Virus host shifts

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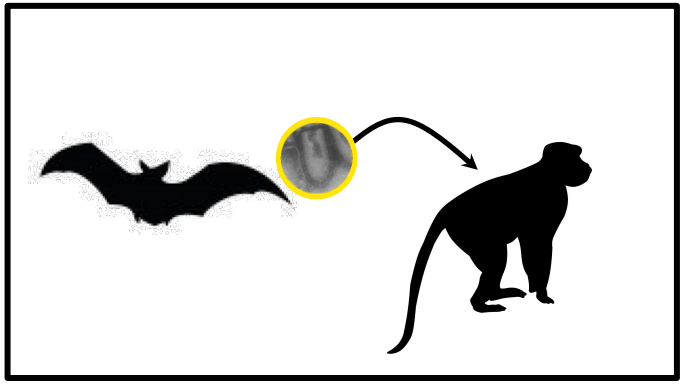
UNIVERSITY OF EXETER

wellcome

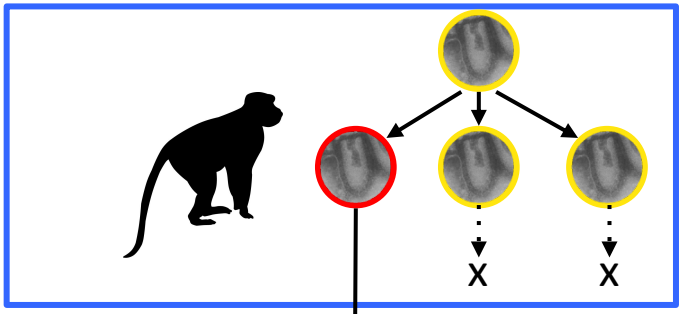
THE ROYAL SOCIETY

Host shifts

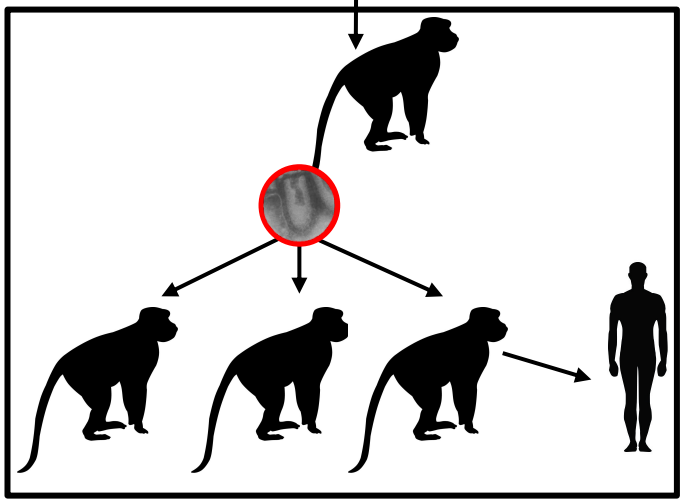
Exposure



Infection and evolution



Transmission

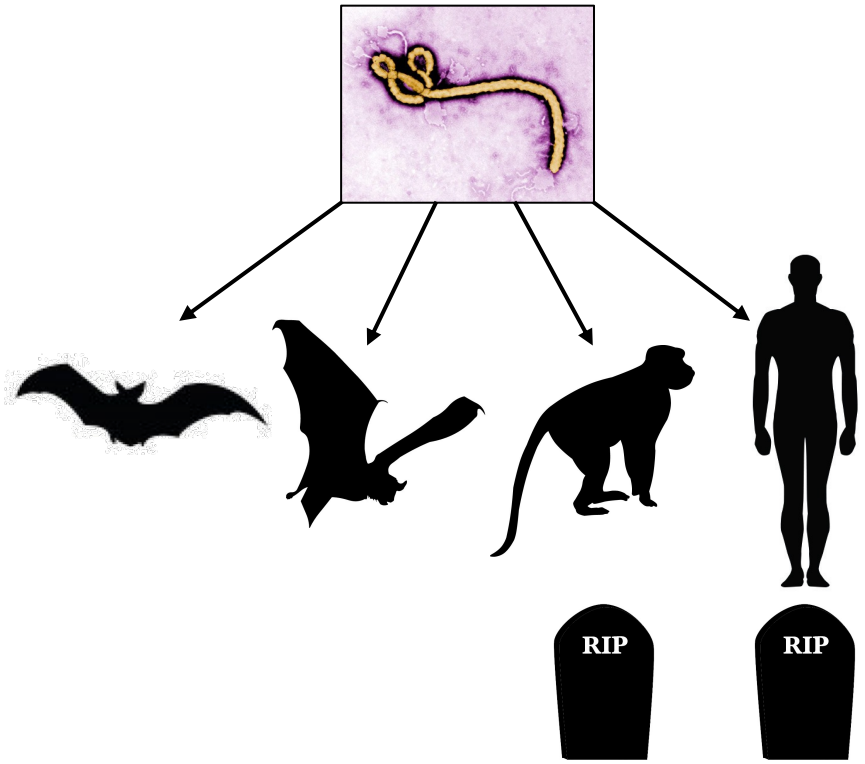


Changes in virulence following host shifts

- Virulence = the harm a parasite does to its host

- Virulence following a host shift can be high, e.g:

  - Ebola
  - Influenza
  - SARS coronavirus
  - Hendra virus

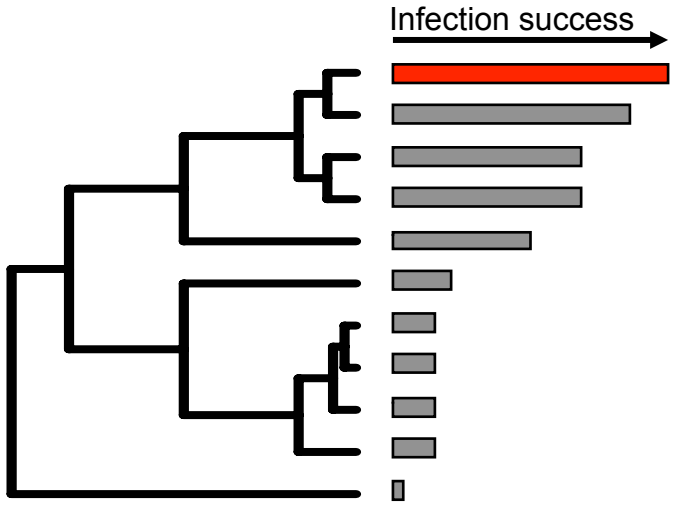


The host phylogeny and virulence

- Host phylogeny is important determinant of host shifts

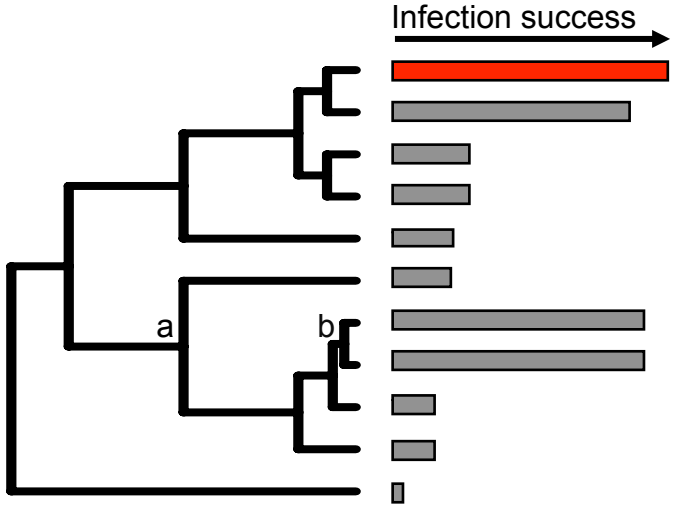
▪genetic distance from the natural host

= ‘distance effect’



▪groups of related hosts show similar levels of susceptibility independent of distance from natural host

= ‘phylogenetic effect’



Longdon et al 2011 PLoS Pathogens tinyurl.com/Longdon-2011a

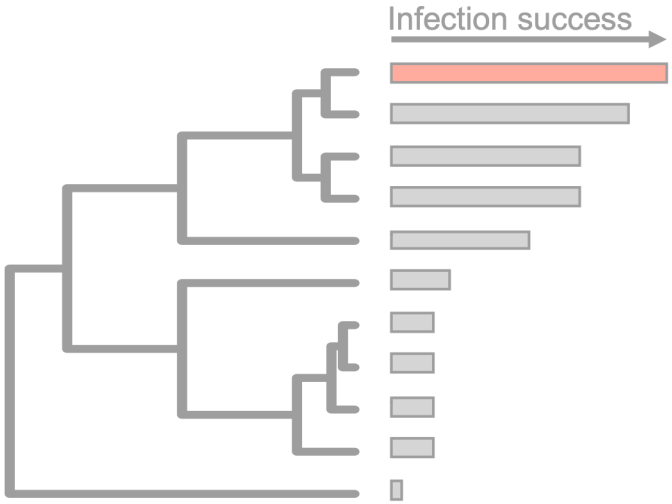
Reviewed in Longdon et al 2014 PLoS Pathogens tinyurl.com/Longdon-2014

The host phylogeny and virulence

- Host phylogeny is important determinant of host shifts

  - genetic distance from the natural host

    = 'distance effect'



  - groups of related hosts show similar levels of susceptibility independent of distance from natural host

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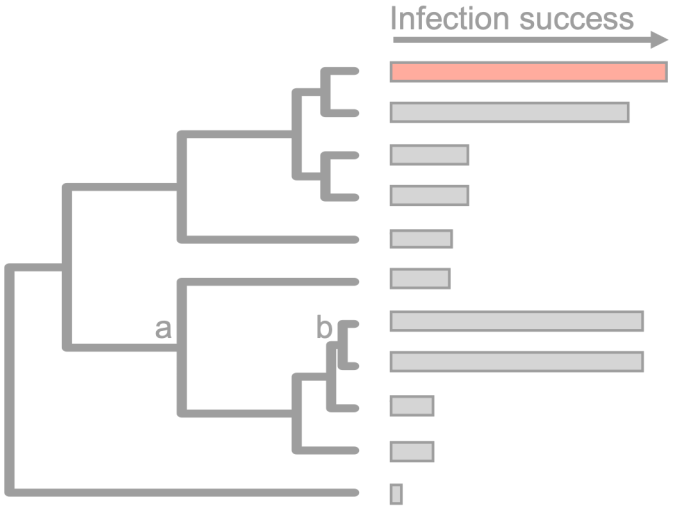
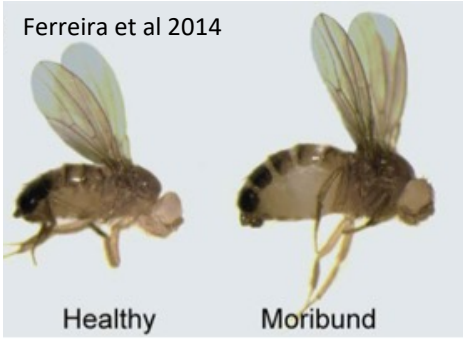


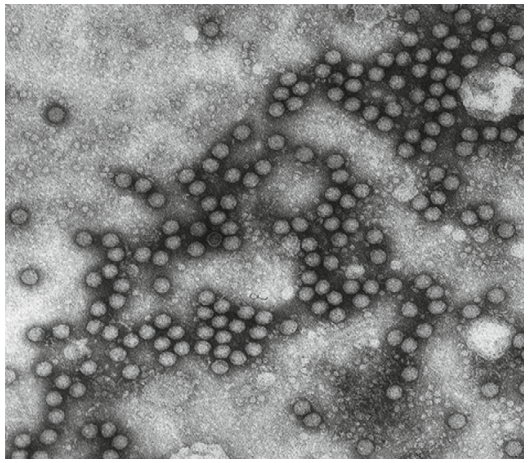
- Is pathogen virulence determined by the host phylogeny?

Study system

- Hosts: 48 species of Drosophilidae

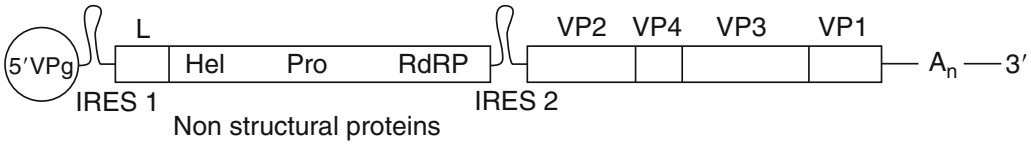
- Pathogen: Drosophila C virus (DCV)
  - positive sense RNA virus in the family *Dicistroviridae*
  - naturally infects *D. melanogaster*
  - horizontally transmitted





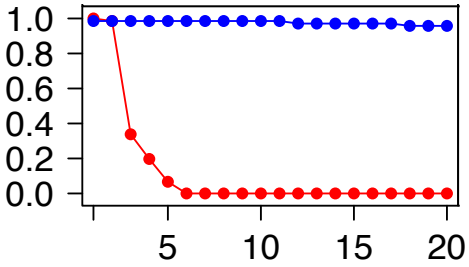
Images: Huszar and Imler 2008

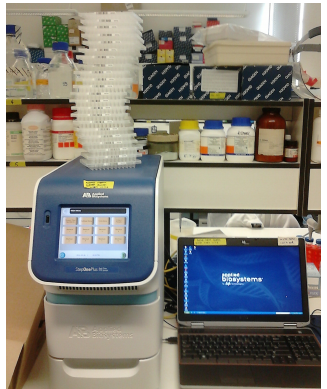
Dicistrovirus



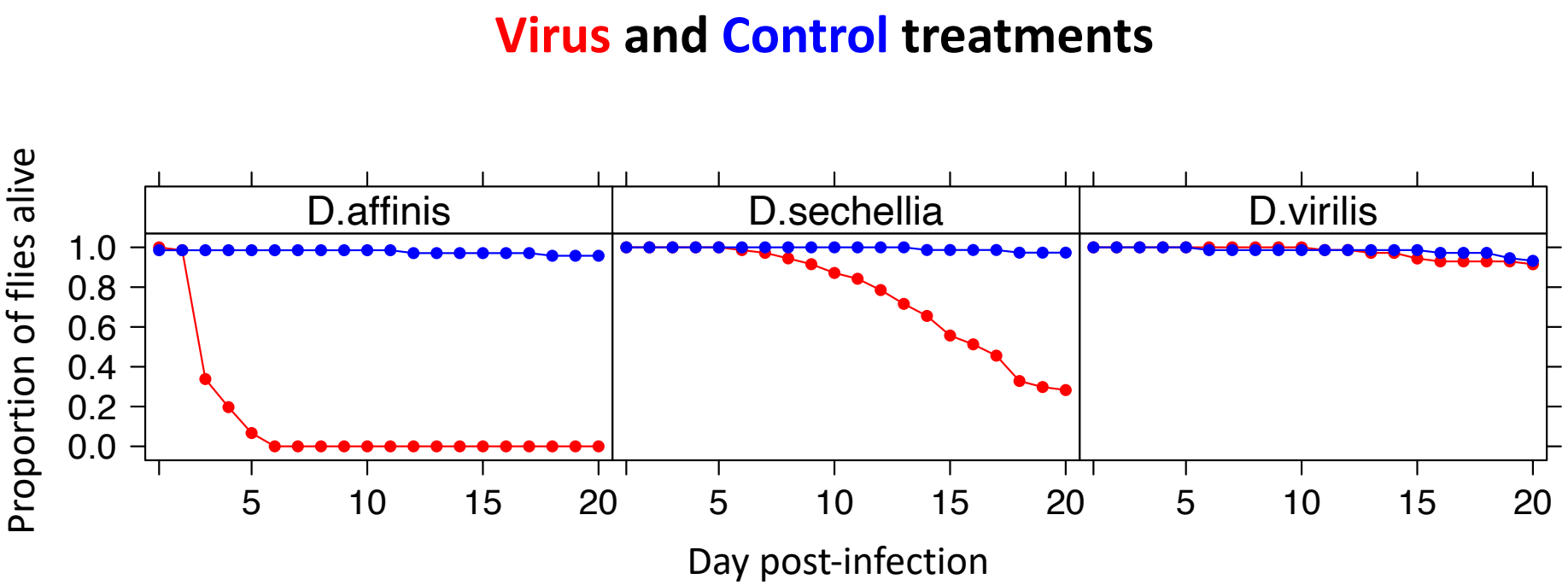
Experimental design

- Infected 48 species of fly with DCV
- Virulence= mortality for 20 days post-infection
- Also measured the change in RNA viral load with qRT-PCR

