

# GENOMICS OF PARASITIC FLATWORMS (Class Trematoda)

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# Neglected Tropical Disease

- Of the 17 WHO-listed NTDs, 8 are caused by helminths (nematodes/trematodes/cestodes).

Buruli Ulcer

Chagas disease

Dengue

Human African trypanosomiasis

Leishmaniasis

Leprosy

Rabies

Trachoma

Yaws

Dracunculiasis

Lymphatic filariasis

Onchocerciasis

Soil transmitted

helminthiasis

Cysticercosis

Echinococcosis

Food-borne trematode infections

Schistosomiasis

Trematodiasis, caused by parasitic flatworms (Class Trematoda)

# Trematodiasis

- Human parasites

Water-borne *Schistosoma* spp.

Food-borne *Clonorchis sinensis*  
*Opisthorchis* spp.  
*Fasciola* spp.  
*Paragonimus* spp.  
*Echinostoma* spp.



## Diverse modes of transmission

### Water-borne



### Food-borne

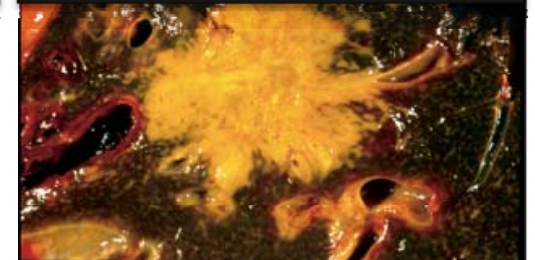


## Long-lived parasites; chronic infections

### Bladder cancer



### Bile duct cancer



- Parasites of other mammals

Food-borne *Fasciola* spp.  
*Fascioloides magna*  
*Dicrocoelium* spp.

- Reliance on praziquantel

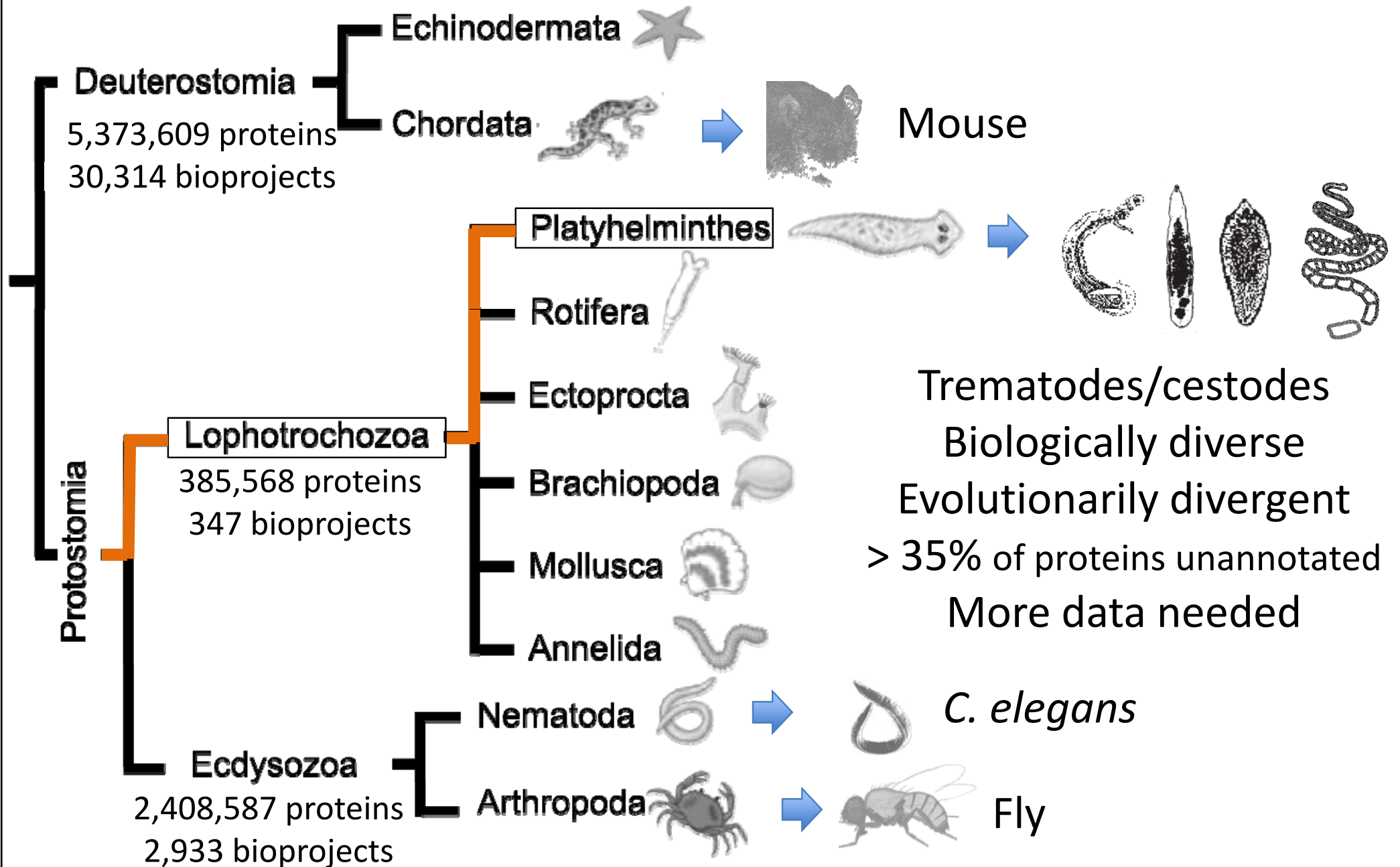
INSIGHTS INTO TREMATODE BIOLOGY BY  
CHARACTERISING THEIR GENOMES AND  
TRANSCRIPTOMES



