



A look into the genome of *Trichuris trichuria*

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Intro. to Genomics (485)

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Selected paper

ARTICLES

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Whipworm genome and dual-species transcriptome analyses provide molecular insights into an intimate host-parasite interaction

Bernardo J Foth^{1,7}, Isheng J Tsai^{1,2,7}, Adam J Reid^{1,7}, Allison J Bancroft^{3,7}, Sarah Nichol¹, Alan Tracey¹, Nancy Holroyd¹, James A Cotton¹, Eleanor J Stanley¹, Magdalena Zarowiecki¹, Jimmy Z Liu⁴, Thomas Huckvale¹, Philip J Cooper^{5,6}, Richard K Grencis³ & Matthew Berriman¹

Whipworms are common soil-transmitted helminths that cause debilitating chronic infections in man. These nematodes are only distantly related to *Caenorhabditis elegans* and have evolved to occupy an unusual niche, tunneling through epithelial cells of the large intestine. We report here the whole-genome sequences of the human-infective *Trichuris trichiura* and the mouse laboratory model *Trichuris muris*. On the basis of whole-transcriptome analyses, we identify many genes that are expressed in a sex- or life stage-specific manner and characterize the transcriptional landscape of a morphological region with unique biological adaptations, namely, bacillary band and stichosome, found only in whipworms and related parasites. Using RNA sequencing data from whipworm-infected mice, we describe the regulated T helper 1 (T_H1)-like immune response of the chronically infected cecum in unprecedented detail. *In silico* screening identified numerous new potential drug targets against trichuriasis. Together, these genomes and associated functional data elucidate key aspects of the molecular host-parasite interactions that define chronic whipworm infection.

My organism: Taxonomy

- SK: Eukaryota
 - K: Metazoa
 - P: Nematoda
 - C: Enoplea
 - O: Trichinellida
 - F: Trichuridae
 - ***G: Trichuria***
 - ***S: trichuris***

