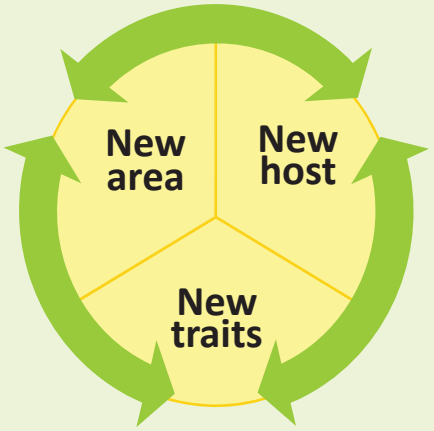
Aude Gilabert
Post-doctorante

Pathogen emergence: Evolution of parasitism and host adaptation

PATHOGEN EMERGENCE

Host-pathogen-environment interface & emerging disease



Engering et al. (2013) Emerg. Microbes Infect., 2: e5

QUESTION: Evolution of signalling pathways

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↳ The dauer signalling pathways

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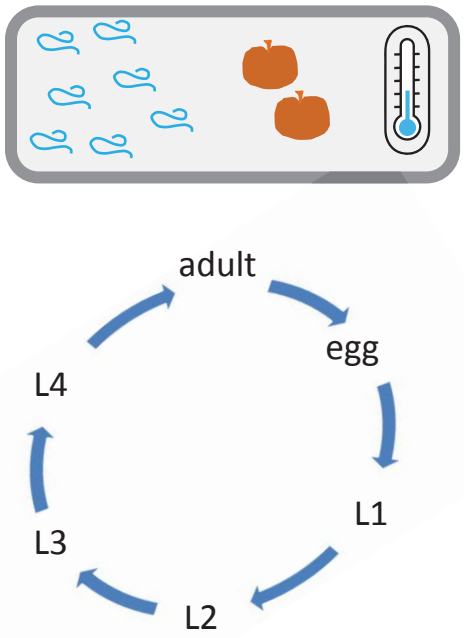
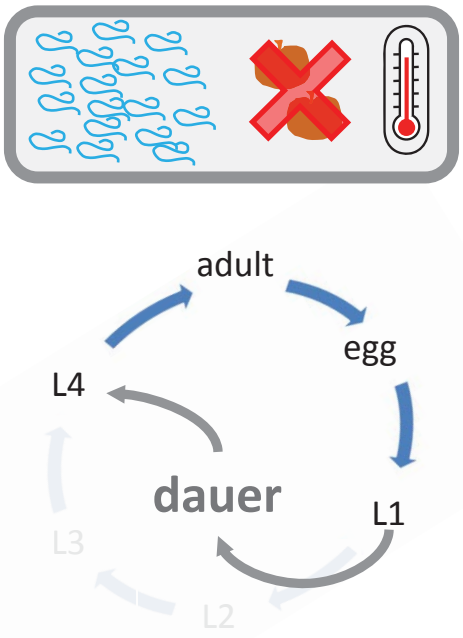
C. elegans life cycle





QUESTION: Evolution of signalling pathways

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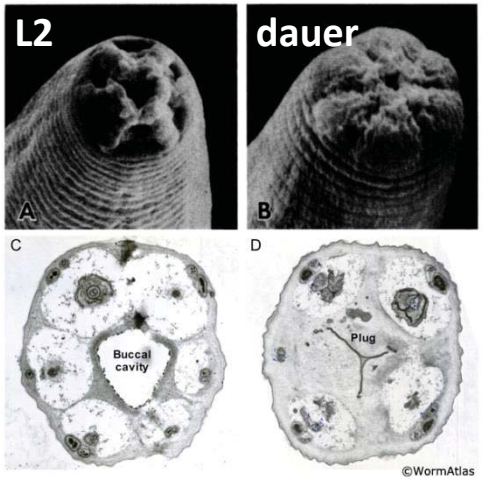
C. elegans life cycle

Daure larva:

- Arrested developmental stage
- Non-feeding
- Morphological characteristics
- ↓ metabolism
- Resistant to environmental stresses



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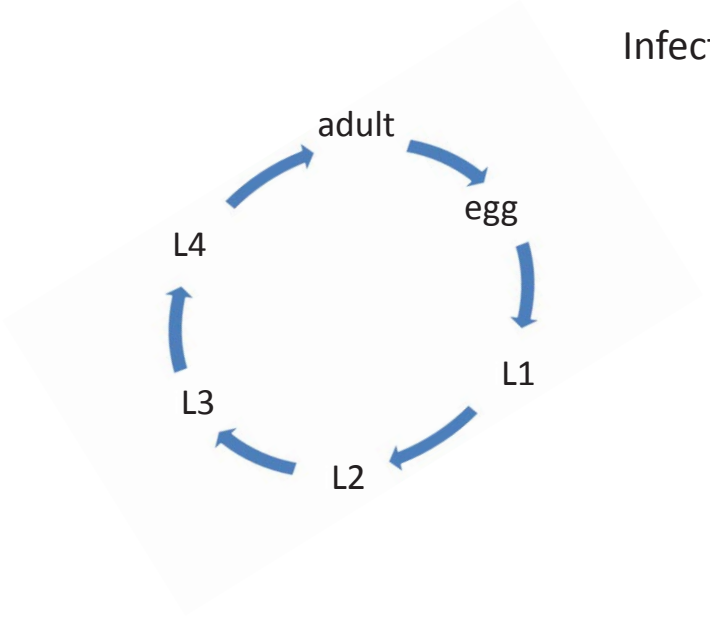
Parasitic nematodes' life cycle



Infective larva (iL)

Specialised stage for infestation

QUESTION: Evolution of signalling pathways

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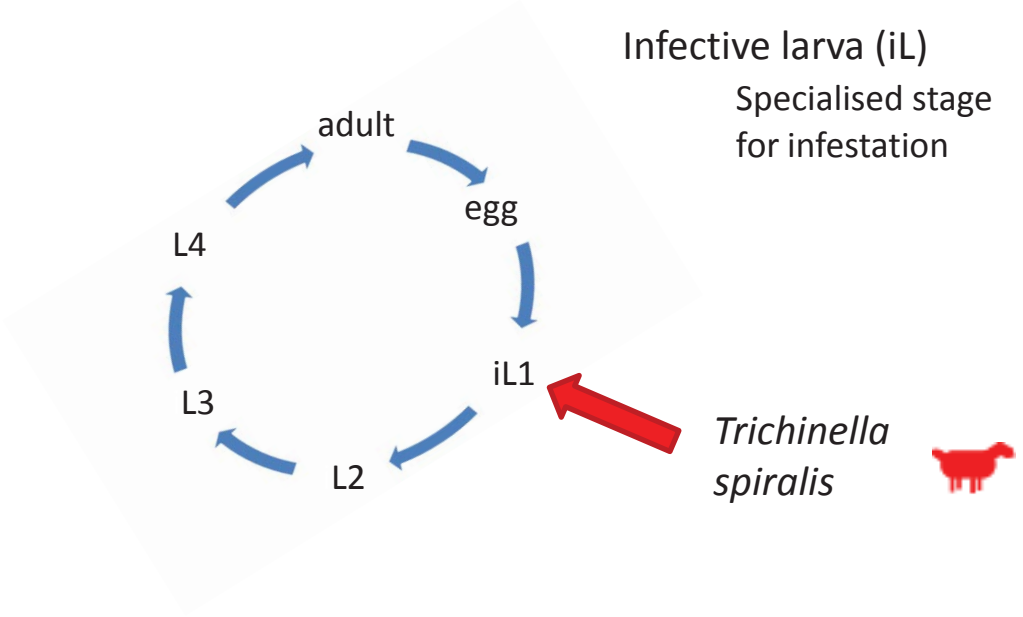

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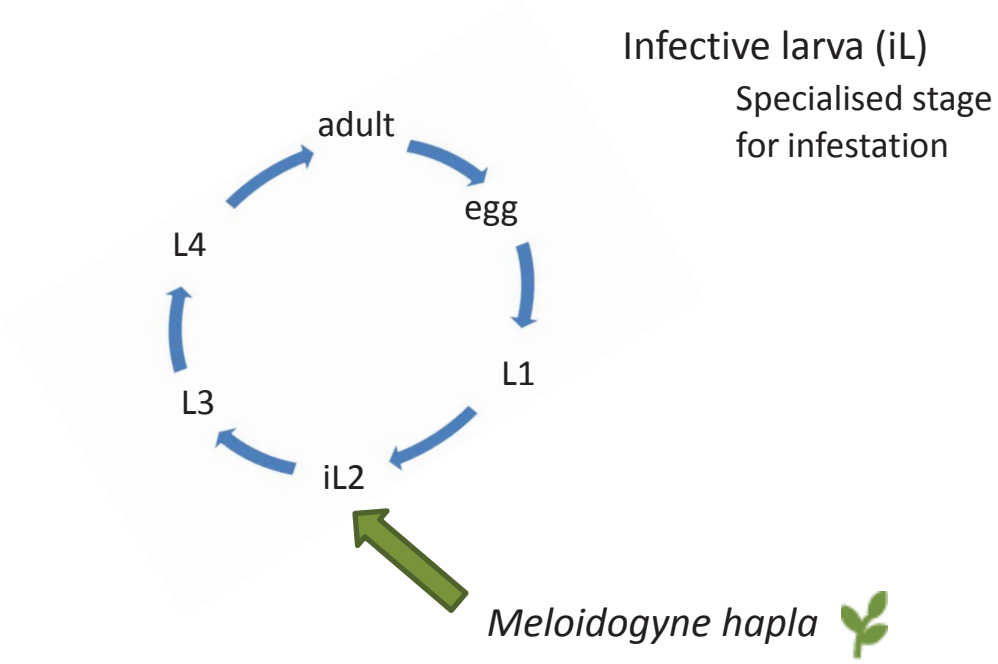

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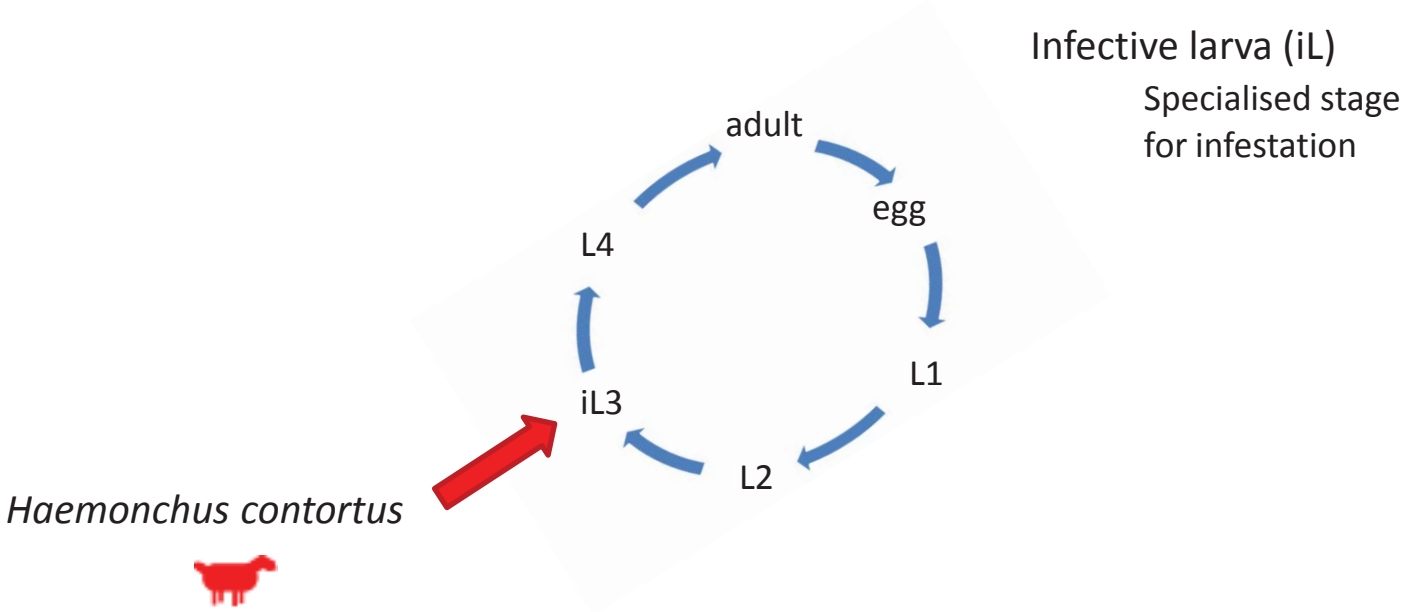

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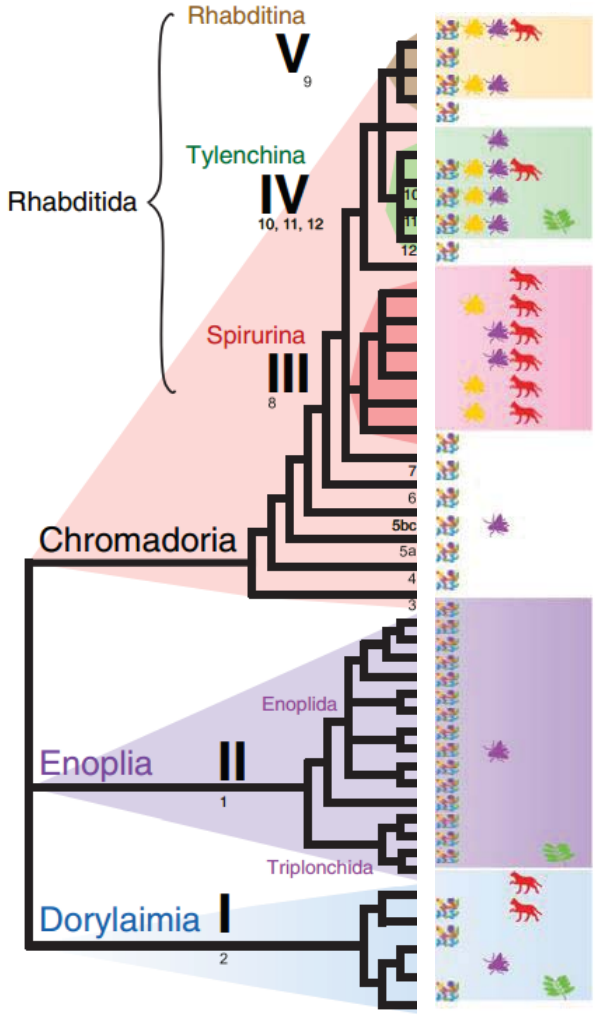
EVOLUTION OF PARASITISM IN NEMATODES