*Fascioloides magna*

# Genomic resources for flatworms

NCBI submissions (Nov 2013)







Faculty of Veterinary Science  
**Parasitology**

# Update on current programs

- Transcriptome assembly and curation of a trematode sequence database
- Assembly and annotation of trematode genomes (e.g. *Schistosoma haematobium*)

# Published food-borne trematode transcriptomes



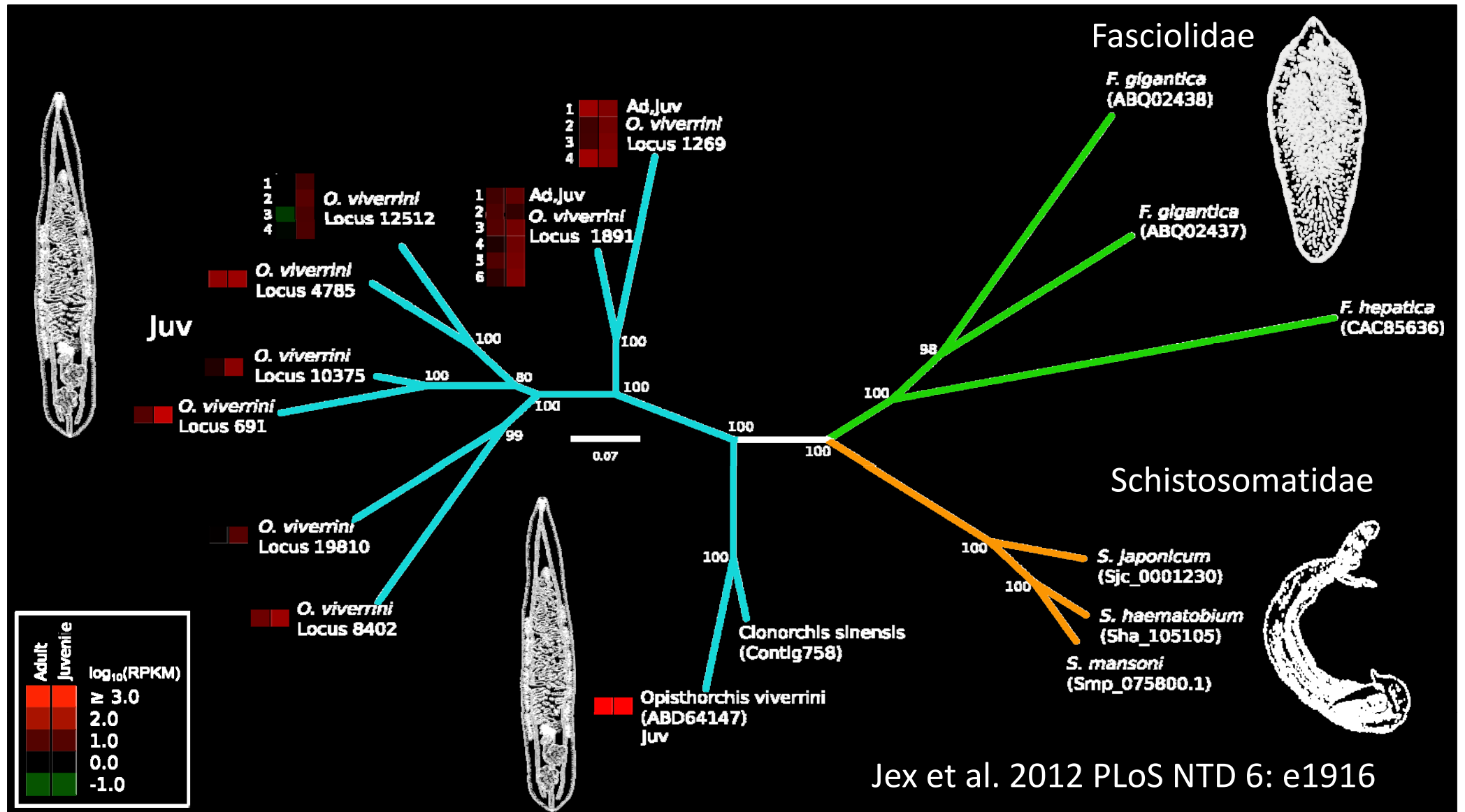
	Opisthorchiidae		Fasciolidae		
	<i>Opisthorchis viverrini</i>	<i>Clonorchis sinensis</i>	<i>Fasciola hepatica</i>	<i>Fasciola gigantica</i>	<i>Fascioloides magna</i>
Roche 454	642,918	574,448	590,927		
Illumina	22.4 million			21.9 million	54 million
Transcripts	21,026	50,769	44,597	30,513	20,140

