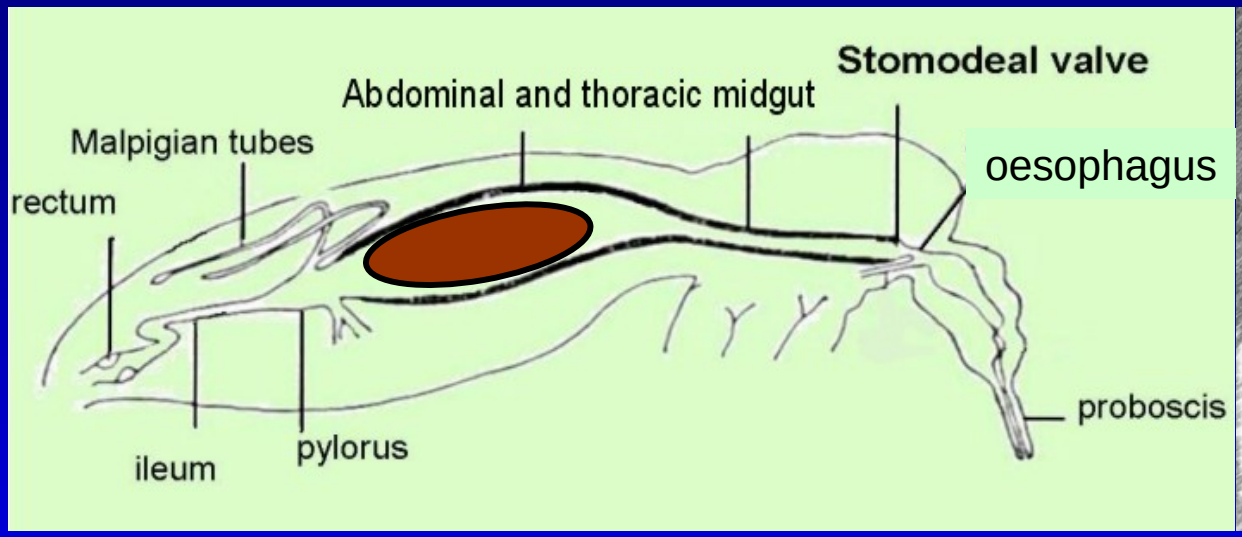
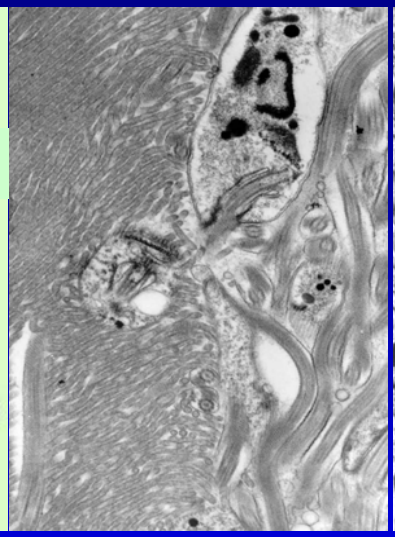
Petr Volf: Critical steps during *Leishmania* development in sand fly vector: midgut attachment





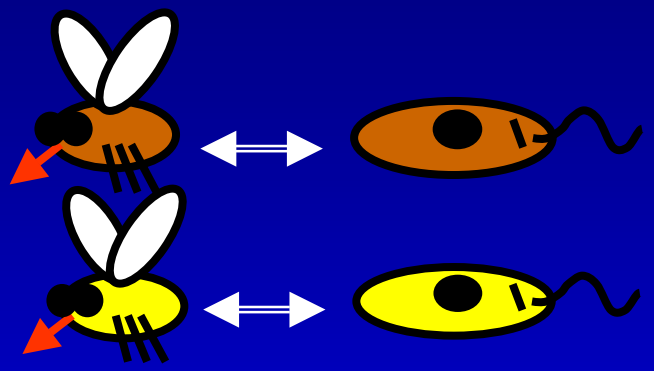
1. Early stage: peritrophic matrix, activity of proteases and antimicrobial peptides
2. Establishment of the infection:
   correlated with ability to attach to midgut epithelium
3. Late stage: mechanical block of the cardia, damage of the stomodeal valve

Establishment of *Leishmania* infection
Specificity of sand fly – *Leishmania* interaction

