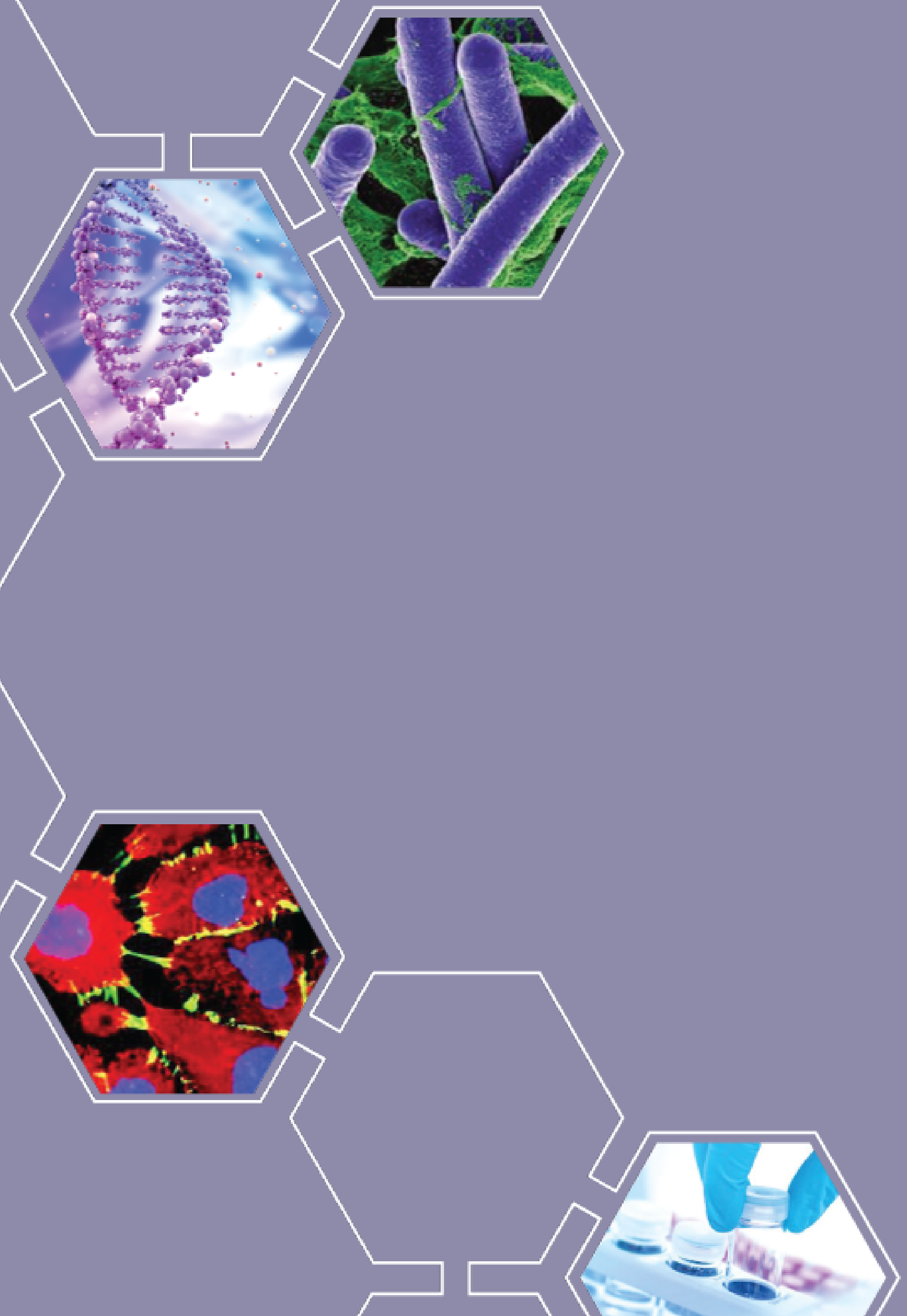
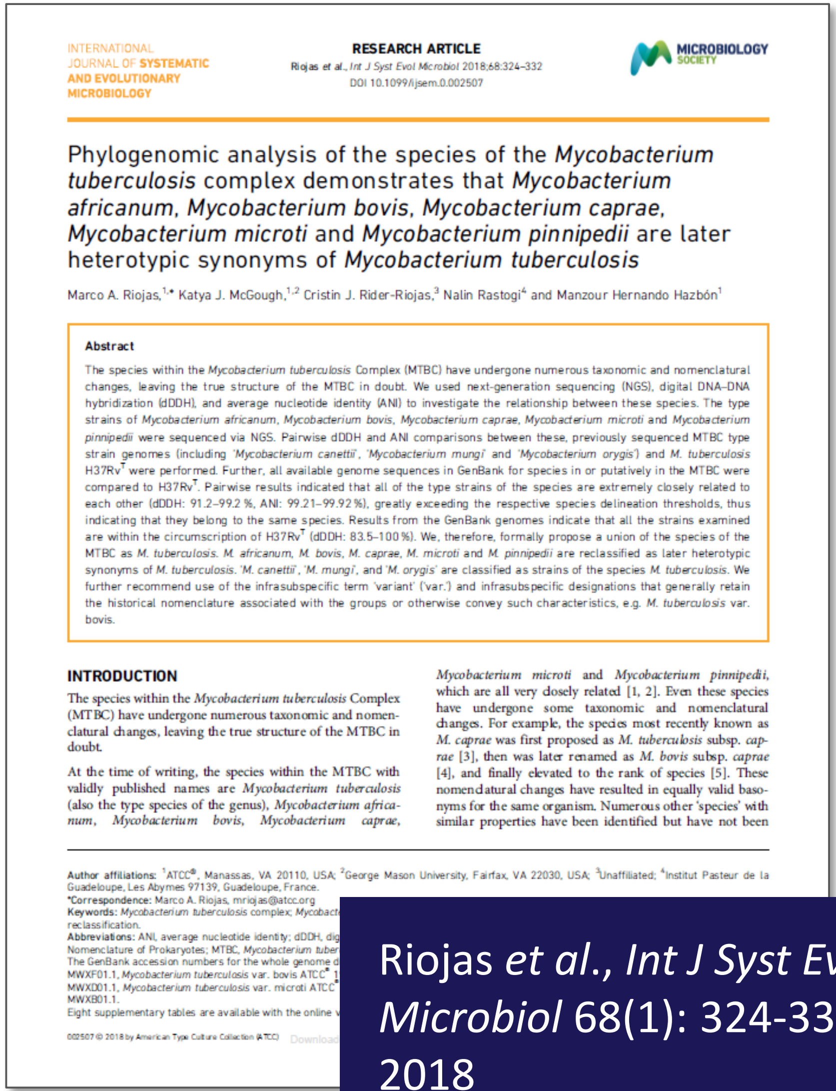


Reclassification of the *Mycobacterium tuberculosis* Complex (MTBC) Species as *Mycobacterium tuberculosis*

Marco A. Riojas, Ph.D.
Scientist, ATCC/BEI Resources

Outline



INTERNATIONAL
JOURNAL OF **SYSTEMATIC
AND EVOLUTIONARY
MICROBIOLOGY**

RESEARCH ARTICLE
Riojas *et al.*, *Int J Syst Evol Microbiol* 2018;68:324–332
DOI 10.1099/ijsem.0.002507

MICROBIOLOGY SOCIETY

Phylogenomic analysis of the species of the *Mycobacterium tuberculosis* complex demonstrates that *Mycobacterium africanum*, *Mycobacterium bovis*, *Mycobacterium caprae*, *Mycobacterium microti* and *Mycobacterium pinnipedii* are later heterotypic synonyms of *Mycobacterium tuberculosis*

Marco A. Riojas,[1,*] Katya J. McGough,[1,2] Cristin J. Rider-Riojas,[3] Nalin Rastogi[4] and Manzour Hernando Hazbón[1]

Abstract

The species within the *Mycobacterium tuberculosis* Complex (MTBC) have undergone numerous taxonomic and nomenclatural changes, leaving the true structure of the MTBC in doubt. We used next-generation sequencing (NGS), digital DNA–DNA hybridization (dDDH), and average nucleotide identity (ANI) to investigate the relationship between these species. The type strains of *Mycobacterium africanum*, *Mycobacterium bovis*, *Mycobacterium caprae*, *Mycobacterium microti* and *Mycobacterium pinnipedii* were sequenced via NGS. Pairwise dDDH and ANI comparisons between these, previously sequenced MTBC type strain genomes (including '*Mycobacterium canettii*', '*Mycobacterium mungi*' and '*Mycobacterium orygis*') and *M. tuberculosis* H37Rv^T were performed. Further, all available genome sequences in GenBank for species in or putatively in the MTBC were compared to H37Rv^T. Pairwise results indicated that all of the type strains of the species are extremely closely related to each other (dDDH: 91.2–99.2 %, ANI: 99.21–99.92 %), greatly exceeding the respective species delineation thresholds, thus indicating that they belong to the same species. Results from the GenBank genomes indicate that all the strains examined are within the circumscription of H37Rv^T (dDDH: 83.5–100 %). We, therefore, formally propose a union of the species of the MTBC as *M. tuberculosis*. *M. africanum*, *M. bovis*, *M. caprae*, *M. microti* and *M. pinnipedii* are reclassified as later heterotypic synonyms of *M. tuberculosis*. '*M. canettii*', '*M. mungi*', and '*M. orygis*' are classified as strains of the species *M. tuberculosis*. We further recommend use of the infrasubspecific term 'variant' ('var.') and infrasubspecific designations that generally retain the historical nomenclature associated with the groups or otherwise convey such characteristics, e.g. *M. tuberculosis* var. bovis.

INTRODUCTION

The species within the *Mycobacterium tuberculosis* Complex (MTBC) have undergone numerous taxonomic and nomenclatural changes, leaving the true structure of the MTBC in doubt.

At the time of writing, the species within the MTBC with validly published names are *Mycobacterium tuberculosis* (also the type species of the genus), *Mycobacterium africanum*, *Mycobacterium bovis*, *Mycobacterium caprae*, *Mycobacterium microti* and *Mycobacterium pinnipedii*, which are all very closely related [1, 2]. Even these species have undergone some taxonomic and nomenclatural changes. For example, the species most recently known as *M. caprae* was first proposed as *M. tuberculosis* subsp. *caprae* [3], then was later renamed as *M. bovis* subsp. *caprae* [4], and finally elevated to the rank of species [5]. These nomenclatural changes have resulted in equally valid basonyms for the same organism. Numerous other 'species' with similar properties have been identified but have not been

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***Correspondence:** Marco A. Riojas, mriojas@atcc.org

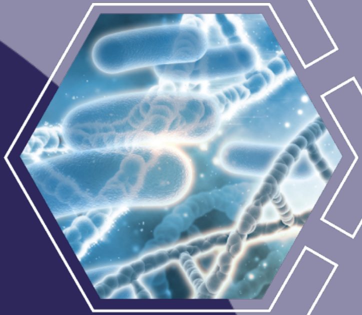
Keywords: *Mycobacterium tuberculosis* complex; *Mycobact*
reclassification.

