Evolution of *Trypanosoma evansi* and *T. equiperdum*: how, and how often?

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Overview

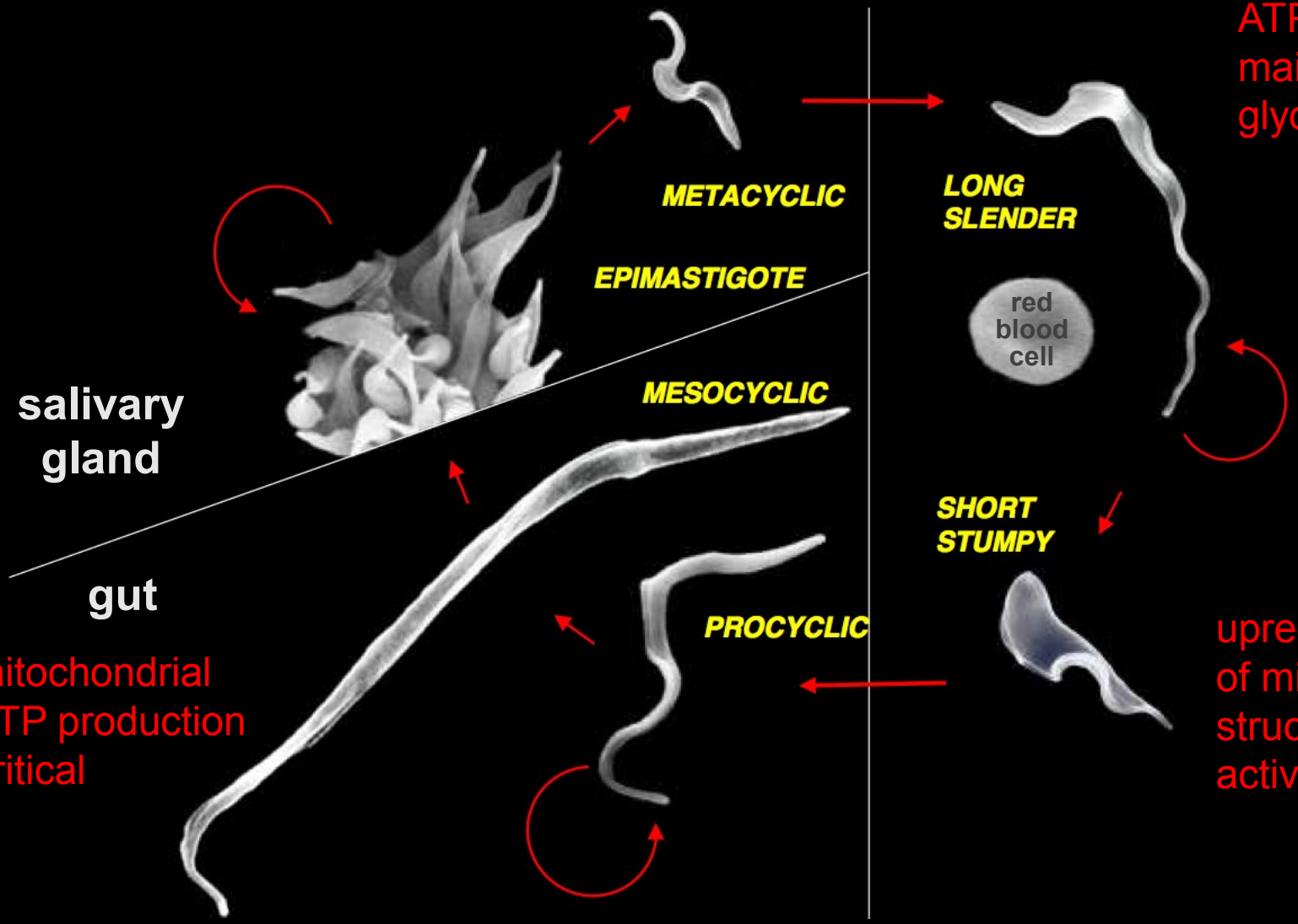
Evolution of *Trypanosoma (b.) evansi* and *T. (b.) equiperdum*

- **Development of stable tsetse-independent transmission**
- **Development of dyskinetoplastidy**

Phylogenetic relationship of *T. evansi* / *T. equiperdum* to *T. brucei*

- **How many times did *Tev*/*Teq* evolve from *Tbb*?**
- **How does the *T. equiperdum* strain responsible for the Italian 2011 outbreak fit in?**

Life cycle of *T. brucei*



ATP production mainly via glycolysis

mitochondrial ATP production critical

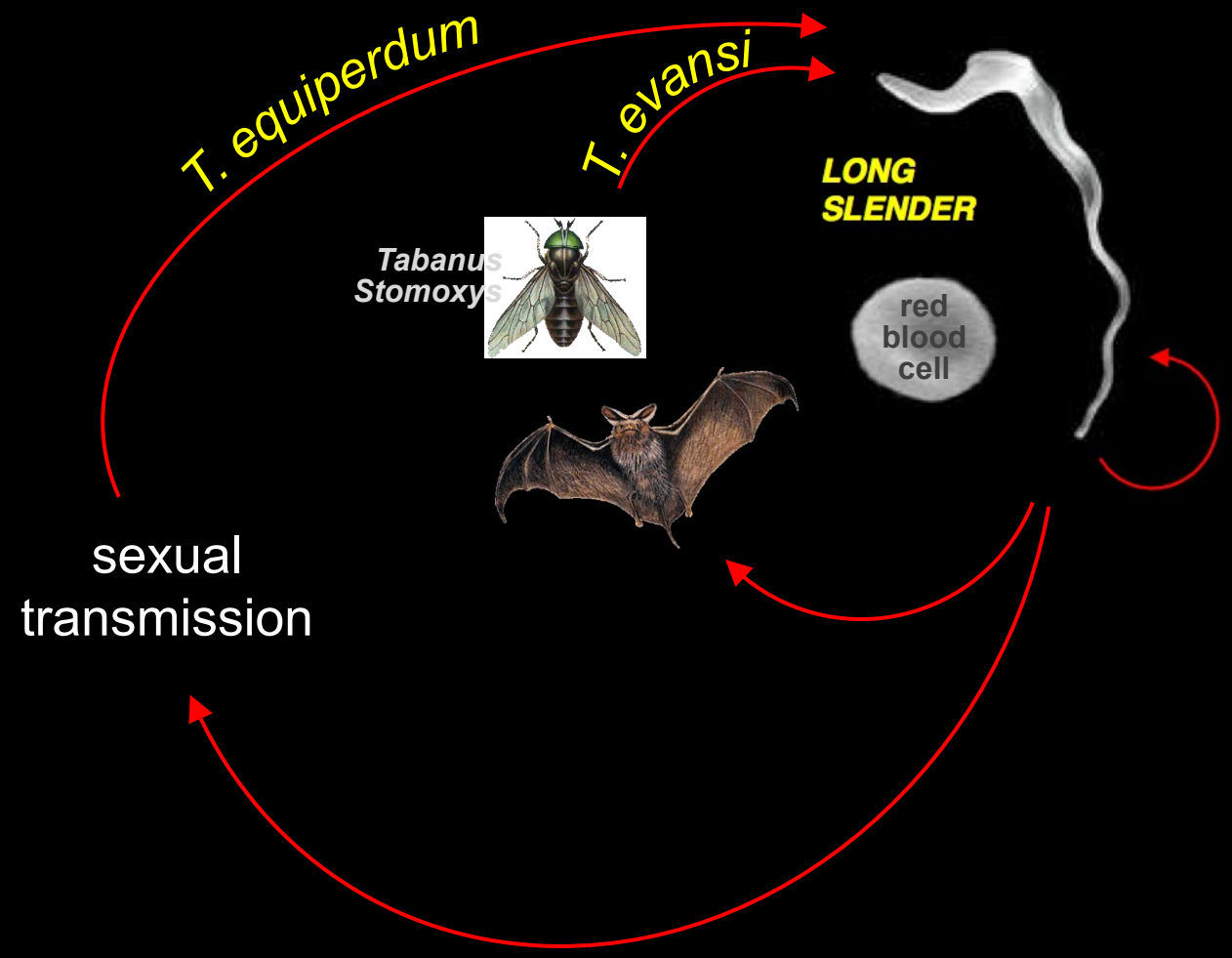
upregulation of mitochondrial structure and activity

