# Analysis of a translation initiation factor of *Schistosoma mansoni* as potential drug target

Sophie Welsch[1], Francesca Magari[2], Simone Häberlein[1], Arnold Grünweller[2], Christoph G. Grevelding[1]

[1]Institute of Parasitology, Justus Liebig University, Schubertstrasse 81, 35392 Giessen
[2]Institute of Pharmaceutical Chemistry, Philipps University, Marbacher Weg 6, 35032 Marburg

## BACKGROUND & OBJECTIVE

- Schistosomiasis is a neglected tropical disease caused by parasites of the genus *Schistosoma*
- Fear of upcoming resistance against Praziquantel (only available drug) → urgent need of new targets and drugs
- Candidate target: Eukaryotic translation initiation factor 4AI (eIF4AI)[1]
  - ✓ RNA helicase that unwinds secondary structures in the 5'-untranslated region of selected mRNAs as a prerequisite for protein synthesis[2]

**What is the function of *S. mansoni* eIF4AI, and is it a potential drug target?**

## MATERIAL & METHODS

**RNA interference (RNAi) against *Smeif4a1* of adult *S. mansoni in vitro***

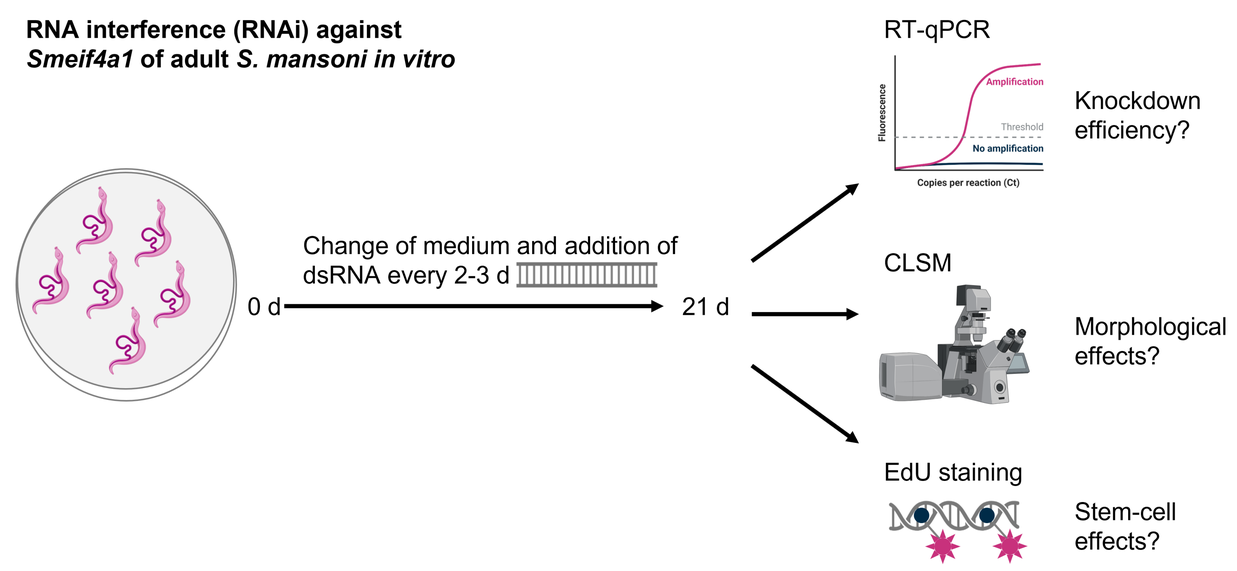


**Fig. 1: Overview of experimental procedure.**
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## RESULTS

### 1. Transcript level of *Smeif4a1* was reduced by ≥ 88% after 21 d of RNAi.

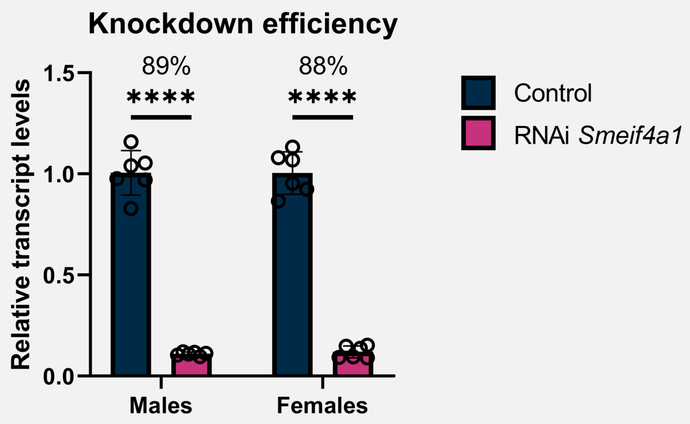


**Fig. 2: Relative transcript levels of *Smeif4a1* were reduced by ≥ 88% in males and females after 21 d of RNAi.** Analysis was performed by RT-qPCR, using a housekeeping gene as standard. Data are shown as mean ± SD, and were obtained from six independent experiments (n = 6).

