NAC2023
18th NSTDA Annual Conference
การประชุมวิชาการประจำปี สวทช. ครั้งที่ ๑๘

Infectious Disease Genomics and Their Application

ศ.นพ.ประสิทธิ์ ผลิตผลการพิมพ์

คณะวิทยาศาสตร์ มหาวิทยาลัยมหิดล

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GENOMICS THAILAND

Prasit Palittapongarnpim, M.D.

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Department of Microbiology, Faculty of Science, Mahidol University

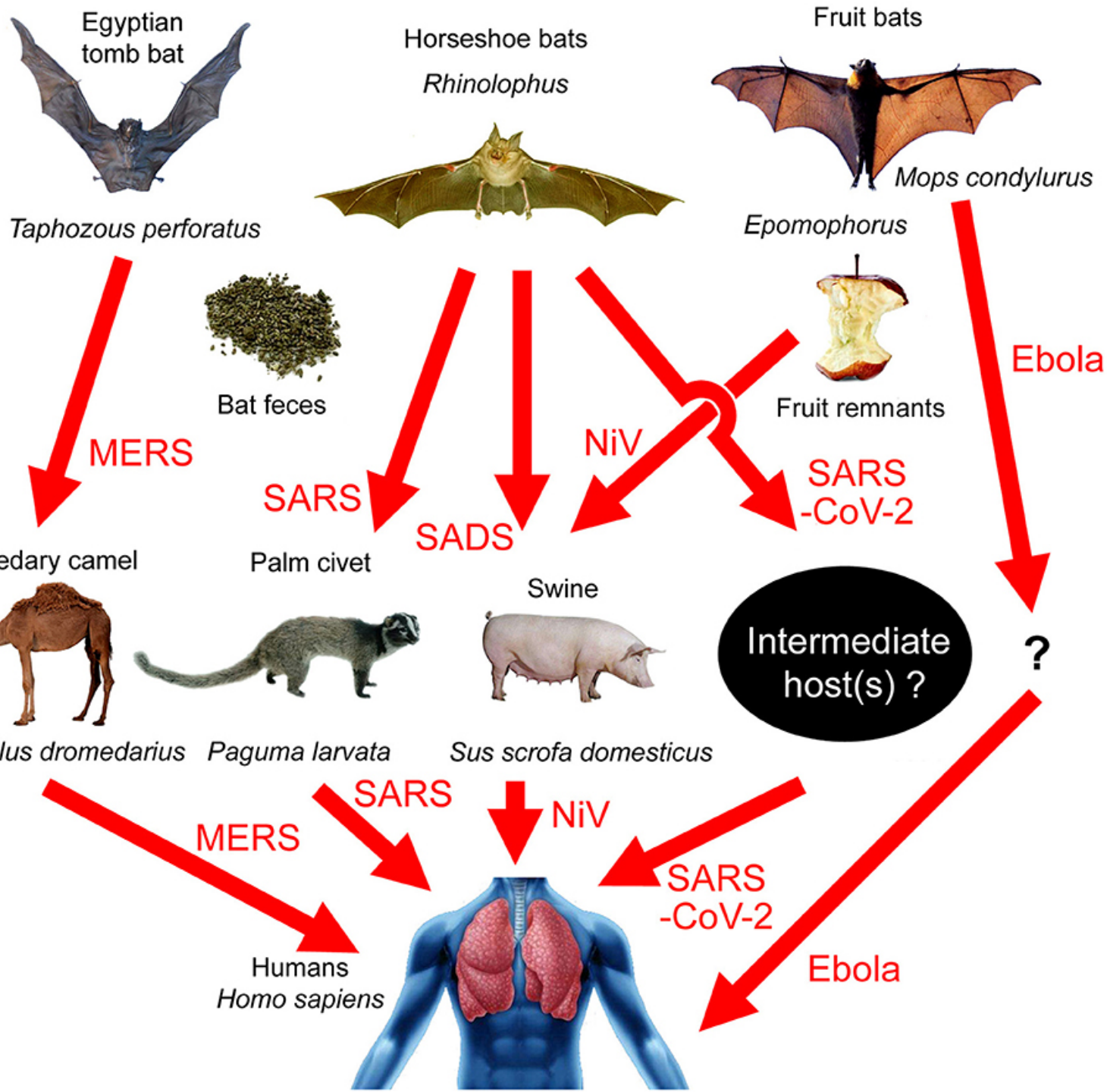
Genomics of Infectious Diseases

frontiers in Veterinary Science

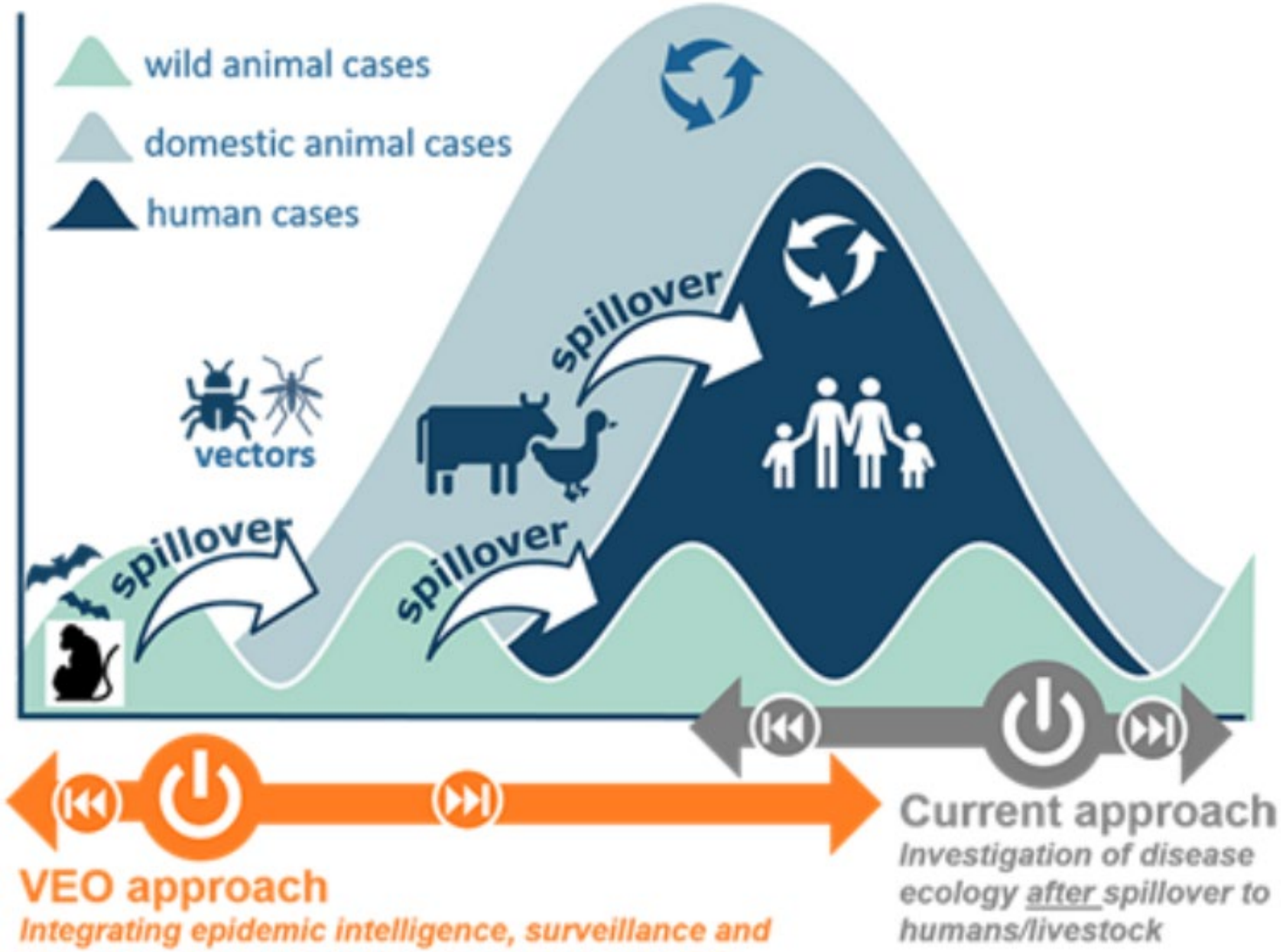
published: 09
doi: 10.3389/fvets.2

Analysis of Possible Intermediate Hosts of the New Coronavirus SARS-CoV-2

Shu Yuan [1], Si-Cong Jiang [2] and Zi-Lin Li [3]*



Swine acute diarrhea syndrome (SADS)



https://www.veo-europe.eu/about-veo

Versatile Emerging infectious disease Observatory (VEO)

The general model of EID is pathogens transmit from wildlife, adapt to domestic animals and then human.

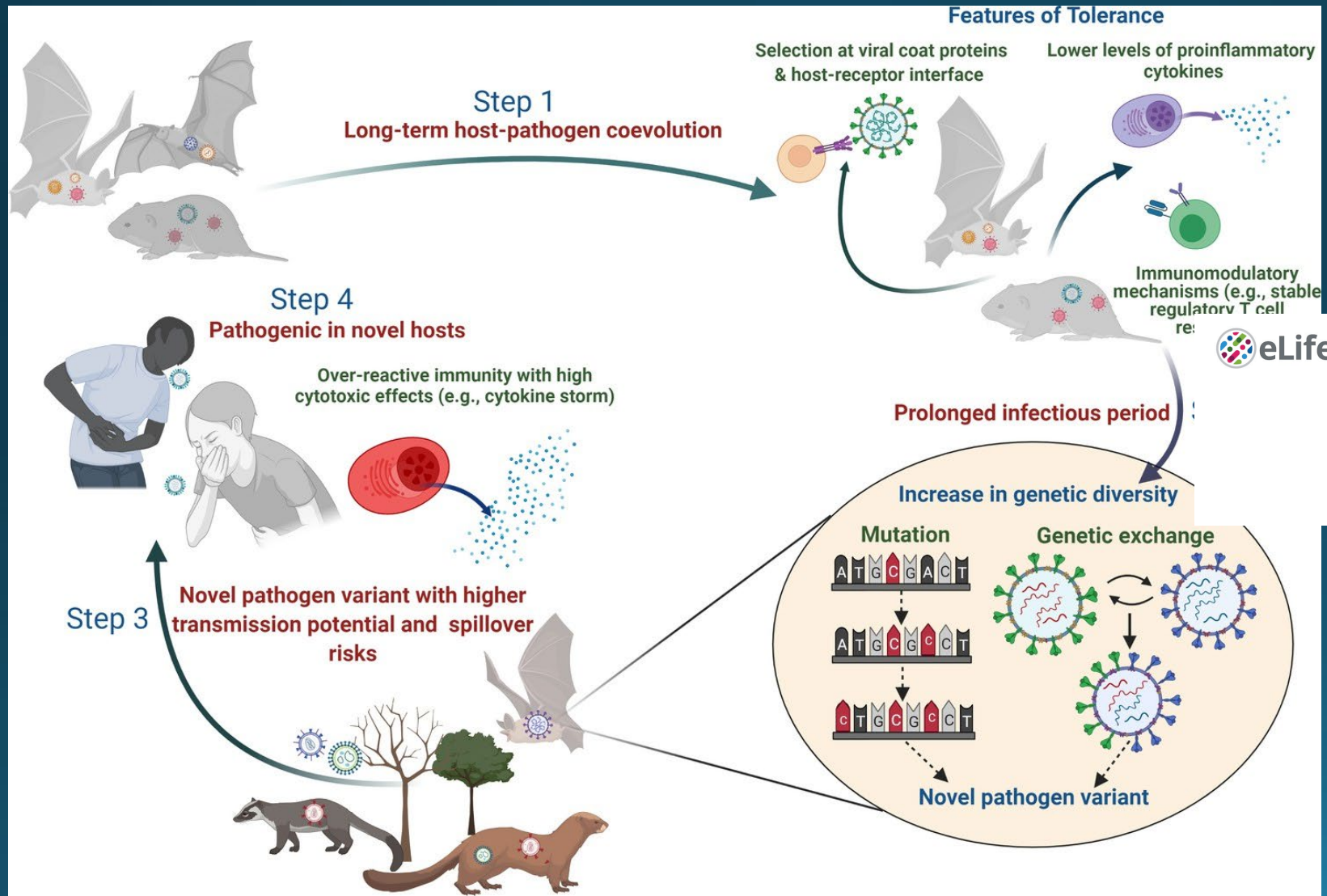
Q: Can we detect and respond to this threat very early and stop the pandemic even before it reach human population?

