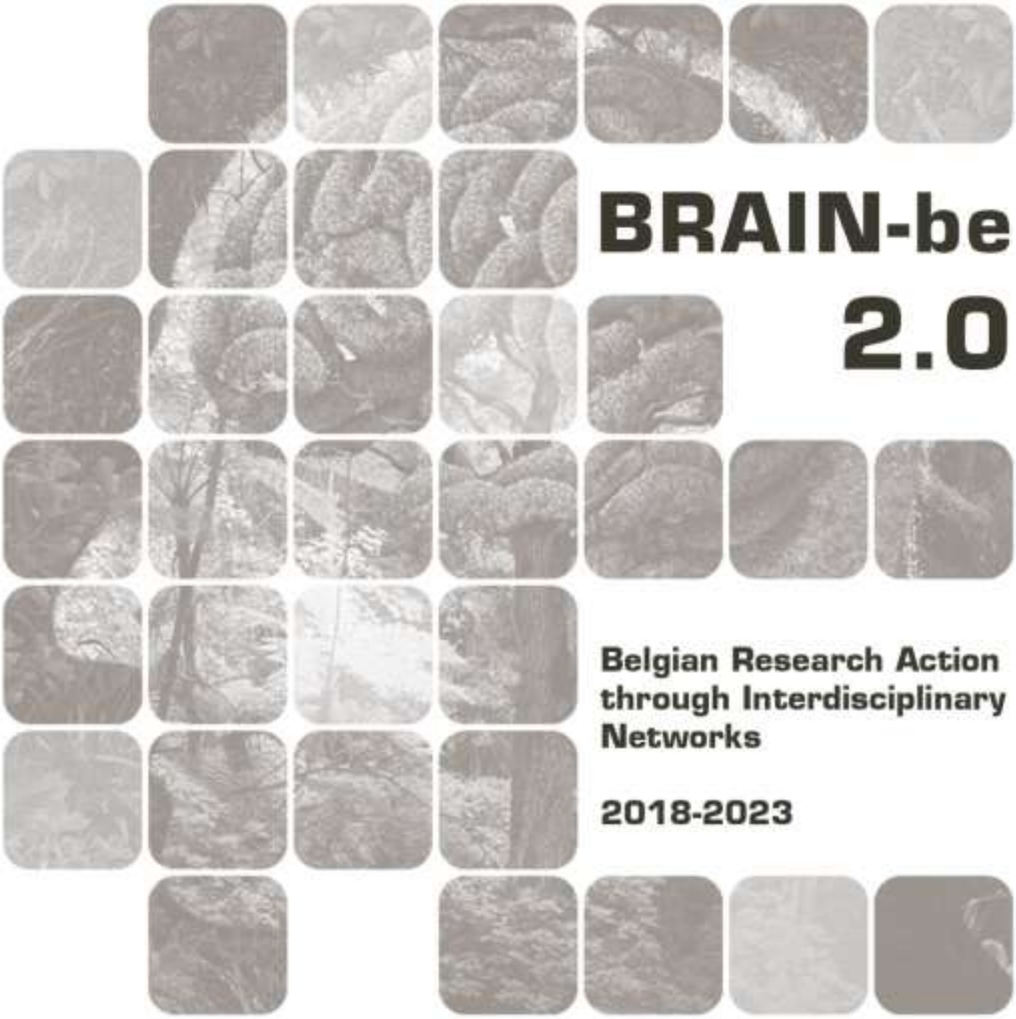

MicroResist

The influence of snail host microbiome in trematode parasite resistance

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Summary EN

Pillar 1: Challenges and knowledge of the living and non-living world

Trematodiases, or snail-borne diseases, are caused by trematode parasite infections and have a global impact. An estimated 250 million people, over a billion livestock animals, and unquantified numbers of wild animals are affected, resulting in decreased life expectancy, diminished quality of life, significant economic losses, and threats to conservation. The spread and establishment of freshwater snails and their parasitic trematodes are exacerbated by globalized transport, environmental changes, and climatic shifts, altering transmission dynamics in endemic regions and facilitating their spread to new areas.

Despite widespread efforts to control trematodiases, the success of these initiatives has been hindered by ineffective strategies, anthropogenic factors, parasite hybridization, and the role of animal reservoirs. Drug-based treatments alone have proven insufficient, emphasizing the need for complementary methods targeting snail hosts. Recently, the microbiome of freshwater snails has emerged as a promising target for disease control, with the potential to enhance resistance in wild snail populations. Variations in snail resistance to trematodes, ranging from full susceptibility to complete resistance, highlight the microbiome's role as a key driver of resistance. While insights from other vector-borne systems, such as mosquito-borne diseases, have shown the microbiome's influence on vector competence, research into the microbiome of freshwater snails remains limited, restricting the implementation of microbiome-based disease control measures.

