ABSTRACT

Unveiling the Role of SmFES Kinase in Schistosoma mansoni: Functional Insights and Novel Compounds for Schistosomiasis Control

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Abstract
The SmFES protein kinase is implicated in signal transduction pathways in *Schistosoma mansoni*, particularly during larval transformation after host penetration. Previous studies from our group identified SmFES as essential for parasite reproduction, hepatic granuloma formation in murine models, and parasite attraction to host mucus molecules. This study further investigates SmFES functionality and screens compounds that may disrupt the parasite's lifecycle. Mice infected with Smfes-knocked-down schistosomula exhibited a 23% higher mortality rate compared to the nonspecific control group exposed to GFP-dsRNA. Liver cytokine analyses showed reductions of 72.3% in CCL2 and 46.3% in IL-6. Histological examination of liver tissues revealed increased collagen deposition and reduced cellularity. Fluorescence in situ hybridization detected Smfes transcription in reproductive regions (uterus, ootype, vitellaria) and the encephaloesophageal region in adult female worms. To explore control strategies, in silico-predicted SmFES-binding compounds were tested on egg and intermediate life stages of the parasite. SmFES17 reduced miracidia hatching rates by 8-12.9%. Compounds SmFES9, SmFES15, SmFES18, and SmFES22 decreased miracidia attraction to *Biomphalaria glabrata* mucus. Snails exposed to miracidia treated with these compounds showed a 30.7% to 58% reduction in cercariae release after 40 days. These findings suggest Smfes influences immune modulation, cellular recruitment, and fibrosis in the liver, contributing to increased mortality in Smfes-knocked-down infections. Its transcription in reproductive and neurological regions highlights potential roles in egg-laying and neural processes. Identified compounds demonstrated efficacy in reducing cercariae release and miracidia hatching, offering promising avenues for schistosomiasis control.
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