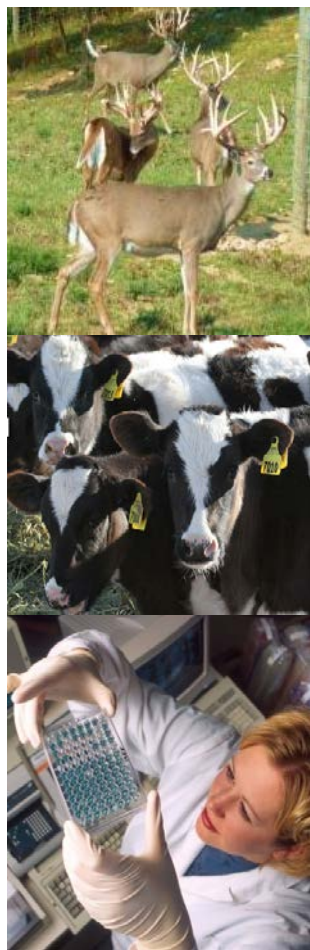


Veterinary Services

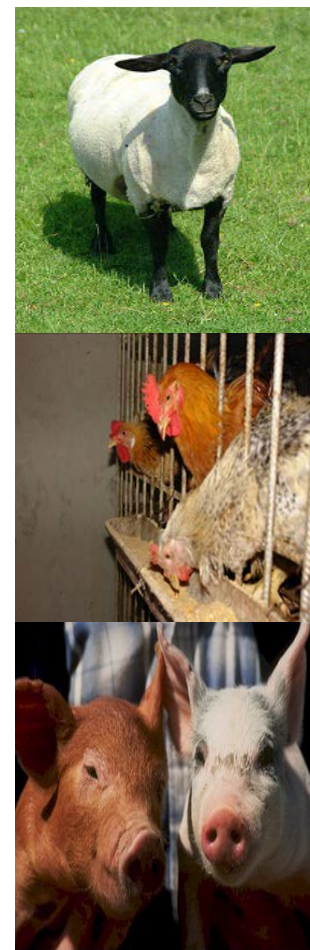


USAHA TB committee

Mycobacterium bovis phylogenetics

Suelee Robbe-Austerman, DVM, PhD
Mycobacteria Brucella Section Head
National Veterinary Services Laboratories

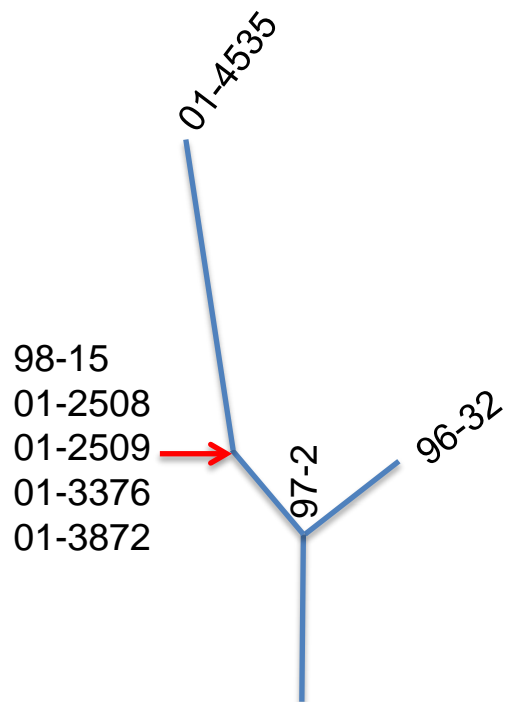
U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services
STAS
10/18/2014



