HOST SPECIFICITY OF BACTERIAL PATHOGENS IN RODENT COMMUNITIES

Jessie Abbate
MIVEGEC / IRD
2 Oct 2018

Population Biology of Multihost Pathogens

Mark E. J. Woolhouse,* Louise H. Taylor, Daniel T. Haydon

The majority of pathogens, including many of medical and veterinary importance, can infect more than one species of host. Population biology has yet to explain why perceived evolutionary advantages of pathogen specialization are, in practice, outweighed by those of generalization. Factors that predispose pathogens to generalism include high levels of genetic diversity and abundant opportunities for cross-species transmission, and the taxonomic distributions of generalists and specialists appear to reflect these factors. Generalism also has consequences for the evolution of virulence and for pathogen epidemiology, making both much less predictable. The evolutionary advantages and disadvantages of generalism are so finely balanced that even closely related pathogens can have very different host range sizes.

Most pathogens are capable of infecting more than one host species. This includes the 60% of human pathogen species that are zoonotic (*1*), causing diseases of major public health concern such as influenza, sleeping sickness, Lyme disease, food poisoning, and variant CJD. It also includes more than 80% of pathogens of domestic animals (*2*), notably those causing 57 of the 70 livestock diseases of greatest international importance (*3*), such as rinderpest, foot-and-mouth disease, and heartwater. Pathogens such as influenza A virus, rabies virus, and *Blastocystis hominis* can infect hosts not only of different species but from different orders or classes (*2*). Yet, despite their ubiquity and importance, multihost pathogens have been largely neglected by population biologists in favor of the simpler paradigm of a single-host species.

Many, though not all, pathogens that can infect multiple hosts can also be transmitted by multiple hosts, and these can be regarded as ecological generalists rather than specialists. The advantages of generalism are poorly understood: it has been suggested that evolution should favor specialism, either because of the existence of functional trade-offs that limit the fitness of generalists in any one habitat or because evolution may proceed faster within narrower niches (*4*); these arguments apply especially to pathogens because they are under selection pressure to coevolve with their hosts (*5*). Yet paradoxically, only a minority of pathogens are specialists in the sense that they exploit a single host species.

So what processes lead to pathogens having multiple hosts, and why do multihost pathogens seem so pervasive? The evolution of generalism requires that pathogens have both the capability to exploit potential alternative host species and the opportunity to transmit to them. The subsequent maintenance of generalism depends on the consequences of an increased host range for pathogen population biology, especially such features as pathogenicity and epidemiology.

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Capability to Infect Multiple Hosts

Pathogens are usually, though not always, less infectious to a different host species. This is referred to as the species barrier (*6*), and there are two main strategies for overcoming it. Some pathogens have an inherent ability to infect multiple host species; for example, *Trypanosoma brucei rhodesiense* has a number of variant surface glycoprotein genes that encode for receptors with different affinities to specific mammalian transferrins (*7*). More commonly, pathogens produce many different genetic variants, some of which become associated with different host species, e.g., rabies (*8*). Gene products involved in host specificity have been identified for some pathogens, such as human immunodeficiency virus (HIV), mouse hepatitis virus, and *Citrobacter rodentium* (*9*).

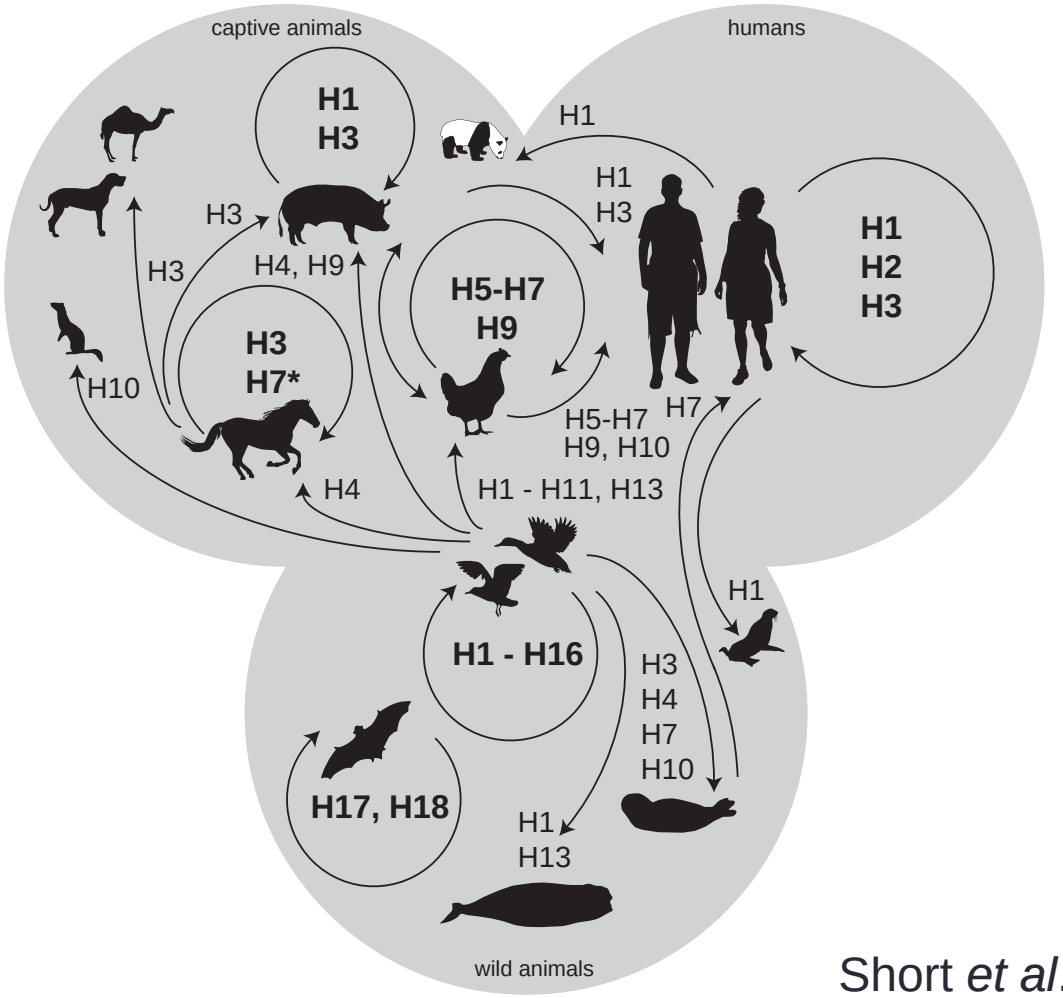
Genetic change associated with host switching constitutes host adaptation. This may involve a small number of nucleotide substitutions or more major genetic changes such as reassortment, e.g., influenza A (*10*), or the acquisition of genetic elements (sometimes associated with virulence as well as host specificity), e.g., *Salmonella typhimurium* (*11*). Host adaptation can be so rapid that pathogen lineages adapt to different host tissues (*12*) or to vector versus host cells (*13*).

Species barriers are routinely crossed by some pathogens (such as rabies virus, which is regarded as a true multihost pathogen), but much more rarely by others [such as simian immunodeficiency virus, which is thought to have been transmitted to humans from other primates only very rarely and to have diverged rapidly into new single-host pathogens, HIV-1 and HIV-2 (*14*)]. Another example of pathogen

Woolhouse *et al*. 2001 *Science*

Host specificity is important for disease transmission and emergence

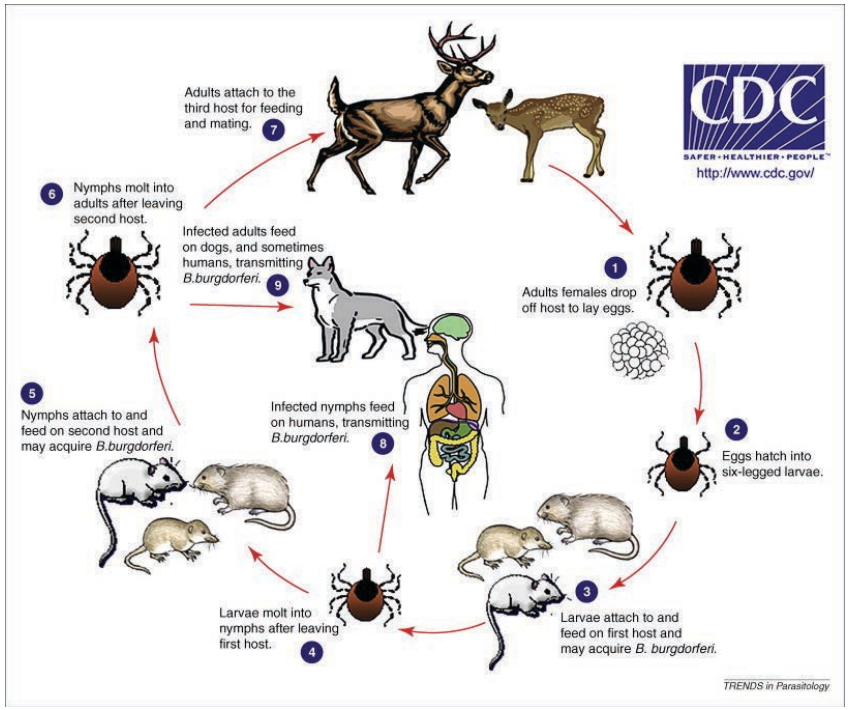
Influenza virus



Short *et al*. 2015 *One Health*

Cross-species transmission of multi-host pathogen species

- Is assumed to be commonplace in the absence of ecological barriers.



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- Is assumed to be commonplace in the absence of ecological barriers.
- Is likely important for persistence (and zoonosis) in multi-host communities.