The expanding concept of health

https://www.lshtm.ac.uk/newsevents/events/one-health-ecohealth-and-planetary-health-bridging-disciplines-post-covid-19

https://timesofindia.indiatimes.com/city/vijayawada/planetary-health-key-to-avoiding-future-pandemics-experts/articleshow/88529601.cms

Infectious diseases are the results of co-evolution between pathogens and hosts.

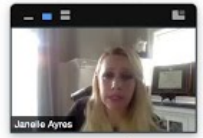


eLife
REVIEW ARTICLE

Evolution of pathogen tolerance and emerging infections: A missing experimental paradigm

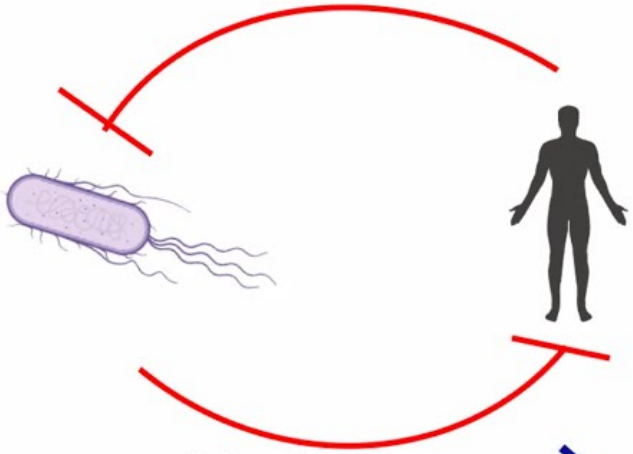
Srijan Seal[1]*, Guha Dharmarajan[2], Imroze Khan[1]*

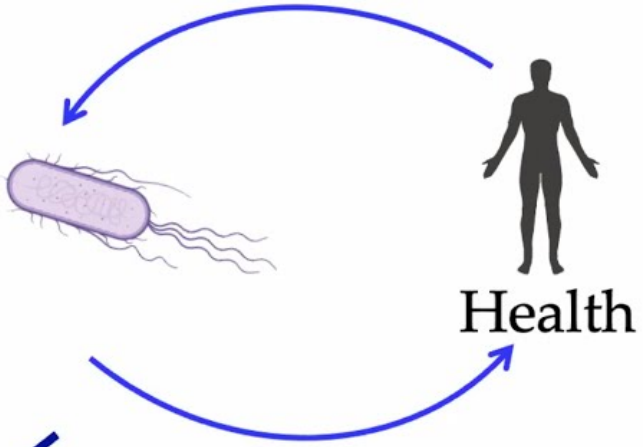
Antagonistic and cooperative defenses "cooperate" to promote evolution of attenuation



Antagonism

Co-operative





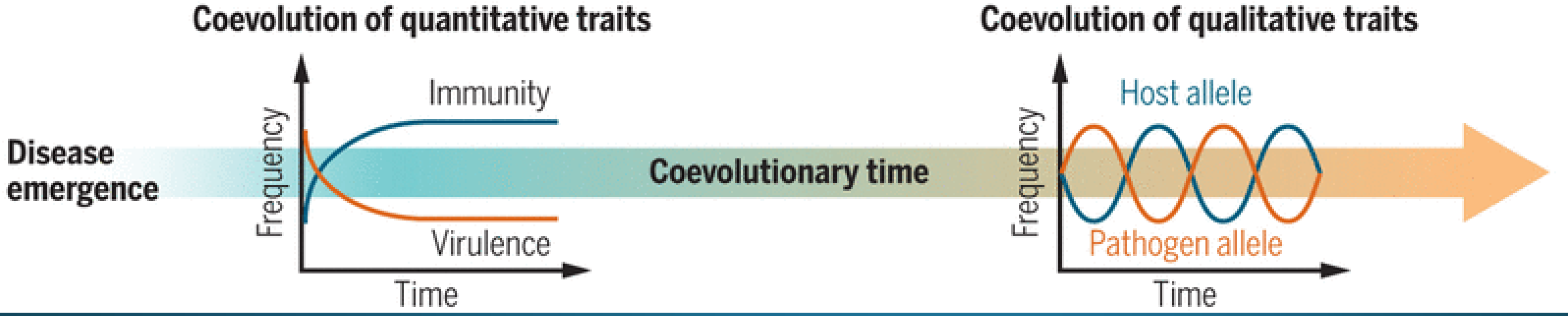
Adaptive immune response provides selective pressure for evolution of attenuation

Attenuation

Phenotypic attenuation metabolically satisfy pathogen

The evolution of antagonistic coevolutionary relationships

Coevolution in emerging or relatively new infectious disease systems is likely to be characterized by quantitative resistance, whereas infectious disease systems with a long coevolutionary history are likely to be characterized by the evolution of qualitative resistance.



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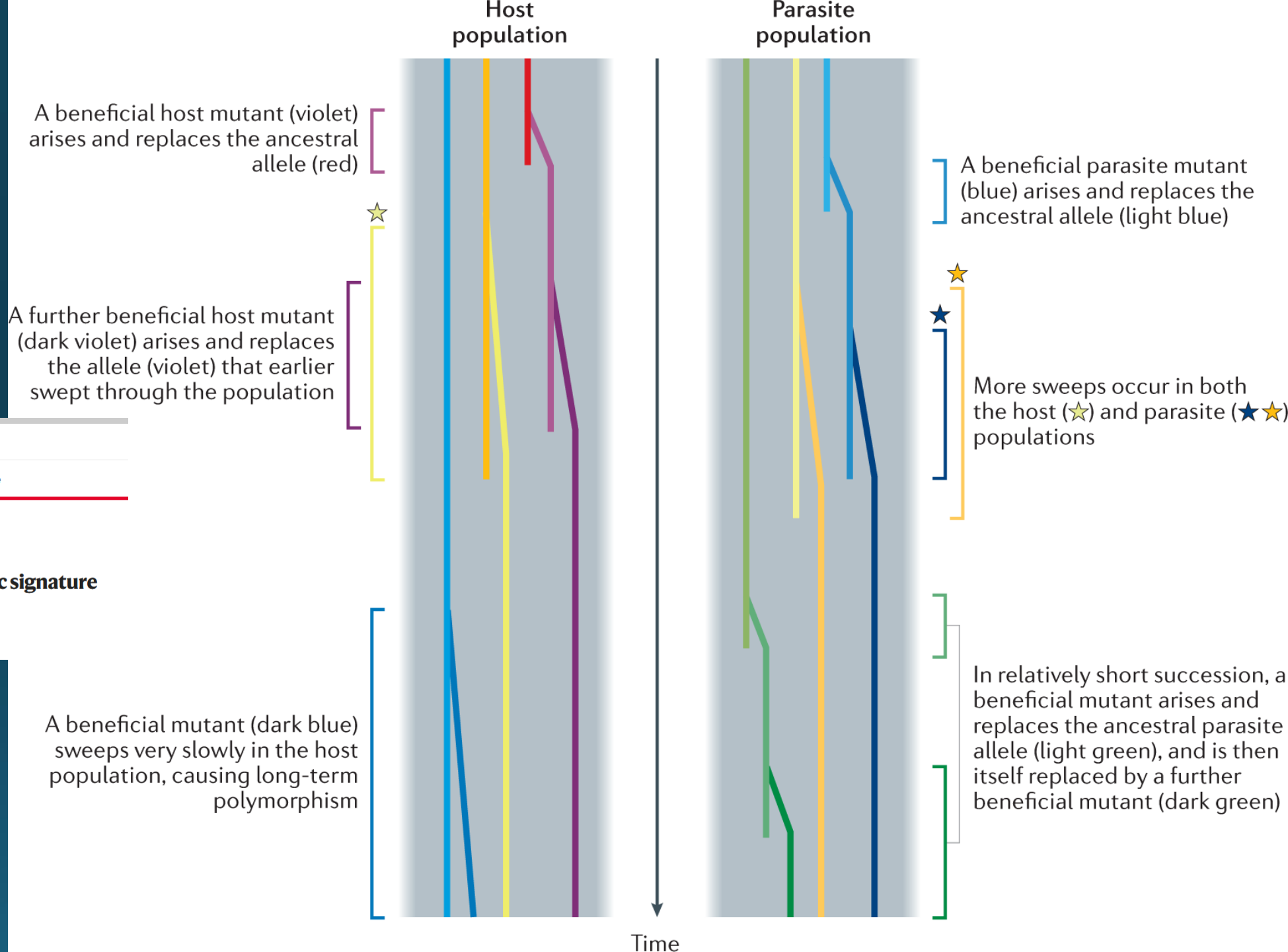
Review Article | Published: 28 August 2020