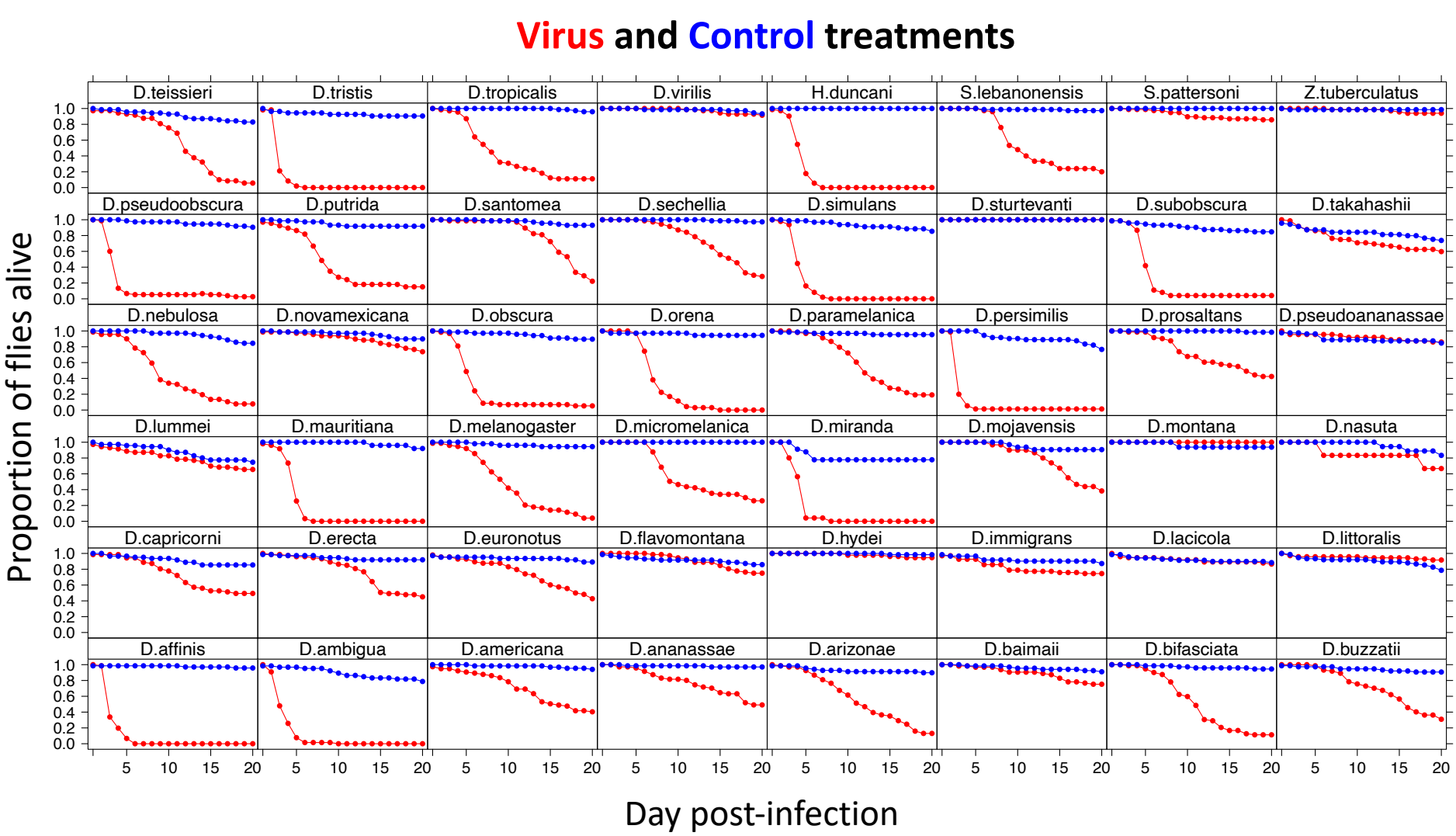




Virulence

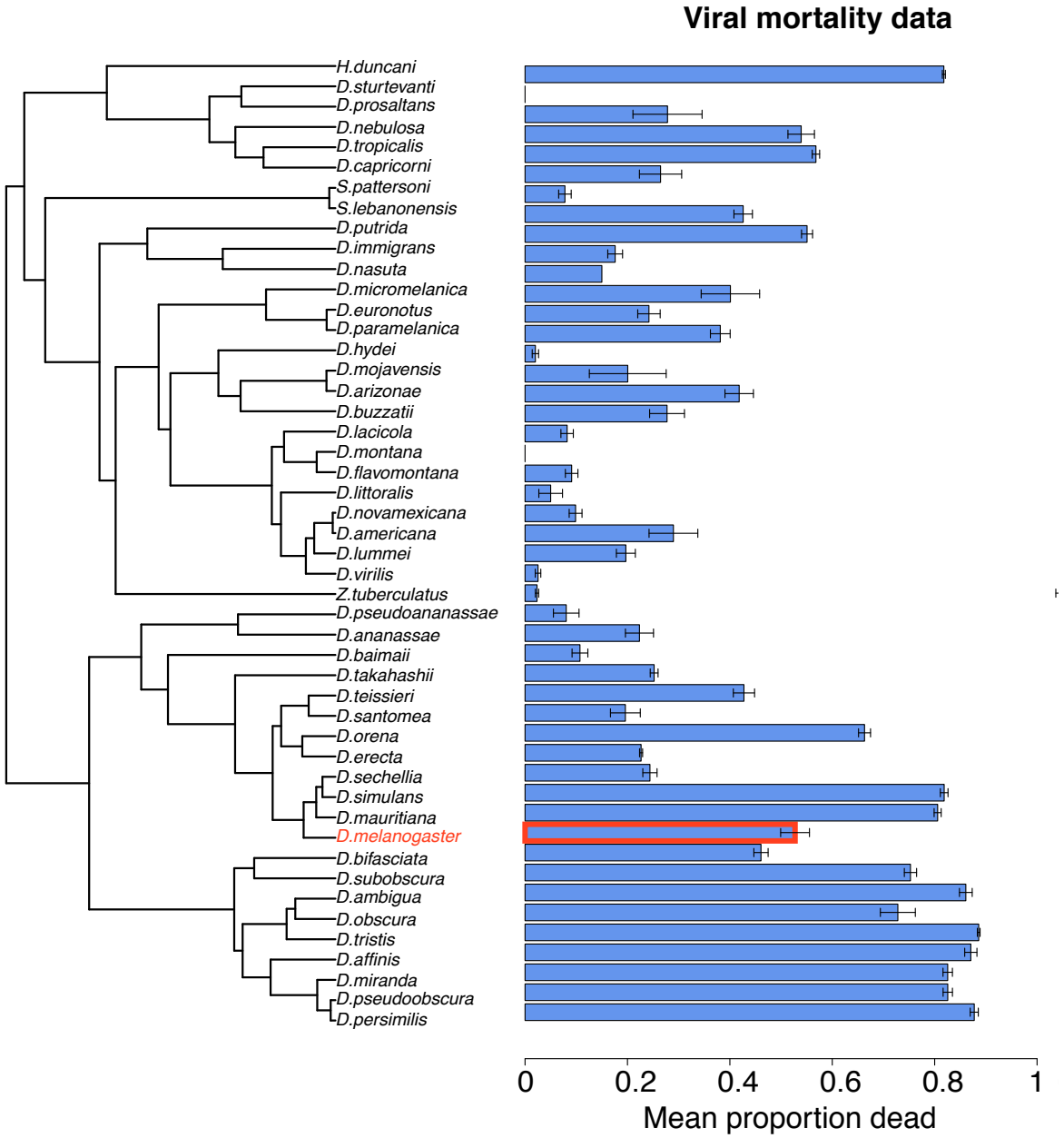

Virus and Control treatments
D.affinis
D.sechellia
D.virilis
Proportion of flies alive
1.0
0.8
0.6
0.4
0.2
0.0
5
10
15
20
Day post-infection

Virulence



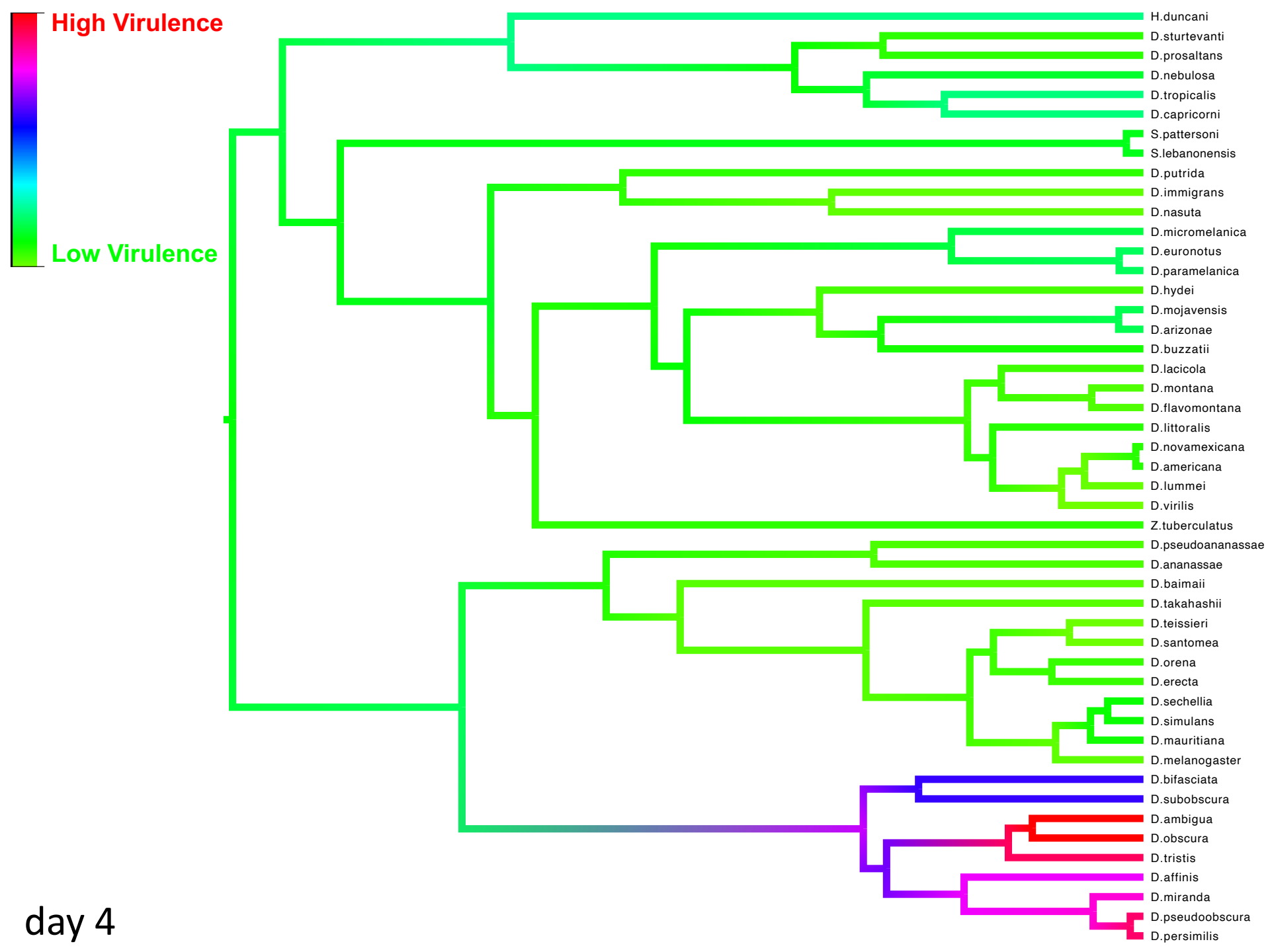
Longdon et al (2015) PLoS Path tinyurl.com/Longdon-2015