Some sand fly species
specific for *Leishmania* they transmitt

Phlebotomus papatasi - L. major
Phlebotomus sergenti - L. tropica

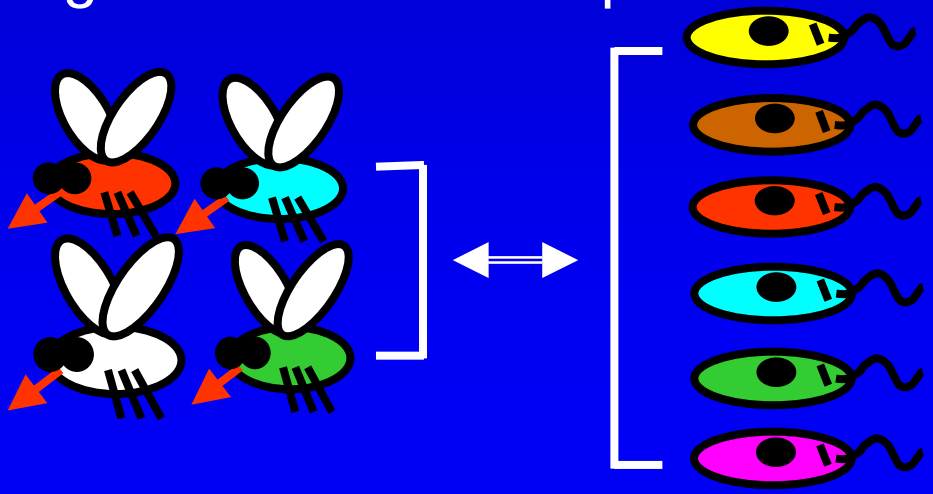
= specific vectors



Others susceptible for a broad range of *Leishmania* species

Lu. longipalpis, *P. argentipes*
P. halepensis, *P. arabicus*

= permissive vectors



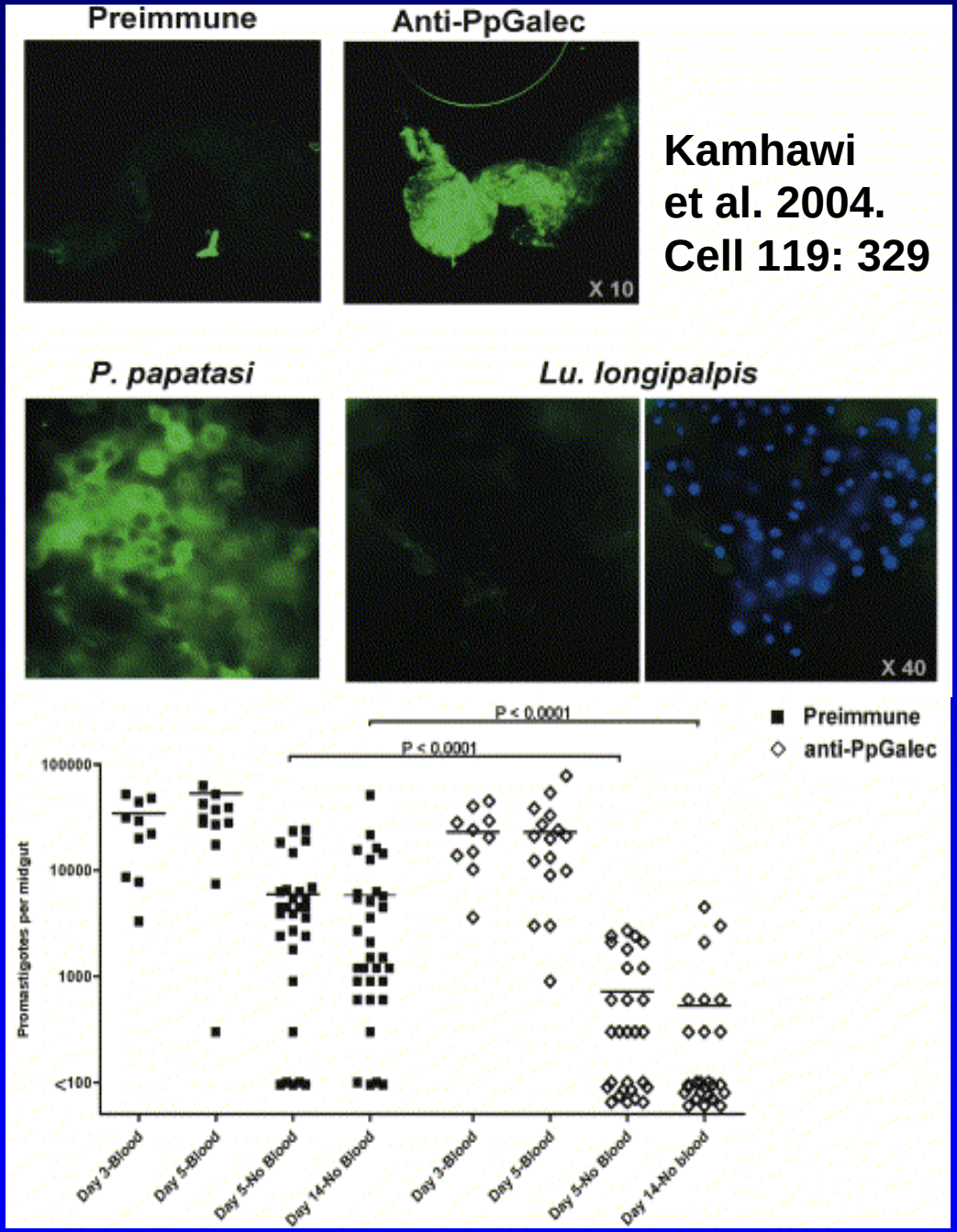
Attachment in specific vectors

promastigotes must attach to survive defecation

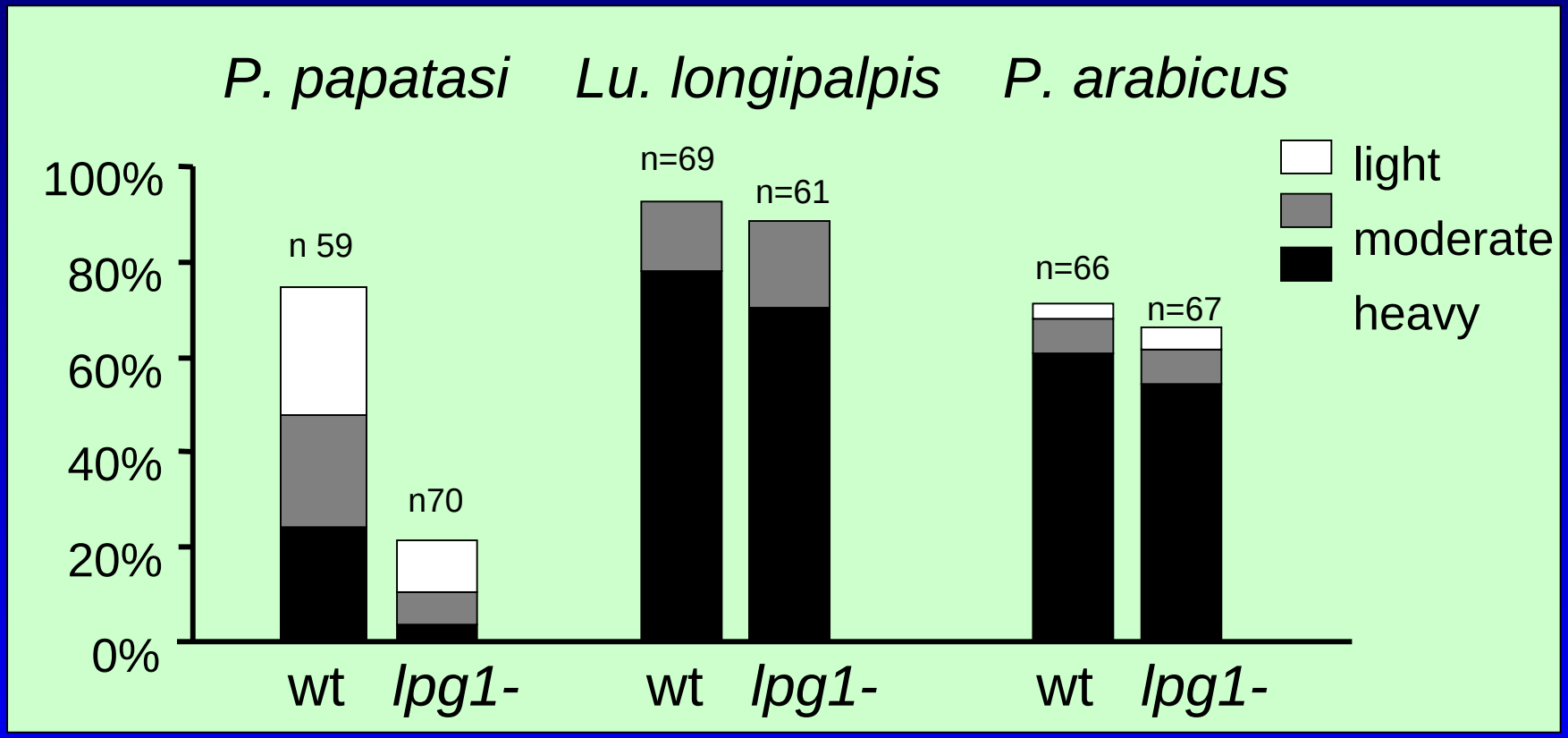
P. papatasi – L. major

Parasite LPG is essential
(Pimenta et al. 1992, 1994)

