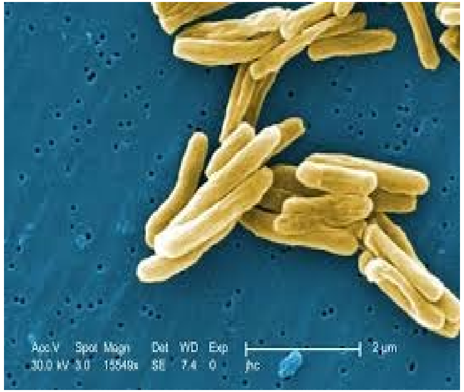
Swiss TPH

Host Specificity in Human and Animal Tuberculosis through the Lens of Genomics

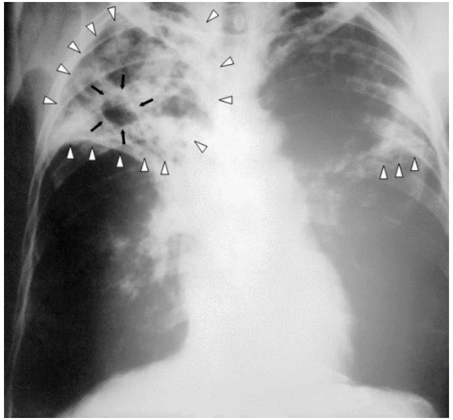
Daniela Brites 22.03.2023

Human Tuberculosis - the partners

Mycobacterium tuberculosis



Homo sapiens



TB Disease enhances bacterial transmission

~10 million TB cases each year
~1.6 million deaths

Zoonotic Tuberculosis - the partners

Mycobacterium bovis

~ 140,000 zTB (~1.4% of all TB)
~ 8% deaths

https://www.who.int/publications/m/item/zoonotic-tb-factsheet

Reverse zoonotic Tuberculosis

Mycobacterium tuberculosis

M. Bovis has a broad host range

Some M. Bovis hosts

https://pixabay.com/

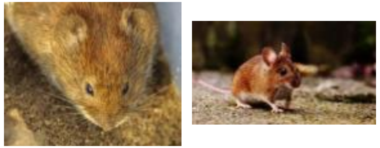
Other close relatives of *M. tuberculosis* & *M. bovis*

M. bovis

M. caprae

https://pixabay.com/

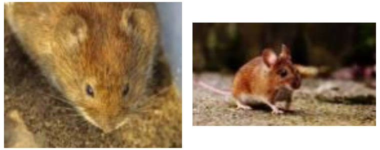
Other close relatives of *M. tuberculosis* & *M. bovis*



M. microti

https://pixabay.com/

Other close relatives of *M. tuberculosis* & *M. bovis*



M. microti

M. pinnipedii

https://pixabay.com/

Other close relatives of *M. tuberculosis* & *M. bovis*

M. mungi

M. suricattae

Dassie bacillus

Chimp bacillus

https://pixabay.com/

Other close relatives of *M. tuberculosis* & *M. bovis*

M. orygis

https://pixabay.com/

Mycobacterium tuberculosis Complex (MTBC)

M. bovis

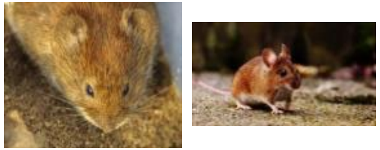
M. suricattae

M. caprae

Chimp bacillus

M. pinnipedii

Dassie bacillus



M. microti

M. mungi

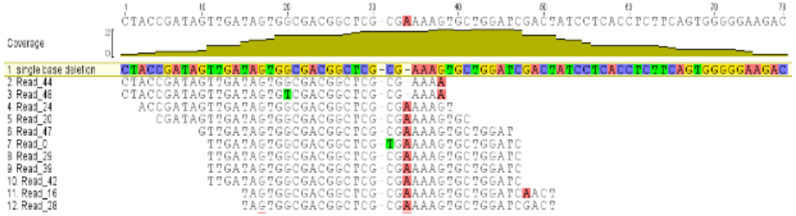
M. orygis

M. tuberculosis

99.95 % nucleotide similarity

https://pixabay.com/

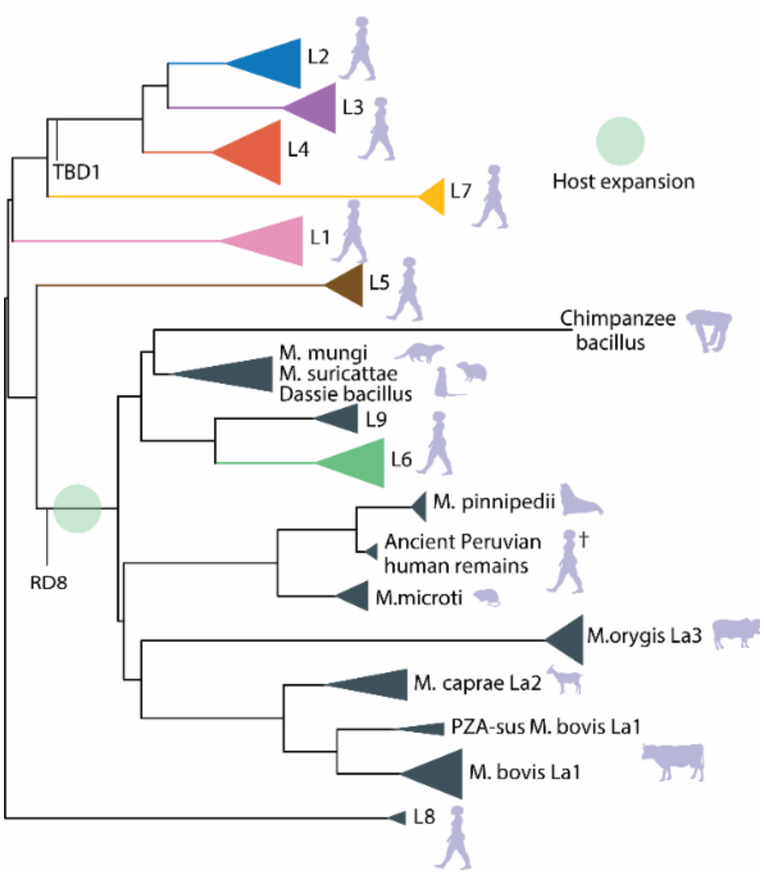
Learning about MTBC host range from comparative genomics



```
                      1        10        20        30        40        50        60        70  73
                      CTACCGATAGTTGATAGTGGCGACGGCTCG-CGAAAAGTGCTGGATCGACTATCCTCACCTCTTCAGTGGGGAAGAC
Coverage
1. single base deletion  CTACCGATAGTTGATAGTGGCGACGGCTCG-CG-AAAGTGCTGGATCGACTATCCTCACCTCTTCAGTGGGGAAGAC
2. Read_44            CTACCGATAGTTGATAGTGGCGACGGCTCG-CG-AAAA
3. Read_48            CTACCGATAGTTGATAGTGTCGACGGCTCG-CG-AAAA
4. Read_24              ACCGATAGTTGATAGTGGCGACGGCTCG-CGAAAAGT
5. Read_20                CGATAGTTGATAGTGGCGACGGCTCG-CGAAAAGTGC
6. Read_47                     GTTGATAGTGGCGACGGCTCG-CGAAAAGTGCTGGAT
7. Read_0                       TTGATAGTGGCGACGGCTCG-TGAAAAGTGCTGGATC
8. Read_29                      TTGATAGTGGCGACGGCTCG-CGAAAAGTGCTGGATC
9. Read_39                      TTGATAGTGGCGACGGCTCG-CGAAAAGTGCTGGATC
10. Read_42                     TTGATAGTGGCGACGGCTCG-CGAAAAGTGCTGGATC
11. Read_16                         TAGTGGCGACGGCTCG-CGAAAAGTGCTGGATCAACT
12. Read_28                         TAGTGGCGACGGCTCG-CGAAAAGTGCTGGATCGACT
```

