True *Schistosoma mansoni* eggs-cretome revealed by laser microdissection of infected mouse liver and intestine

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Schistosoma mansoni eggs are the central drivers of schistosomiasis pathology and transmission, yet the proteins they release within host tissues remain poorly defined due to limitations of conventional in vitro approaches. Here, we provide the first in situ characterization of egg-derived proteins present in host tissues. Using laser microdissection, we selectively isolated periovular granuloma microenvironments from the livers and small intestines of infected mice during the acute and chronic phases of infection, followed by high-resolution mass spectrometry. Across all samples, we identified a conserved core set of 149 parasite proteins, representing a true in vivo egg excretory/secretory repertoire. Egg-associated protein profiles varied markedly by organ and infection phase. In the liver, acute infection was characterized by a richer and more abundant repertoire of immunomodulators (including omega-1 and IPSE), proteases, protease inhibitors, antioxidant proteins, and micro-exon gene and venom allergen-like proteins, whereas chronic liver granulomas showed a reduced and altered profile. In contrast, intestinal granulomas exhibited fewer qualitative changes between phases and a more uniform protein composition over time, despite an overall decline in protein detectability. These patterns likely reflect fundamental differences in egg fate and tissue context, as hepatic eggs remain permanently trapped whereas intestinal eggs transit out of the host. This study provides the first in situ snapshot of schistosome egg-derived proteins within host tissues, revises assumptions about intestinal granuloma chronicity, and defines core and context-dependent egg proteins that are likely to shape granuloma biology, host modulation, and parasite transmission.