LPG binds to receptor on midgut microvilli
P. papatasi galectin
(Kamhawi et al. 2004. Cell)



Attachment in permissive vectors: LPG is not required

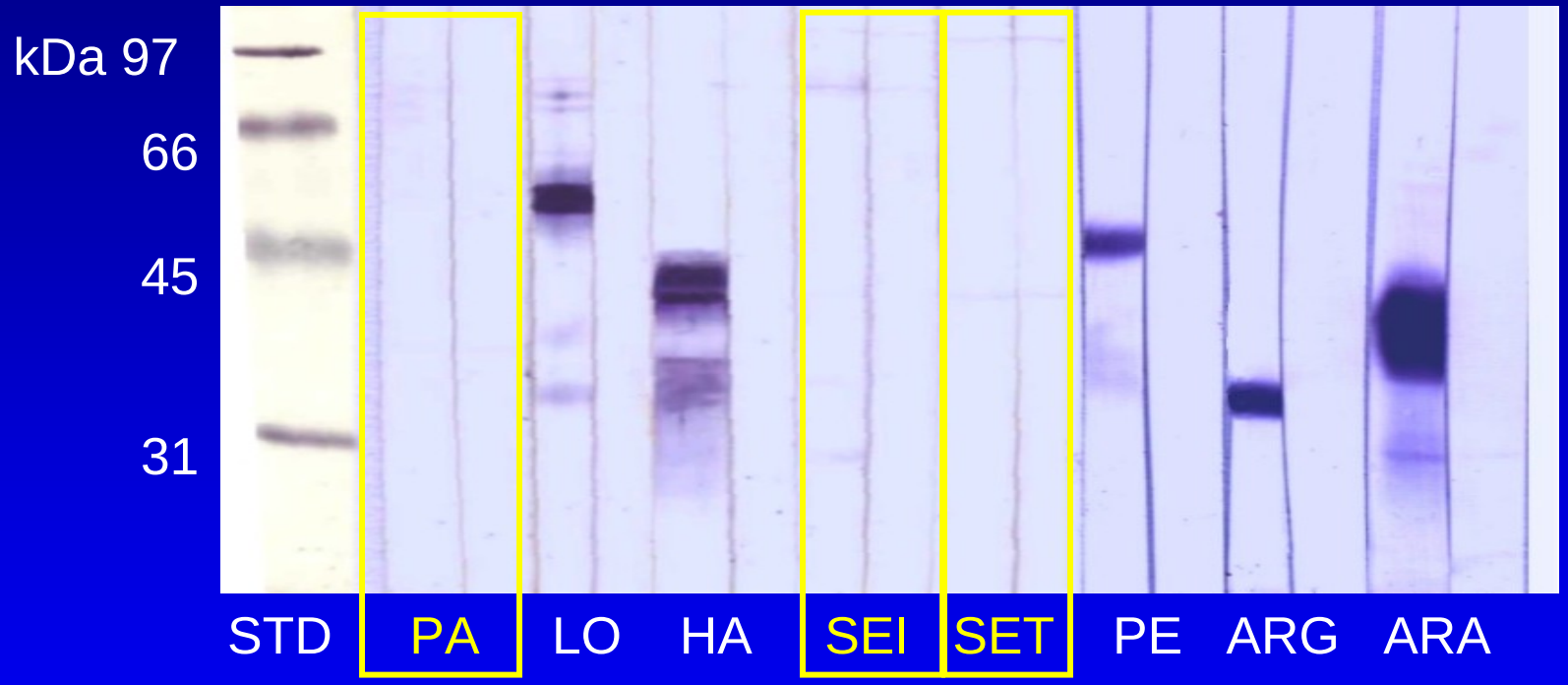


lpg1- mutants develop poorly in *P. papatasi*
but vigorously in *Lu. longipalpis* and *P. arabicus*

Myskova et al. 2007. Microb Infect.

O-glycosylation: in permissive species only, not in specific vectors

reaction of midgut lysates with HPA

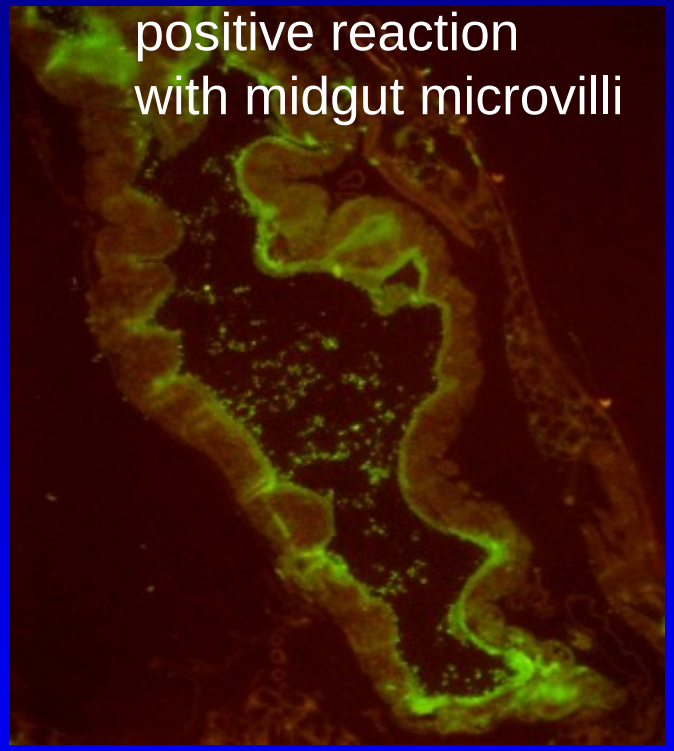


O-glycosylated proteins present in various permissive vectors, but not in *P. papatasi* and *P. sergenti*

Myskova et al. 2007. Microb Infect.