Adult *F. magna* secreted proteins (Cantacessi et al. 2012 Mol Cell Proteom 11: 1340)

*O. viverrini* stage-specific transcriptomes (Jex et al. 2012 PLoS NTD 6: e1916)

# *Opisthorchis viverrini* juvenile-enriched peptidases

- Asparaginyl endopeptidase (legumain or C13) – 236 transcripts
- Lysosomal endopeptidase but component of the ES
- Transactivates cathepsin B – but what else???



# Published food-borne trematode transcriptomes






	Opisthorchiidae		Fasciolidae		
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Curation of “orthologues”, conserved functional domains, gene ontology vocabulary and KEGG biological pathways/protein family classification

HelmDB

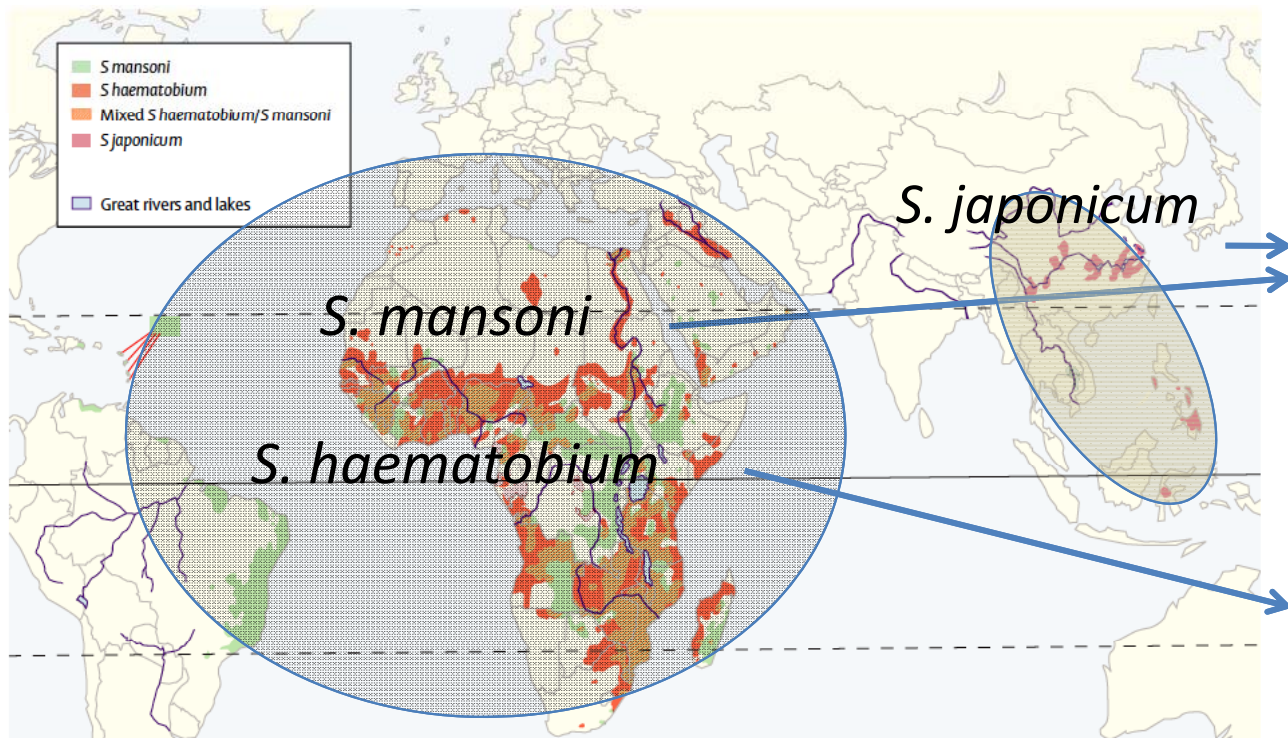
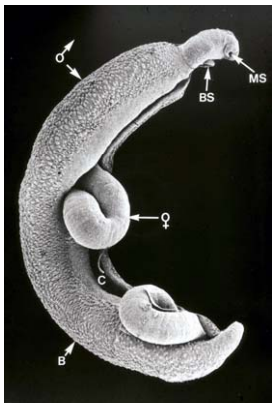