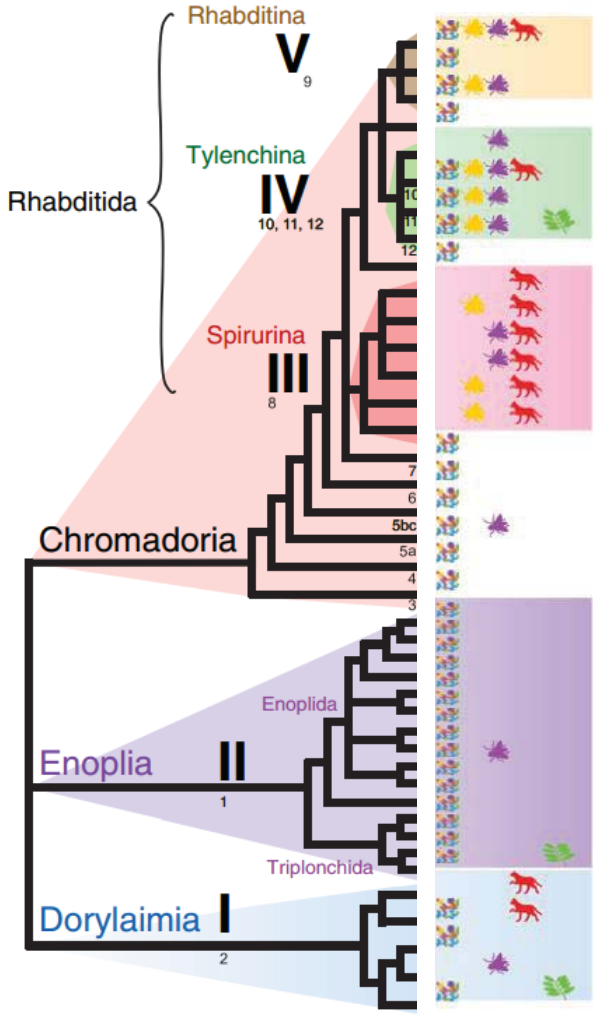


⇒ Multiple independent transitions

- Dauer hypothesis

  Pre-adaptation to parasitism

EVOLUTION OF PARASITISM IN NEMATODES



⇒ Multiple independent transitions

- Dauer hypothesis

  Pre-adaptation to parasitism

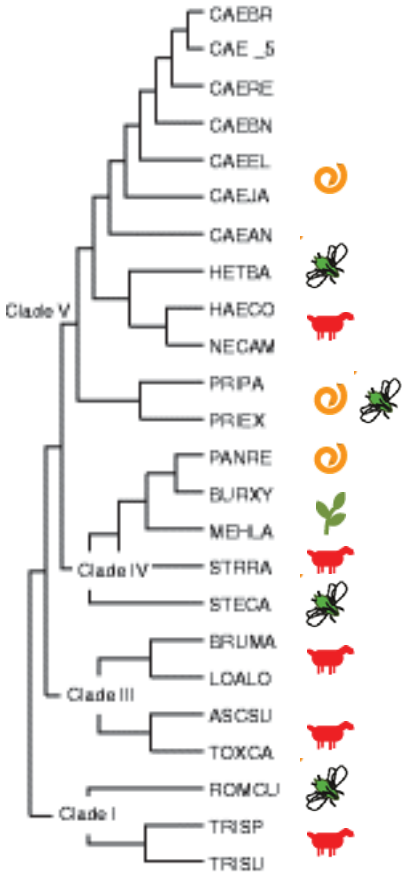
- *Existence of common genetic pathways that would likely control the dauer transition across the phylum?*

⇒ Gene candidate approach

Blaxter & Koutsovoulos (2015) Parasitology, 142 (S1): S26-S39

EVOLUTION OF PARASITISM IN NEMATODES

- Bioinformatic search of orthologues
  - 47 genes involved in the dauer transition
  - 24 species



Free-living Animal parasites Plant parasites

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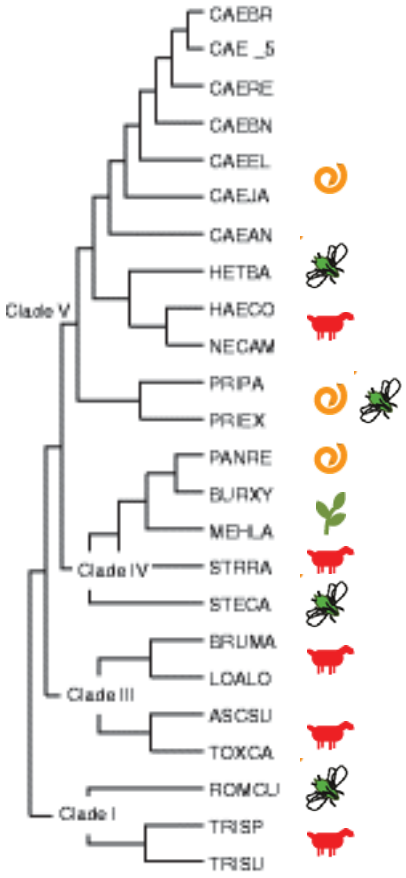

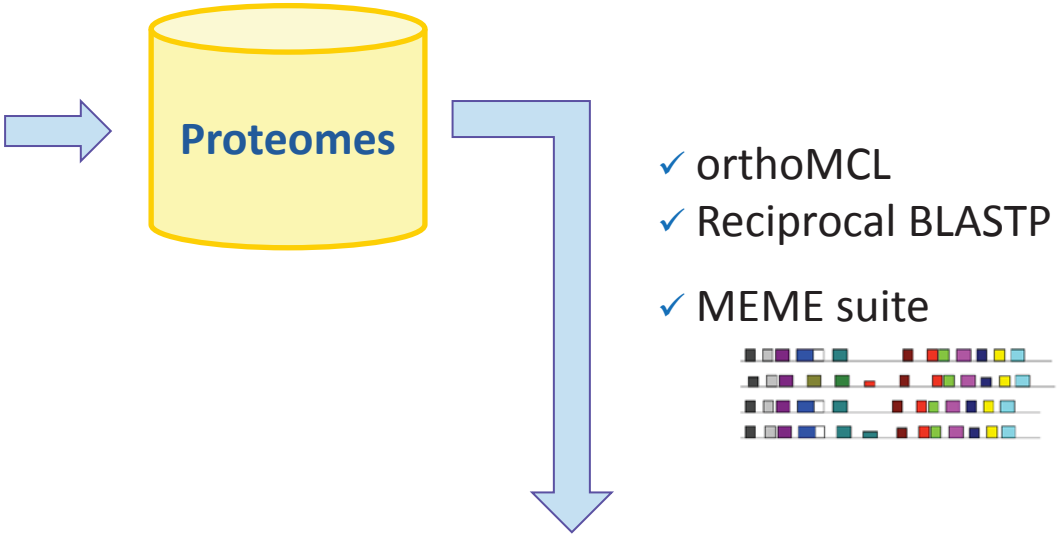

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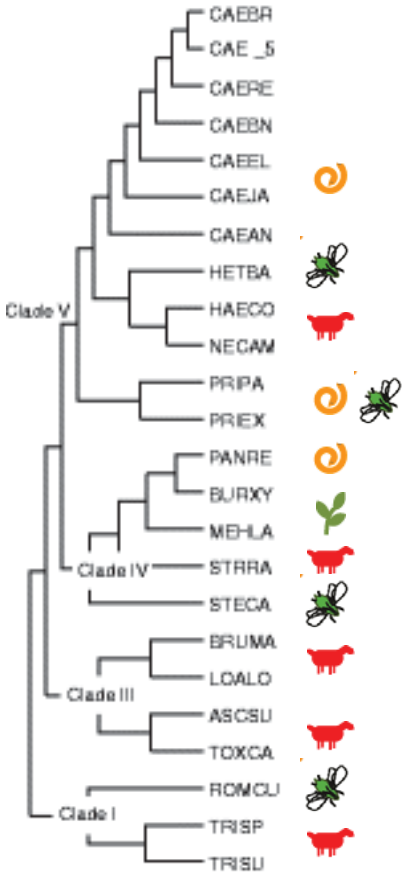

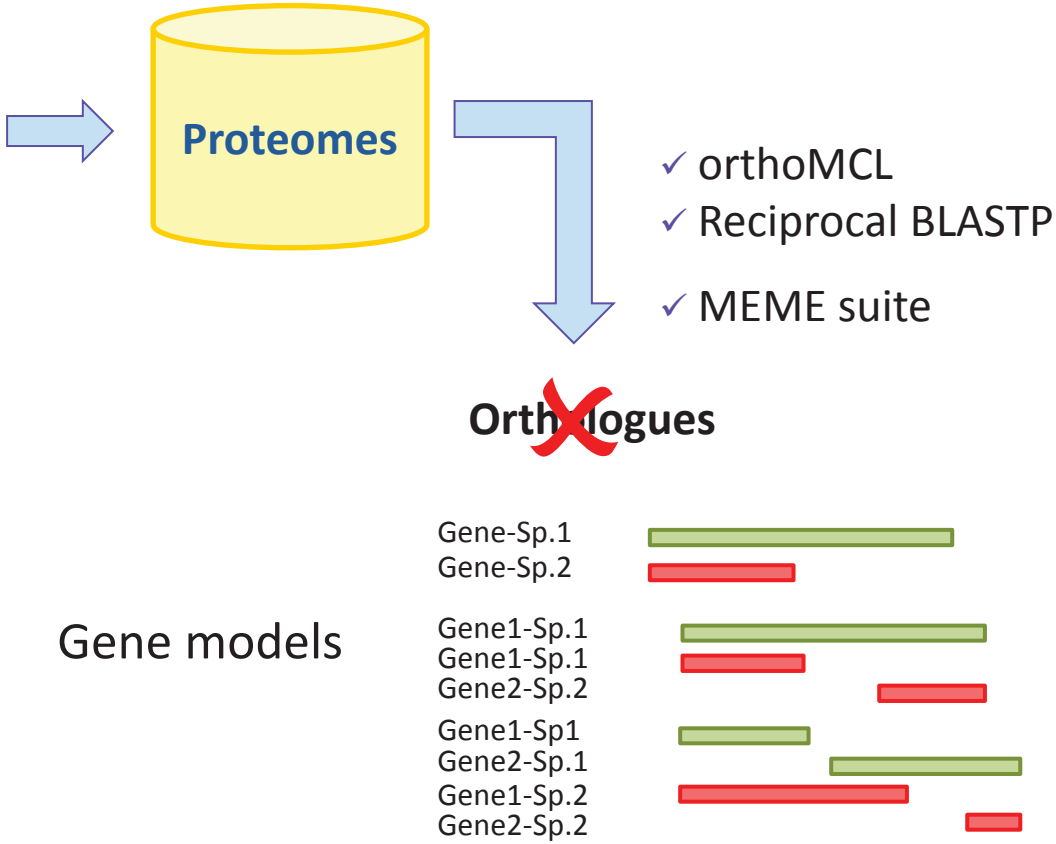

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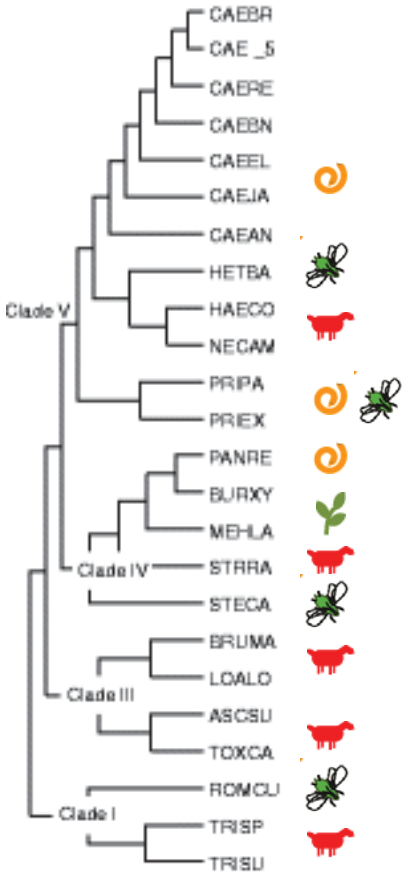

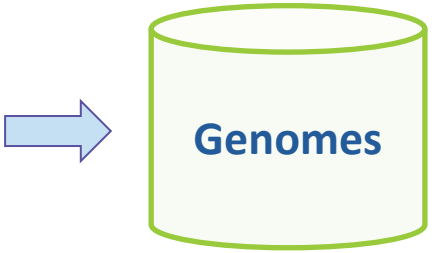

Free-living Animal parasites Plant parasites

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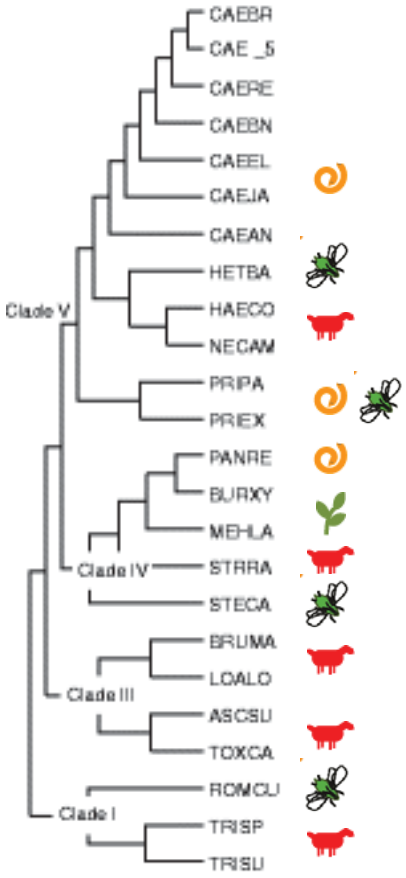
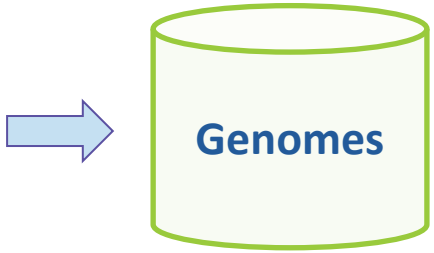
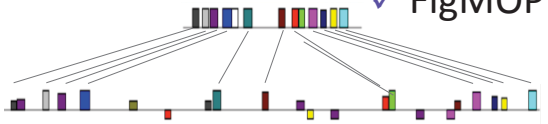
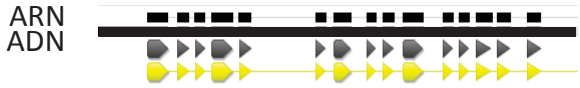




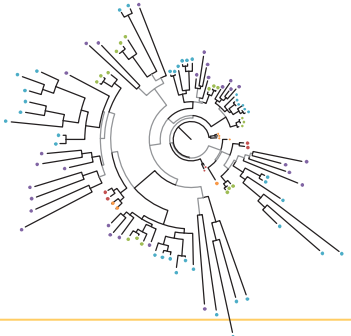
- ✓ Reciprocal TBLASTN
- ✓ DNA reads-to-protein alignments
  - ✓ DIAMOND
- ✓ Protein-to-genome alignments
  - ✓ spaln
  - ✓ FigMOP