> 12’000 Public MTBC WGS sequences

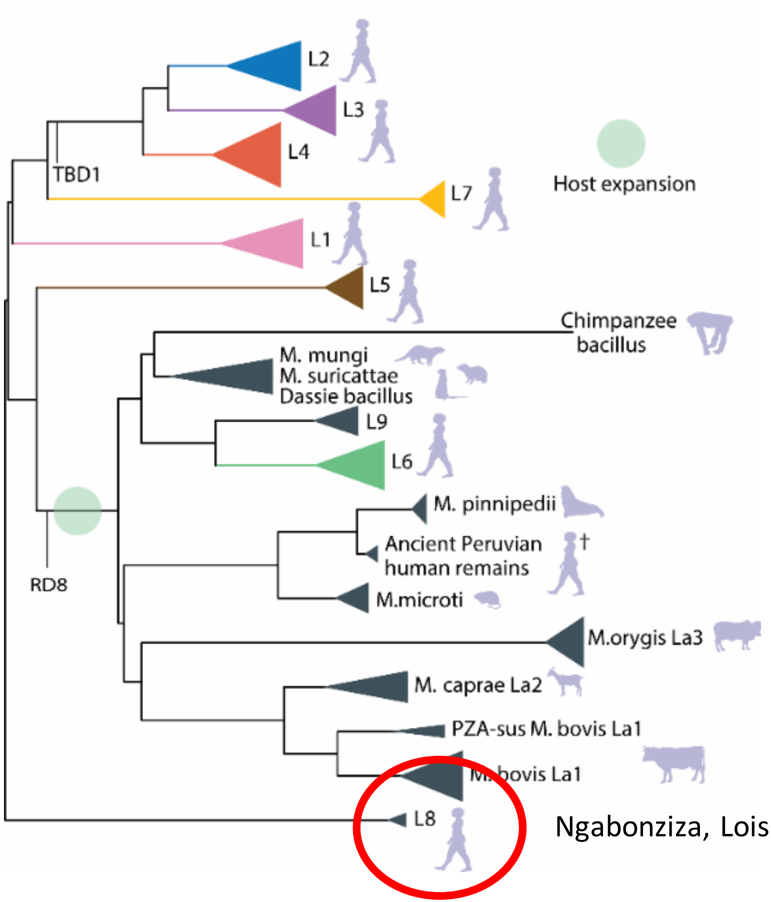
Mycobacterium tuberculosis complex (MTBC)



Brites et al, 2018
Ngabonziza, Loiseau et al, 2020
Coscolla et al, 2021

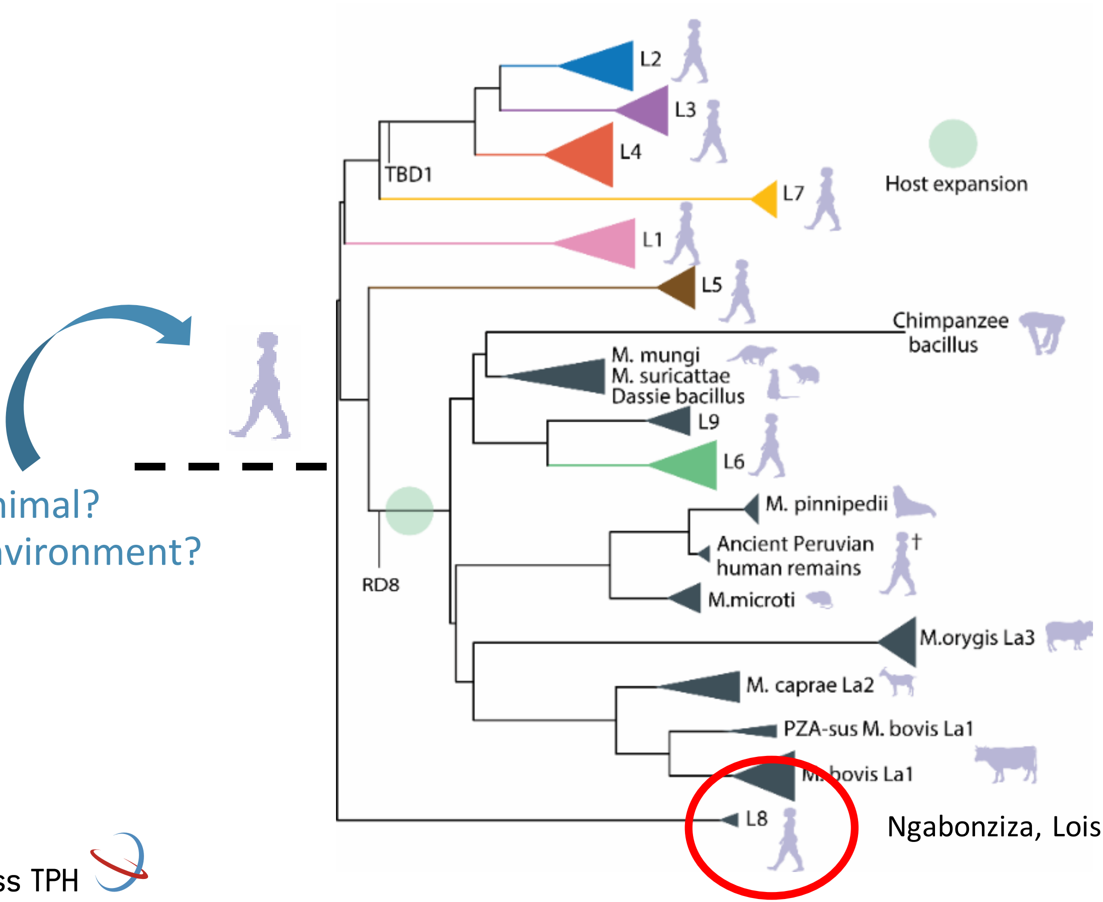
Adapted from C. Loiseau (2020)

MTBC – host transitions



Ngabonziza, Loiseau et al, 2020

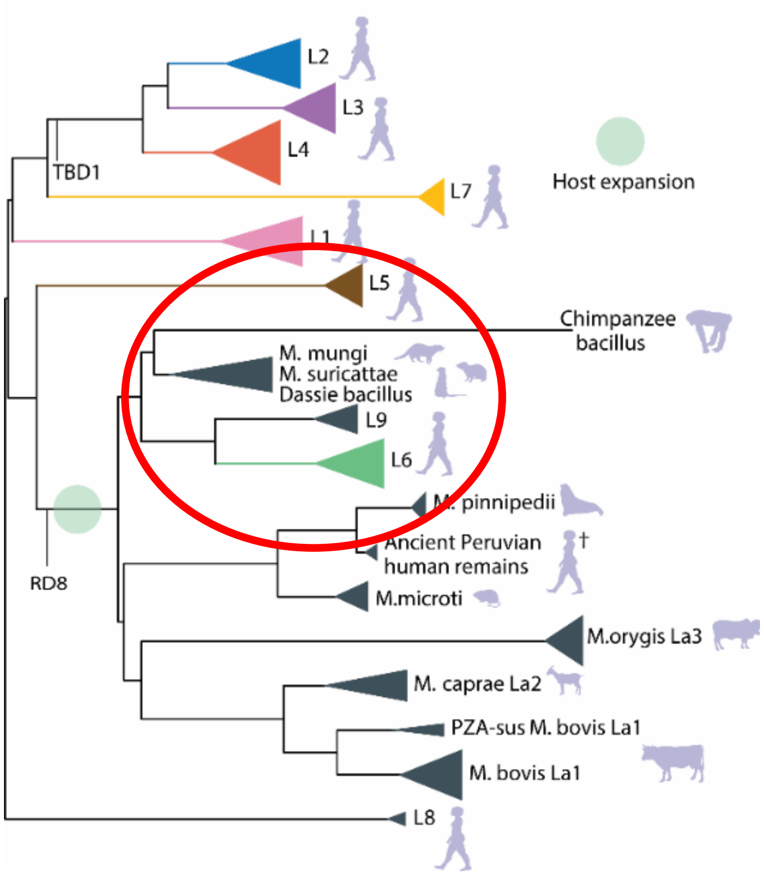
MTBC – host transitions



Animal?
Environment?

Ngabonziza, Loiseau et al, 2020

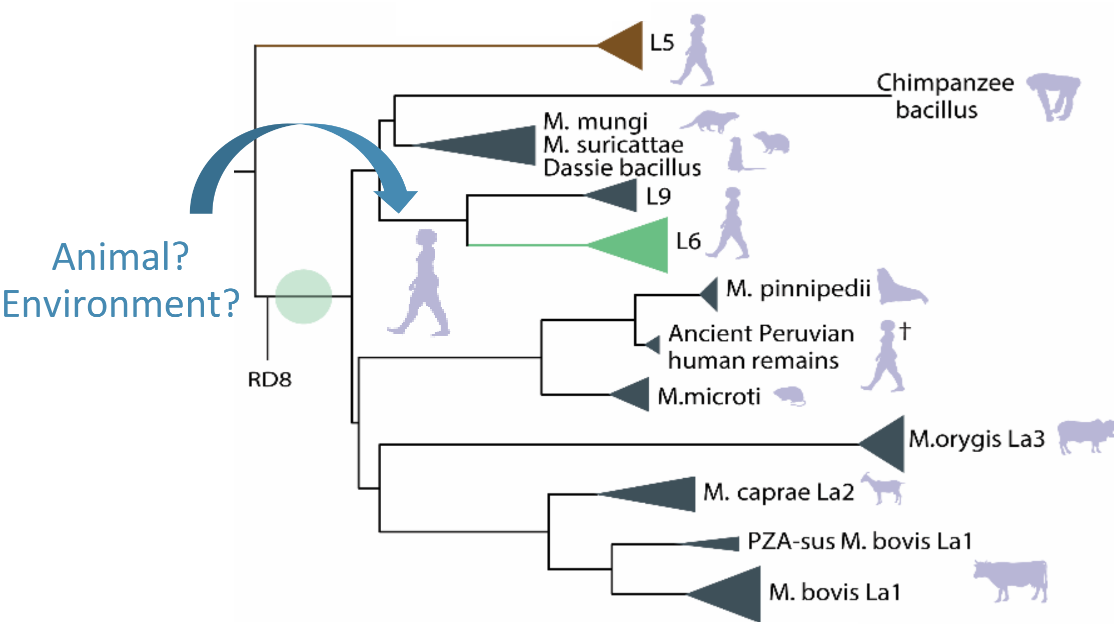
MTBC – host transitions



Brites et al, 2018
Coscolla et al, 2021

Adapted from C. Loiseau (2020)