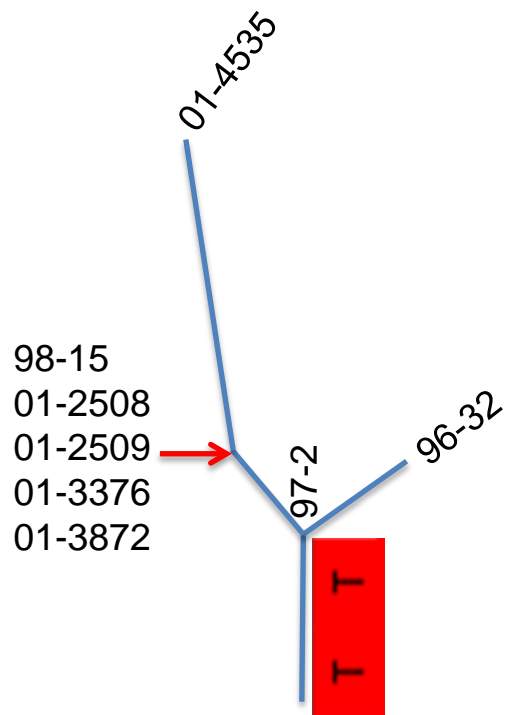
Objectives

- Reading phylogenetic trees and SNP tables
- Describe the last 10 years of *M. bovis* cases recovered in the USA
- Describe human *M. bovis* isolates in our database

	A	CN	CO	CP	CQ	CR	CS	CT
		chrom1-2824728	chrom1-1126954	chrom1-3005112	chrom1-3816582	chrom1-1258903	chrom1-2913998	chrom1-862227
1	reference_pos	chrom1-2824728	chrom1-1126954	chrom1-3005112	chrom1-3816582	chrom1-1258903	chrom1-2913998	chrom1-862227
2	reference_call	C	C	G	A	G	C	A
85	97-2MIDNRdeerAlp	T	T	G	A	G	C	A
86	96-32MIDNRdeerAlp	T	T	T	A	G	C	A
87	98-15MIDNRdeerAlp	T	T	G	C	G	C	A
88	01-2508_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
89	01-2509_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
90	02-3376_MI_Osco_Beef_20-Val	T	T	G	C	G	C	A
91	01-3872_MI_Alpe_Beef_15-Val	T	T	G	C	G	C	A
92	01-4535_MI_Alpe_Beef_15-Val	T	T	G	C	A	A	G

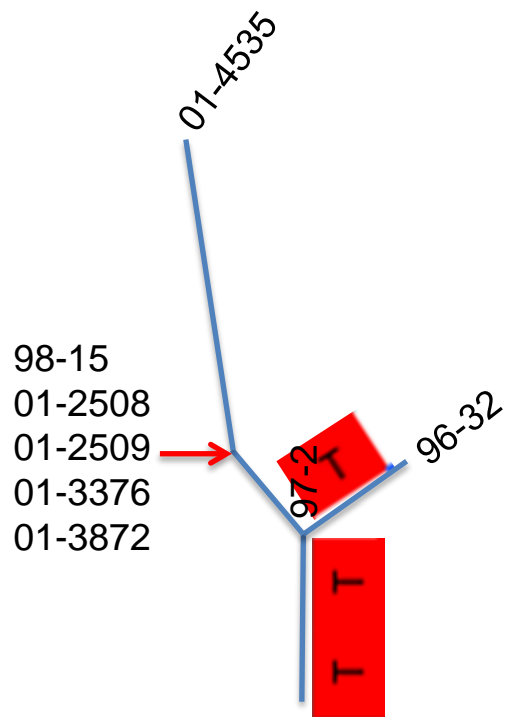


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2	reference_call	C	C	G	A	G	C	A
85	97-2MIDNRdeerAlp	T	T	G	A	G	C	A
86	96-32MIDNRdeerAlp	T	T	T	A	G	C	A
87	98-15MIDNRdeerAlp	T	T	G	C	G	C	A
88	01-2508_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
89	01-2509_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
90	02-3376_MI_Osco_Beef_20-Val	T	T	G	C	G	C	A
91	01-3872_MI_Alpe_Beef_15-Val	T	T	G	C	G	C	A
92	01-4535_MI_Alpe_Beef_15-Val	T	T	G	C	A	A	G

