Winners vs. Losers - comparative transcriptomic analysis of *Schistosoma mansoni* mature and immature eggs from gut and liver

L. Konečný [a,b*], K. Peterková [a,b], M. Sombetzki [c], J. Dvořák [d,e]

[a] Department of Parasitology, Faculty of Science, Charles University, Prague, Czechia
[b] Department of Zoology and Fisheries, Centre of Infectious Animal Diseases, Czech University of Life Sciences, Prague, Czechia
[c] University Medical Center Rostock, Germany
[d] Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Prague, Czechia
[e] Centre For Infectious Animal Diseases, Faculty of Environmental Sciences Czech University of Life Sciences, Prague, Czechia

The eggs of the blood fluke *Schistosoma mansoni* are the main cause of the clinical manifestations of chronic schistosomiasis. It is important to note, however, that only the egg "losers" trapped in the host tissues, especially in the liver, are responsible for these manifestations. After laying, the egg "winners", on the other hand, manage to attach to the endothelium of the mesenteric vein, and after a period of development, induce the growth of a small granuloma which facilitates their passage through the intestinal wall to gut lumen. "Losers" carried with a blood stream to non-specific tissues also undergo full development and induce a big granuloma formation, but their life ends there. Although these trapped eggs represent a dead end in the parasite life cycle, vast majority of transcriptomic, proteomic and secretomic studies attempting to describe the biology of the *S. mansoni* eggs have studied these liver-trapped "losers" instead of gut-attached "winners". Thus, the fundamental question is if and possibly how the gene expression of the egg is affected by the surrounding tissues.

In our study, we isolated *S. mansoni* eggs from the liver and intestinal tissues of experimentally infected mice, divided these eggs into mature and immature and compared their transcriptomic profiles. In addition, we evaluated viability of these eggs via hatching assays. Our results clearly show that gene expression in *S. mansoni* eggs is critically dependent on tissue localization. In addition to the crucial differences in expression between eggs derived from the two tissues, the expression profiles of liver-derived eggs are very similar regardless of their developmental stage, whereas gut-derived eggs show remarkable changes during their maturation. Among most differentially expressed genes of interest between these tissues are mitochondrial genes, which together with proteases and protease inhibitors, are substantially more active in intestinal eggs. In stark contrast, IPSE/alpha-1, Omega-1, as well as the majority of micro-exon genes (MEGs), which are often proposed as the primary egg immunomodulators, are, in fact, restricted to liver losers.

We argue that such differential expression of many important groups of molecules directly reflects the environment in which the egg is located. While in the case of the gut eggs, the up-regulated molecules probably represent the tools for successful passage to the external environment, in the case of the liver-trapped eggs, the high expression of immunomodulatory molecules may serve as a bait for the immune system for the benefit of the intestinal eggs.

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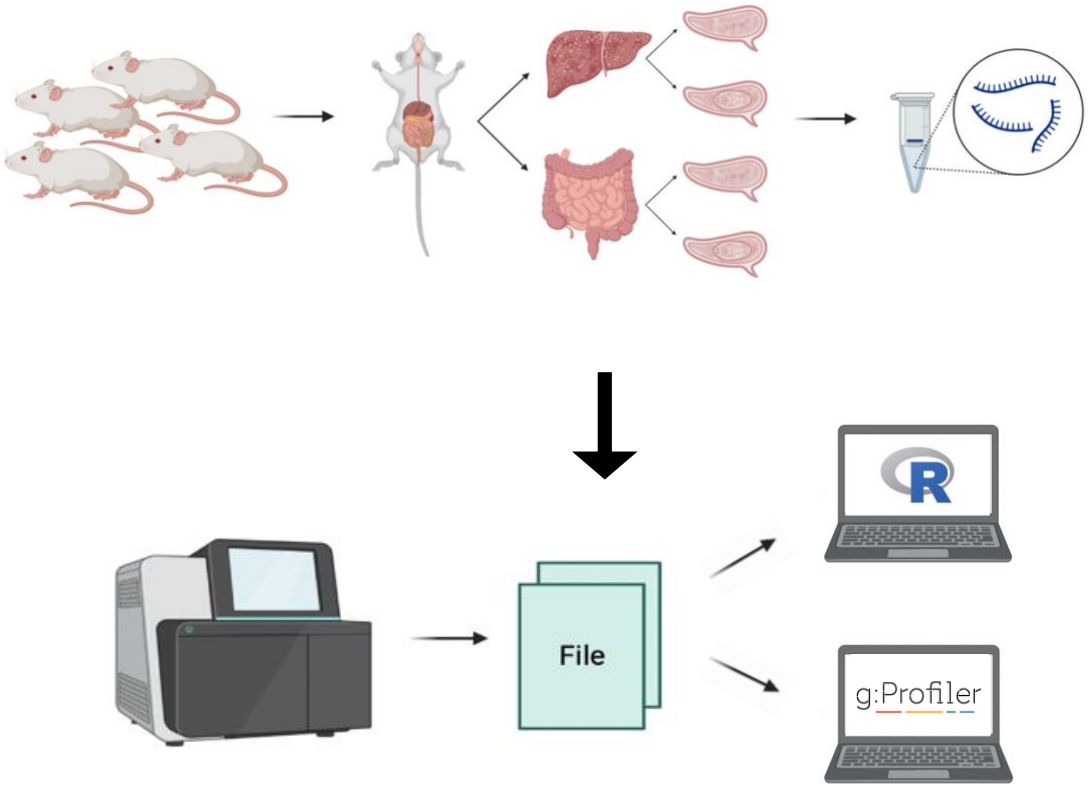