Phylogeny and virulence



Longdon et al (2015) PLoS Path

tinyurl.com/Longdon-2015


High Virulence
Low Virulence
H.duncani
D.sturtevanti
D.prosaltans
D.nebulosa
D.tropicalis
D.capricorni
S.pattersoni
S.lebanonensis
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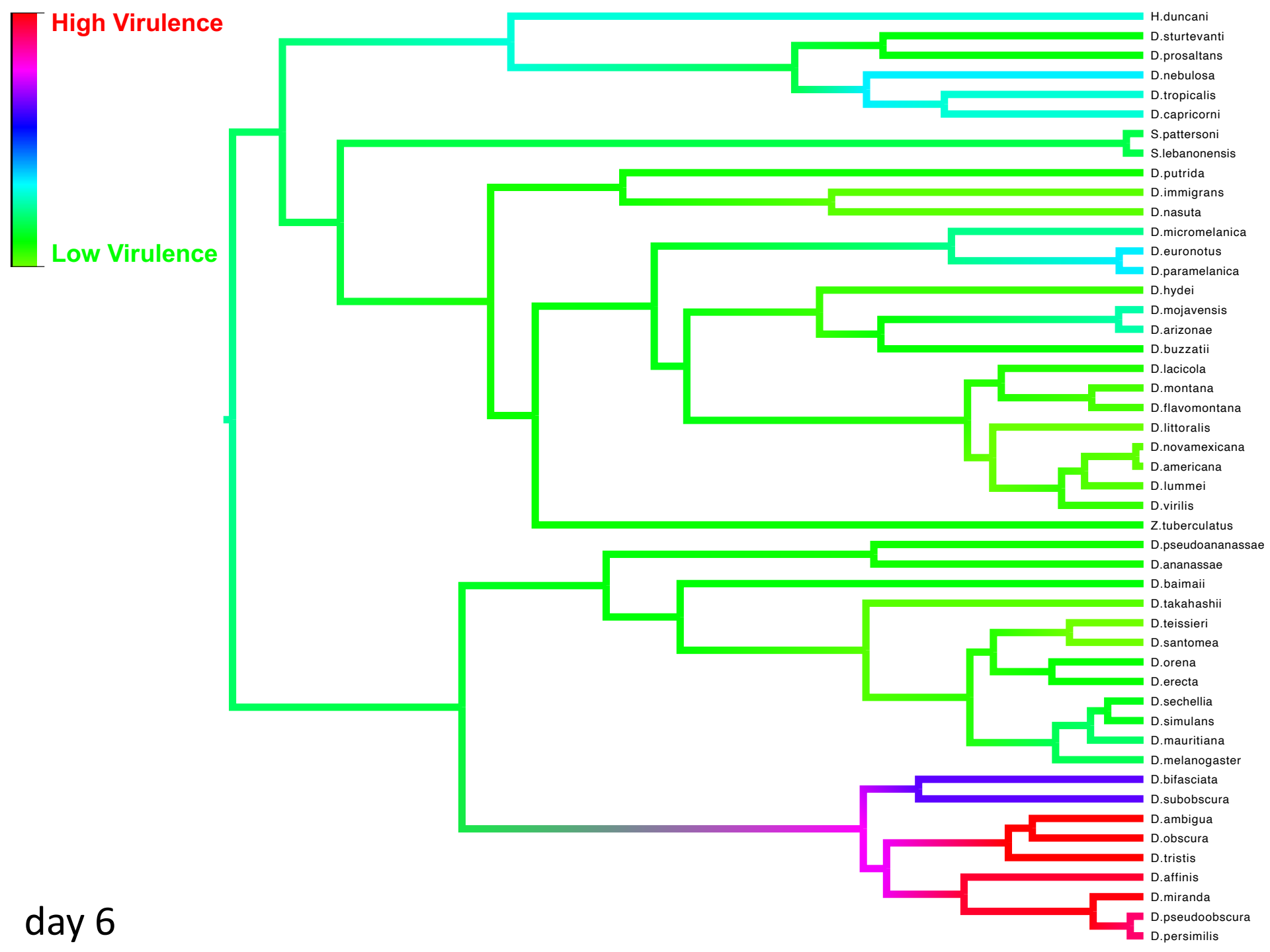
D.orena
D.erecta
D.sechellia
D.simulans
D.mauritiana
D.melanogaster
D.bifasciata
D.subobscura
D.ambigua
D.obscura
D.tristis
D.affinis
D.miranda
D.pseudoobscura
D.persimilis
day 4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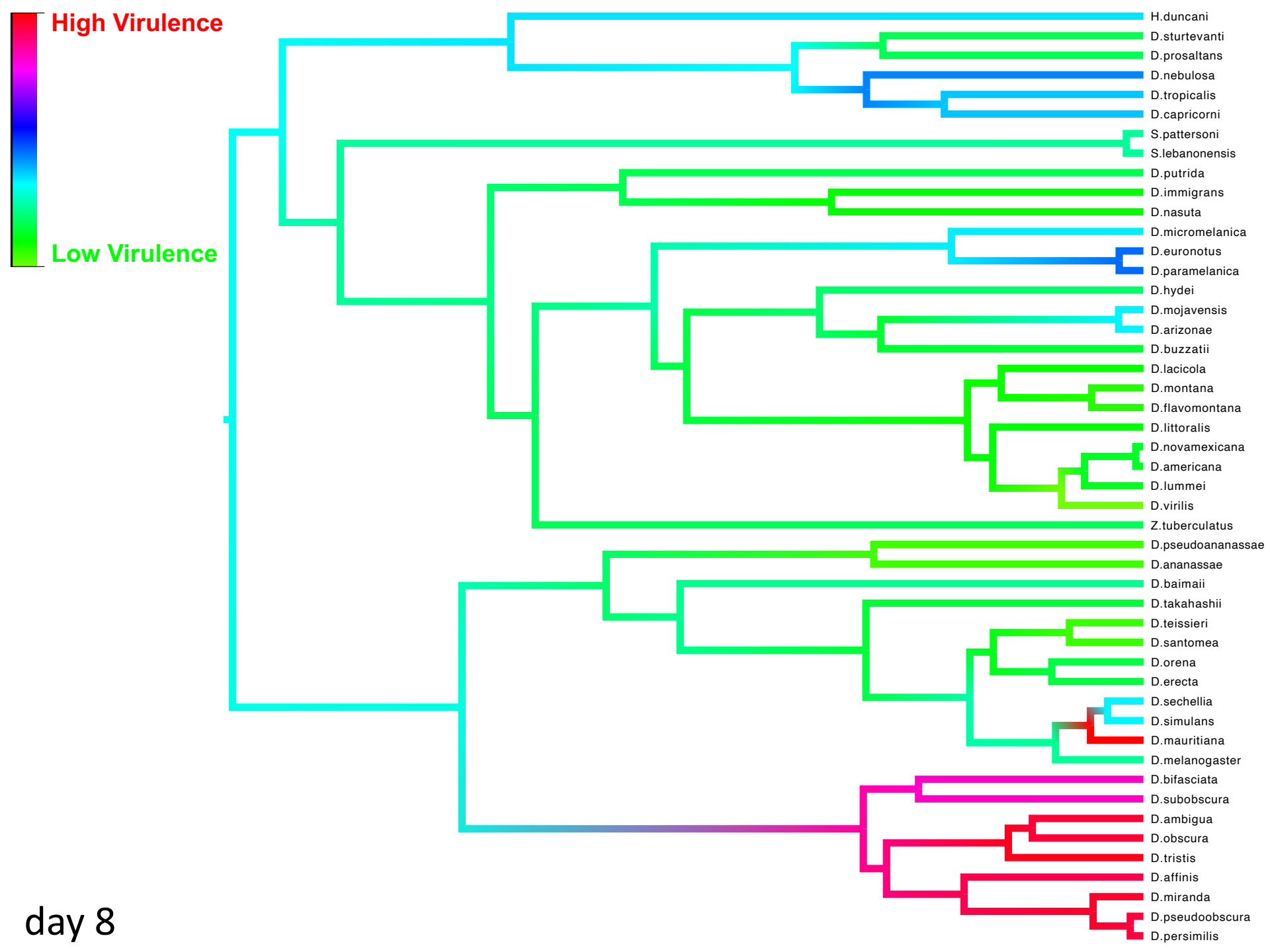
day 6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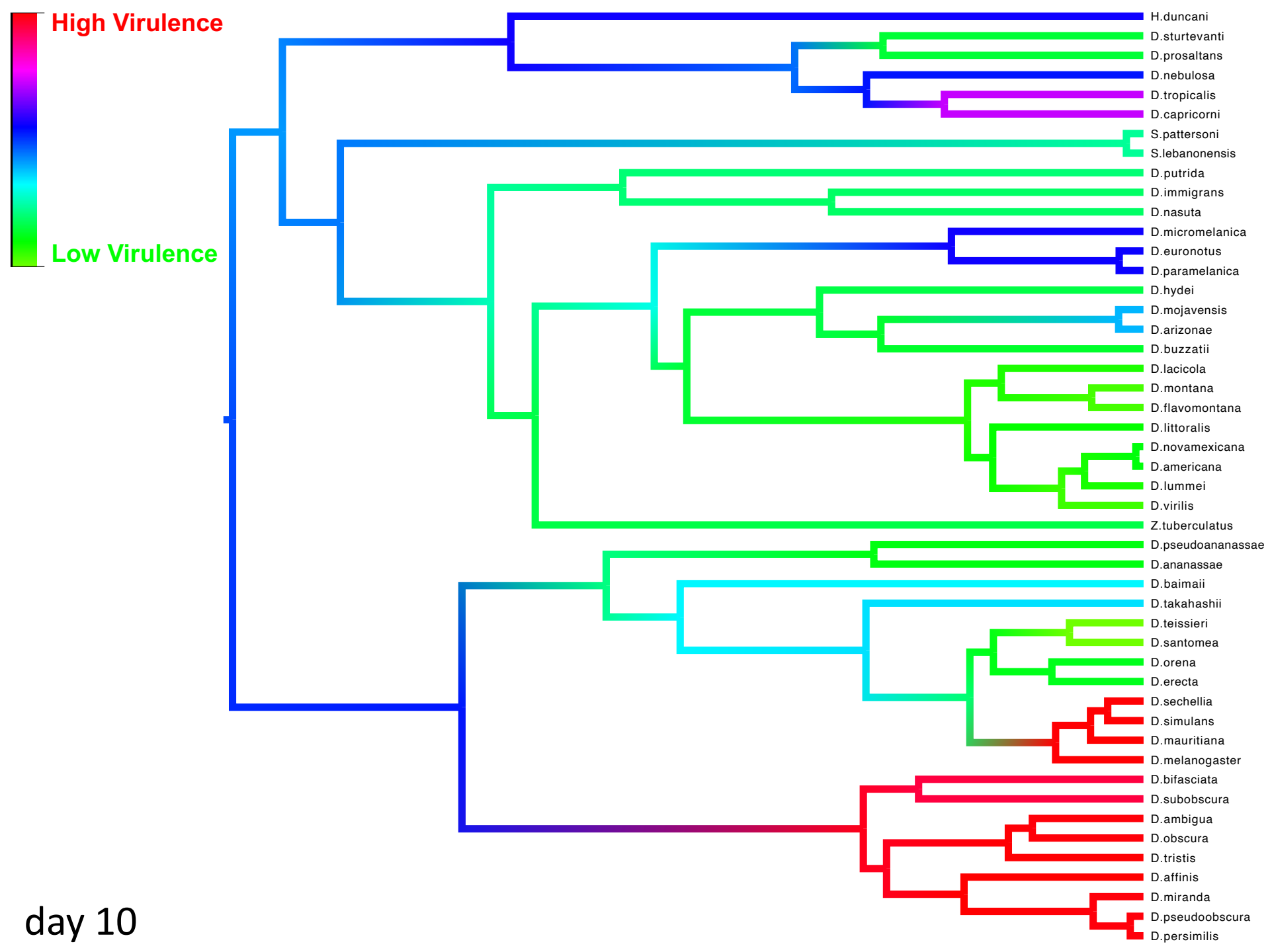
day 8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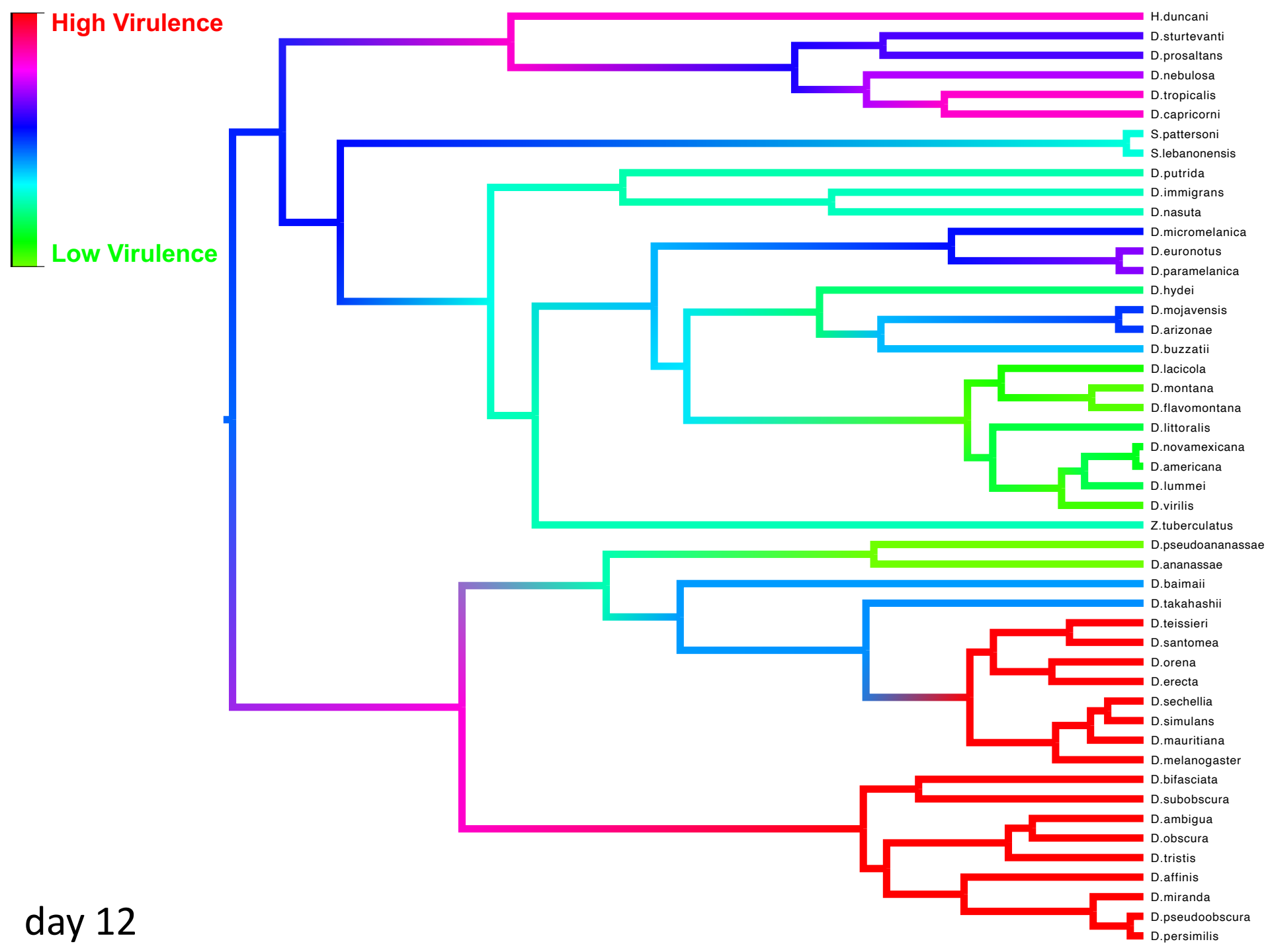
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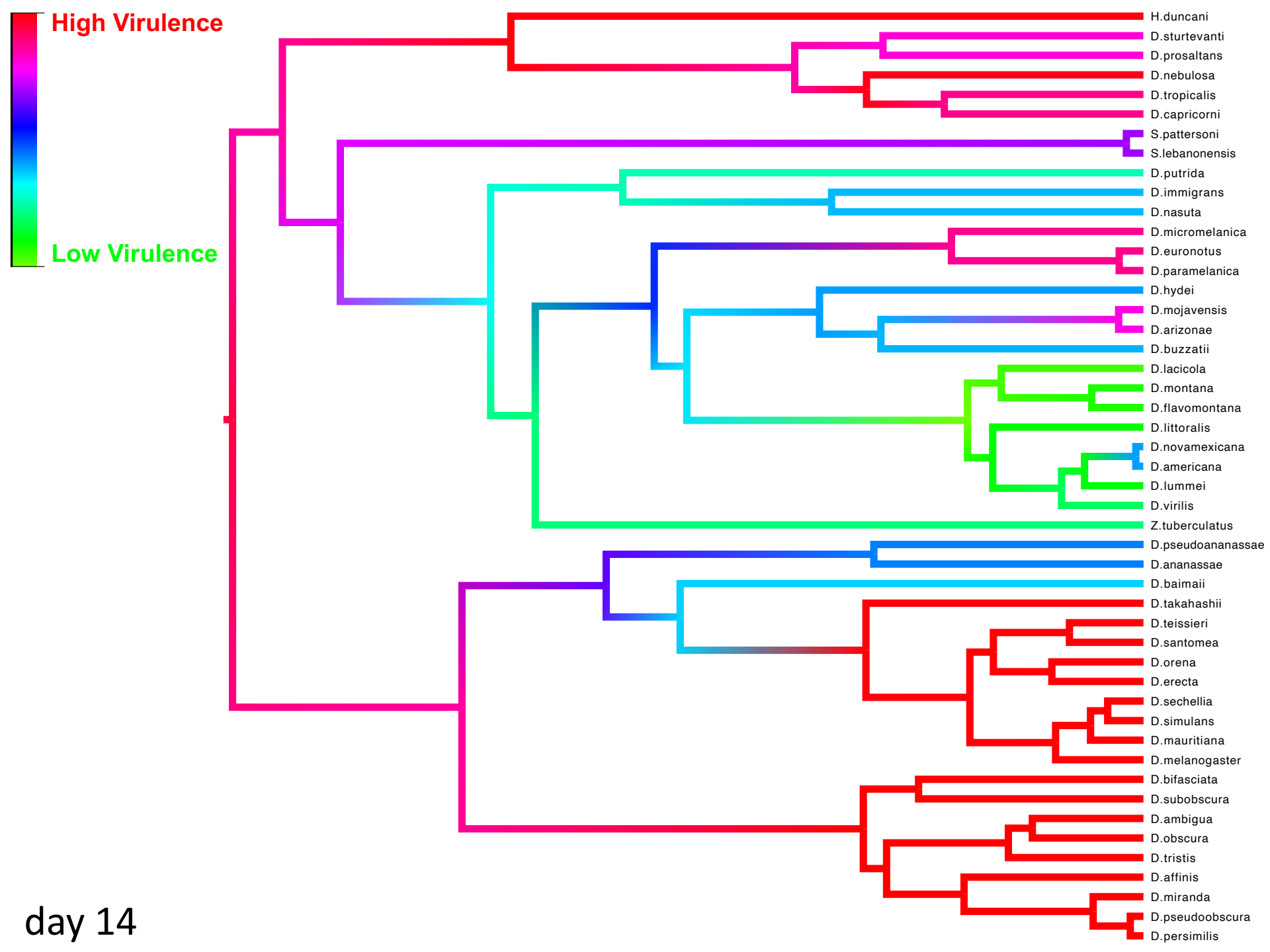
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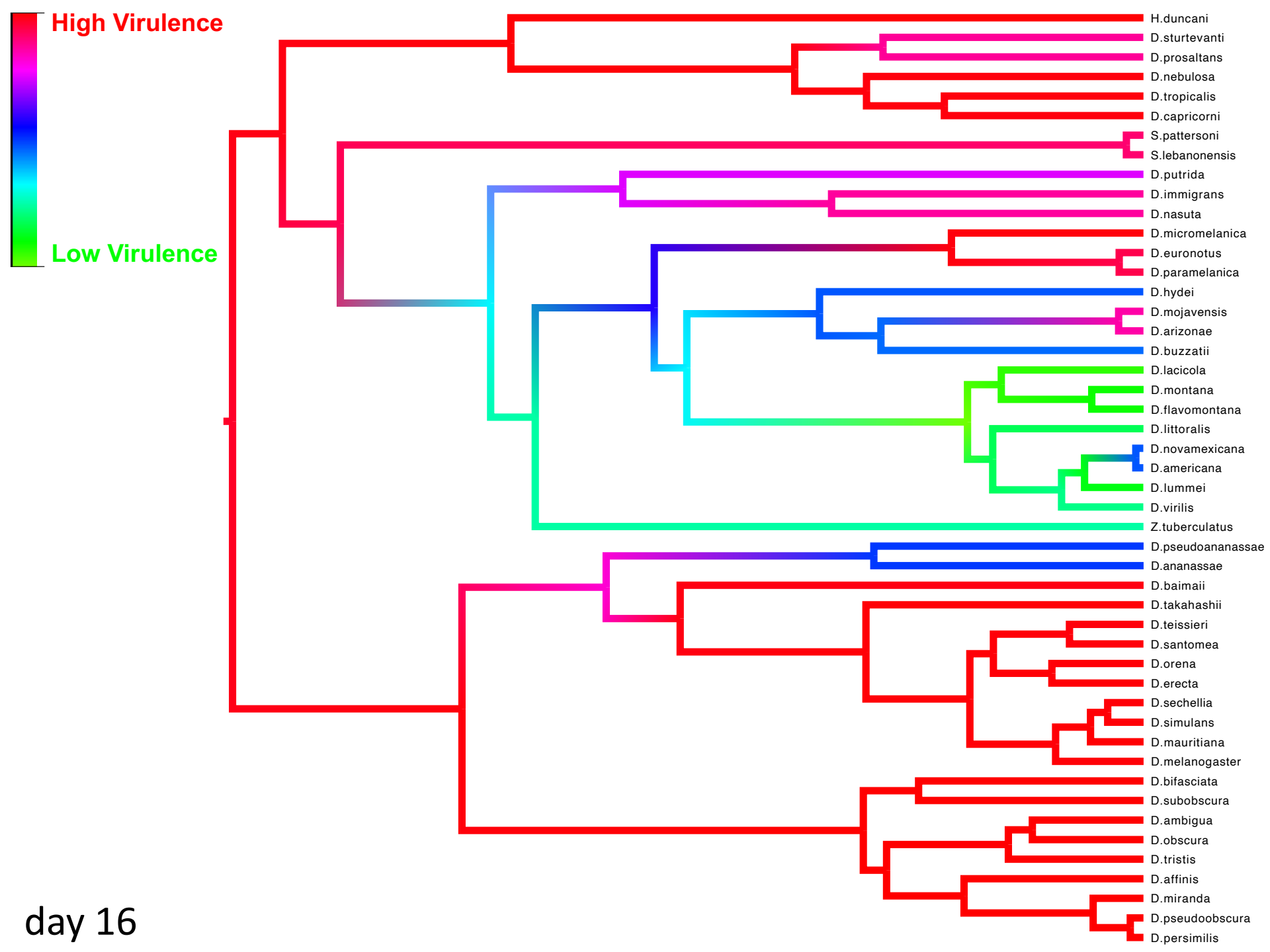
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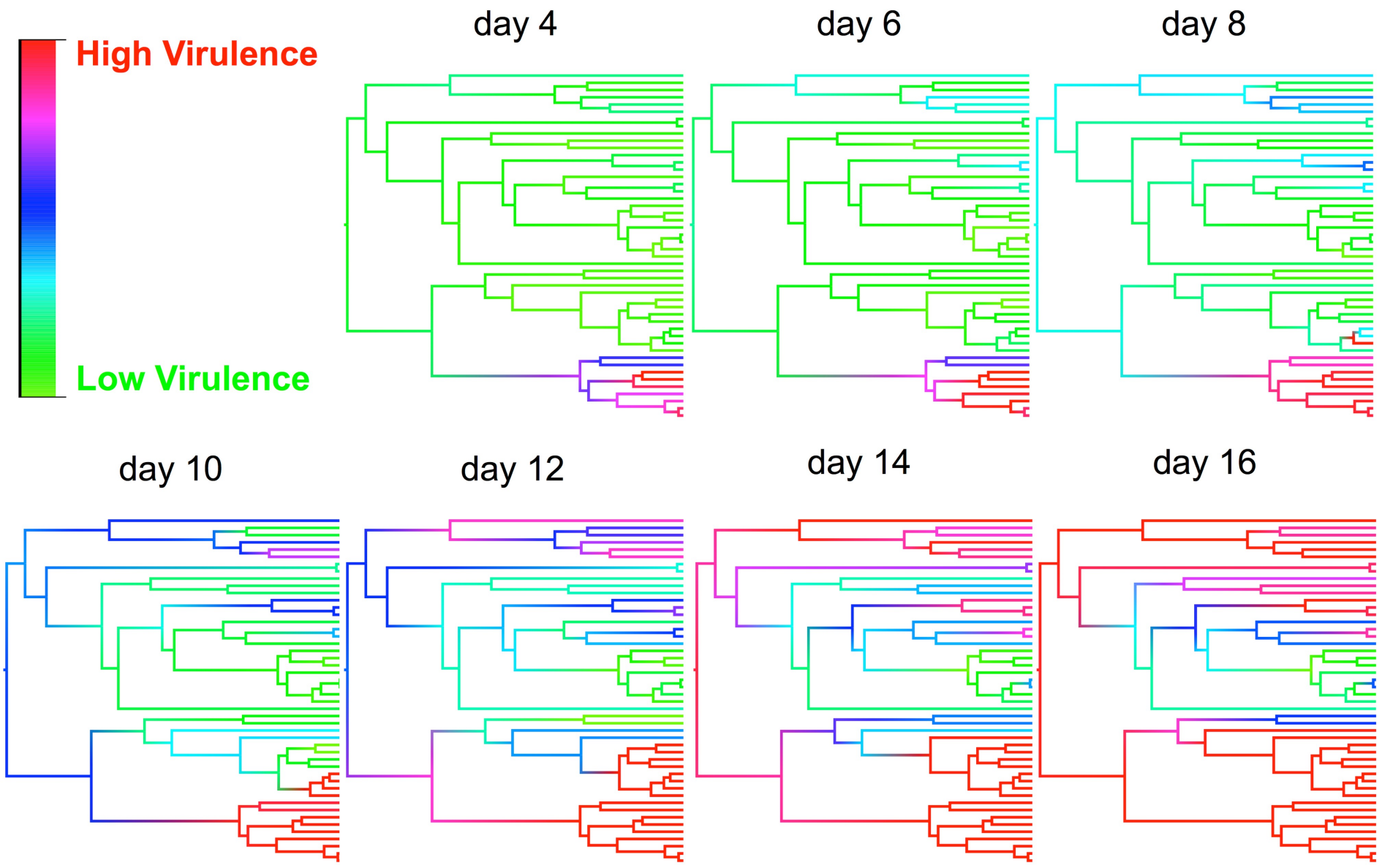
day 16