tsetse fly

mammal

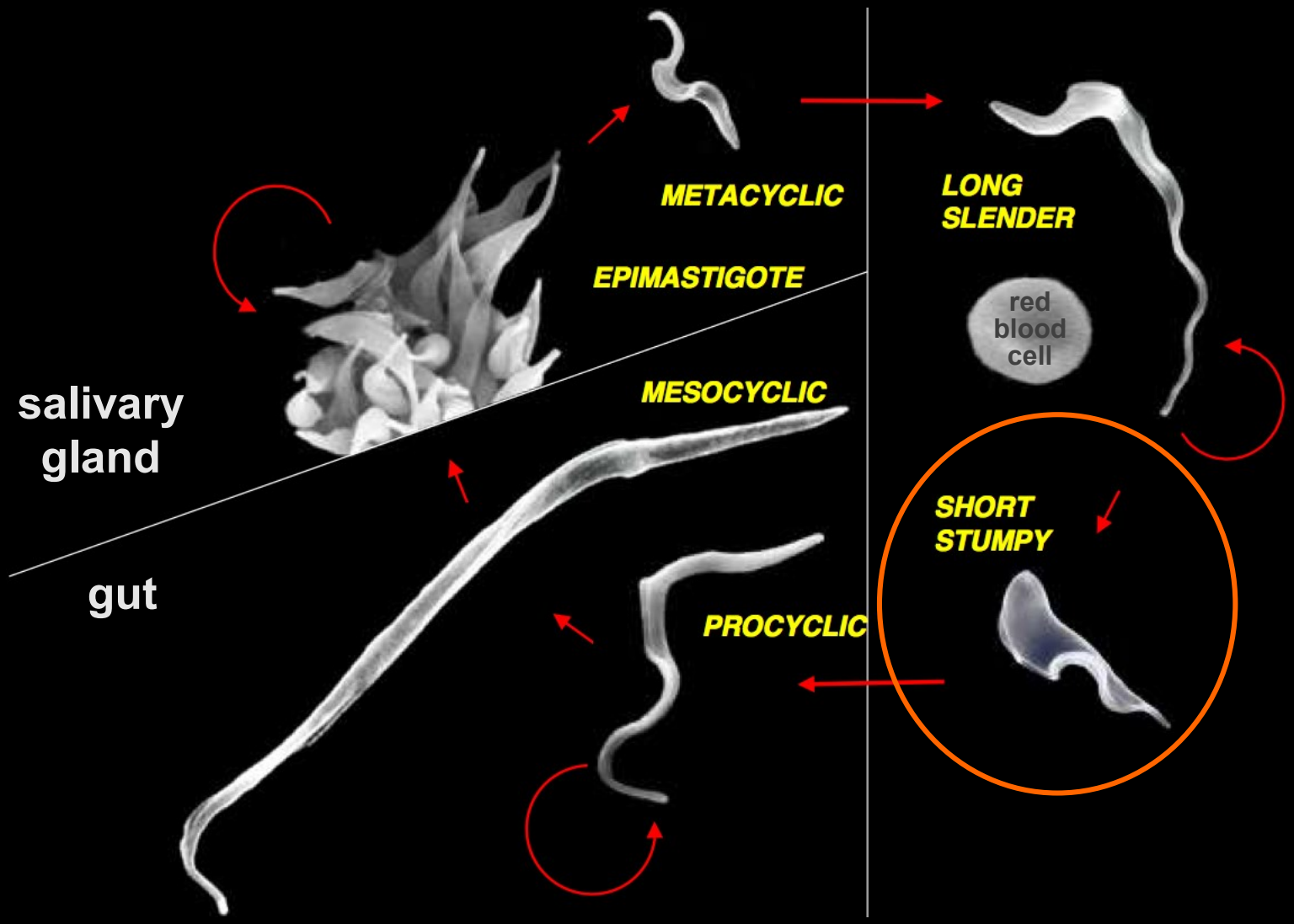
Image credit: Dave Barry, Glasgow

Life cycle of *T. equiperdum* / *T. evansi*



mammal

Life cycle of *T. brucei*

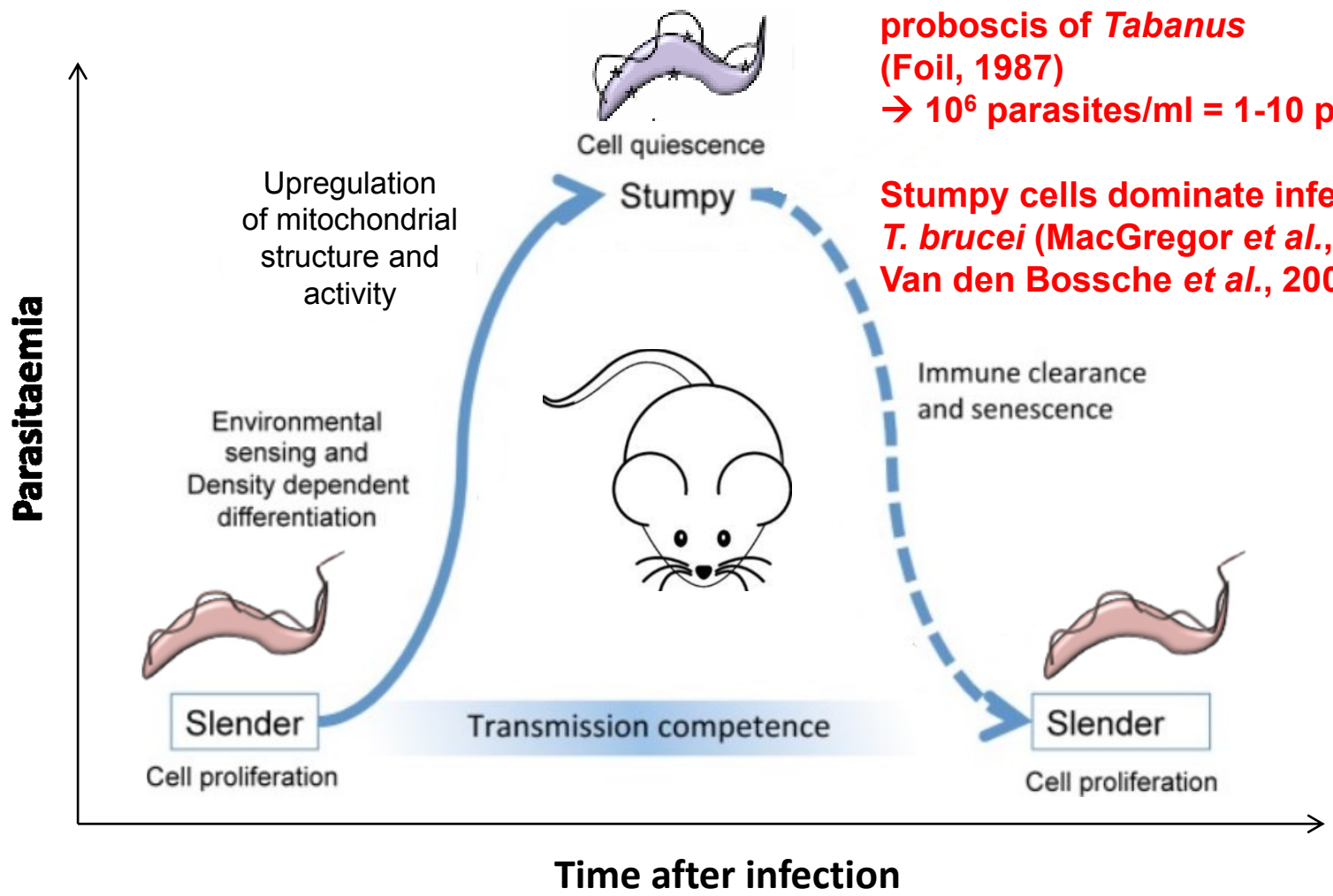


tsetse fly

mammal

Image credit: Dave Barry, Glasgow

Density-dependent differentiation of long slender *T. brucei* into transmission competent stumpy cells

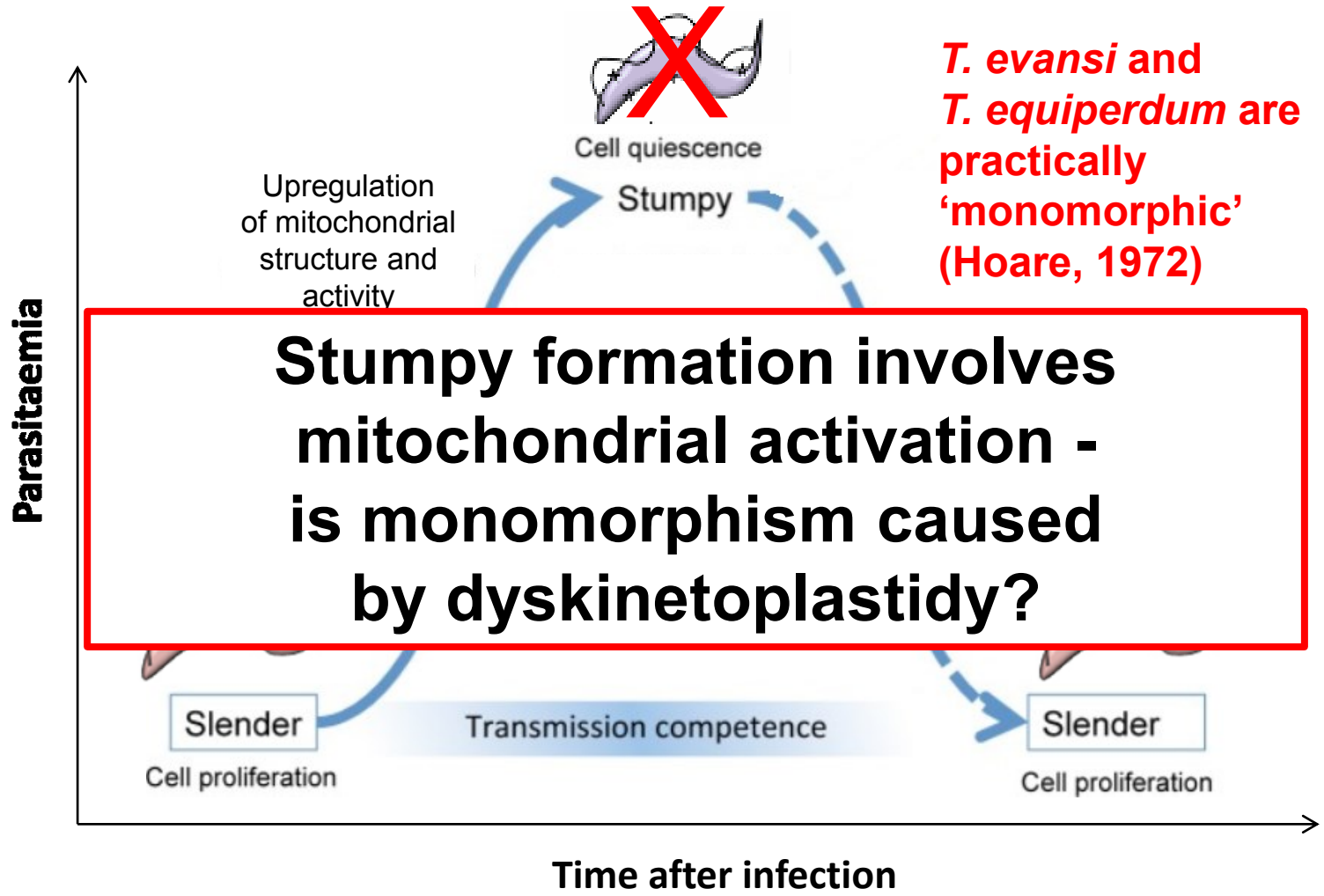


~1-10 nl of blood retained at proboscis of *Tabanus* (Foil, 1987)
→ 10^6 parasites/ml = 1-10 parasites