Permissive vectors: O-glycosylated epitopes are present on the luminal surface of the midgut

Sections of *Lutzomyia longipalpis* abdomen

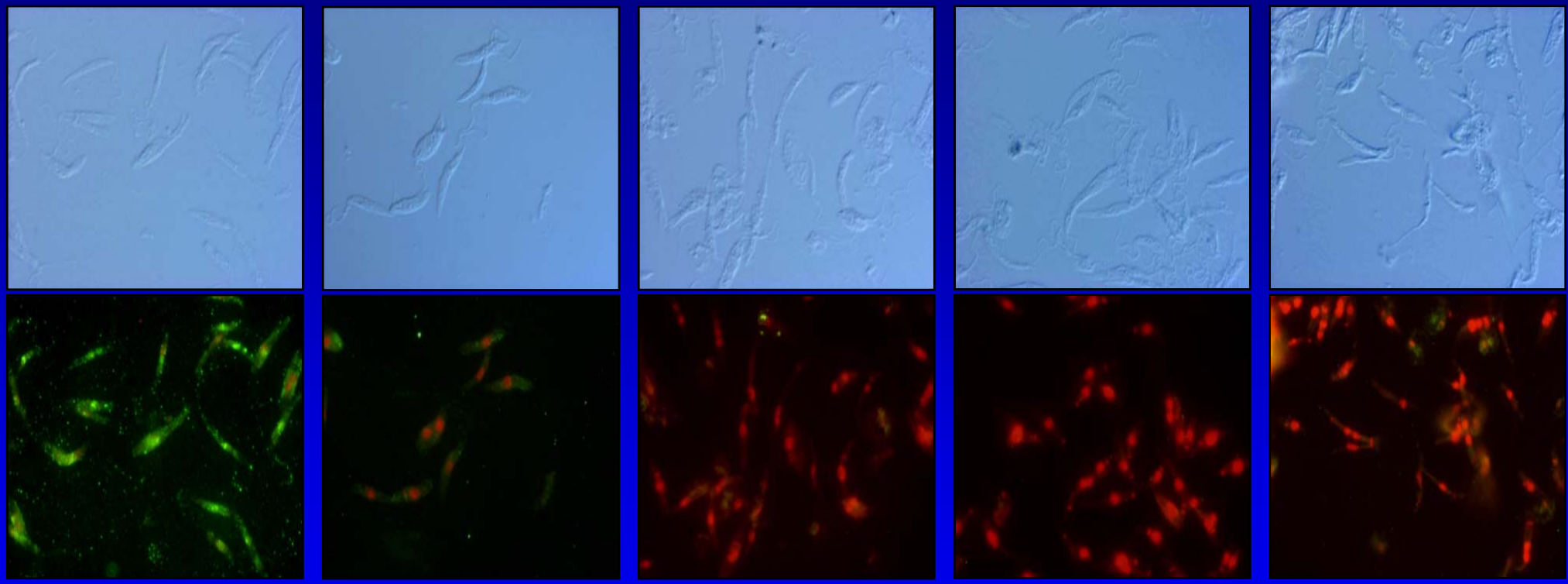


HPA / FITC

(HPA / FITC + NAcGal)

Myskova et al. 2007. Microb Infect.

Permissive vectors: midgut O-glycosylated components bind to *Leishmania* in-vitro



P. halepensis midgut lysate + HPA / FITC

GalNAc preincubated with *P. halepensis* lysate or *Leishmania*

P. papatasi midgut lysate + HPA / FITC

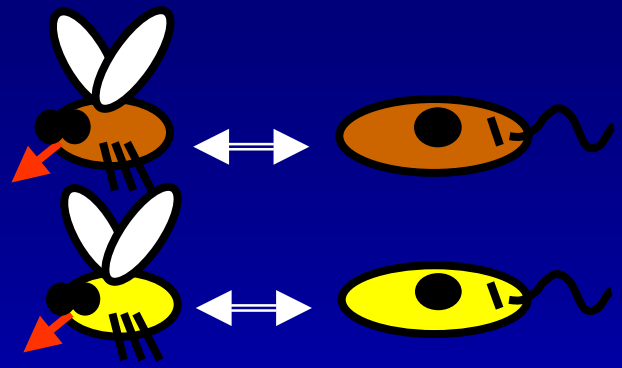
HPA / FITC

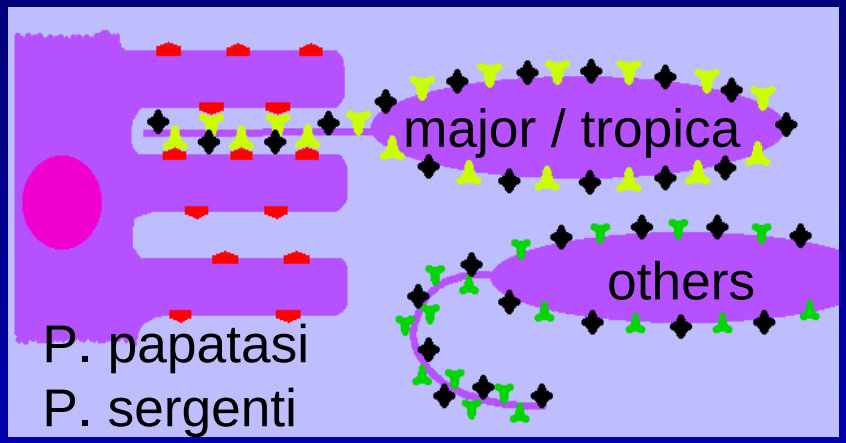
Myskova et al. 2007. Microb Infect.

Different mechanisms of attachment:

1

Specific vectors

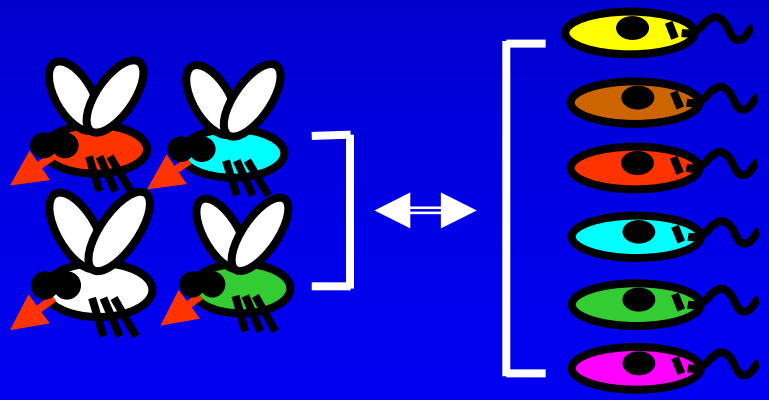


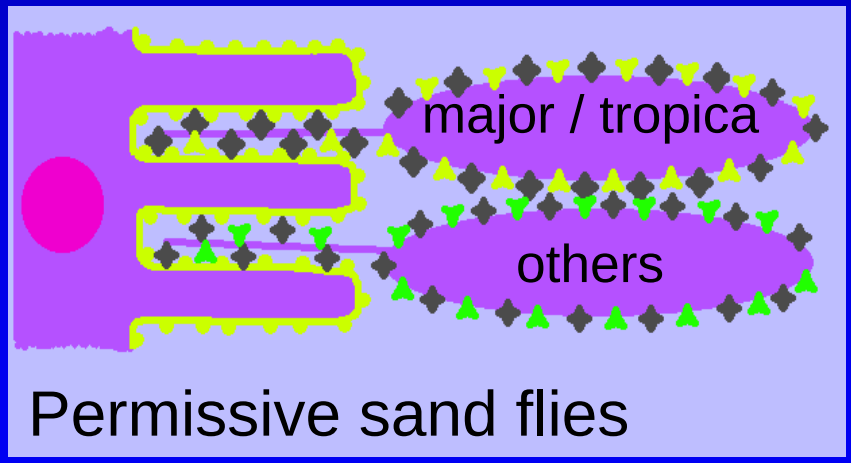


No O-glycosylation:
Attachment by LPG receptor. Coevolution: selection of the unique, highly substituted LPG of *L. major* and *L. tropica*. LPG essential.