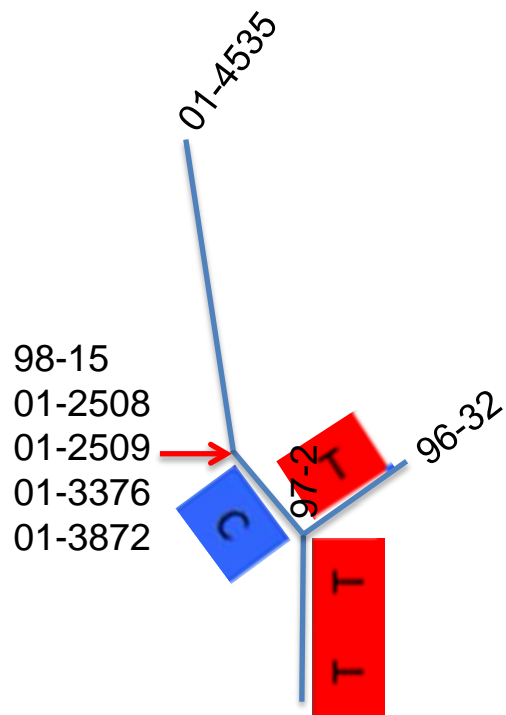




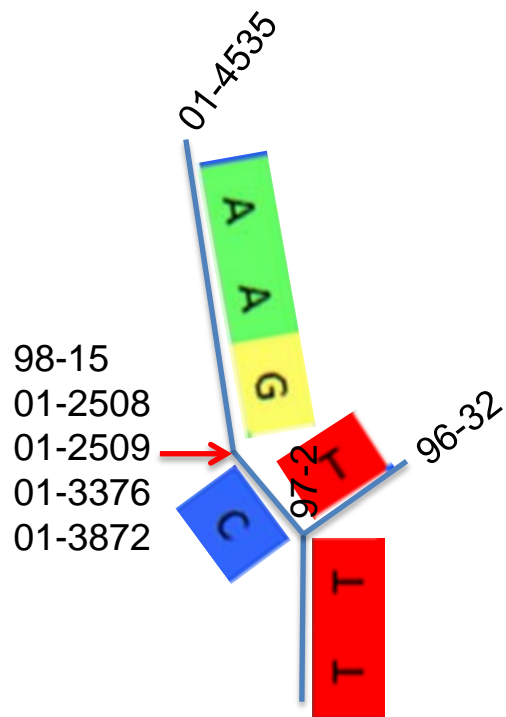
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2	reference_call	C	C	G	A	G	C	A
85	97-2MIDNRdeerAlp	T	T	G	A	G	C	A
86	96-32MIDNRdeerAlp	T	T	T	A	G	C	A
87	98-15MIDNRdeerAlp	T	T	G	C	G	C	A
88	01-2508_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
89	01-2509_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
90	02-3376_MI_Osco_Beef_20-Val	T	T	G	C	G	C	A
91	01-3872_MI_Alpe_Beef_15-Val	T	T	G	C	G	C	A
92	01-4535_MI_Alpe_Beef_15-Val	T	T	G	C	A	A	G