Stumpy cells dominate infection in *T. brucei* (MacGregor *et al.*, 2011; Van den Bossche *et al.*, 2005)

Adapted from Rico *et al.* (2013)

Density-dependent differentiation of long slender *T. brucei* into transmission competent stumpy cells

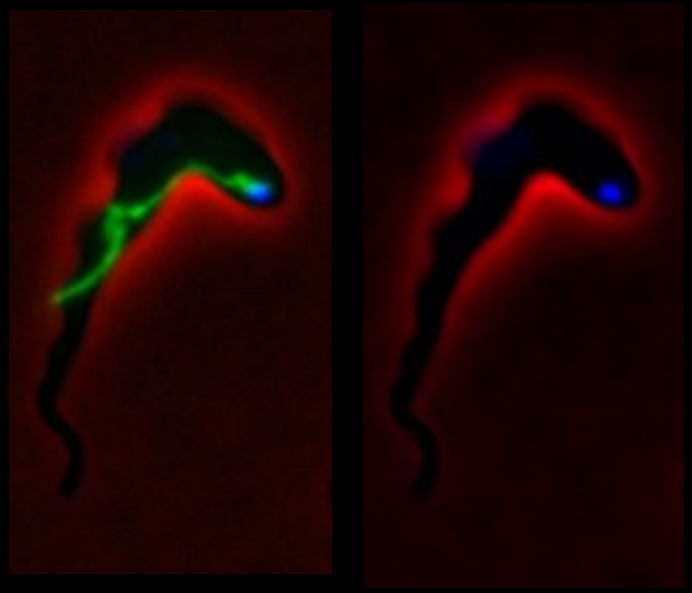


***T. evansi* and *T. equiperdum* are practically 'monomorphic' (Hoare, 1972)**

Stumpy formation involves mitochondrial activation - is monomorphism caused by dyskinetoplastidy?

Adapted from Rico *et al.* (2013)

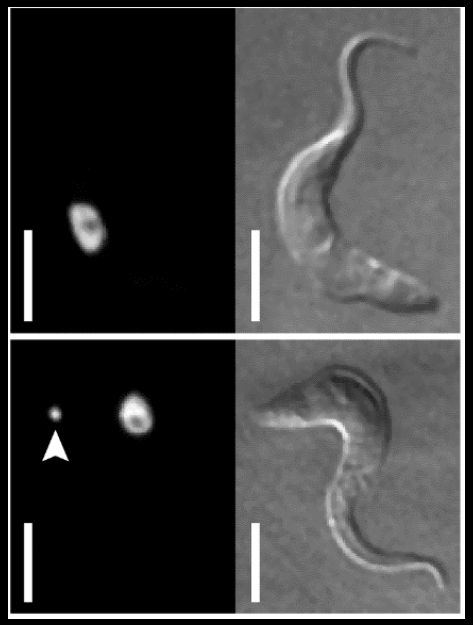
T. evansi and *T. equiperdum* are 'dyskinetoplastic'



mitochondrion

mtDNA = kinetoplast

- essential (Schnaufer *et al.*, 2001)
- important target for anti-trypanosomatid drugs (Gould & Schnaufer, 2014)



DAPI phase contrast

'akinetoplastic' ($kDNA^0$)
= complete loss of the kinetoplast

'dyskinetoplastic' ($kDNA^-$)
= dysfunctional kinetoplast

Bloodstream *T. brucei* $kDNA^0$ are viable in presence of certain mutations in ATPase subunit gamma (Dean *et al.*, 2013)

T. brucei mtDNA (kinetoplast, kDNA)

Human mtDNA

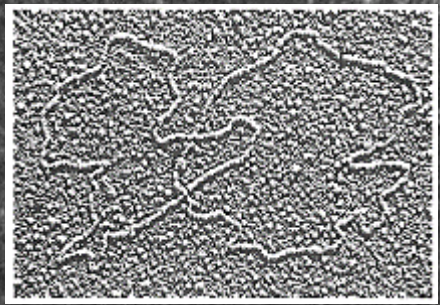
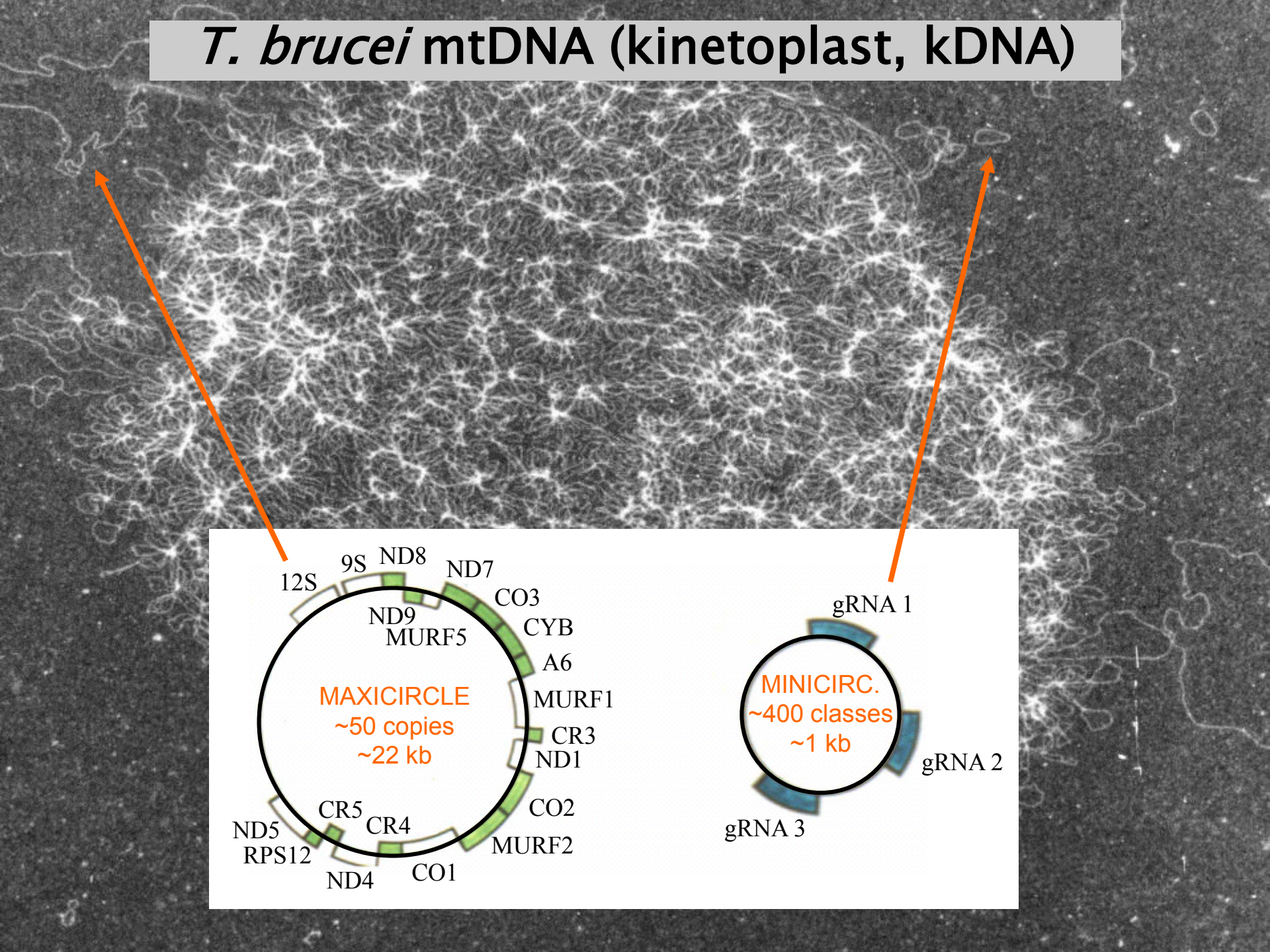
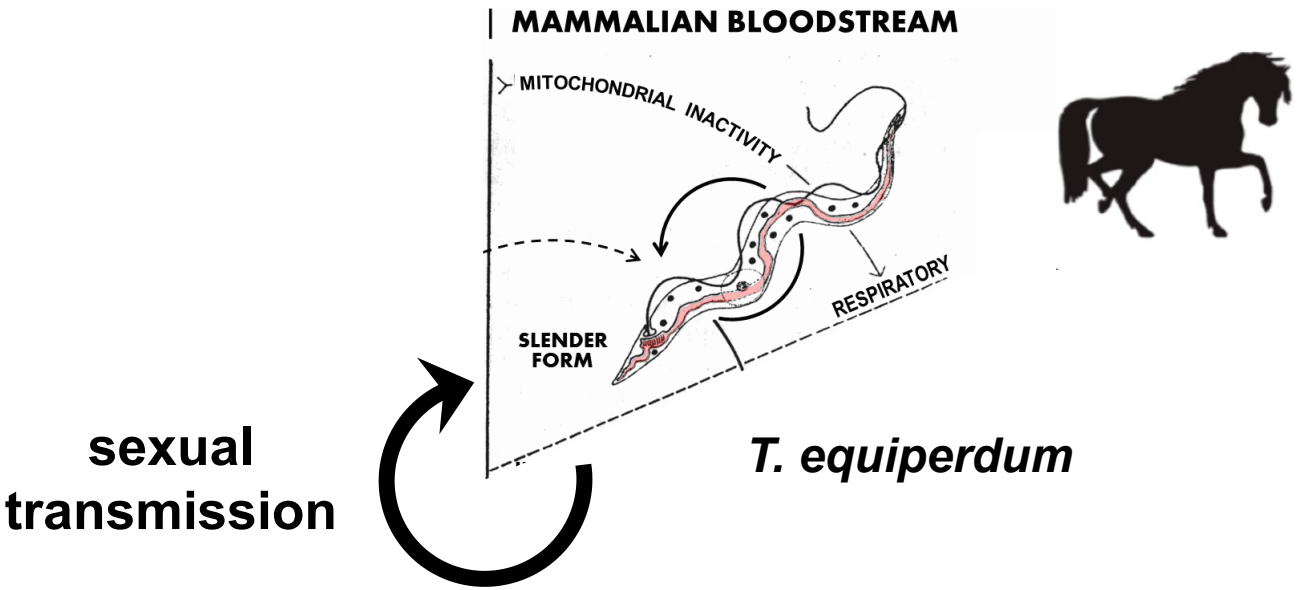
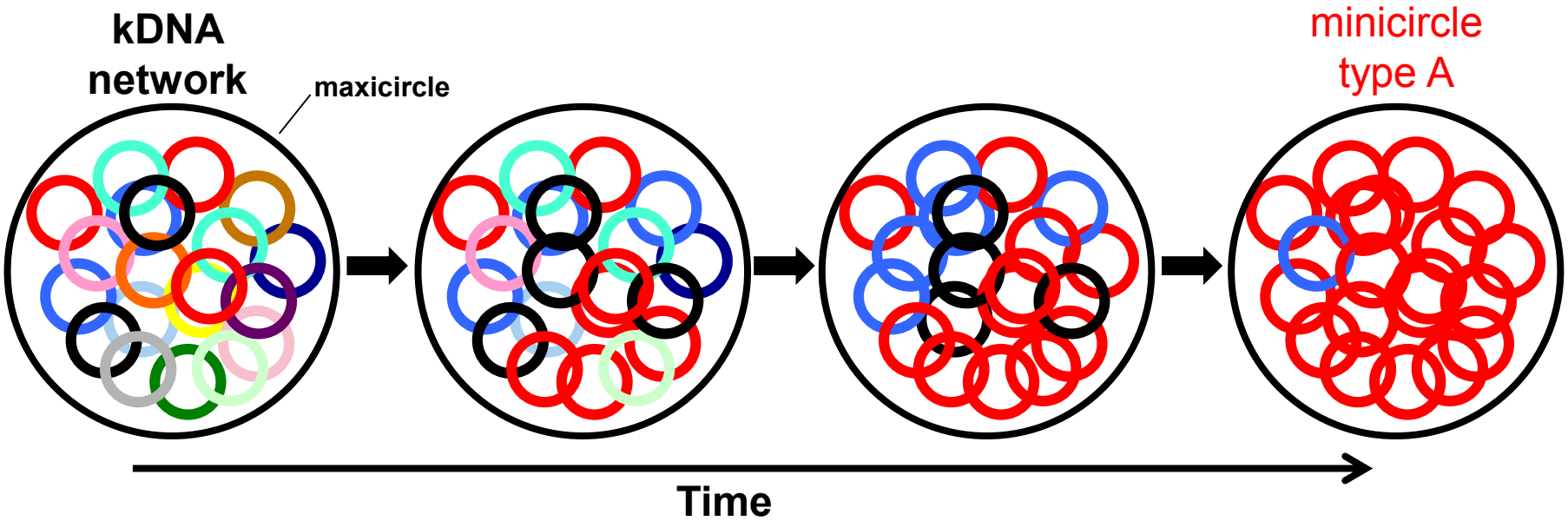