- ✓ ARN-to-ADN alignments



- ✓ RAxML



Orthologues

Free-living | Animal parasites | Plant parasites | Exons | CDS

EVOLUTION OF PARASITISM IN NEMATODES

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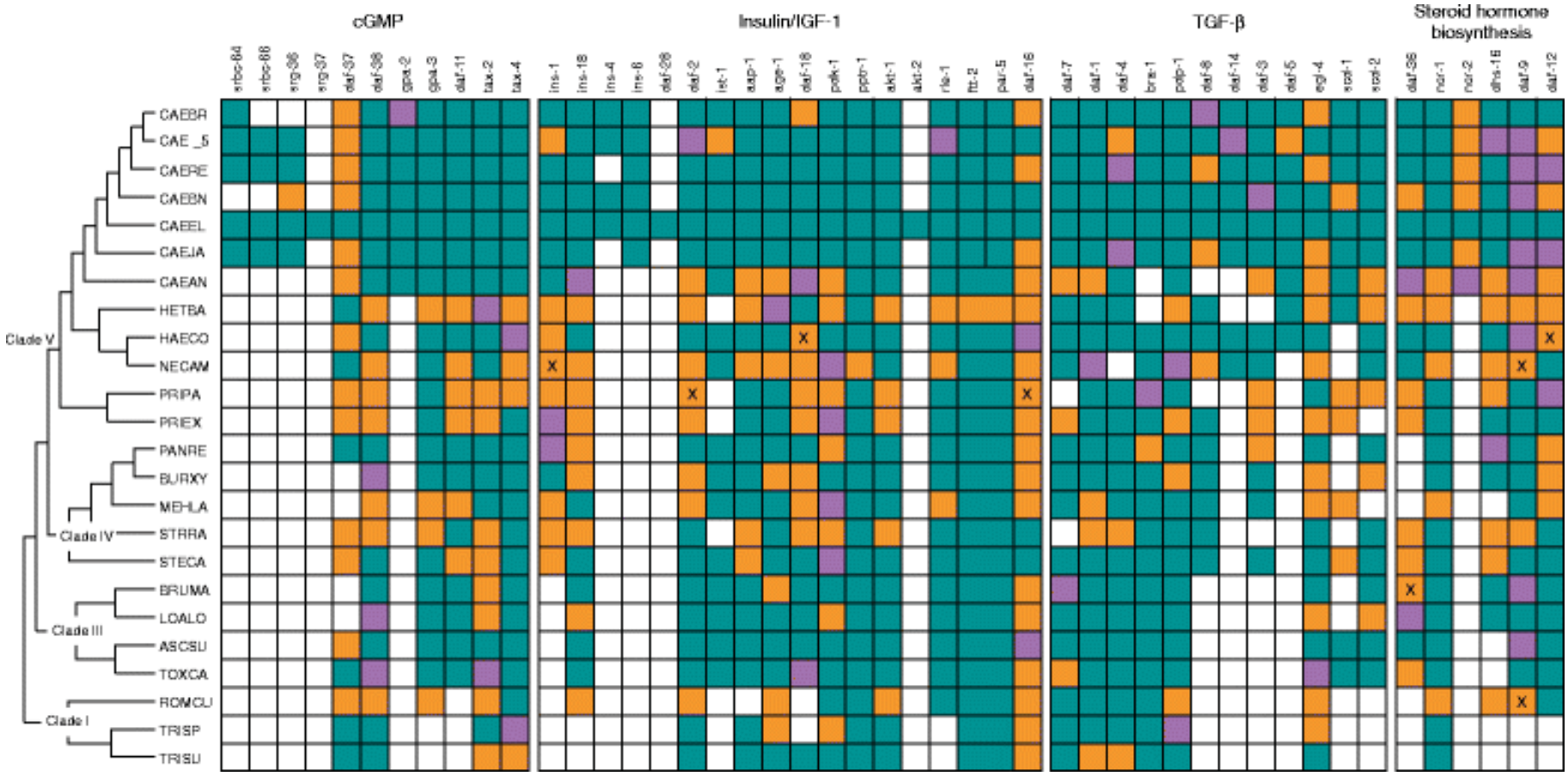
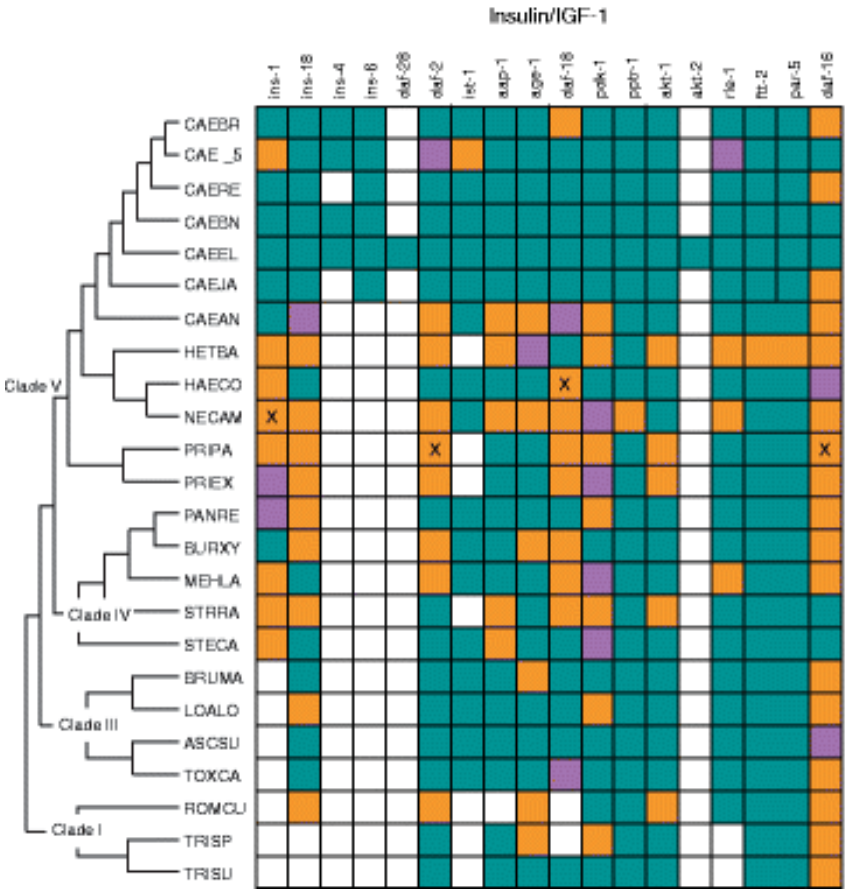
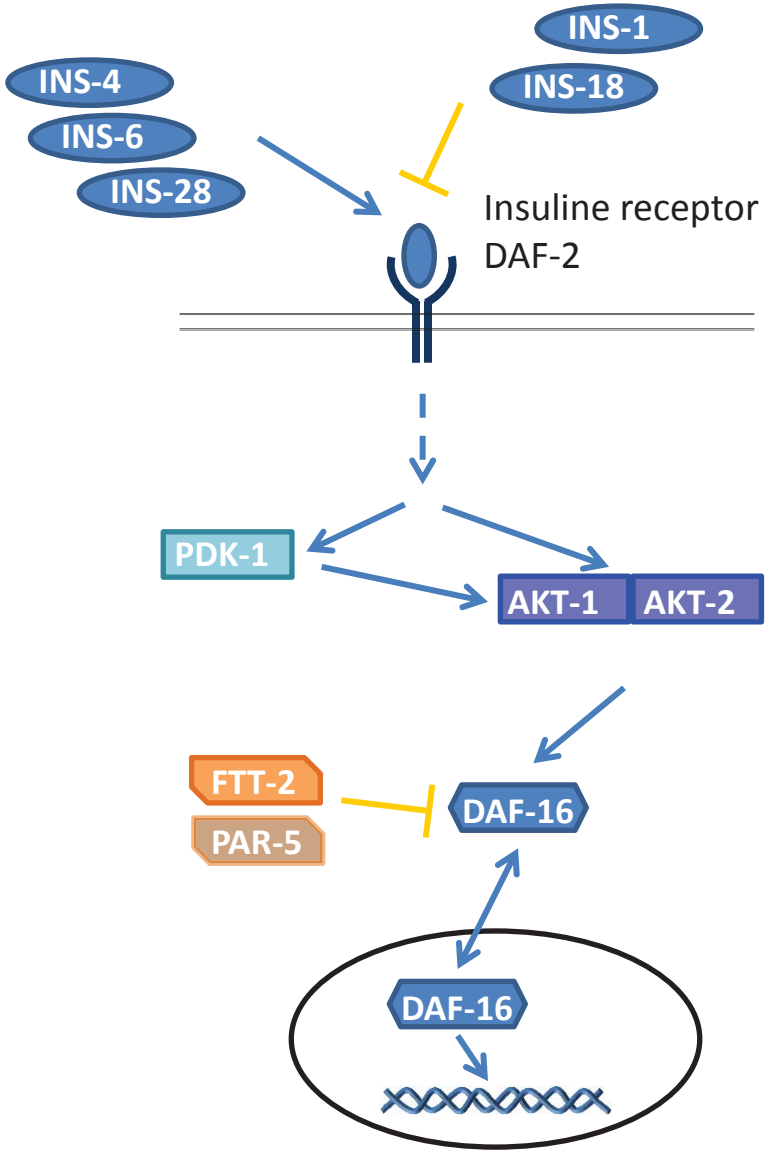


Other search strategies

Not found | Reciprocal BLAST | Minor changes | Major changes

EVOLUTION OF PARASITISM IN NEMATODES





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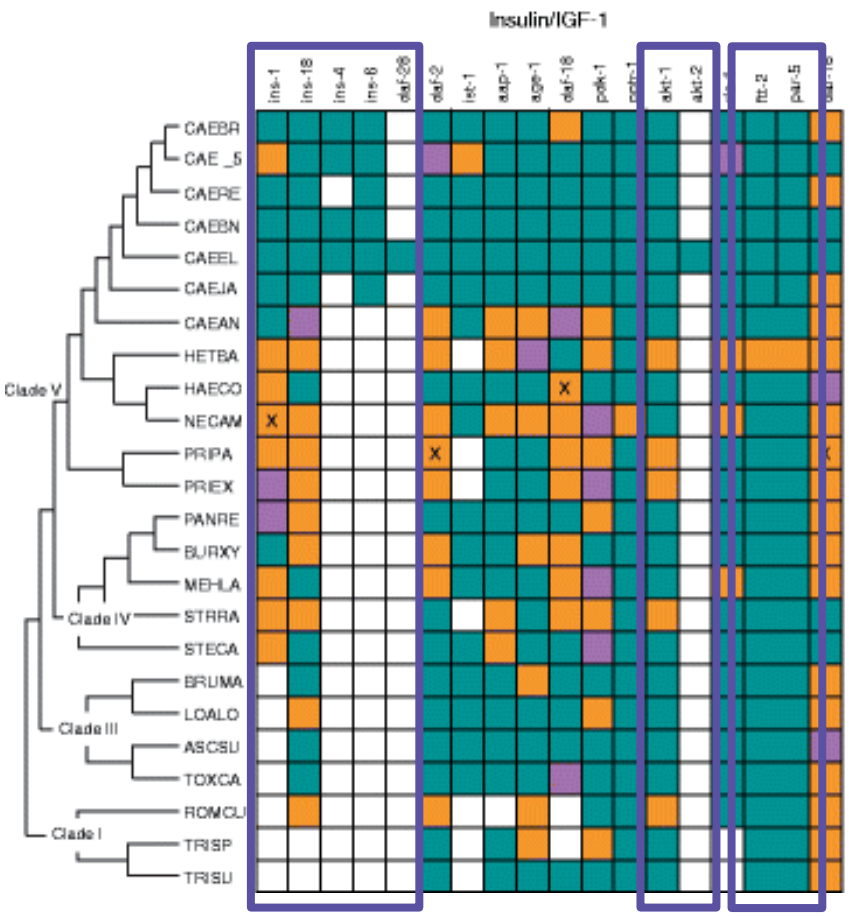
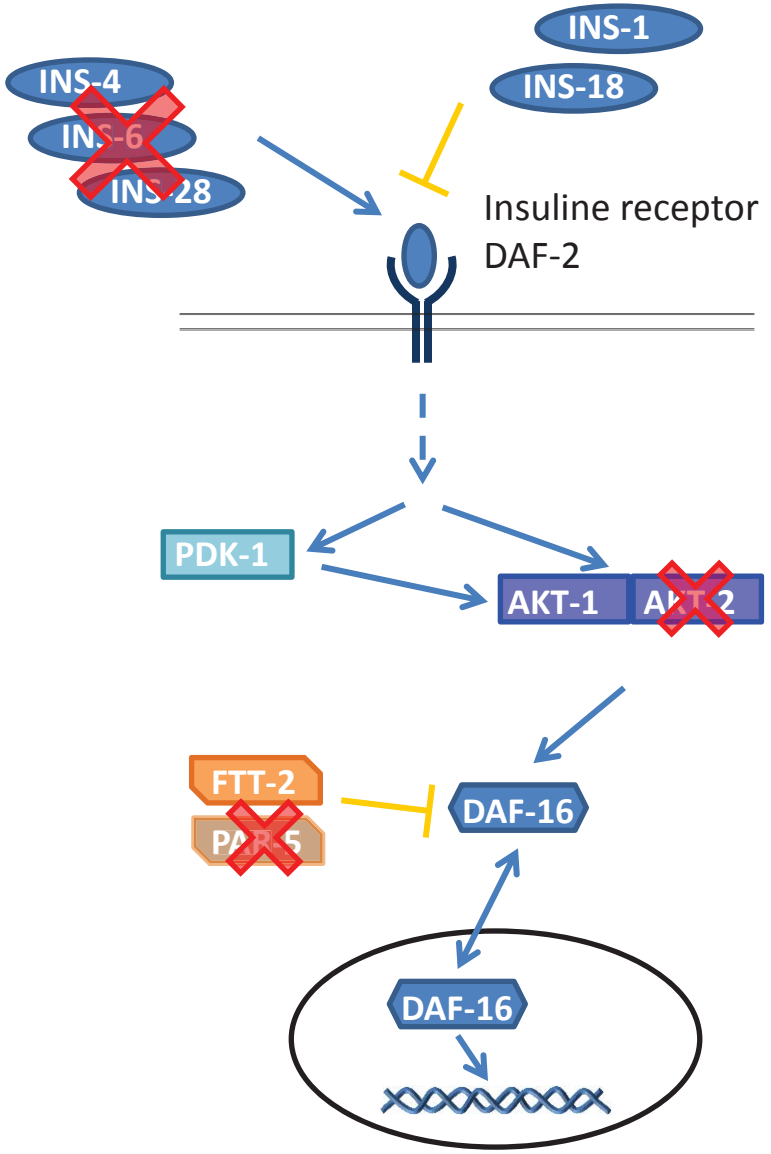
EVOLUTION OF PARASITISM IN NEMATODES

Non-*Caenorhabditis*





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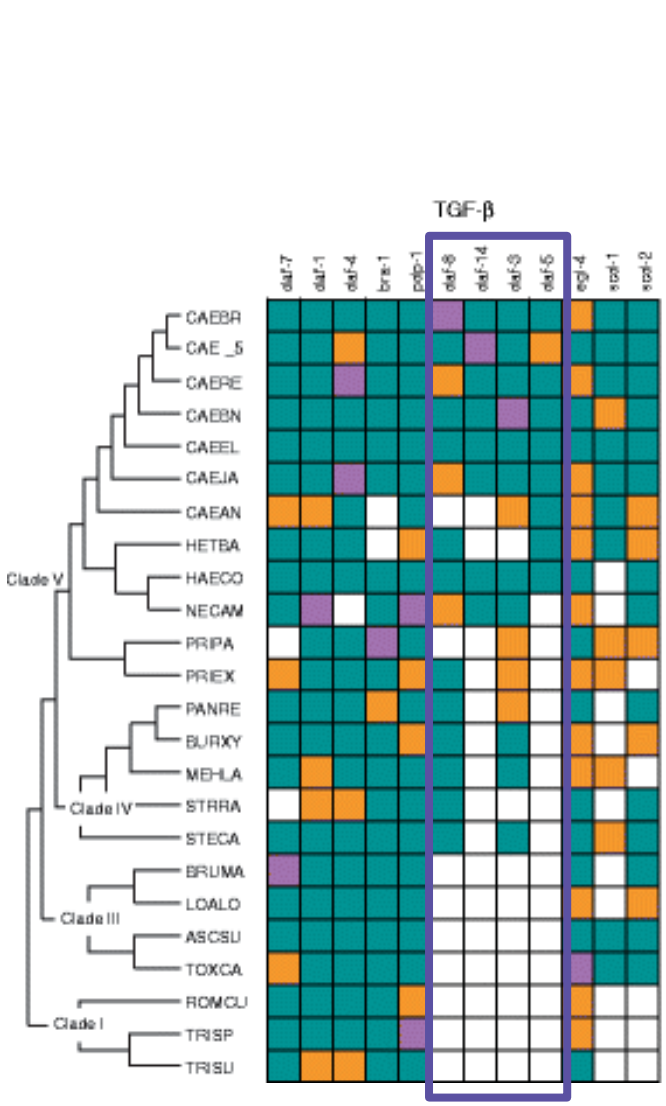

