Functional genomics for schistosomes: retroviral-based transgenesis and CRISPR-Cas9

Gabriel Rinaldi[1], Sutas Suttiprapa[2], Christina Cochran[2], Isheng J. Tsai[1], Wannaporn Ittiprasert[2], Victoria H. Mann[2], Nancy Holroyd[1], Sergey Iordanskiy[2], Michael I. Bukrinsky[2], Matt Berriman[1] & Paul J. Brindley[2]

1. Wellcome Trust Sanger Institute, Cambrideshire, UK
2. The George Washington University, Washington DC, USA

Functional genomic studies will facilitate the characterization of newly genome sequences of schistosomes. VSVG-pseudotyped murine leukemia virus (MLV) can transduce eggs of *Schistosoma mansoni* leading to chromosomal integration and germline transmission of transgenes, facilitating the development of stable transgenic lines. Nonetheless, robust expression of transgenes has been a challenge. Accordingly, perturbation of epigenetic marks, exogenous *cis*-regulatory, e.g. conditional promoters, schistosome tissue-specific promoters, codon optimization of reporters, and antibiotic selection of transduced parasites are being evaluated. Lentiviruses, including VSVG-pseudotyped human immunodeficiency virus type 1 (HIV-1) likely can facilitate transgenesis of schistosomes. We showed that early steps of lentivirus infection including attachment of virions to the schistosome tegument, proviral cDNA synthesis, and genome integration take place. High throughput sequencing analyses revealed widespread genome integration of HIV. Transgenesis combined with the genome editing technology CRISPR-Cas9 (clustered regularly interspaced short palindromic repeats-CRISPR associated 9) has shifted the landscape for manipulating the genome by introducing specific mutations in the DNA. New findings suggested that Cas9-gRNAs ribonucleoprotein complexes delivered into schistosomules by electroporation induced INDEL mutation in a model locus, the gene coding for interleukin-4-inducing principle of *S. mansoni* eggs (IPSE). Retroviral-based approaches coupled with CRISPR-Cas9-driven genome editing will facilitate functional genomics investigations for this neglected tropical disease pathogen.

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