Cross-species transmission of multi-host pathogen species

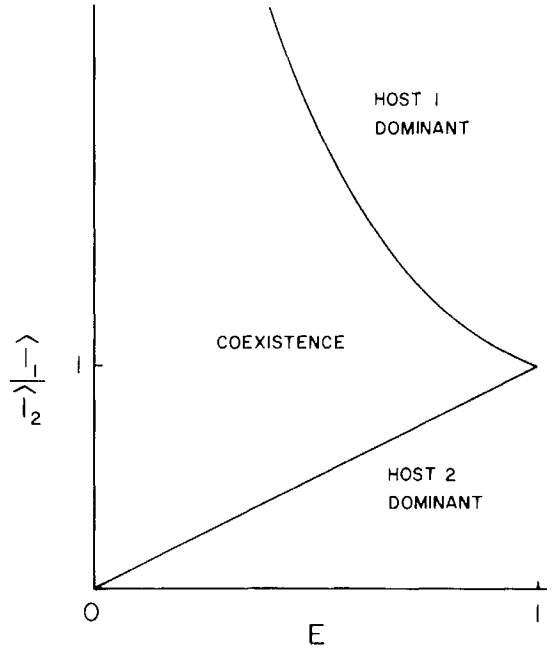
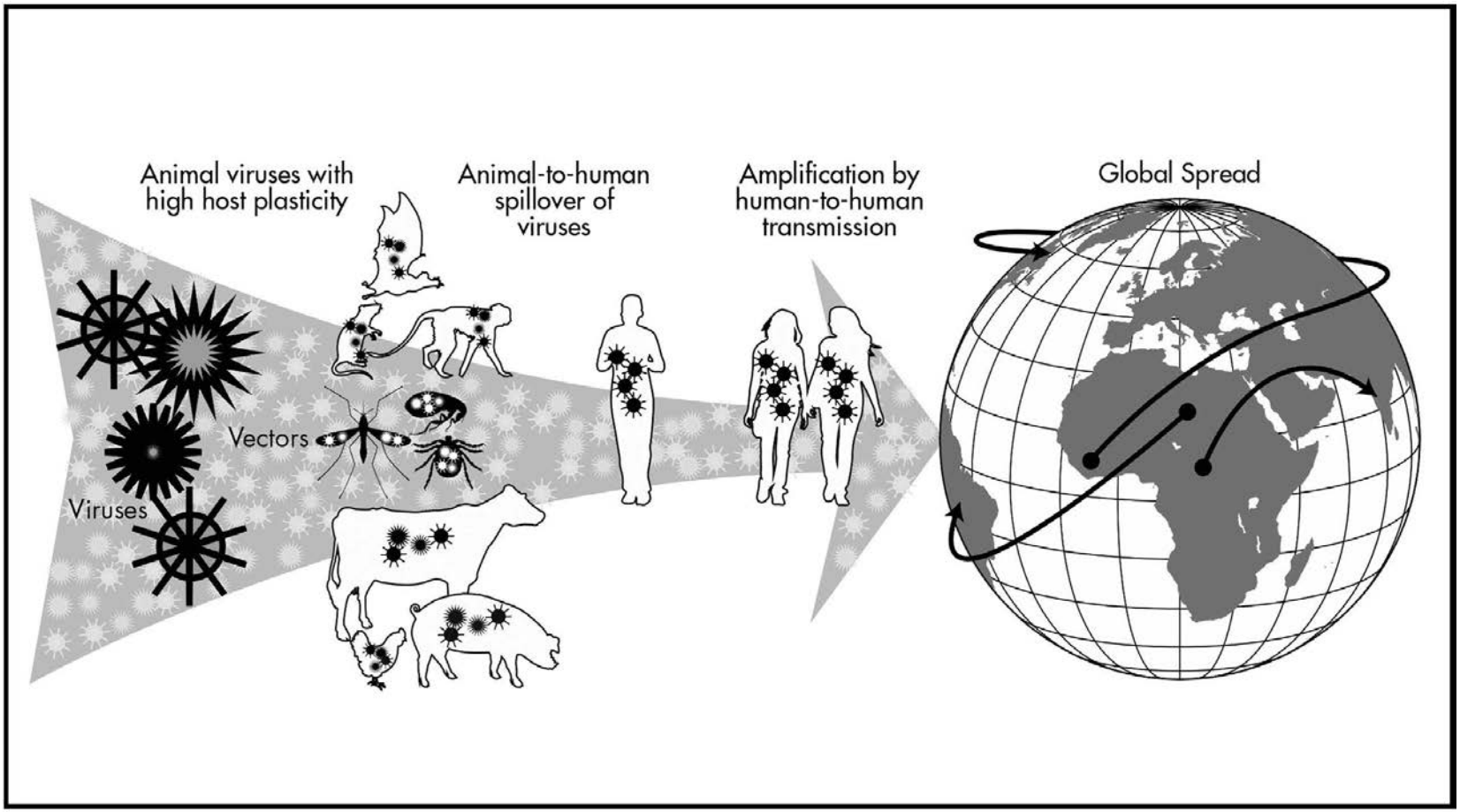


FIG. 2.—Coexistence conditions for symmetrical transmission dynamics. The quantity E scales between-species transmission as a function of within-species transmission (see text). Coexistence requires the ratio $\hat{I}_1/\hat{I}_2$ to lie within the indicated bounds.

Holt & Pickering 1985 *American Naturalist*

Cross-species transmission of multi-host pathogen species

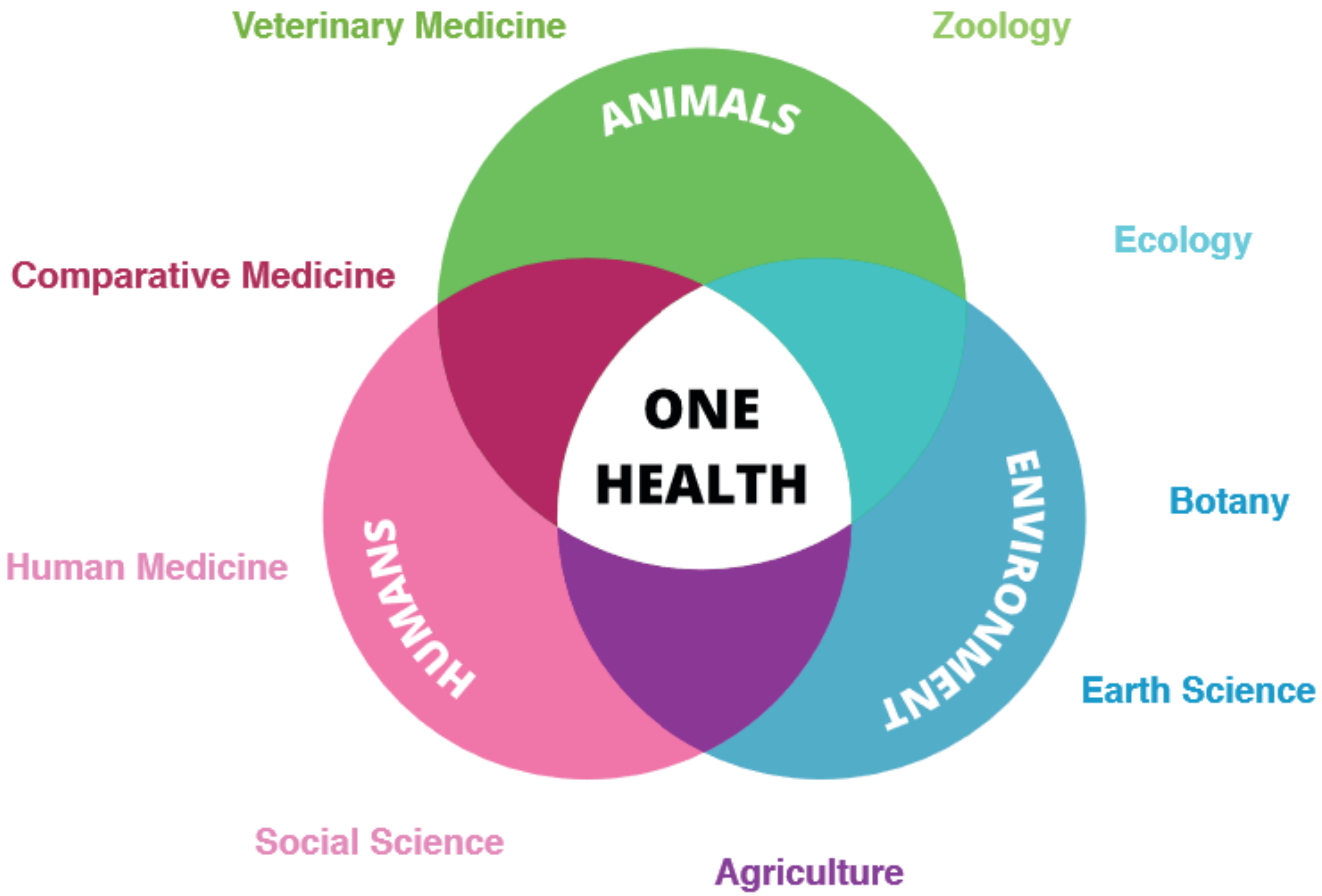


Kreuder Johnson *et al*. 2015 *Scientific Reports*

Cross-species transmission of multi-host pathogen species

- *Batrachochytrium dendrobatidis*

Cross-species transmission of multi-host pathogen species



Cross-species transmission of multi-host pathogen species

- Is assumed to be commonplace in the absence of ecological barriers.
- Is likely important for persistence (and zoonosis) in multi-host communities.
- … may be greatly over-estimated.