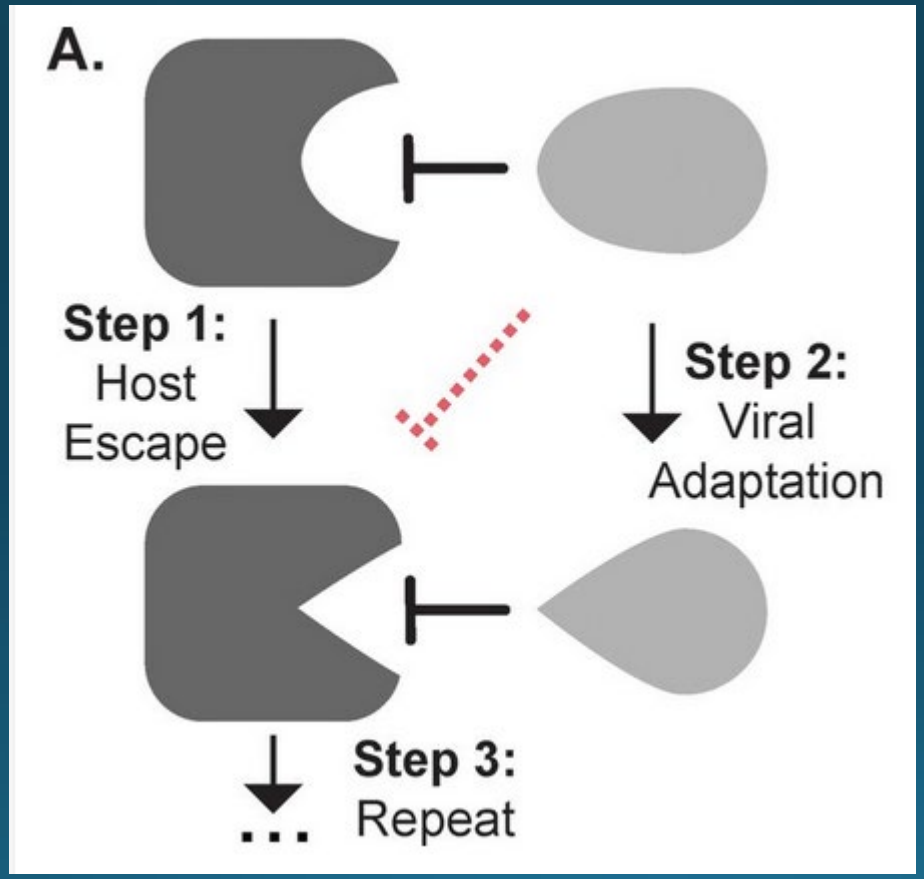
Host–parasite co-evolution and its genomic signature

Dieter Ebert & Peter D. Fields

Nature Reviews Genetics **21**, 754–768 (2020) | Cite this article



Evolutionary Arm Race



Immediate Applications of Genomics of Infectious Diseases

- Long term preparedness of emerging infectious diseases
- Metagenomic Diagnosis
- Tracing transmission
- Diagnosis of drug resistance
- Susceptibility to infection
- Microbial genomics and pharmacogenetics of therapy

Important Areas of Studying Genomics of Infectious Diseases

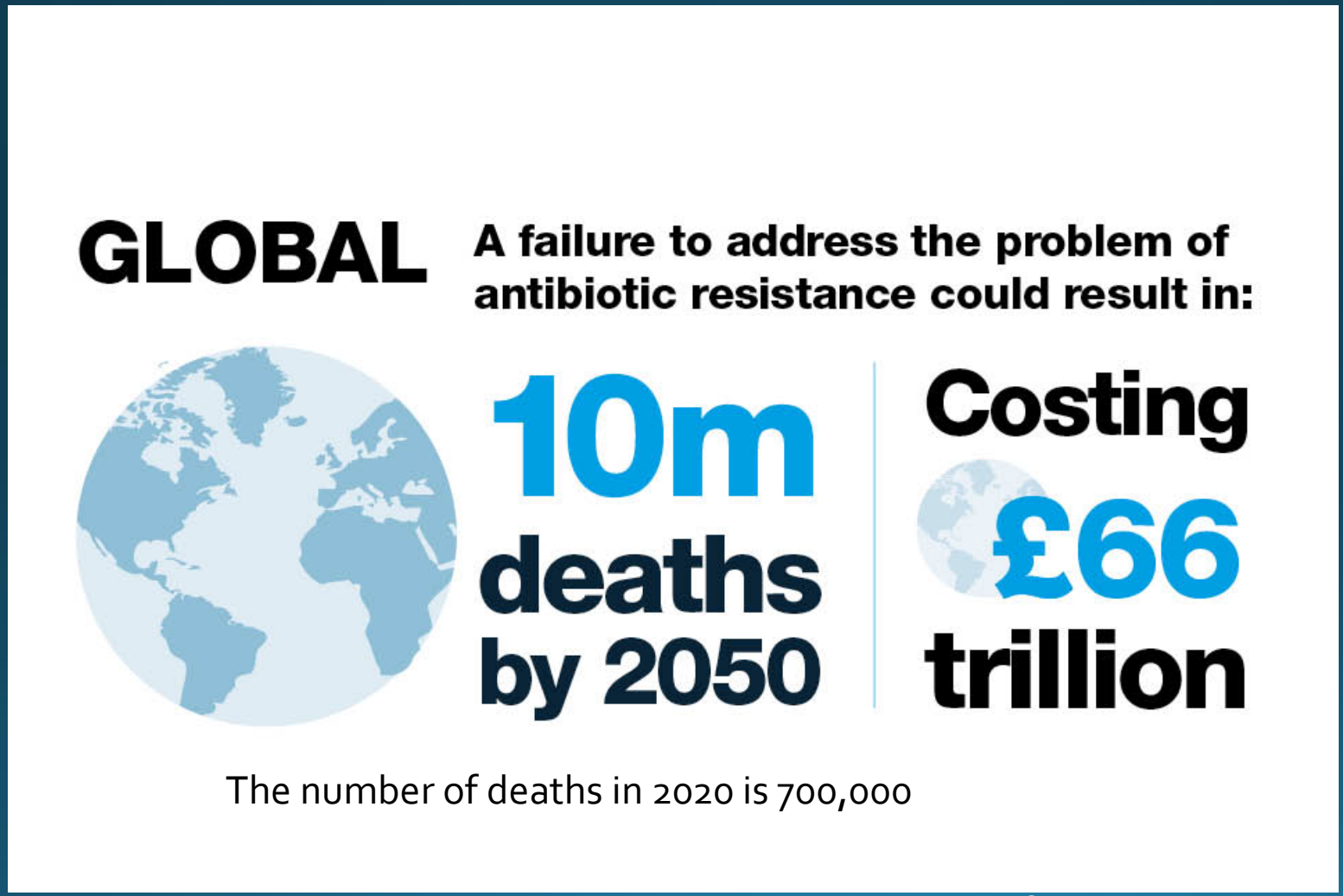
Microbial Genomics

- Origins
  - Emerging pathogens
  - Long-standing pathogens
- Host specificity
  - Obligate human pathogens
  - Life cycles through multiple hosts
  - Animal reservoirs
  - Environmental reservoirs
- Determinants of virulence
  - Infectiousness
  - Severity
- Mobile genetic elements

Human Genomics

- Human genetic groups which correlate with
  - Ethnicity
  - Geography
- Single nucleotide polymorphisms
  - Susceptibility to infection
  - Determinants of clinical forms
  - Determinants of severity
- Effects of ages

One health is essential for preventing the next Pandemic.



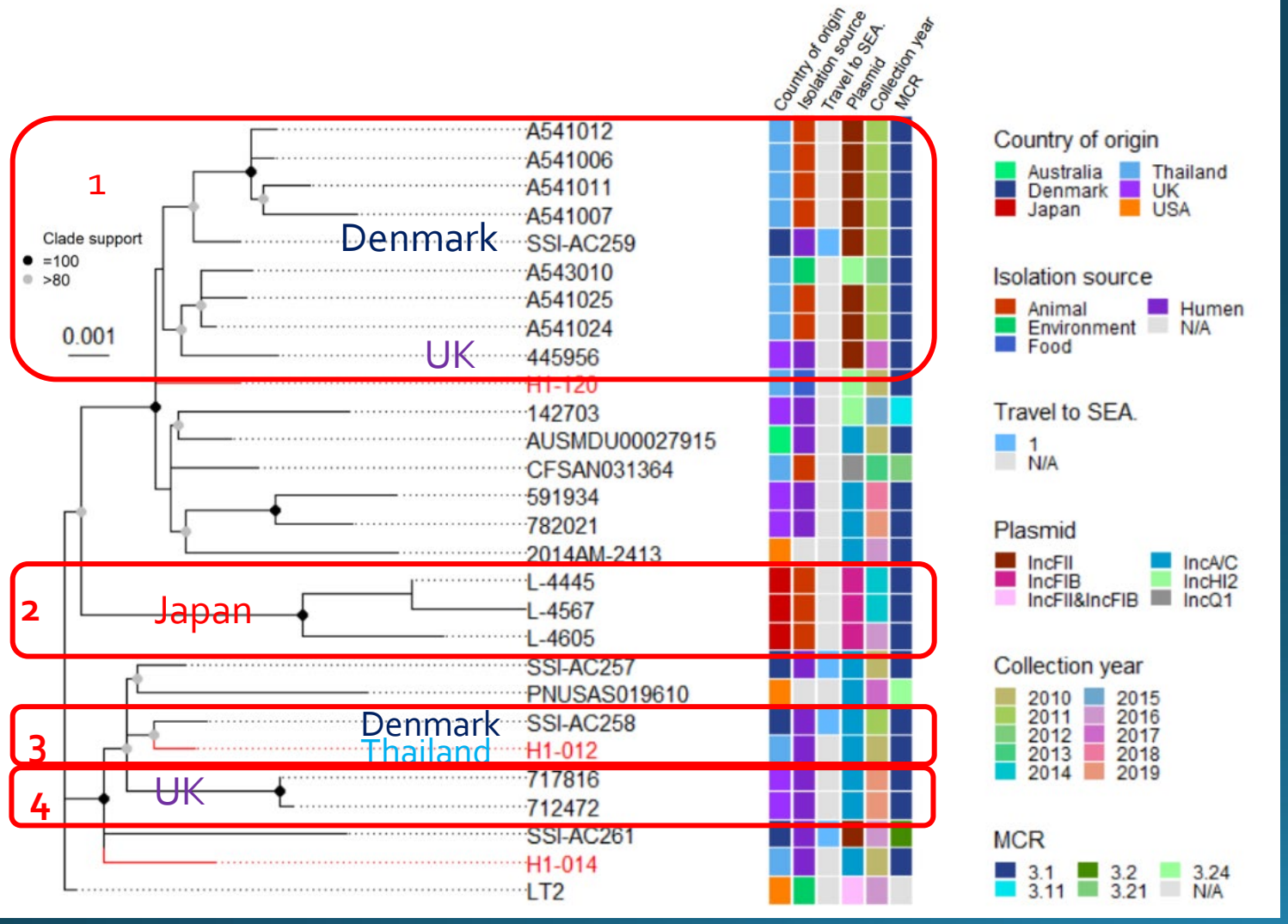
The number of deaths in 2020 is 700,000

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/image_data/file/47286/Health_Matters_AMR_960x6404.jpg

mcr-3 carrying Monophasic Variant of *Salmonella* Typhimurium (*S.* 4,5,[12]:i:-)

- **3 isolates of colistin resistant MVST** (*S.* 4,5[12]:i:-) in Thailand was sequenced by both **short read** and **long read** sequencing.
- Many colistin resistant MVST have been reported in Europeans, who had a history of visiting China and SEA.
- **+WGS (short read) of 24 global isolates from NCBI.**
- **Similarity of isolates evaluated by**
  - **Pairwise SNV distances**
  - ***flbAB-hin* deletion profiles**
  - **Plasmid profiles**
- Revised manuscript submitted to Sci Rep.