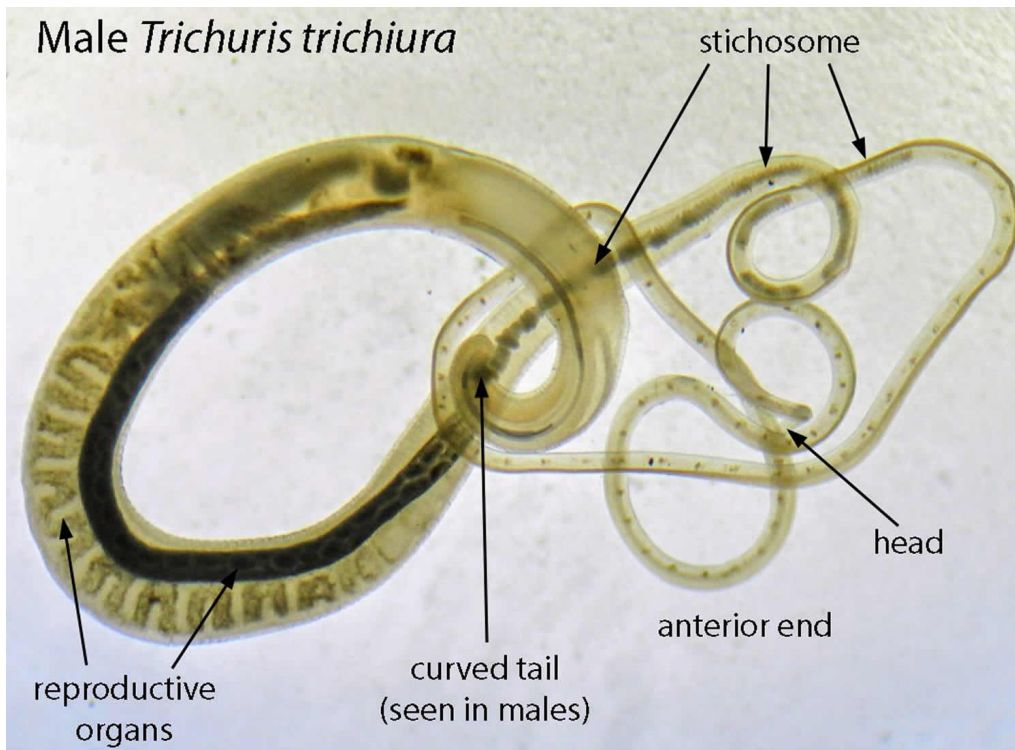
My organism: Physical characteristics

- Adult size: ♂ 38 cm, ♀ 43 cm
- Egg size: 20 x 50 μm
- Bulbous posterior end harbors reproductive organs.