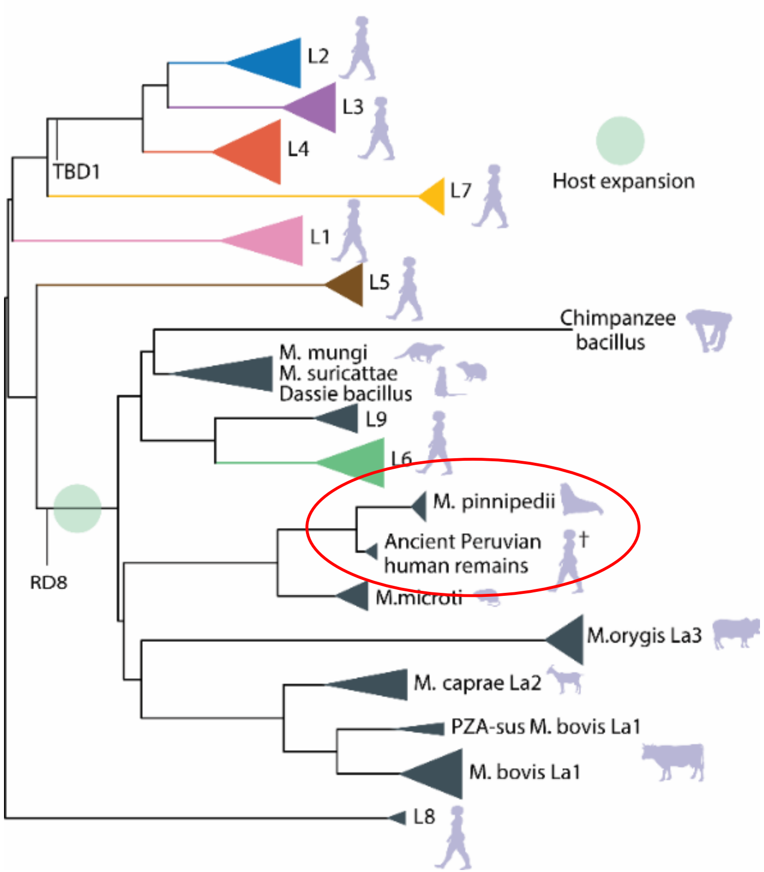
MTBC – host transitions



Brites et al, 2018

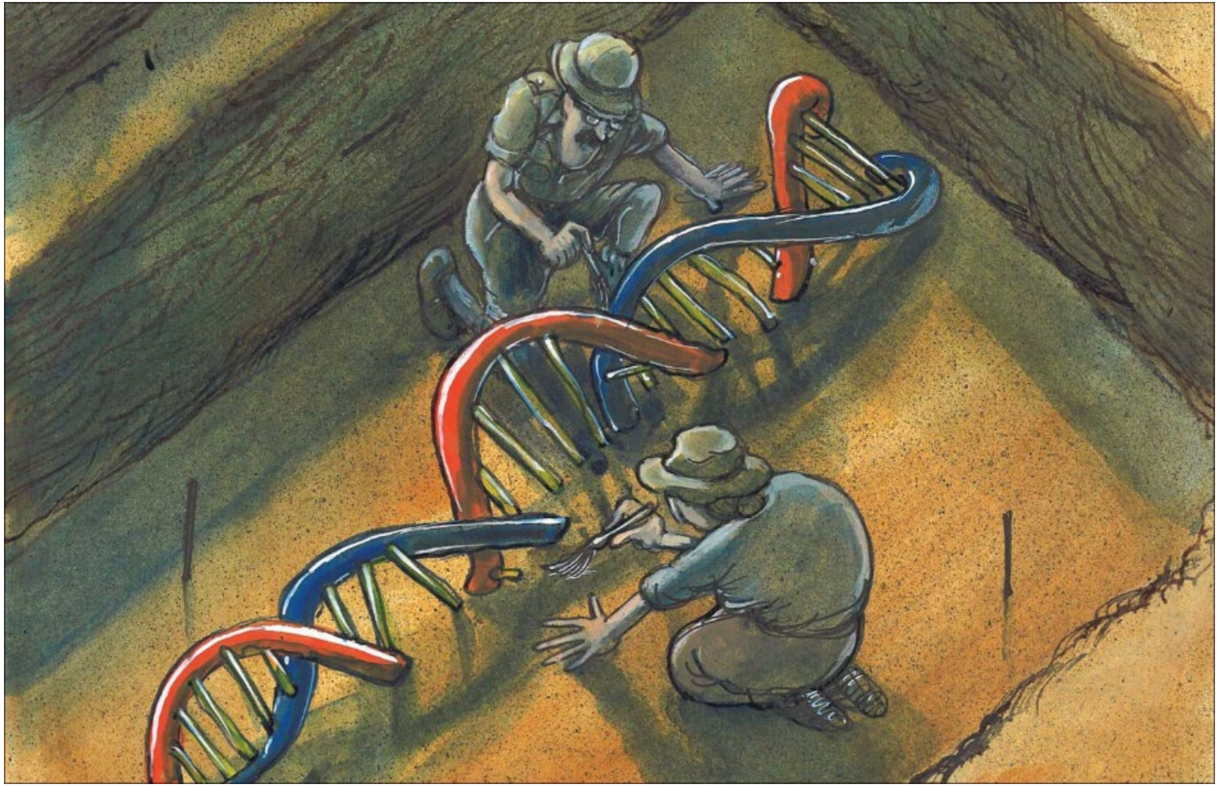
Adapted from C. Loiseau (2020)

MTBC – host transitions



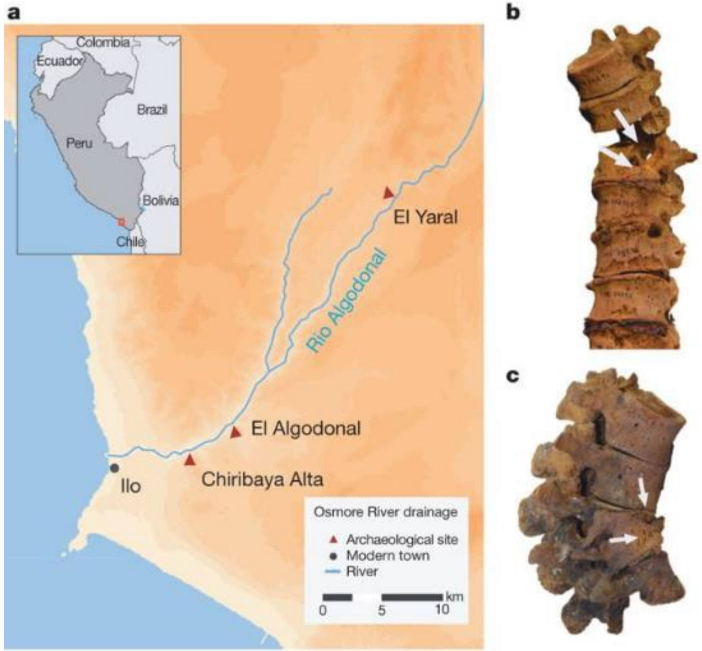
Adapted from C. Loiseau (2020)