Ancestral trait reconstructions



Analysis

- Phylogenetic mixed model (MCMCglmm)
- Fixed effect= distance from the natural host
- Random effects= V_p (phylogeny), V_s (species), V_e (residual)
- Phylogenetic effect= $V_p / (V_p + V_s)$

Model: Distance effect

- No effect of distance from the “natural” host on virulence

Model: Phylogenetic effect

- No effect of distance from the “natural” host on virulence

- The host phylogeny explains a large amount of the variation in:

    - Virulence: **75%** (95% CI= 48%-97%)

Longdon et al (2015) PLoS Path tinyurl.com/Longdon-2015

Model: Phylogenetic effect

- No effect of distance from the “natural” host
- The host phylogeny explains a large amount of the variation in:
  - Virulence: **75%** (95% CI= 48%-97%)
  - Viral load: **67%** (95% CI= 33%-93%)

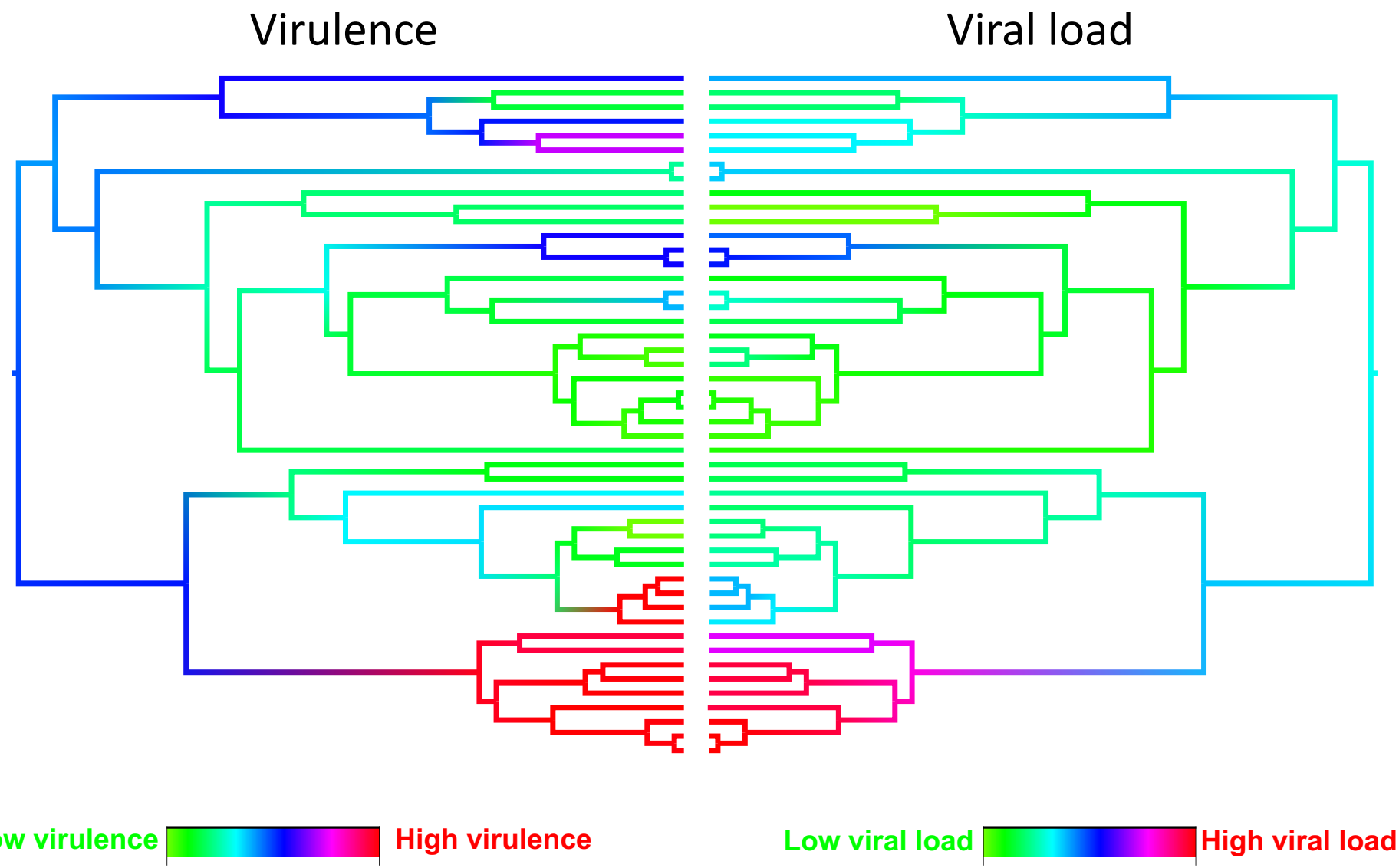
Longdon et al (2015) PLoS Path tinyurl.com/Longdon-2015

Phylogenetic effect

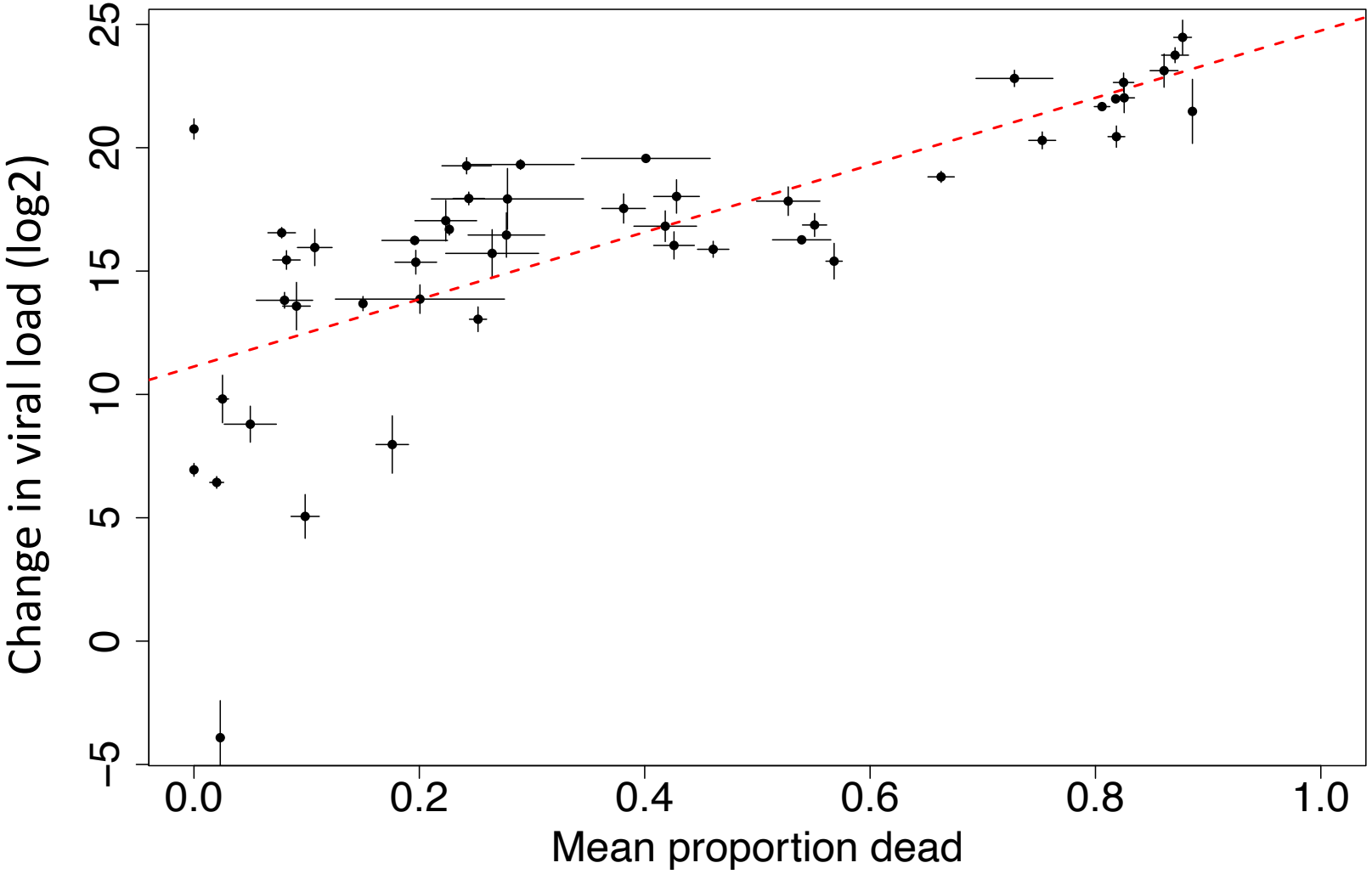
- No effect of distance from the “natural” host
- The host phylogeny explains a large amount of the variation in:
  - Virulence: **75%** (95% CI= 48%-97%)
  - Viral load: **67%** (95% CI= 33%-93%)
- Closely related species have similar levels of virulence and viral loads

Longdon et al (2015) PLoS Path tinyurl.com/Longdon-2015

Phylogenetic effect: ancestral traits

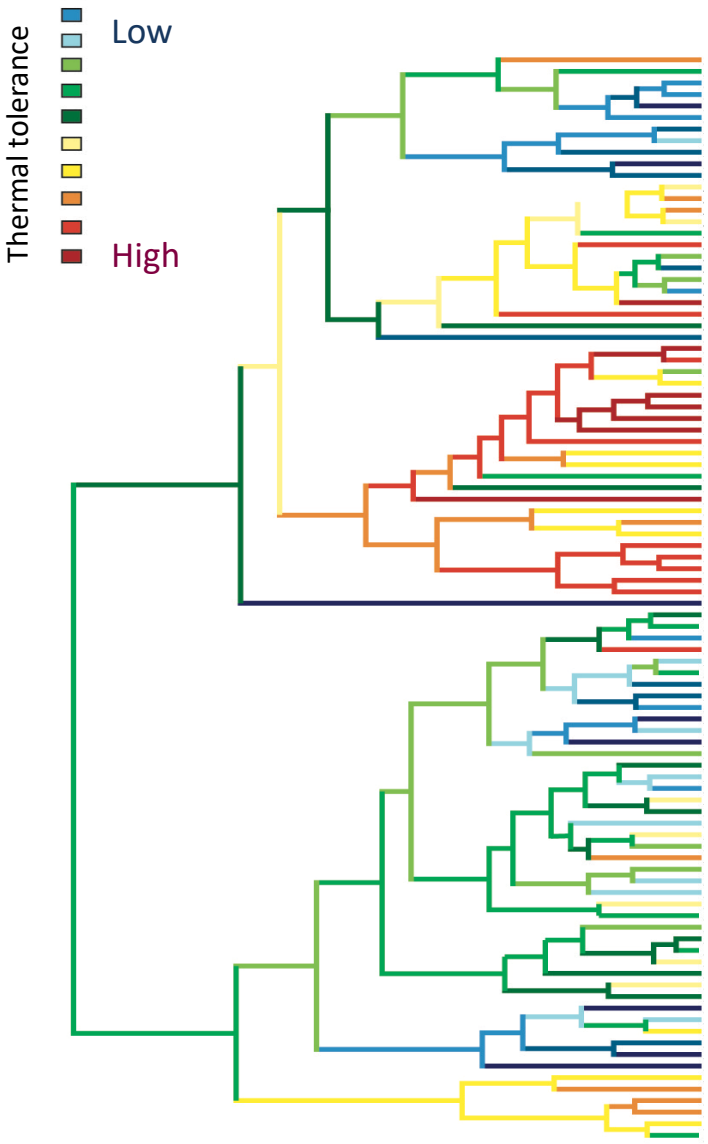


Correlation between viral load and virulence



Phylogenetic correlation = 0.76 (0.44-0.99)

