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Corresponding author(s): Cornelis H. Hokke

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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☐	☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Softwares used for data collection include FlexControl 3.4 Build 119 (Bruker Daltonics), Empower 3 (Waters Corp.) and Chromeleon7, version 7.1.2.1478 (Thermo Fisher Scientific).
Data analysis	Sotwares used for data analysis include FlexAnalysis (Version 3.4, Build 50, Bruker Daltonics), Compass DataAnalysis, Version 5.0, Build 203 (Bruker DaltonicsGlycoWorkBench (Version 3, 29 June 2007), GLAD (version 3.1 glycotoolkit.com/Tools/GLAD/), Agilent Technologies Feature Extraction Software (version 7.0), GenePix Pro 7.0 (Molecular Devices) and the R/Bioconductor software package limma, run under the R version 3.5.0.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

MALDI-TOF–MS(/MS) and PGC-nano-LC-MS(/MS) data supporting our findings have been made available in Figures 1,4-6, Figures S1-7 and Tables S1-4. In addition, all raw MS data presented in this study have been deposited in Glycopost (https://glycopost.glycosmos.org/, project ID: GPST000602). Glycan microarray screening output files can be found in Github (https://github.com/lmcpetralia/Major-human-schistosome-species-express-different-glycans).

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	In this study, glycan microarrays were screened using sera from schistosome-infected children and from non-infected individuals (non-endemic). Male and female human subjects were grouped based solely on infection status. Therefore, sex and gender were not considered as variables in the analysis and are not reported.
Reporting on race, ethnicity, or other socially relevant groupings	In this study, glycan microarrays were screened with sera from children originating from areas highly endemic for schistosomiasis and from individuals in non-endemic areas. Human subjects were grouped solely based on infection status. Thus, this study does not report on race, ethnicity, or other socially relevant groupings.
Population characteristics	Sera for glycan array screening were obtained from children aged 5–11 years living in two geographic areas highly endemic for urinary or intestinal schistosomiasis. Both sexes were represented. Infection status was confirmed using microscopy□based diagnostic methods: microscopic egg counting following urine filtration (Schistosoma haematobium, urinary schistosomiasis) and the Kato-Katz technique (Schistosoma mansoni, intestinal schistosomiasis).
Recruitment	Participants were recruited through random selection from the aforementioned geographic areas. For the Piida study (Schistosoma mansoni infection sera), the recruitment targeted individuals aged 5–59 years, and pregnant women were excluded from participation. Given the high endemicity of schistosomiasis, the study aimed to capture a representative sample of the community.
Ethics oversight	Ethical approval for the Piida study (Schistosoma mansoni infection sera) was obtained from the Uganda National Council for Science and Technology (UNCST) and cleared by the Office of the President. The study was also supported by the Cambridge Local Research Ethics Committee. The Lambaréné study (Schistosoma haematobium infection sera) was approved by ethics committees of the University of Tübingen and International Foundation of the Albert Schweitzer Hospital, Lambaréné, Gabon.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The sample size of parasitic material used in this study was guided by the amount of biological material required to generate high quality mass spectrometry (MS)-based glycomic data and to enable successful construction of glycan microarrays. Because parasitic biomass and infected host material are inherently limited, no formal a priori power calculation could be performed. Instead, sample amounts were chosen to meet established minimum thresholds for reliable glycan detection and structural characterization within MS workflows. For the glycan microarray screening experiments, the available clinical sera determined the cohort sizes (Schistosoma haematobium–infected sera, n = 18; Schistosoma mansoni–infected sera, n = 21; non endemic control sera, n = 9). These sample sizes are typical of exploratory antigen profiling studies and reflect the feasibility of obtaining well characterized sera from endemic regions. They are large enough to determine qualitative differences between the groups by glycan microarray analyses. Furthermore, to address the modest cohort sizes, we employed empirical Bayes statistical methods to stabilize variance estimates and improve the reliability of differential signal detection, an approach widely used in high dimensional datasets where sample numbers are limited. Finally, technical replication, use of internal controls, and validated analytical pipelines further supported the robustness of the resulting datasets.