DNA can be sequenced from archeological samples



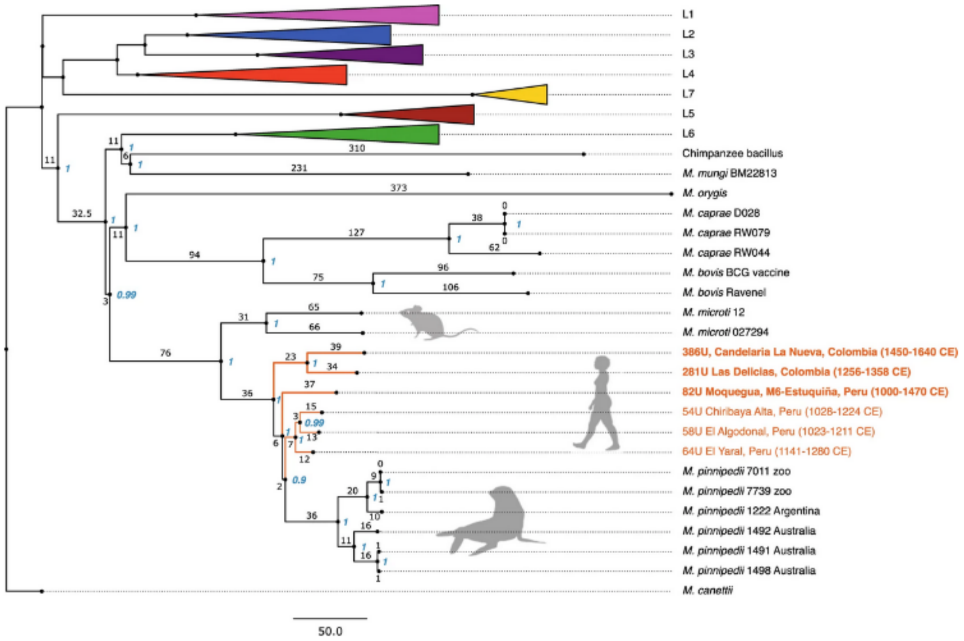
Fonte: https://newhumanist.org.uk/articles/5335/what-ancient-dna-says-about-us

Before Europeans got to the Americas there was TB there already



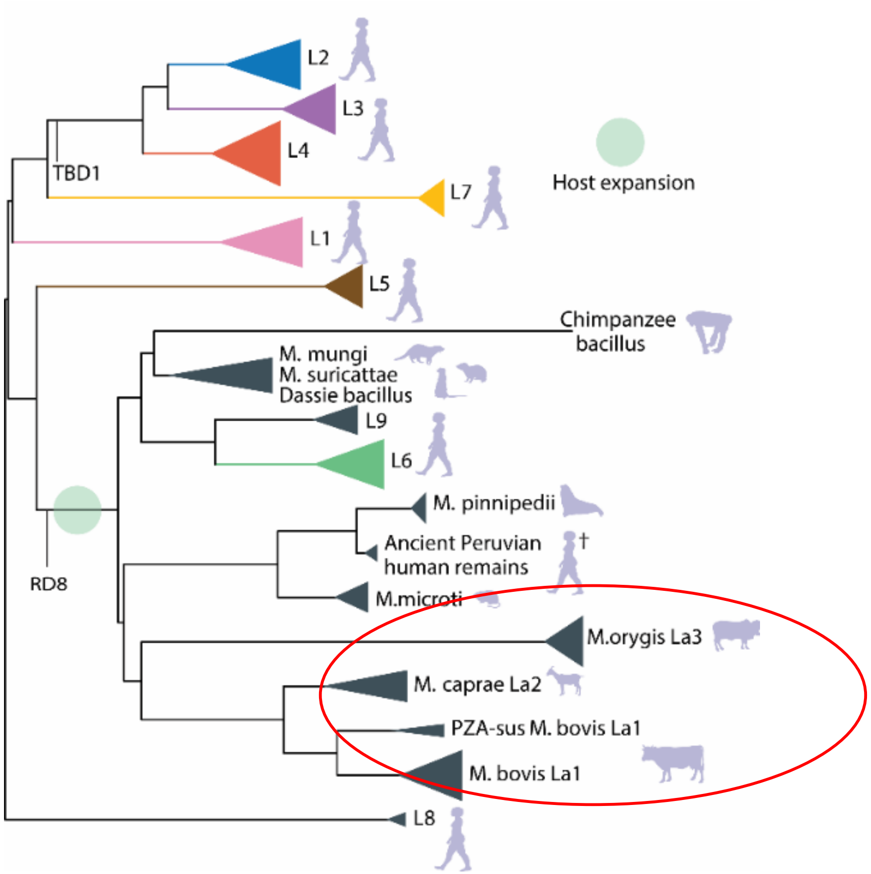
Bos et al, Nature, 2014; Vagene et al, Nature Comm 2022

In the 11th century TB in humans was caused by strains closely related to *M. pinnipedii* know to infect seals today



Bos et al, Nature, 2014; Vagene et al, Nature Comm 2022

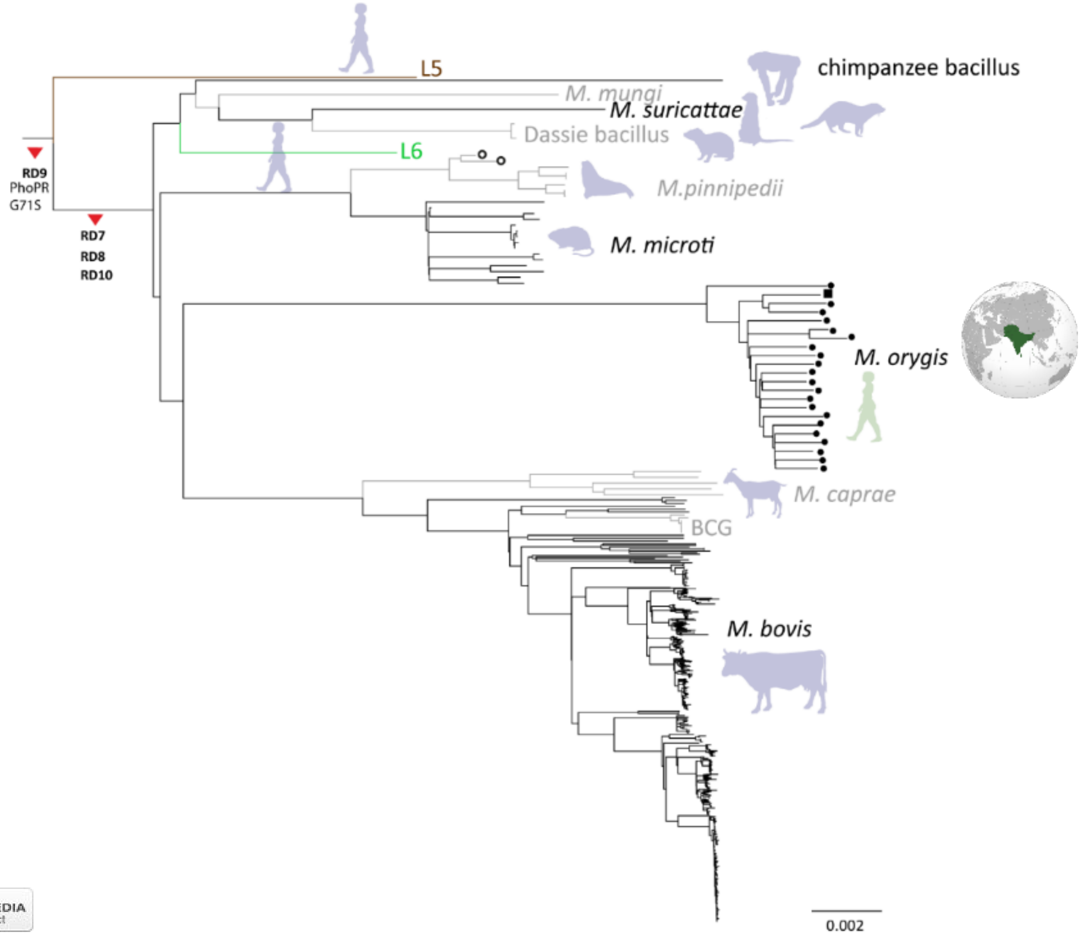
What about zoonosis today?