Fig. 1 – Methodological approach – graphical abstract

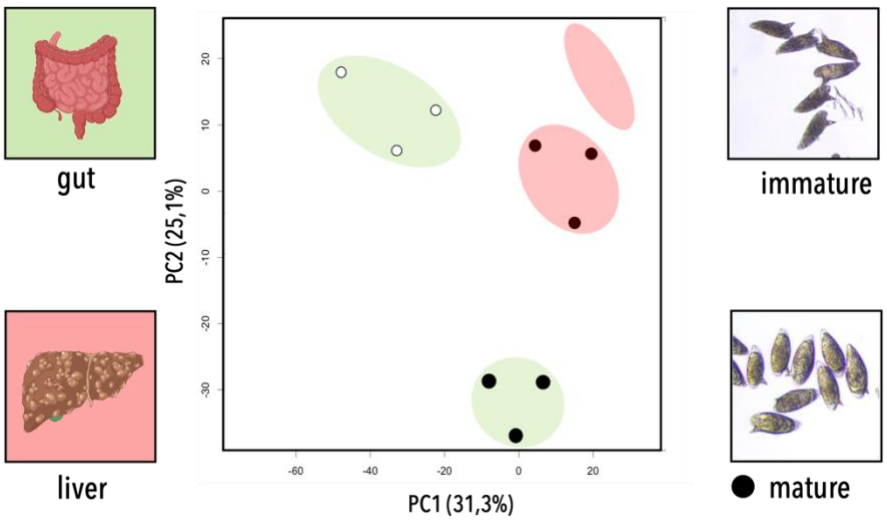

Fig. 2 – PCA analysis

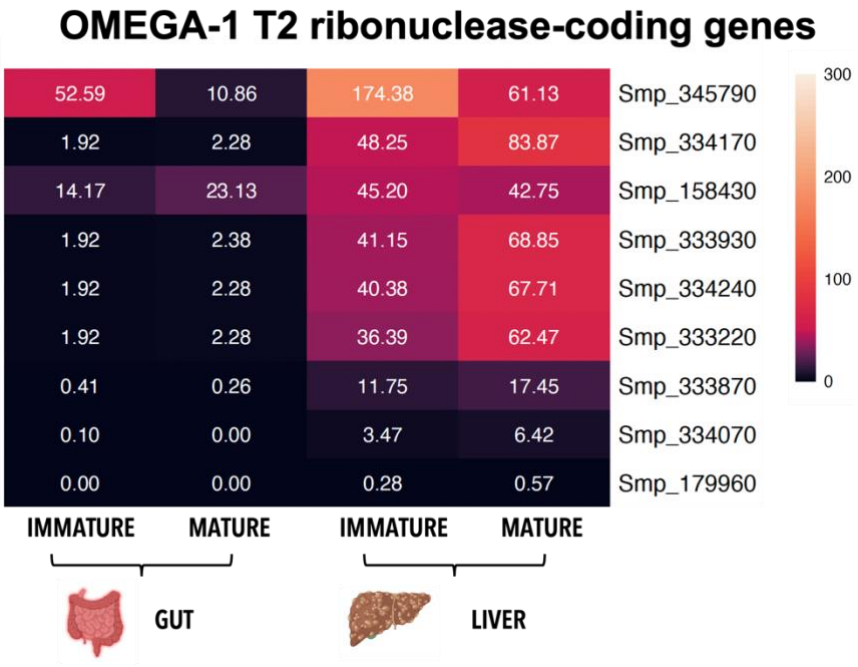

Fig. 3 – Reads per million for Omega-1 coding genes in different samples

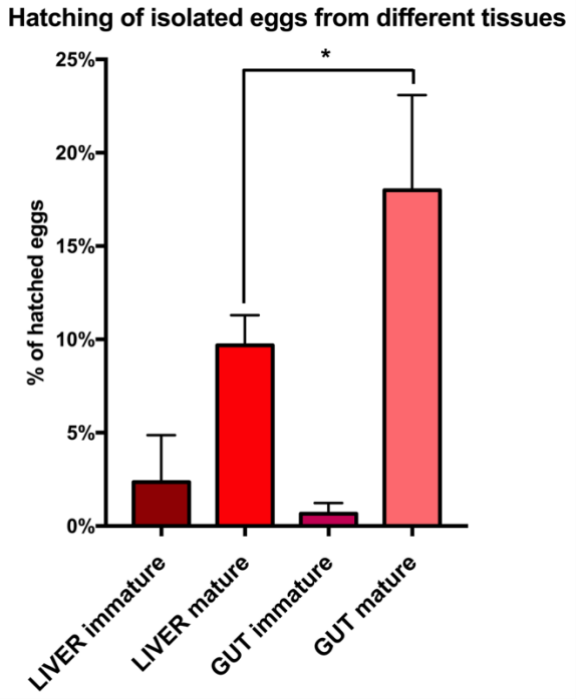

Fig. 4 – Hatching assays