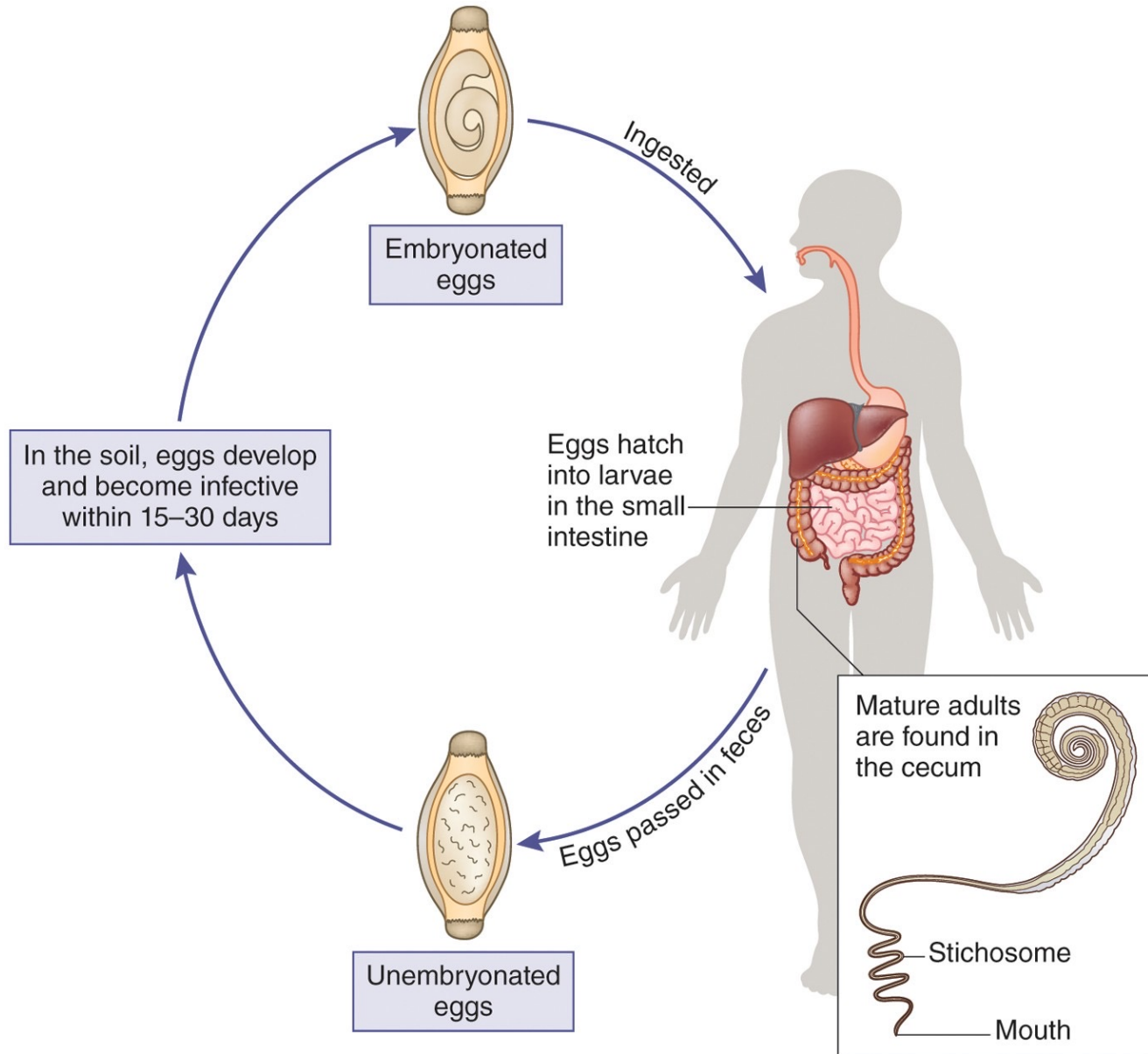


My organism: Physical characteristics

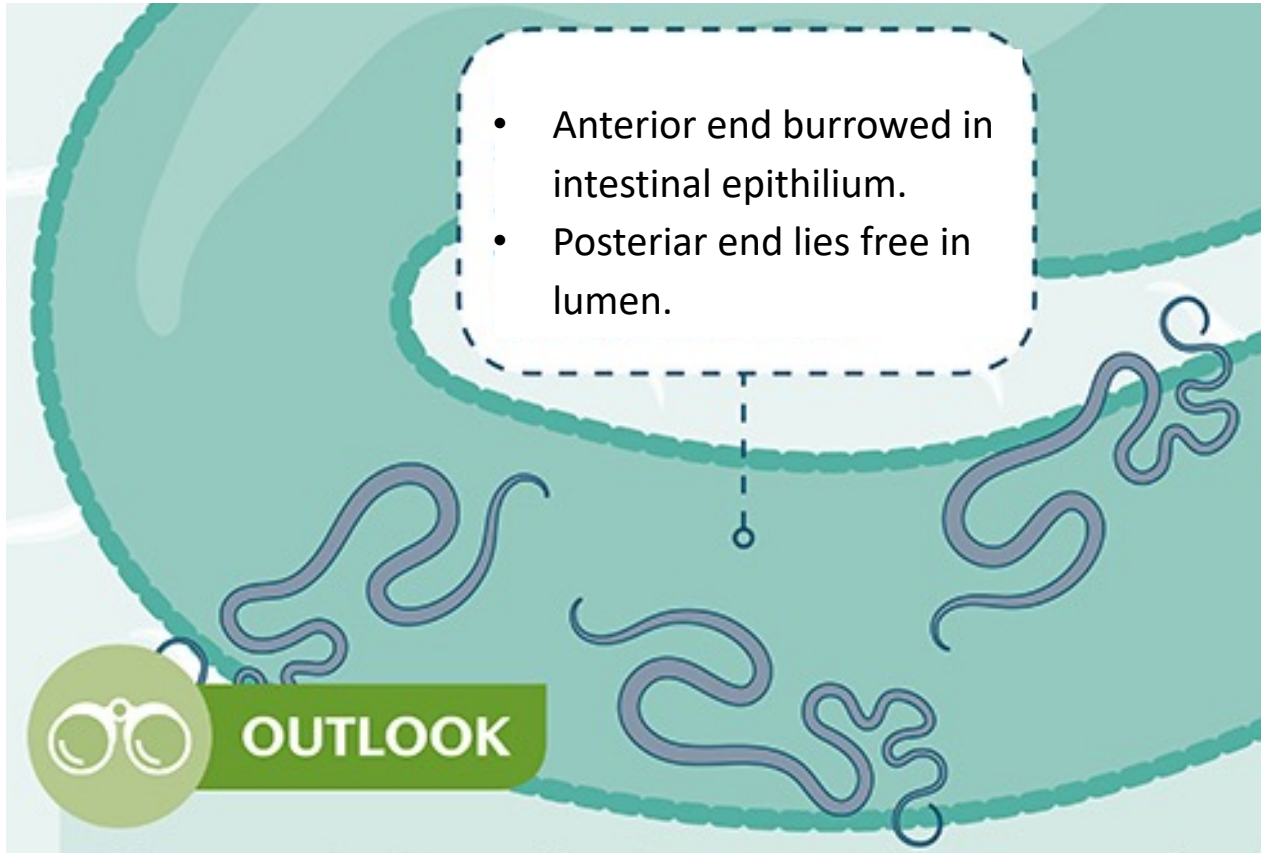
- Bacillary cells and stichocytes in anterior part.
 - Involved in host-parasite interactions, immunomodulation and feeding.