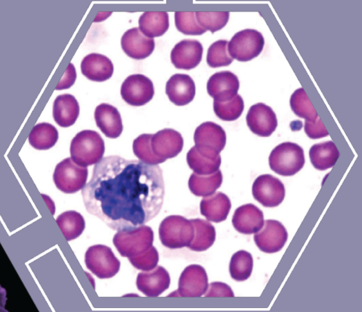
Abbreviations: ANI, average nucleotide identity; dDDH, dig
Nomenclature of Prokaryotes; MTBC, *Mycobacterium tuber*
The GenBank accession numbers for the whole genome d
MWXF01.1, *Mycobacterium tuberculosis* var. bovis ATCC® 1
MWXD01.1, *Mycobacterium tuberculosis* var. microti ATCC®
MWXB01.1.
Eight supplementary tables are available with the online v

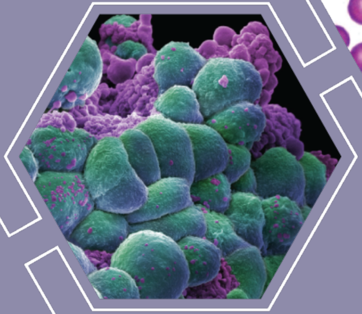
Riojas *et al.*, *Int J Syst Evol Microbiol* 68(1): 324-332, 2018

- About ATCC
- Determination of species
  - What is a species?
  - How are species assigned?
  - DNA-DNA hybridization (DDH)
  - Digital DDH (dDDH)
- Research results and conclusions
  - MTBC results
  - Nomenclatural proposal

About ATCC





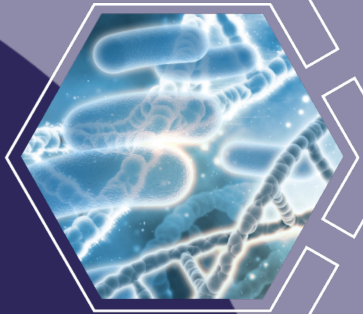


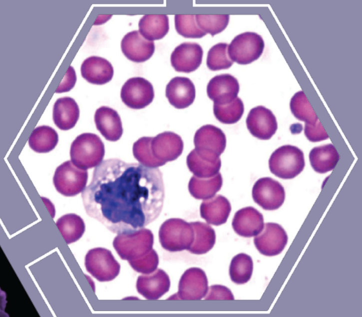
About ATCC

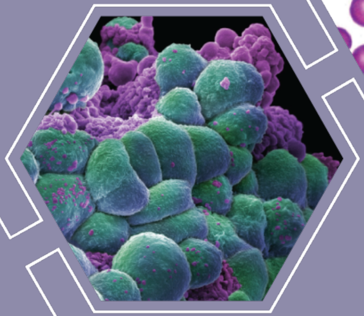
- Founded in 1925, ATCC is a non-profit organization with HQ in Manassas, VA, and an R&D and Services center in Gaithersburg, MD
- World's premier biological materials resource and standards development organization
  - 5,000 cell lines
  - 80,000 microorganisms
  - Genomic & synthetic nucleic acids
  - Media/reagents
- ATCC collaborates with and supports the scientific community with industry-standard biological products and innovative solutions
  - Growing portfolio of products and services
  - Sales and distribution in 150 countries, 15 international distributors
- Talented team of 450+ employees, over one-third with advanced degrees

An innovative global partner for authentic biomaterials, standards and services

Determination of Species







How are Species Defined?

- Each species is represented by a **type strain** and a description of that strain
  - Usually the first strain identified
  - Not necessarily the most typical or the representative of the species
  - Designated with a superscripted, uppercase T after the strain name (*e.g.*, *Mycobacterium tuberculosis* H37Rv^T)
  - **The type strain is essentially the "definition" of a species**
- Serves as the comparative reference point for the identification of new strains and the assignment to existing species

How is a New Strain Assigned to a Species?

- The characteristics of the new strain are compared to the characteristics of species type strains
  - Historically: phenotypic characteristics

- A strain that shares enough of the essential characteristics of a type strain is said to be within the **circumscription** of that species/type strain
  - Therefore, it belongs to that species

Species A^{T}
Gram +
Aerobic
Motile
Nitrate +

Species B^{T}
Gram +
Anaerobic
Motile
Nitrate –

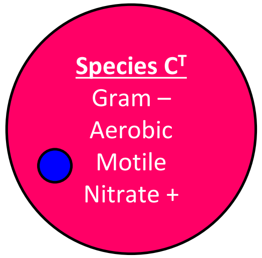
Species C^{T}
Gram –
Aerobic
Motile
Nitrate +

Species D^{T}
Gram –
Anaerobic
Non-motile
Nitrate –

●
Gram –
Aerobic
Motile
Nitrate +

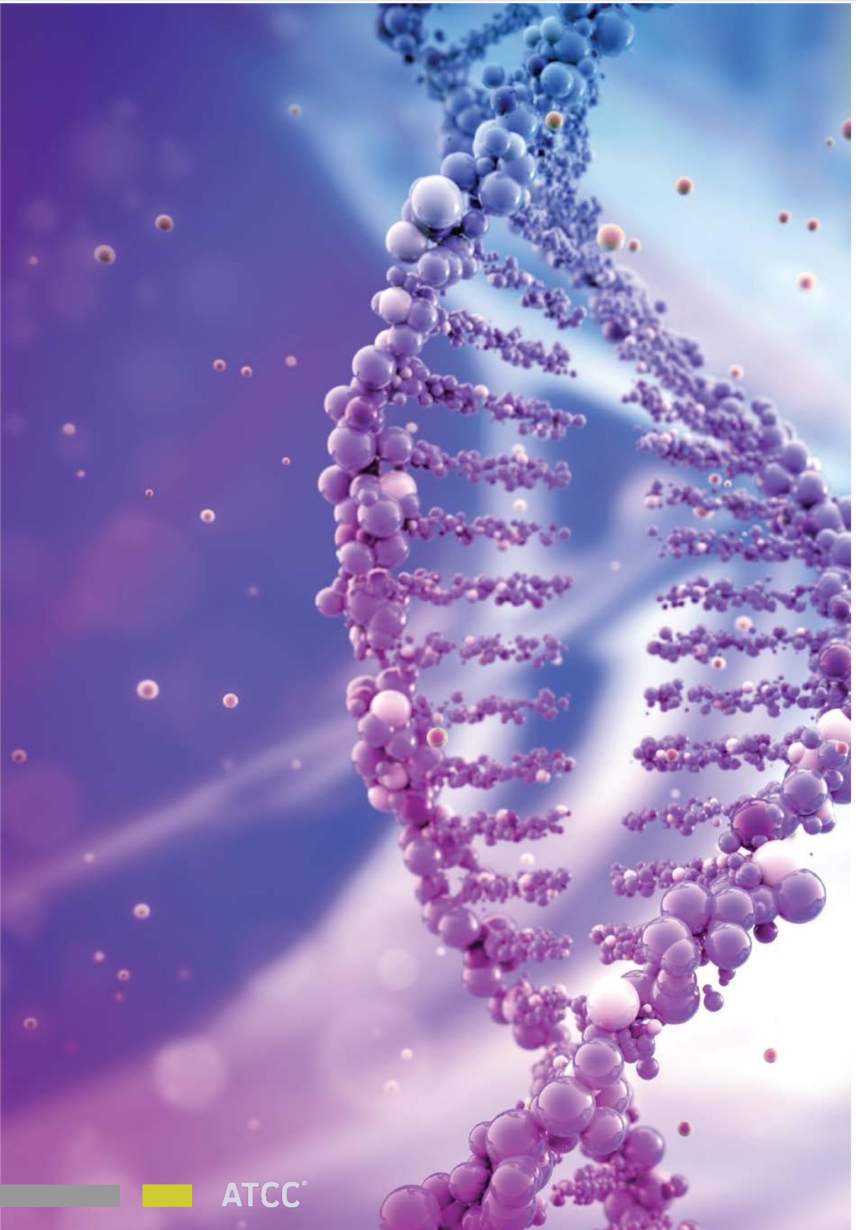
How is a New Strain Assigned to a Species?

- Recognizing that phenotypes can be quite unreliable, today we rely more heavily on genotypic comparisons
  - 16S rRNA genes, *hsp65*, *rpoB*
  - Multilocus Sequence Typing (MLST)

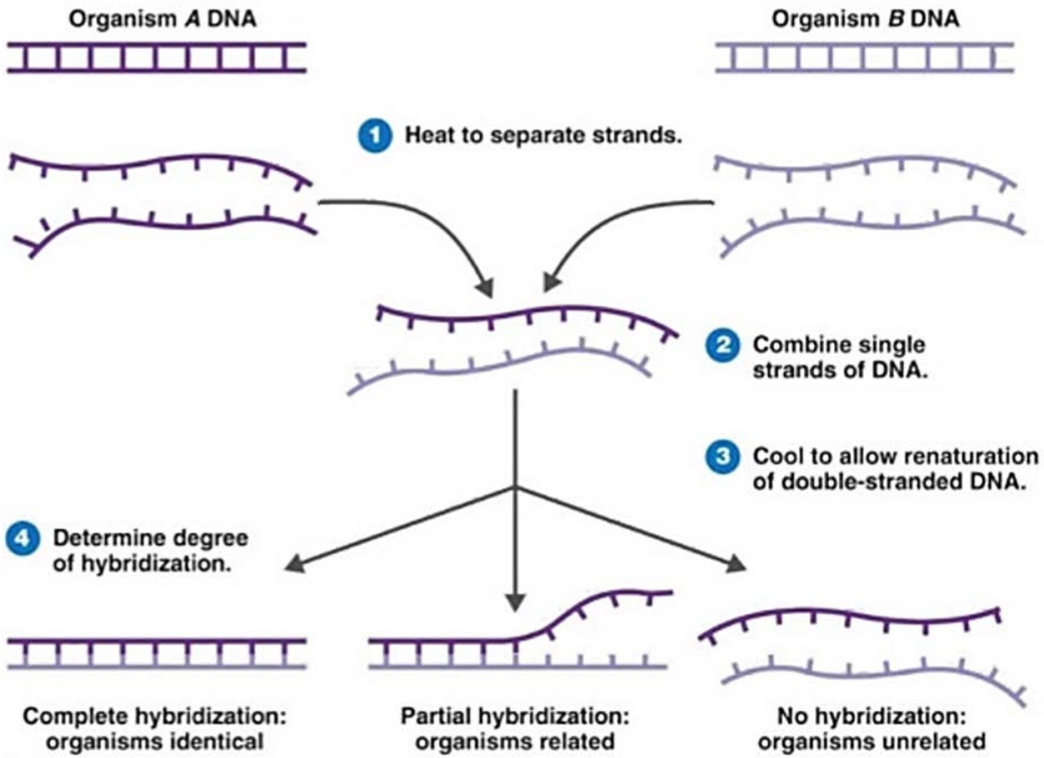

Species C^T
Gram –
Aerobic
Motile
Nitrate +

- Single or small numbers of genes can still provide misleading results
  - Vulnerable to selection bias
- The most objective and accurate comparison would be between whole genomes