image: Hudson &Vinograd

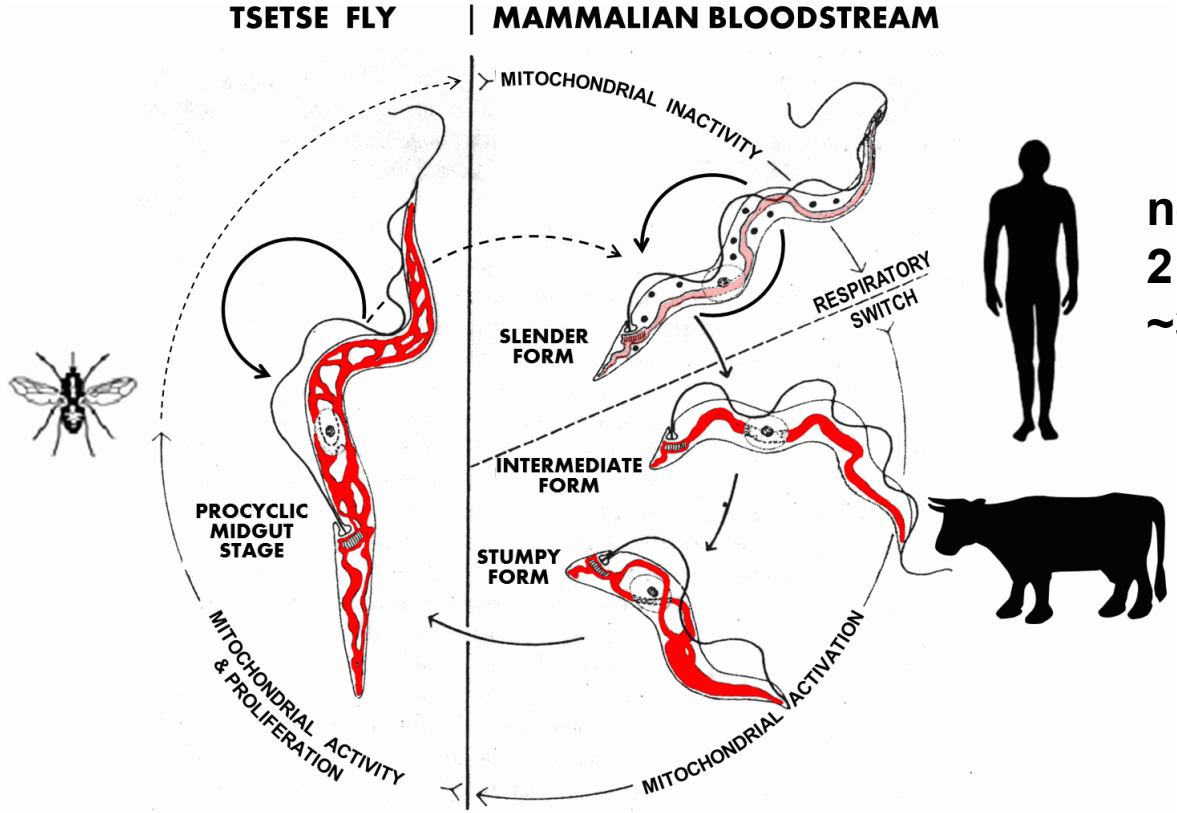
T. brucei mtDNA (kinetoplast, kDNA)



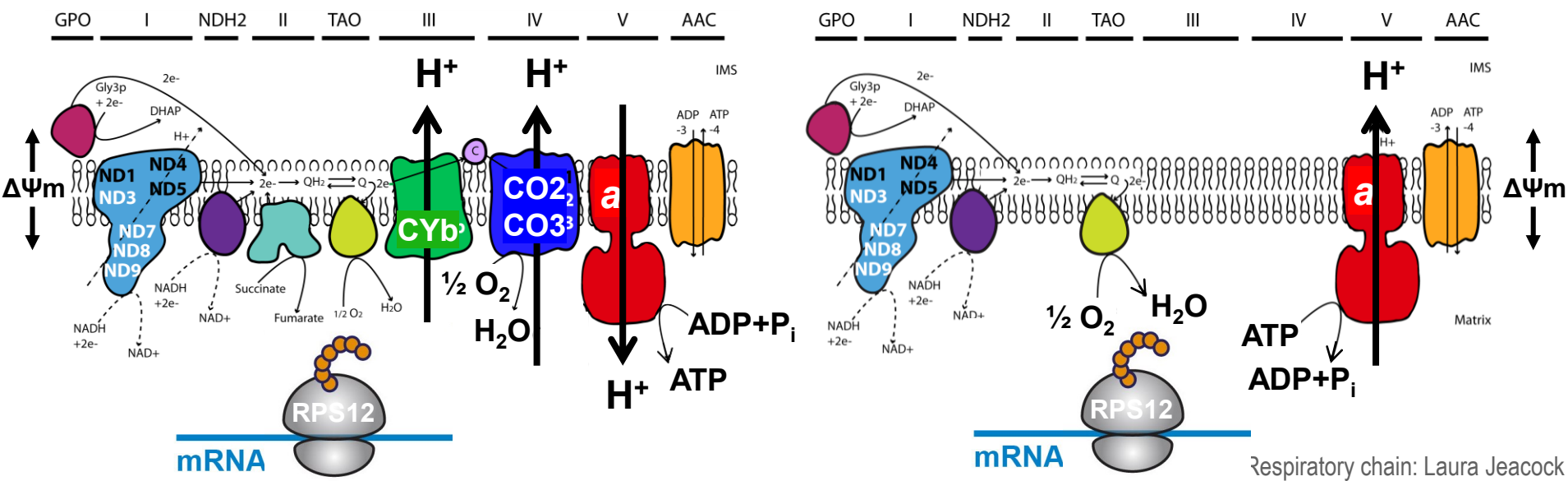

MAMMALIAN BLOODSTREAM
MITOCHONDRIAL INACTIVITY
SLENDER FORM
RESPIRATORY
sexual transmission
T. equiperdum