My organism: Life Cycle



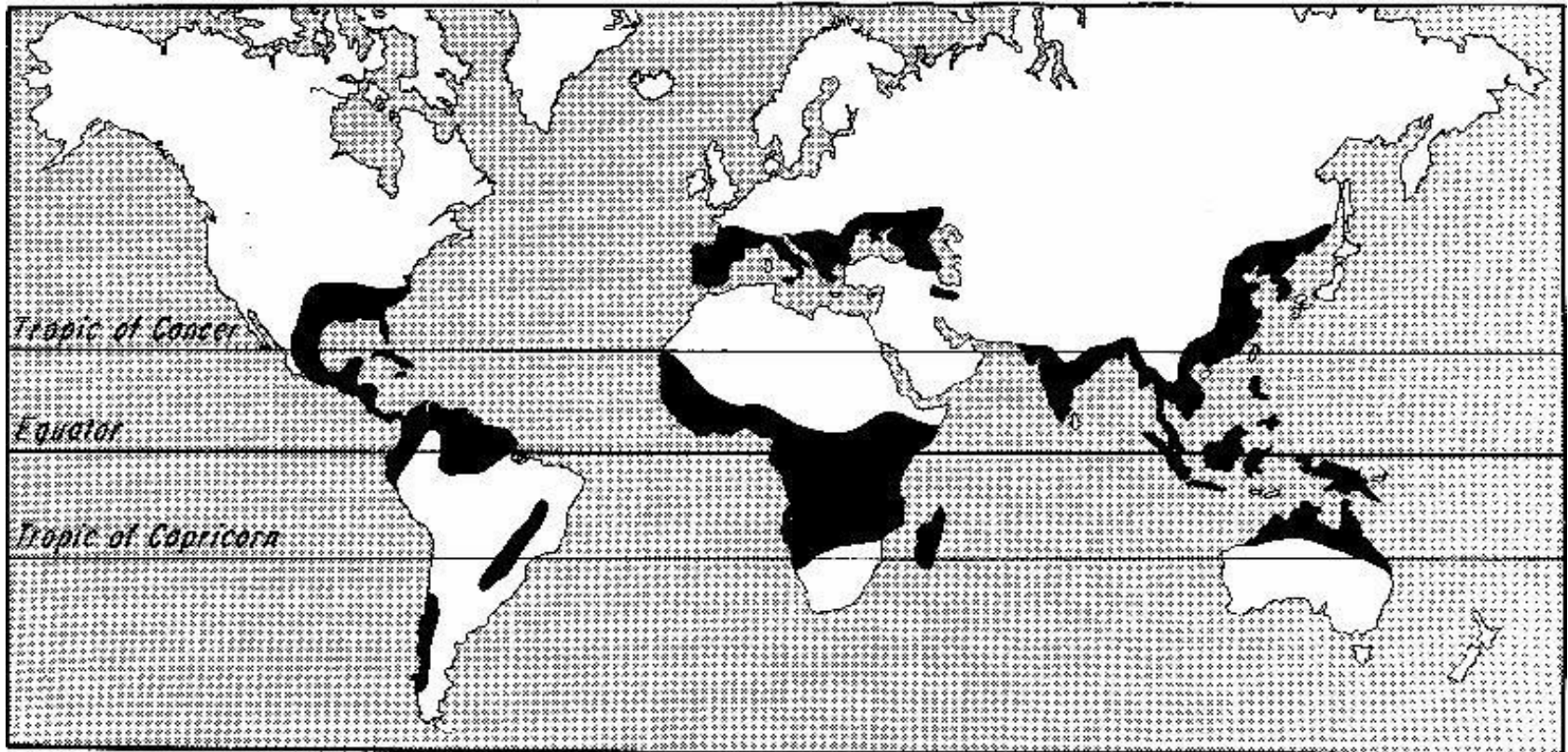
My organism: Parasitism



- Could cause colitis, anemia, and *Trichuris* dysentery syndrome.