Core genome phylogenetic tree of the 27 MVST. The phylogenetic clades correlated with chromosomal *fljAB-hin* deletion and plasmid profiles. Several groups are related by transmission.



PeerJ

Whole-genome characterisation of multidrug resistant monophasic variants of *Salmonella* Typhimurium from pig production in Thailand

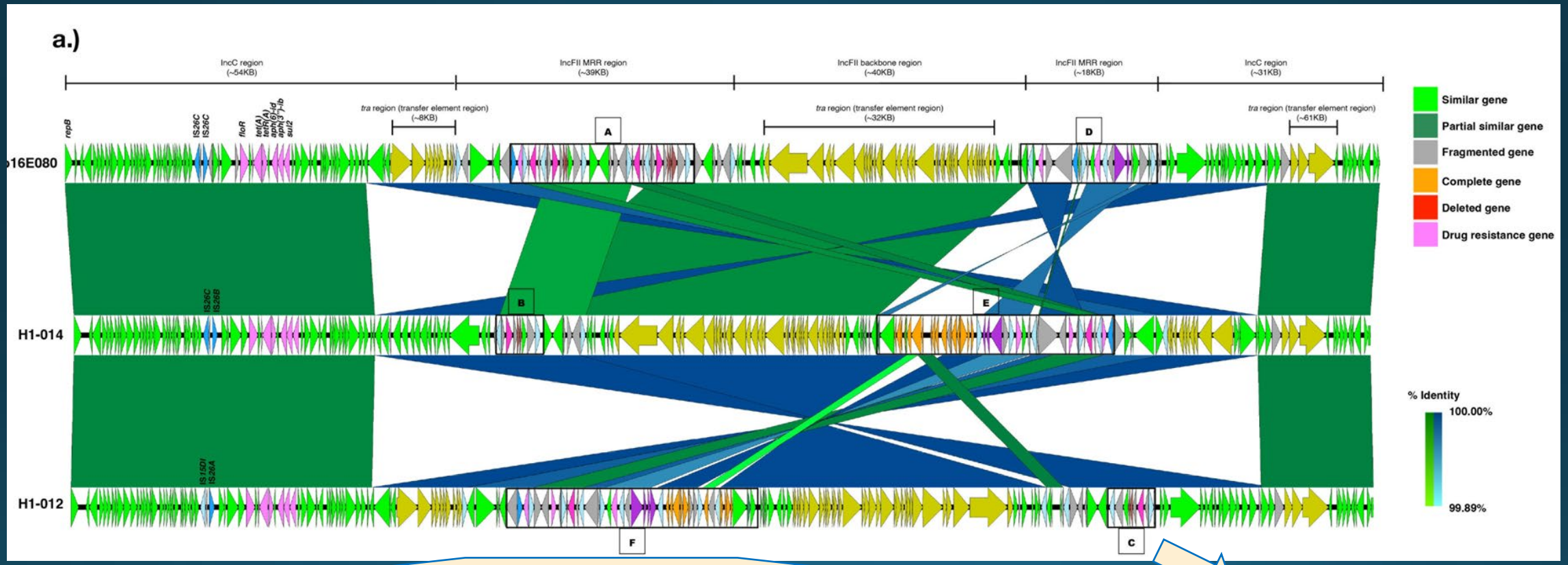
Prapas Patchanee[1], Prawitchaya Tanamai[1], Phacharaporn Tadee[2], Matthew D. Hitchings[3], Jessica K. Calland[4], Samuel K. Sheppard[4,5], Dethaloun Meunsene[6], Ben Pascoe[4,5] and Pakpoom Tadee[1]

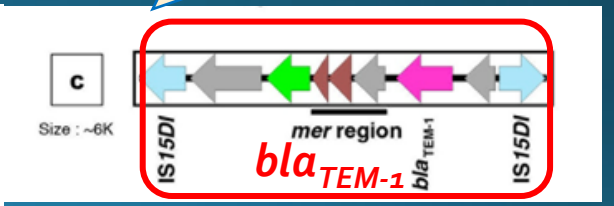
RAPID COMMUNICATIONS

Plasmid-borne colistin resistance gene *mcr-3* in *Salmonella* isolates from human infections, Denmark, 2009–17

E Litrup [1], K Kiil [1], AM Hammerum [1], L Roer [1], EM Nielsen [1], M Torpdahl [1]
1. Department of Bacteria, Parasites and Fungi, Statens Serum Institut, Copenhagen, Denmark
Correspondence: Eva Litrup (evl@ssi.dk)

bla_{TEM-1}, $bla_{CTX-M-55}$ and *mcr3.1* are all co-located in IncA/C plasmids in Thai isolates. Defining structures of drug resistance gene segments facilitate further tracing of transmission





Risk for Prison-to-Community Tuberculosis Transmission, Thailand, 2017–2020

Reiko Miyahara, Pundharika Piboonsiri, Boonchai Chiyasirinroje, Worarat Imsanguan, Supalert Nedsuwan, Hideki Yanai, Katsushi Tokunaga, Prasit Palittapongarnpim, Megan Murray, Surakameth Mahasirimongkol

Settings: Population based study in Chiangrai 2017-2020

Pairwise SNV distances cutoff: 20

Large genetic cluster: >10 patients

Figure 1. Phylogenetic tree of patients with pulmonary tuberculosis of *Mycobacterium tuberculosis* lineage in study of risk for prison-to-community tuberculosis transmission, Chiang Rai Province, Thailand, 2017–2020. Scale bar indicates 0.01 substitutions per site SNP, single-nucleotide polymorphism.

2018

The use of next-generation sequencing technologies for the detection of mutations associated with drug resistance in *Mycobacterium tuberculosis* complex: technical guide

World Health Organization

FIND
Because diagnosis matters
WHO collaborating centre for the evaluation of new diagnostic technologies

Catalogue of mutations in *Mycobacterium tuberculosis* complex and their association with drug resistance

World Health Organization

Journal of Global Antimicrobial Resistance 3 (2015) 262–266

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

Genetic characterisation of a *whiB7* mutant of a *Mycobacterium tuberculosis* clinical strain

Saradee Warit [a], Saranya Phunpruch [b,c], Chaitas Jityam [b], Sarinya Jaitrong [a], Pamaree Billamas [a], Angkana Chaiprasert [d], Prasit Palittapongarnpim [a,e], Therdsak Prammananan [a,*]

c.191delG mutation in ***whiB7*** resulted in overexpression tiof *whiB7* and king it sensitivity to **clarithromycin**.

ARTICLES
https://doi.org/10.1038/s41564-022-01130-y

nature microbiology

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OPEN

CRISPRi chemical genetics and comparative genomics identify genes mediating drug potency in *Mycobacterium tuberculosis*

Shuqi Li[1,5], Nicholas C. Poulton[1,5], Jesseon S. Chang[1], Zachary A. Azadian[1], Michael A. DeJesus[1], Nadine Ruecker[2], Matthew D. Zimmerman[3], Kathryn A. Eckartt[1], Barbara Bosch[1], Curtis A. Engelhart[2], Daniel F. Sullivan[2], Martin Gengenbacher[3,4], Véronique A. Dartois[3,4], Dirk Schnappinger[2] and Jeremy M. Rock[1]✉

Mechanisms of the effect of c.191delG. c.191delG is specific to **L1.2.2 (EAI2), whose incidence =800,000 /y**

