XVII INTERNATIONAL SYMPOSIUM ON
SCHISTOSOMIASIS
PERSPECTIVES ON SCHISTOSOMIASIS ELIMINATION
NOVEMBER 10-13TH 2024 | SALVADOR - BAHIA

Indicate the format in which you wish to present your work: ☐ Poster ☒ Oral Presentation

TITLE

ROLES OF THE SCHISTOSOMA MANSONI TYROSINE KINASE SMFES IN SCHISTOSOMIASIS: FUNCTIONAL CHARACTERIZATION AND EVALUATION OF COMPOUND ACTIVITY

AUTHORS

Torres, G.P.*[1]; Tavares N.C.[1] ; Azevedo, G.L.A.[1]; Lopes, B.L.M.[1]; Montresor, L.C.[1]; Caldeira, R.L.[1]; Gava, S.G.[1]; Mourão, M.M.[1]

AFFILIATIONS

[1] Grupo de Helmintologia e Malacologia Médica, Instituto René Rachou/Fundação Oswaldo Cruz, Belo Horizonte/MG

ABSTRACT

The SmFES protein kinase is hypothesized to play a key role in the signal transduction pathways of Schistosoma mansoni, particularly in larval transformation following host penetration. Our previous research identified SmFES as an essential protein for parasite reproduction, hepatic granuloma formation in a murine model, and attraction to host mucus molecules. In this study, first, we explored the function of SmFES in cell recruitment for granuloma formation, immune response, and potential strategies to disrupt the parasite's lifecycle. Thus, we assessed the impact of reduced liver granulomas on the survival of infected mice, observing a 23% increase in mortality compared to the nonspecific control group. Histological analysis of liver tissue revealed an increase in fibrosis and decreased cellular profile in the SmFES-knockdown group relative to controls. Then, to investigate immune factors associated with cell recruitment in the livers of mice infected with SmFES-depleted parasites, we measured TNF-α, IFN-γ, IL-10, IL-6, CCL2, and IL-12p70 levels in liver homogenates. Mice infected with SmFES-knockdown schistosomula exhibited a 72.3% and 46.3% reduction in CCL2 and IL-6 concentrations, respectively. To detect SmFES expression patterns in adult female S. mansoni worms, fluorescence in situ hybridization was employed, showing transcription in the encephaloesophageal and reproductive regions, including the uterus, ootype, and vitellaria. This suggests a role in oviposition and potential neurological functions. Then, since it has been demonstrated that miracidia were unable to sense the snail host and explore control strategies to interrupt the parasite's cycle, we evaluated in silico-predicted SmFES-binding compounds with anti-Schistosoma activity. Compounds were tested on egg cultures, assessing miracidia hatching, attraction, and infectivity in Biomphalaria glabrata. Compound SmFES17 reduced hatching rates by 8-12.9%. Miracidia exposed to SmFES9, SmFES15, SmFES18, and SmFES22 showed decreased attraction to B. glabrata mucus. Moreover, snails were challenged with hatched miracidia from eggs exposed to the five compounds. After 40 days, cercariae release was evaluated, resulting in a reduction of 30.7% for SmFES9-exposed parasites to 58% for SmFES17. These findings suggest that SmFES influences cytokine production in the liver, affecting immune modulation, diminished cellular recruitment, and increased fibrosis, potentially contributing to increased mortality in SmFES-knockdown infections due to insufficient retention of toxic egg proteins. SmFES expression in female reproductive organs indicates a role in oviposition, while its presence in the encephaloesophageal region hints at neurological involvement. Moreover, the identified compounds offer potential for new schistosomiasis control strategies by reducing miracidia hatching and cercariae release, a mathematical models would aid in stating its potential.

KEYWORDS

RNA Interference; Protein Kinase; Functional Characterization; Inflammatory Response; Drug Discovery

FINANCIAL SUPPORT

CAPES; CNPq; Fapemig; Rene Rachou Institute/ Fiocruz Minas.