in aged snails the gene loci relocation is not possible neither in the presence of parasite nor heat-shock. We have evidence to support that the rapid relocation of gene loci is due to the presence of nuclear motor activity in young snails which is lacking in aged snails. Interference with this mechanism negatively affects chromatin dynamics and gene expression in response to an infection or a heat shock stimulation. This lack of chromobility recapitulates a recent finding in aged human cells (senescent) that normal nuclear motor activity for rapidly relocating chromosomes is also lacking, making *B. glabrata* a new model organism in which to study genome behaviour in relation to ageing.

Since we know this gene movement and subsequent upregulation of gene expression are involved in an active schistosome infection, we hypothesis that aged snails would be less able to be infected by *S. mansoni*, making this nuclear motor complex and dynamics mechanism a target with respect to controlling infection of this human parasite in the snail.