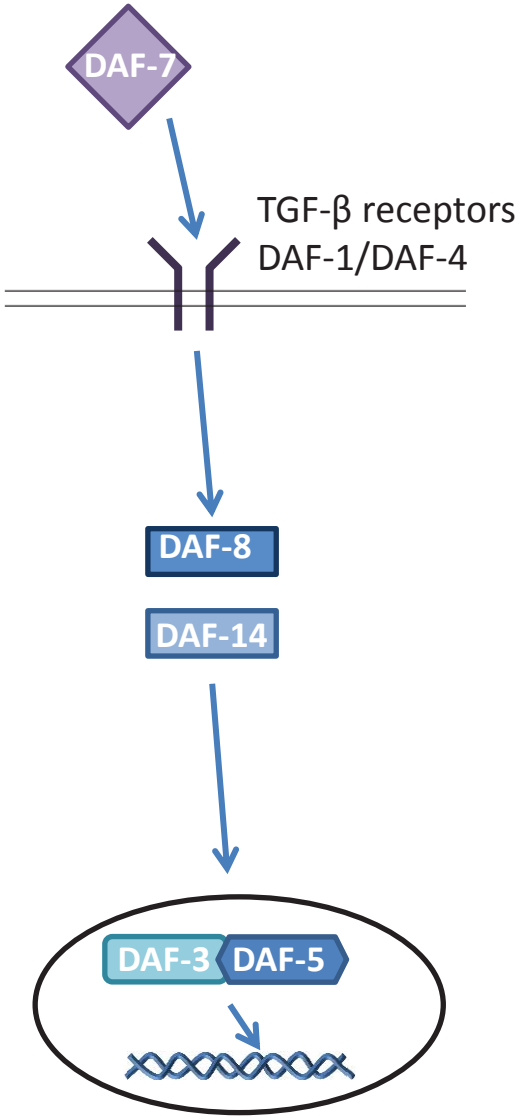

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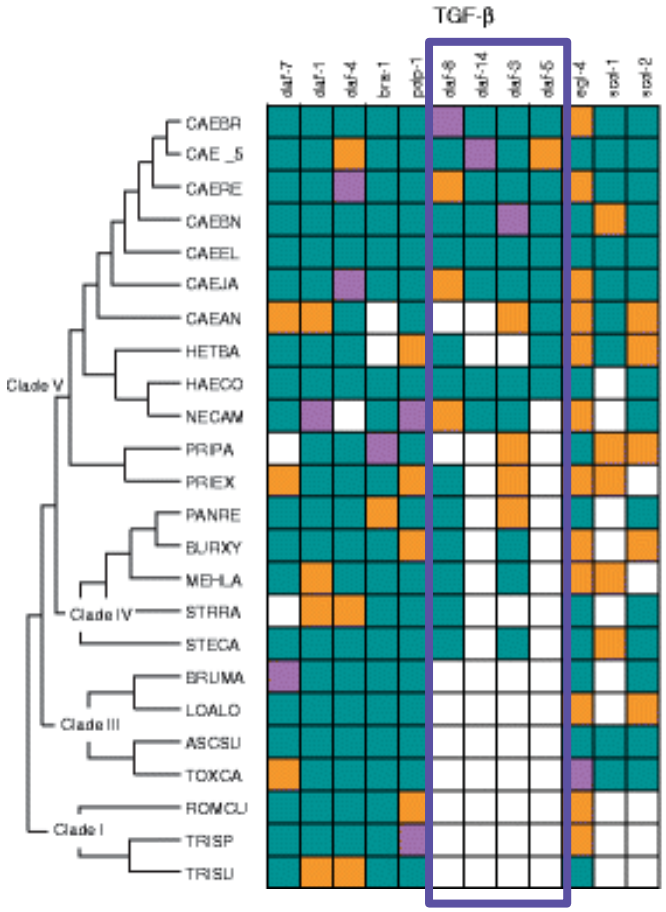

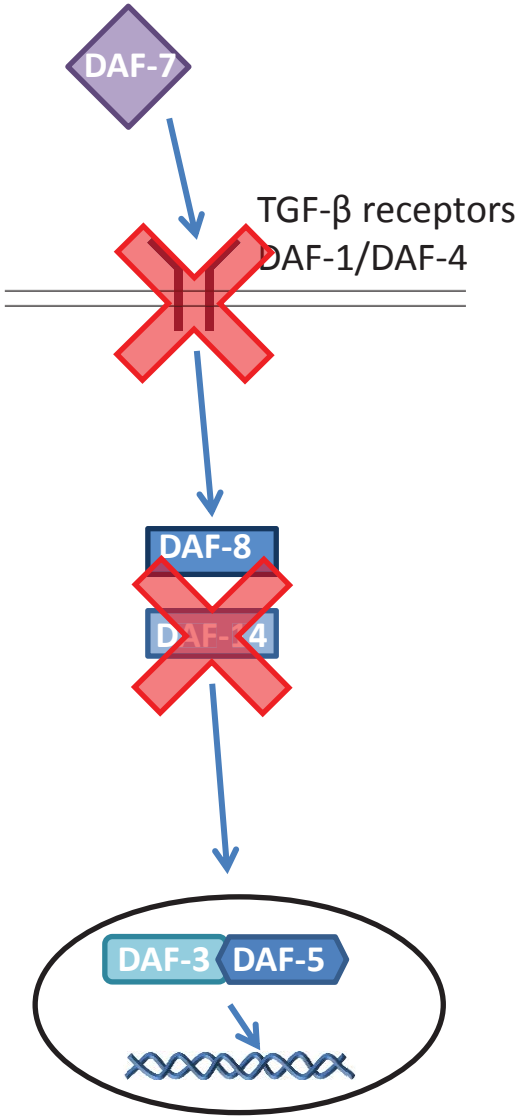

Phenotypes:

Dauer development
Egg-laying

Other search strategies

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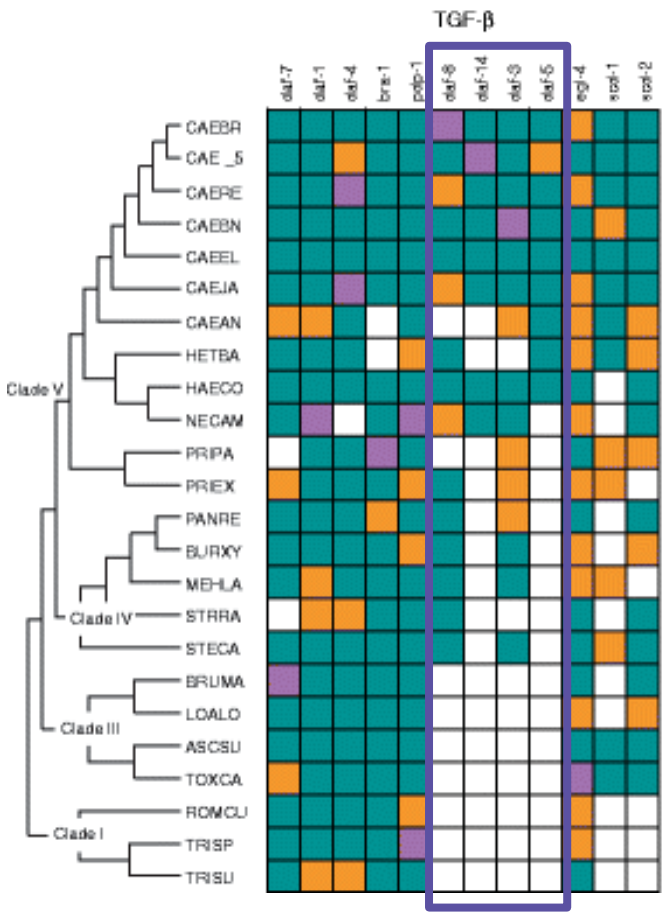

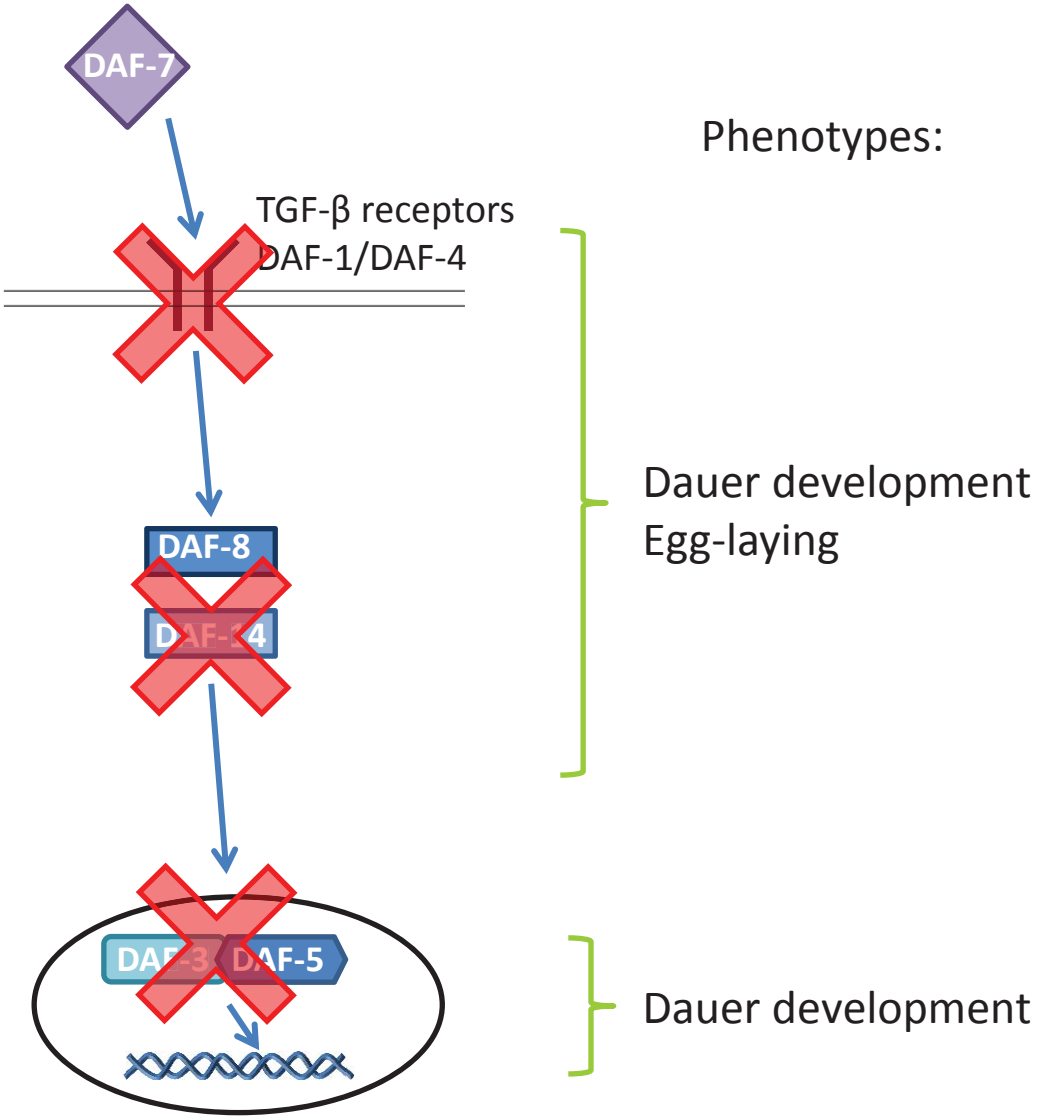

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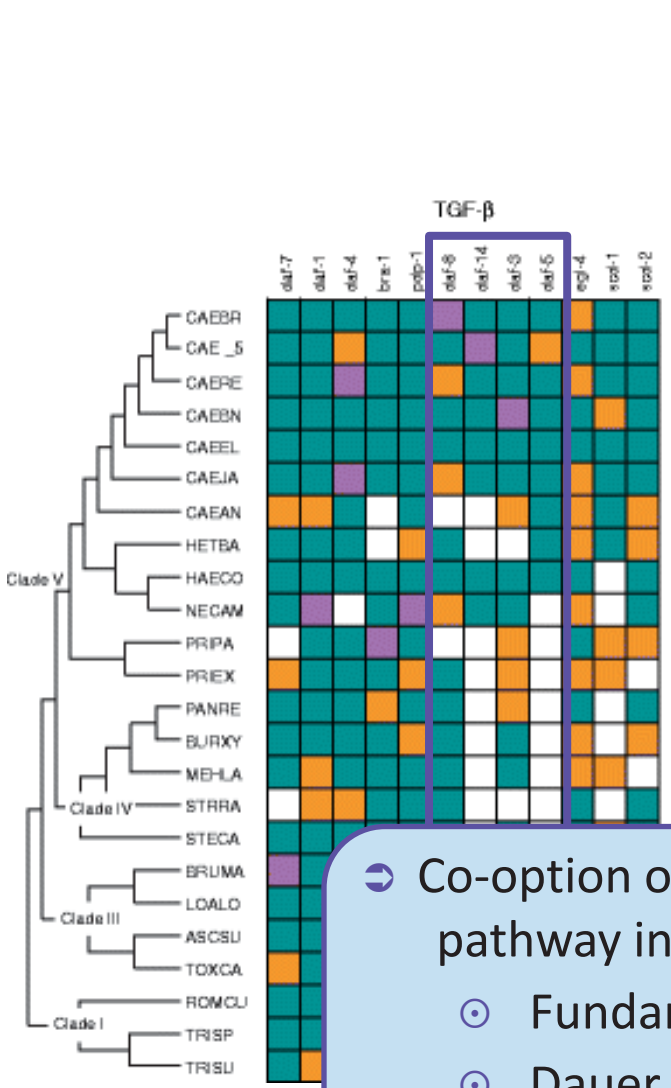

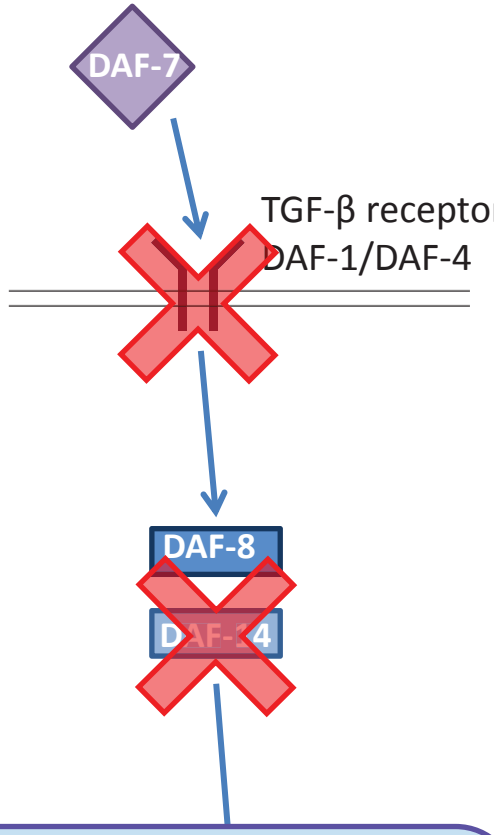

Phenotypes:

Dauer development
Egg-laying

- Co-option of the DAF-7–TGF-β pathway into dauer control
  - Fundamental ancestral role
  - Dauer control in clade V nematodes

