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## New insights into the role of DNA methylation in *Biomphalaria glabrata* infection susceptibility

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### Introduction

As for many transmissible diseases non-pharmacological interventions are one of the most effective ways to control schistosoma infections. One of these, the control of the intermediate host, is also recognized by WHO as a key element to eradication of the disease in humans.

*Biomphalaria* snails can show remarkable resistance to schistosomes and prevalence is low in snail populations even in regions where the parasite is highly present in the vertebrate host. Resistance is a heritable trait, but it shows also high plasticity *e.g.*, snails can become resistant to the same parasite strain after a primary infection. One of the components of heritable plasticity is epigenetic information that refers to the heritable but reversible changes in gene function, and one of the bearers of epigenetic information is DNA methylation. We reasoned that modifying DNA methylation in the snail would have potentially positive effects on resistance traits.

### Methods

We developed chemical DNA methylation modulators to which the snails were exposed to modify their pan-genomic methylation and we established a method for targeted DNA

methylation modifications based on dCas9/Crispr. For heritability of resistance measure we used epigenetic recombinant inbred lines (EpiRILs) and experimental infections.

### **Results**

We applied a dCas9-SunTag-DNMT3A complex and synthetic sgRNA to transfect *B. glabrata* embryos and observed an increase of CpG methylation at the target site in 50% of the hatching snails. DNA methylations were also introduced in an inbred *B.glabrata* line by chemical treatment in F0. This led to phenotypic variation in F3 and methylation differences in F3. Both increase and decrease (up to 100% and down to 20% prevalence from 86% control) of infection success indicating variation in complex resistance/compatibility trait.

### **Conclusions**

We show that DNA methylation can be modified in *B.glabrata* both chemically and dCas-based, and pan-genomic or targeted. These modifications produce heritable phenotypic variants and have an influence on infection susceptibility confirming the epigenetic component of this trait. A rationale of DNA methylation-based vector control will be presented.

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The 20-min presentation is part of the Roundtable 10, theme “New approaches on the intermediate host studies” and it is scheduled for November 23rd from 09:00 to 10:40 hours.