Adapted from C. Loiseau (2020)

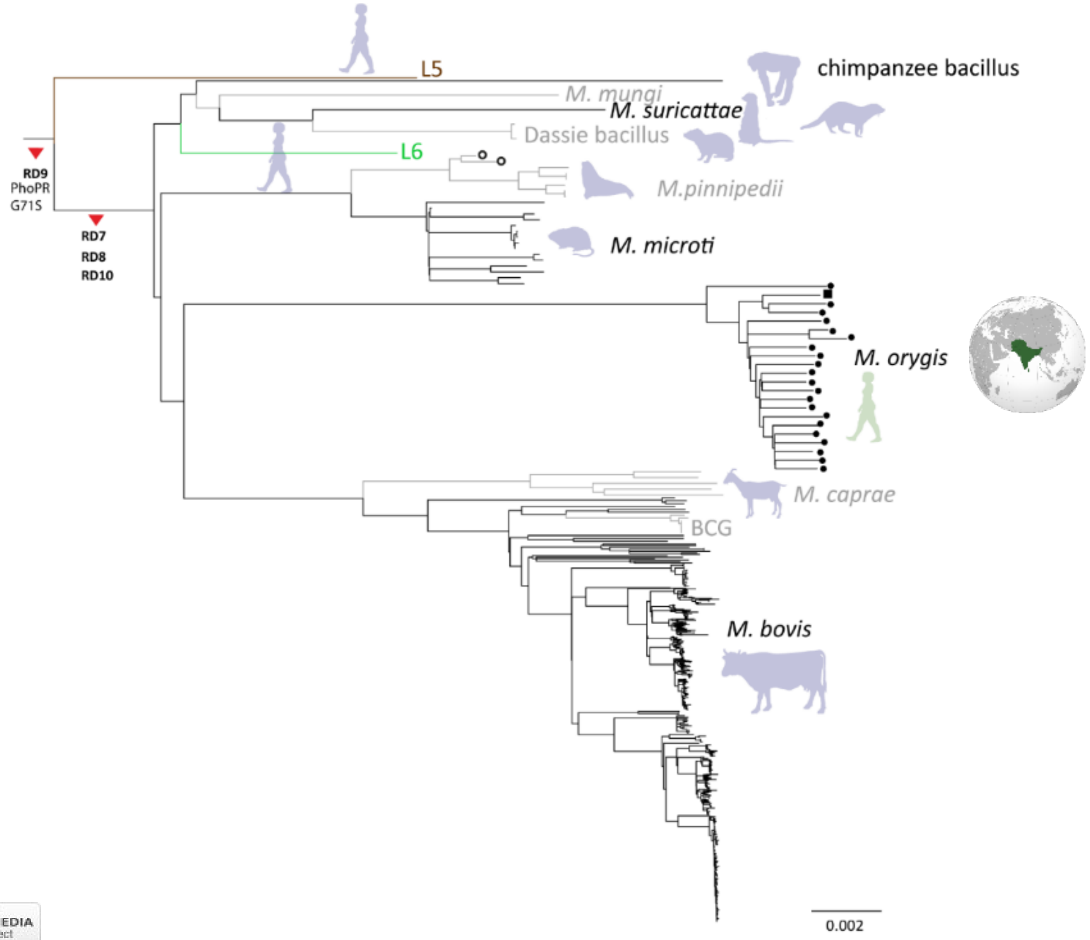
Swiss TPH

M. bovis, *M. caprae* and *M. ogyris* share a recent common ancestor



Brites et al 2018

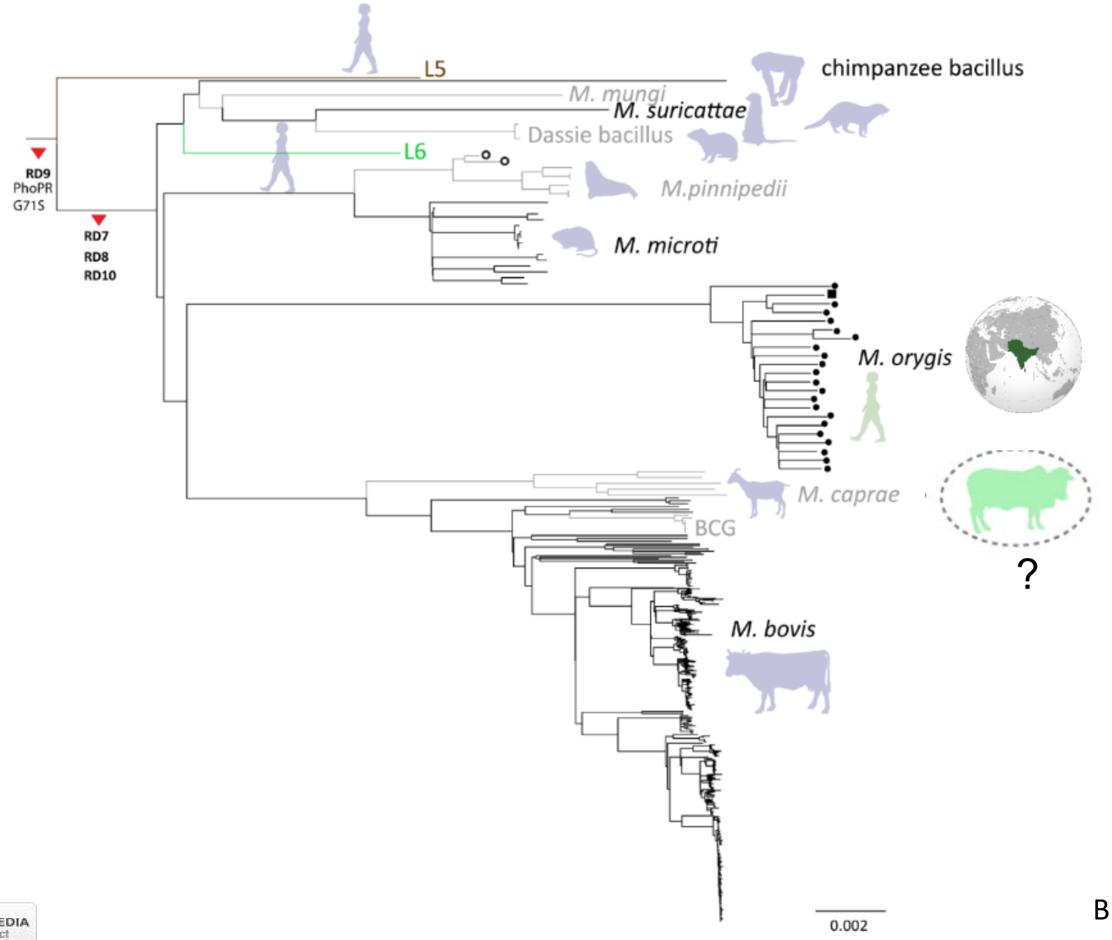
Host range of *M. orygis*



Host range:
Antilopes
buffalos
rhinos
humans
cattle
deers
monkey

Brites et al 2018

Is *M. orygis* the equivalent of *M. bovis* in South Asia?



Host range:
Antilopes
buffalos
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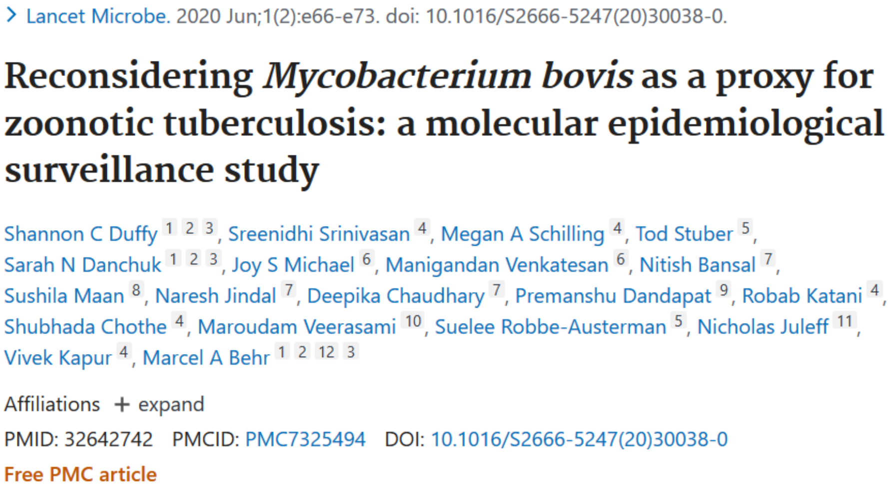
Brites et al 2018



› Lancet Microbe. 2020 Jun;1(2):e66-e73. doi: 10.1016/S2666-5247(20)30038-0.