2

Permissive vectors





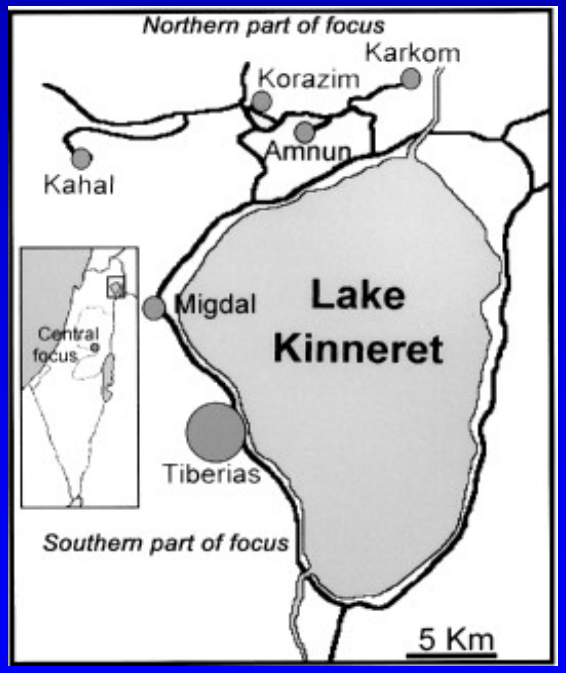
O-glycosylated epitopes: Attachment by another mechanism, LPG is not required.

Volf and Myskova 2007. Trends Parasitol

Transmission cycles of *Leishmania tropica* in Israel

Rural foci around Lake Kinneret (Sea of Galilee)
Rock hyraxes (Procavia capensis) incriminated as reservoir hosts

Jacobson et al., 2003. J Infect Dis

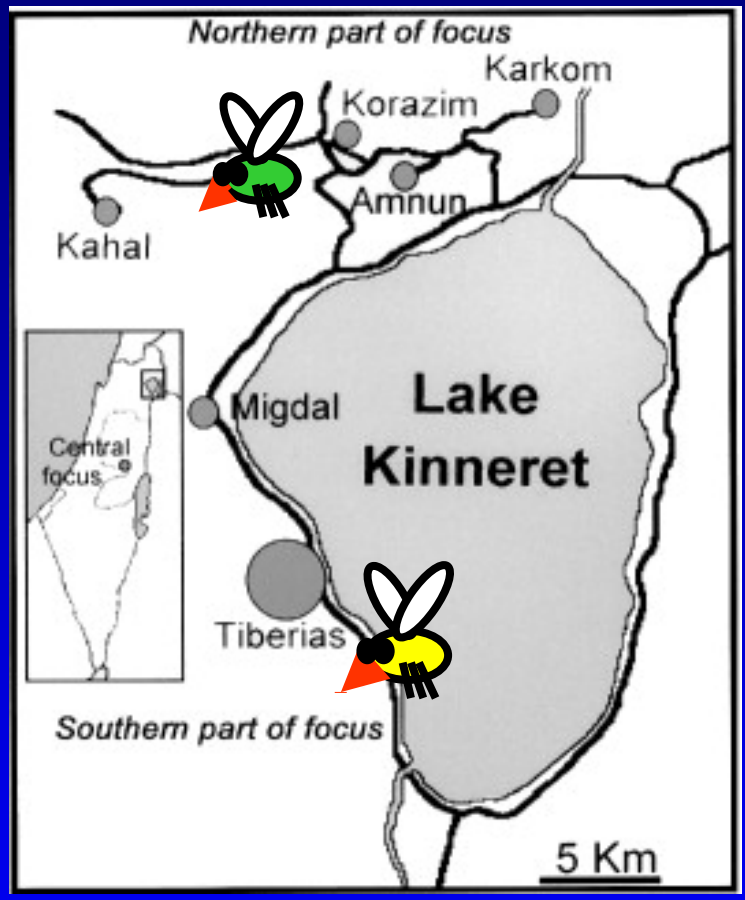


Leishmania tropica in Israel: two types of foci

1. Foci with typical vector *P. sergenti*

2. Northern focus in Galilee region
P. sergenti present (24%)
but vector is *P. arabicus* (20%)
5% positivity of *P. arabicus*