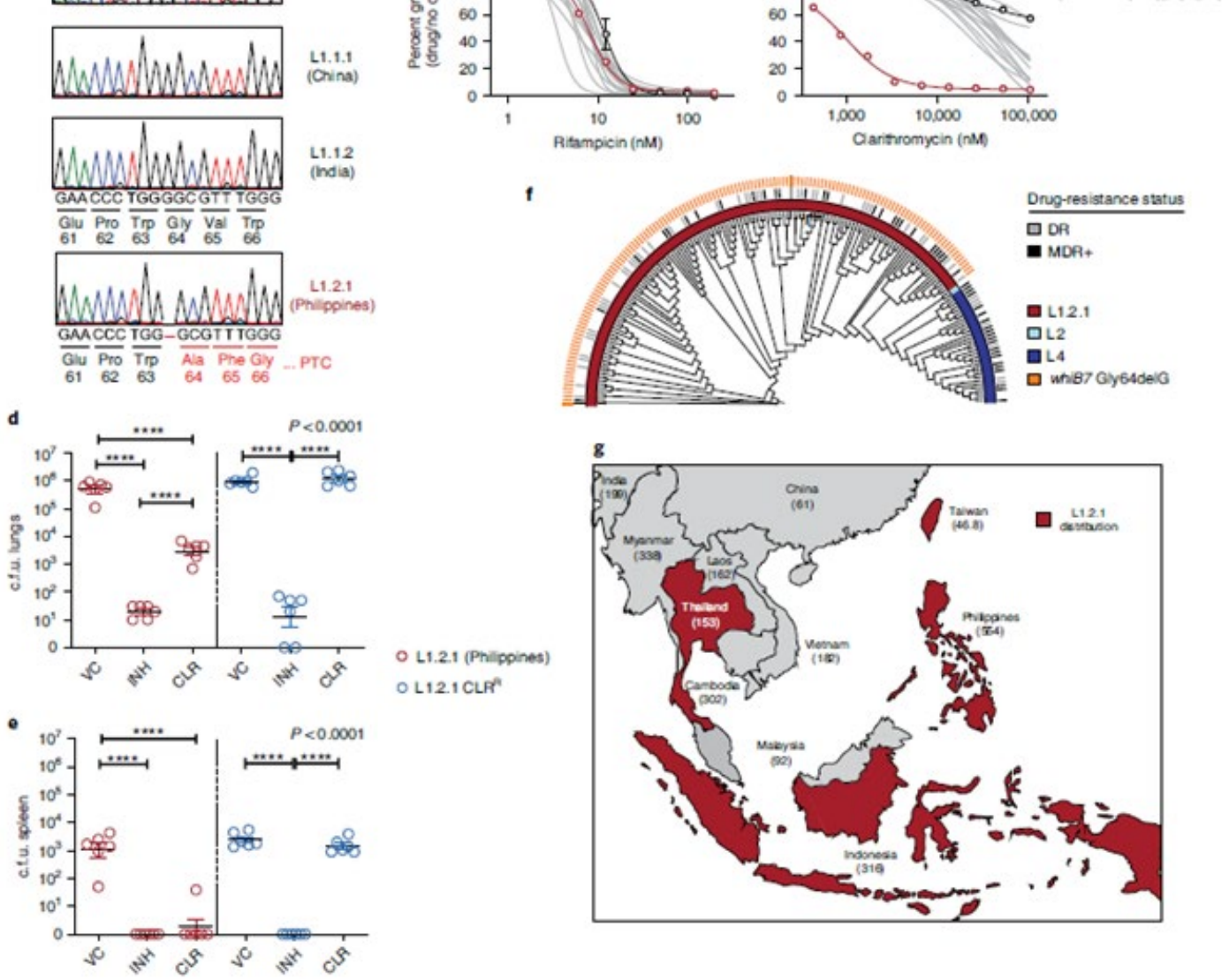


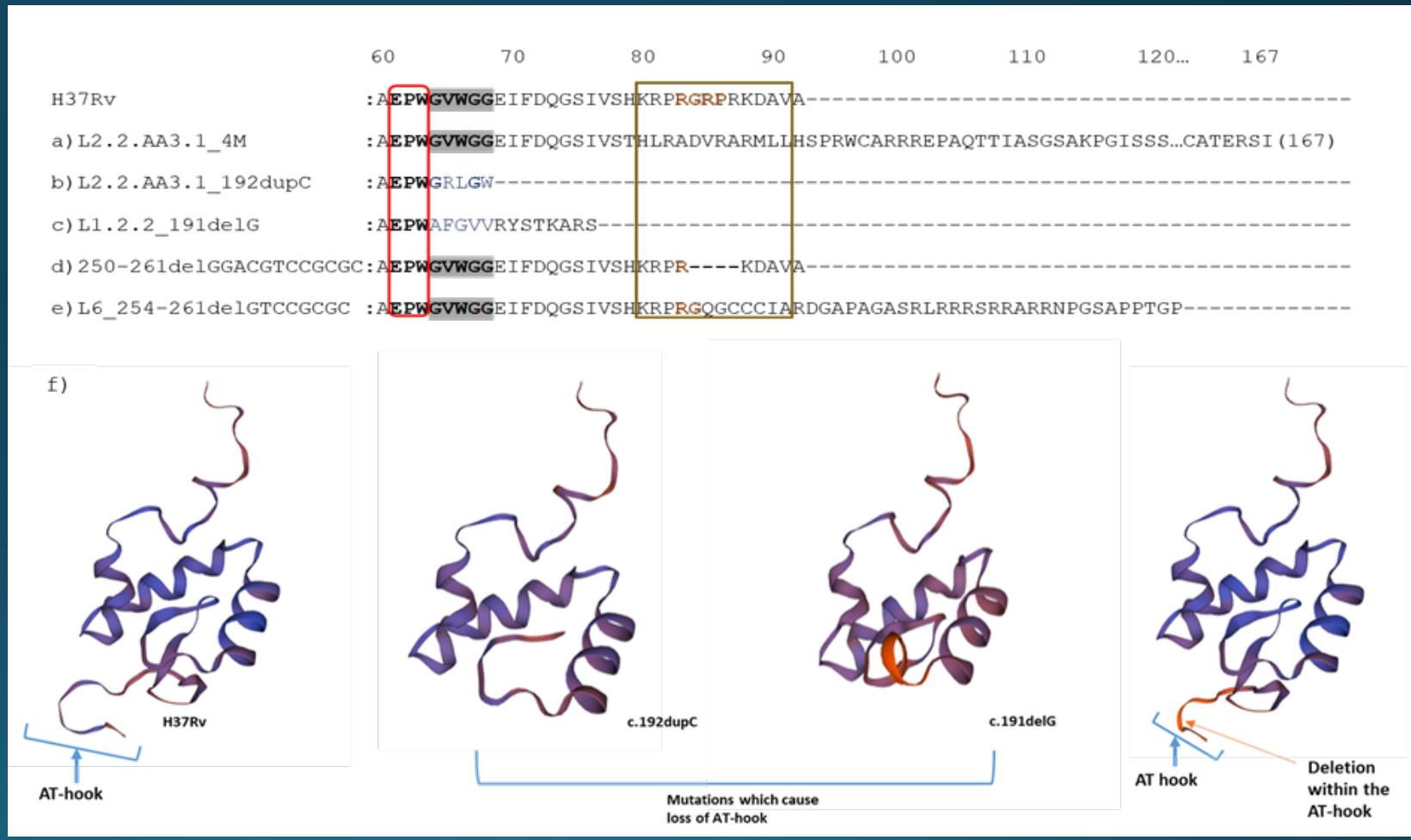
Fig. 6 | A loss-of-function mutation in *whiB7* renders an endemic Indo-Oceanic Mtb lineage hypersusceptible to macrolides. a, Diagram of Mtb *whiB7* with the eight most common *whiB7* variants observed in our clinical strain genome database. Pie chart depicts the observed frequencies of each variant. L, dominant lineage in which variant is observed. **b**, Sanger sequencing of *whiB7* from the indicated Mtb clinical strains and their country of origin. PTC, premature termination codon. The colour of each peak represents the base at the indicated position (black, G; green, A; red, T; blue, C). **c**, Dose-response curves (mean ± s.e.m., $n = 3$ biological replicates) were measured for a reference set of Mtb clinical and lab strains. **d**,**e**, Lung (**d**) and spleen (**e**) Mtb c.f.u. (mean ± s.e.m.) in BALB/c mice after 24 d of INH (25 mg kg^{-1}) or CLR (200 mg kg^{-1}) treatment. Statistical significance was assessed by one-way ANOVA followed by Tukey's post-hoc test. VC, vehicle control; CLR^R, clarithromycin-resistant (23S rRNA A2297G). Black line, median. $n = 6$ mice per group/condition. **f**, Phylogenetic tree of 178 Mtb clinical strains isolated during the 2012 nationwide drug resistance survey in the Philippines[10] (Source Data Fig. 6). The presence of the *whiB7* Gly64delG mutation and genotypically predicted drug-resistance status are shown as in Fig. 5f. **g**, Map showing L1.2.1 distribution in Southeast Asia and TB incidence rates of each country[71].

Analysis of *whiB7* in *MTB* reveals novel AT-hook deletion mutations

Olabisi Flora Davies-Bolorunduro, Bharkboom Jaemsai, Wuthiwat Ruangchai, Worakorn Phumiphanjarphak, P Aiewsakun[1], P Palittapongarnpim

- 40500 WGS of global isolates including L1-L8.
- c.191delG specificity to L1.2.2 is confirmed.
- c.191delG results in the loss of β-turn structure and C-terminal AT hook.
- Other mutations causing loss of AT hook have been identified
  - 192dupG
  - 4 M mutations
  - Deletion of core amino acid of AT hook in 17 sublineages.

Manuscript submitted



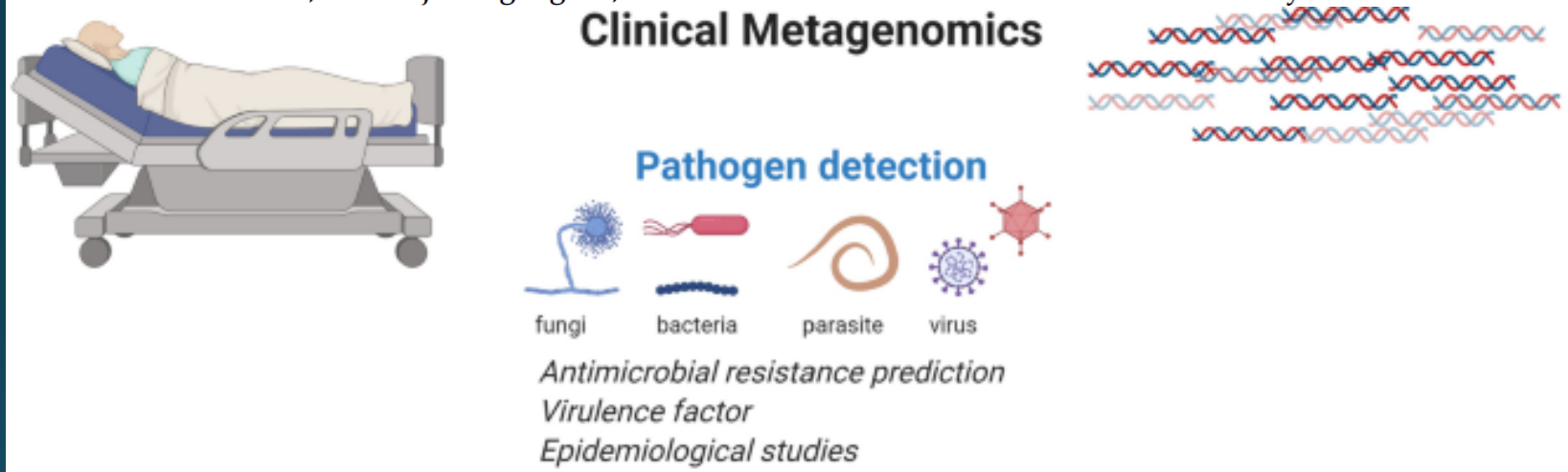
viruses

MDPI

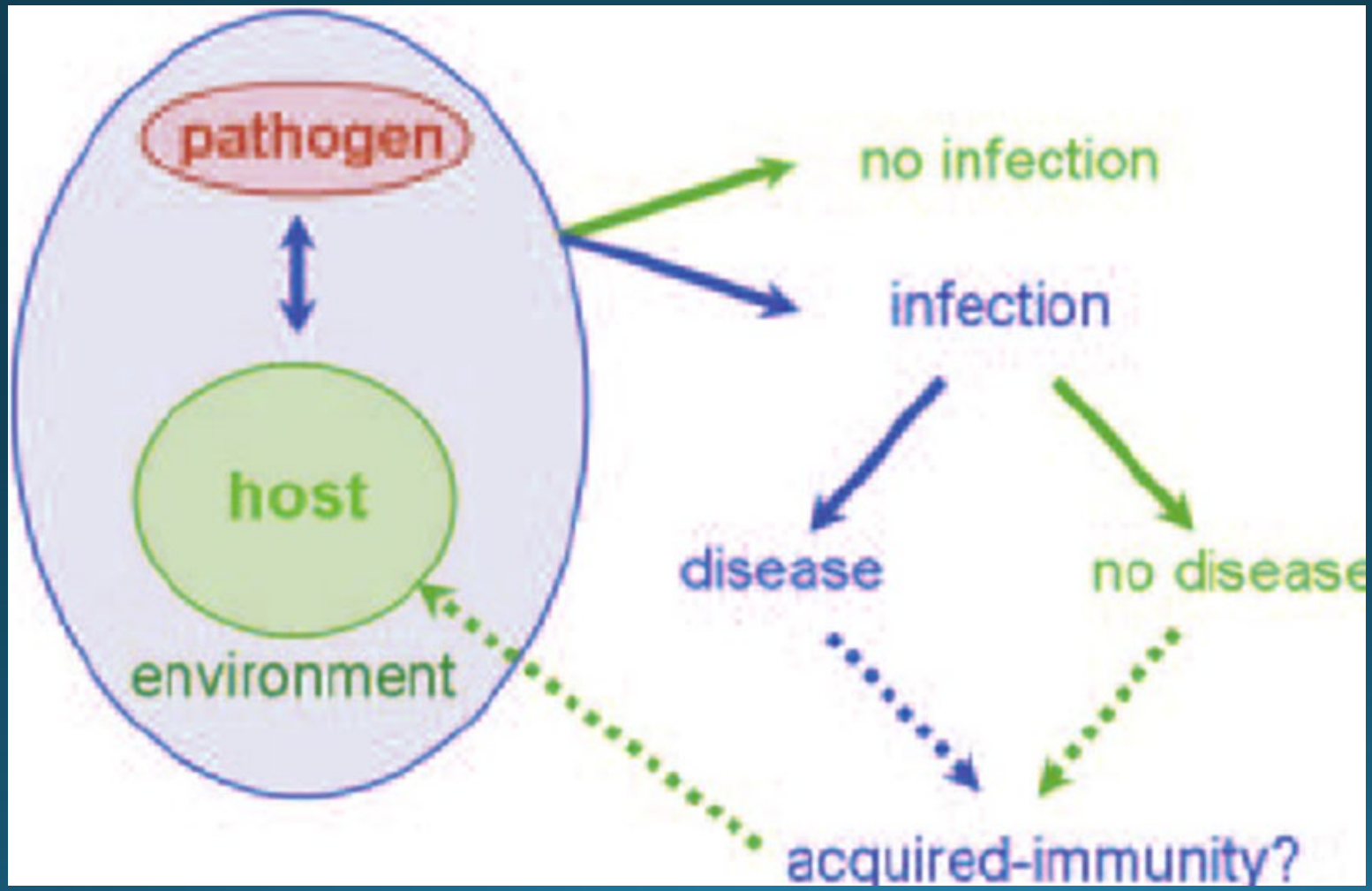
Article

Target Enrichment Metagenomics Reveals Human Pegivirus-1 in Pediatric Hematopoietic Stem Cell Transplantation Recipients