Cryptic pathogen species / Covert host specificity

- Known to occur in several host-pathogen systems

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  - e.g., *Microbotryum* spp. on Caryophyllaceae hosts

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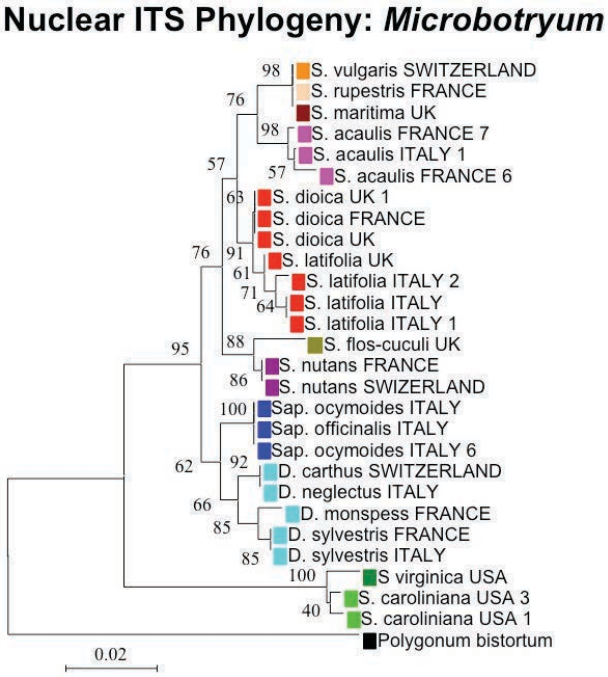

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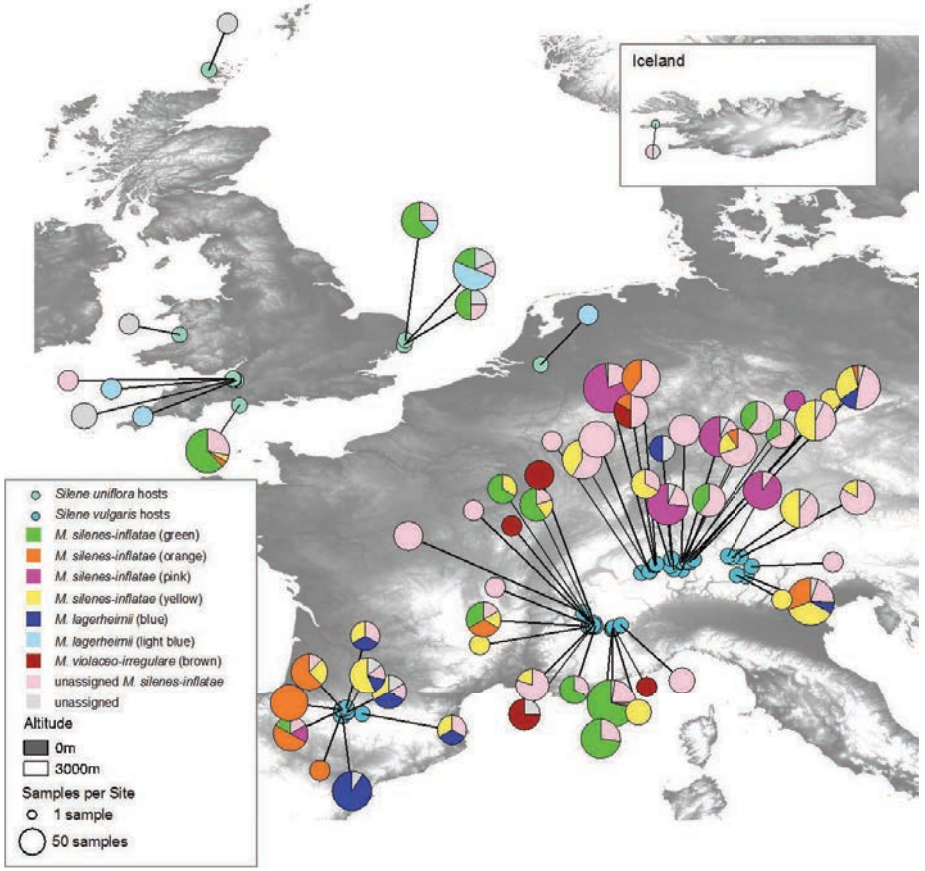

Abbate *et al*. 2018 *Mol Ecol*

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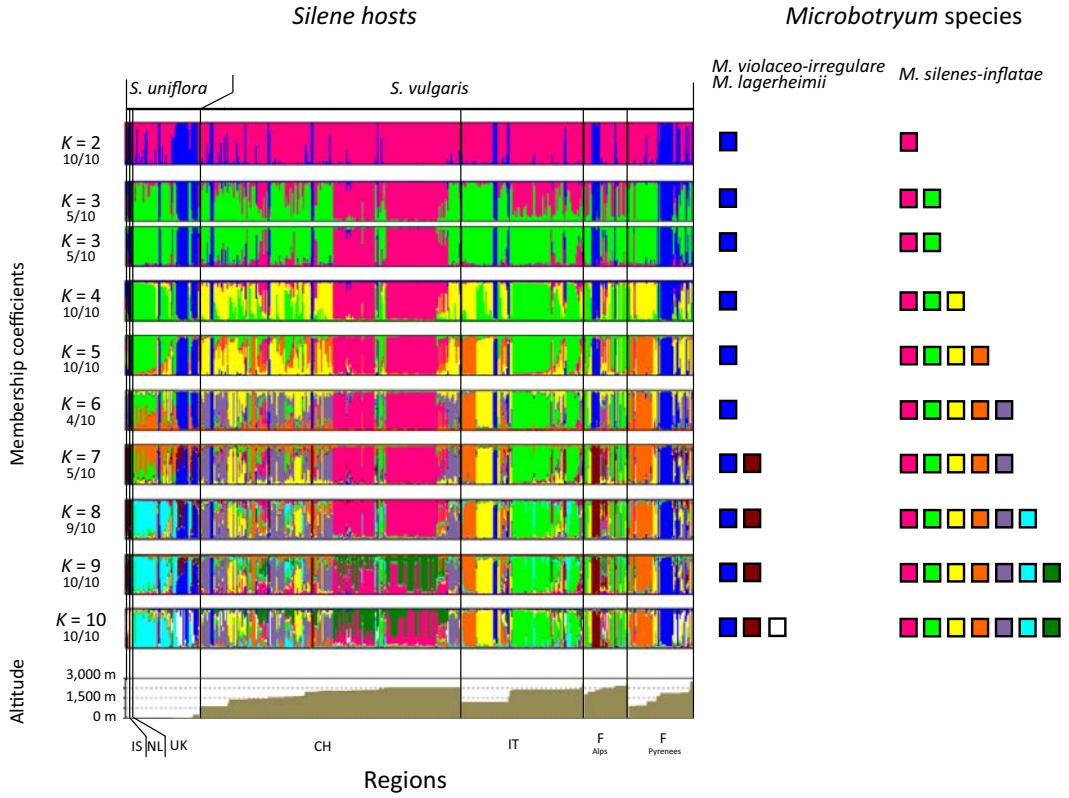

Abbate *et al*. 2018 *Mol Ecol*

Cryptic pathogen species / Covert host specificity

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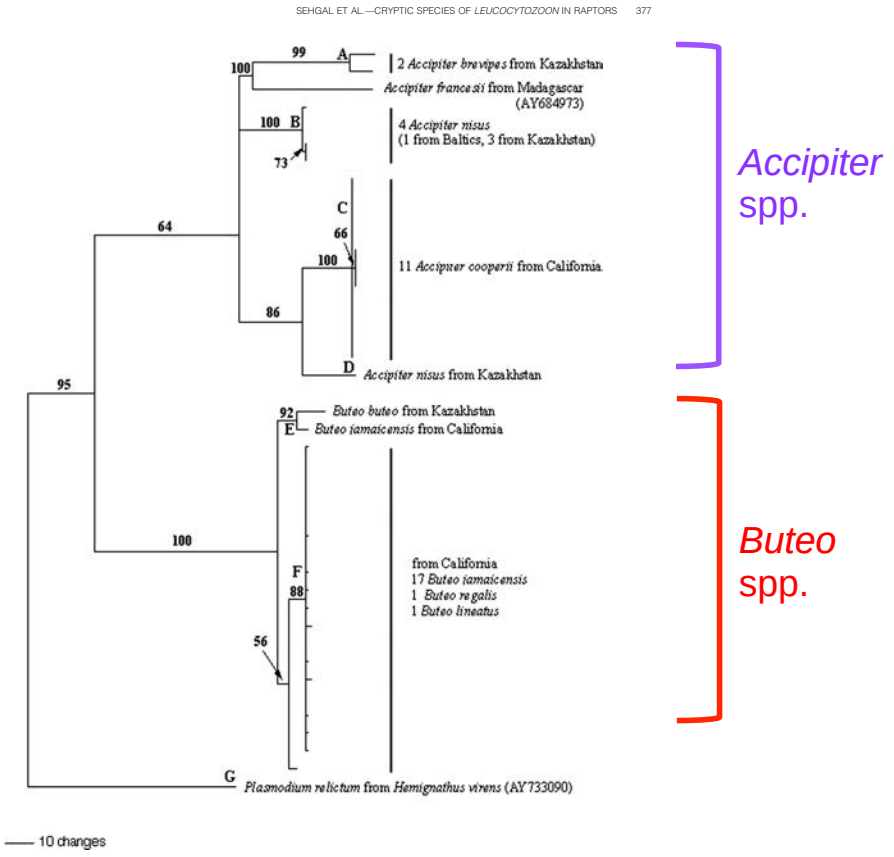
  - e.g., 10% sequence divergence between haplotypes of protozoan parasites (*Leucocytozoon toddi*) correlates with host raptor family