Jacobson et al., 2003. J Infect Dis

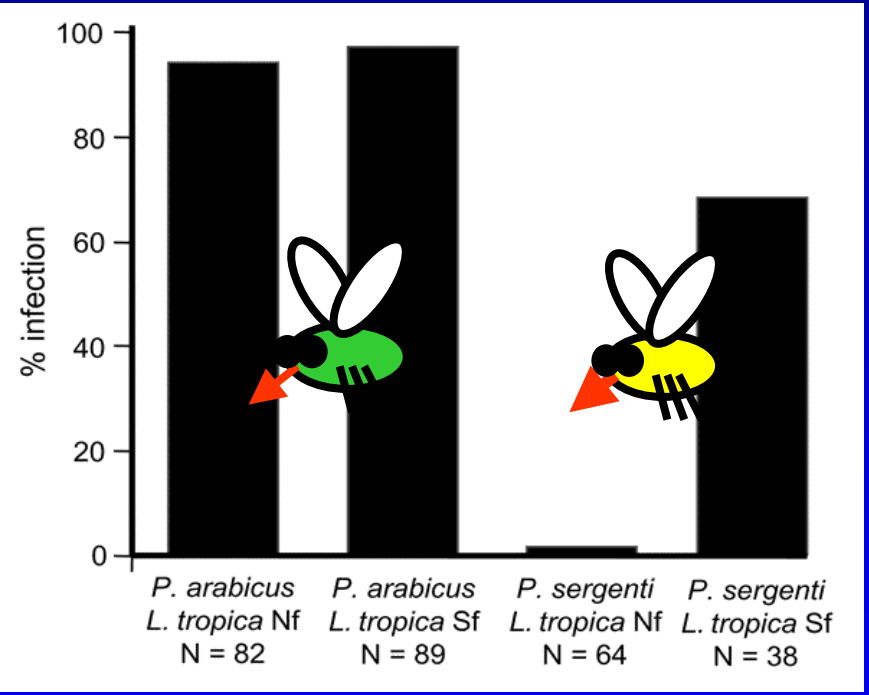


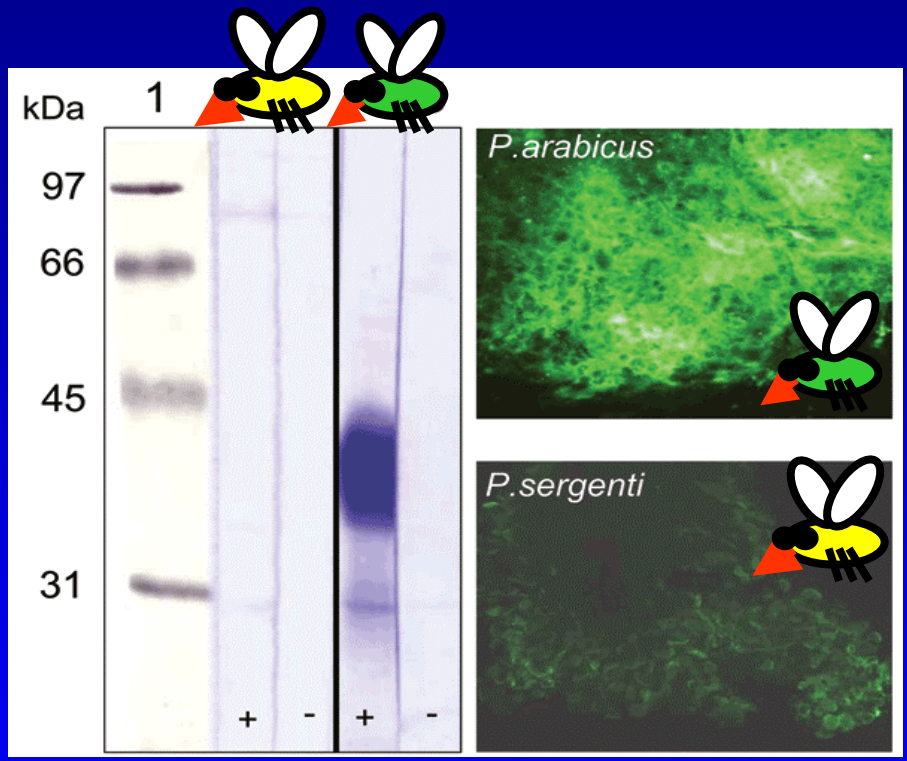
Vectorial competence of *P. arabicus* confirmed by experimental infections

Svobodova et al. 2006. Microbes and Infection

Leishmania tropica in Israel: two types of foci

LPG of Southern form: „typical“ = side chains with terminal Glc or Ara
LPG of Northern form: terminal Gal not capped with Glc *(Soares et al., 2004)*





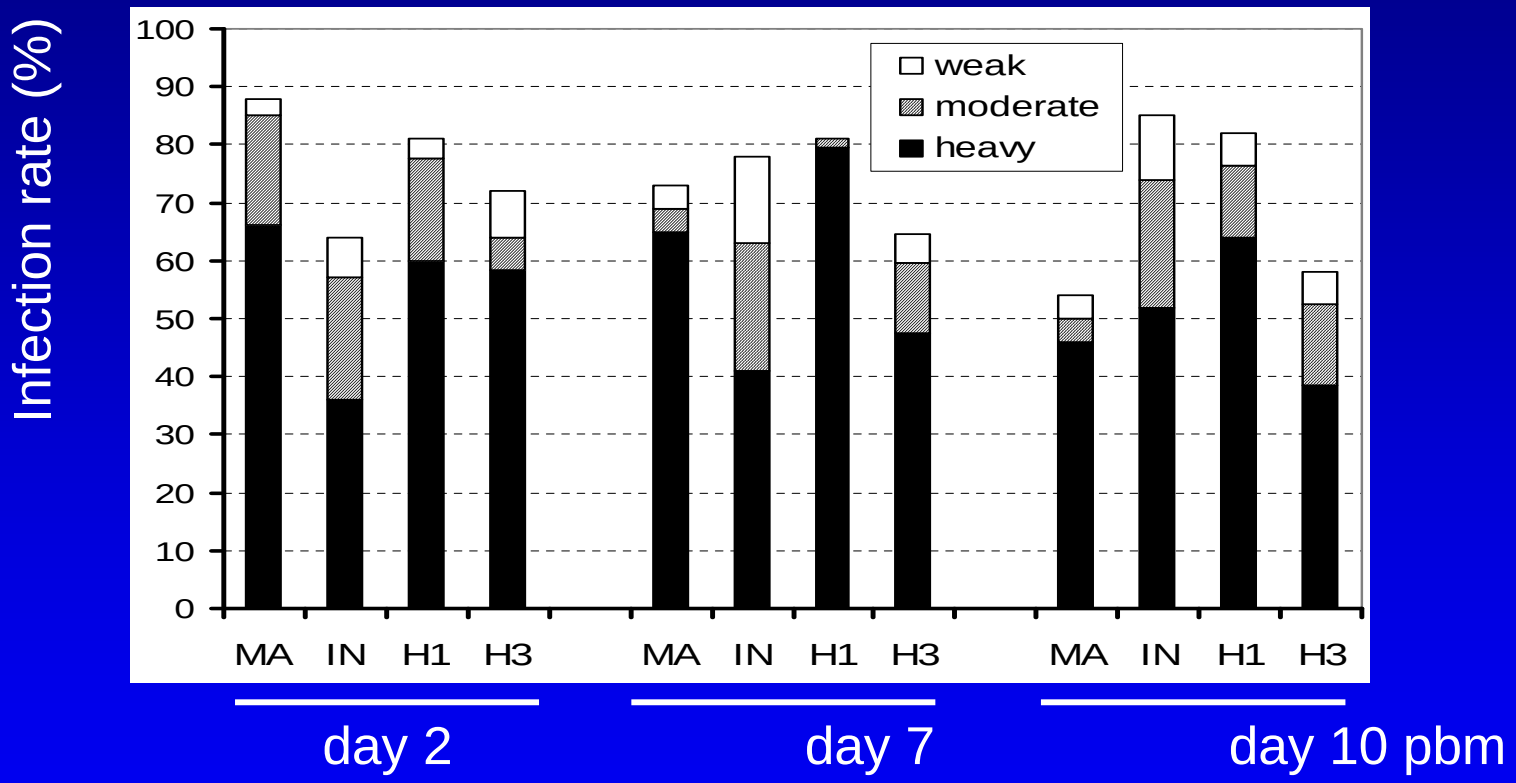
P. arabicus: O-glycosylated midgut epitopes, permisive