kDNA network
maxicircle
minicircle type A
Time

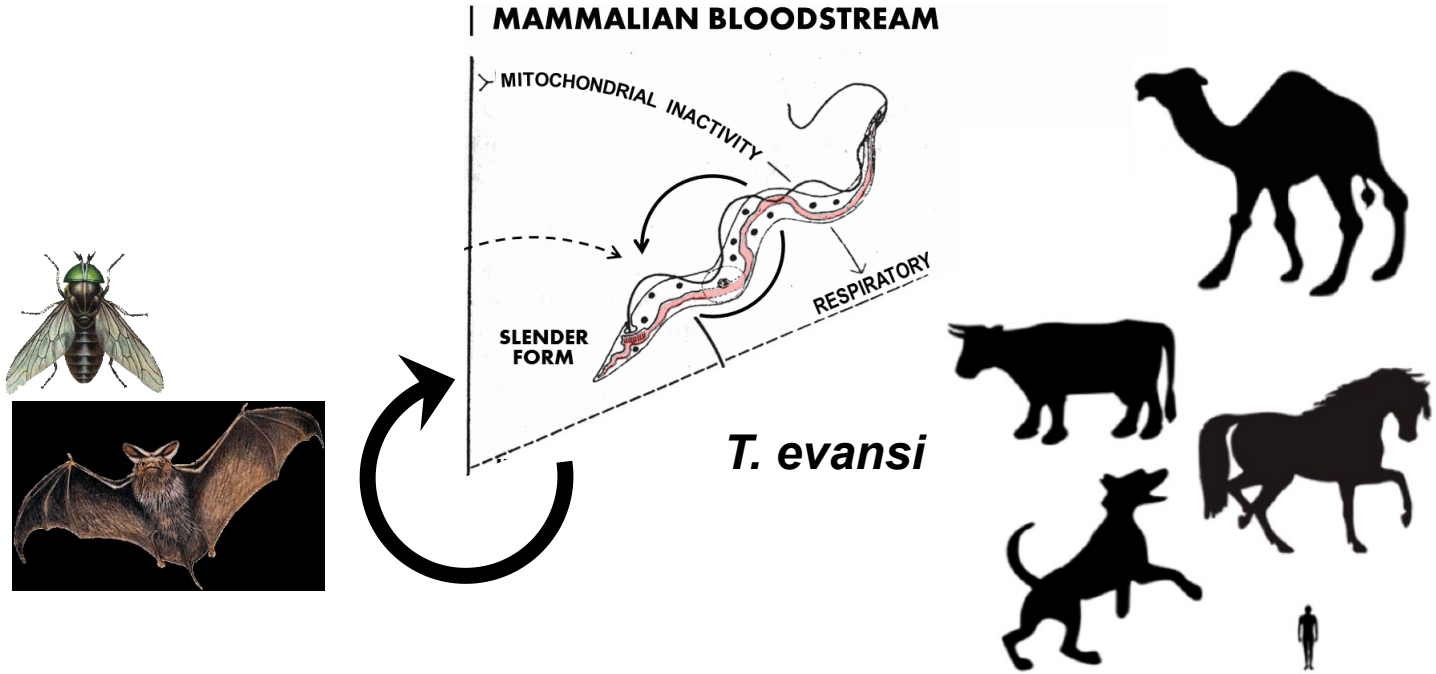
needed:
≥5 mt proteins
> 70 gRNAs



needed:
2 mt proteins
~30 gRNAs



Respiratory chain: Laura Jeacock


MAMMALIAN BLOODSTREAM
MITOCHONDRIAL INACTIVITY
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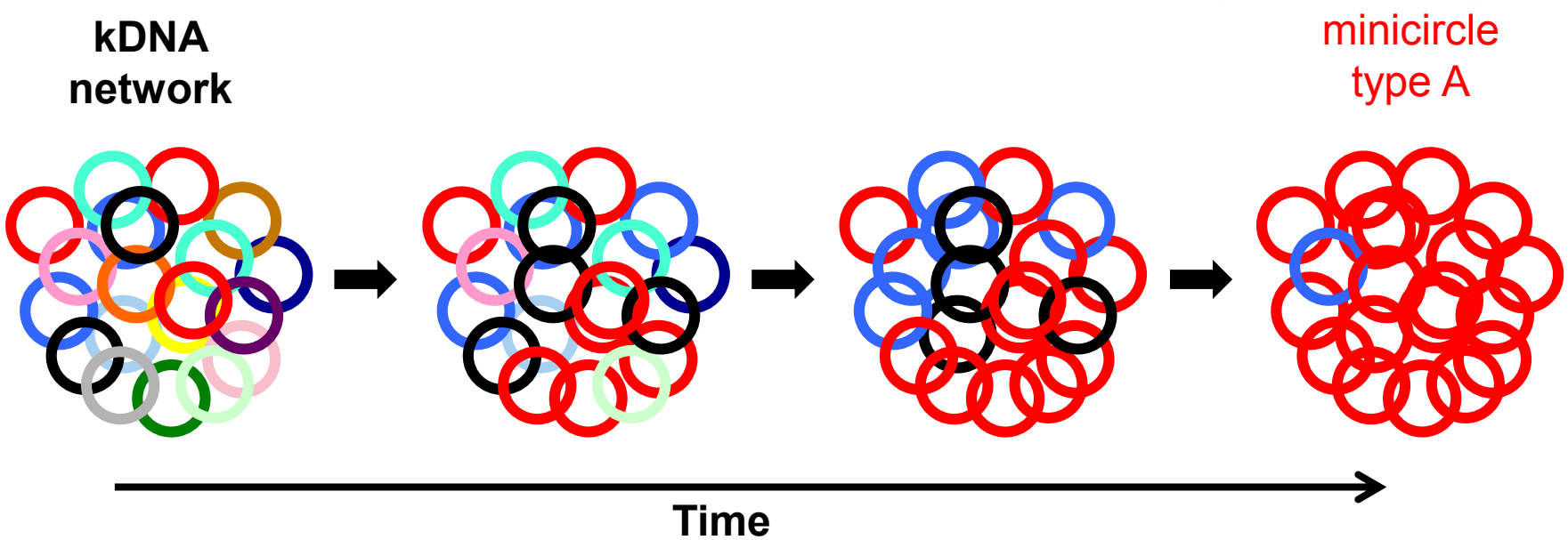
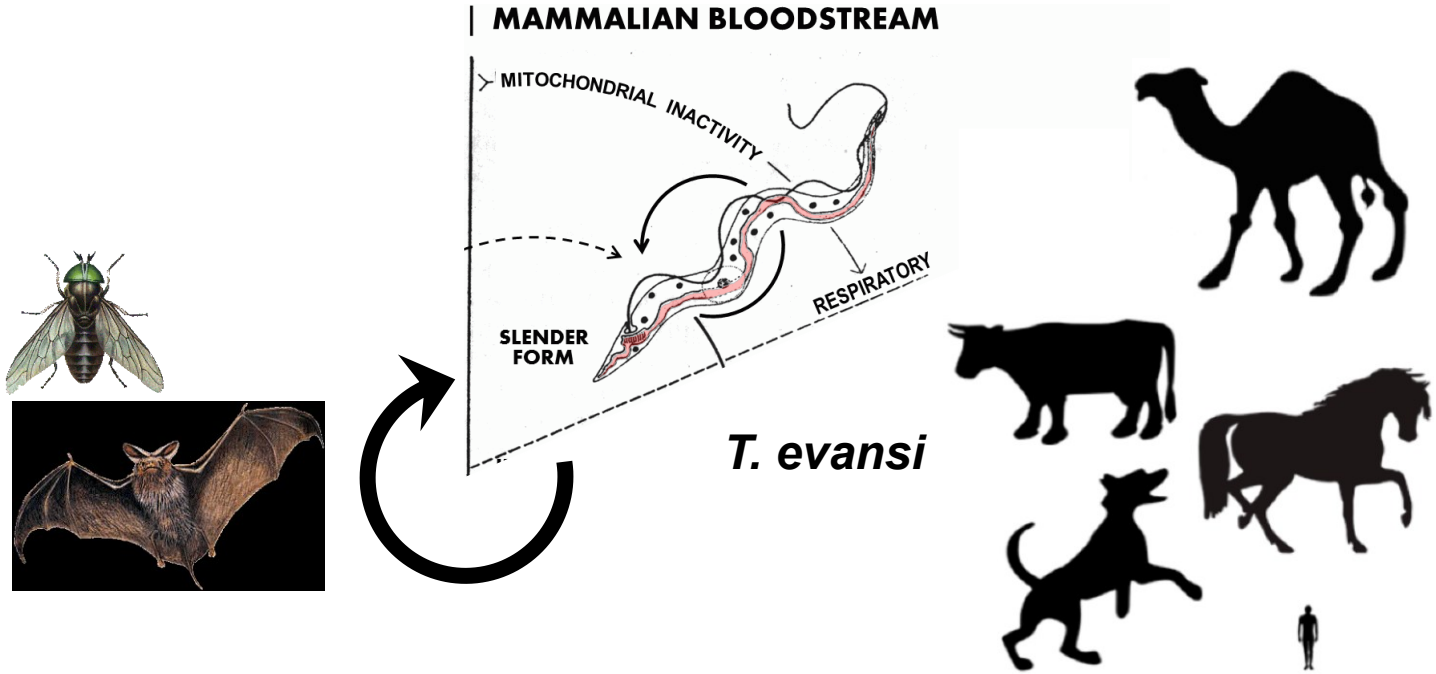
T. evansi