An integrative database of curated transcriptomes of key nematodes and trematodes for functional annotation-improvement

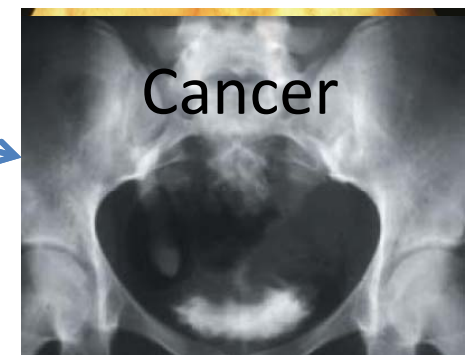


# Schistosomiasis (bilharziasis/snail fever)

- 200 million infected; > 200,000 deaths p.a.
- Water-borne infection, chronic
- Treatment – praziquantel, no vaccine



Gryseels et al. 2006 Lancet; 368: 1106



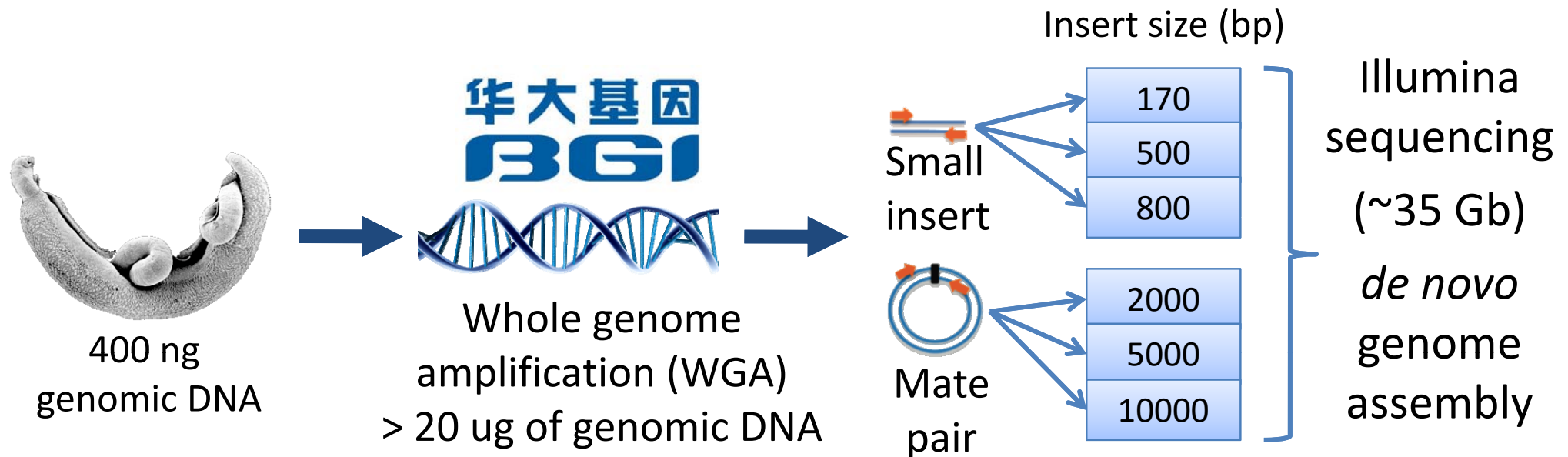
# Urogenital schistosomiasis

## *Schistosoma haematobium*

- Important NTD (Rollinson 2009 Parasitology; 136:1593)
- Difficult to culture/passage (snail host)
- Laboratory infection (hamster – atypical)