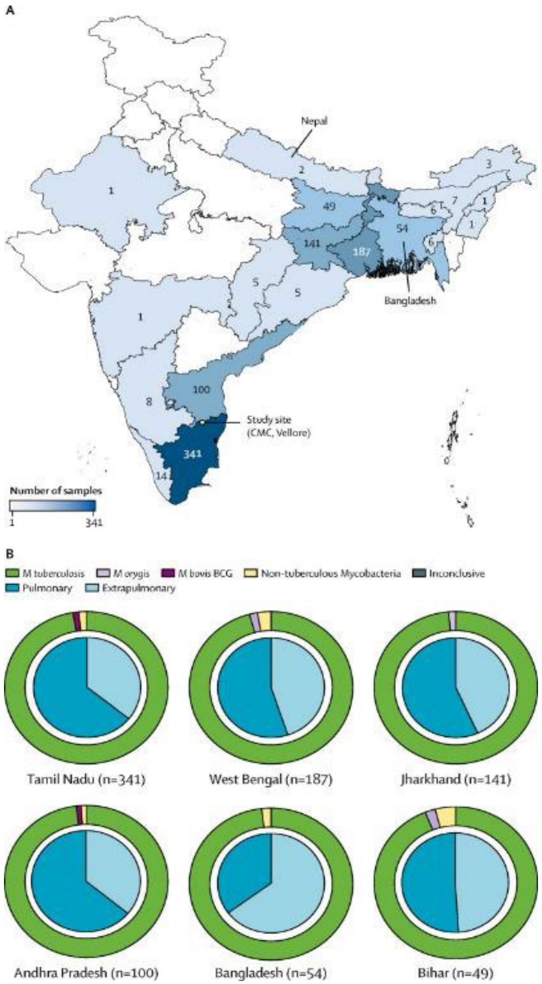
Reconsidering *Mycobacterium bovis* as a proxy for zoonotic tuberculosis: a molecular epidemiological surveillance study

Shannon C Duffy [1] [2] [3], Sreenidhi Srinivasan [4], Megan A Schilling [4], Tod Stuber [5], Sarah N Danchuk [1] [2] [3], Joy S Michael [6], Manigandan Venkatesan [6], Nitish Bansal [7], Sushila Maan [8], Naresh Jindal [7], Deepika Chaudhary [7], Premanshu Dandapat [9], Robab Katani [4], Shubhada Chothe [4], Maroudam Veerasami [10], Suelee Robbe-Austerman [5], Nicholas Juleff [11], Vivek Kapur [4], Marcel A Behr [1] [2] [12] [3]

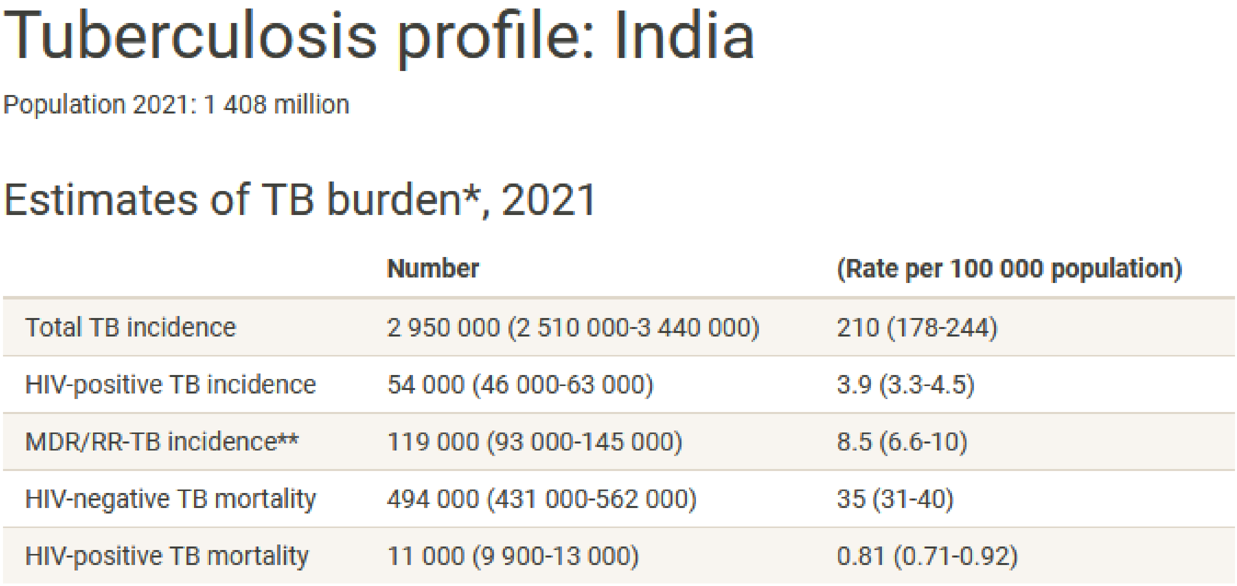
Affiliations + expand

PMID: 32642742 PMCID: PMC7325494 DOI: 10.1016/S2666-5247(20)30038-0

Free PMC article



India has the largest burden of human tuberculosis globally



Tuberculosis profile: India

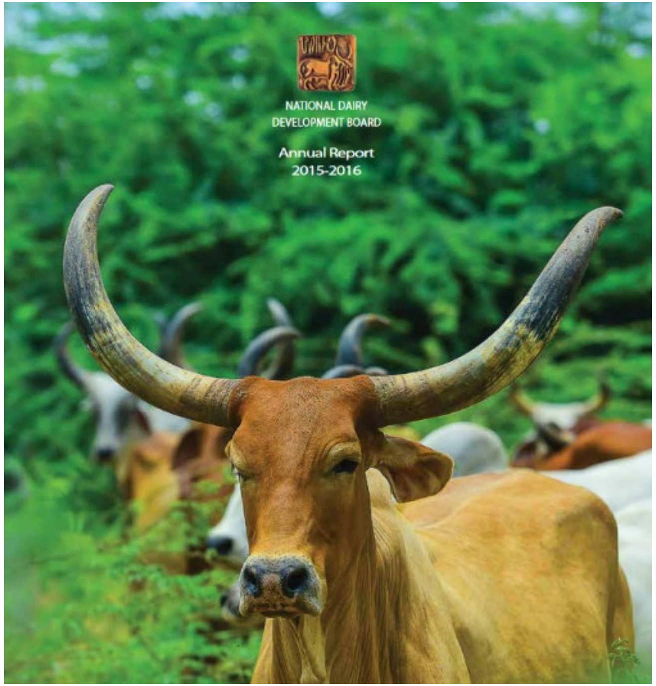
Population 2021: 1 408 million

Estimates of TB burden*, 2021

	Number	(Rate per 100 000 population)
Total TB incidence	2 950 000 (2 510 000-3 440 000)	210 (178-244)
HIV-positive TB incidence	54 000 (46 000-63 000)	3.9 (3.3-4.5)
MDR/RR-TB incidence**	119 000 (93 000-145 000)	8.5 (6.6-10)
HIV-negative TB mortality	494 000 (431 000-562 000)	35 (31-40)
HIV-positive TB mortality	11 000 (9 900-13 000)	0.81 (0.71-0.92)

WHO TB report 2021

India has the largest cattle population in world



NATIONAL DAIRY
DEVELOPMENT BOARD
Annual Report
2015-2016

https://www.nddb.coop/sites/default/files/NDDB_AR_2015-16Eng.pdf

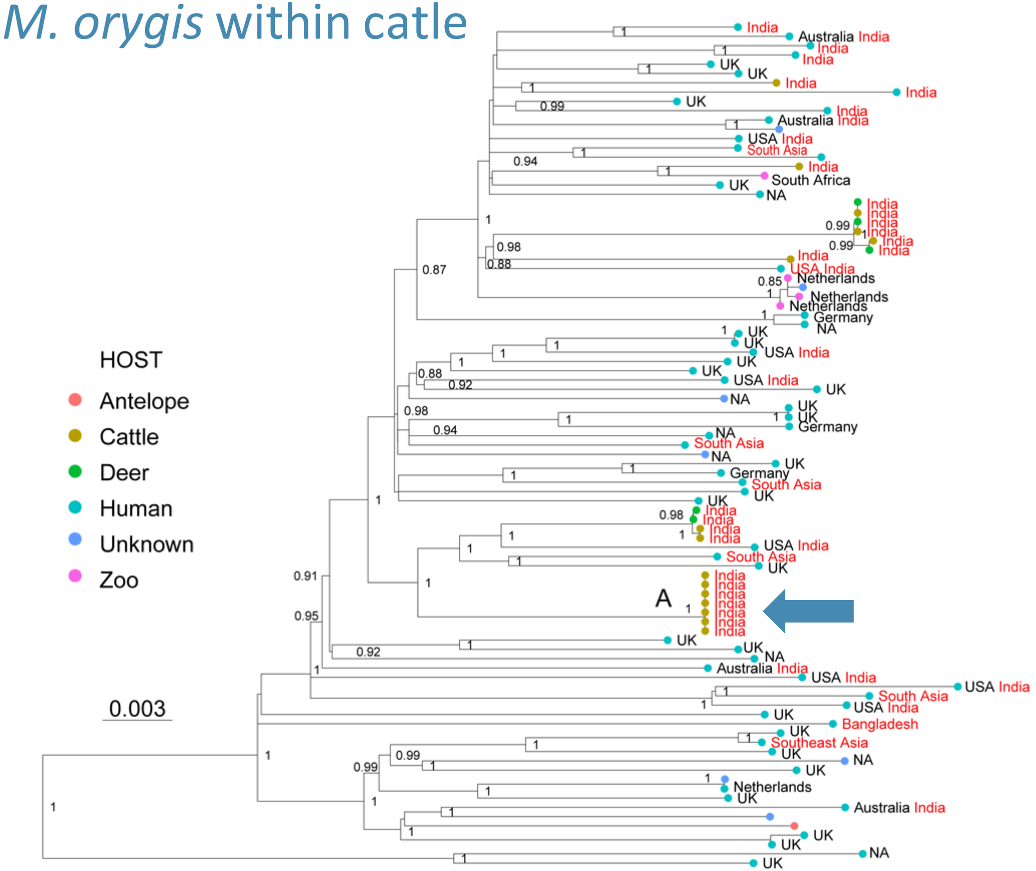
303 Million in 2020

bTB is endemic in India

Prevalence of bTB in cattle in India is estimated to be **7.3%** ~ 21 Million cases