kDNA network
minicircle type A
Time


MAMMALIAN BLOODSTREAM
MITOCHONDRIAL INACTIVITY
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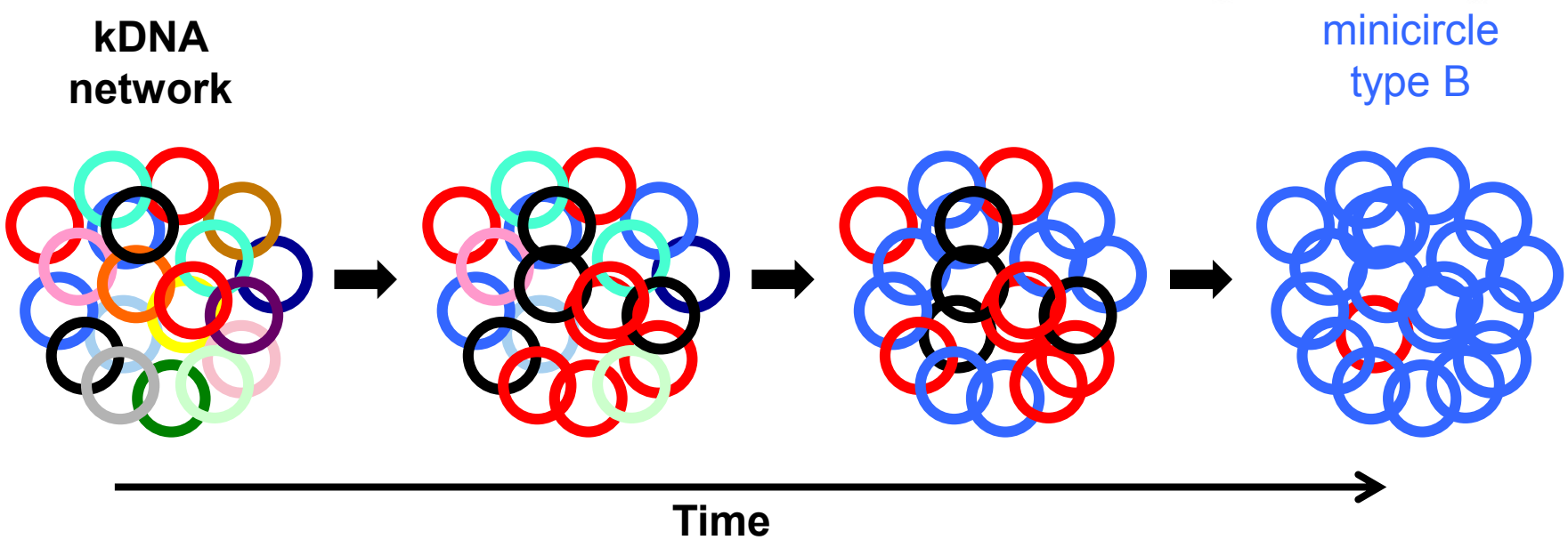
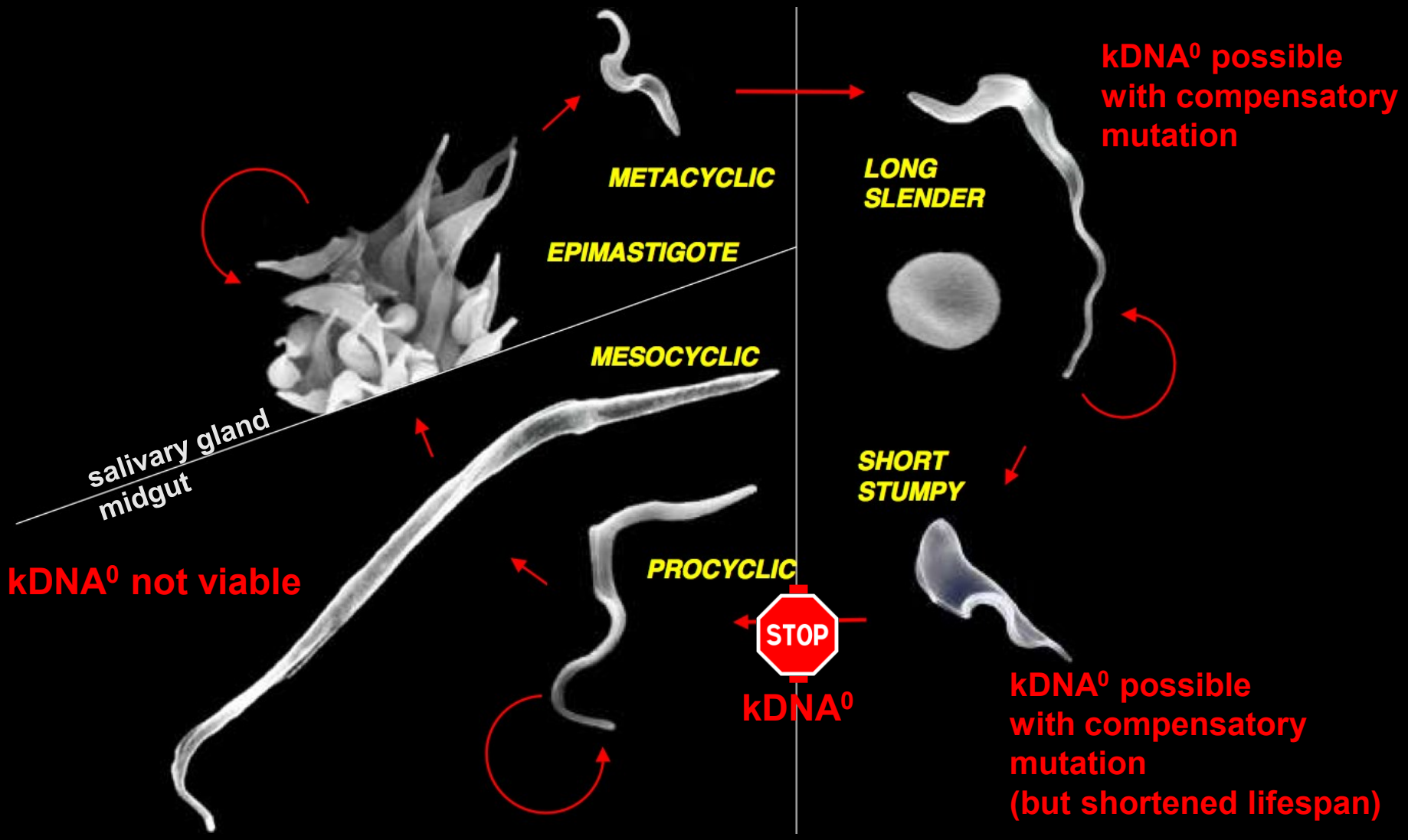
RESPIRATORY
T. evansi


kDNA network
minicircle type B
Time

kDNA function during the life cycle of *T. brucei*



tsetse fly

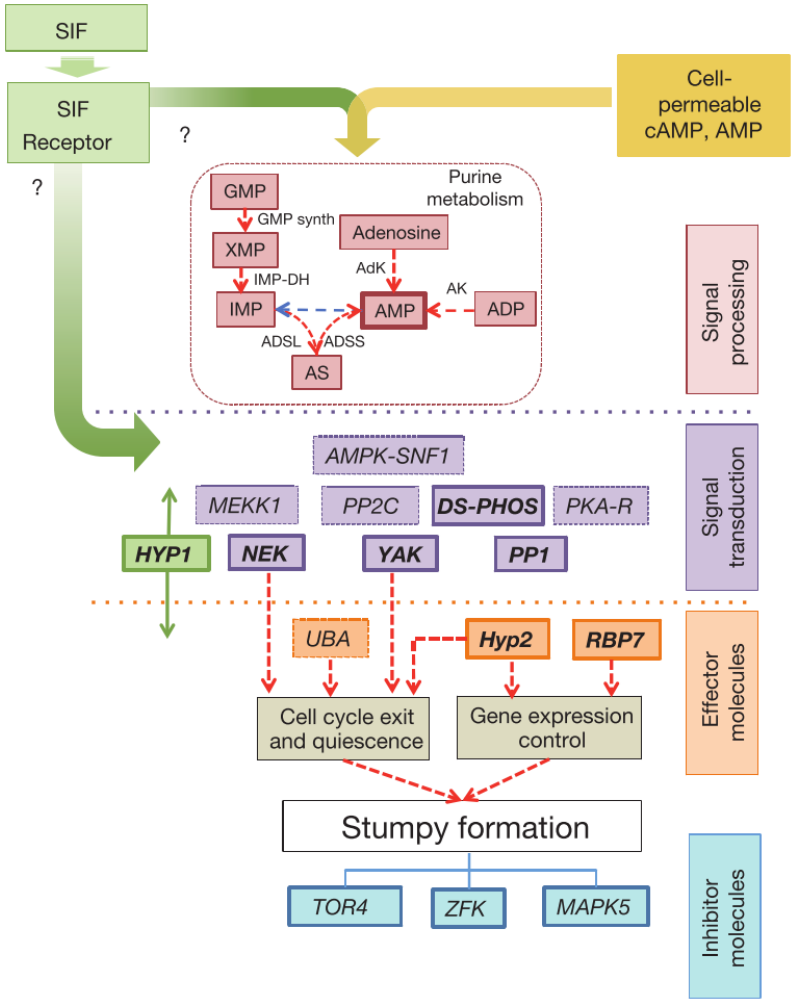
mammal

Image credit: Dave Barry, Glasgow

What is the cause of monomorphism in *T. evansi* / *T. equiperdum*?