P. sergenti: no O glycosylation, specific for L. tropica with typical LPG

Svobodova et al. 2006. Emerg Infect Dis

Development of *Leishmania major/L. infantum* hybrids in various sand flies

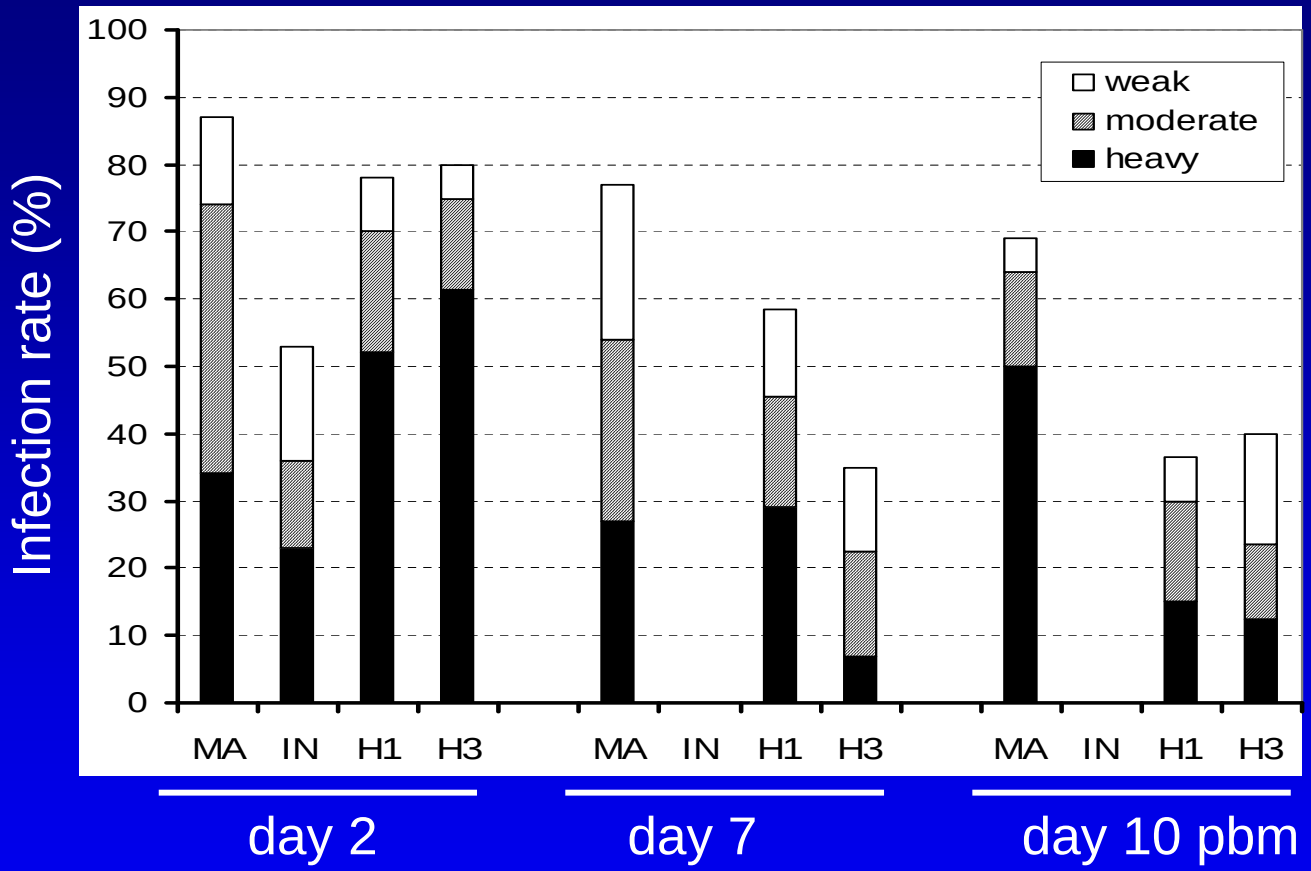
Leishmania development in *Lutzomyia longipalpis*

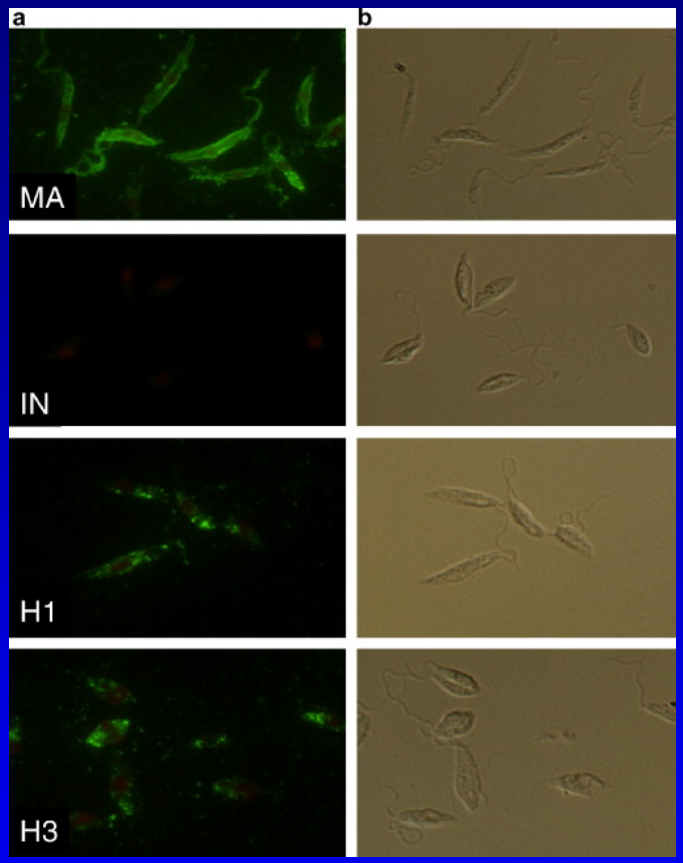


In permissive vector *L. longipalpis* all parasites developed well
LPG is not required

Volf et al. 2007. Int J Parasitol

Development of *Leishmania* hybrids in *Phlebotomus papatasi*



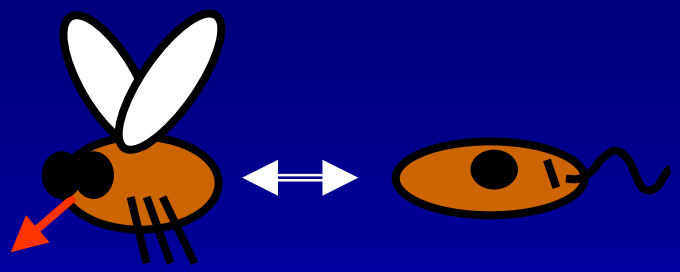


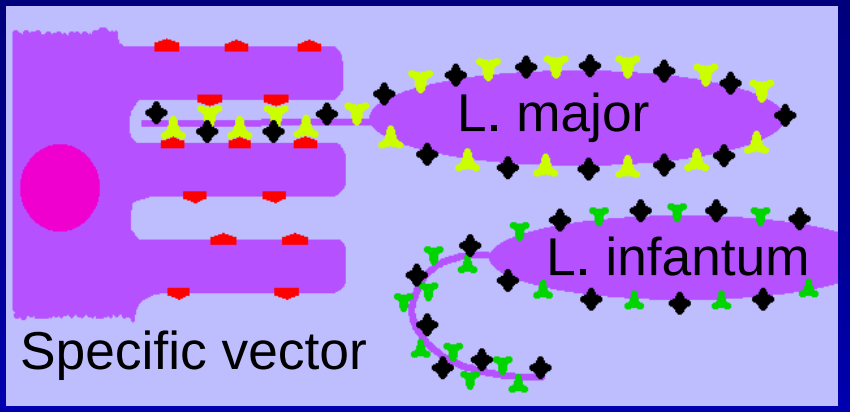
Hybrids attach in *P. papatasi* midgut and develop late stage infections.
Hybrids express *L. major* LPG – enhanced fitness in this vector