Sehgal *et al*. 2006 *J Parasitol*

Cryptic pathogen species / Covert host specificity

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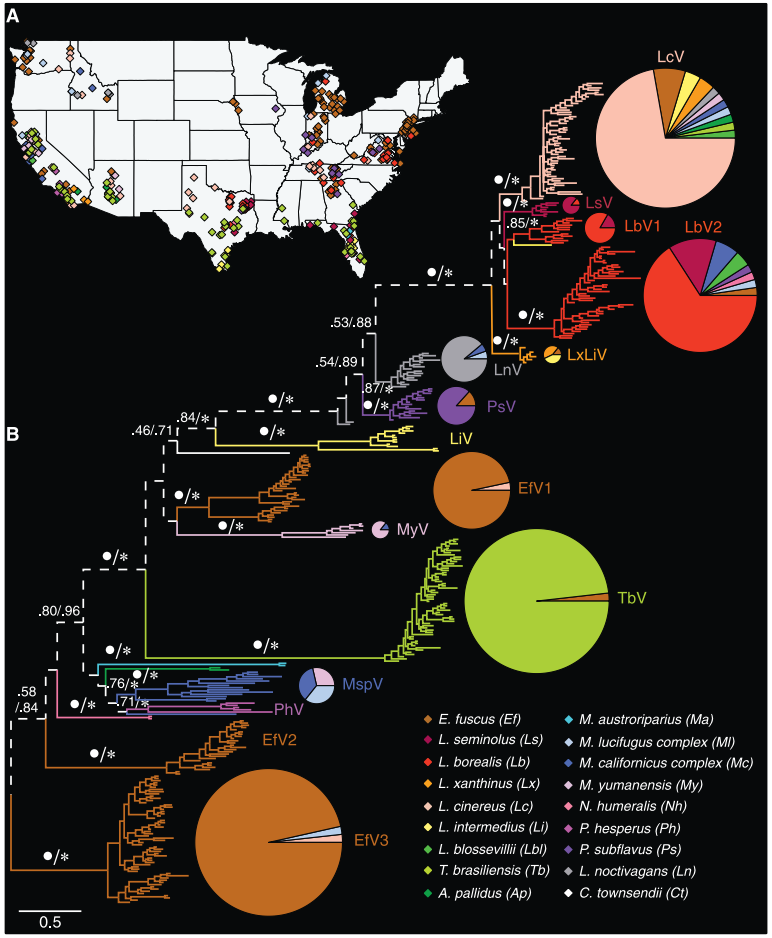
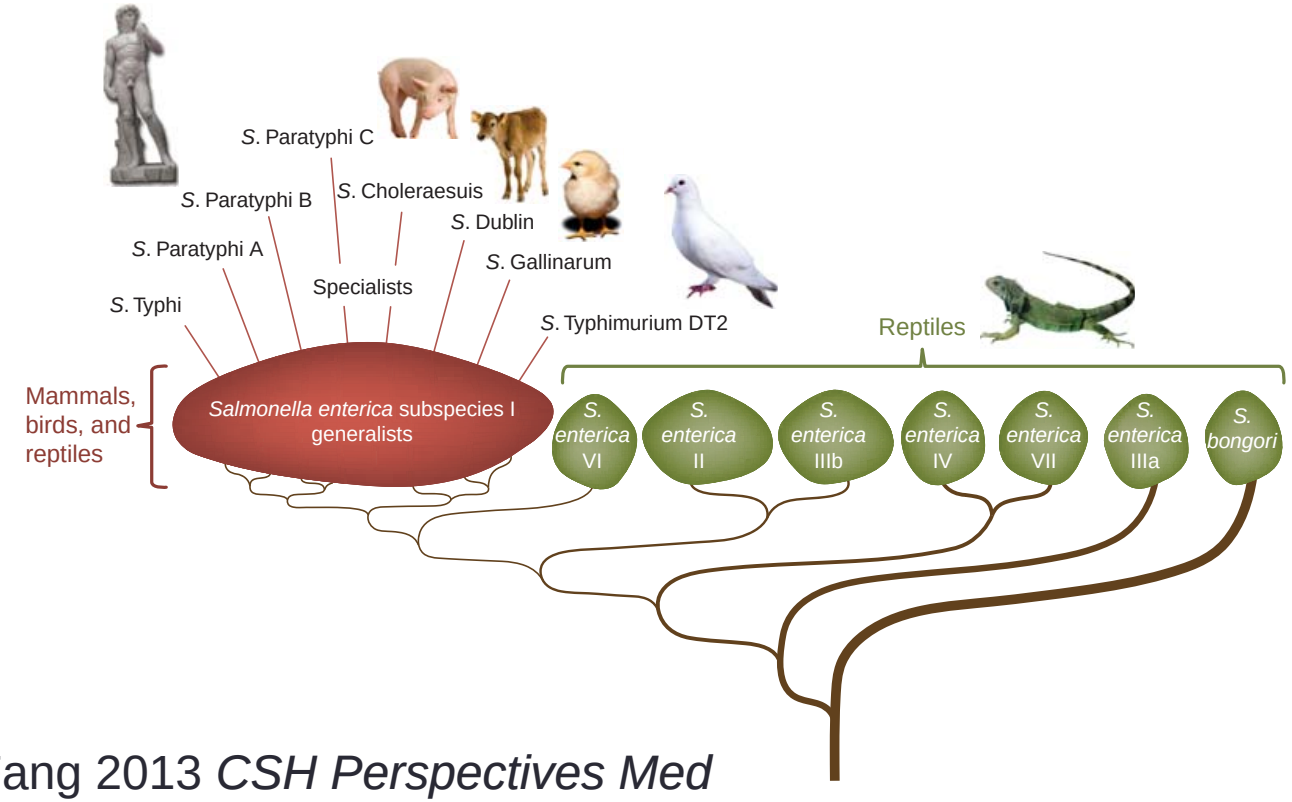
  - e.g., Rabies viral lineages are constrained by host phylogeny



Streicker *et al*. 2010 *Science*

Cryptic pathogen species / Covert host specificity

- Known to occur in several host-pathogen systems
  - e.g., *Salmonella* species include both generalists and specialists



Baumler & Fang 2013 *CSH Perspectives Med*

Cryptic pathogen species / Covert host specificity

- Also occurs in bacterial pathogens of rodents

Journal of Animal Ecology

British Ecological Society

Journal of Animal Ecology 2016 doi: 10.1111/1365-2656.12568

Multihost *Bartonella* parasites display covert host specificity even when transmitted by generalist vectors

Susan M. Withenshaw[1,2]*, Godefroy Devevey[3], Amy B. Pedersen[3] and Andy Fenton[1]

[1]*Institute of Integrative Biology, University of Liverpool, Crown Street, Liverpool, Merseyside L69 7ZB, UK;* [2]*NERC Centre for Ecology and Hydrology, Maclean Building, Benson Lane, Crowmarsh Gifford, Oxfordshire OX10 8BB,UK; and* [3]*School of Biology & Centre for Immunity, Infection and Evolution, University of Edinburgh, Ashworth Laboratories, Charlotte Auerbach Road, Edinburgh EH9 3FL, UK*

Whitenshaw *et al*. 2016 *J Animal Ecology*

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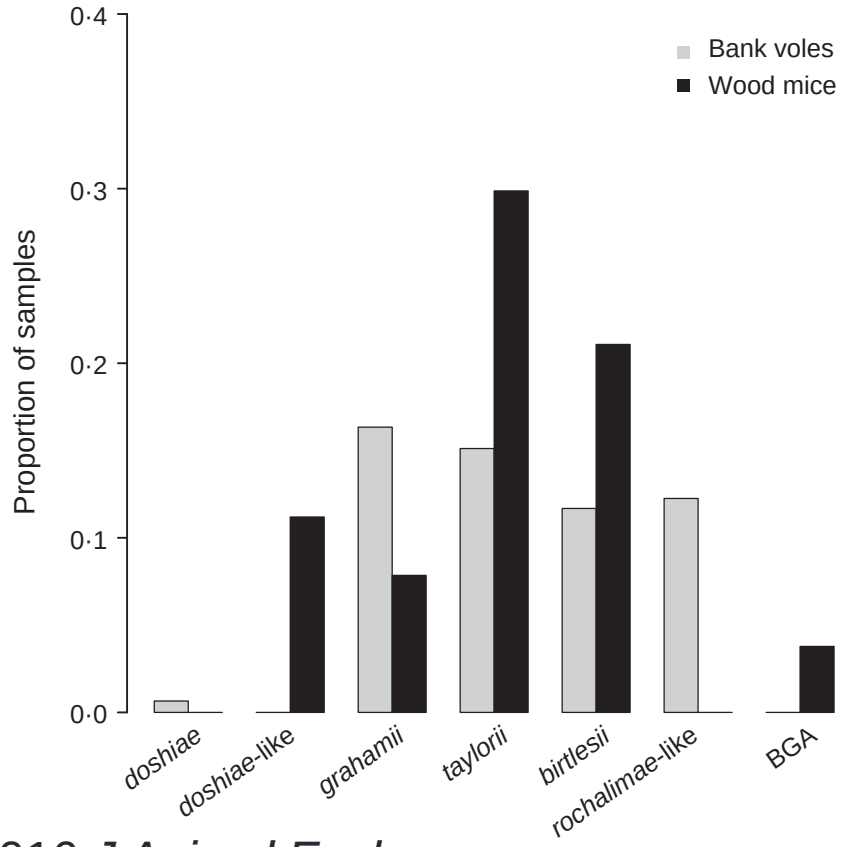

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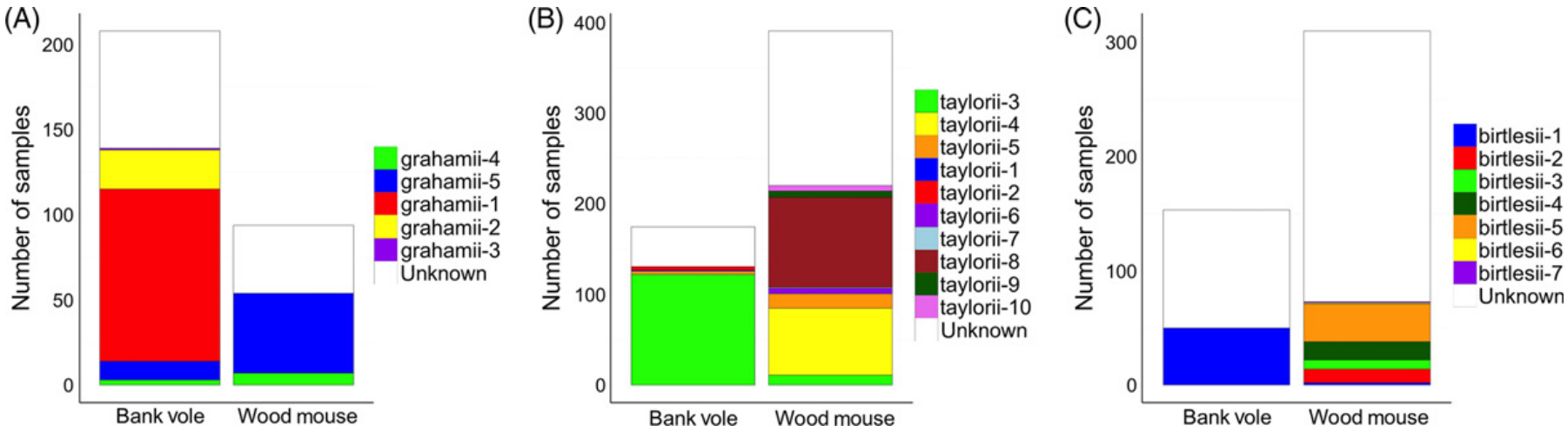