DNA-DNA Hybridization (DDH)

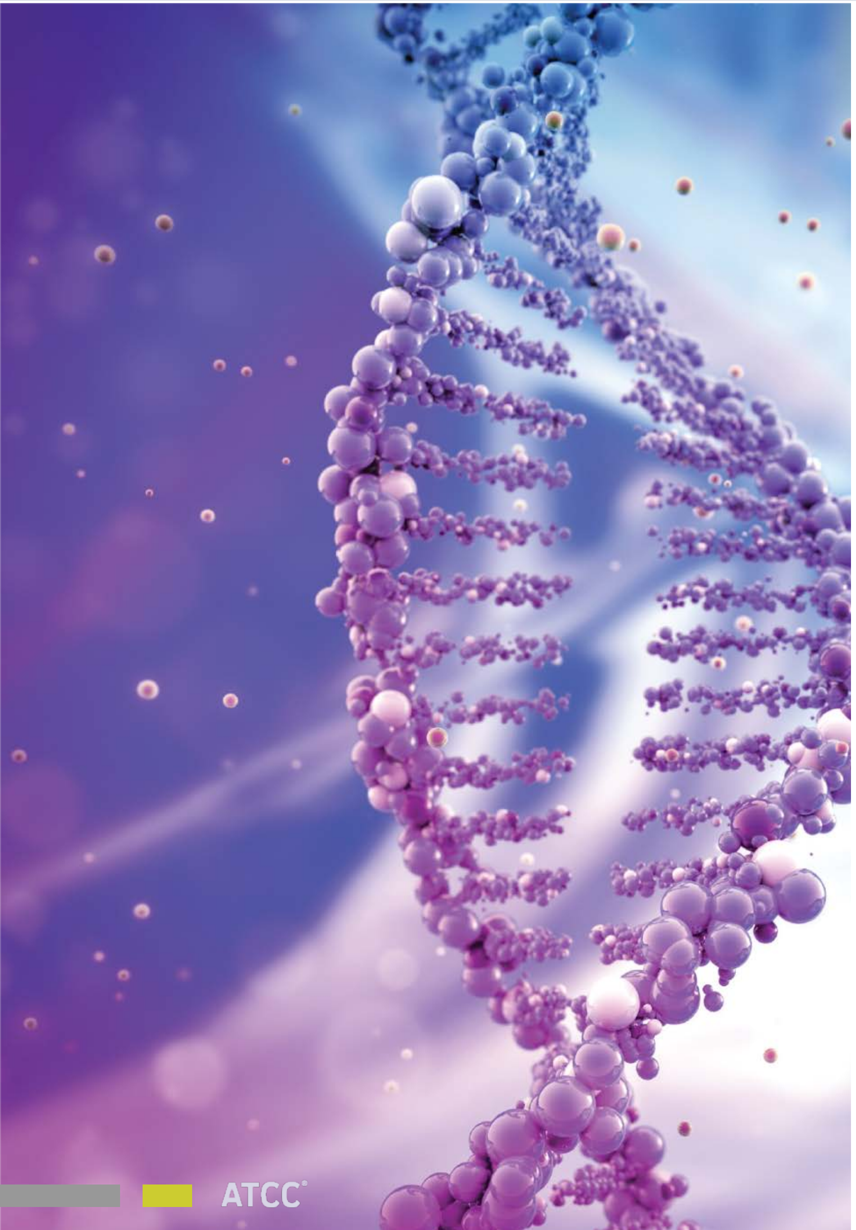


- Denature genomic DNA (gDNA) mixture for organisms A and B
- Allow gDNA to anneal; hybrids result
- Reassociation of gDNA ≈ sequence similarity



Malhotra S, *et al. J Mol Genet Med* 8:142, 2014.

DNA-DNA Hybridization (DDH)



- Denature genomic DNA (gDNA) mixture for organisms A and B
- Allow gDNA to anneal; hybrids result
- Reassociation of gDNA ≈ sequence similarity

- **DDH similarity >70%: same species**
- **DDH similarity <70%: different species**

- Considered the gold standard for species definition
  - A putatively new species must be shown to have <70% DDH similarity to existing species (*i.e.*, type strains) to be recognized as a legitimately new species

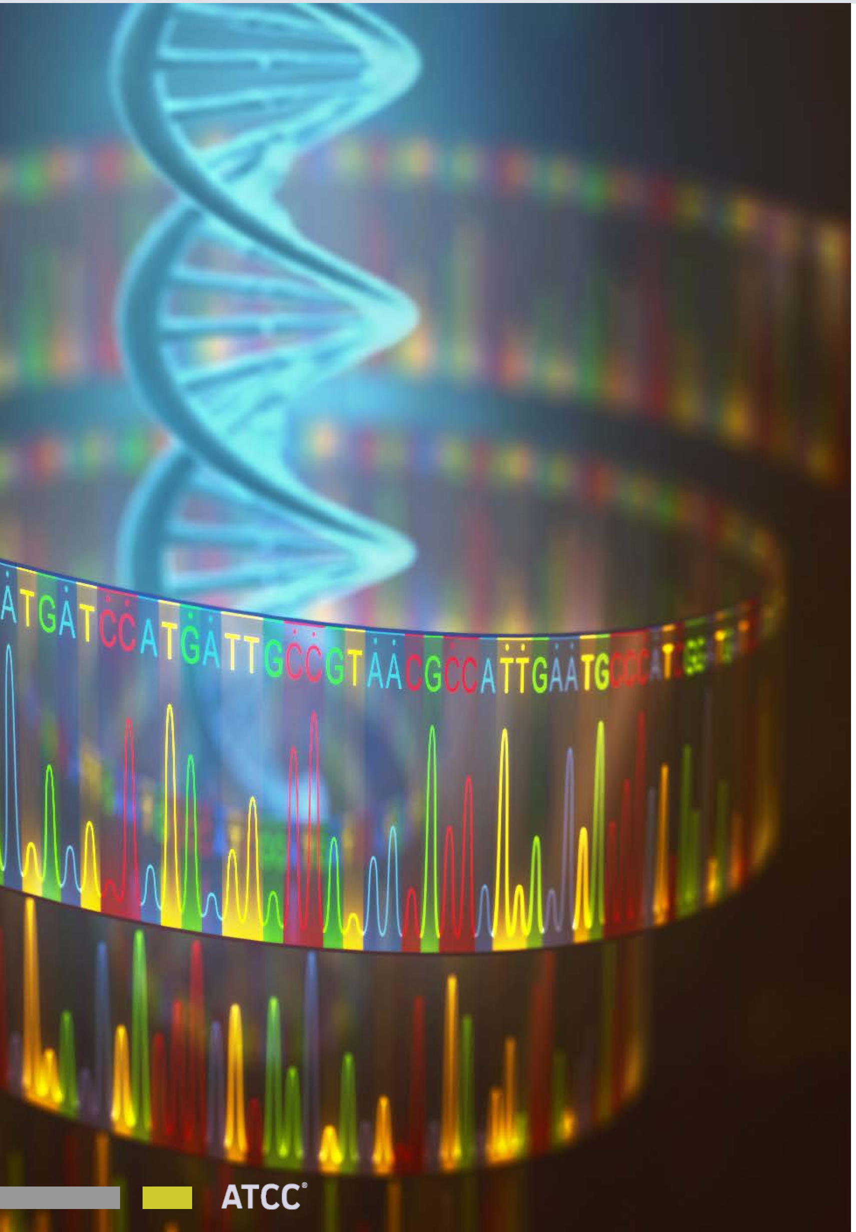
DNA-DNA Hybridization (DDH)

- DDH poses significant challenges
  - Highly labor intensive
  - Time consuming
  - Error prone
  - Poorly reproducible

- To overcome these challenges, an analogous sequence-based method has been developed
  - Digital DDH (dDDH)

- This method uses the whole-genome sequence of two strains to compare the strains bioinformatically and infer their distance from each other

Digital DNA-DNA Hybridization (dDDH)



- Available via web server
  - GGDC: Genome-to-Genome Distance Calculator

    ggdc.dsmz.de

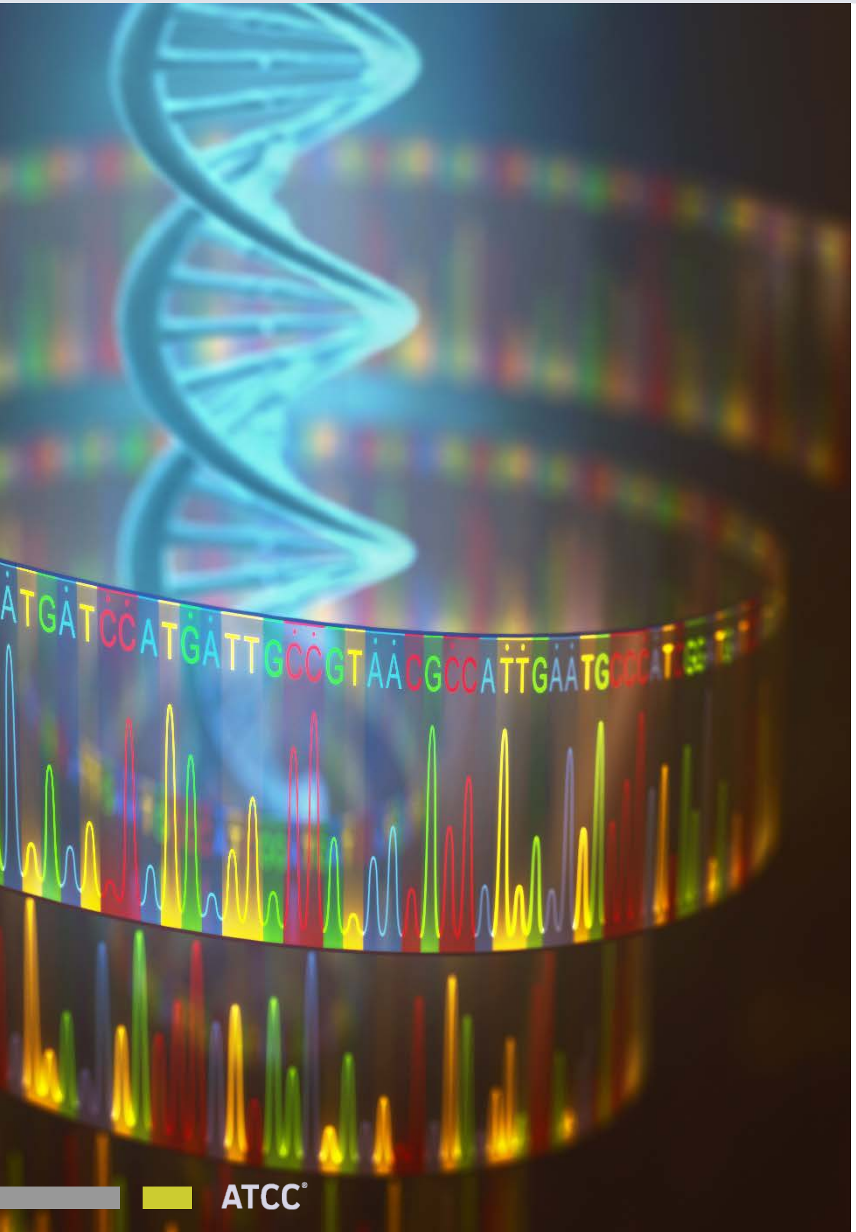
- Calibrated to the DDH 70% threshold
  - No difference in scale, *e.g.*, 95% average nucleotide identity (ANI)