My organism: Geographic distribution

- Soil and climate determine the distribution.
- Tropical weather: sub-Saharan Africa and Southeast Asia.

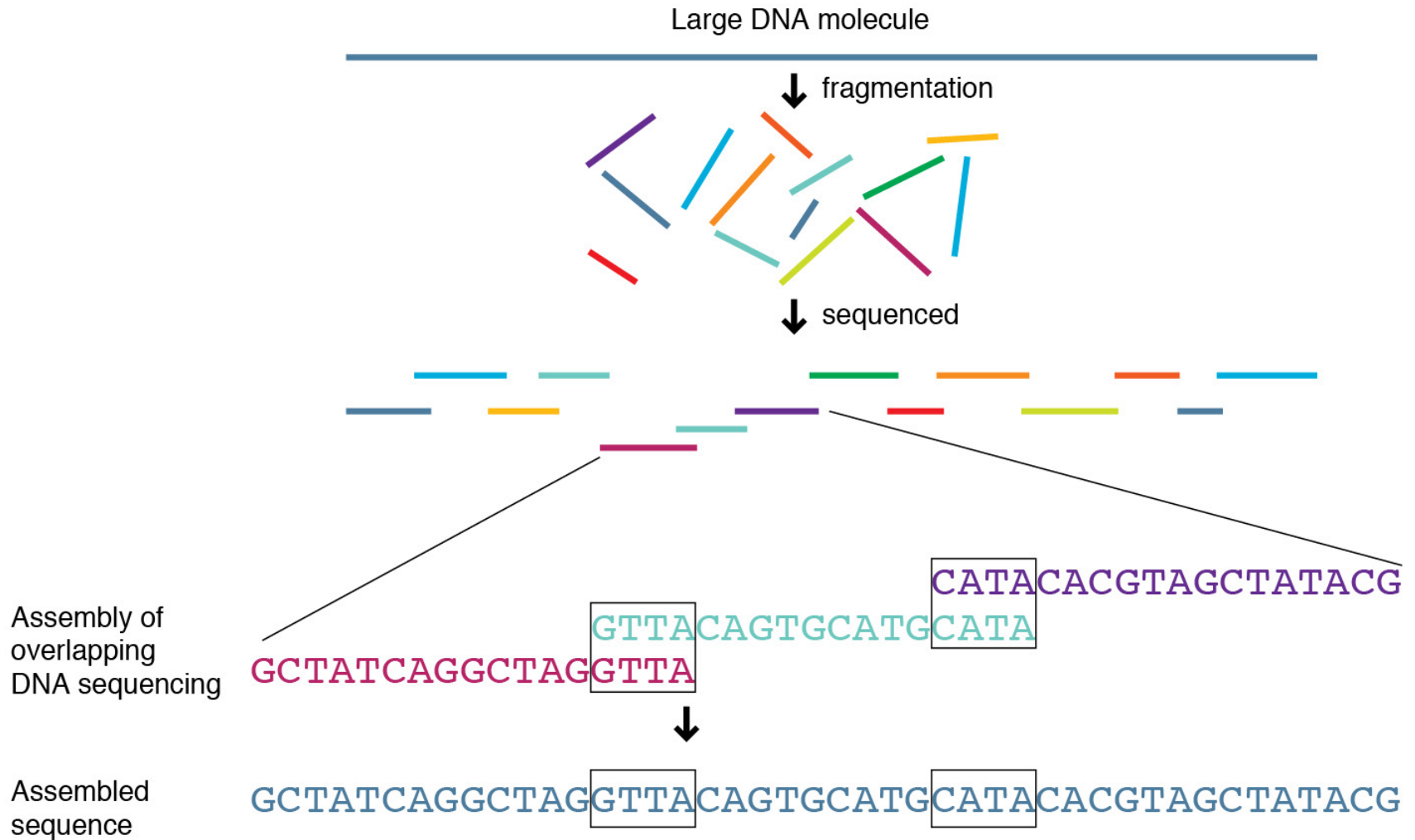


Sequenced sample info

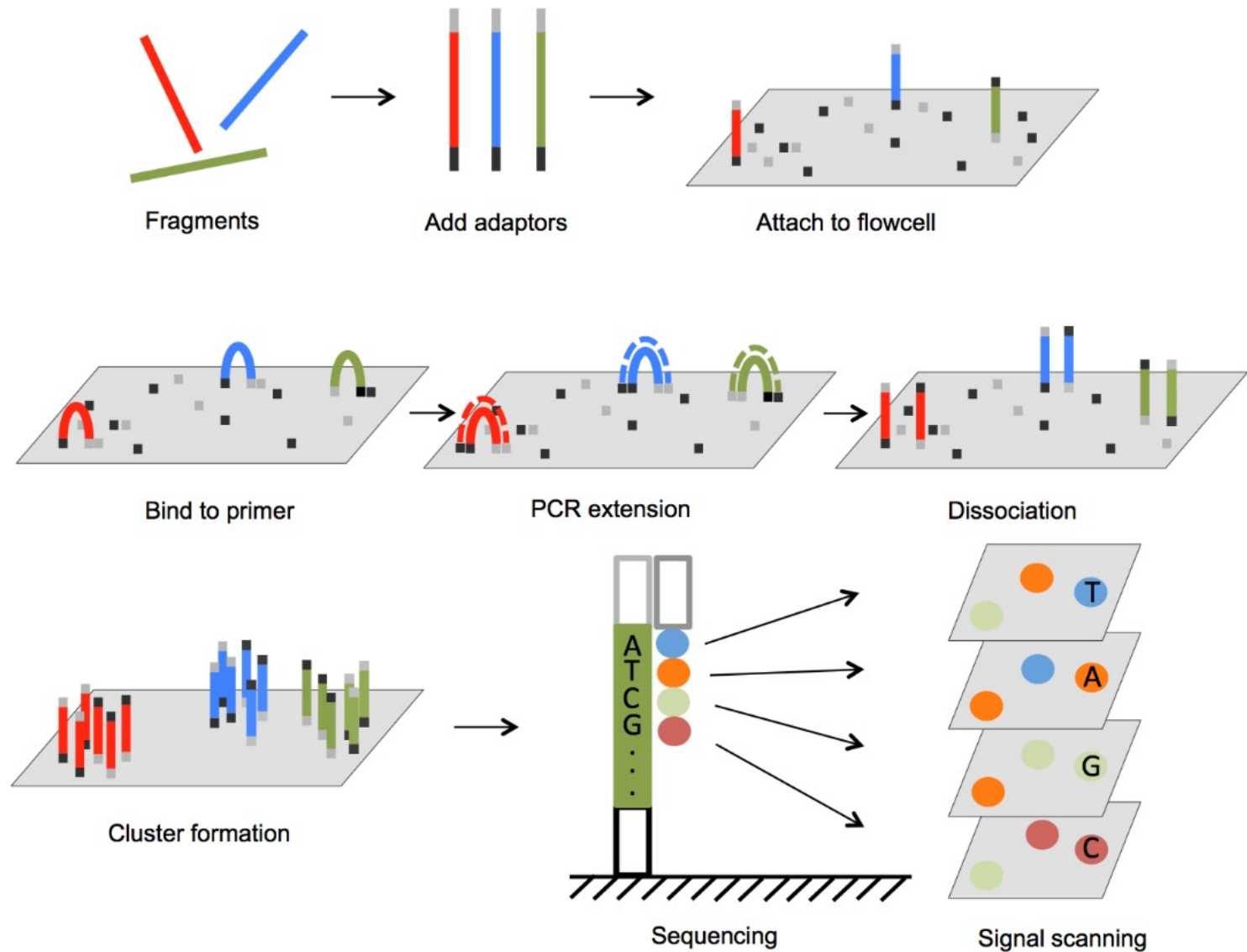
- Adult male *T. trichuria*
- Isolated DNA: 234 ng