Sequence one pair of worms (male/female)



# Genome assembly

	<i>S. haematobium</i>	<i>S. mansoni</i> v5	<i>S. japonicum</i>
Scaffolds	99,953	885	25,048
Genome size (Mb)	385	365	403
N50 scaffold length	306,738	32,100,000	176,868
Number of genes	13,073	10,852	13,469
GC content	35.9%	35.3%	34.1%

## Draft *S. haematobium* genome from a single pair of worms

LETTERS

Nature Genetics 2012; 44, 221-225

nature  
genetics

### Whole-genome sequence of *Schistosoma haematobium*

Neil D Young<sup>1,11</sup>, Aaron R Jex<sup>1,11</sup>, Bo Li<sup>2,11</sup>, Shiping Liu<sup>2</sup>, Linfeng Yang<sup>2</sup>, Zijun Xiong<sup>2</sup>, Yingrui Li<sup>2</sup>, Cinzia Cantacessi<sup>1</sup>, Ross S Hall<sup>1</sup>, Xun Xu<sup>2</sup>, Fangyuan Chen<sup>2</sup>, Xuan Wu<sup>2</sup>, Adhemar Zerlotini<sup>3</sup>, Guilherme Oliveira<sup>3</sup>, Andreas Hofmann<sup>1,4</sup>, Guojie Zhang<sup>2</sup>, Xiaodong Fang<sup>2</sup>, Yi Kang<sup>2</sup>, Bronwyn E Campbell<sup>1</sup>, Alex Loukas<sup>5</sup>, Shoba Ranganathan<sup>6,7</sup>, David Rollinson<sup>8</sup>, Gabriel Rinaldi<sup>9,10</sup>, Paul J Brindley<sup>10</sup>, Huanming Yang<sup>2</sup>, Jun Wang<sup>2</sup>, Jian Wang<sup>2</sup> & Robin B Gasser<sup>1</sup>

Genome added to SchistoDB:

<http://schistodb.net/>

SchistoDB Version 3.0 1 Jul 12  
Schistosoma Genomic Resources

A EuPathDB Project

Gene ID: Smp\_043030 Gene Text Search: synth\*

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# Transcriptome – annotation and gene expression

RNA-Seq  
RPKM= expression

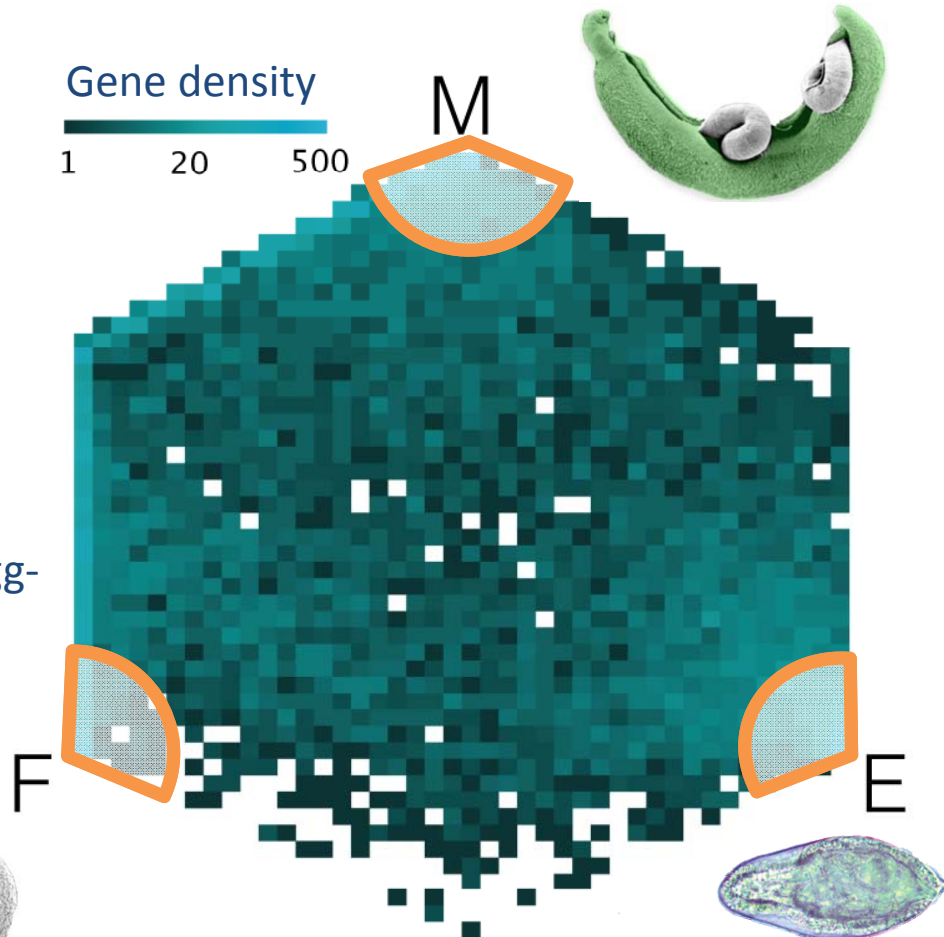
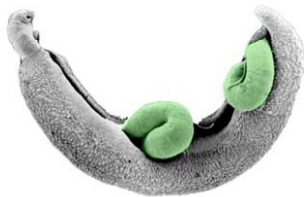
Gene density  
1 20 500