- Data supports the use of dDDH for assignment of subspecies
  - Delineation threshold proposed at 79–80%

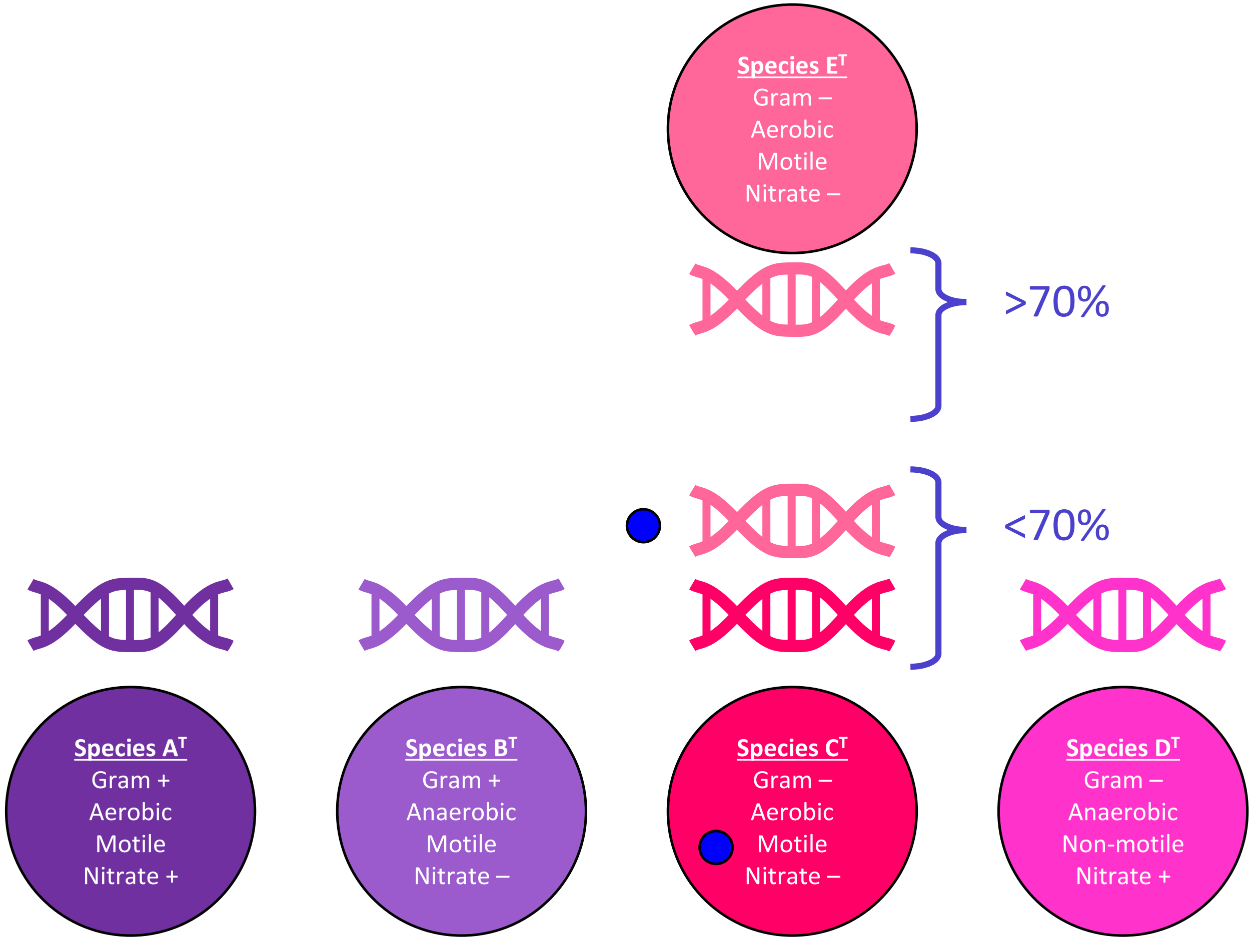
dDDH Range	Interpretation	
≥ 80%	Same species	Same subspecies
70 – 80%	Same species	Different subspecies
< 70%	Different species	

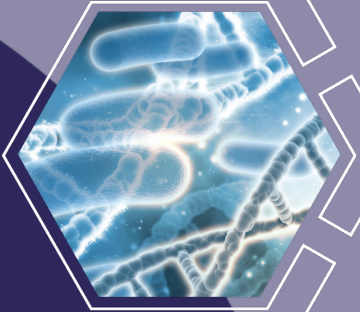
Meier-Kolthoff JP, *et al*. (2014); Meier-Kolthoff JP, *et al*. (2013); Auch, *et al*. (2013a); Auch, *et al*. (2013b).

Transfer of Species Based on Genomic Data

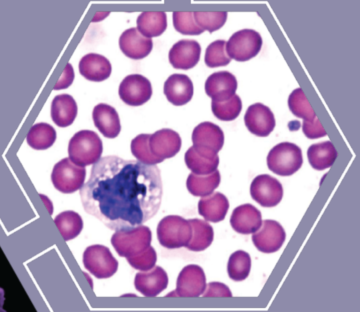


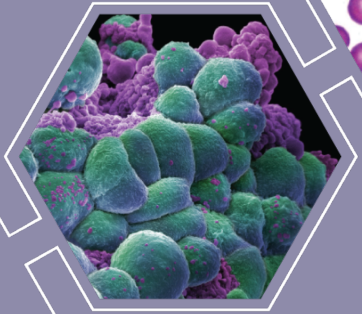
- Genomic analysis can provide updated taxonomy





Mycobacterium tuberculosis Complex





Mycobacterium tuberculosis Complex (MTBC)

- Consists of six officially recognized (validly published) species, all very closely related
  - *Mycobacterium tuberculosis*
  - *Mycobacterium africanum*
  - *Mycobacterium bovis*
  - *Mycobacterium caprae*
  - *Mycobacterium microti*
  - *Mycobacterium pinnipedii*
  - Not validly published
    - “Mycobacterium canettii”
    - “Mycobacterium mungi”
    - “Mycobacterium orygis”

- It has been hypothesized for several decades that these may actually represent a single species

Mycobacterium tuberculosis Complex (MTBC)

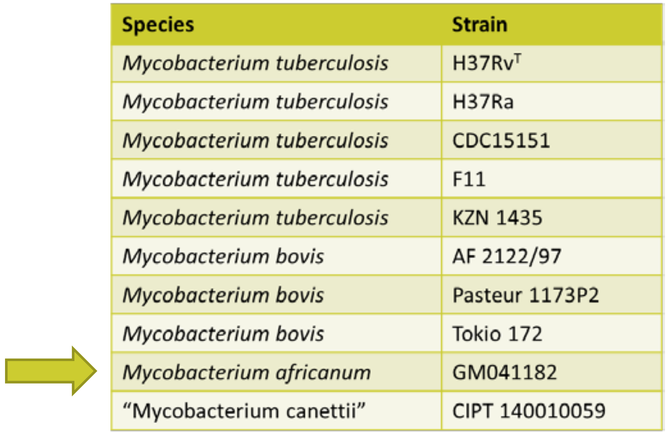
- Recent work has shown that some strains of the related species fall within the circumscription of *M. tuberculosis* H37Rv^T

Species	Strain
Mycobacterium tuberculosis	H37Rv^T
Mycobacterium tuberculosis	H37Ra
Mycobacterium tuberculosis	CDC15151
Mycobacterium tuberculosis	F11
Mycobacterium tuberculosis	KZN 1435
Mycobacterium bovis	AF 2122/97
Mycobacterium bovis	Pasteur 1173P2
Mycobacterium bovis	Tokio 172
Mycobacterium africanum	GM041182
"Mycobacterium canettii"	CIPT 140010059

Garcia-Betancur JC, *et al. Infect Genet Evol* 12:819–826, 2012.

Mycobacterium tuberculosis Complex (MTBC)

- Recent work has shown that some strains of the related species fall within the circumscription of *M. tuberculosis* H37Rv^{T}
  - However, all strains compared were **<u>non-type strains</u>**
  - Conclusion: “mycobacterial scientists should agree an accord that designates MTBC as a single species in the official taxonomic rules of nomenclature.”
  - Only applicable to *<u>those</u>* strains, not the species as a whole



Species	**Strain**
Mycobacterium tuberculosis	H37Rv^{T}
Mycobacterium tuberculosis	H37Ra
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Mycobacterium tuberculosis	KZN 1435
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Mycobacterium bovis	Tokio 172
Mycobacterium africanum	GM041182
“Mycobacterium canettii”	CIPT 140010059

Garcia-Betancur JC, *et al. Infect Genet Evol* 12:819–826, 2012.