### 2. *Smeif4a1* RNAi resulted in morphological changes of testis and ovary.

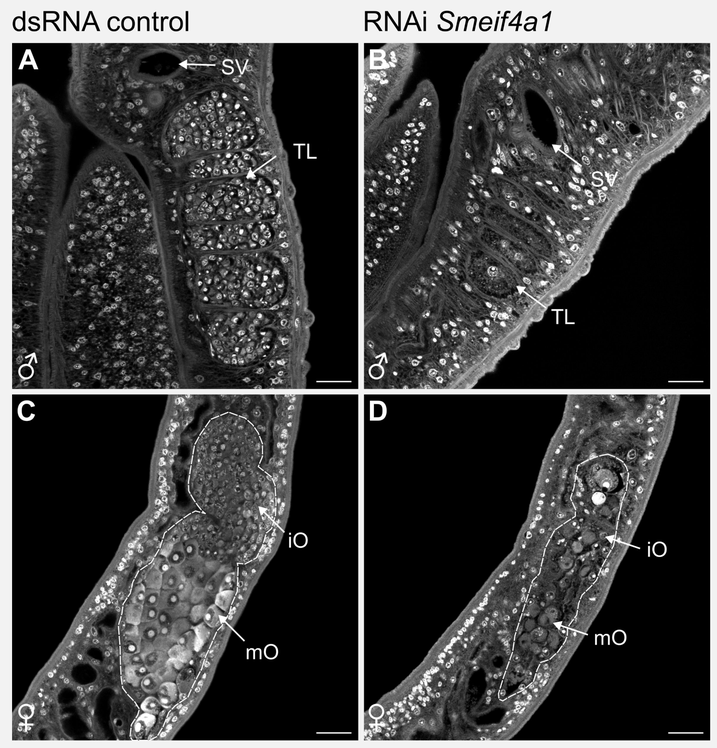


**Fig. 3: Morphological analysis of males (A, B) and females (C, D) treated with non-schistosomal dsRNA (A, C) or dsRNA of *Smeif4a1* (B, D) for 21 d.** Representative images of three independent experiments (n = 3). iO = immature oocyte, mO = mature oocyte, SV = sperm vesicle, TL = testicular lobes. Scale bars: 25 µm.