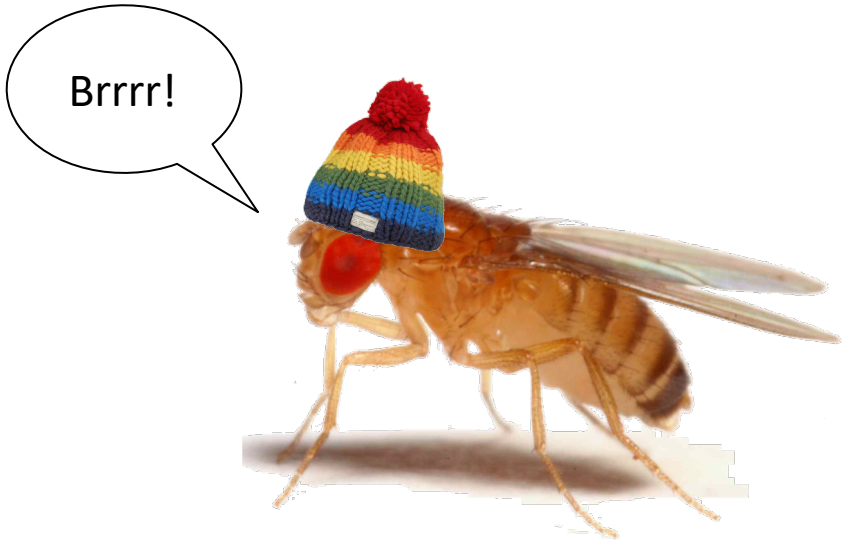
Environmental factors



Katherine Roberts

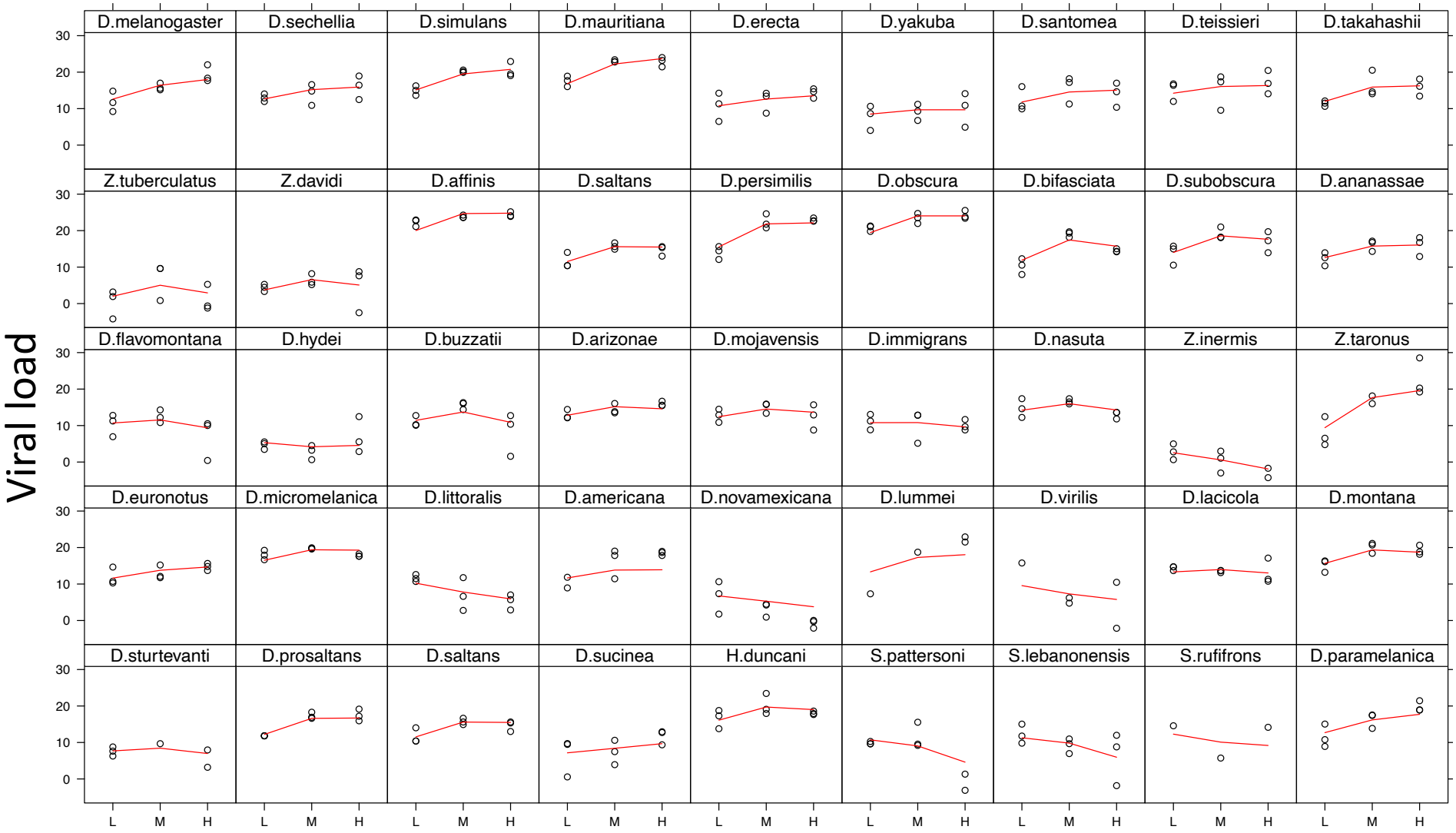
- Phylogenetic signal in thermal tolerances of Drosophila
- Thermal optimas and virus susceptibility

Data from Kellerman et al 2012 Evolution
tinyurl.com/Kellerman-2012


Brrrr!

Phew!

Effect of temperature



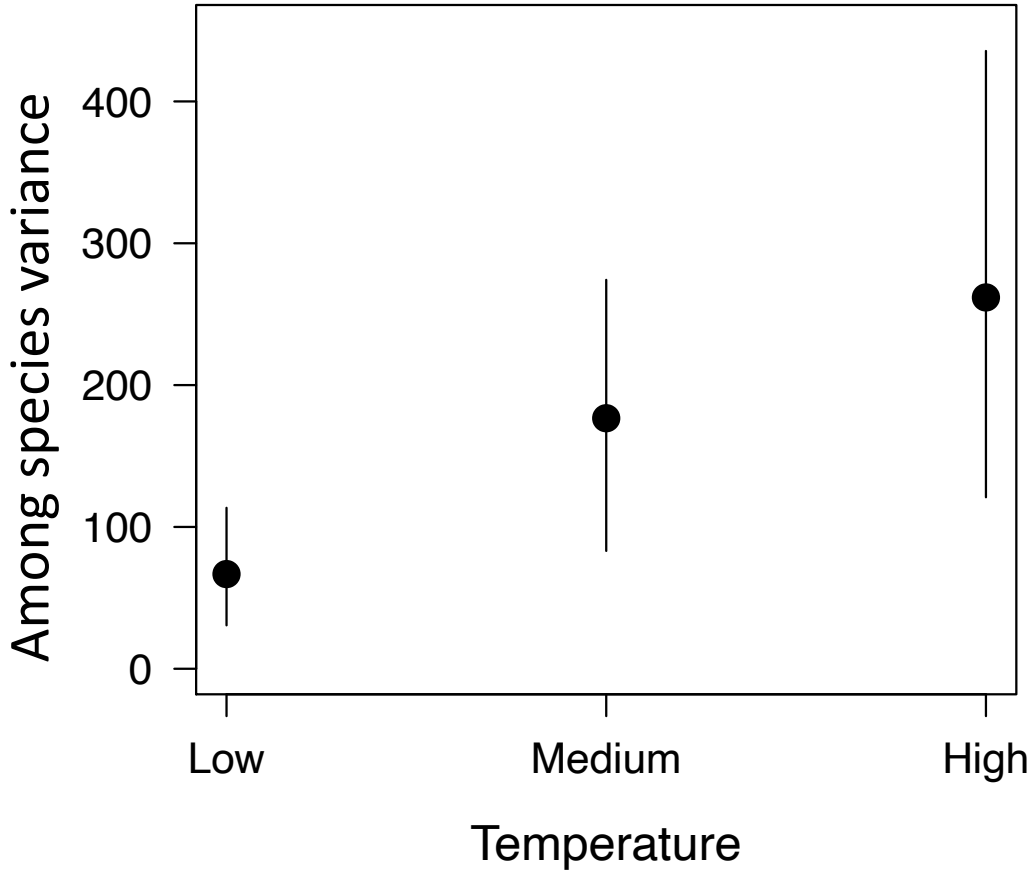
Roberts et al 2018 PLoS Path tinyurl.com/KatRoberts-2018

Effect of temperature

Strong correlations in viral load across temperatures

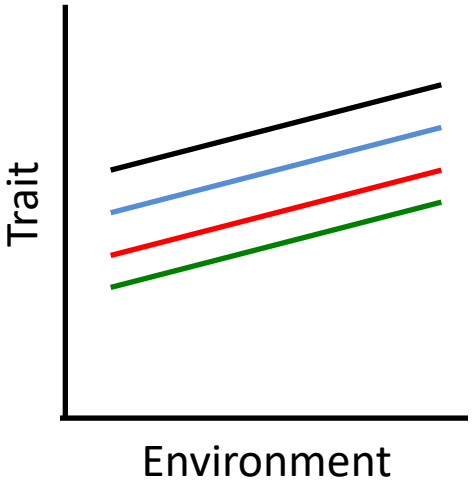
Temperatures	Correlations	95 % CI's
Low-Medium	0.92	0.90-0.99
Low-High	0.89	0.77-0.98
Medium-High	0.97	0.93-0.99

Variance increases with temperature

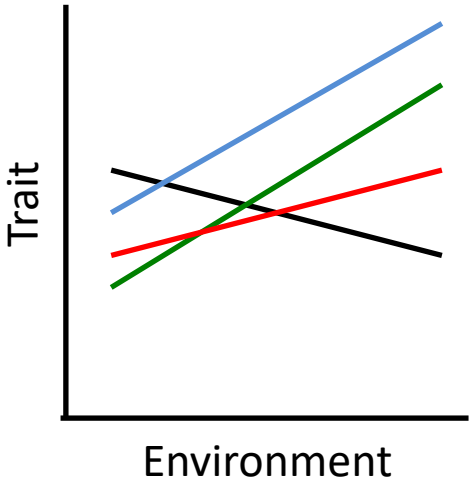


Temperature	Intercepts		Between-species Variance (v_p)	
	Mean	95% CIs	Mean	95% CIs
Low	11.9	9.5, 14.6	65.3	32.3, 110.3
Medium	14.3	11.7, 17.1	172.2	90.2, 278.8
High	13.5	10.8, 16.7	260.6	119.7, 413.7

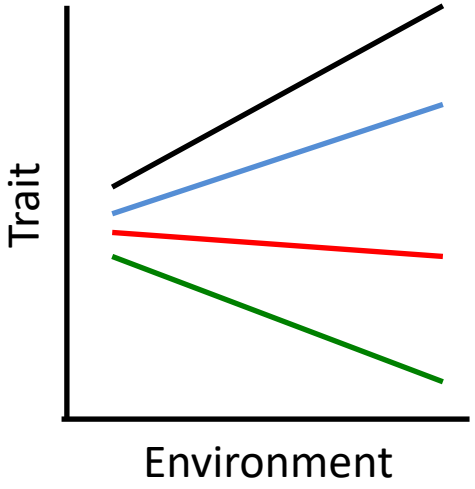
Interactions



No interaction



Cross over of reaction norms, rank changes between environments

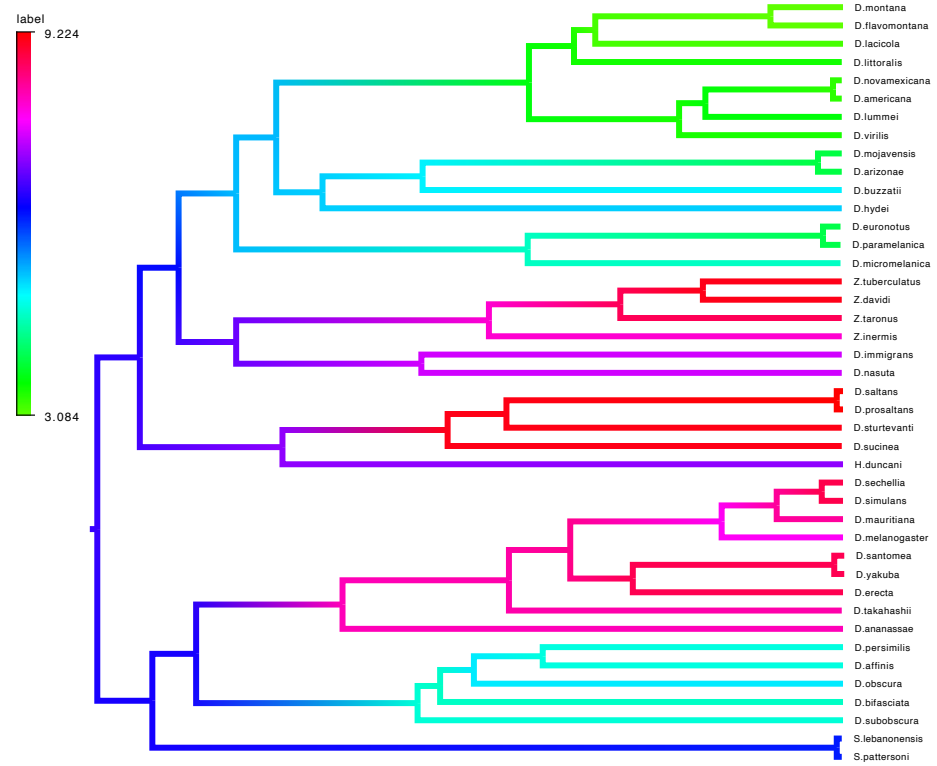


Variation but not rank order differs between environments

Adapted from Inglebury et al 2010 JEB

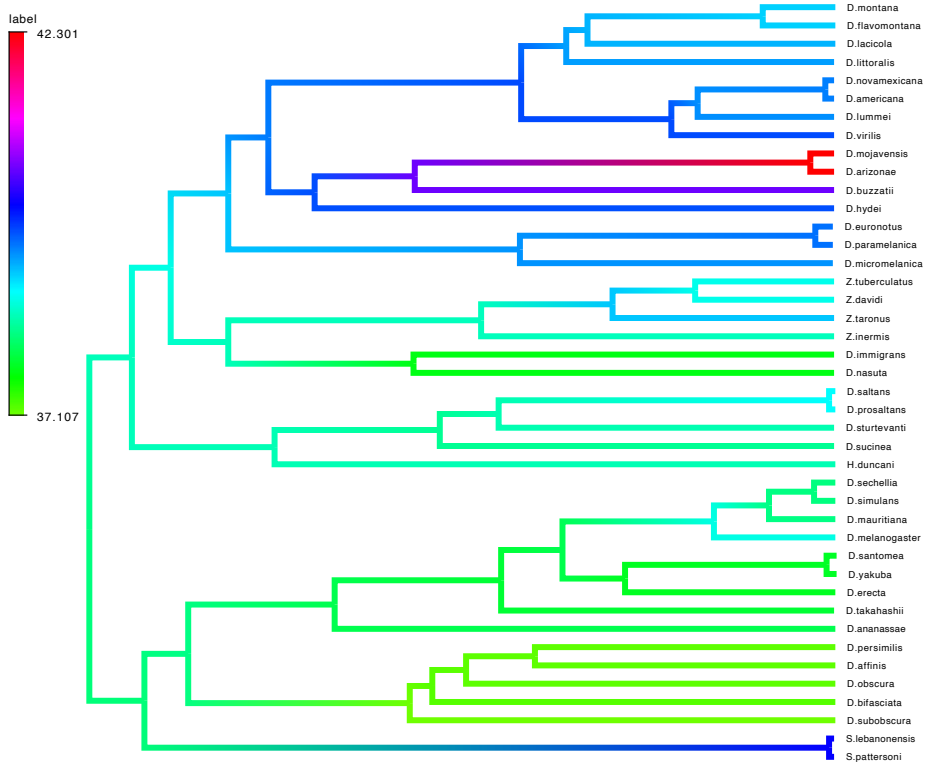
Effect of temperature

CT min



Variance explained by phylogeny:
0.72 (0.61-0.84)

CT max



Variance explained by phylogeny:
0.65 (0.52-0.79)

Roberts et al 2018 PLoS Path tinyurl.com/KatRoberts-2018

What about diet?

What about diet?

Diet

27 Drosophilidae species

P:C Ratio

High 1:5 or Medium 1:10 or Low 1:20

Survival assay

↓

DCV or control inoculation. Mortality checks for 21 days

Viral load assay

↓

DCV inoculation – frozen day 0 or day 2 post-infection

Roberts and Longdon 2021 JEB tinyurl.com/KatRoberts-2021

Diet

- Strong positive inter-species correlations in both viral load and mortality across diets

Roberts and Longdon 2021 JEB tinyurl.com/KatRoberts-2021

Diet

- Strong positive inter-species correlations in both viral load and mortality across diets

- Protein:carbs just one aspect of diet – increasing evidence lipids may be important…

(Zanco et al 2021 eLIFE and Chtarbanova et al 2014 J of Virology)

Roberts and Longdon 2021 JEB tinyurl.com/KatRoberts-2021

Why are some species more susceptible than others?

PLOS BIOLOGY

RESEARCH ARTICLE

Tissue tropism and transmission ecology predict virulence of human RNA viruses

Liam Brierley¤*, Amy B. Pedersen, Mark E. J. Woolhouse

Centre for Immunity, Infection and Evolution, Institute of Evolutionary Biology, University of Edinburgh, Edinburgh, United Kingdom

Abstract

Novel infectious diseases continue to emerge within human populations. Predictive studies have begun to identify pathogen traits associated with emergence. However, emerging pathogens vary widely in virulence, a key determinant of their ultimate risk to public health. Here, we use structured literature searches to review the virulence of each of the 214 known human-infective RNA virus species. We then use a machine learning framework to determine whether viral virulence can be predicted by ecological traits, including human-to-human transmissibility, transmission routes, tissue tropisms, and host range. Using severity of clinical disease as a measurement of virulence, we identified potential risk factors using predictive classification tree and random forest ensemble models. The random forest approach predicted literature-assigned disease severity of test data with mean accuracy of 89.4% compared to a null accuracy of 74.2%. In addition to viral taxonomy, the ability to cause systemic infection was the strongest predictor of severe disease. Further notable predictors of severe disease included having neural and/or renal tropism, direct contact or respiratory transmission, and limited ($0 < R_0 \leq 1$) human-to-human transmissibility. We present a novel, to our knowledge, comparative perspective on the virulence of all currently known human RNA virus species. The risk factors identified may provide novel perspectives in understanding the evolution of virulence and elucidating molecular virulence mechanisms. These risk factors could also improve planning and preparedness in public health strategies as part of a predictive framework for novel human infections.