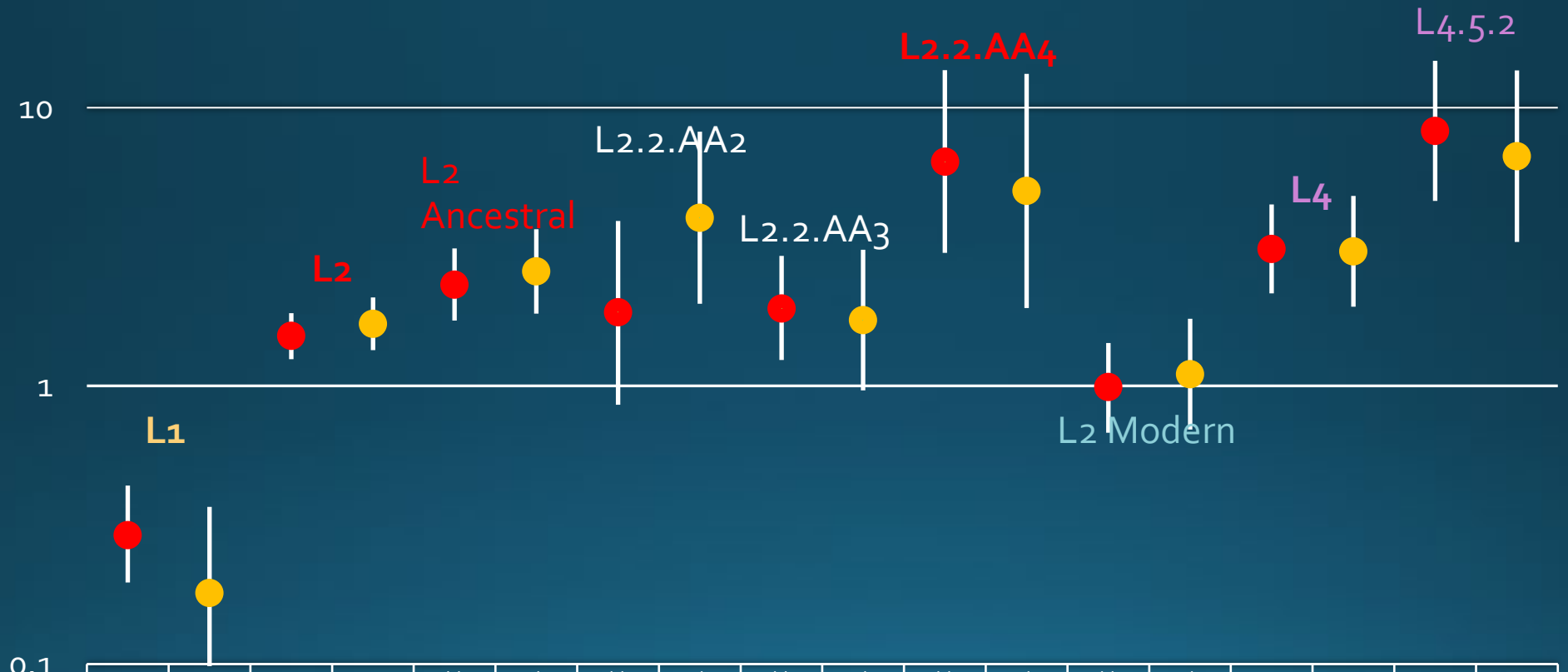
Natali Ludowyke [1], Worakorn Phumiphanjarphak [1,2], Nopporn Apiwattanakul [3], Suwimon Manopwisedjaroen [1], Samart Pakakasama [3], Insee Sensorn [4], Ekawat Pasomsub [5], Wasun Chantratita [4], Suradej Hongeng [3], Pakorn Aiewsakun [1,2,*] and Arunee Thitithanyanont [1,2,*]



Host-Pathogen Interactions: Whose genetics determine what?



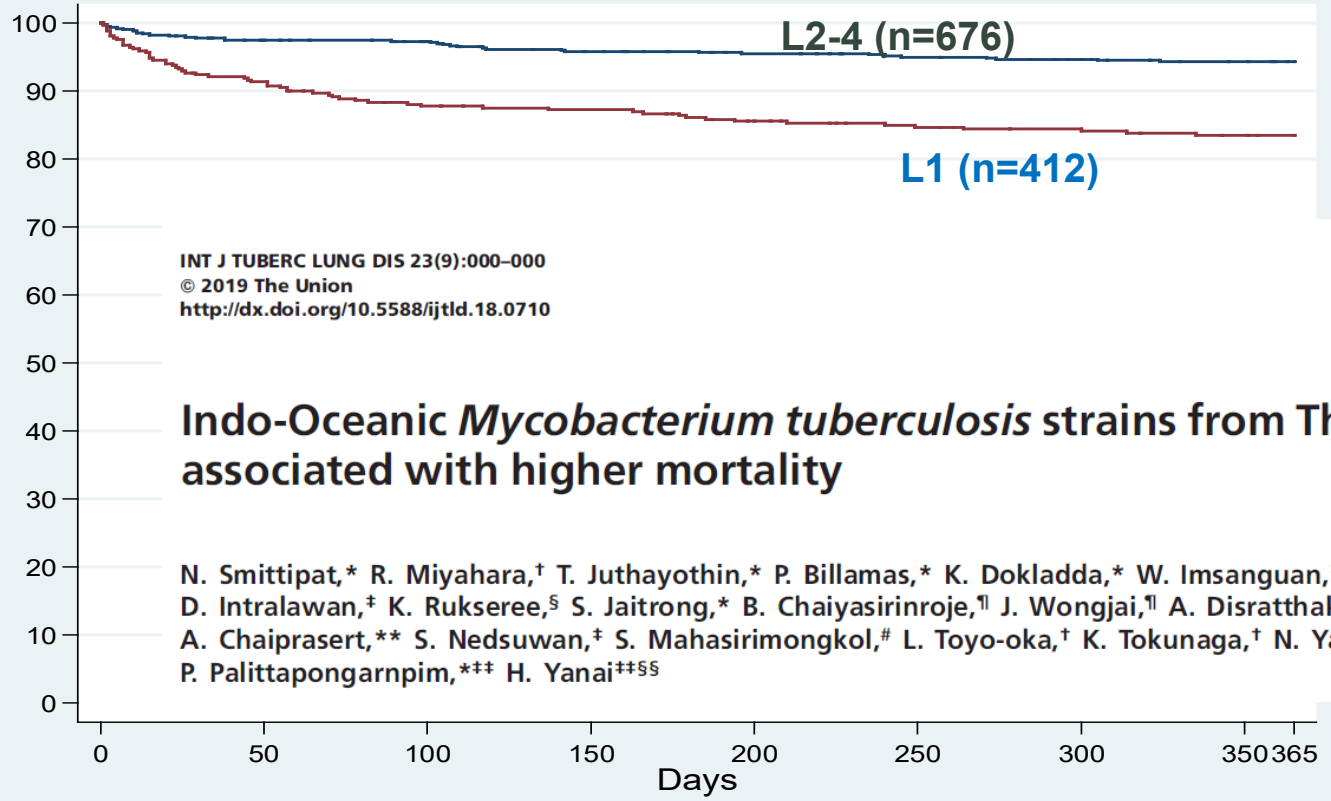
Risk Ratios of infections by selected lineages and sublineages of Akha and Lahu populations compared to Thais.



	Ahka L1	Lahu L1	Ahka L2	Lahu L2	Ahka Ancestral Beij	Lahu Ancestral Beij	Ahka Ancestral 2	Lahu Ancestral 2	Ahka Ancestral 3	Lahu Ancestral 3	Ahka Ancestral 4	Lahu Ancestral 4	Ahka Modern Beij	Lahu Modern Beij	Ahka L4	Lahu L4	Ahka L4.5.2	Lahu L4.5.2
	0.43	0.36	1.79	2.04	3.06	3.59	3.84	8.04	2.88	3.03	13.4	12.99	1.4	1.71	4.41	4.73	14.46	13.36
	0.2	0.09	1.27	1.37	1.75	1.85	0.87	2.01	1.26	0.98	3.06	1.94	0.69	0.71	2.19	1.96	4.71	3.35
	0.29	0.18	1.51	1.67	2.31	2.58	1.84	4.02	1.9	1.72	6.4	5.02	0.99	1.1	3.1	3.04	8.25	6.69

Mortality of L1 and L2-4 in Chiangrai one year after diagnosis

increased the mortality risk compared with East-Asian strains (adjusted hazard ratio [aHR] 1.42, 95%CI 1.02–1.99) or modern lineages (aHR 1.49, 95%CI 1.08–2.06) in the 172 patients who died within 1 year after TB diagnosis. The former also caused significantly higher mortality than modern lineages among patients who died within 6 months after TB diagnosis (aHR 1.62, 95%CI 1.12–2.35). No significant association was found between drug resistance and death.