Dauer development

Other search strategies

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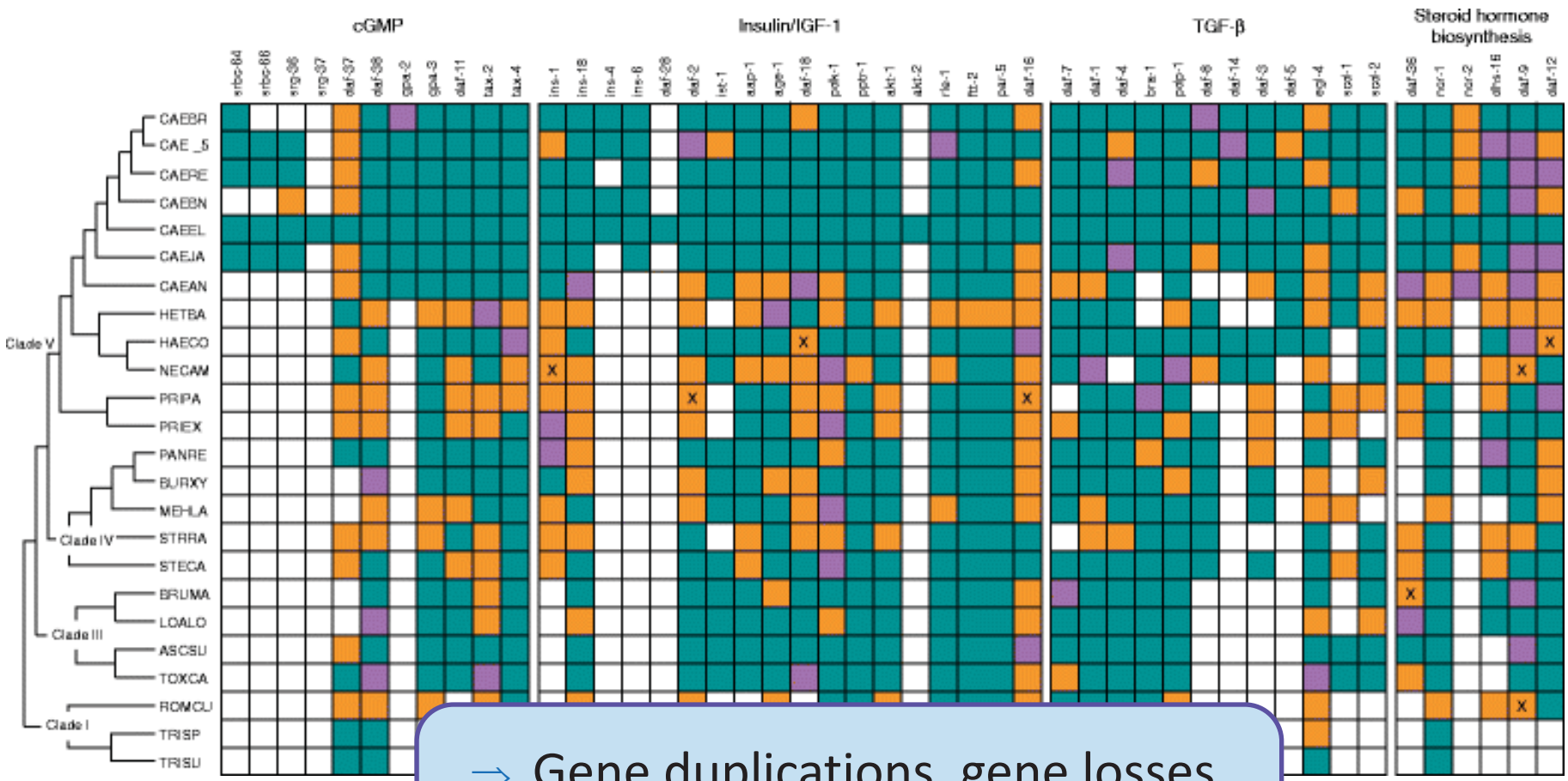
EVOLUTION OF PARASITISM IN NEMATODES



⇒ Gene duplications, gene losses & pathway co-option

Other search strategies

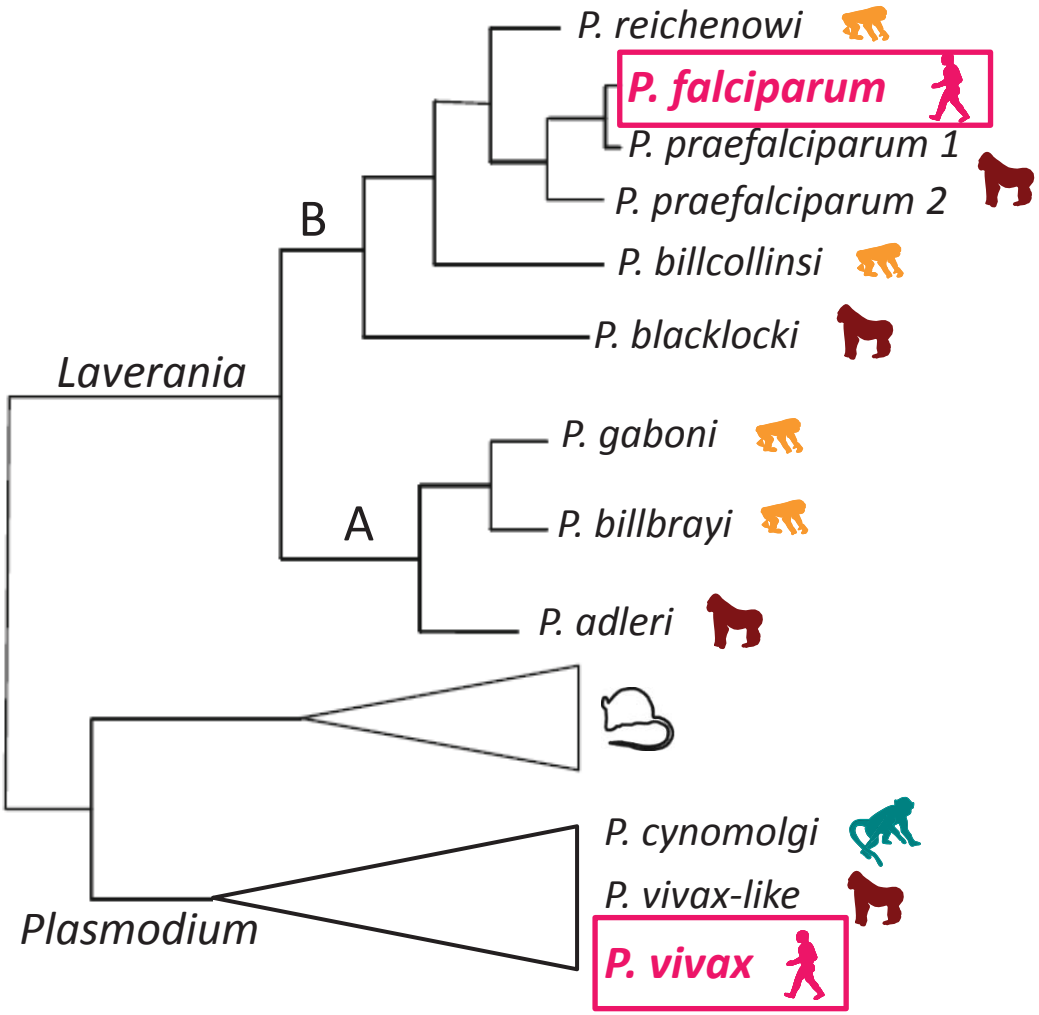
Not found | Reciprocal BLAST | Minor changes | Major changes

HOST ADAPTATION IN *PLASMODIUM* SPECIES

QUESTION: Human pathogens emergence

↳ *Plasmodium falciparum & Plasmodium vivax*,
malaria causing pathogens

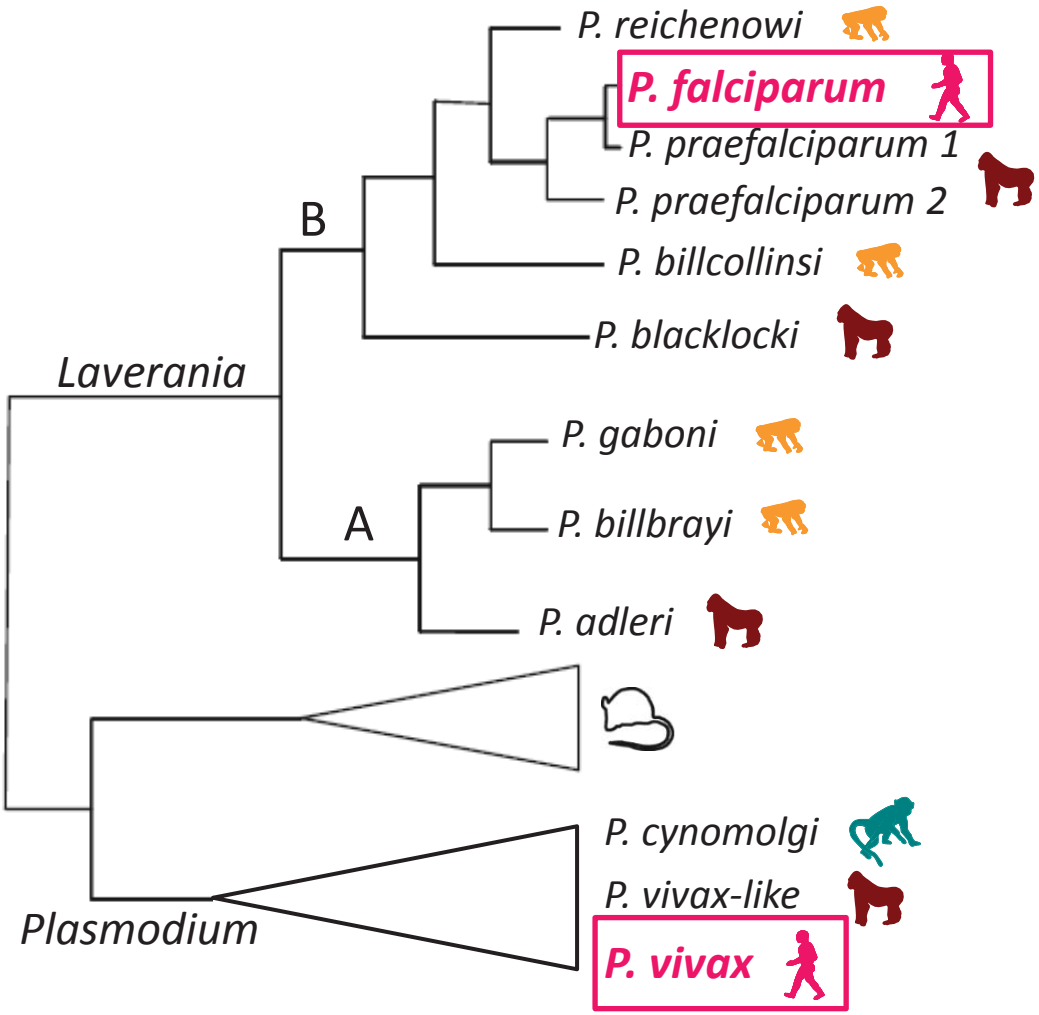
HOST ADAPTATION IN *PLASMODIUM* SPECIES



Gonzalez *et al.* (2013) Curr Top Microbiol Immunol, 365:337-53

Human Chimpanzee Gorilla Rodents Asian monkeys

HOST ADAPTATION IN *PLASMODIUM* SPECIES



⇒ Origins

⇒ Host adaptation

⇒ Comparative genomics

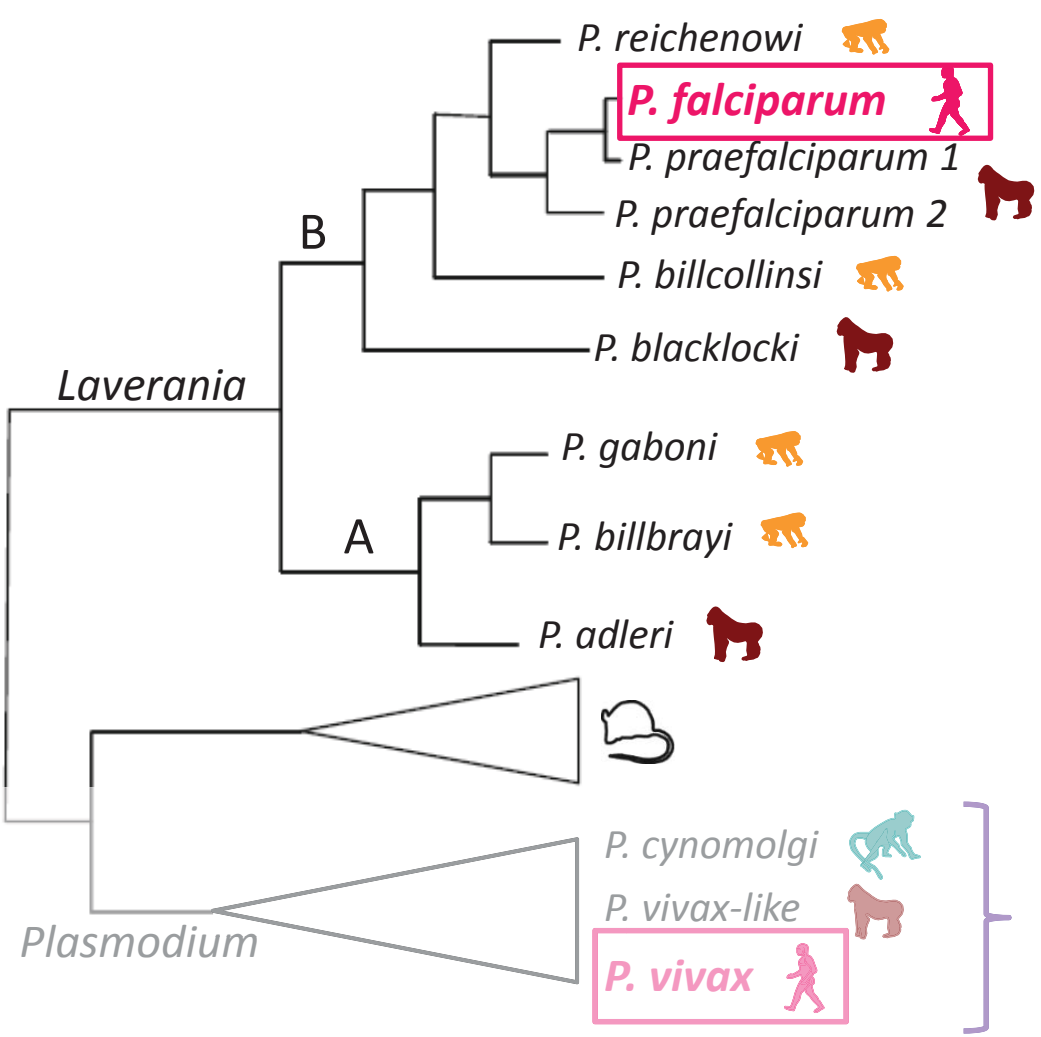
wellcome trust sanger institute

Gonzalez *et al.* (2013) Curr Top Microbiol Immunol, 365:337-53

Human Chimpanzee Gorilla Rodents Asian monkeys

HOST ADAPTATION IN *PLASMODIUM* SPECIES

- Comparative genomics & bioinformatics



i. **Gene transfer, convergent evolution**
ii. *Selection*
iii. *Multi-genic families*

Diversity & genetic differenciation (SNPs)

Human Chimpanzee Gorilla Rodents Asian monkeys

SNP : Single Nucleotide Polymorphism

HOST ADAPTATION IN *PLASMODIUM* SPECIES

- *Laverania* genomics

Technical challenges:

- Low parasitemia
- Co-infections
- Host contamination
- AT rich

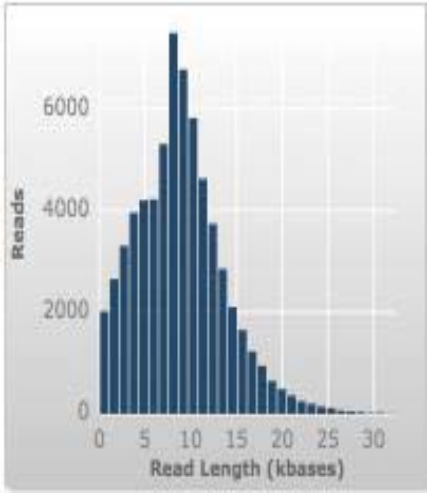
- *Laverania* genomics

Technical challenges:

- Low parasitemia
- Co-infections
- Host contamination
- AT rich

⇒ CF11 cellulose columns,
whole genome amplification (WGA)
& PacBio

long reads
(mean = 10kb)