### 3. *Smeif4a1* RNAi reduced worm vitality and egg production.

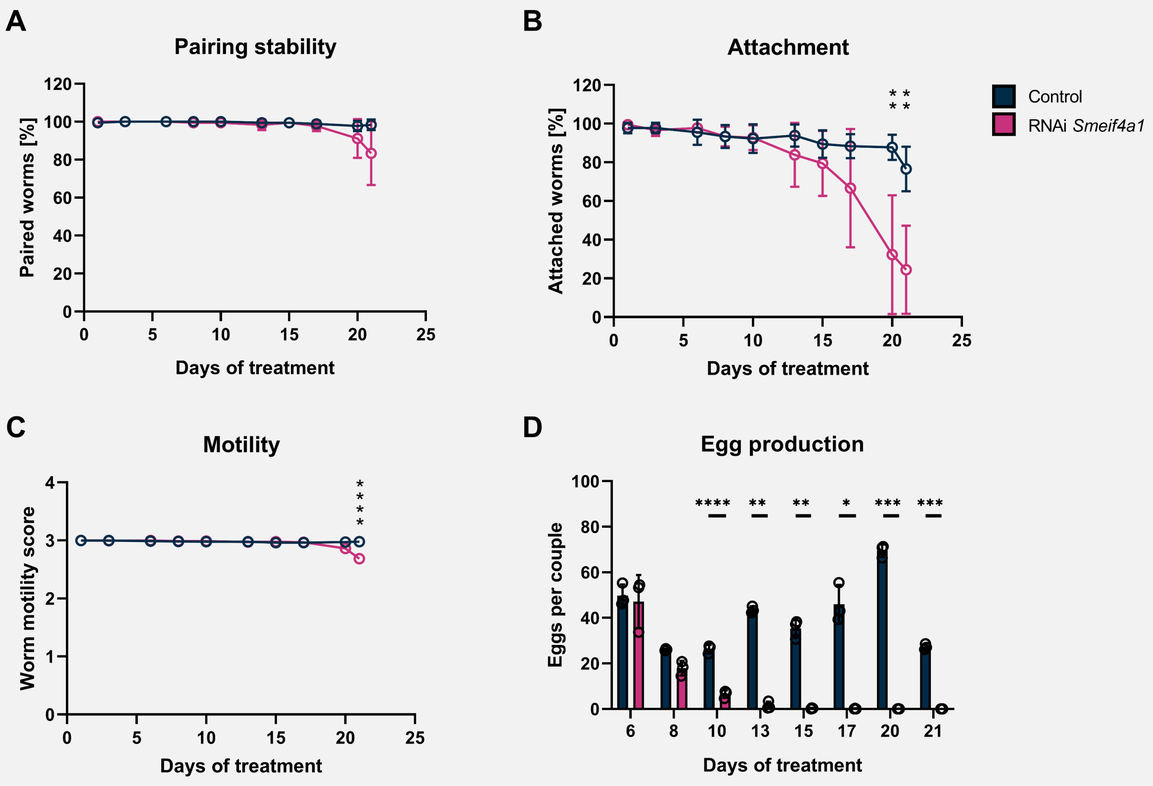


**Fig. 4: RNAi of *Smeif4a1* affected worm vitality after 20 d of treatment and egg production after 10 d of treatment. A** Percentage of paired worms. **B** Percentage of attached worms. Only males (paired and unpaired) were included in the analysis. **C** Worm motility score 4 = hyperactive, 3 = normal, 2 = reduced motility, 1 = minimal activity, 0 = dead. **D** Total egg production per couple. **A-C** n = 6, **D** n = 3. Paired two-tailed t-test with $p < 0.05$*, $p < 0.01$**, $p < 0.0005$***, $p < 0.0001$****.

### 4. *Smeif4a1* RNAi impaired the stem-cell proliferation.

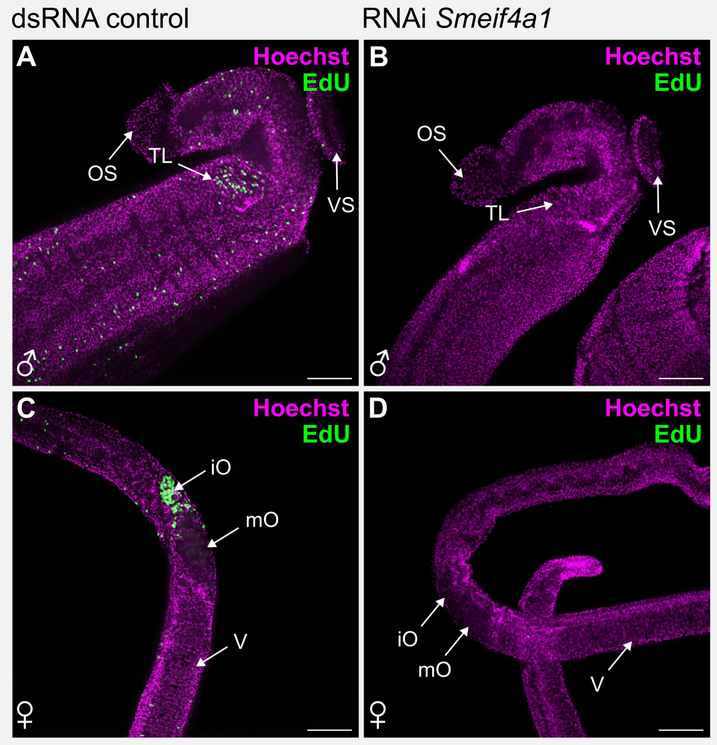


**Fig.5: EdU assay of males (A, B) and females (C, D) treated with non-schistosomal dsRNA (A, C) or dsRNA of *Smeif4a1* (B, D).** Representative images of three independent experiments (n = 3). iO = immature oocyte, mO = mature oocyte, OS = oral sucker, TL = testicular lobes, V = vitellarium, VS = ventral sucker. Scale bars: 50 µm.

## CONCLUSION & OUTLOOK

SmeIF4AI seems to be involved in stem-cell proliferation, oogenesis and spermatogenesis. This affects the overall egg production, which is the pathogenic factor of the disease. Thus, SmeIF4AI represents a promising drug target. EIF4A inhibitors are currently tested on adult *S. mansoni in vitro*. Binding of these inhibitors to recombinant SmeIF4A are currently investigated by thermal shift assays.

## REFERENCES

[1]Obermann et al. (2023), *Sci Rep.*, *13*(1):9297
[2]Parsyan et al. (2011), Nat Rev Mol Cell Biol., *12*(4):235-245.

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