Volf et al. 2007. Int J Parasitol

Specific versus premissive vectors

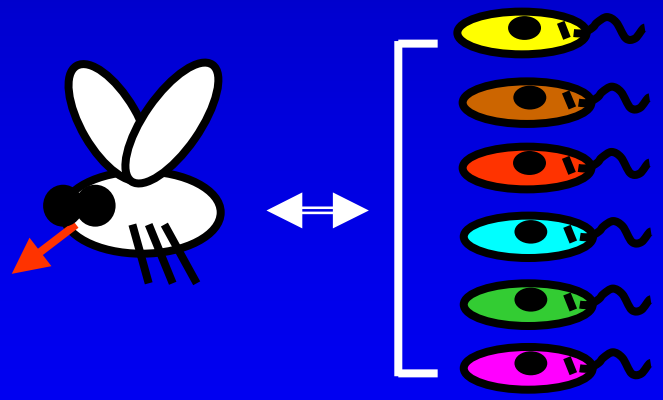
P. papatasi

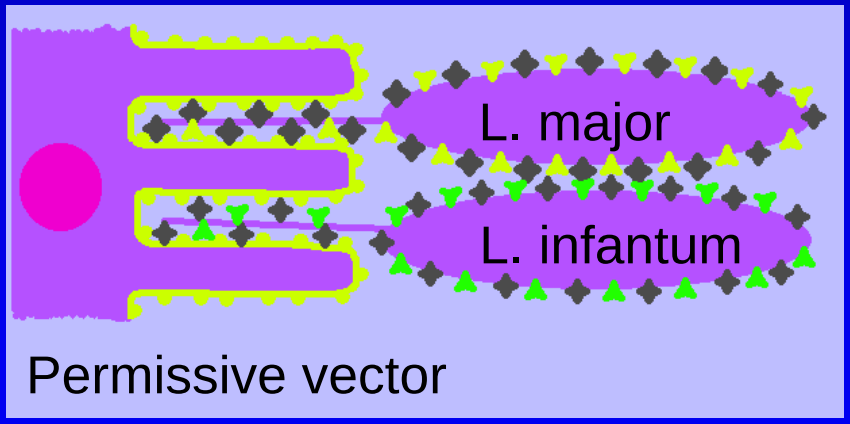




No O-glycosylation:
Attachment by LPG receptor.
Coevolution: selection of the unique, highly substituted LPG of *L. major.*

Lutzomyia longipalpis





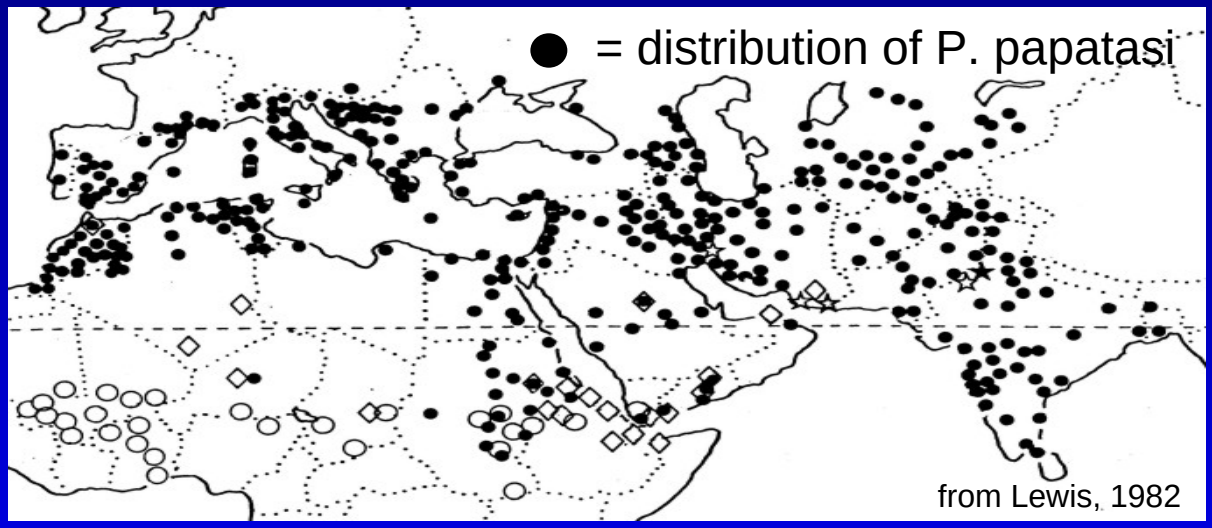
O-glycosylated epitopes: Attachment by another mechanism

Volf and Myskova 2007. Trends Parasitol

Enhanced fitness of *L. major/ infantum* hybrids

Hybrids develop late stage infections in *P. papatasi*

→ Important epidemiological consequences



→ Genetic exchange enhances fitness and transmission potential

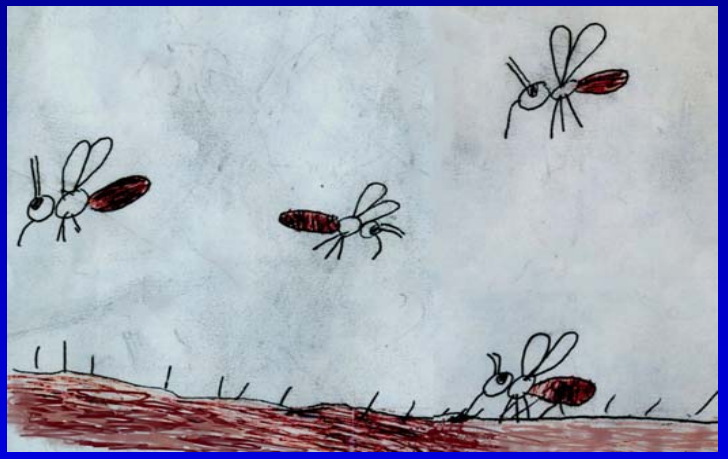
Ayala F. 1998: Is sex better? Parasites say “no”. *PNAS 95, 3346-3348*

Victoir K., Dujardin J.C. 2002: How to succeed in parasitic life without sex. Asking *Leishmania*. *Trends Parasitol. 18, 81-85*

Our conclusion: sex is good, even for *Leishmania*.

Volf et al. 2007. Int J Parasitol

Charles University
Dept. Parasitology
Vector Biology lab



GA ČR

wellcome trust