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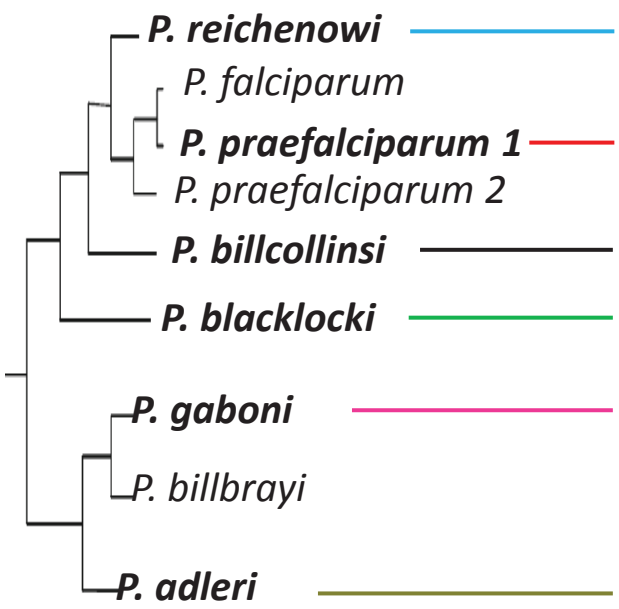
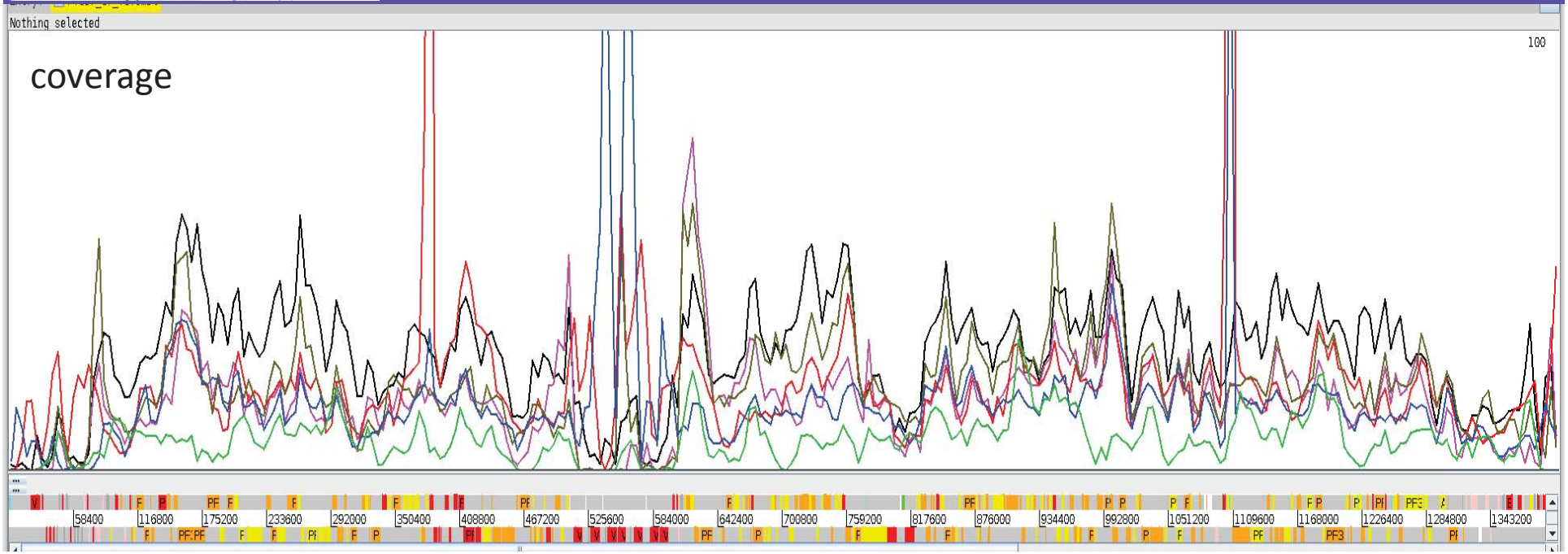


	Sample	Sample preparation
P. reichenowi	Fresh blood	CF11 / WGA
P. praefalciparum 1	Fresh blood	CF11 / WGA
P. billcollinsi	Fresh blood	CF11 / WGA
P. blacklocki	Frozen blood	CF11 / WGA + sWGA
P. gaboni	Fresh blood	CF11 / WGA
P. adleri	Fresh blood	CF11 / WGA

HOST ADAPTATION IN *PLASMODIUM* SPECIES



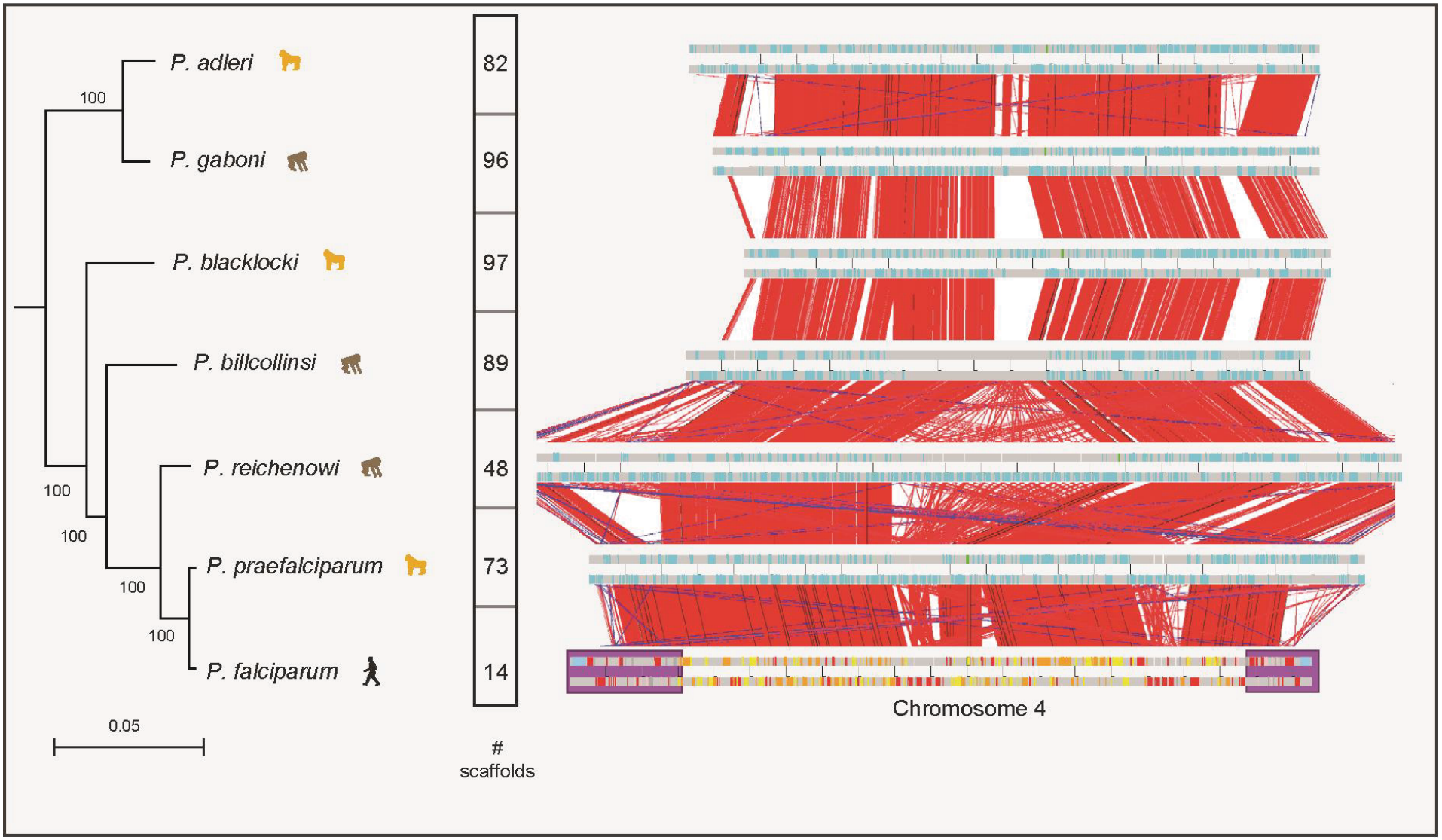
	Sample	Sample preparation	# genes
P. reichenowi	Fresh blood	CF11 / WGA	5941
P. falciparum			5548
P. praefalciparum 1	Fresh blood	CF11 / WGA	6476
P. praefalciparum 2			
P. billcollinsi	Fresh blood	CF11 / WGA	5637
P. blacklocki	Frozen blood	CF11 / WGA + sWGA	5346
P. gaboni	Fresh blood	CF11 / WGA	5421
P. billbrayi			
P. adleri	Fresh blood	CF11 / WGA	5515

4269 one-to-one orthologues

HOST ADAPTATION IN *PLASMODIUM* SPECIES

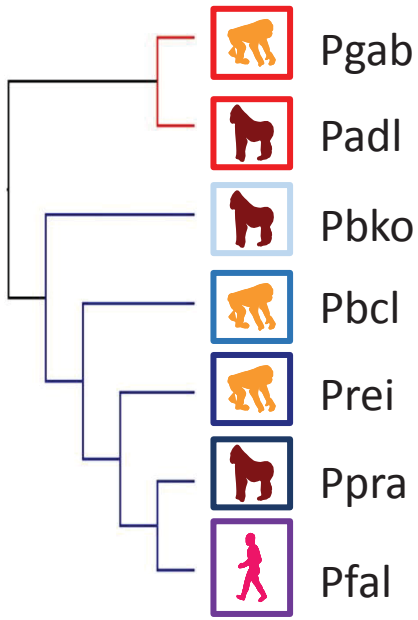
Species tree

Reference genome assemblies



- Gene transfer & convergent evolution

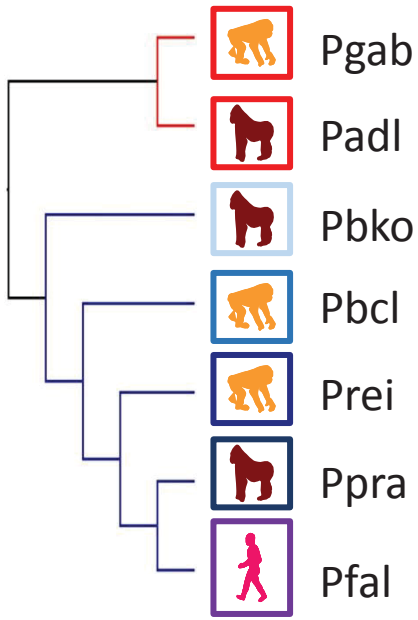
Species tree topology



4269 CDS

- Gene transfer & convergent evolution

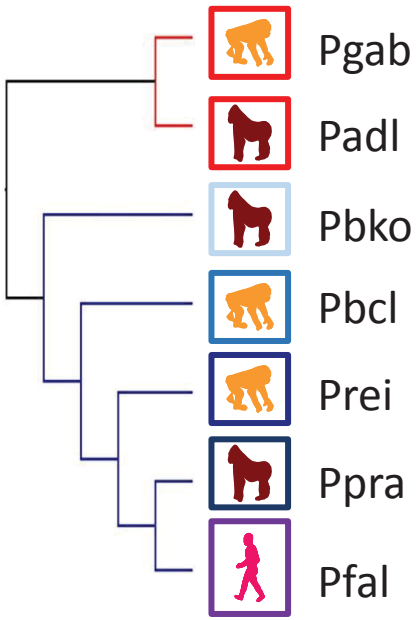
Species tree topology



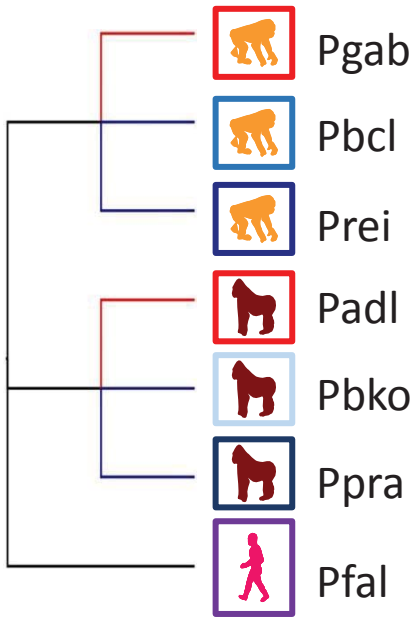
4269 CDS ⇒ 4251 CDS

- Gene transfer & convergent evolution

Species tree topology



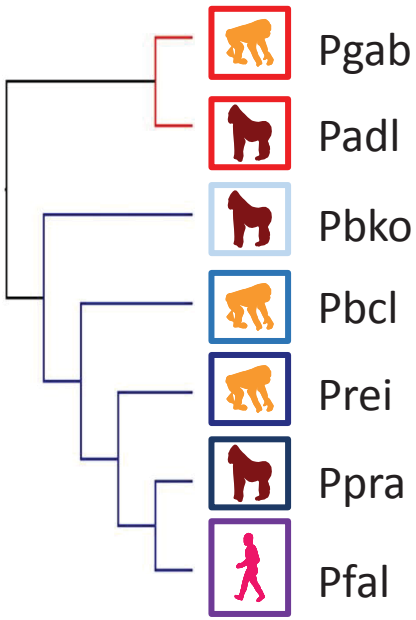
Host-mediated convergent evolution topology



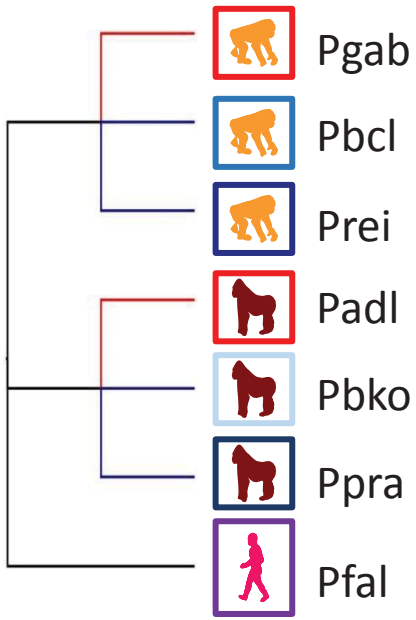
4269 CDS ⇒ 4251 CDS

- Gene transfer & convergent evolution

Species tree topology



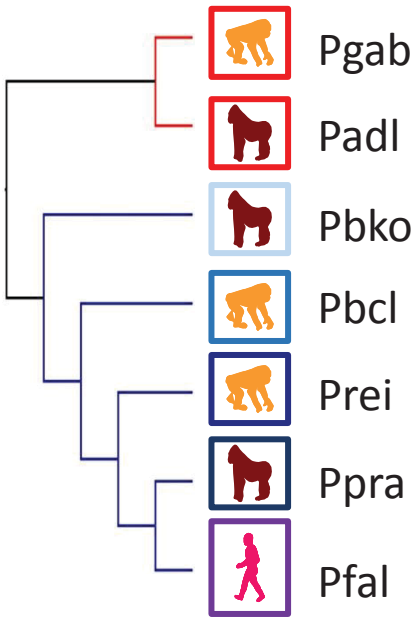
Host-mediated convergent evolution topology