Sequencing strategy: Whole genome shotgun



Sequencing method: Illumina



Sequencing method: Illumina

- PCR-free short fragment Illumina library

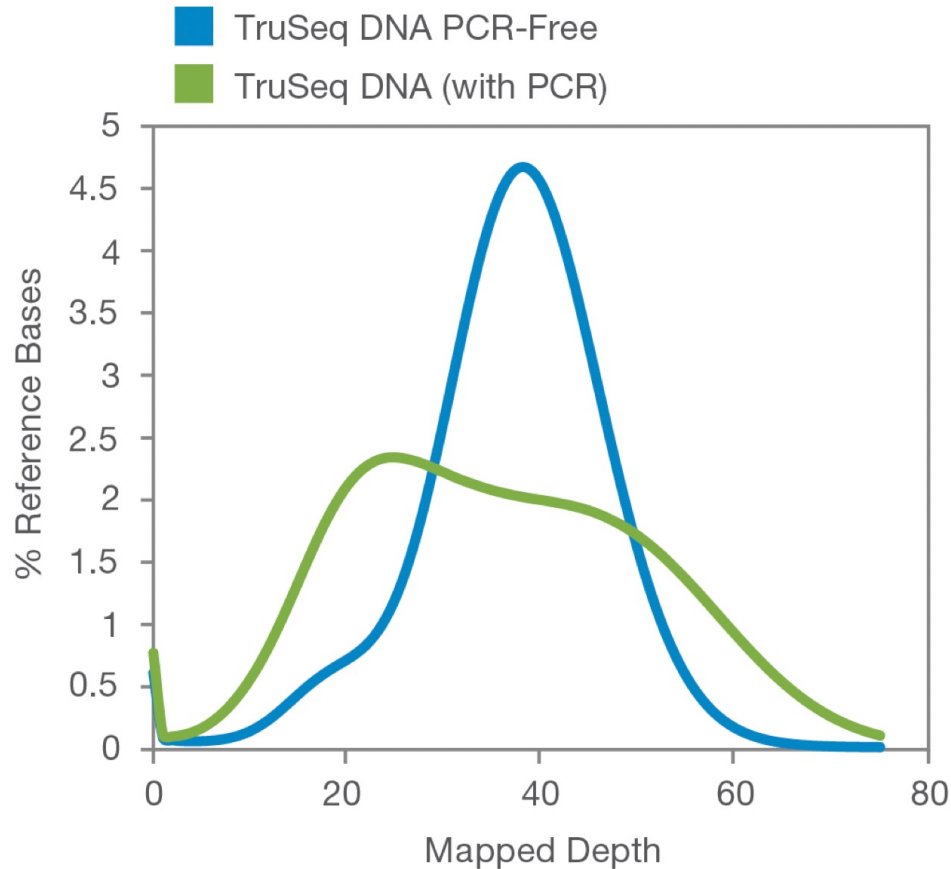


Figure 4: Greater Coverage Uniformity—TruSeq DNA PCR-Free libraries provide greater coverage uniformity across the genome when compared to those generated using the TruSeq DNA (with PCR) protocol.

Genome assembly

- De novo
 - First assembly using SGA (450 bp)
 - Second assembly using Velvet (> 500 bp)
 - Hybridization: SGA + Velvet (> 15 kb scaffolds)
 - Further scaffolding by multiple programs
- Improved manually and computationally
- Assembly v2.1