Genome-wide dissection of the quorum sensing signalling pathway in *Trypanosoma brucei*

Binny M. Mony[1]*, Paula MacGregor[1]*, Alasdair Ivens[1], Federico Rojas[1], Andrew Cowton[1], Julie Young[1], David Horn[2] & Keith Matthews[1]



Mony *et al.*, *Nature* 2014

Summary Part 1

Evolution of *Trypanosoma (b.) evansi* and *T. (b.) equiperdum*

Development of stable tsetse-independent transmission

Factors favouring tsetse-independent transmission:

***Tev*:** **Monomorphism probably important**

→ Mutation in stumpy differentiation pathway?

Host able to tolerate high levels of parasitaemia

→ Camels, Asian buffaloes (Desquesnes *et al.* 2013)

***Teq*:** **Genital tropism (Biteau *et al.* 2016; Trindade *et al.* 2016)**

Development of dyskinetoplastidy

Mutations in ATPase subunit gamma obviate the need for functional kDNA (Dean *et al.* 2013)

Loss of functional kDNA results in loss of tsetse infectivity

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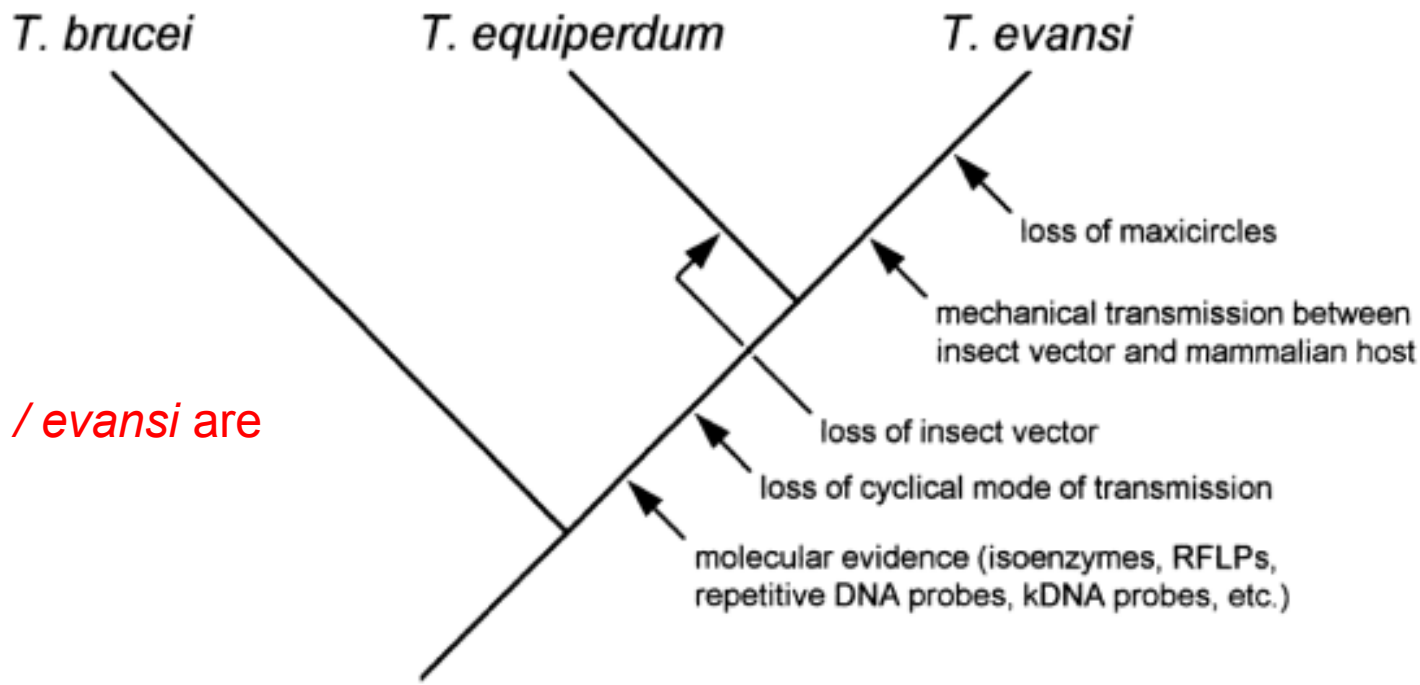
How does the *T. equiperdum* strain responsible for the Italian 2011 outbreak fit in?

How often did *T. equiperdum* / *T. evansi* evolve from *T. brucei*?

Trypanosoma evansi and *T. equiperdum*: distribution, biology, treatment and phylogenetic relationship (a review)

Veterinary Parasitology 79 (1998) 95–107

Reto Brun[a,*], Hermann Hecker[a], Zhao-Rong Lun[b]



T. equiperdum / evansi are monophyletic

Opinion TRENDS in Parasitology Vol.21 No.7 July 2005

Full text provided by www.sciencedirect.com
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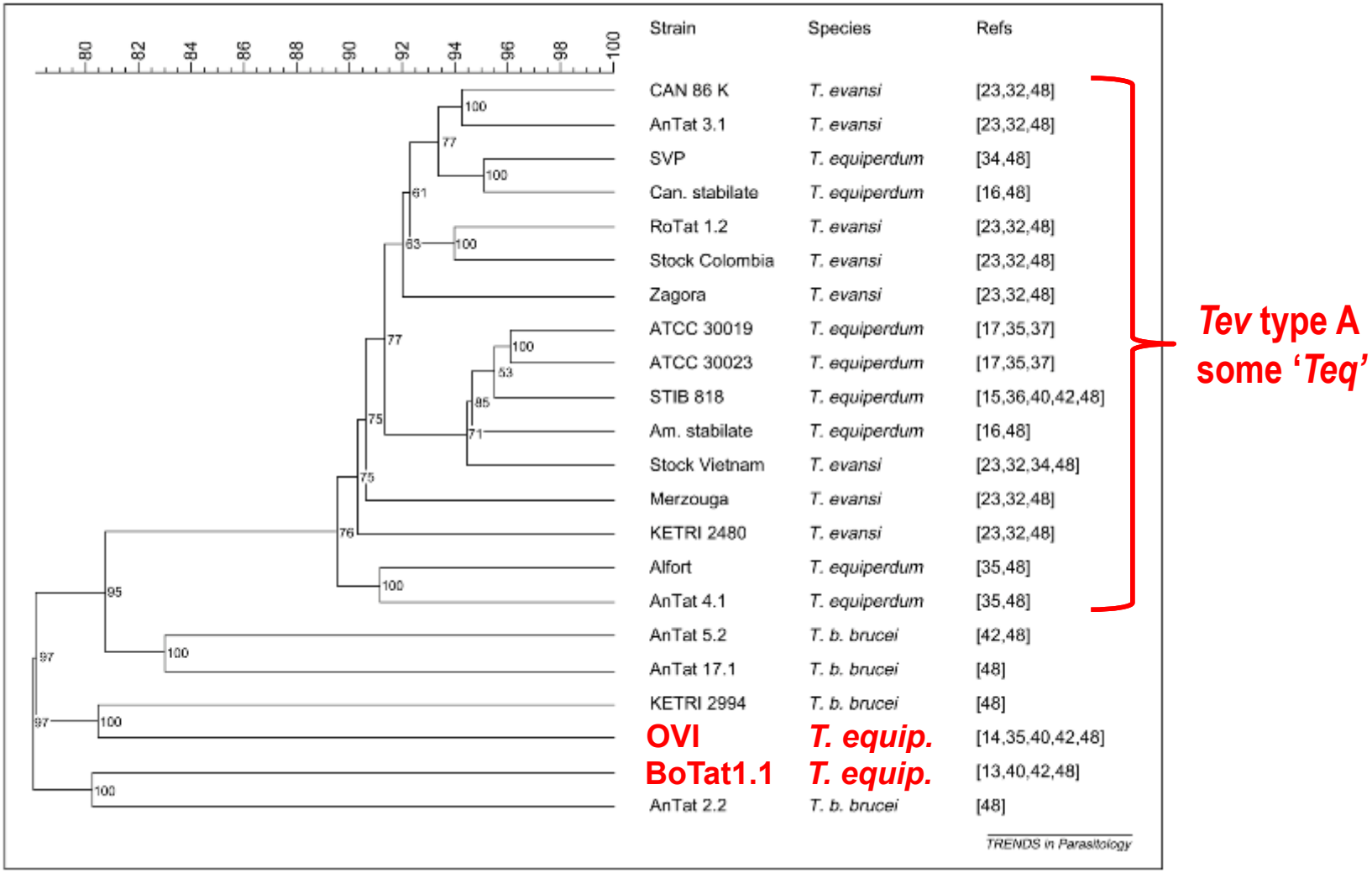
Trypanosoma equiperdum: master of disguise or historical mistake?