Sequencing of MTBC Type Strains

- Extracted DNA from the *type strains* of the missing five species
- Phylogenomically compared the WGS sequences of these 5 species, *M. tuberculosis* H37Rv$^{\mathrm{T}}$, and 3 non-validly published “species”, plus 2 outgroups
  - Digital DNA-DNA hybridization (dDDH)
  - Average nucleotide identity (ANI)

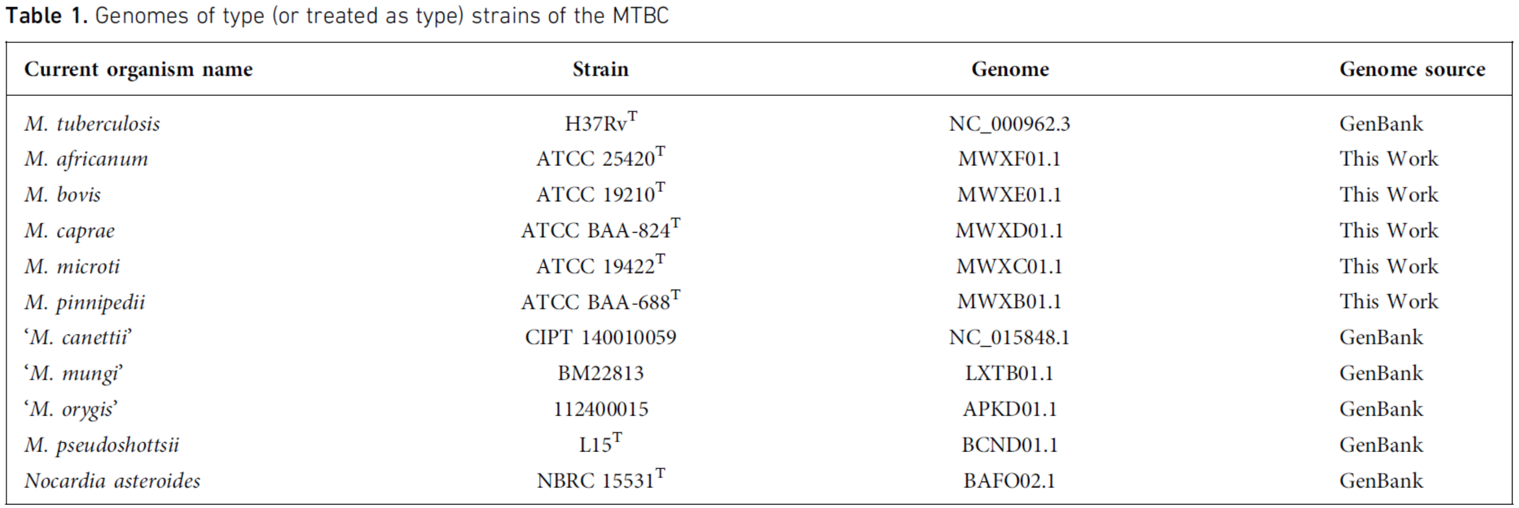
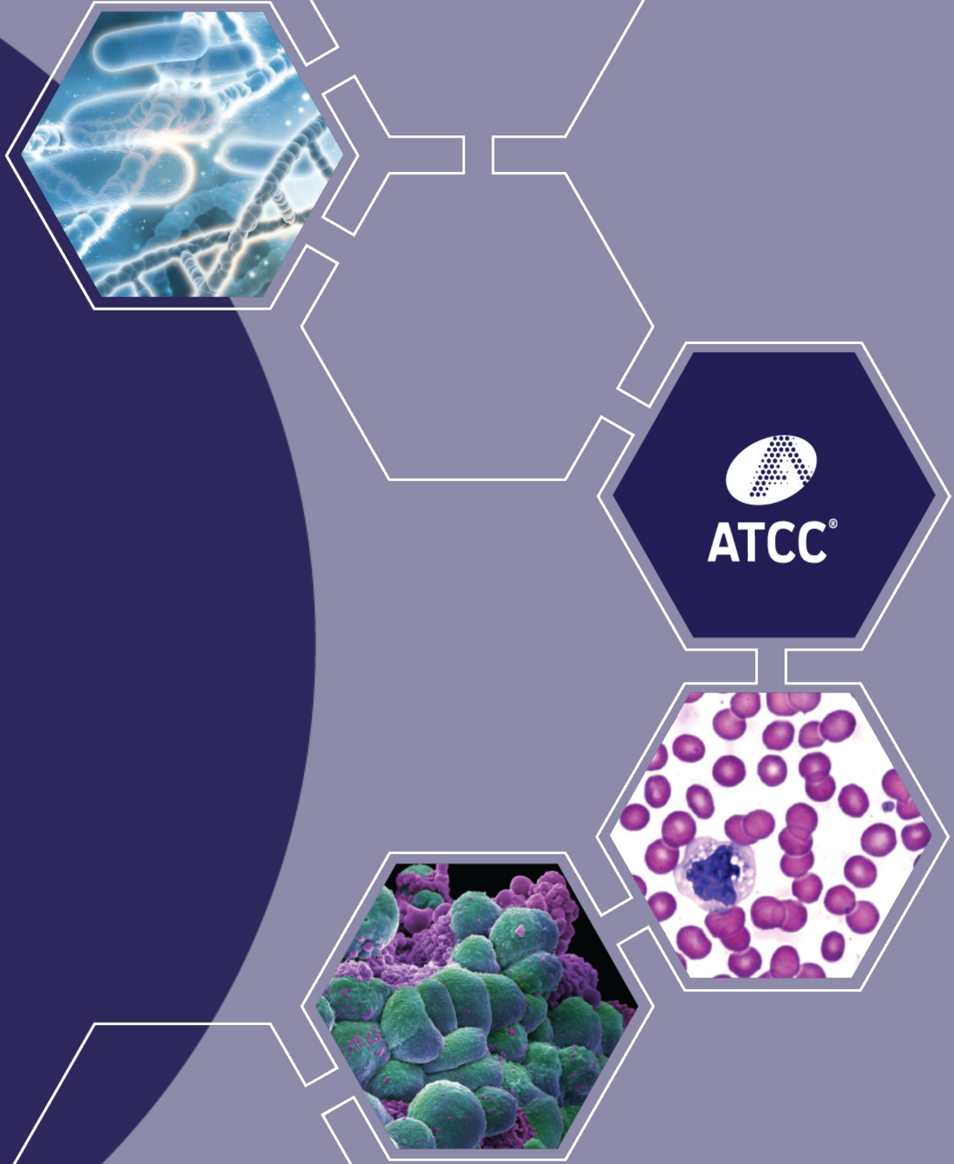


Table 1. Genomes of type (or treated as type) strains of the MTBC

Current organism name	Strain	Genome	Genome source
M. tuberculosis	H37Rv$^{\mathrm{T}}$	NC_000962.3	GenBank
M. africanum	ATCC 25420$^{\mathrm{T}}$	MWXF01.1	This Work
M. bovis	ATCC 19210$^{\mathrm{T}}$	MWXE01.1	This Work
M. caprae	ATCC BAA-824$^{\mathrm{T}}$	MWXD01.1	This Work
M. microti	ATCC 19422$^{\mathrm{T}}$	MWXC01.1	This Work
M. pinnipedii	ATCC BAA-688$^{\mathrm{T}}$	MWXB01.1	This Work
‘*M. canettii*’	CIPT 140010059	NC_015848.1	GenBank
‘*M. mungi*’	BM22813	LXTB01.1	GenBank
‘*M. orygis*’	112400015	APKD01.1	GenBank
M. pseudoshottsii	L15$^{\mathrm{T}}$	BCND01.1	GenBank
Nocardia asteroides	NBRC 15531$^{\mathrm{T}}$	BAFO02.1	GenBank

Riojas, *et al. Int J Syst Evol Microbiol* 68:324–332, 2018.

Research Results and Conclusions



Genomic Comparison of MTBC Type Strains

Table 2. Genomic Distance Analysis of type strains of members of the MTBC

Pairwise genome-to-genome distances (GGDs) for the type strains of the species within the *Mycobacterium tuberculosis* complex ('MTBC') and two outgroups ('OUT'). Results from digital DNA–DNA hybridization (dDDH) are shown above the self-comparison diagonal, and average nucleotide identity (ANI) results are shown below the diagonal. Species delineation thresholds used were 80 % for dDDH and 96 % for ANI.

	Species/ Strain \ dDDH / ANI	MTBC1	MTBC2	MTBC3	MTBC4	MTBC5	MTBC6	MTBC7	MTBC8	MTBC9	OUT1	OUT2
MTBC1	*M. tuberculosis* H37Rv^T	100	97.7	97.5	97.9	98.7	97.3	91.2	97.9	97.6	.1	18.8
MTBC2	*M. africanum* ATCC® 25420^T	99.88	100	98	98.5	98.9	98.2	92.2	98.9	98.4	.2	18.8
MTBC3	*M. bovis* ATCC® 19210^T	99.78	99.82	100	98.2	98.2	97.8	91.6	98.1	97.8	.3	19
MTBC4	*M. caprae* ATCC® BAA-824^T	99.86	99.87	99.83	100	98.8	97.7	91.7	98.6	98.2	.1	18.8
MTBC5	*M. microti* ATCC® 19422^T	99.89	99.8	99.79	9.91	100	99.2	93.3	99	98.9	.3	18.9
MTBC6	*M. pinnipedii* ATCC® BAA-688^T	99.84	99.86	99.78	99.84	99.92	100	91.6	98.3	97.6	.1	18.8
MTBC7	"*M. canettii*" CIPT 140010059	99.25	99.28	99.21	99.26	99.36	99.26	100	92.5	91.8	.2	19
MTBC8	"*M. mungi*" BM22813	99.88	99.91	99.81	99.88	99.92	99.89	99.31	100	98.6	.2	18.8
MTBC9	"*M. orygis*" 112400015	99.85	99.87	99.80	99.87	99.91	99.86	99.28	99.88	100	.1	18.8
OUT1	*M. pseudoshottsii* L15^T	79.33	79.27	79.21	79.34	79.34	79.25	79.29	79.25	79.37	100	19.2
OUT2	*Nocardia asteroides* NBRC 15531^T	70.92	70.76	70.96	70.94	70.88	71.02	70.99	71.00	70.84	70.75	100

Color Key	
ANI	**dDDH**
Self-Comparison	Self-Comparison
96 – 100	80 – 100
< 96	< 80

Riojas, *et al. Int J Syst Evol Microbiol* 68:324–332, 2018.