4269 CDS ⇒ 4251 CDS ⇒ 0 CDS

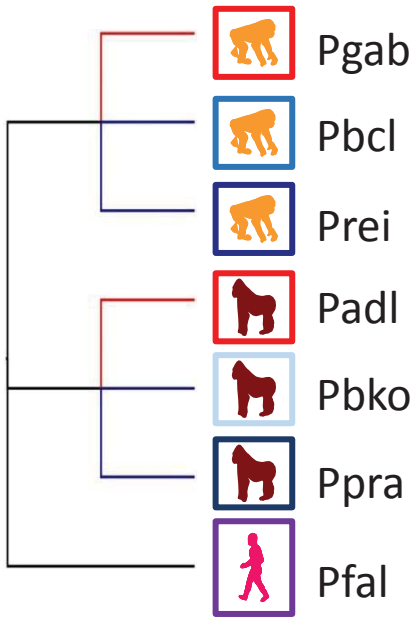
- Gene transfer & convergent evolution

Species tree topology

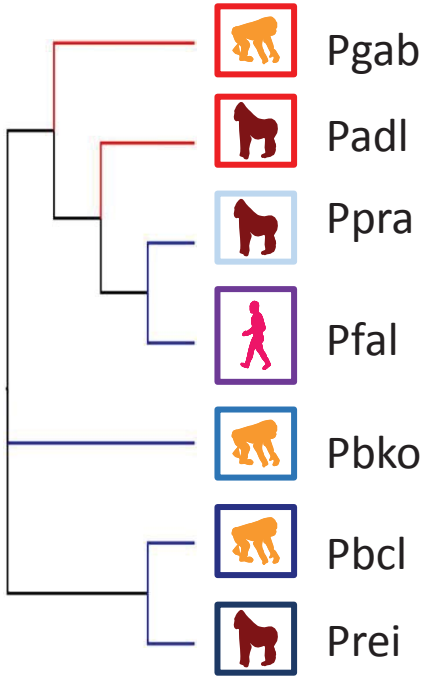


4269 CDS ⇒ 4251 CDS

Host-mediated convergent evolution topology

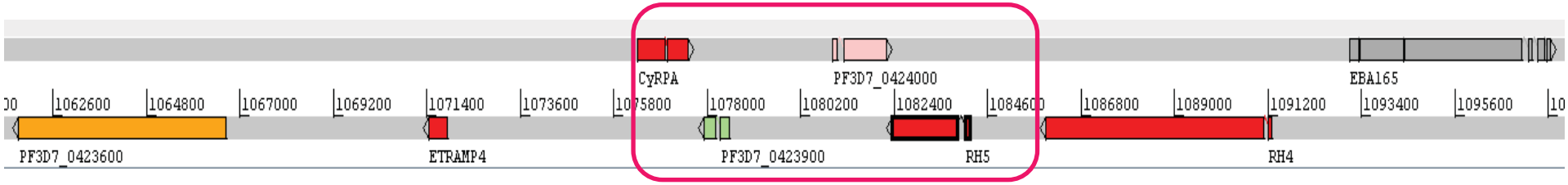


⇒ 0 CDS



⇒ 4 CDS

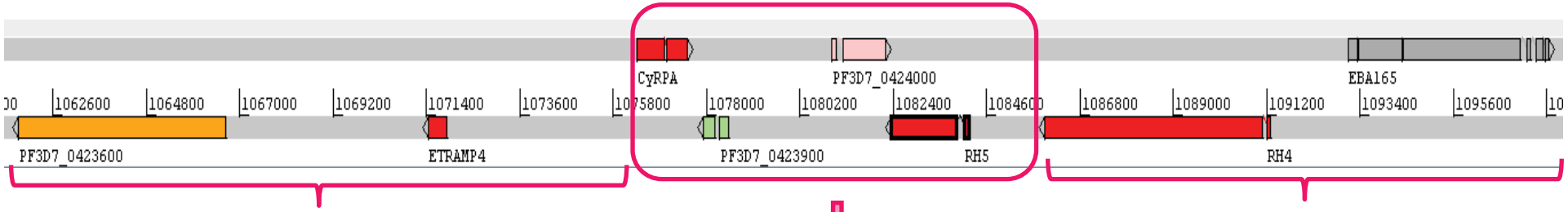
- Gene transfer & convergent evolution



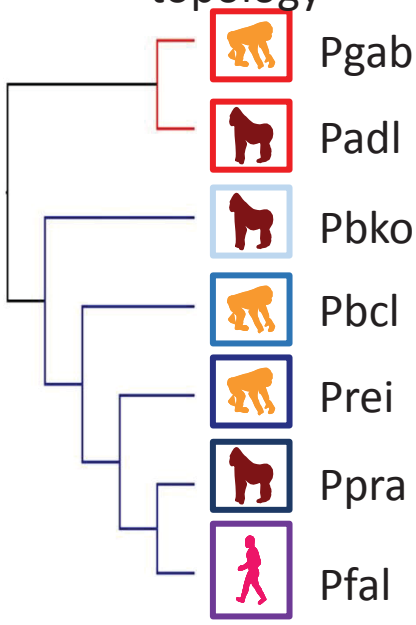
Human Chimpanzee Gorilla

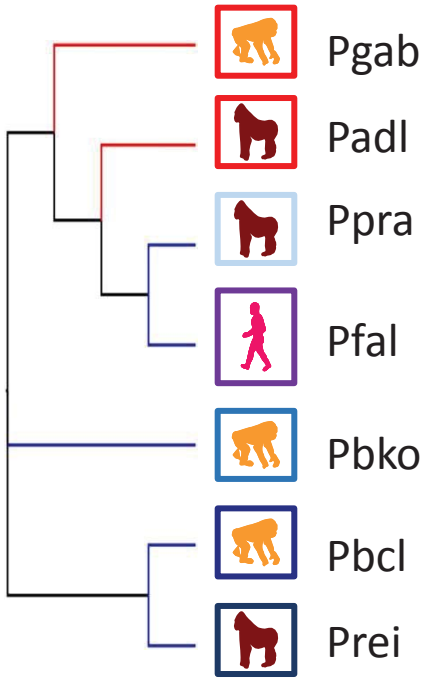
- Gene transfer & convergent evolution

CDS & intergenic regions

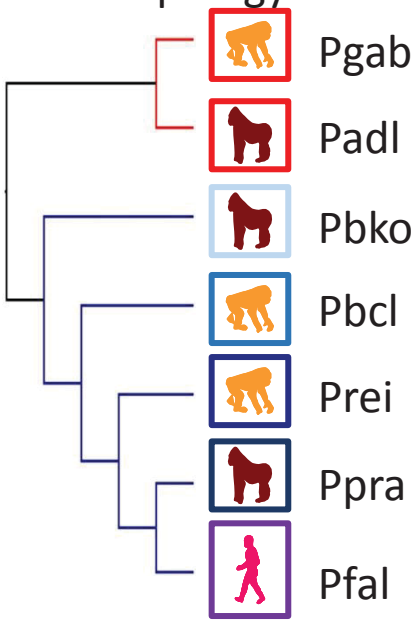


Species tree topology





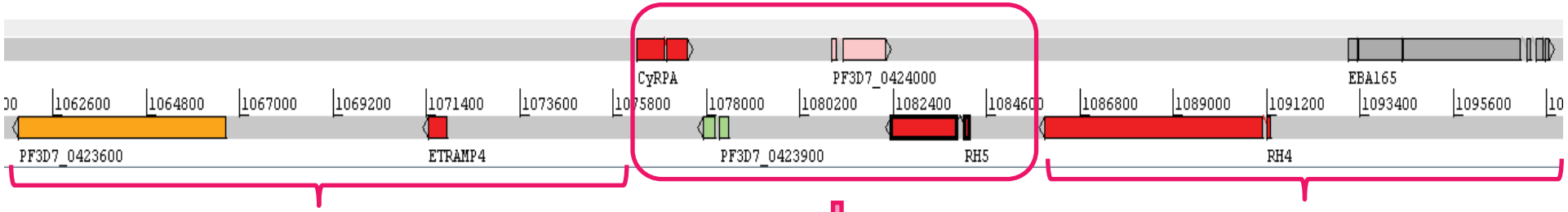
Species tree topology



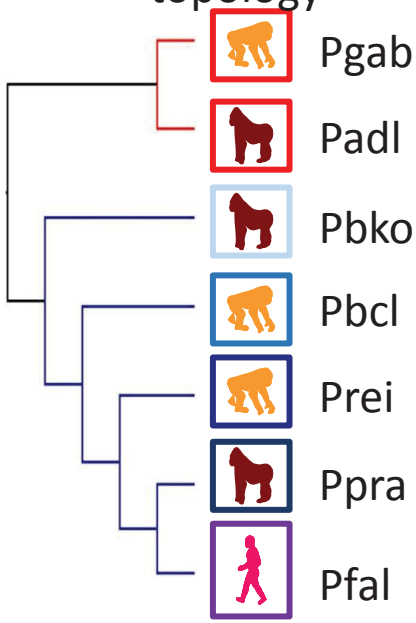
Human Chimpanzee Gorilla

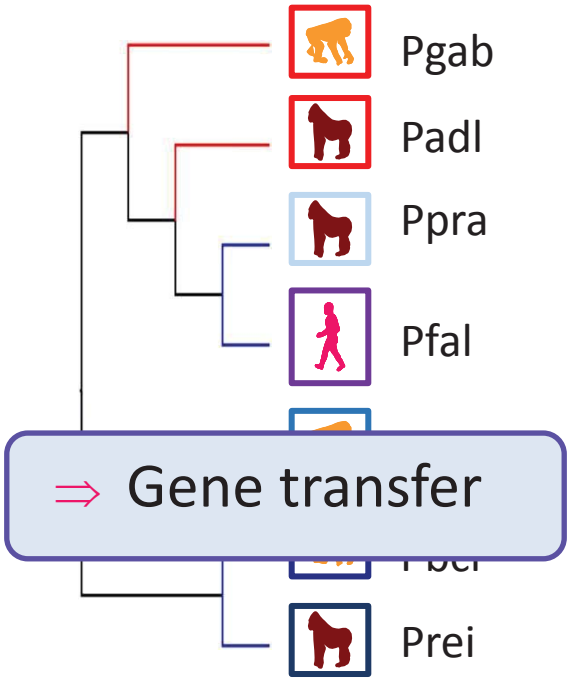
- Gene transfer & convergent evolution

CDS & intergenic regions



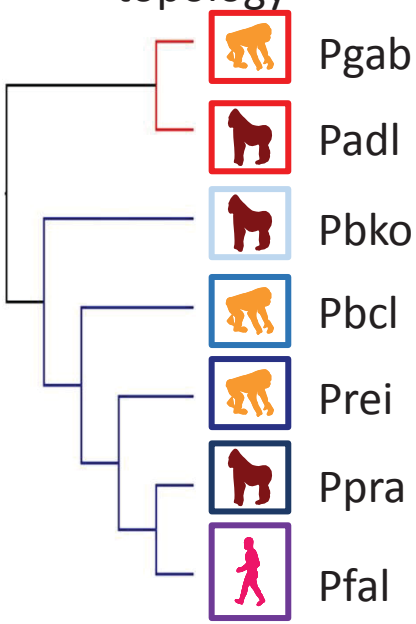
Species tree topology





⇒ Gene transfer

Species tree topology

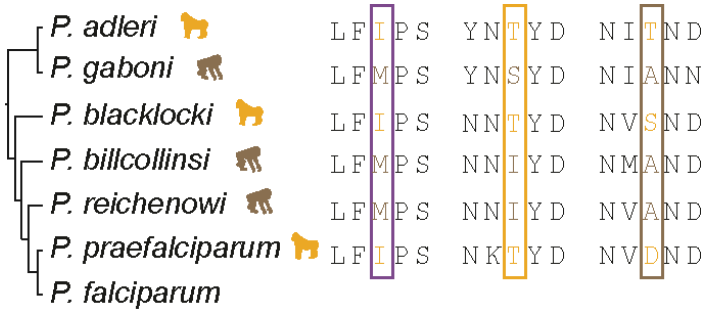


Human Chimpanzee Gorilla

HOST ADAPTATION IN *PLASMODIUM* SPECIES

- Convergent evolution

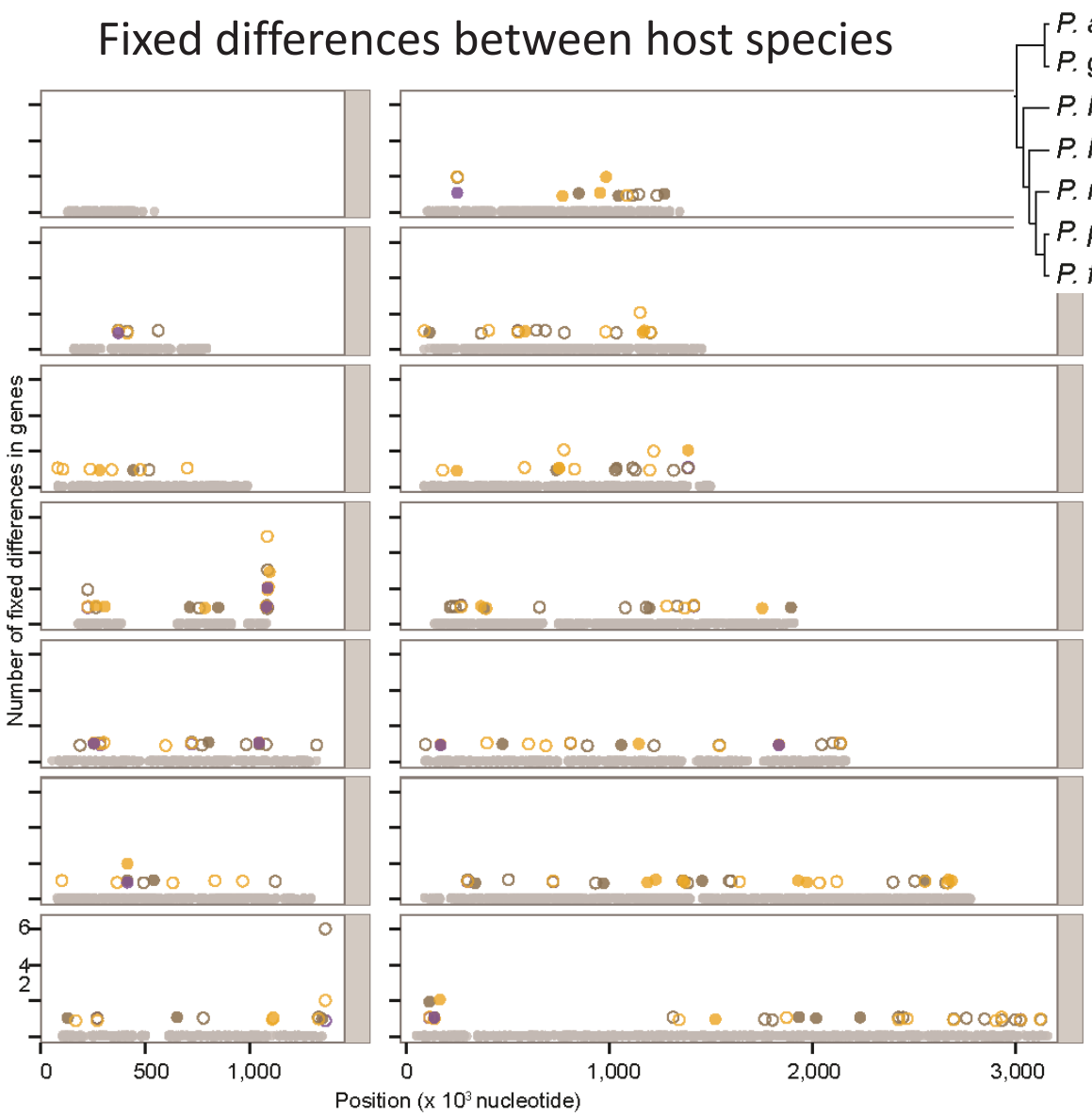
  Fixed differences between host species