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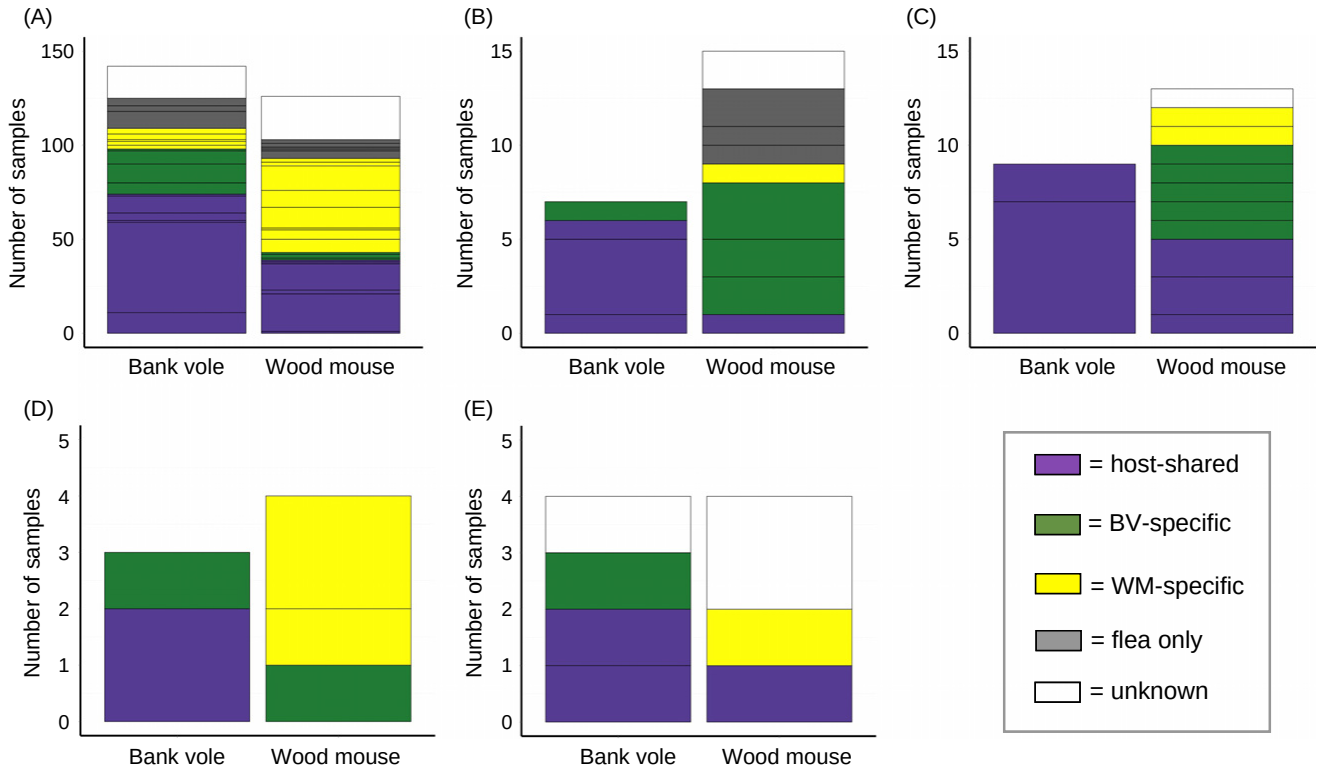


Whitenshaw *et al*. 2016 *J Animal Ecology*

Cryptic pathogen species / Covert host specificity

- Also occurs in bacterial pathogens of rodents

- Detection via 16S meta-barcoding

Pathobiome diversity (natural history) & co-infection patterns

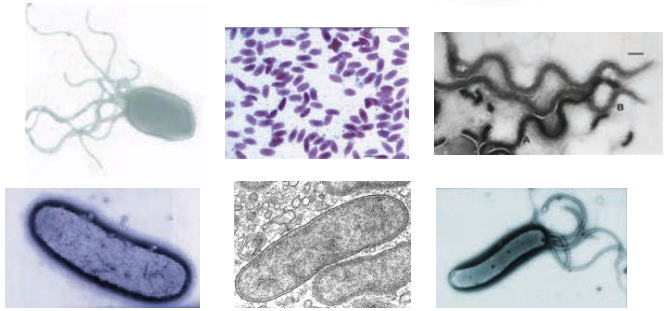
Pathobiome diversity and co-infection patterns in a community of rodents.

Abbate JL, Galan M, Yannick C, Gotteland C, Razzauti M, Sironen T, Voutilainen L, Henttonen H, Gasqui P, Cosson J-F, Charbonnel N.

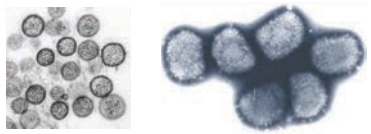
Pathobiome diversity (natural history) & co-infection patterns

Rodent blood infections

- Splenic microbiota (16S MiSeq)



- Viral seropositivity



Abbate *et al*. in prep

Pathobiome diversity (natural history) & co-infection patterns

Rodent blood infections

Cricetidae

Microtus agrestris (field vole)

Microtus arvalis (common vole)

Microtus subterraneus (European pine vole, Common pine vole)

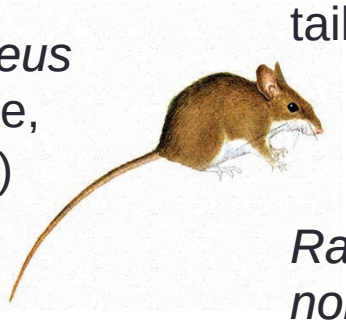
Myodes glareolus (bank vole)

Arvicola scherman (Montane water vole)

Muridae

Apodemus sylvaticus (wood mouse)

Apodemus flavicolus (yellow tailed mouse)



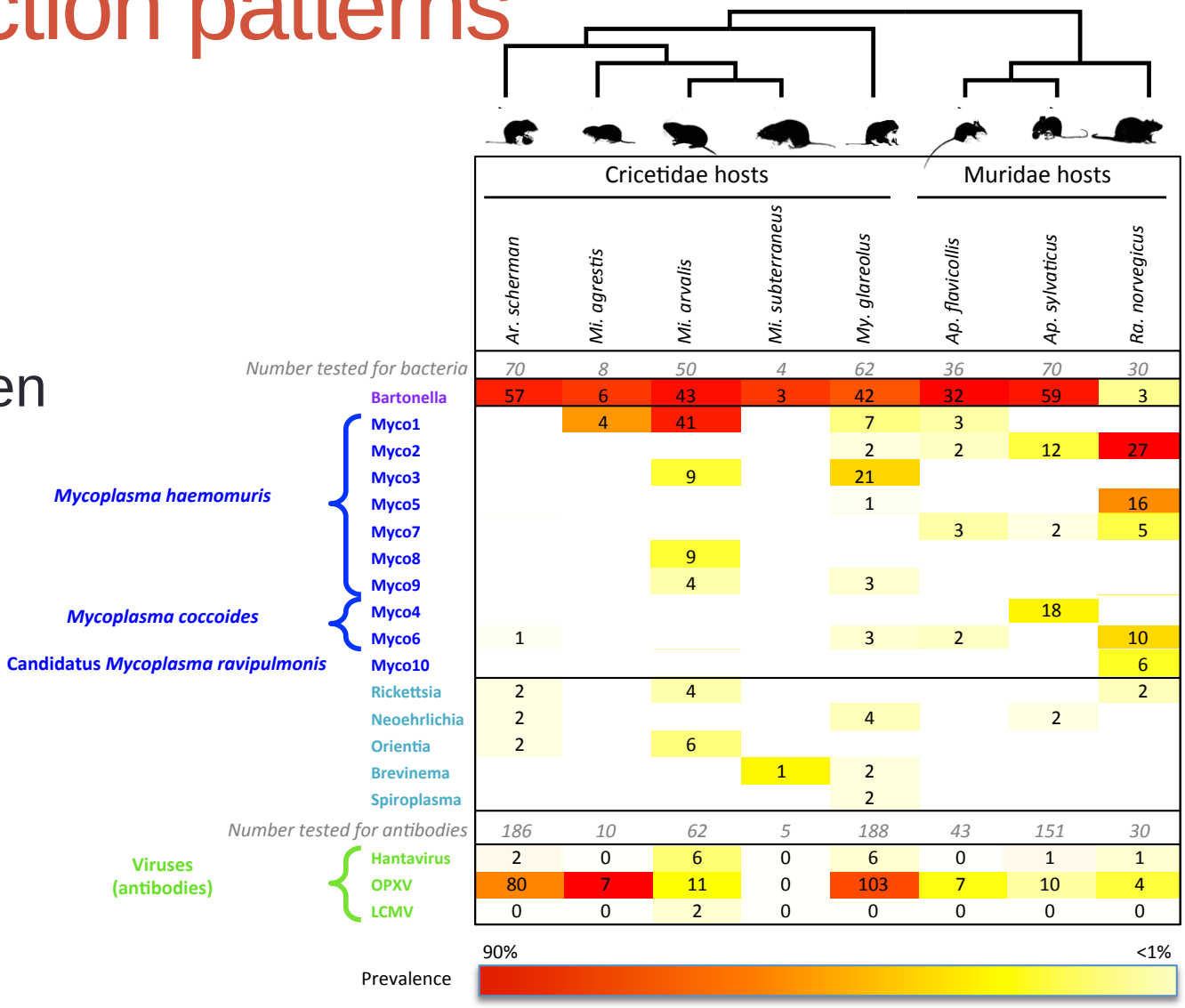
Rattus norvegicus (brown rat)