Filip Claes[1,2], Philippe Büscher[2], Louis Touratier[3] and Bruno Maria Goddeeris[1]



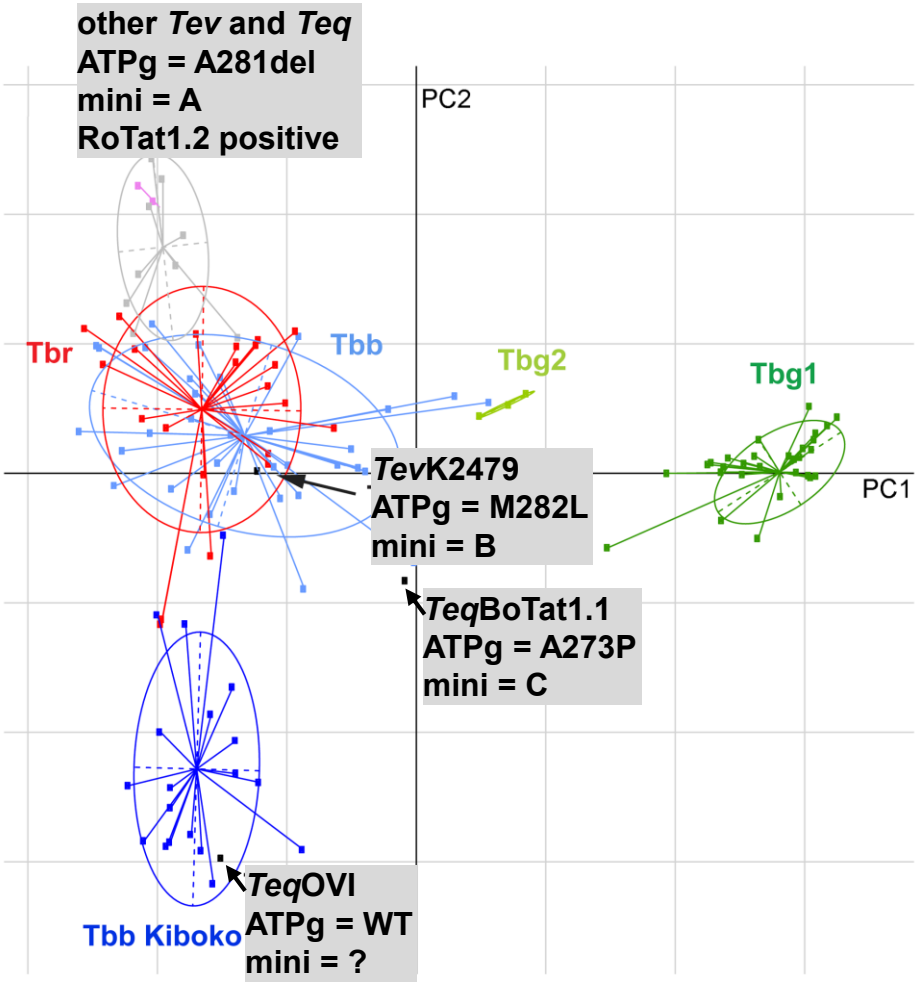
Genome and Phylogenetic Analyses of *Trypanosoma evansi* Reveal Extensive Similarity to *T. brucei* and Multiple Independent Origins for Dyskinetoplasty

PLOS | NEGLECTED TROPICAL DISEASES

January 2015 | Volume 9 | Issue 1 | e3404

Jason Carnes[1], Atashi Anupama[1], Oliver Balmer[2], Andrew Jackson[3], Michael Lewis[4], Rob Brown[1], Igor Cestari[1], Marc Desquesnes[5,6], Claire Gendrin[1], Christiane Hertz-Fowler[7], Hideo Imamura[8], Alasdair Ivens[9], Luděk Kořený[10,11¤], De-Hua Lai[10,11,12], Annette MacLeod[13], Suzanne M. McDermott[1], Chris Merritt[1], Severine Monnerat[1], Wonjong Moon[1], Peter Myler[1], Isabelle Phan[1], Gowthaman Ramasamy[1], Dhileep Sivam[1], Zhao-Rong Lun[12]*, Julius Lukeš[10,11,14]*, Ken Stuart[1,15]*, Achim Schnaufer[9,16]*

suggest at least four independent origins for *T. equiperdum / evansi*



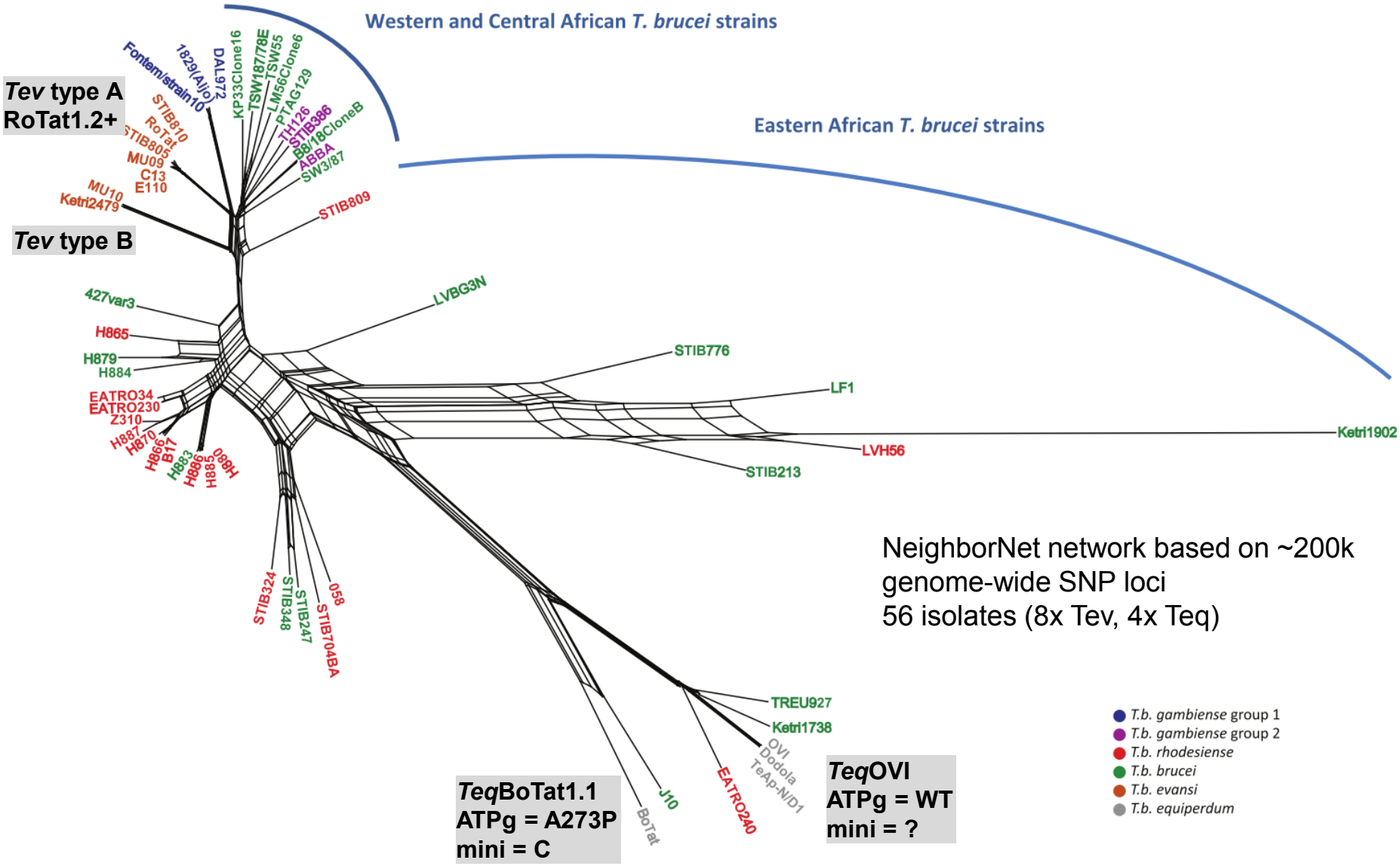
Principal component analysis of microsatellite data

GBE

Genome Biol. Evol. 9(8):1990–1997.

Genome-Wide SNP Analysis Reveals Distinct Origins of *Trypanosoma evansi* and *Trypanosoma equiperdum*

Bart Cuypers[1,2], Frederik Van den Broeck[1], Nick Van Reet[1], Conor J. Meehan[1], Julien Cauchard[3], Jonathan M. Wilkes[4], Filip Claes[5], Bruno Goddeeris[6], Hadush Birhanu[7], Jean-Claude Dujardin[1,8], Kris Laukens[2], Philippe Büscher[1], and Stijn Deborggraeve[1,*]



NeighborNet network based on ~200k genome-wide SNP loci
56 isolates (8x Tev, 4x Teq)

2011 Italian Dourine Outbreak

Region	Province	Equids		
		Present	*Positive*	*With symptoms*
Sicilia	Catania	5	1	0
Sicilia	Catania	27	1	1
Campania	Napoli	3	1	0
Campania	Napoli	8	2	0
Campania	Napoli	17	5	5
Campania	Caserta	59	9	1
Puglia	Bari	49	1	1
		168	**20**	**8**

Slide from Ilaria Pascucci

Preliminary molecular characterization

- ICT 2011 tested **negative** for all maxicircle kDNA PCR
- ICT 2011 tested **negative** to the PCR for RoTat1.2 VSG
  - *T. equiperdum* OVI tested **positive** for all maxicircle kDNA PCR
  - *T. equiperdum* OVI tested **negative** to the PCR for RoTat1.2 VSG
  - *T. evansi* (Kazakistan) tested **negative** for all maxicircle kDNA PCR
  - *T. evansi* (Kazakistan) tested **positive** to the PCR for RoTat1.2 VSG

Maurilia Marcacci, Marco Di Domenico, Ilaria Pascucci, Cesare Cammà
IZSAM, Teramo, Italy

Slide from Ilaria Pascucci

Phylogenetic analysis of ICT2011 and other isolates using microsatellite markers

15 markers; 133 isolates: 73x Tbb/Tbr, 48x Tev, 12x Teq

Achim Schnaufer, Julie Wallis, Gloria Amegatcher, Caroline Dewar, Alasdair Ivens, Keith Matthews, Norah Saarman, Kirstin Dion, Christine M Kamidi, Adalgisa Caccone, Maurilia Marcacci, Marco Di Domenico, Ilaria Pascucci, Cesare Cammà

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Constentin Dieme
Brice Rotureau

Liverpool School of Tropical Medicine

Aitor Casa-Sanchez
Alvaro Acosta-Serrano

Image: Ilaria Pascucci