Genomic Comparison of MTBC Type Strains

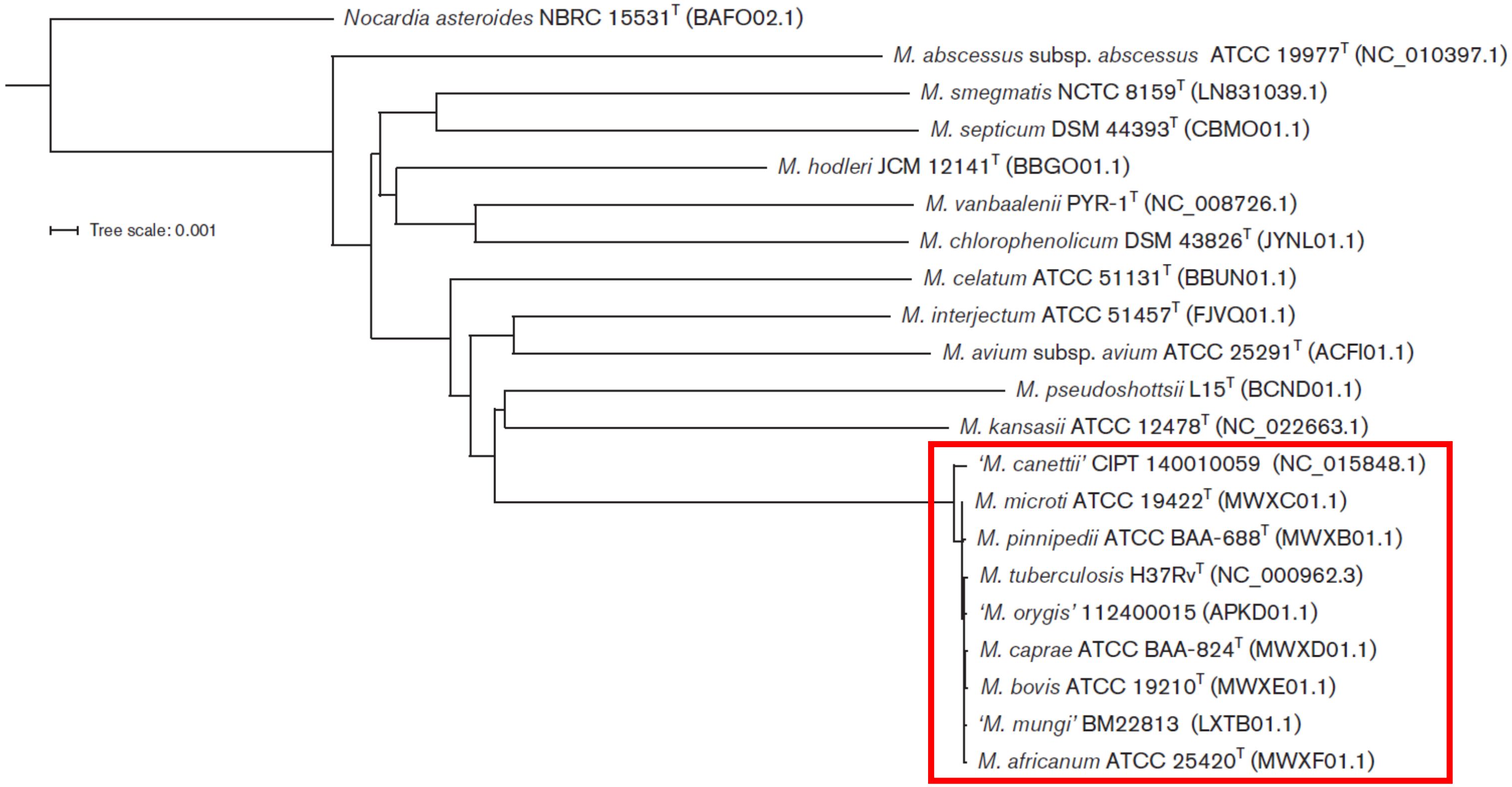
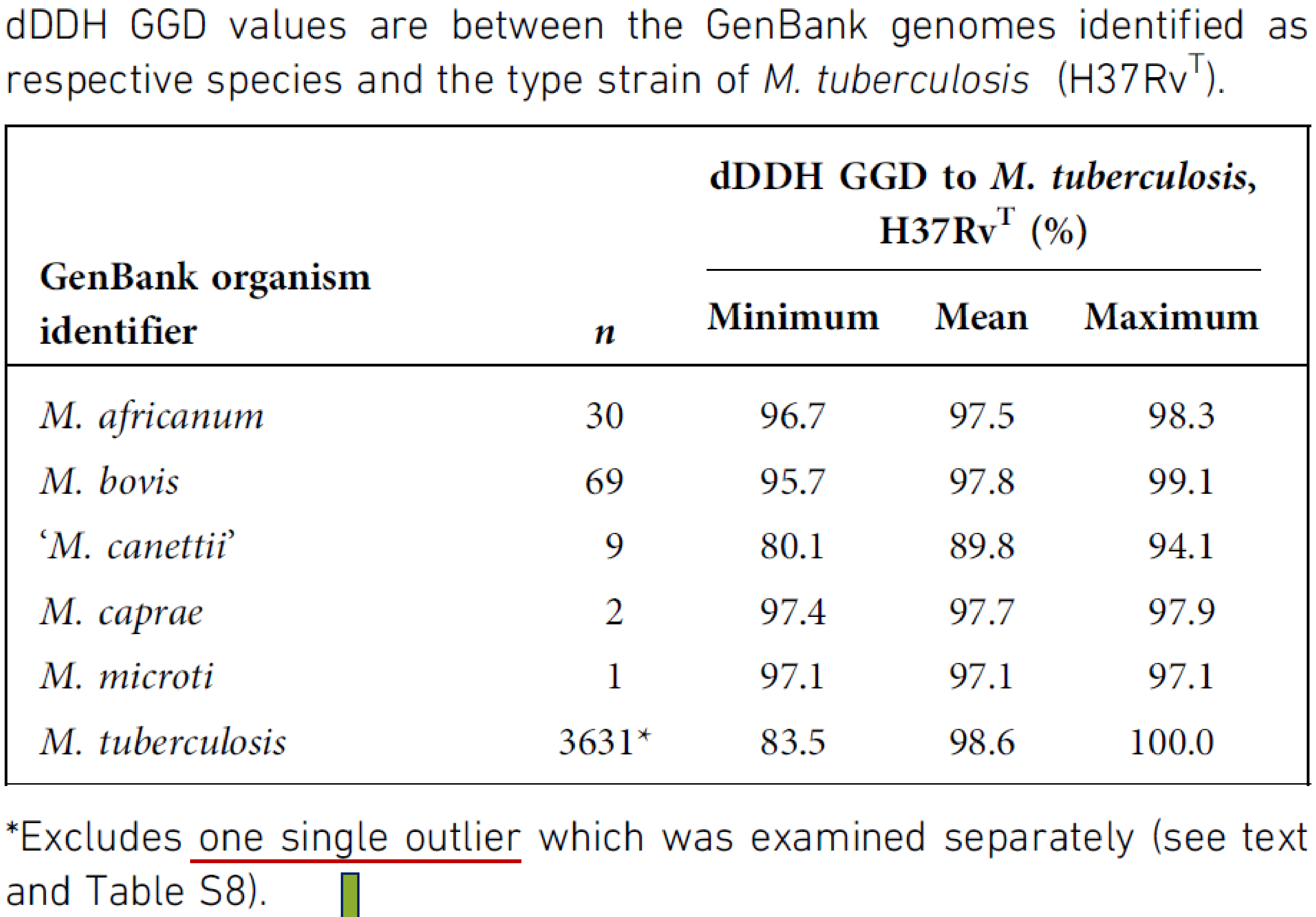


Fig. 1. Phylogenomic tree showing the relationship between the whole genomes of type strains of species of MTBC and the type strains of various other species of the genus *Mycobacterium* with *Nocardia asteroides* as an outgroup. Bar, 0.001 substitutions per site.

Riojas, *et al. Int J Syst Evol Microbiol* 68:324–332, 2018.

Genomic Comparison of MTBC Type Strains



dDDH GGD values are between the GenBank genomes identified as respective species and the type strain of *M. tuberculosis* (H37Rv^T).

GenBank organism identifier	*n*	dDDH GGD to *M. tuberculosis*, H37Rv^T (%)		
		Minimum	**Mean**	**Maximum**
M. africanum	30	96.7	97.5	98.3
M. bovis	69	95.7	97.8	99.1
'*M. canettii*'	9	80.1	89.8	94.1
M. caprae	2	97.4	97.7	97.9
M. microti	1	97.1	97.1	97.1
M. tuberculosis	3631*	83.5	98.6	100.0

*Excludes one single outlier which was examined separately (see text and Table S8).

dDDH: 22.2%, ANI: 79.39%

Riojas, *et al. Int J Syst Evol Microbiol* 68:324–332, 2018.

Genomic Comparison of MTBC Type Strains

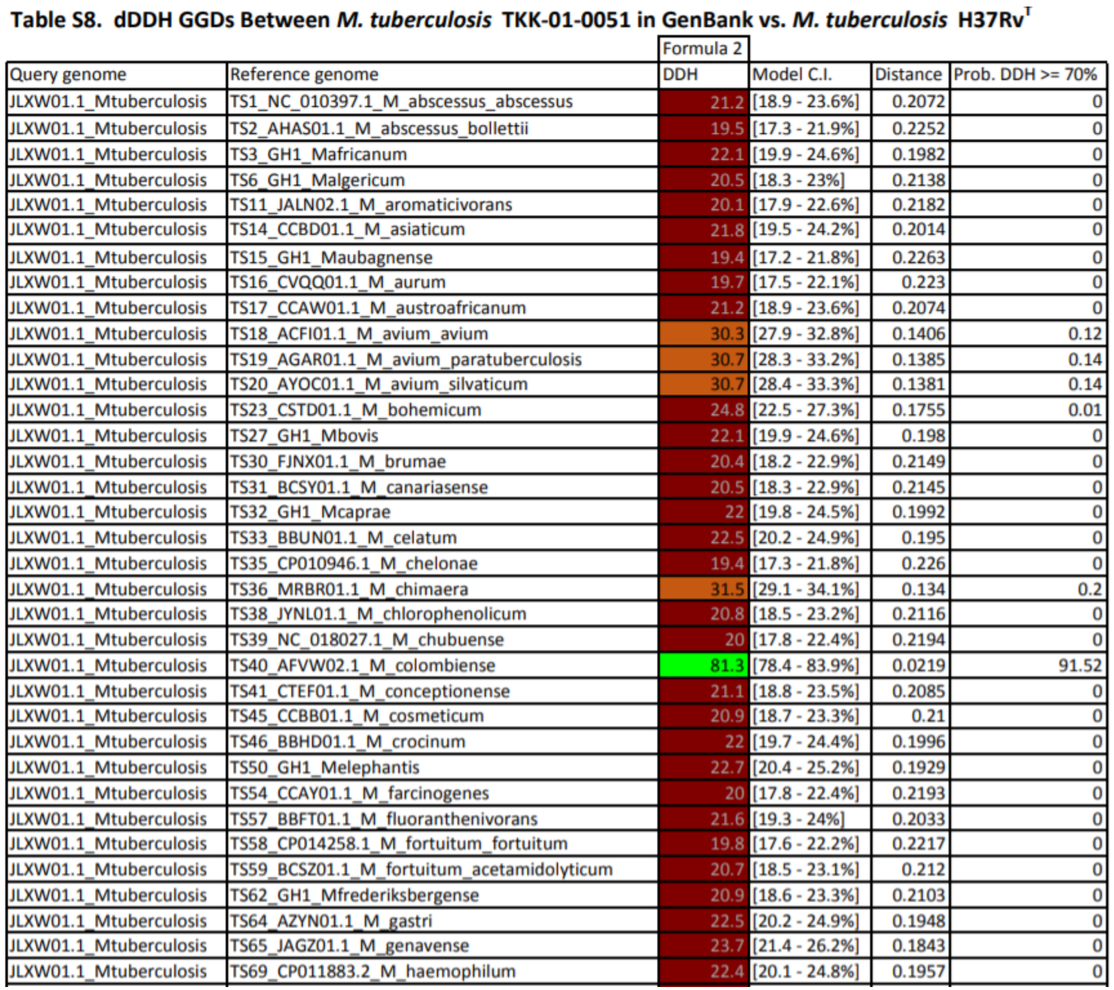
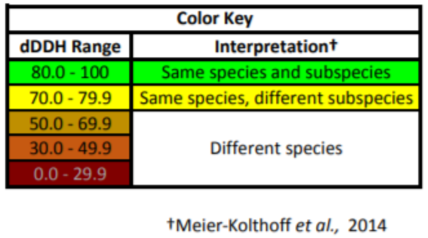


Table S8. dDDH GGDs Between *M. tuberculosis* TKK-01-0051 in GenBank vs. *M. tuberculosis* H37Rv^T