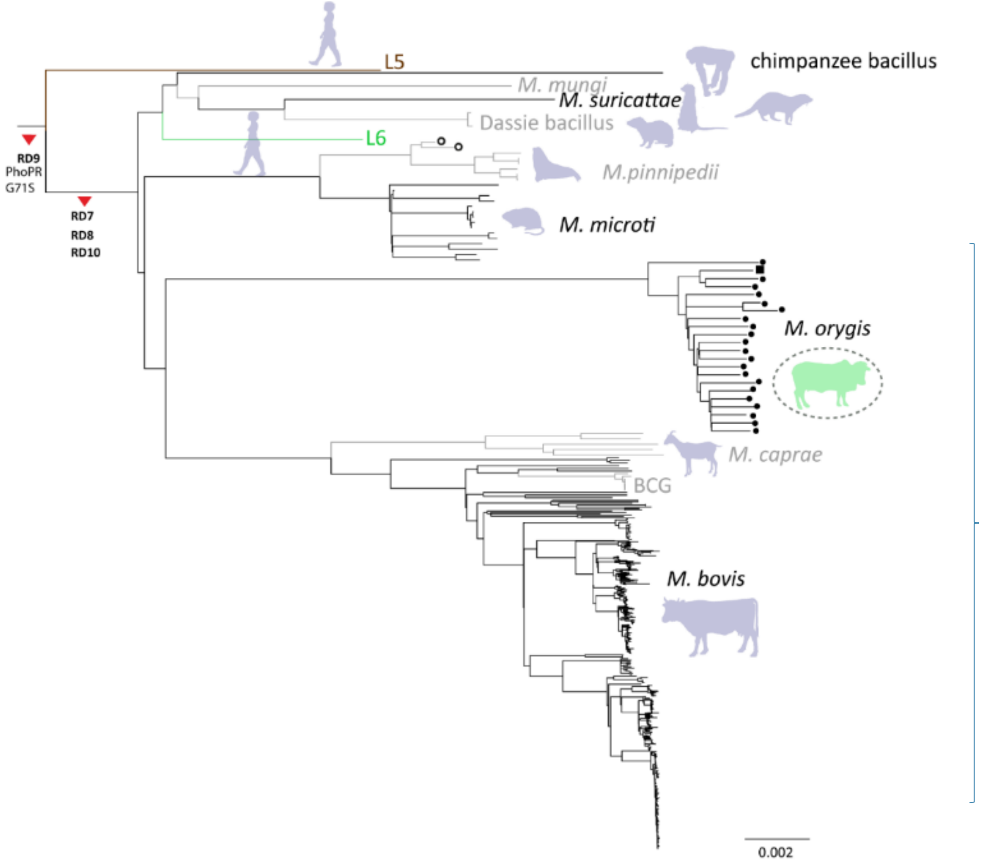
Ramanujam H, Palanivandi K, *One Health* 2023

Transmission of *M. orygis* within catle



Zwyer M et al, *Open Research Europe*, 2021

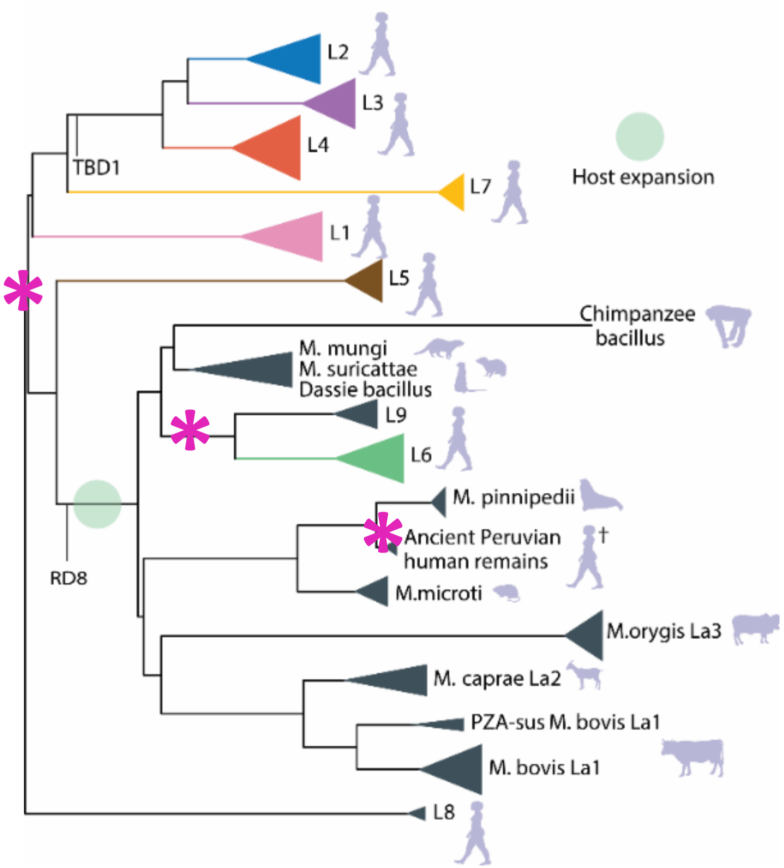
M. orygis, M. caprae, M. bovis - livestock associated MTBC



Livestock pathogens?

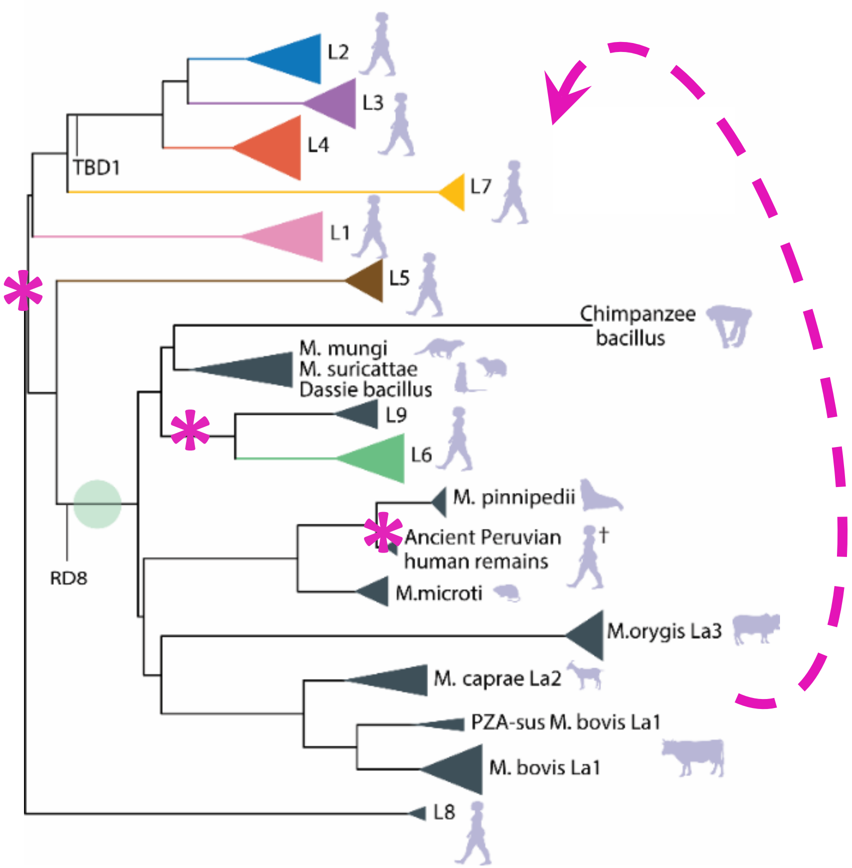
Brites et al 2018

MTBC (re)-adapted to humans at least three times



Adapted from C. Loiseau (2020)