## Oogenesis

(superoxide dismutase, egg-shell proteins, female specific protein 800)

## Tegument

(tetraspanin-1)



## Cell growth

(cadherin, innexin, connexin)

## Muscle development

(titin, myosin, paramyosin)

## Egg proteins (CP391S-like)

## Growth/Development


(tubulin, annexin, sphingosine kinase, calcium binding proteins)

## Immune-related?


(TNF-associated factor, secreted frizzled-related protein, VALs)

# GENOMIC RESOURCES FOR TREMATODES

■ Transcriptomic   ■ Genomic  
■ Proteomic   ■ Small RNA

*F. hepatica* 

*F. gigantica* 

*F. magna* 

*O. viverrini* 

*C. sinensis* 

*D. dendriticum* 

*S. haematobium* 

*S. mansoni* 

*S. japonicum* 

Food-borne

Water-borne

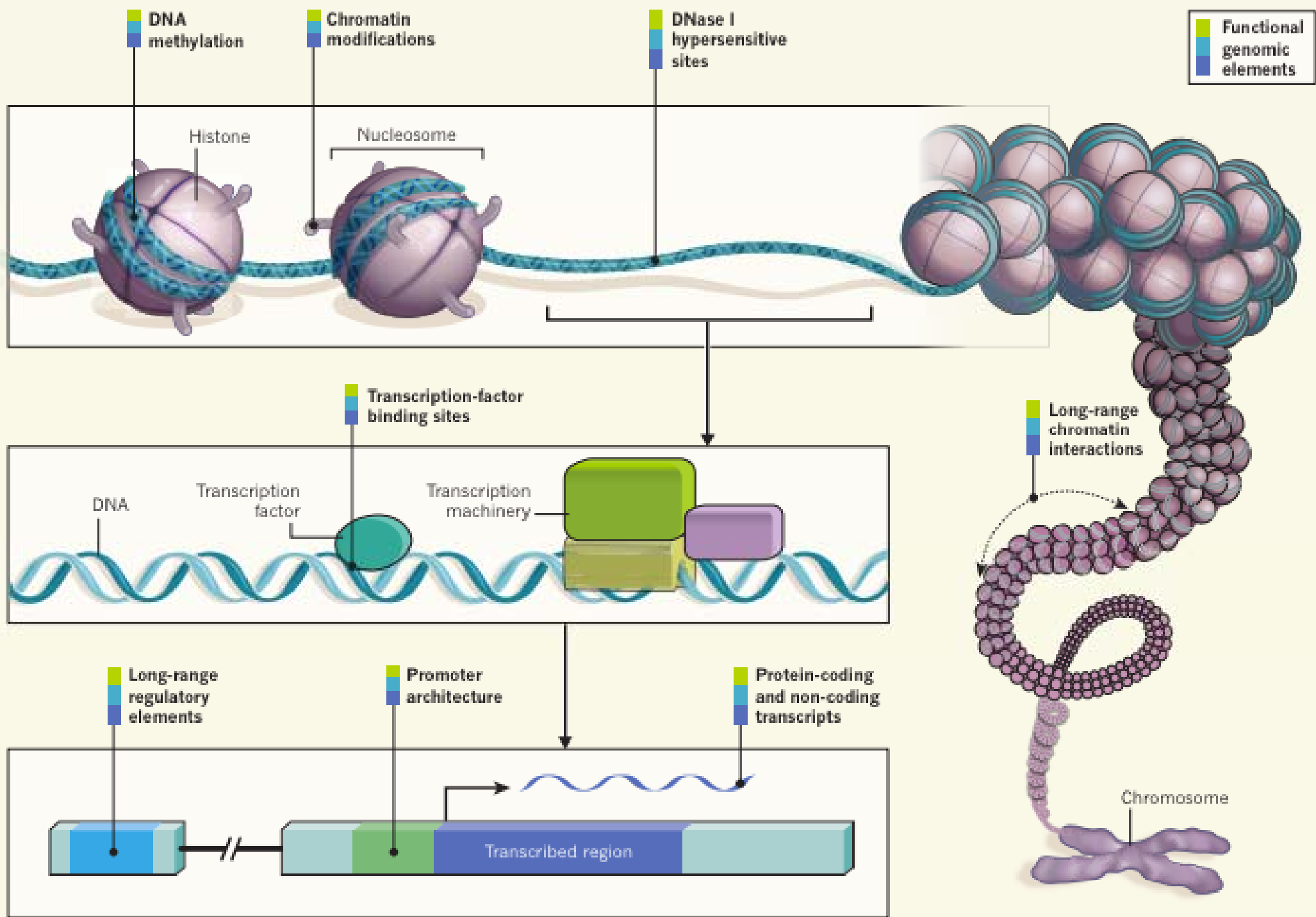
Fasciolidae

Opisthorchiidae

Dicrocoelidae

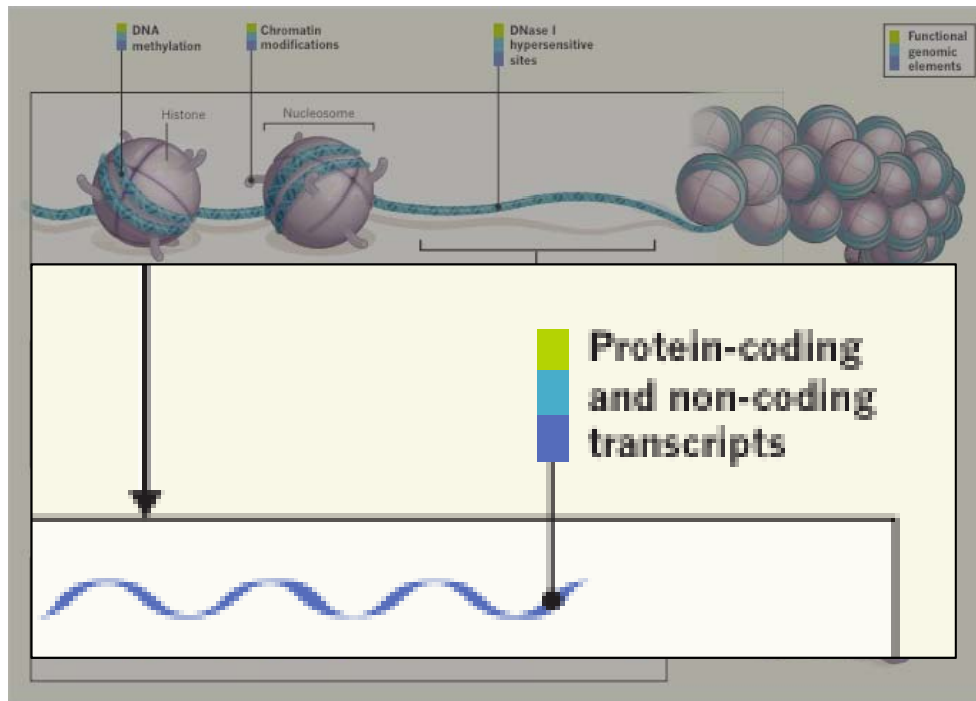
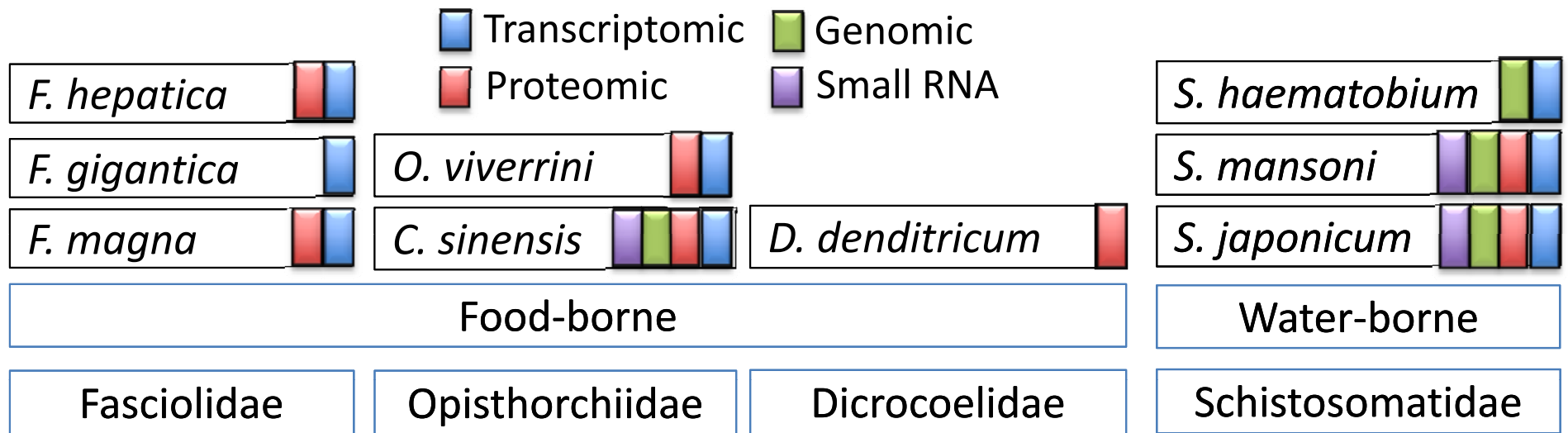
Schistosomatidae