Data exclusions	No data were excluded from the statistical analysis.
Replication	For the structural glycomic studies of Schistosoma haematobium and Schistosoma mansoni, biological replicates were generated on two different occasions for each glycan class and parasite life-stage studied. Consistent results were obtained and are presented in the supplementary data. In addition, our study replicates previous results for Schistosoma mansoni published (https://doi.org/10.1074/mcp.M115.048280) and unpublished (C.H. Smit, Chapter 3 of PhD thesis, ISBN: 978-94-6299-396-9). Microarray design include triplication of glycan samples. Consistency of the triplicates can be observed in the provided glycan array raw data. In addition, our results of previous glycan microarray screening with sera from Schistosoma mansoni-infected individuals (https://doi.org/10.1371/journal.pntd.0001922 and C.H. Smit, Chapter 3 of PhD thesis, ISBN: 978-94-6299-396-9) were successfully replicated in the present study.
Randomization	Sera used for glycan microarray screening were non-randomly allocated based on infection status: Schistosoma haematobium-infected, Schistosoma mansoni-infected or non infected (non-endemic). Samples (infection and control sera) were randomly distributed across microarray slides (8 samples per slide), regardless of group assignment, using a randomization tool. Covariates were controlled by studying a relatively homogenous age group (children infected with either Schistosoma haematobium or Schistosoma mansoni).
Blinding	Blinding was not implemented in this study, as the outcome of the mass spectrometry and glycan microarray measurements were entirely objective. Specifically, for the glycan microarray, the infection and control sera were randomly allocated across the microarray slides (8 samples per slide), independent of group assignment (see 'Randomization' above). As a result, each slide contained sera from multiple groups, ensuring that no slide could be handled differently in a way that might bias the results. Furthermore, signal intensities were quantified using a scanner that reports median fluorescence intensity for each spot on the microarray. The data acquisition is automated and not subject to interpretation, preventing the risk of bias influencing the results.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Four carbohydrate-binding monoclonal antibodies (273-3F2-A, 291-4D10-A, 291-5D5-A and 100-4G11) were used for microarray validation. 273-3F2-A was applied to the microarray slides in 1:100 dilution ration, while 291-4D10-A, 291-5D5-A and 100-4G11 were applied at a 1:200 dilution ratio. The mAbs were produced in house by hybridomas generated from mice infected with schistosomes (described in Figure S9).
Validation	Reactivity of the mAbs used in this study towards specific glycan motifs have been previously determined in the following publications: https://doi.org/10.1093/glycob/10.6.601, https://doi.org/10.1093/glycob/10.6.601, https://10.1017/s0031182004006390, https://10.1016/j.ab.2010.07.008, https://10.1093/glycob/cwg025.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Various life stages of Schistosoma mansoni (Puerto Rican strain) and Schistosoma haematobium (Egyptian NAMRU-3 strain) were used in this study. They were obtained from life cycles maintained at the Leiden University Medical Center in male Golden Syrian hamsters (RjHan:AURA strain) and from Biomphalaria glabrata and Bulinus truncatus snails.
Wild animals	N/A
Reporting on sex	The present glycomic study of Schistosoma mansoni and Schistosoma haematobium was conducted on a mixture of male and female adult worms. While the study addresses developmental characteristics of the parasite by analyzing several life stages separately, it was beyond the scope of this work to investigate sex-specific glycomic features of adult worms. This limitation is partly due to the

	practical challenges associated with reliably separating male and female worms, found in copula and exhibiting overlapping morphological traits. Moreover, obtaining sufficient quantities of sex-specific biological material for glycomic analysis is technically demanding, further constraining the feasibility of such comparisons within the current study.
Field-collected samples	The study did not involved parasitic samples collected from the field, as the various life stages of the parasite used in this study were obtained from laboratory hamsters.
Ethics oversight	The various life stages of Schistosoma mansoni and Schistosoma haematobium used in this study were obtained from laboratory hamsters in which the parasite life cycles are maintained at the Leiden University Medical Center in accordance with the Guide for the Care and Use of Laboratory Animals of the Institute for Laboratory Animal Research and have received approval from the Dutch 'Central Authority for Scientific Procedures on Animals' (CCD, License number: AVD11600202215904).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A