Abbate *et al*. in prep

Pathobiome diversity (natural history) & co-infection patterns

Rodent blood infections

- occurred often in more than one host species

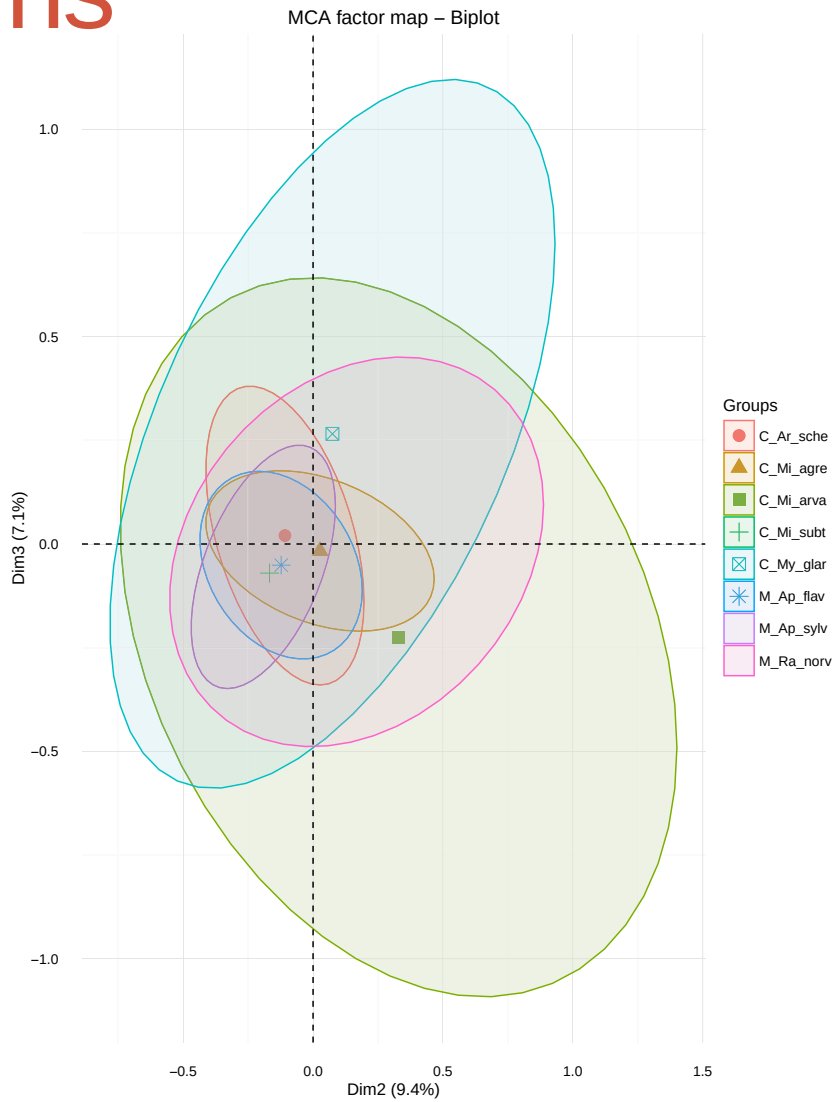


Abbate *et al*. in prep

Pathobiome diversity (natural history) & co-infection patterns

Rodent blood infections

- presence/ absence structured mainly by host species

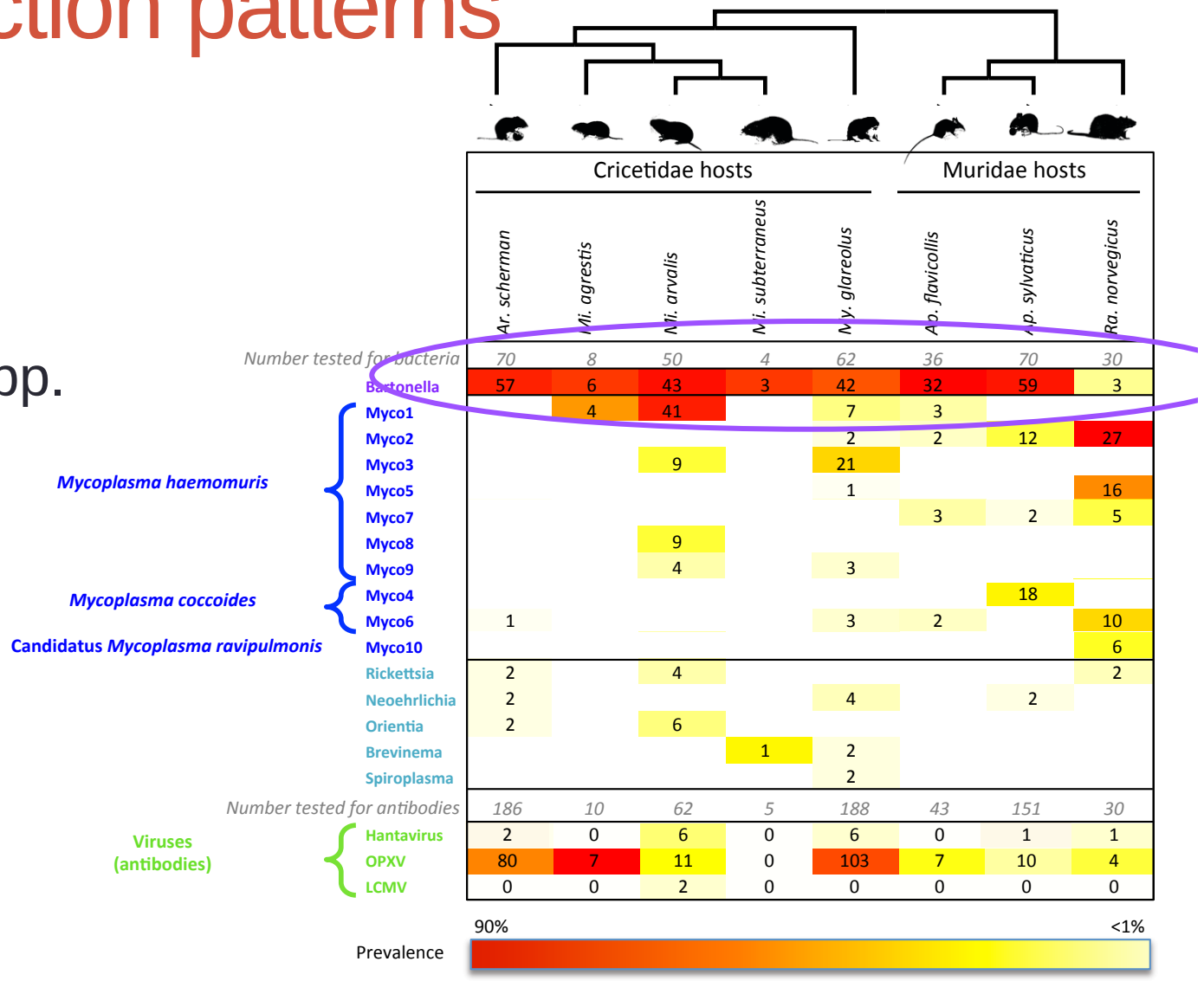


Abbate *et al*. in prep

Pathobiome diversity (natural history) & co-infection patterns

Rodent blood infections

- *Bartonella* spp.



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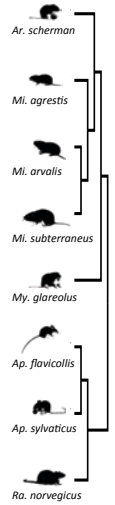
Pathobiome diversity (natural history) & co-infection patterns

Rodent blood infections

- *Bartonella* spp.

Individual	Host Spp	Genbank Ma	% Match	Bacterial Species	Genbank Host Species
BB10070	ArSher	KJ361629	100	Undescribed	Myodes spp.
BR11357	ArSher	KJ361629	100	Undescribed	Myodes spp.
BB10008	MiAgre	KJ361629	100	Undescribed	Myodes spp.
BR11195	MiAgre	KJ361629	100	Undescribed	Myodes spp.
BB10025bis	MiArv	NR_02505	100	B. birtlesii	Apodemus spp.
BR11280	MiArv	NR_02505	100	B. birtlesii	Apodemus spp.
BB10236	MiSubter	KJ361629	100	Undescribed	Myodes spp.
BB10018	MyGlar	AB529507	100	B. grahamii	Myodes glareolus
BR10114bis	MyGlar	AB529507	100	B. grahamii	Myodes glareolus
BB10091	ApFlav	NR_02505	100	B. birtlesii	Apodemus spp.
BR11269	ApFlav	NR_02505	100	B. birtlesii	Apodemus spp.
BB10003	ApSylv	NR_02505	100	B. birtlesii	Apodemus spp.
BR10046bis	ApSylv	NR_02505	100	B. birtlesii	Apodemus spp.
BR11181	RatNorv	NR_02527	100	B. tribocorum	Rattus norvegicus
BR11274bis	RatNorv	NR_02527	100	B. tribocorum	Rattus norvegicus