Genome annotation

Table 1 Genome and gene statistics for nine nematodes

	<i>Trichuris trichiura</i> ^a	<i>Trichuris muris</i> ^b	<i>Trichuris muris</i> ^c (v4)	<i>Trichinella spiralis</i> ^d	<i>Ascaris suum</i> ^d	<i>Brugia malayi</i> ^d	<i>Loa loa</i> ^d	<i>Meloidogyne hapla</i> ^d	<i>Bursaphelenchus xylophilus</i> ^d	<i>Caenorhabditis elegans</i> ^d
Nematode clade	I	I	I	I	III	III	III	IV	IV	V
Haploid chromosome number	NA	3	3	3	12	6	6	16	6	6
Genome assembly size (Mb)	75.18	85.00	89.31 ^e	61.15	266.07	94.12	89.7	52.96	73.10	100.29
Number of scaffolds	3,711	1,123	1,069	3,853	2,414	9,805	3,452	3,389	3,555	7
N50 scaffolds (kb)	71.2	1,580	4,834	7,554	419.1	191.1	177.1	37.6	988.2	17,494
N50 scaffolds (<i>n</i>)	263	15	6	3	171	62	126	372	21	3
Longest scaffold (kb)	533.8	7,990	17,505	12,041	3,795	5,236	1,325	360.4	3,612	20,924
Mean scaffold length (kb)	20.3	75.7	83.5	15.9	110.2	9.6	26.0	15.6	20.6	14,327
Gaps, combined length (kb)	14.5	227.9	4,542	4,987	7,429	7,759	3,847	0	1,476	0
Number of genes	9,650	11,004		16,380	15,260	14,219	14,907	14,420	18,074	20,501
Mean protein length (aa)	435	416		318	396	320	334	348	344	404
Median protein length (aa)	329	290		192	288	209	213	250	262	329

Structural annotation

# of coding exons	55,156
# of introns	45,506
Encoded proteins	2,014
Genes shared with other nematodes	6,641
Species specific genes	2,350

Functional Genome annotation

- I. In *Trichuris*, 75 genes encode serine proteases
 - Involved in digestion and host-immunomodulation.
- II. From *T. muris*, genes encoding SLPI-like proteins (protease inhibitor)
 - Inhibit inflammation in host intestinal tissue
 - Nematode clade I specific functions
 - Expressed in anterior region
- III. Dnase II-like proteins, released during invasion of host cells.
 - Limit immune responses
 - Expressed in anterior region

Functional Genome annotation (*T. muris*)

- *T. muris* infection causes changes in the expression of genes associated with inflammatory diseases.

Supplementary Table 12a: Overlap between mouse genes differentially expressed in *T. muris* infection and human orthologs identified as involved in different traits identified by GWAS.

Disease/Trait	Associated SNPs	Overlap with genes differentially expressed in <i>T. muris</i> infection	P value
Crohn's disease	140	34	0.0002
Ulcerative colitis	133	33	0.00067
Inflammatory bowel disease	163	38	0.00071
Celiac disease	38	11	0.0012
Type 1 diabetes	54	15	0.0024
Body mass index	73	6	0.33
Height	192	23	0.52

Note: Inflammatory bowel disease SNPs are those that are associated with Crohn's disease, ulcerative colitis or both.

Interesting fact: Therapeutic infection

- During infection, production of cytokines (IL-10, IL-22) might have a role in tissue repair.
 - Trichuris suis as medicine for treating inflammatory bowel disease!
 - Colonize humans briefly without causing disease.
 - Inhibit intestinal inflammation by mechanisms different from current medications.

Questions

- Which part of the whipworm is embedded in the intestinal epithelium, anterior or posterior?
- What is the sequencing strategy and method used in my paper?

References

- CDC - DPDx – Trichuriasis <https://www.cdc.gov/dpdx/trichuriasis/index.html>
- Mohamed D. Abd-Alla, Jonathan I. Ravdin, Chapter 44 - Mucosal Immune Response to Parasitic Infections, Mucosal Immunology (Third Edition), Academic Press, 2005, Pages 815-829, <https://doi.org/10.1016/B978-012491543-5/50048-6>.
- R W Summers, D E Elliott, J F Urban Jr, R Thompson, J V Weinstock. Trichuris suis therapy in Crohn's disease. INFLAMMATORY BOWEL DISEASE. 2005;54:87–90. Iowa city, USA. doi: 10.1136/gut.2004.041749

Any questions?

Thank you!