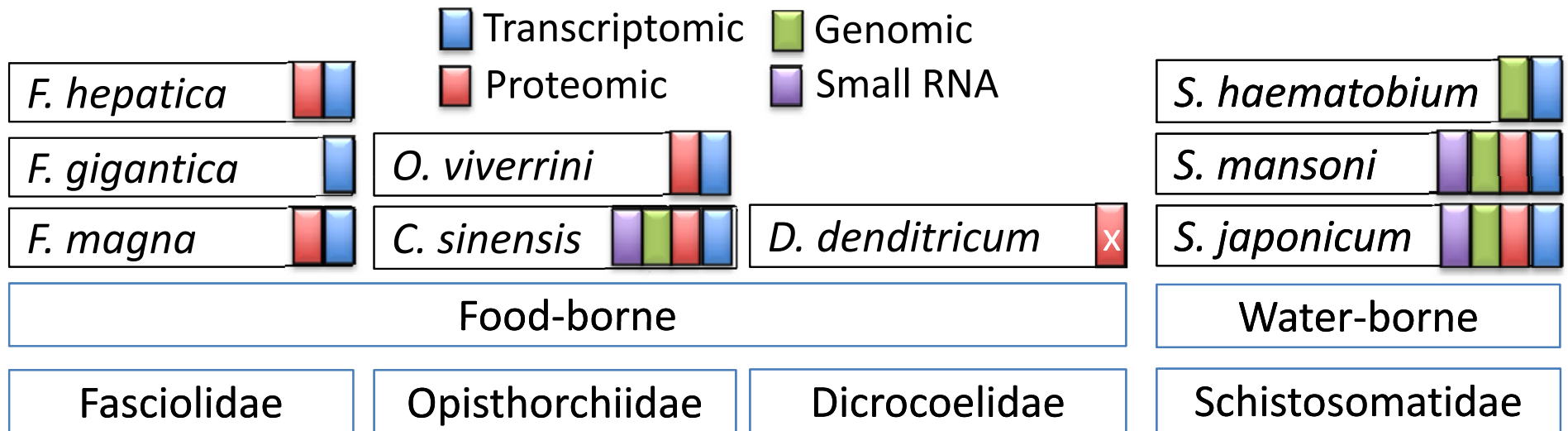


Ecker et al. 2012. "Genomics: ENCODE explained." Nature 489(7414): 52-55.

# GENOMIC RESOURCES FOR TREMATODES



“2% of the human genome contains genes..... around 80% of the genome is actively doing something..... involved in controlling when and where proteins are produced”  
Ewan Birney ENCODE PROJECT



**COMPARE and CONTRAST**

Vaccine candidates (e.g. Tetraspanin 2)  
 Helminth proteins (HDMs, SCP/TAPS)  
 Trematode proteins (AEPs)  
 Drug discovery/repurposing  
 Adaptations to life in blood/bile duct

**CONFIRM FUNCTION**

Transcription = Expression  
 Phenotype (RNAi)  
 Localisation (IHC)  
 Enzyme activity  
 Receptor specificity

New intervention strategies for trematodiasis



# Future work

- Sequencing trematode genomes (using WGA)
- Population genetics
- Drugs / vaccines – predict, prioritise and consolidate
- Curate resource for proteomics and functional genomics
- Non-coding elements (conserved/novel)



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Visit the Gasser lab: <http://www.gasserlab.org/>