Tissue Tropism

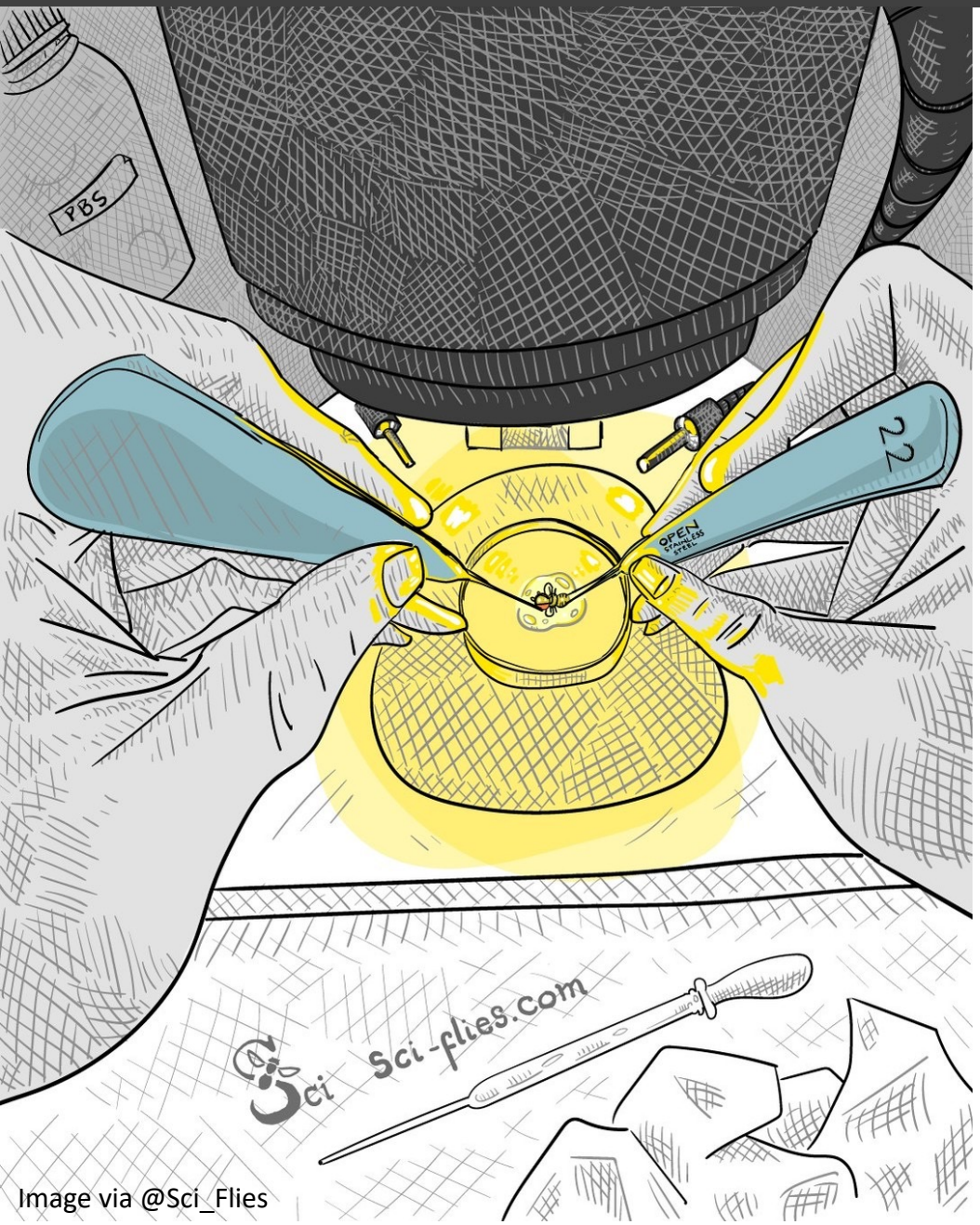


Image via @Sci_Flies

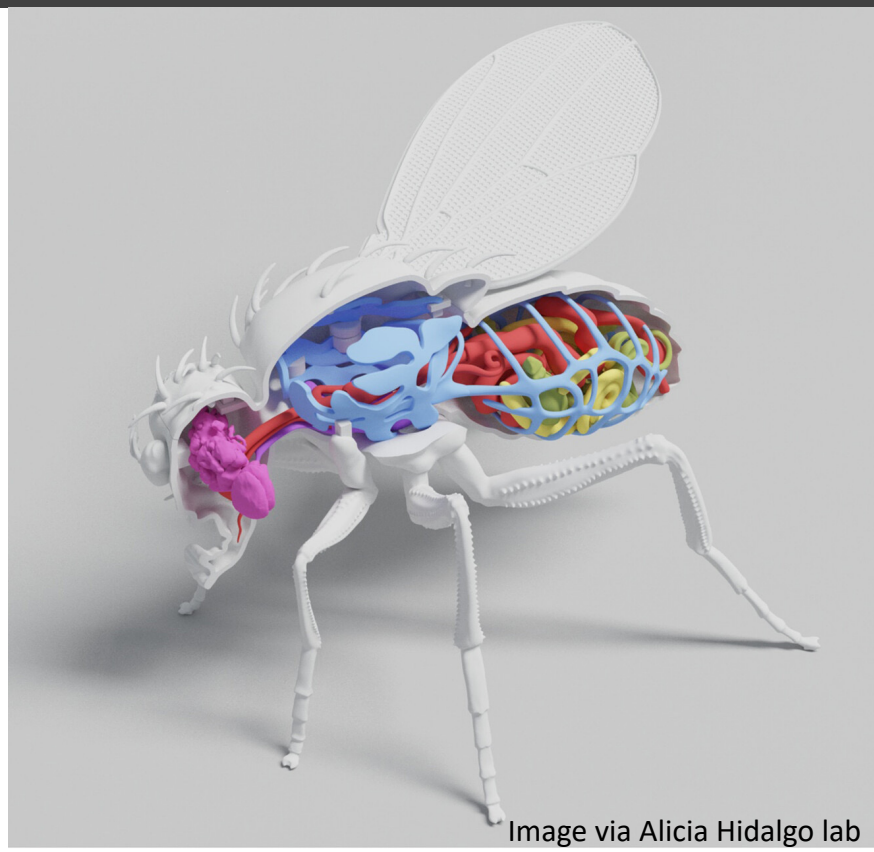
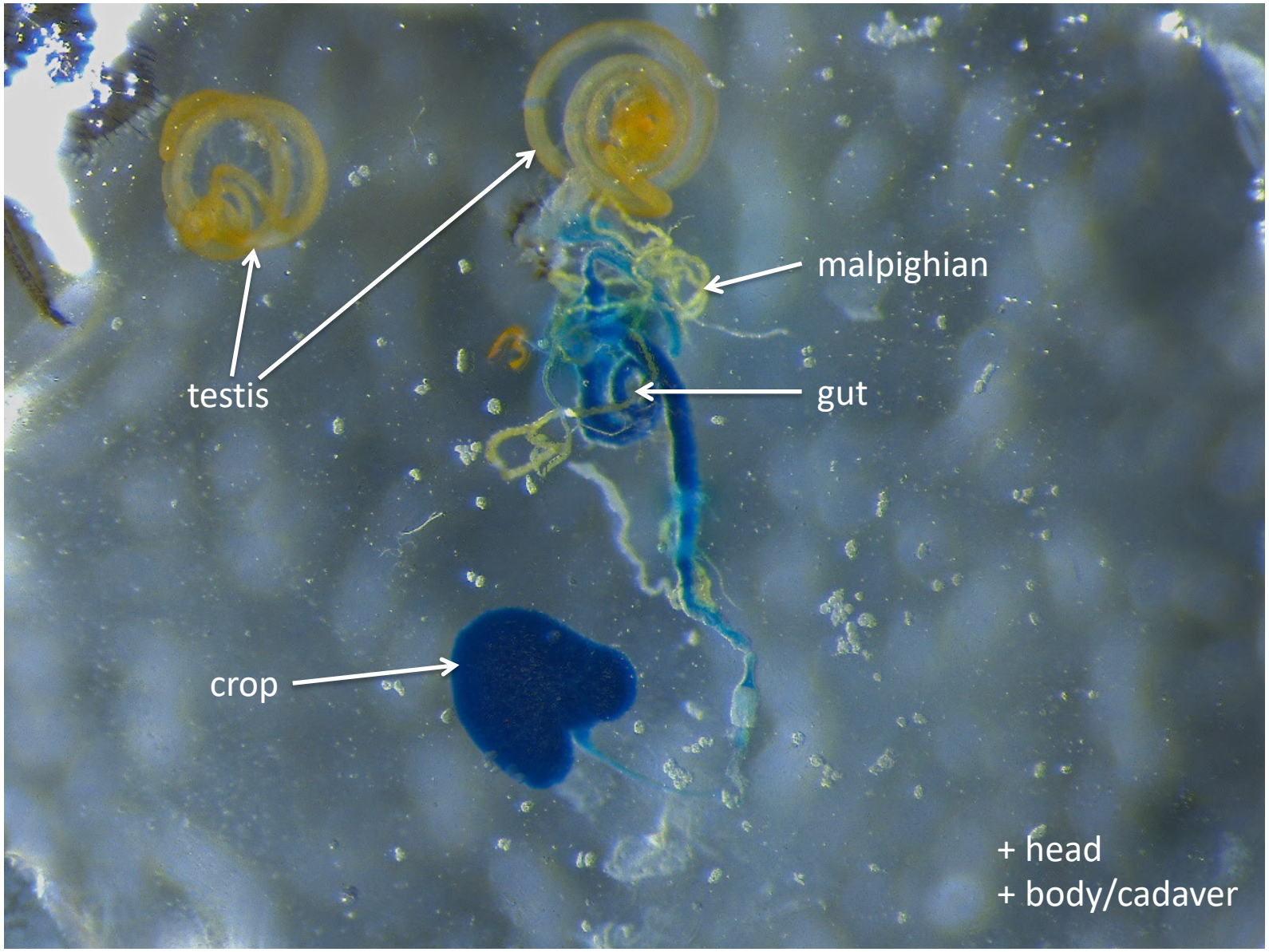
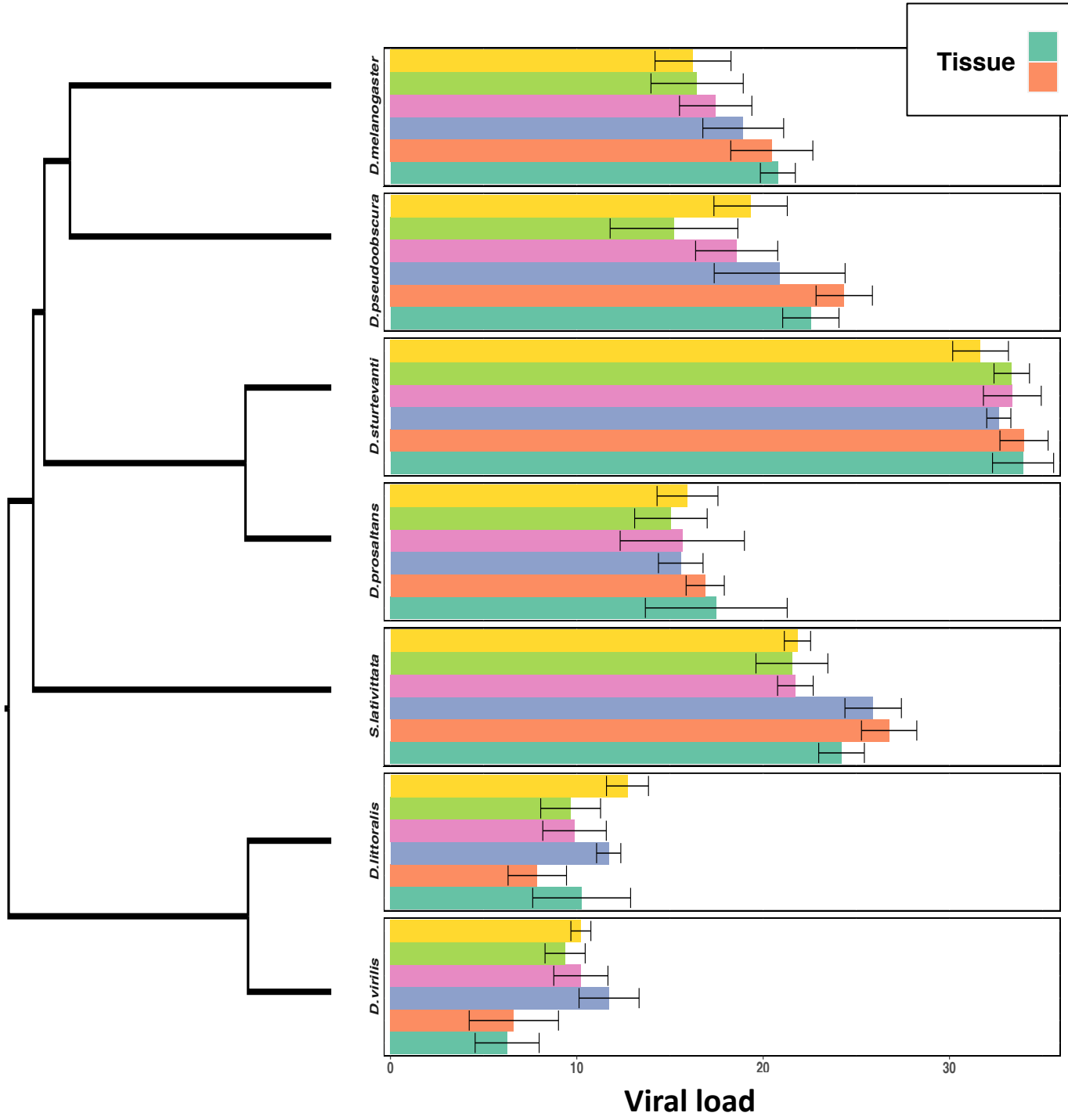


Image via Alicia Hidalgo lab

- Head
- Crop
- Gut
- Malpighian tubules
- Sex tissues
- Body

Tissue Tropism



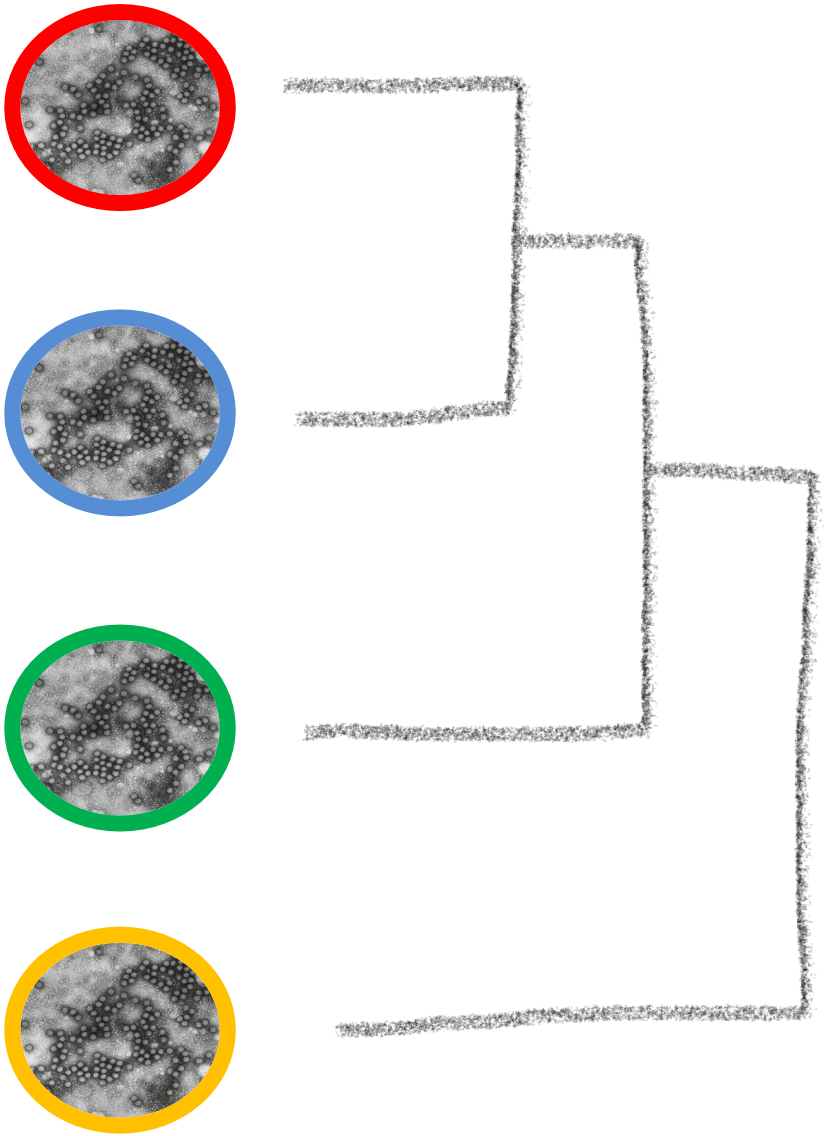


Detect effects of tissue type and species on viral load

No evidence for a tissue-by-species interaction

Roberts et al. Unpublished

How does susceptibility vary to different pathogens?



QUANTIZED COLUMNS

What Other Coronaviruses Tell Us About SARS-CoV-2

29 |

As COVID-19 cases continue to increase, our extensive knowledge of other coronaviruses informs our understanding.

Coronavirus: How is the deadly virus different to SARS and Ebola?

Lessons from containing past virus outbreaks could help in tackling coronavirus, experts say, but how do the viruses differ?