The first objective of the MicroResist project focused on a laboratory-based infection experiment designed to investigate how the snail microbiome changes during the maturation of schistosome infections. This included examining the bacterial component of the microbiome during key stages of parasite development, assessing the impact of different schistosome species on the snail’s bacterial profiles, and comparing these effects in single-parasite versus co-infection scenarios.

The second objective sought to validate and enhance the axenic tool originally developed by Chernin (1957), laying the groundwork for a robust transplant protocol for the bacterial component of freshwater snail microbiomes.

The third objective explored a possible connection between the bacterial aspect of the microbiome in a globally invasive snail species and its resistance to trematode infections through a reciprocal transplant experiment.

Lastly, the project shifted focus from the microbiome to investigate the anthropogenic pressures influencing snail-parasite interactions in man-made lakes, highlighting the ecological and human-driven factors shaping these dynamics.

The MicroResist project investigated the interactions between snails and the bacterial aspect of the microbiome as determined by 16S rRNA gene metabarcoding to uncover mechanisms of resistance to trematode infections. It studied bacterial communities in *Biomphalaria glabrata* snails exposed to *Schistosoma* trematodes, finding correlations between parasite species, co-infection dynamics, developmental stages, and microbial profiles. These findings emphasize the importance of accounting for parasite-related microbial shifts in future studies. A new protocol for creating germ-free snails and successfully transplanting microbiomes in freshwater snails was developed as confirmed by 16S rRNA gene metabarcoding, paving the way for experiments to determine causal relationships between microbiome composition and resistance. Moreover, the phylogenetic relatedness of the donor host significantly affected recipients’ survival probability, corroborating the phylosymbiosis pattern in freshwater snails. This tool enables future work to decipher a potential causative role of the microbiome in freshwater snail biology, unlocking a new and potentially vital new avenue of mollusc research.

In *Pseudosuccinea columella*, a globally invasive snail linked to liver fluke infections, microbiome transplant experiments between resistant and susceptible populations showed no immediate impact on resistance to *Fasciola hepatica*. However, bacterial community shifts following parasite exposure characterized through 16S rRNA gene metabarcoding indicate potential transgenerational effects mediated by microbiomes. Additionally, the MicroResist project documented trematode parasites of the common hippopotamus (*Hippopotamus amphibius*) in artificial water systems of Zimbabwe through an integrative taxonomic approach, combining molecular data and morphometrics of museum and new samples. The resulting publication highlights the ecological consequences of invasive snails, demonstrating that the introduction of *P. columella* to habitats with *H. amphibius* increases liver fluke transmission, threatening wild herbivore populations through parasite spillback.

A microbiome-based intervention to address the global impact of trematodiases remains elusive for now. Our results indicate that the microbiome might not be directly causing resistance to trematode parasites in freshwater snails. Nevertheless, more research including alternative snail species and additional populations is required before microbiome-based control measures targeting the intermediate snail host could be excluded completely as a potential avenue. Additionally, microbiome-mediated control of trematodiases could be valuable from other perspectives by, for example, increasing the fitness of resistant snail populations which could then outcompete susceptible snail populations. Furthermore, the MicroResist project revealed that there is a need to strengthen biosecurity measures and systematic monitoring efforts to prevent the spread of invasive snail species and mitigate their ecological impact. Collaborations between conservation efforts and public health initiatives should be promoted to address shared challenges posed by trematodiases in wildlife and human communities. Educational campaigns are needed to raise awareness about snail-borne diseases and the importance of community involvement in control efforts, particularly in endemic areas and recently also in Europe as schistosomiasis colonized Corsica, France. Lastly, international cooperation in research, surveillance, and control measures is essential to tackle the transboundary challenges posed by trematodiases and invasive snail species.

The MicroResist project successfully explored the complex interplay between freshwater snails, their microbiomes, and trematode parasites, revealing that while microbiome transplantation alone did not confer resistance to infection in some *P. columella* populations, trematode infections consistently altered the snail-associated microbiome in species- and stage-specific ways. These microbial shifts may be linked to immune responses, tissue damage, or parasite-driven modulation, highlighting the need for further mechanistic studies. Although microbiome-mediated resistance remains elusive, the findings underscore the potential of targeting the microbiome—of either the host or the parasite—for future control strategies. Moving forward, integrating multi -omics perspectives, high-resolution in situ visualization, and broader ecological and genetic background will be essential to uncover functional interactions and identify pathways of resistance for sustainable trematode control within a *One Health* framework.

Keywords (5):
Schistosomiasis, microbiome, parasite resistance, museum collections, transplant experiments