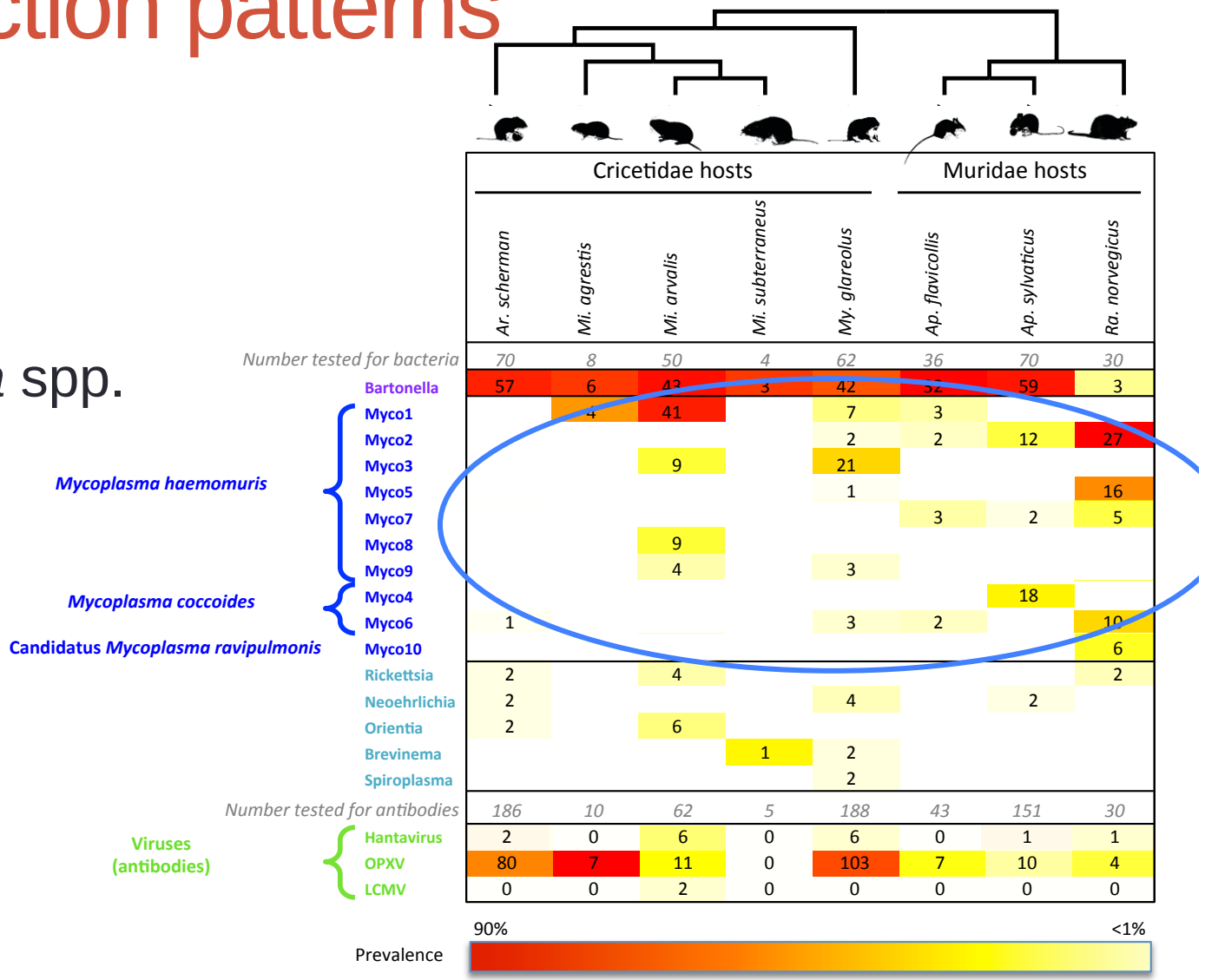


Abbate *et al*. in prep

Pathobiome diversity (natural history) & co-infection patterns

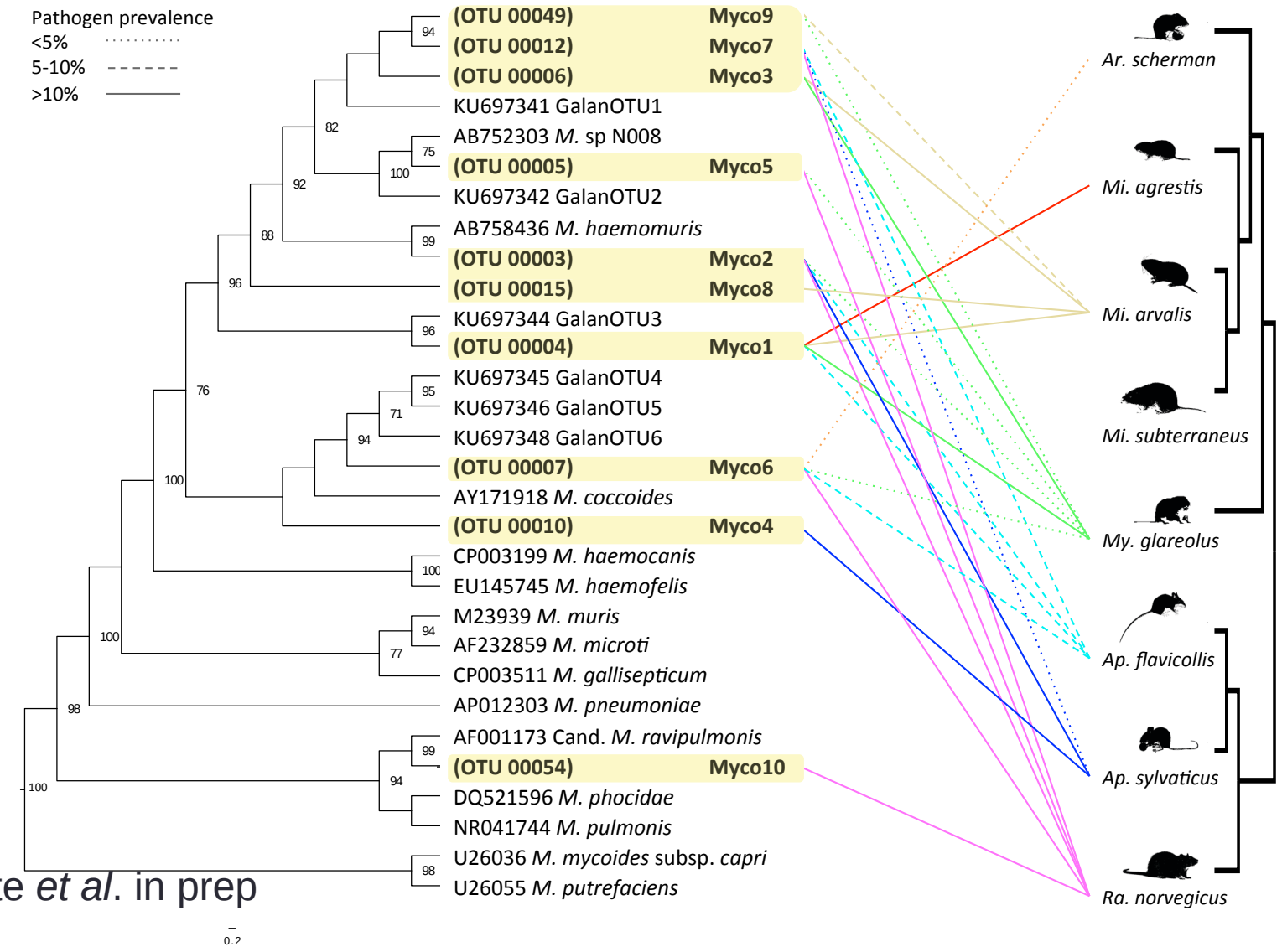
Rodent blood infections

- *Mycoplasma* spp.



Abbate *et al*. in prep

Mycoplasma species diversity



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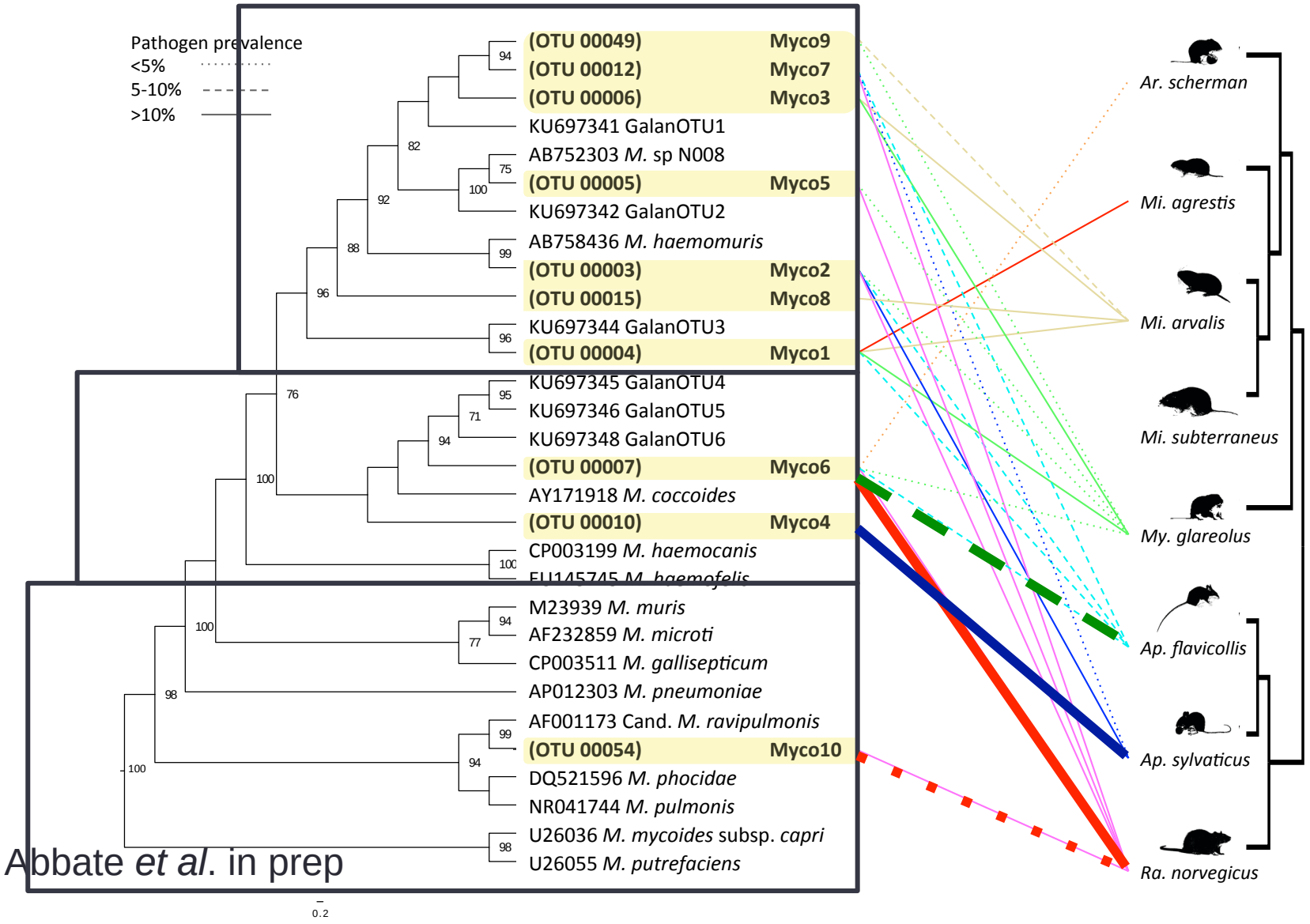
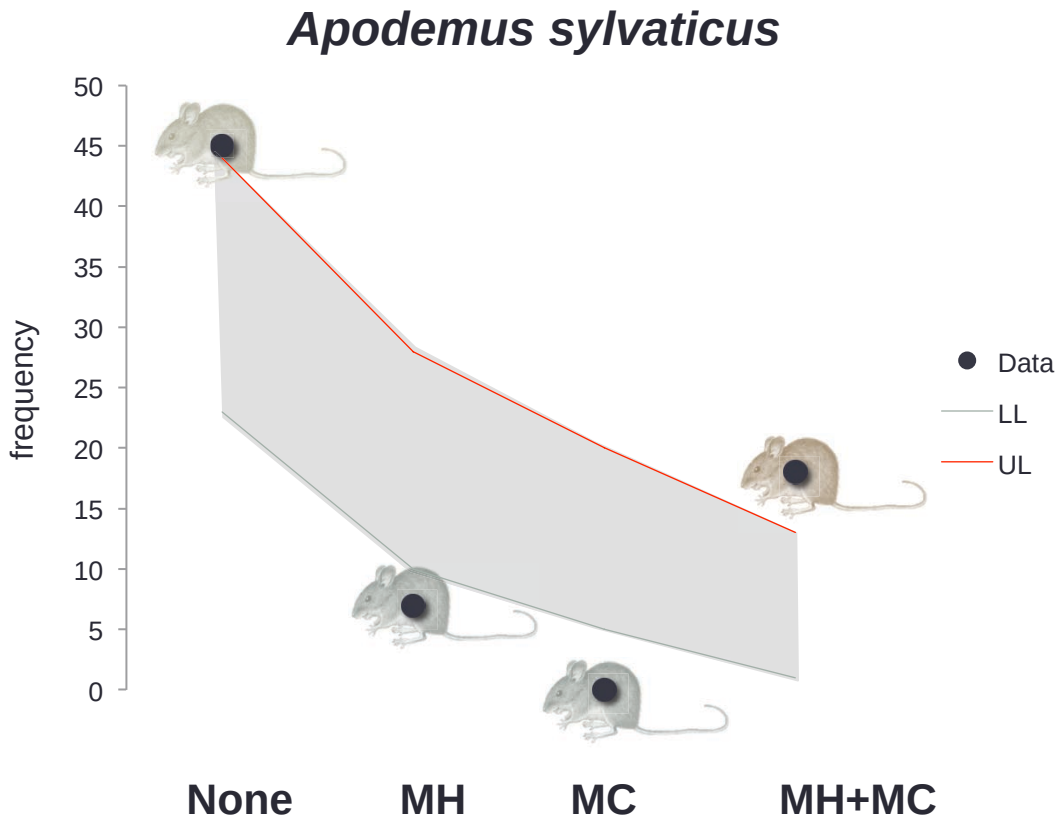