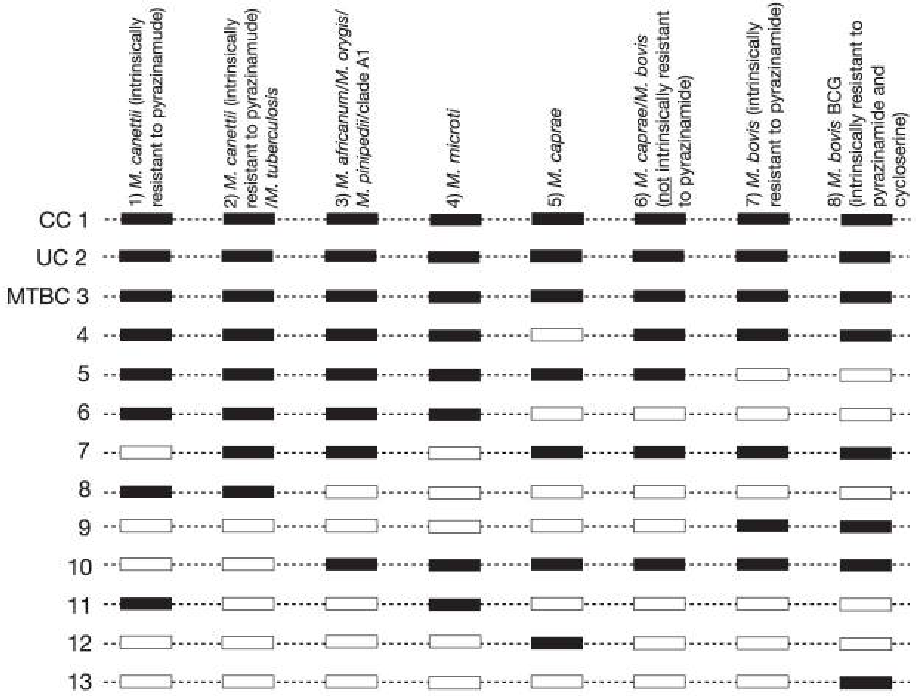
This is why we should worry about zTB



Adapted from C. Loiseau (2020)

894 phylogenetically diverse genomes of the MTBC

Hain Lifescience GenoType MTBC

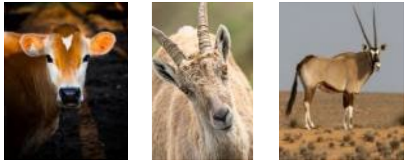


	1) *M. canettii* (intrinsically resistant to pyrazinamude)	2) *M. canettii* (intrinsically resistant to pyrazinamude) /*M. tuberculosis*	3) *M. africanum*/*M. orygis*/ *M. pinipedii*/clade A1	4) *M. microti*	5) *M. caprae*	6) *M. caprae*/*M. bovis* (not intrinsically resistant to pyrazinamide)	7) *M. bovis* (intrinsically resistant to pyrazinamide)	8) *M. bovis* BCG (intrinsically resistant to pyrazinamide and cycloserine)
CC 1	●	●	●	●	●	●	●	●
UC 2	●	●	●	●	●	●	●	●
MTBC 3	●	●	●	●	●	●	●	●
4	●	●	●	●	○	●	●	●
5	●	●	●	●	●	●	○	○
6	●	●	●	●	○	○	○	○
7	○	●	●	○	●	●	●	●
8	●	●	○	○	○	○	○	○
9	○	○	○	○	○	○	●	●
10	○	○	●	●	●	●	●	●
11	●	○	○	●	○	○	○	○
12	○	○	○	○	●	○	○	○
13	○	○	○	○	○	○	○	●

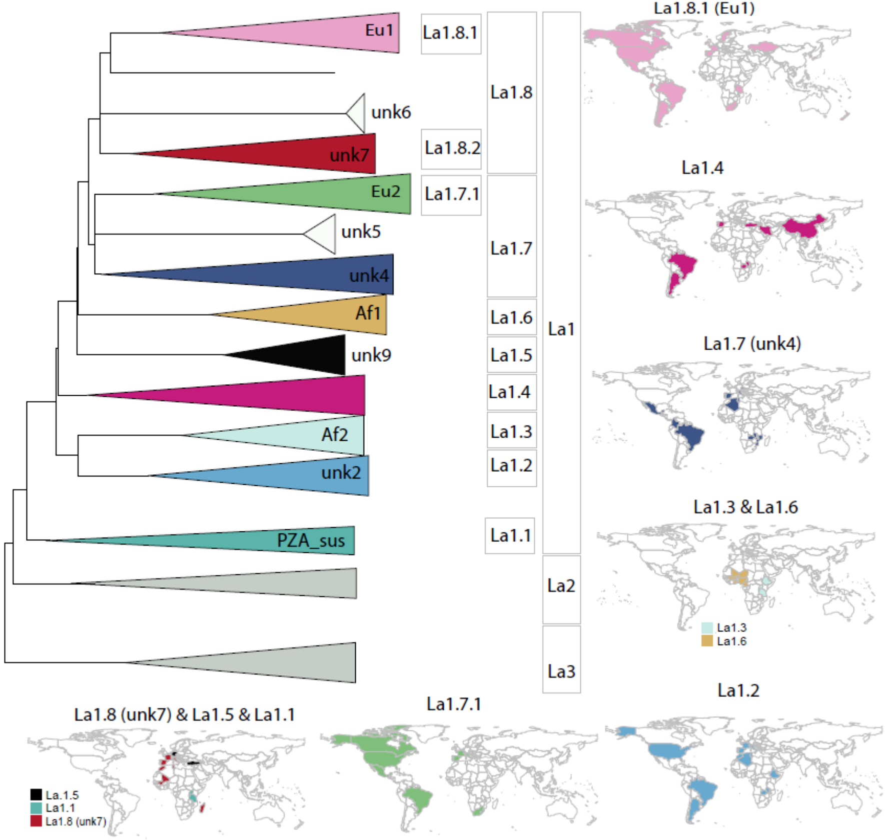
Clade A1: *M. mungi*, *M. suricattae*, Dassie bacillus, Chimpanzee bacillus

Loiseau et al, AAC 2019

Phylogenetic Single Nucleotide Polymorphisms (SNP)



SNP genotyping



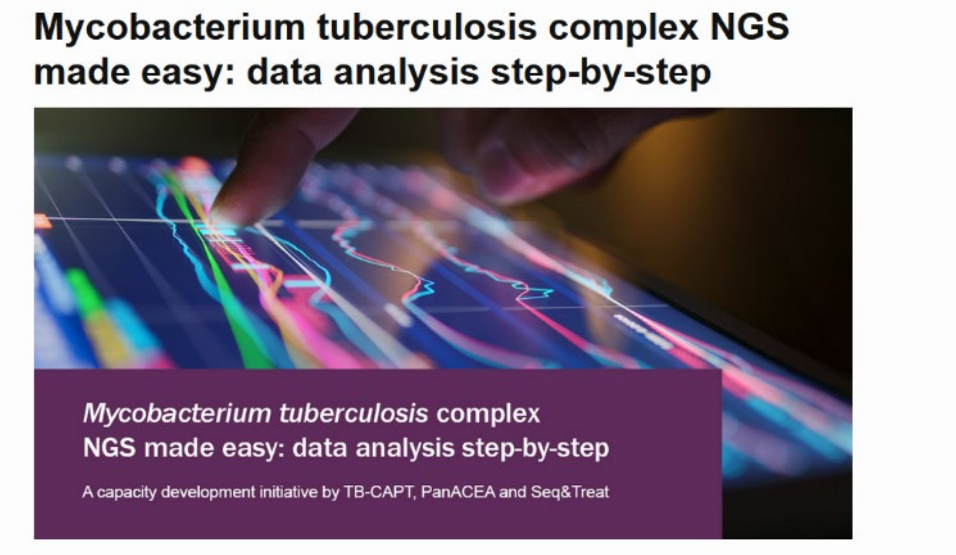
Zwyer M et al, *Open Research Europe*, 2021

Do you have animal isolates that you would like to sequence?

d.brites@swisstph.ch

Do you want to learn how apply to genomics and bioinformatics to TB?

E- Learning Course for self-study



Mycobacterium tuberculosis complex NGS made easy: data analysis step-by-step

Mycobacterium tuberculosis complex NGS made easy: data analysis step-by-step

A capacity development initiative by TB-CAPT, PanACEA and Seq&Treat

https://gallantries.github.io/video-library/modules/mtb-analysis

Live edition (remote)
2-6th October 2023

A join effort brought to you by:

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Swiss Tropical and Public Health Institute

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Swiss Tropical and Public Health Institute

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Caroline Stöhr
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Galo Adrián Goig
Swiss Tropical and Public Health Institute

Arash Ghodousi
IRCCS Ospedale San Raffaele & Università Vita-Salute San Raffaele

Liliana Rutaihwa
FIND

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SANBI/UWC

Federico DiMarco
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Swiss TPH

I.R.C.C.S. Ospedale San Raffaele

FIND Diagnosis for all

Galaxy

Acknowledgement

Thank you!

Swiss TPH

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Michaela Zwyer

Those that provided us with animal MTBC isolates, in particular:

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Erika Scaltriti (Italy)
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Mohammad Uddin (Bangladesh)
Blanka Orłowska (Poland)

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