		Formula 2			
Query genome	Reference genome	DDH	Model C.I.	Distance	Prob. DDH >= 70%
JLXW01.1_Mtuberculosis	TS1_NC_010397.1_M_abscessus_abscessus	21.2	[18.9 - 23.6%]	0.2072	0
JLXW01.1_Mtuberculosis	TS2_AHAS01.1_M_abscessus_bollettii	19.5	[17.3 - 21.9%]	0.2252	0
JLXW01.1_Mtuberculosis	TS3_GH1_Mafricanum	22.1	[19.9 - 24.6%]	0.1982	0
JLXW01.1_Mtuberculosis	TS6_GH1_Malgericum	20.5	[18.3 - 23%]	0.2138	0
JLXW01.1_Mtuberculosis	TS11_JALN02.1_M_aromaticivorans	20.1	[17.9 - 22.6%]	0.2182	0
JLXW01.1_Mtuberculosis	TS14_CCBD01.1_M_asiaticum	21.8	[19.5 - 24.2%]	0.2014	0
JLXW01.1_Mtuberculosis	TS15_GH1_Maubagnense	19.4	[17.2 - 21.8%]	0.2263	0
JLXW01.1_Mtuberculosis	TS16_CVQQ01.1_M_aurum	19.7	[17.5 - 22.1%]	0.223	0
JLXW01.1_Mtuberculosis	TS17_CCAW01.1_M_austroafricanum	21.2	[18.9 - 23.6%]	0.2074	0
JLXW01.1_Mtuberculosis	TS18_ACFI01.1_M_avium_avium	30.3	[27.9 - 32.8%]	0.1406	0.12
JLXW01.1_Mtuberculosis	TS19_AGAR01.1_M_avium_paratuberculosis	30.7	[28.3 - 33.2%]	0.1385	0.14
JLXW01.1_Mtuberculosis	TS20_AYOC01.1_M_avium_silvaticum	30.7	[28.4 - 33.3%]	0.1381	0.14
JLXW01.1_Mtuberculosis	TS23_CSTD01.1_M_bohemicum	24.8	[22.5 - 27.3%]	0.1755	0.01
JLXW01.1_Mtuberculosis	TS27_GH1_Mbovis	22.1	[19.9 - 24.6%]	0.198	0
JLXW01.1_Mtuberculosis	TS30_FJNX01.1_M_brumae	20.4	[18.2 - 22.9%]	0.2149	0
JLXW01.1_Mtuberculosis	TS31_BCSY01.1_M_canariasense	20.5	[18.3 - 22.9%]	0.2145	0
JLXW01.1_Mtuberculosis	TS32_GH1_Mcaprae	22	[19.8 - 24.5%]	0.1992	0
JLXW01.1_Mtuberculosis	TS33_BBUN01.1_M_celatum	22.5	[20.2 - 24.9%]	0.195	0
JLXW01.1_Mtuberculosis	TS35_CP010946.1_M_chelonae	19.4	[17.3 - 21.8%]	0.226	0
JLXW01.1_Mtuberculosis	TS36_MRBR01.1_M_chimaera	31.5	[29.1 - 34.1%]	0.134	0.2
JLXW01.1_Mtuberculosis	TS38_JYNL01.1_M_chlorophenolicum	20.8	[18.5 - 23.2%]	0.2116	0
JLXW01.1_Mtuberculosis	TS39_NC_018027.1_M_chubuense	20	[17.8 - 22.4%]	0.2194	0
JLXW01.1_Mtuberculosis	TS40_AFVW02.1_M_colombiense	81.3	[78.4 - 83.9%]	0.0219	91.52
JLXW01.1_Mtuberculosis	TS41_CTEF01.1_M_conceptionense	21.1	[18.8 - 23.5%]	0.2085	0
JLXW01.1_Mtuberculosis	TS45_CCBB01.1_M_cosmeticum	20.9	[18.7 - 23.3%]	0.21	0
JLXW01.1_Mtuberculosis	TS46_BBHD01.1_M_crocinum	22	[19.7 - 24.4%]	0.1996	0
JLXW01.1_Mtuberculosis	TS50_GH1_Melephantis	22.7	[20.4 - 25.2%]	0.1929	0
JLXW01.1_Mtuberculosis	TS54_CCAY01.1_M_farcinogenes	20	[17.8 - 22.4%]	0.2193	0
JLXW01.1_Mtuberculosis	TS57_BBFT01.1_M_fluoranthenivorans	21.6	[19.3 - 24%]	0.2033	0
JLXW01.1_Mtuberculosis	TS58_CP014258.1_M_fortuitum_fortuitum	19.8	[17.6 - 22.2%]	0.2217	0
JLXW01.1_Mtuberculosis	TS59_BCSZ01.1_M_fortuitum_acetamidolyticum	20.7	[18.5 - 23.1%]	0.212	0
JLXW01.1_Mtuberculosis	TS62_GH1_Mfrederiksbergense	20.9	[18.6 - 23.3%]	0.2103	0
JLXW01.1_Mtuberculosis	TS64_AZYN01.1_M_gastri	22.5	[20.2 - 24.9%]	0.1948	0
JLXW01.1_Mtuberculosis	TS65_JAGZ01.1_M_genavense	23.7	[21.4 - 26.2%]	0.1843	0
JLXW01.1_Mtuberculosis	TS69_CP011883.2_M_haemophilum	22.4	[20.1 - 24.8%]	0.1957	0



Color Key	
dDDH Range	**Interpretation†**
80.0 - 100	Same species and subspecies
70.0 - 79.9	Same species, different subspecies
50.0 - 69.9	Different species
30.0 - 49.9	
0.0 - 29.9	

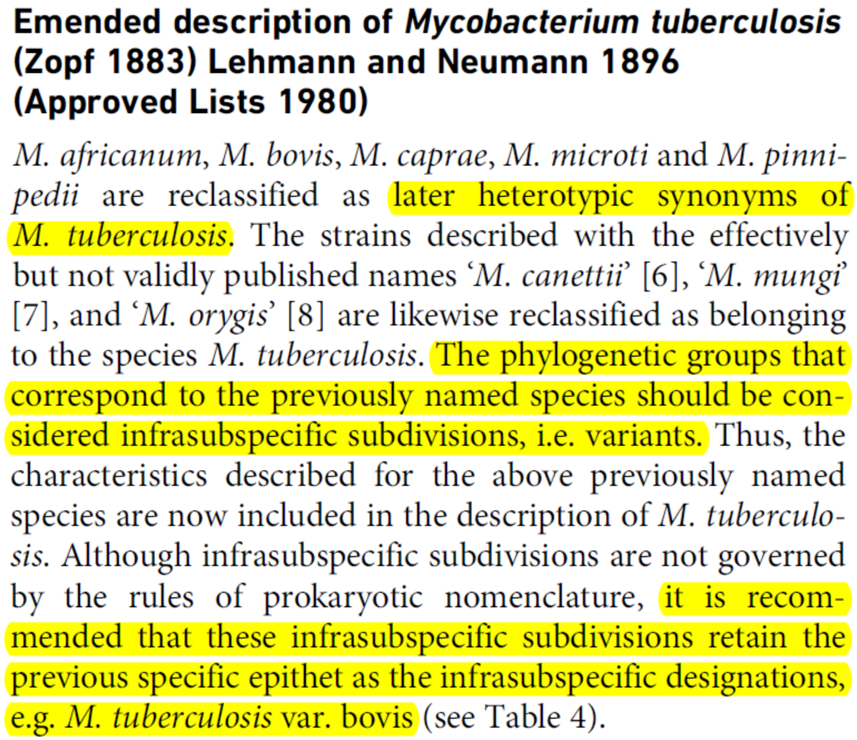
†Meier-Kolthoff *et al.*, 2014

(ANI: 97.73%)

Riojas, *et al. Int J Syst Evol Microbiol* 68:324–332, 2018.

Unification of MTBC Species as *M. tuberculosis*

- Unites the MTBC as *Mycobacterium tuberculosis*
- Submitted emended species description in *IJSEM*
  - Type strain: *M. tuberculosis* H37Rv^T



Emended description of *Mycobacterium tuberculosis* (Zopf 1883) Lehmann and Neumann 1896 (Approved Lists 1980)

M. africanum, *M. bovis*, *M. caprae*, *M. microti* and *M. pinnipedii* are reclassified as later heterotypic synonyms of *M. tuberculosis*. The strains described with the effectively but not validly published names '*M. canettii*' [6], '*M. mungi*' [7], and '*M. orygis*' [8] are likewise reclassified as belonging to the species *M. tuberculosis*. The phylogenetic groups that correspond to the previously named species should be considered infrasubspecific subdivisions, i.e. variants. Thus, the characteristics described for the above previously named species are now included in the description of *M. tuberculosis*. Although infrasubspecific subdivisions are not governed by the rules of prokaryotic nomenclature, it is recommended that these infrasubspecific subdivisions retain the previous specific epithet as the infrasubspecific designations, e.g. *M. tuberculosis* var. bovis (see Table 4).

Riojas, *et al. Int J Syst Evol Microbiol* 68:324–332, 2018.

Unification of MTBC Species as *M. tuberculosis*

- Unites the MTBC as *Mycobacterium tuberculosis*
- Submitted emended species description in *IJSEM*
  - Type strain: *M. tuberculosis* H37Rv^T
  - All other species type strains downgraded to reference strains
    - Recommendation: use former species name as intrasubspecific designation