Abbate *et al*. in prep

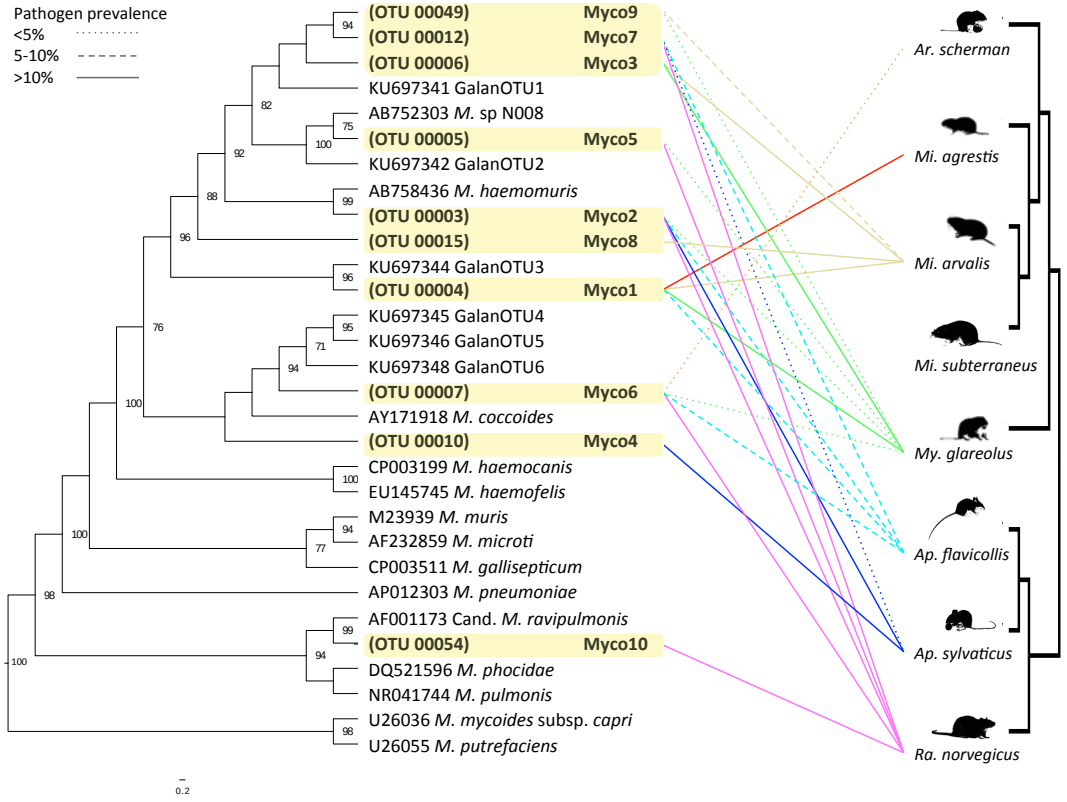
Implications: Within-host associations (co-infection patterns)



Abbate *et al*. in prep

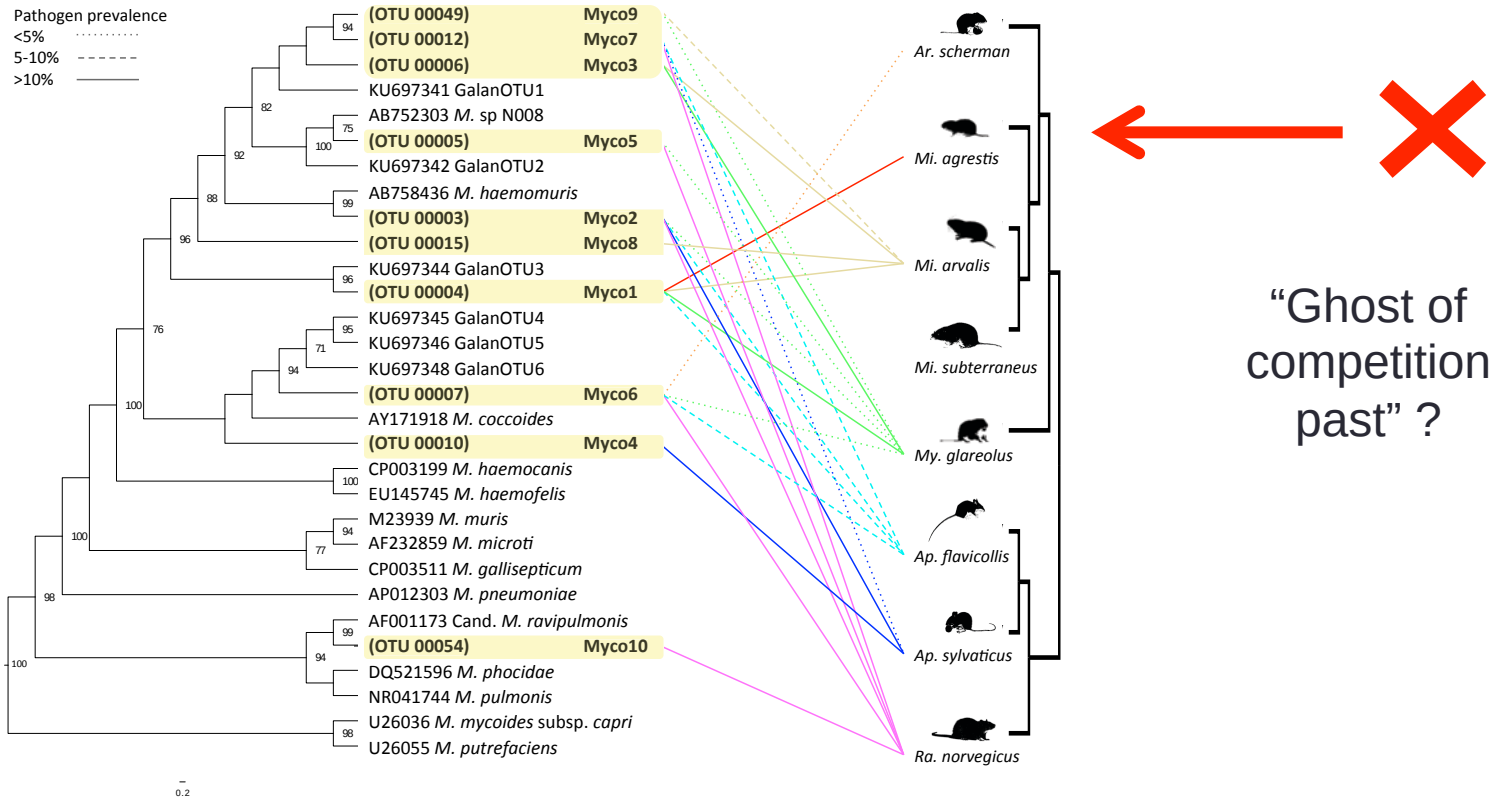
Implications: Within-host associations (co-infection patterns)

- At what taxonomic level should ‘species’ associations be evaluated?



Implications: Within-host associations (co-infection patterns)

- Bias towards detecting facilitation?



Summary

- Reminder: Population genetics and species concepts matter as much for pathogens as for hosts
- Evidence for truly generalist pathogens in natural systems is lacking
- Important implications for
  - predicting disease emergence
  - detecting ecological interactions

Thank you!