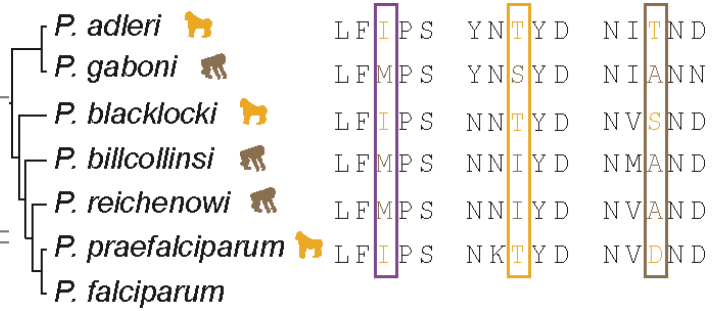


HOST ADAPTATION IN *PLASMODIUM* SPECIES

Convergent evolution

Fixed differences between host species



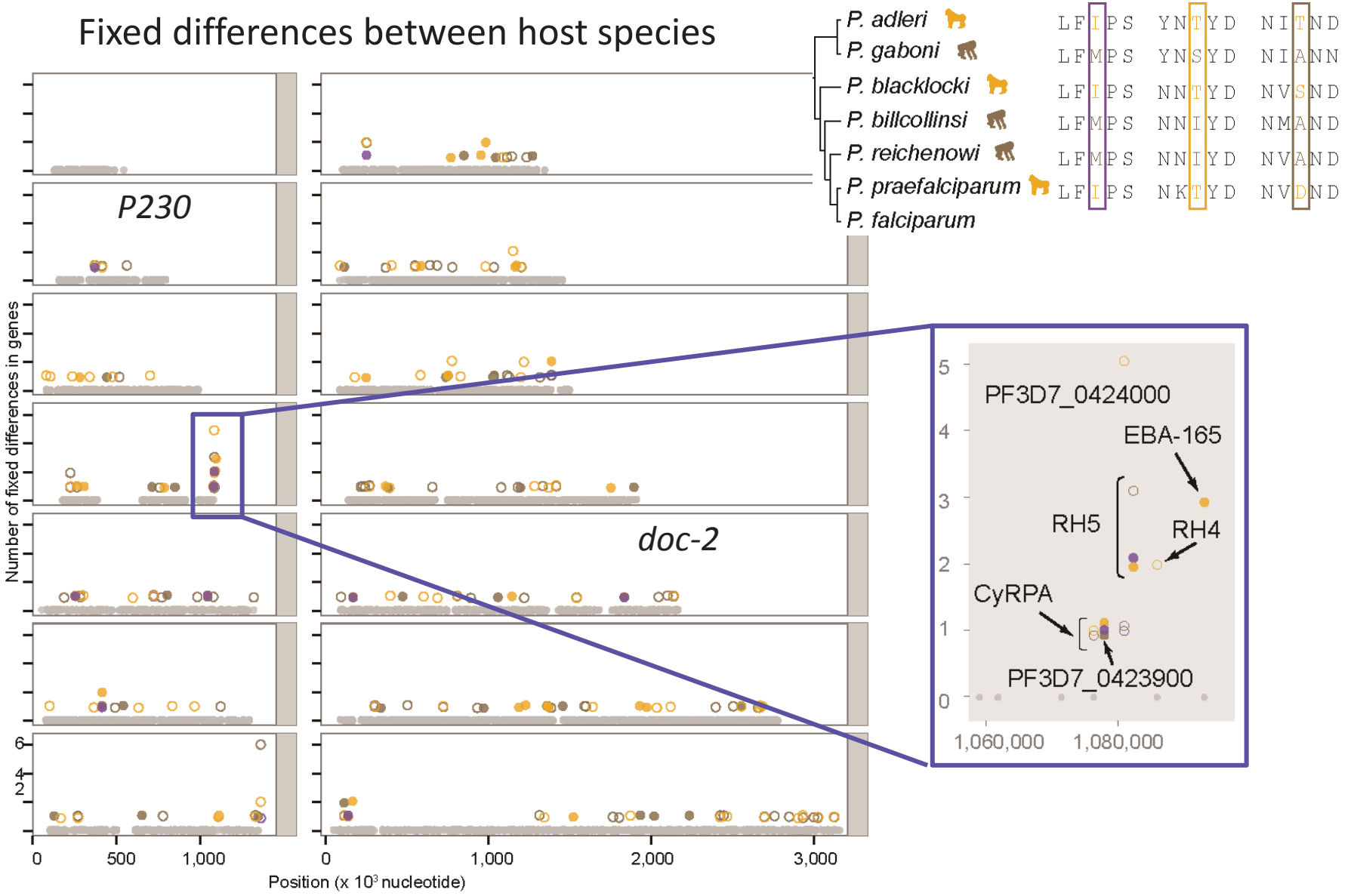


Human Chimpanzee Gorilla

HOST ADAPTATION IN *PLASMODIUM* SPECIES

Convergent evolution

Fixed differences between host species

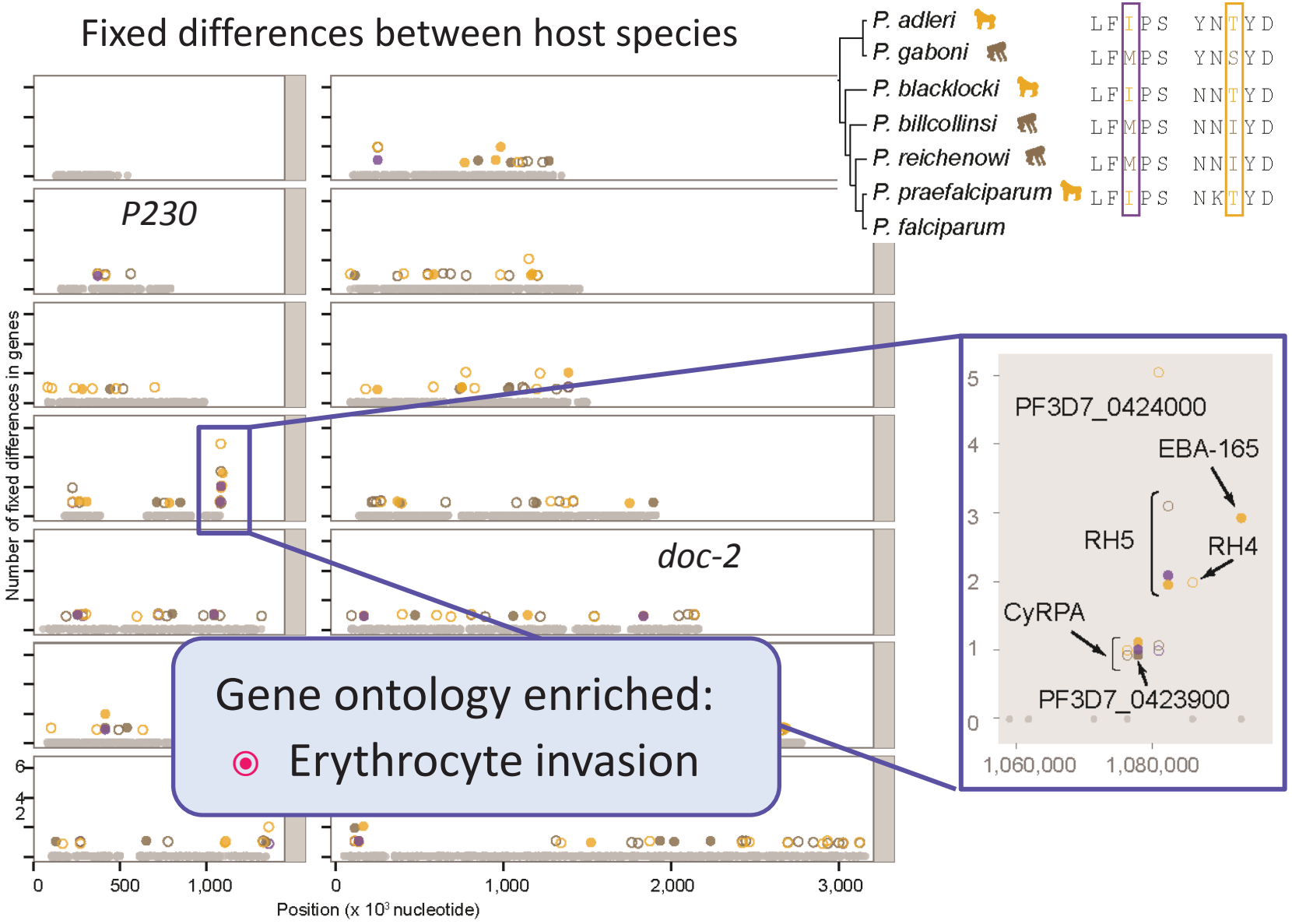


Human Chimpanzee Gorilla

HOST ADAPTATION IN *PLASMODIUM* SPECIES

- Convergent evolution

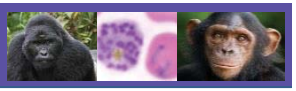
Fixed differences between host species



Gene ontology enriched:

- Erythrocyte invasion

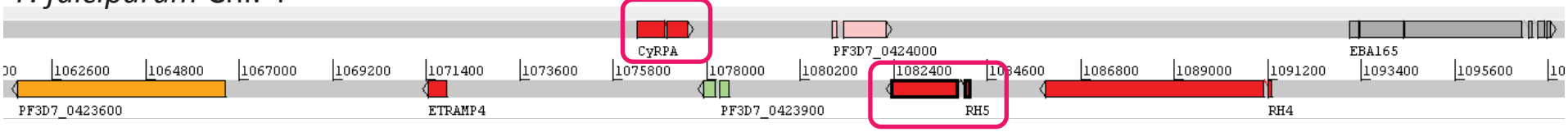
Human Chimpanzee Gorilla



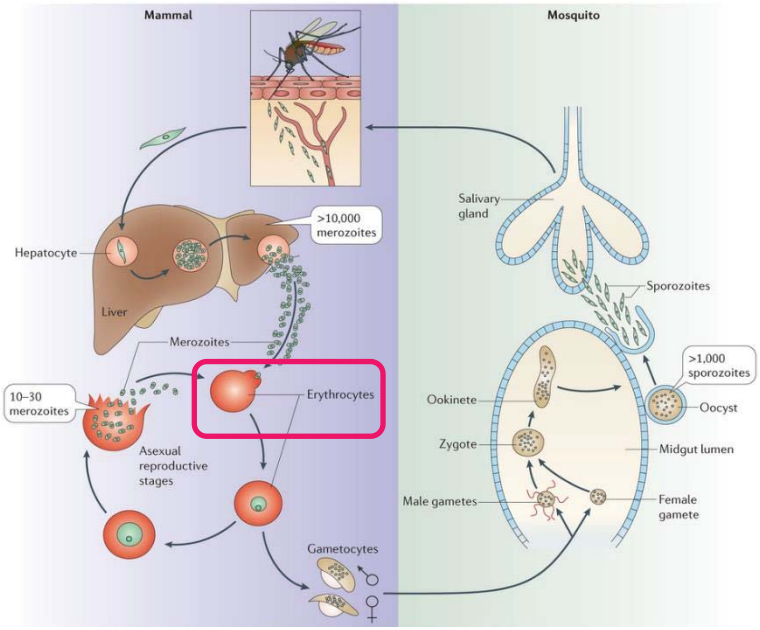
⇒ Gene transfer & convergent evolution

P. falciparum Chr. 4

cysteine-rich protective antigen

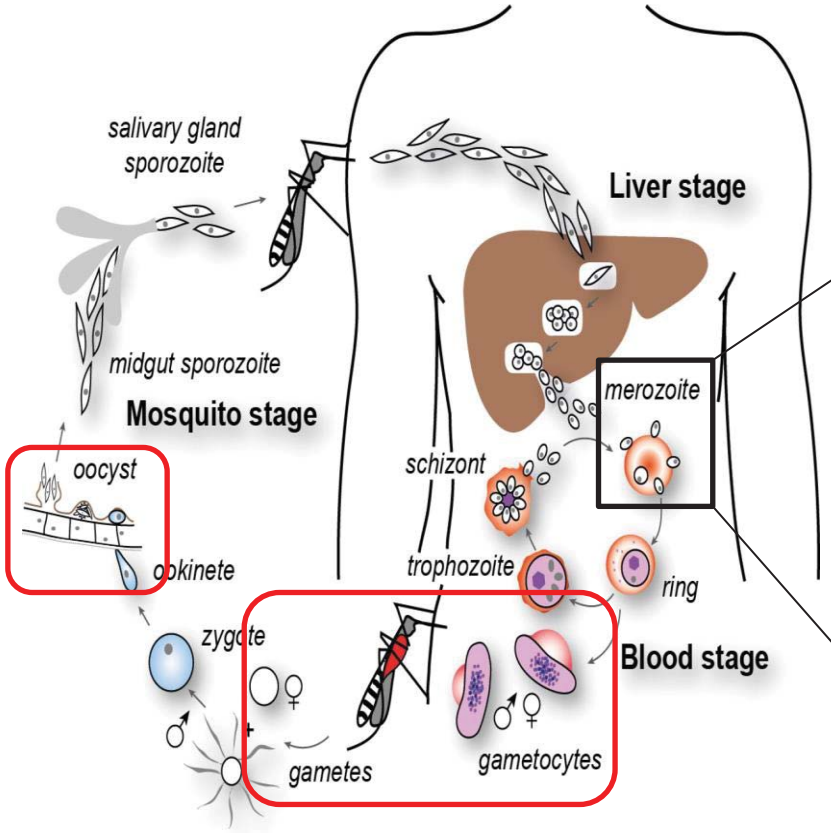


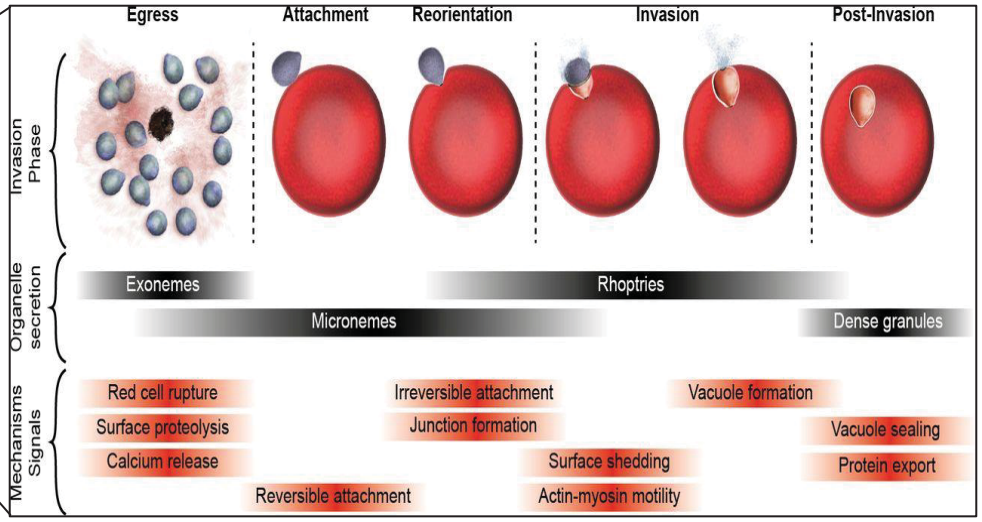
reticulocyte binding protein homologue 5

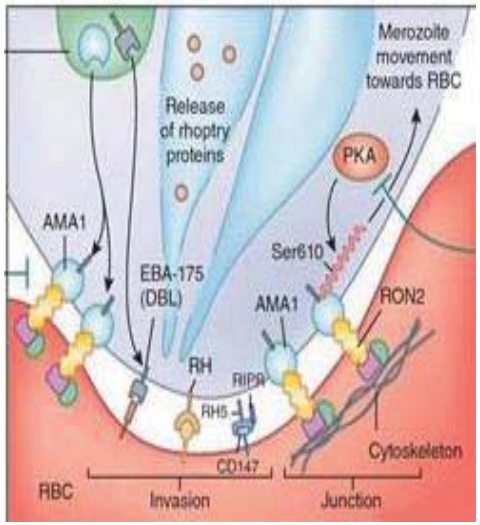


- CyRPA/Ripr/RH5 complex
  - ⇨ Interaction with the human receptor basigin
  - ⇨ Erythrocyte invasion & host tropism

Ménard *et al.* (2013) Nature Reviews Microbiology, 11: 701-711







6-cysteine protein P230
(pre-zygotic reproductive barrier)

DOC2
(Microneme secretion)

RH3, RH5 + CyRPA, EBA-175

Cowman *et al.* (2012) J Cell Biol, 198:961-971

Miller *etal.* (2013) Nature Medicine 19, 156–167

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John Gilleard

NSERC CREATE
Host Parasite Interactions
UCalgary
UAlberta
ULethbridge

Thank you!

MiVEGEC
Maladies Infectieuses et Vecteurs
Écologie, Génétique, Évolution et Contrôle

Céline Arnathau
Lionel Brazier
Patrick Durand
Franck Prugnolle
François Renaud
Virginie Rougeron

wellcome trust sanger institute

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Thomas D Otto
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Chris Newbold