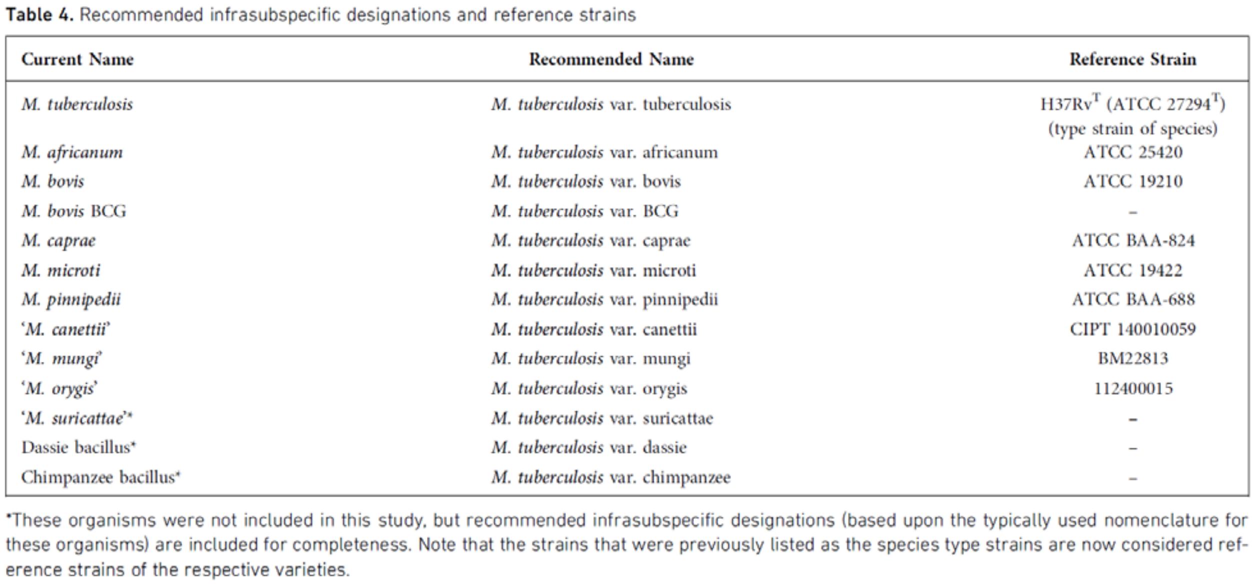


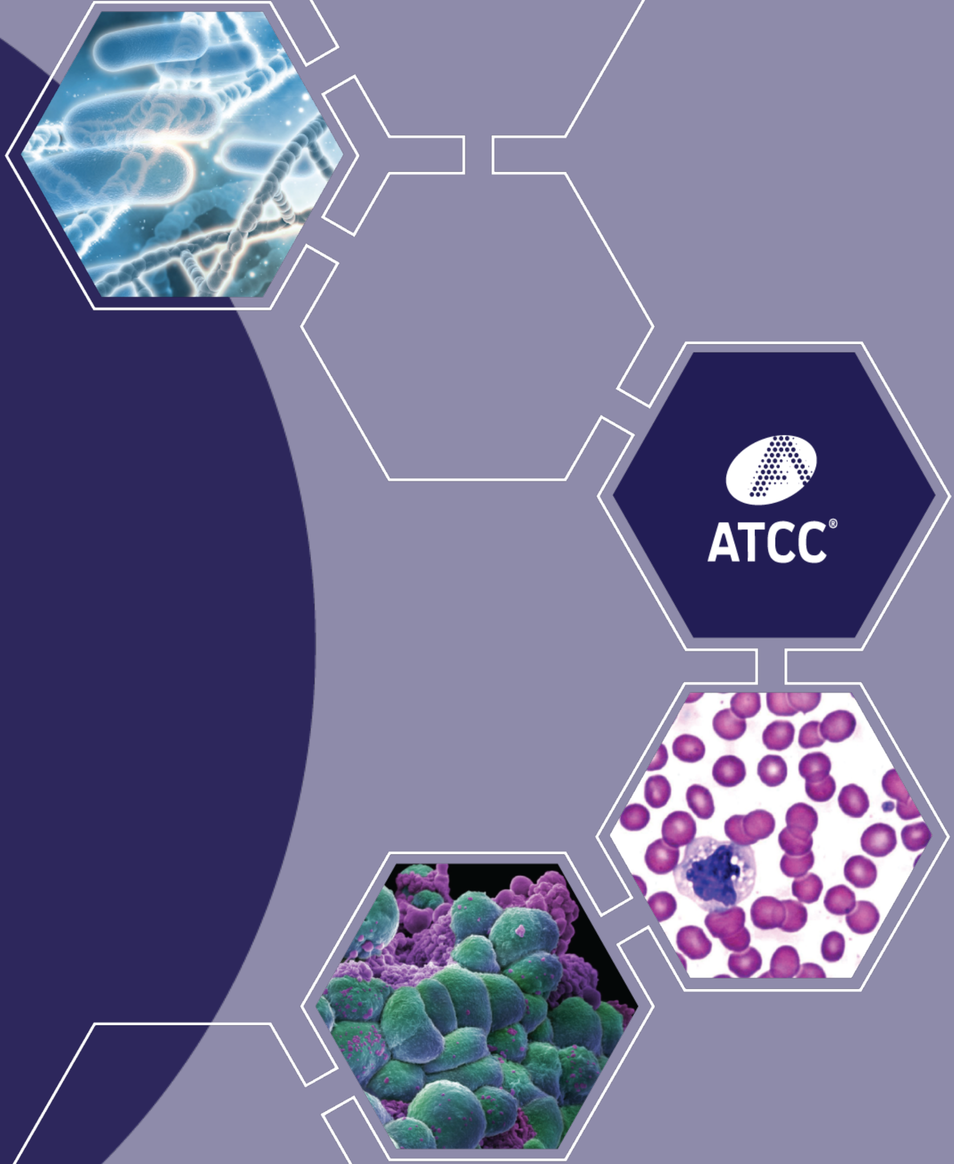
Table 4. Recommended infrasubspecific designations and reference strains

Current Name	Recommended Name	Reference Strain
M. tuberculosis	*M. tuberculosis* var. tuberculosis	H37Rv^T (ATCC 27294^T) (type strain of species)
M. africanum	*M. tuberculosis* var. africanum	ATCC 25420
M. bovis	*M. tuberculosis* var. bovis	ATCC 19210
M. bovis BCG	*M. tuberculosis* var. BCG	–
M. caprae	*M. tuberculosis* var. caprae	ATCC BAA-824
M. microti	*M. tuberculosis* var. microti	ATCC 19422
M. pinnipedii	*M. tuberculosis* var. pinnipedii	ATCC BAA-688
'*M. canettii*'	*M. tuberculosis* var. canettii	CIPT 140010059
'*M. mungi*'	*M. tuberculosis* var. mungi	BM22813
'*M. orygis*'	*M. tuberculosis* var. orygis	112400015
'*M. suricattae*'*	*M. tuberculosis* var. suricattae	–
Dassie bacillus*	*M. tuberculosis* var. dassie	–
Chimpanzee bacillus*	*M. tuberculosis* var. chimpanzee	–

*These organisms were not included in this study, but recommended infrasubspecific designations (based upon the typically used nomenclature for these organisms) are included for completeness. Note that the strains that were previously listed as the species type strains are now considered reference strains of the respective varieties.

Riojas, *et al. Int J Syst Evol Microbiol* 68:324–332, 2018.

Conclusions



Conclusions

- Phylogenomic analysis comparing the type strains of the “species” within the MTBC shows that they are, in fact, a single species
- dDDH comparison against a larger set of sequenced type strains enabled discovery of the identity of a strain misclassified as *M. tuberculosis*
- Whole-genome sequencing of bacterial type strains enables the elucidation of the true relationships between species and strains
    - Modernize taxonomic relationships using complete genetic information
    - Develop detailed phylogenomic trees
    - Determine the identity of unknown sequenced samples

References

- **Riojas MA**, *et al*. Phylogenomic analysis of the species of the *Mycobacterium tuberculosis* complex demonstrates that *Mycobacterium africanum*, *Mycobacterium bovis*, *Mycobacterium caprae*, *Mycobacterium microti* and *Mycobacterium pinnipedii* are later heterotypic synonyms of *Mycobacterium tuberculosis*. *Int J Syst Evol Microbiol* 68: 324–332, 2018.
- **Auch AF**, von Jan M, Klenk HP & Göker M. Digital DNA-DNA hybridization for microbial species delineation by means of genome-to-genome sequence comparison. *Stand Genomic Sci* 2: 117-134, 2010.
- **Auch AF**, Klenk HP & Göker M. Standard operating procedure for calculating genome-to-genome distances based on high-scoring segment pairs. *Stand Genomic Sci* 2: 142-148, 2010.
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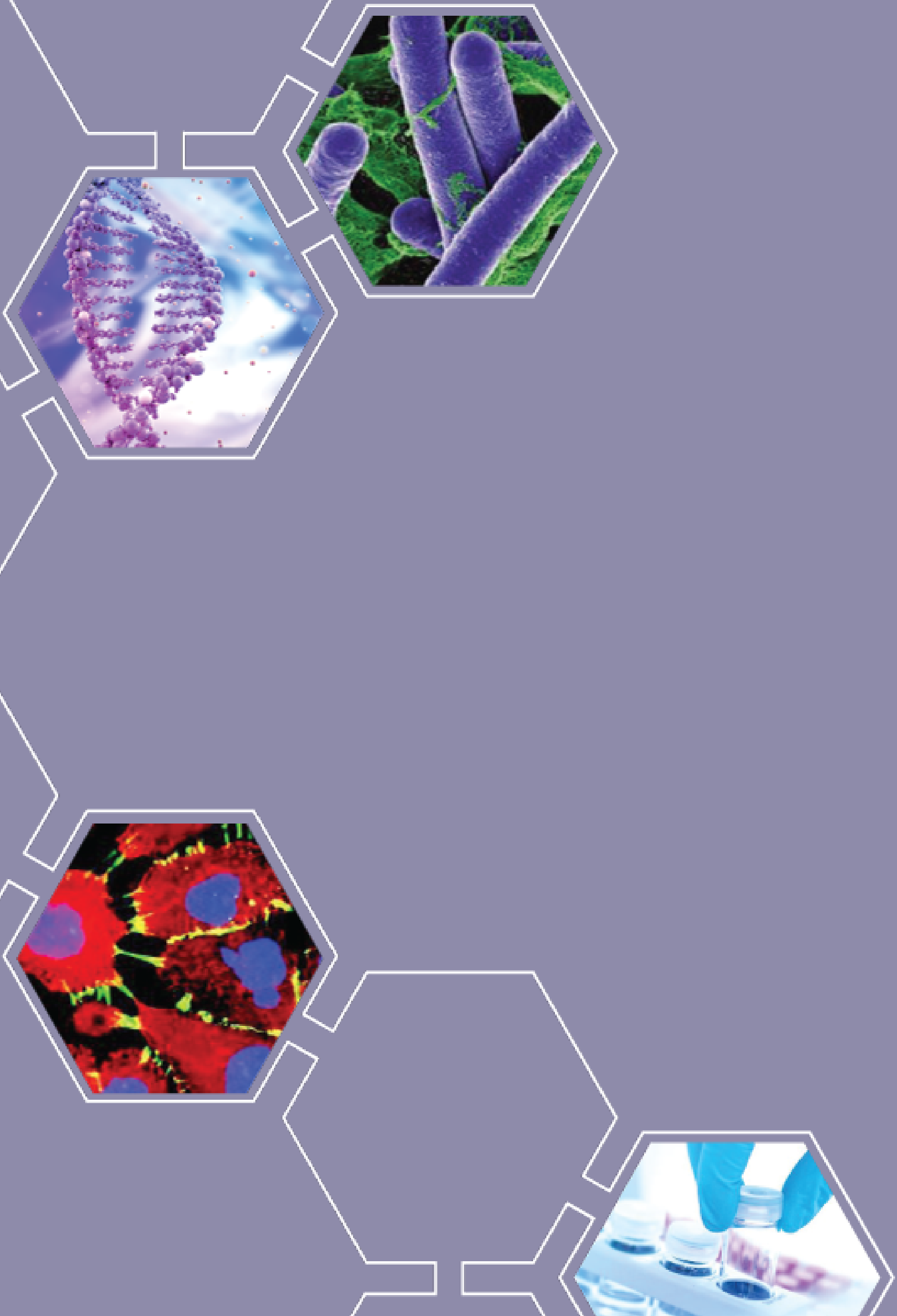
Disclaimers



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