INT J TUBERC LUNG DIS 23(9):000–000

http://dx.doi.org/10.5588/ijtld.18.0710

Indo-Oceanic *Mycobacterium tuberculosis* strains from Thailand associated with higher mortality

N. Smittipat,* R. Miyahara,† T. Juthayothin,* P. Billamas,* K. Dokladda,* W. Imsanguan,‡ D. Intralawan,‡ K. Rukseree,§ S. Jaitrong,* B. Chaiyasirinroje,¶ J. Wongjai,¶ A. Disratthakit,# A. Chaiprasert,** S. Nedsuwan,‡ S. Mahasirimongkol,# L. Toyo-oka,† K. Tokunaga,† N. Yamada,†† P. Palittapongarnpim,*‡‡ H. Yanai‡‡§§

nature communications

Article

https://doi.org/10.1038/s41467-023-36282-w

Genome-wide host-pathogen analyses reveal genetic interaction points in tuberculosis disease

Received: 16 August 2022

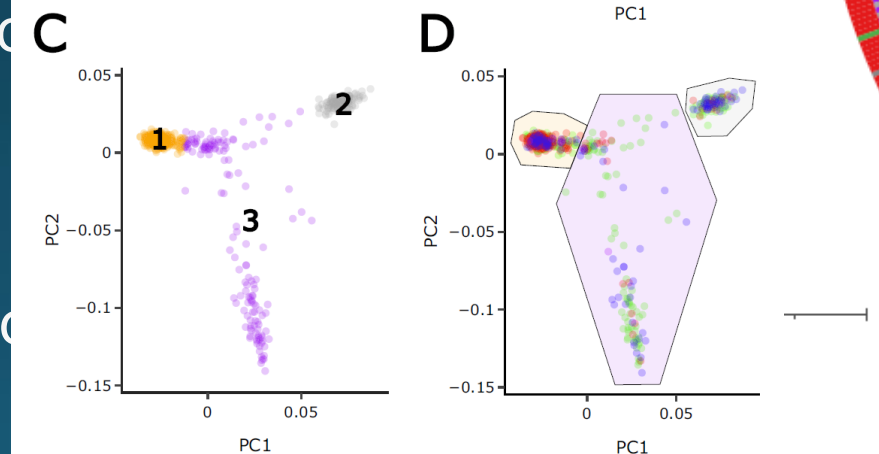
Accepted: 24 January 2023

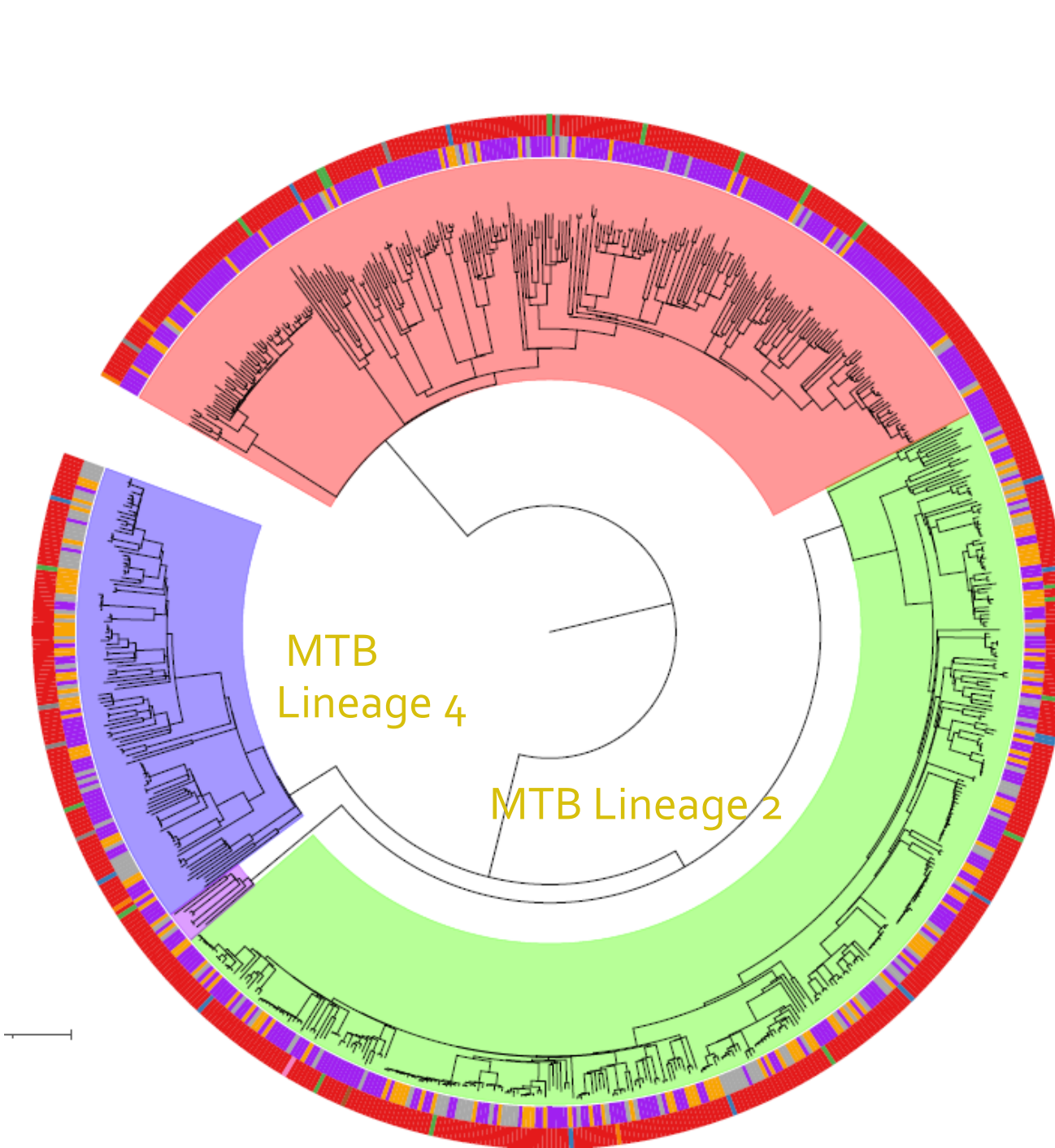
Published online: 01 February 2023

Check for updates

Jody Phelan[1], Paula Josefina Gomez-Gonzalez[1], Nuria Andreu[1], Yosuke Omae[2], Licht Toyo-Oka[2], Hideki Yanai[3], Reiko Miyahara[4], Supalert Nedsuwan[5], Paola Florez de Sessions[6], Susana Campino[1], Neneh Sallah[1], Julian Parkhill[7], Nat Smittipat[8], Prasit Palittapongarnpim[8], Taisei Mushiroda[9], Michiaki Kubo[9], Katsushi Tokunaga[2], Surakameth Mahasirimongkol[10], Martin L. Hibberd[1] & Taane G. Clark[1,11]

- Subjects: 714 culture positive chronic pulmonary TB patients in Chiangrai during 2003-2010.
- Bacteria: Illumina sequencing
- Human: High density SNP typing. (1,000,
- Correlation between MTB Lineages and human PCA gr





All patients

Main human PCA group

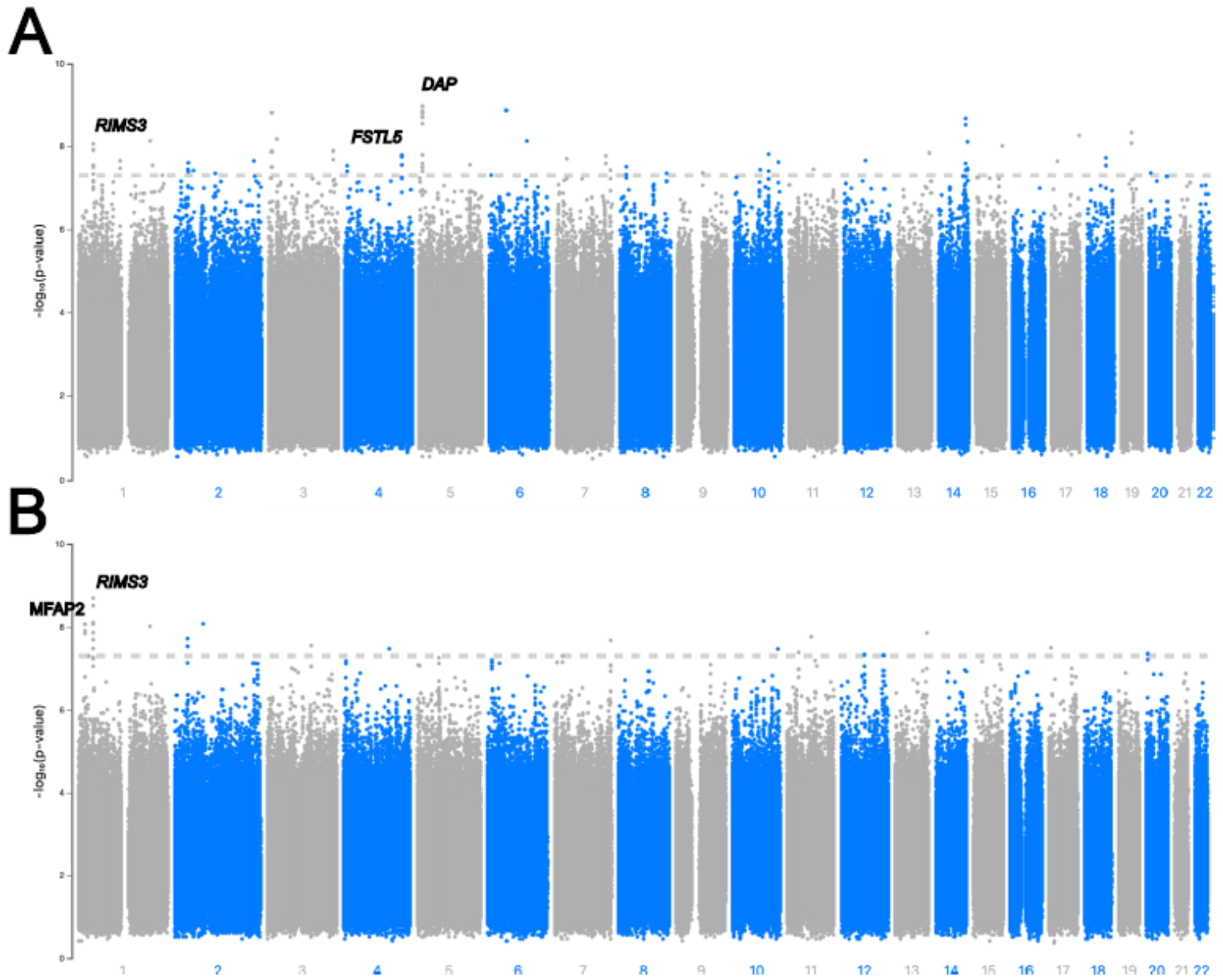


Fig. 2 | Results from the genome-to-genome comparison of host and pathogen data. A Manhattan plot showing the −log10 (*P* value) for each human variant. Results are plotted by chromosomes with alternating grey and blue colouring. The cut-off (5×10^{-8}) is shown with the horizontal red line. Resul whole dataset ($n = 714$), and (**B**) the main host cluster as d component analysis (see Fig. 1C) ($n = 426$).