Yasmeen Abutaleb | Saturday 25 January 2020 10:44 |

The Observer

Experience of Sars a key factor in countries' response to coronavirus

Plans of action to combat the Covid-19 outbreak around the world show huge differences

La Jolla Institute FOR IMMUNOLOGY | Life Without Disease.®

What we can learn from SARS

Researchers comb through hundreds of studies to find clues to beating COVID-19

Global Agenda | COVID-19 | Global Health | Future of Health and Healthcare

Two experts explain what other viruses can teach us about COVID-19 – and what they can't

China

China coronavirus: The lessons learned from the Sars outbreak

By Kelly-Leigh Cooper
BBC News

24 January 2020

SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis

Muge Cevik, Matthew Tate, Ollie Lloyd, Alberto Enrico Maraolo, Jenna Schafers, Antonia Ho

Summary

Background Viral load kinetics and duration of viral shedding are important determinants for disease transmission. We aimed to characterise viral load dynamics, duration of viral RNA shedding, and viable virus shedding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in various body fluids, and to compare SARS-CoV-2, SARS-CoV, and Middle East respiratory syndrome coronavirus (MERS-CoV) viral dynamics.

Lancet Microbe 2020
Published Online
November 19, 2020
https://doi.org/10.1016/S2666-5247(20)30172-5

Why are some species more susceptible than others?

PLOS | BIOLOGY

RESEARCH ARTICLE

Tissue tropism and transmission ecology predict virulence of human RNA viruses

Liam Brierley¤*, **Amy B. Pedersen**, **Mark E. J. Woolhouse**

Centre for Immunity, Infection and Evolution, Institute of Evolutionary Biology, University of Edinburgh, Edinburgh, United Kingdom

PeerJ

Taxonomic patterns in the zoonotic potential of mammalian viruses

Alex D. Washburne[1], Daniel E. Crowley[1], Daniel J. Becker[1], Kevin J. Olival[2], Matthew Taylor[1], Vincent J. Munster[3] and Raina K. Plowright[1]

[1] Department of Microbiology and Immunology, Montana State University, Bozeman, MT, USA
[2] Ecohealth Alliance, New York, NY, USA
[3] National Institute of Allergy and Infectious Disease, Hamilton, MT, USA

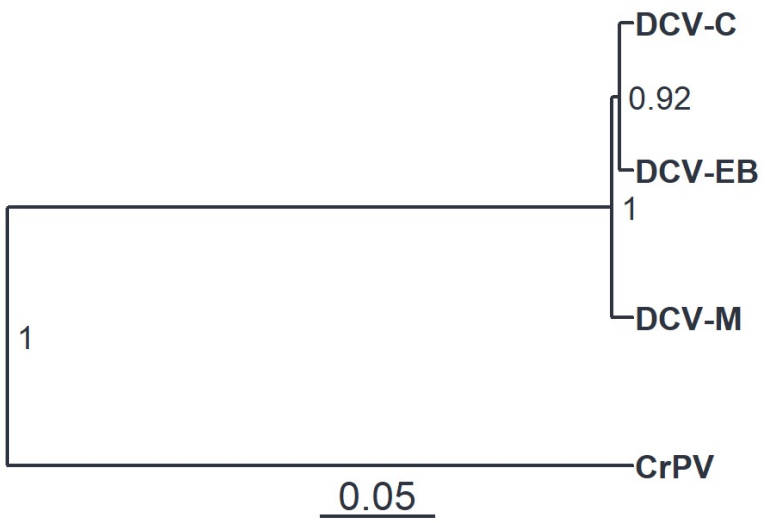
Viral zoonotic risk is homogenous among taxonomic orders of mammalian and avian reservoir hosts

Nardus Mollentze[a,1] **and Daniel G. Streicker**[a,b,1]

[a]Medical Research Council–University of Glasgow Centre for Virus Research, Glasgow G61 1QH, United Kingdom; and [b]Institute of Biodiversity, Animal Health and Comparative Medicine, College of Medical Veterinary and Life Sciences, University of Glasgow, Glasgow G12 8QQ, United Kingdom

How does susceptibility vary to different pathogens?

A.



Ryan Imrie

B.

Virus Isolate Sequence Similarity

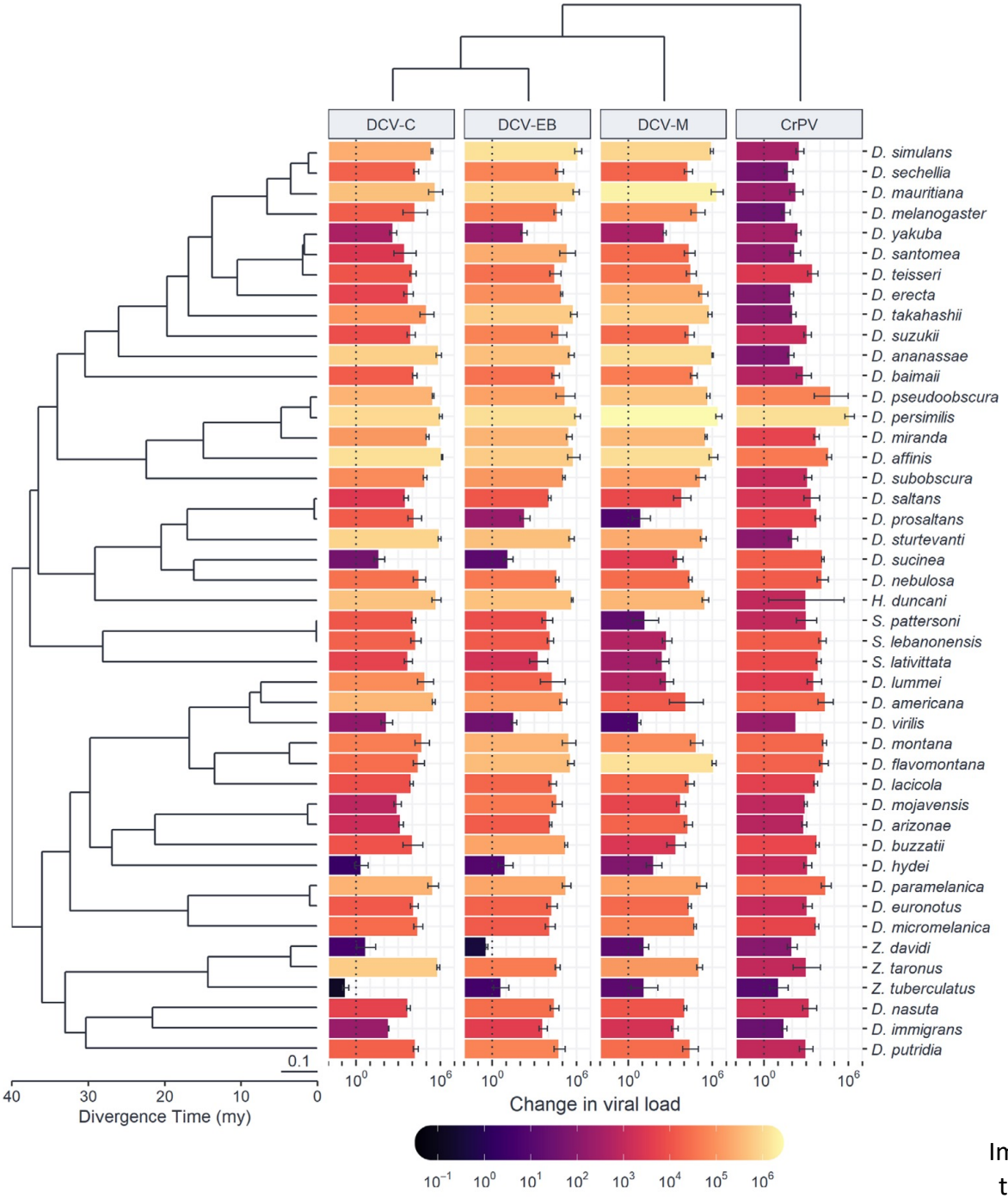
	DCV-C	DCV-EB	DCV-M	CrPV
DCV-C		97.10%	94.00%	57.40%
DCV-EB	98.81%		93.90%	57.30%
DCV-M	98.30%	98.20%		57.40%
CrPV	59.00%	58.70%	58.70%	

= Genome-wide nucleotide % identity.

= ORF1 & ORF2 amino acid % identity.

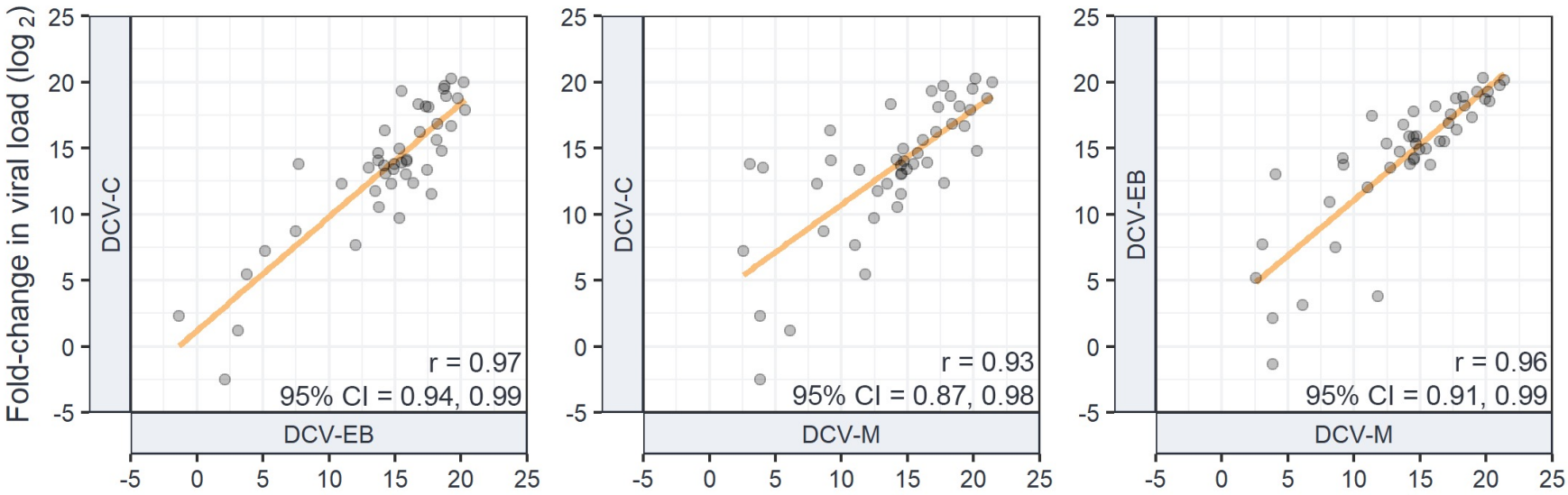
How does susceptibility vary to different pathogens?

	DCV	CrPV
Symptoms	Gut pathology causing intestinal obstruction, reduced faecal excretion rate	No gut pathology or intestinal obstruction
Suppression of immune response	Sequesters dsRNA, interferes with RISC formation	Inhibits Ago-2 slicing activity



Imrie et al. 2021. Evol Letters
tinyurl.com/RyanImrie-2021

Correlations between viruses



Imrie et al. 2021. Evol Letters
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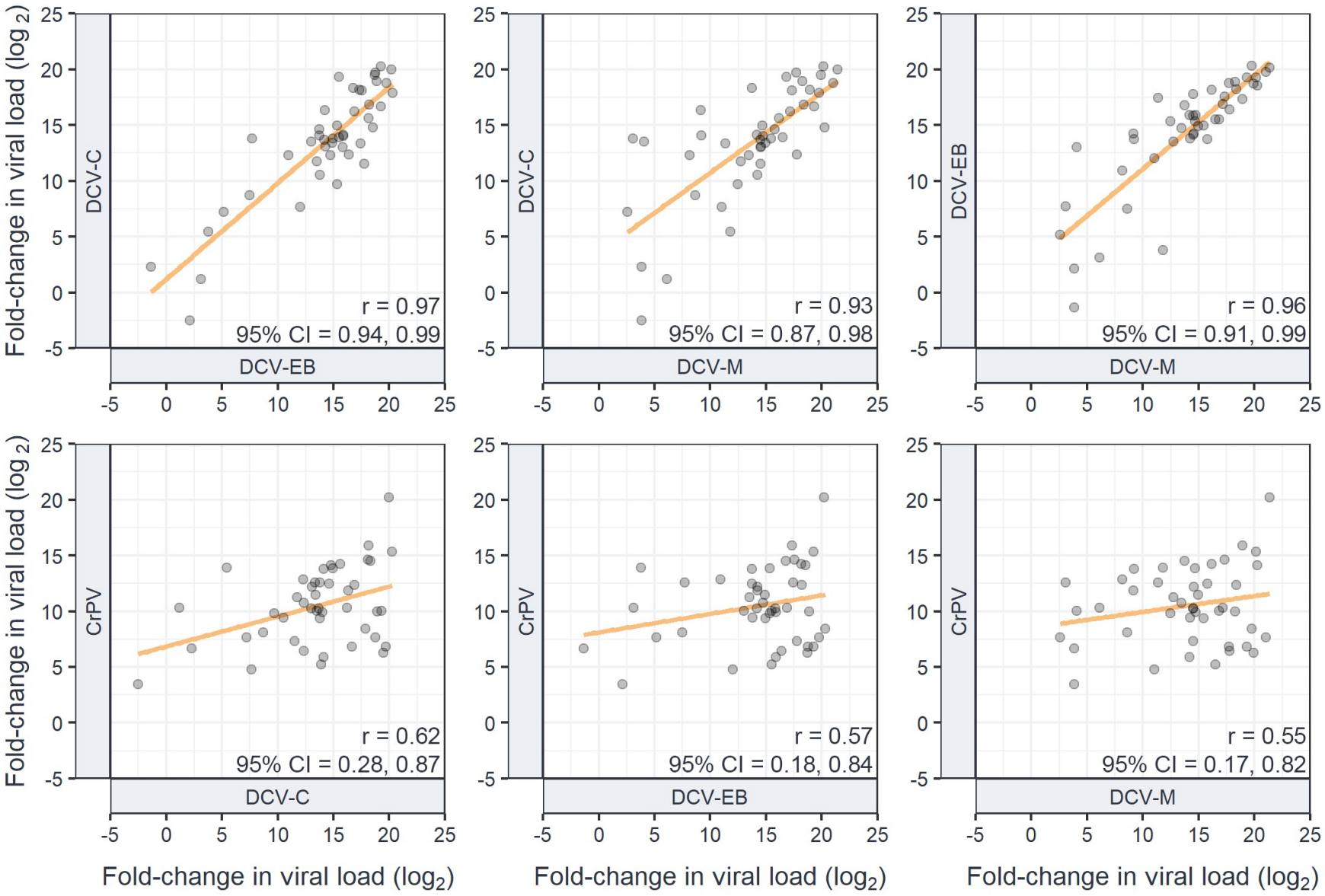
Correlations between viruses



Imrie et al. 2021. Evol Letters

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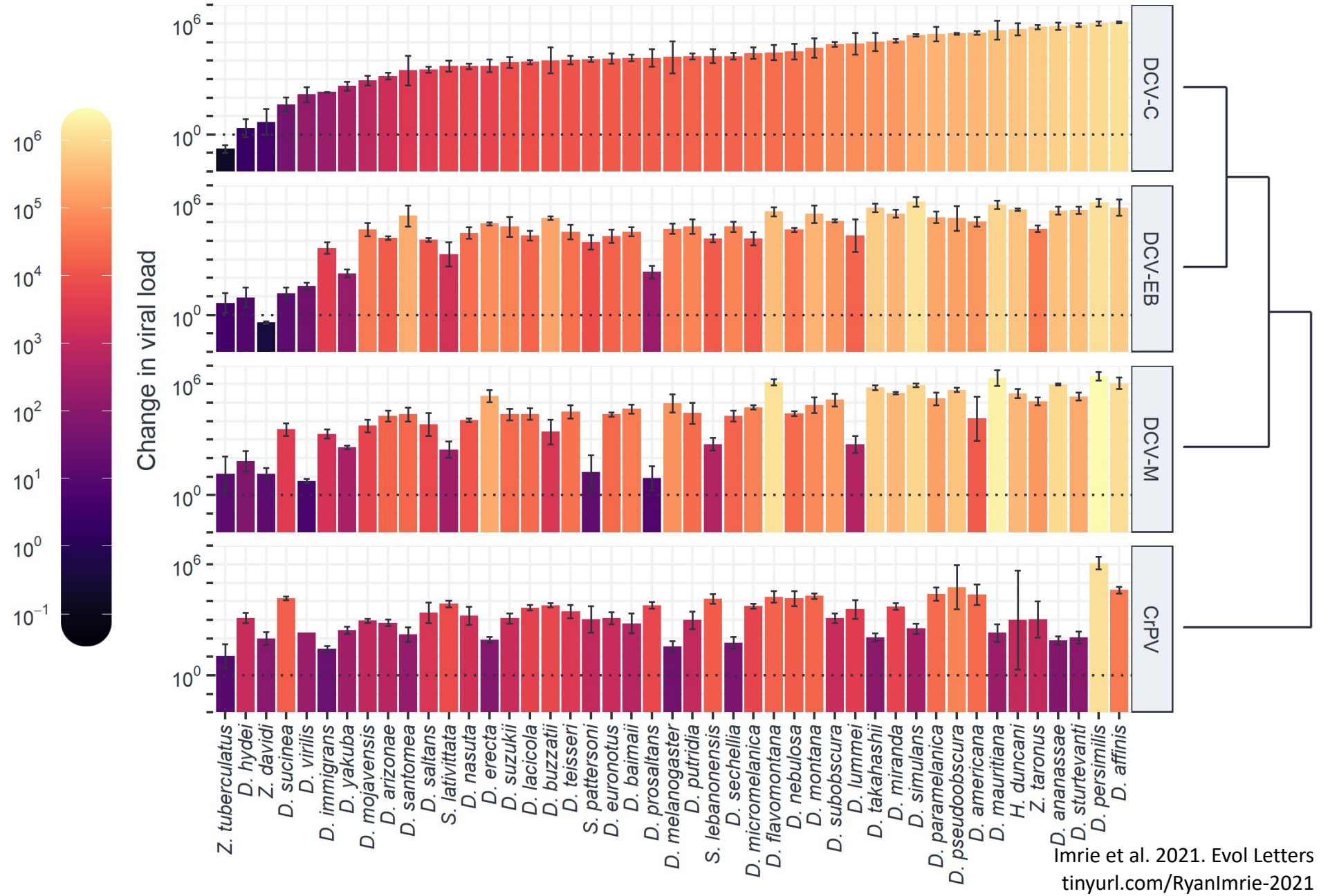
Correlations between viruses