https://doi.org/10.1038/s41467-023-36282-w

Table 1 | Genome-to-genome association results

Host Chr.	Host Region	No. SNPs[a]	SNP[b]	*P* value	Odds ratio	Host Locus	Host Locus Annotation	*Mtb* Clade lineage	Analysis[c]
5	10712199–10758562	18	rs267951	1.41×10^{-9}	40.52	DAP	Intronic	2.2.1	All
14	97134528–97150790	4	rs74875032	2.11×10^{-9}	21.47	Intergenic	–	4.4.2	All
1	17303792–17310019	5	rs529617685	8.57×10^{-9}	129.69	MFAP2	Intronic	2.2.1.1	Main
4	162602209–162620104	10	rs142600697	1.59×10^{-8}	42.49	FSTL5	Intronic	2.2.1	All
2	35360834–35367230	6	rs1118438	2.47×10^{-8}	22.78	Intergenic	–	1.1.3	All, Main
1	41067739–41074312	14	rs558237	2.86×10^{-8}	3.61	RIMS3	Downstream	1.1	All, Main
3	8308620–8310990	3	rs59441182	3.12×10^{-8}	19.79	Intergenic	–	4.4.2	All
8	19413249–19418028	3	rs4563899	4.84×10^{-8}	29.27	CSGALNACT	Intronic	2.2.1	All

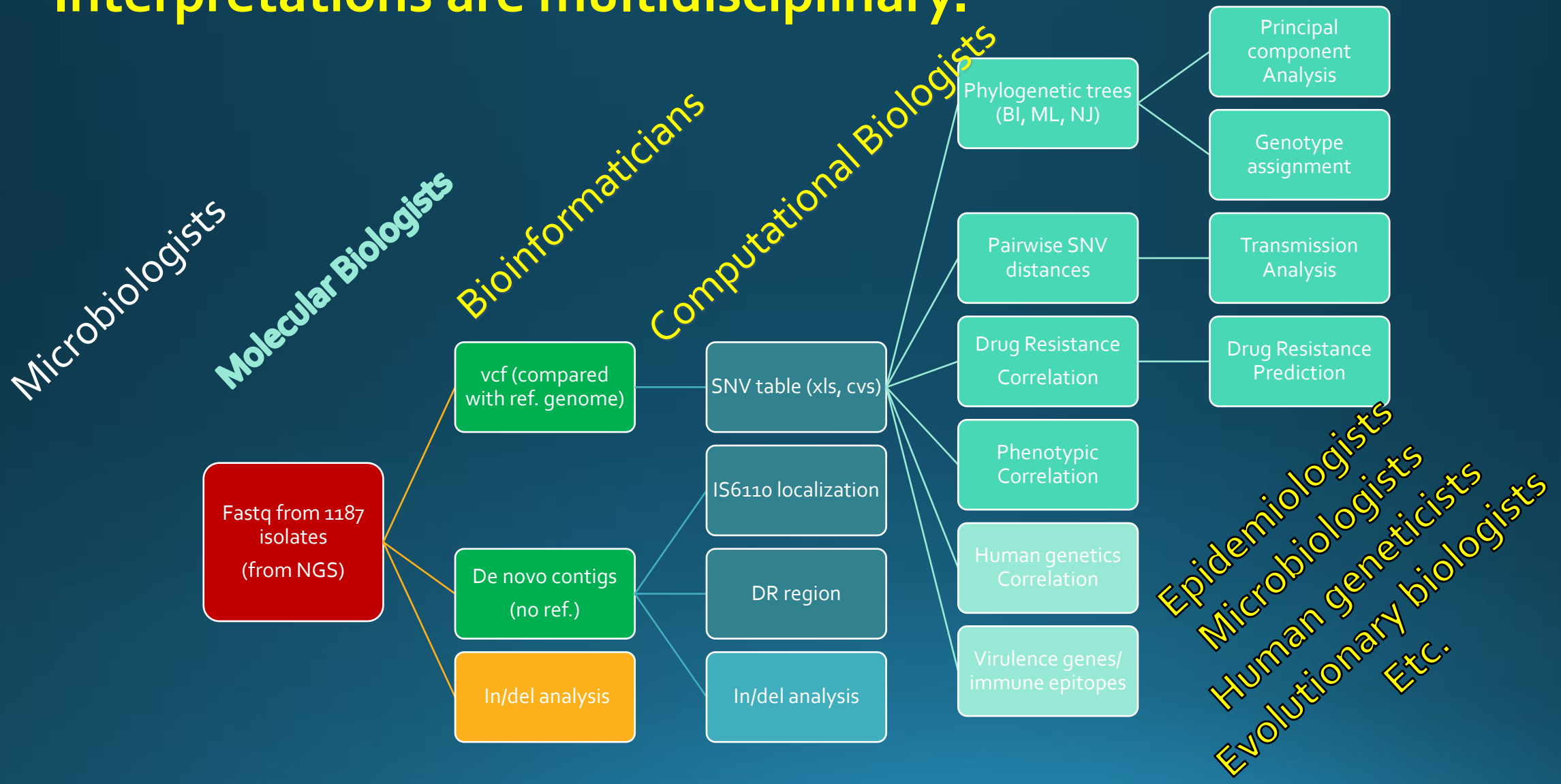
The minimum P-value per gene and the associated odds ratio and lineage of the *M. tuberculosis* variant (*Mtb*).

[a]Number of SNPs with $P < 5\times10^{-8}$;

[b]the SNP with the strongest association (minimum *P* value);

[c]Analyses were performed using all paired samples ($n = 714$) and the main cluster only ($n = 426$) as determined using the first two principal components (see Fig. 1C).

Conclusion: WGS is an essential tool for one health in studying transmission dynamics and host-pathogen genomic interaction. **Interpretations are multidisciplinary.**



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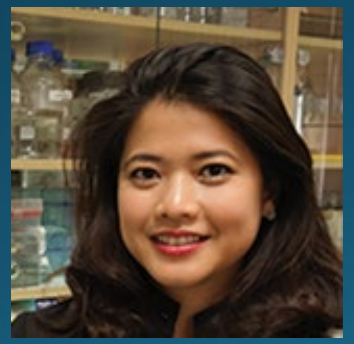

Congratulations to Assoc. Prof. Arunee Thitithanyanont for being selected as an honoree on the Asian Scientist 100 list!

Year 2021

ASIAN SCIENTIST 100

Arunee Thitithanyanont

Mahidol University
Thailand

Thitithanyanont received the L'Oréal Thailand COVID-19 Solidarity Prize in the field of life sciences for her research projects addressing the COVID-19 pandemic, including diagnostic methods, treatments and vaccines. In an early study of 217 recovered COVID-19 patients, Thitithanyanont and her team at the department of microbiology at Mahidol University were able to identify viral clearance as well as the pattern of antibody responses with SARS-CoV-2. This understanding of natural host defenses and antibody duration provides a foundation for further research into controlling the spread of the virus.

(Photo: Loop)



Faculty of Science
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Taa Clark
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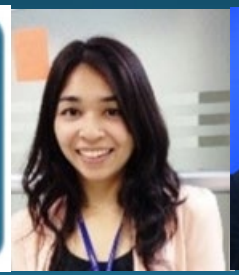
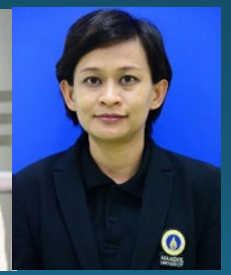
CENTEX Shrimp
BIOTEC





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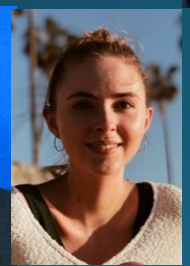

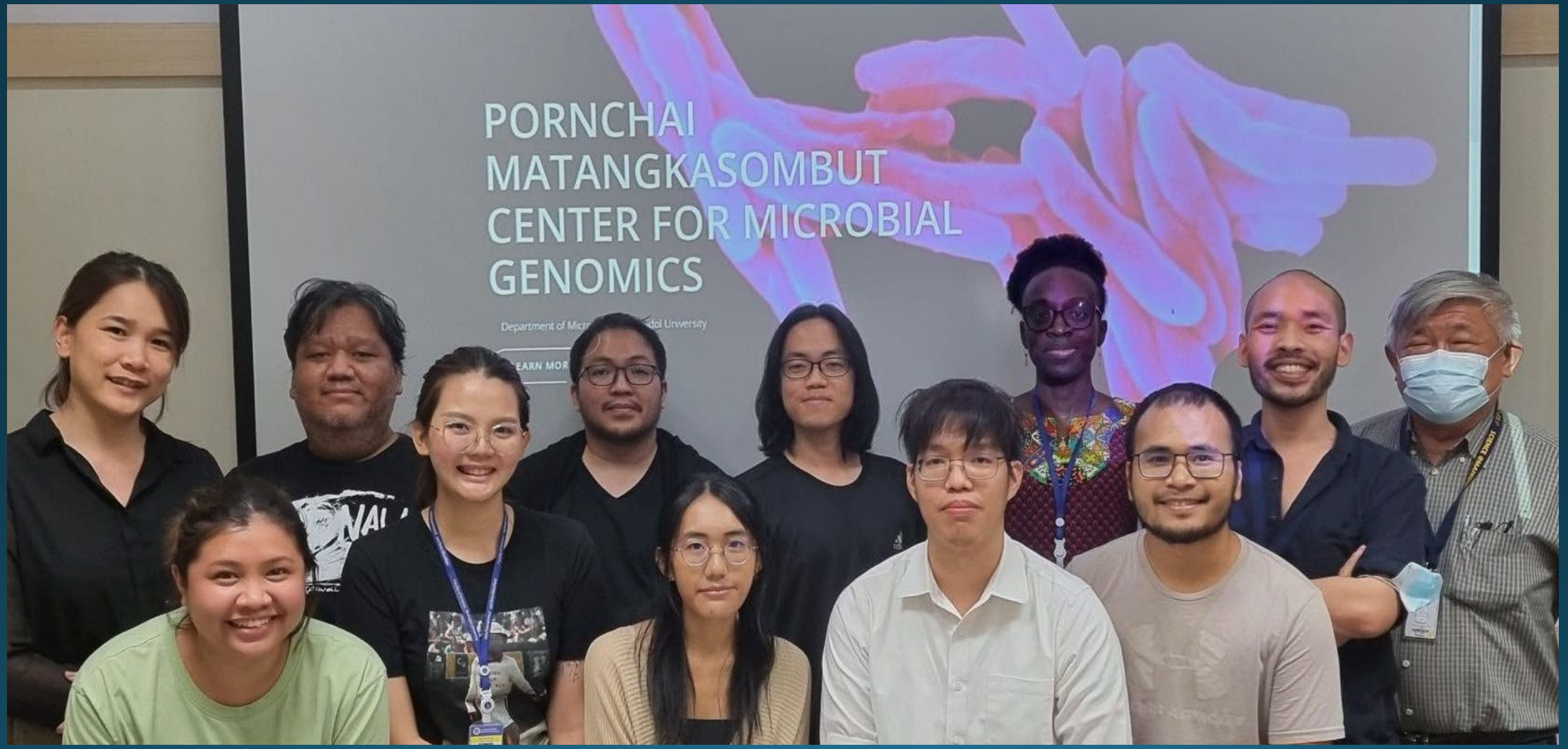
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Infectious Disease Genomics and Their Application

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คณะวิทยาศาสตร์ มหาวิทยาลัยมหิดล

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