Imrie et al. 2021. Evol Letters

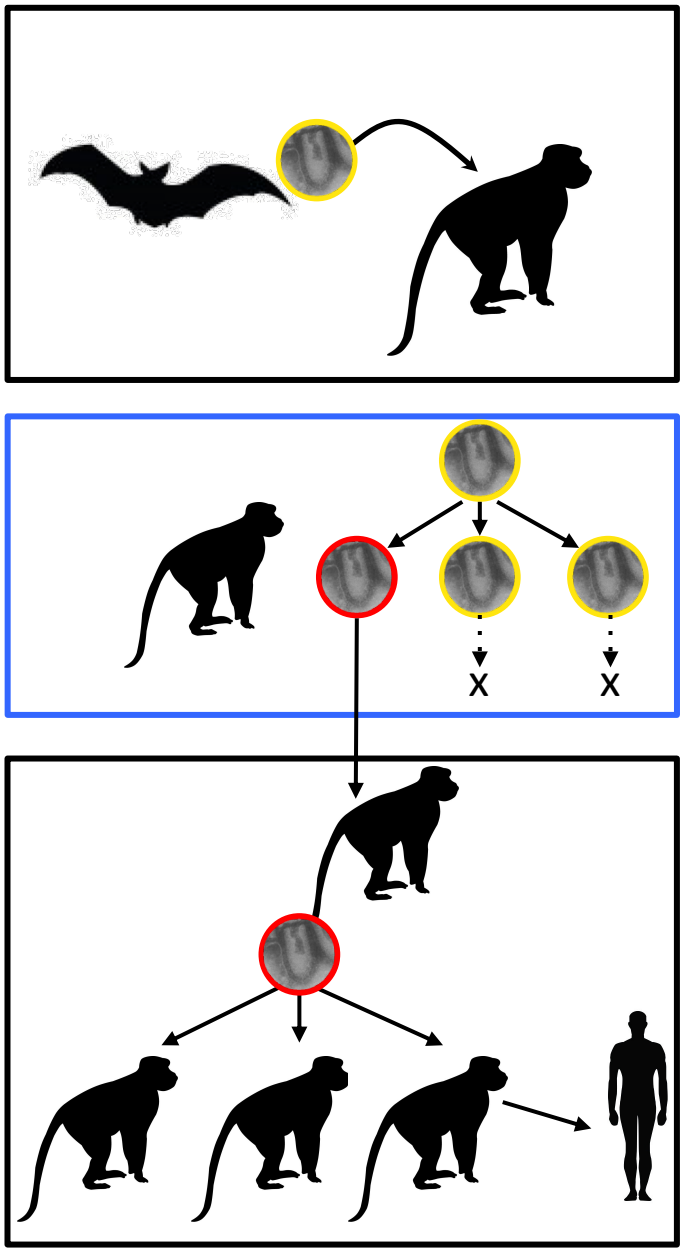
tinyurl.com/RyanImrie-2021

Host shifts

Exposure

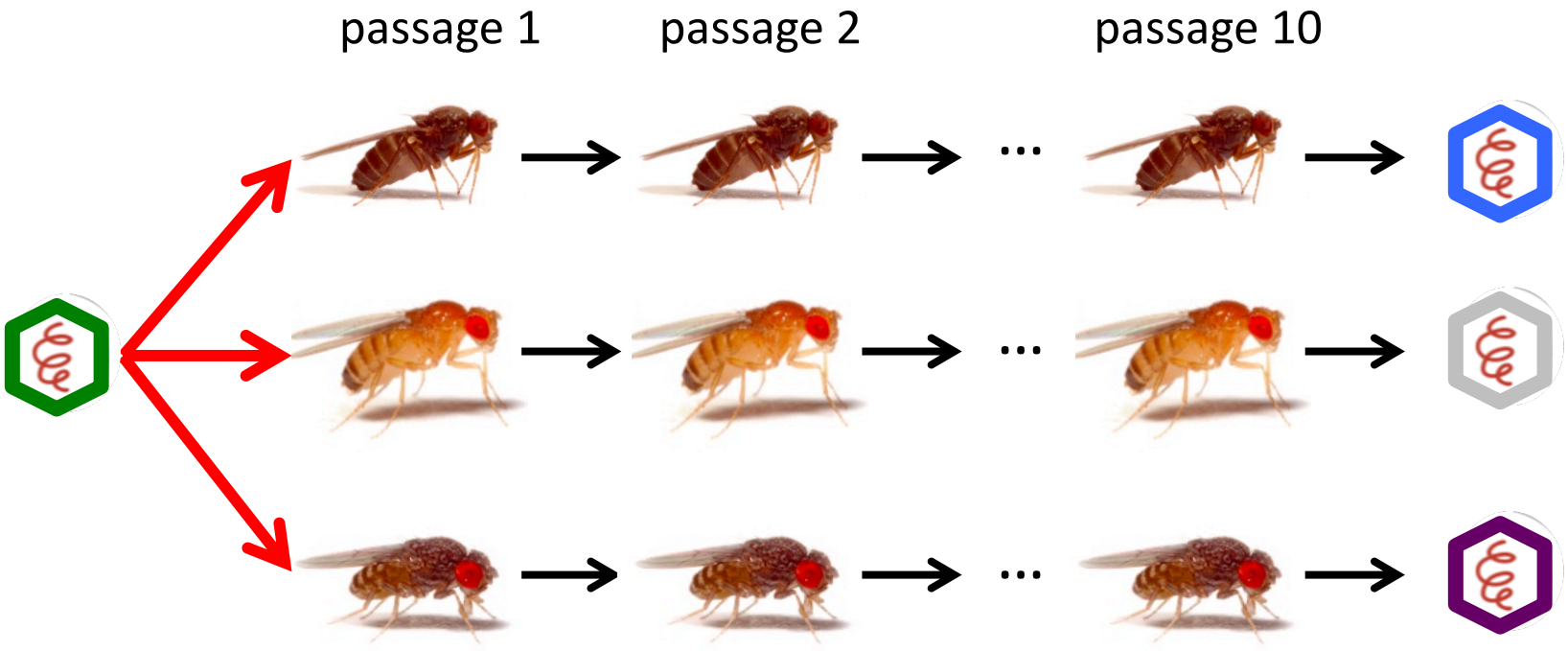
Infection and evolution

Transmission

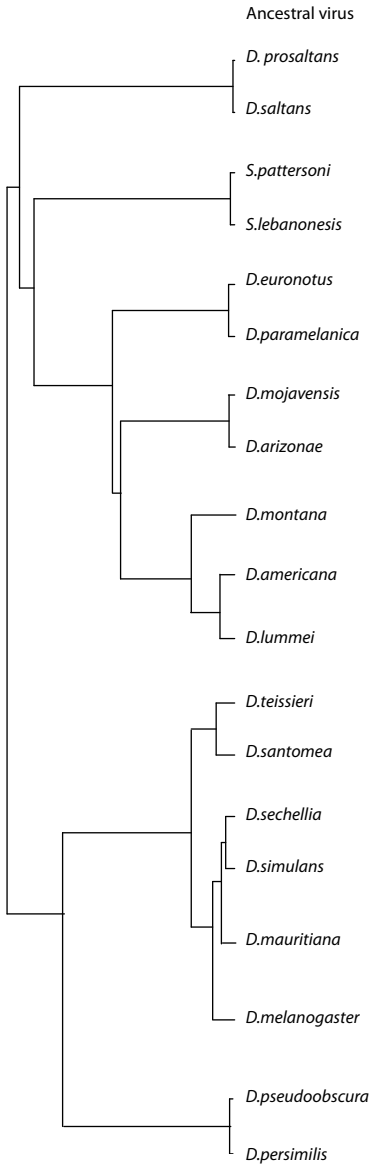


DCV experimental evolution

- 19 host species
- 6-10 lineages per species

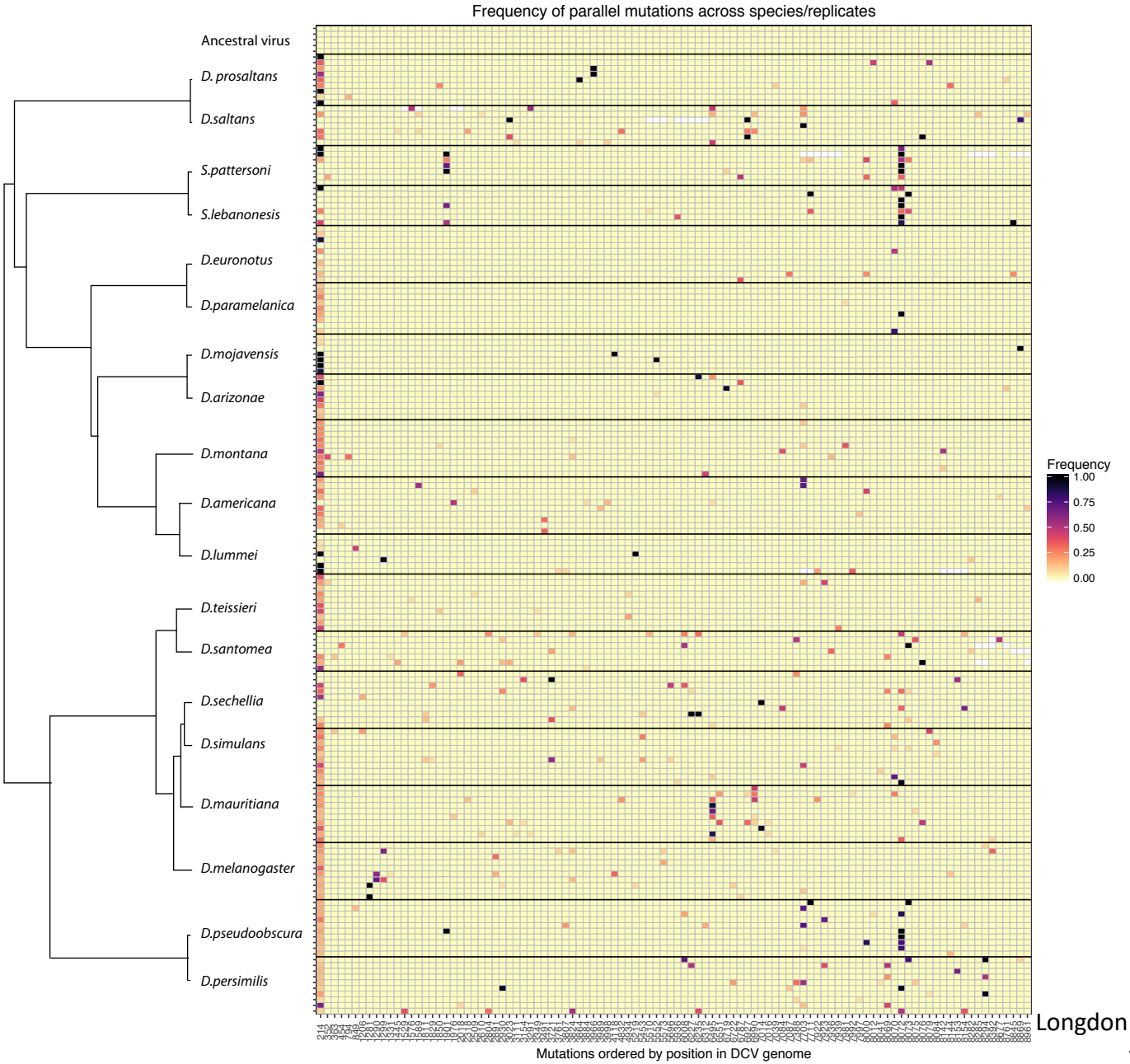


DCV experimental evolution



Longdon et al 2018 PLoS Pathogens
tinyurl.com/Longdon-2018

DCV experimental evolution



Longdon et al 2018 PLoS Pathogens
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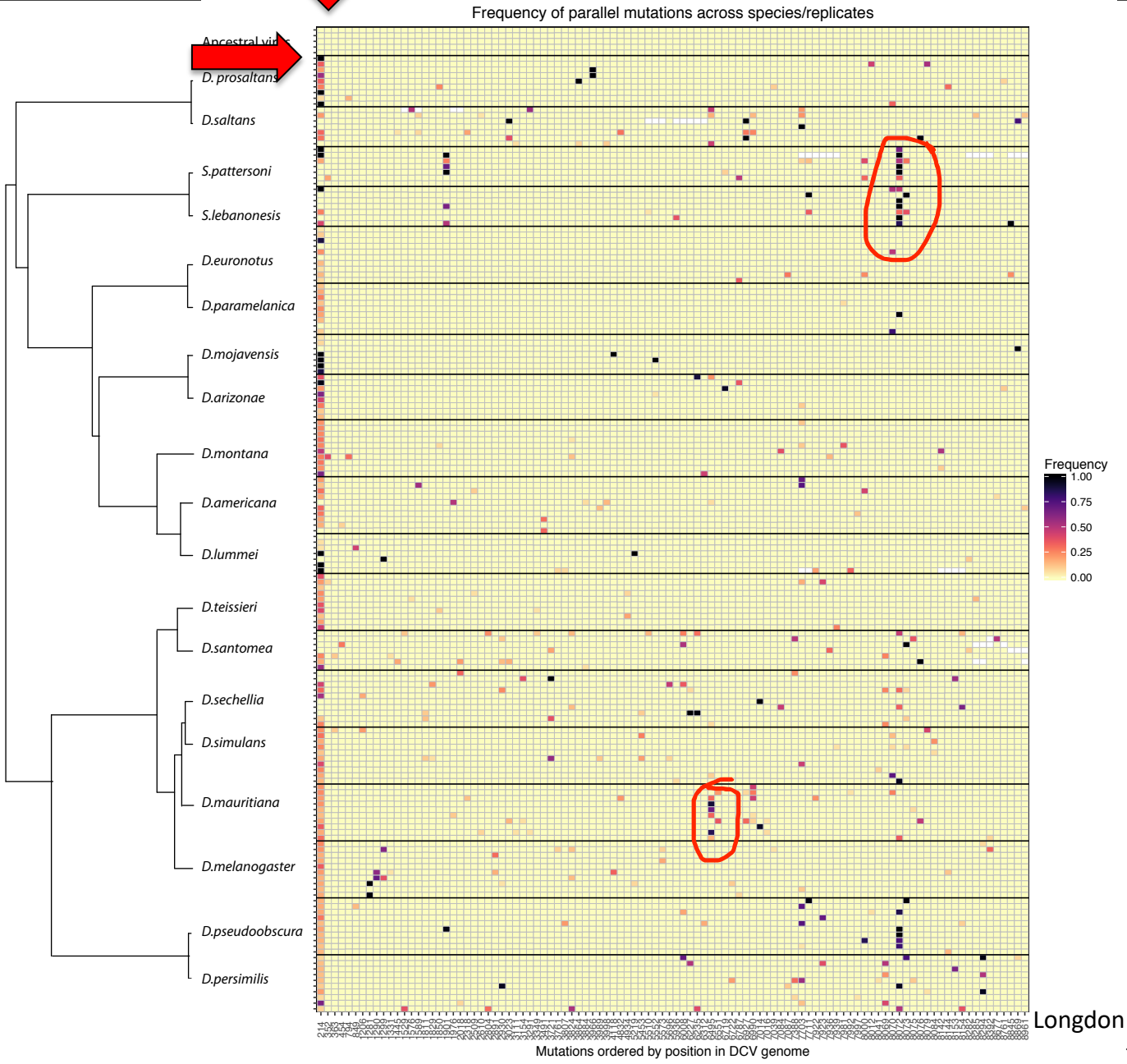
DCV experimental evolution



Longdon et al 2018 PLoS Pathogens
tinyurl.com/Longdon-2018

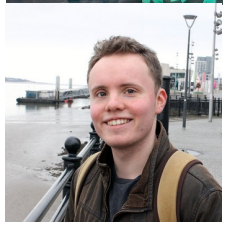
Summary

- The host phylogeny is important for understanding host shifts
- Species' susceptibilities may respond in different ways to changes in temperature
- Related pathogens have similar characteristics in novel hosts

Acknowledgments

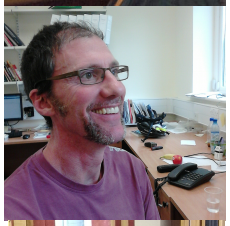
Frank Jiggins

Kat Roberts



Ryan Imrie

Jarrod Hadfield



Jon Day

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Rodrigo Cogni
Tom Houslay
Chuan Cao
Sophie Smith

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Fly photos: Nicolas Gompel and Darren Obbard