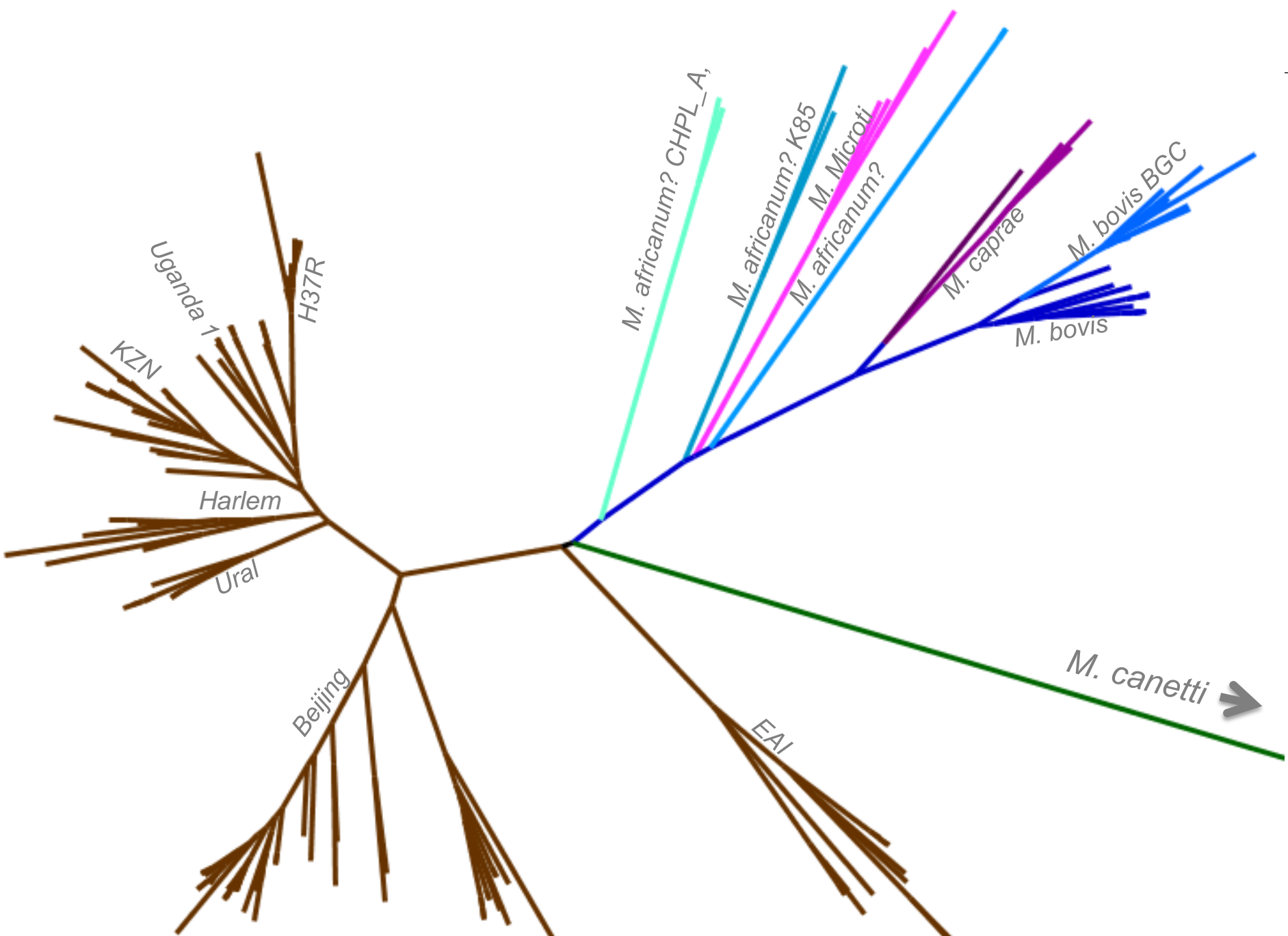


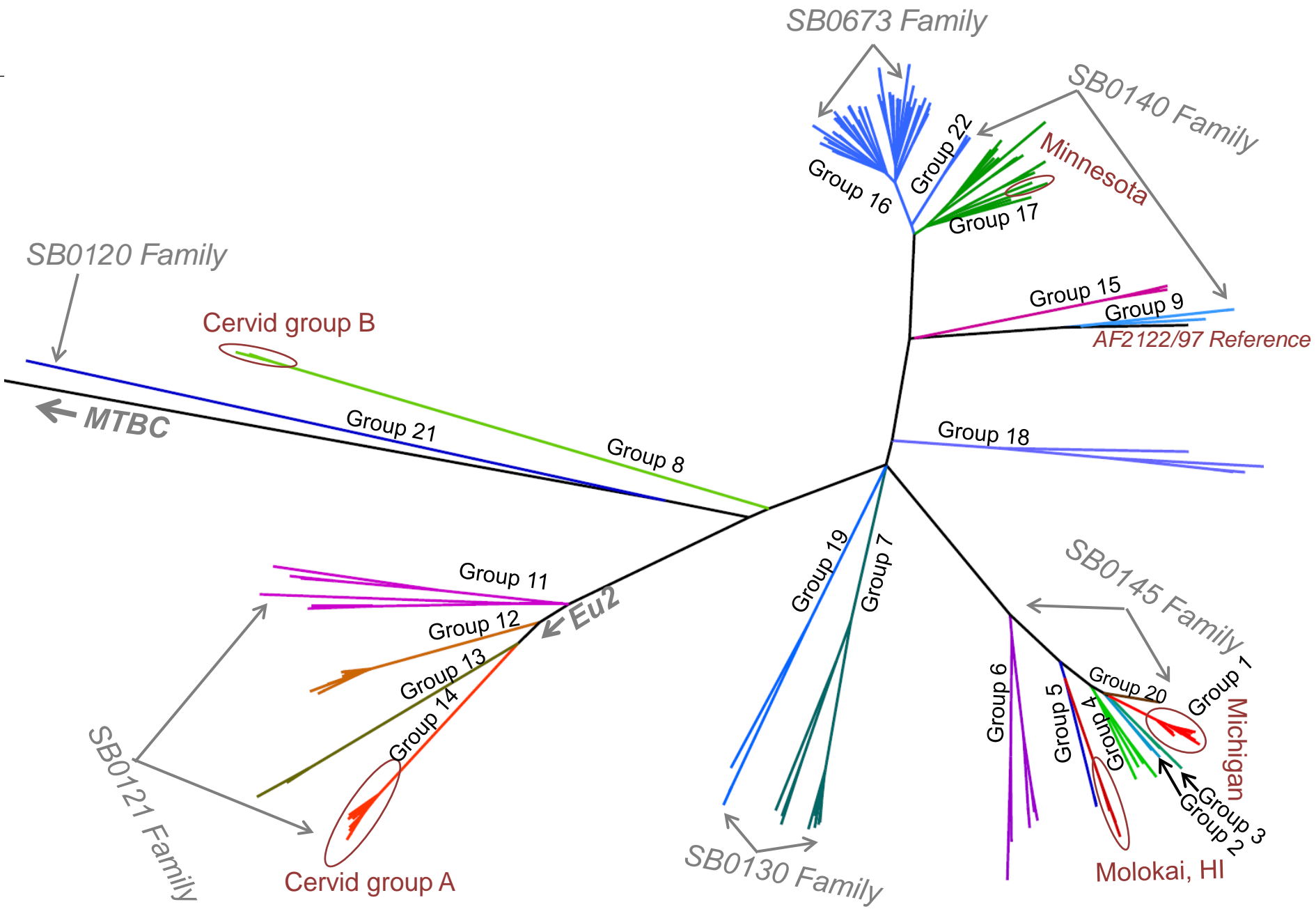
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2	reference_call	C	C	G	A	G	C	A
85	97-2MIDNRdeerAlp	T	T	G	A	G	C	A
86	96-32MIDNRdeerAlp	T	T	T	A	G	C	A
87	98-15MIDNRdeerAlp	T	T	G	C	G	C	A
88	01-2508_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
89	01-2509_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
90	02-3376_MI_Osco_Beef_20-Val	T	T	G	C	G	C	A
91	01-3872_MI_Alpe_Beef_15-Val	T	T	G	C	G	C	A
92	01-4535_MI_Alpe_Beef_15-Val	T	T	G	C	A	A	G



	A	CN	CO	CP	CQ	CR	CS	CT
		chrom1-2824728	chrom1-1126954	chrom1-3005112	chrom1-3816582	chrom1-1258903	chrom1-2913998	chrom1-862227
1	reference_pos	chrom1-2824728	chrom1-1126954	chrom1-3005112	chrom1-3816582	chrom1-1258903	chrom1-2913998	chrom1-862227
2	reference_call	C	C	G	A	G	C	A
85	97-2MIDNRdeerAlp	T	T	G	A	G	C	A
86	96-32MIDNRdeerAlp	T	T	T	A	G	C	A
87	98-15MIDNRdeerAlp	T	T	G	C	G	C	A
88	01-2508_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
89	01-2509_MI_Alpe_Beef_12-Val	T	T	G	C	G	C	A
90	02-3376_MI_Osco_Beef_20-Val	T	T	G	C	G	C	A
91	01-3872_MI_Alpe_Beef_15-Val	T	T	G	C	G	C	A
92	01-4535_MI_Alpe_Beef_15-Val	T	T	G	C	A	A	G







Where are USA bTB cases coming from?

- Low level/ circulation or residual w/in national herd?
 - Expect to see similar strains, no recent anchors to imported animals.
- New introductions
 - Imported cattle
 - Human source
 - Other??

Database of sequenced isolates

1,138 *M. bovis* isolates sequenced

- 123/130 (94.6%) affected USA cattle herds sequenced since 1999.
- 330/385 (85.7%) of fed cattle (import and domestic) since 2000.
 - 306 Mexico origin animals
 - 68 unknown
 - 9 USA origin
 - 2 Canada origin
- ~150 Mexican cattle (mostly dairy)
- 30 Human isolates



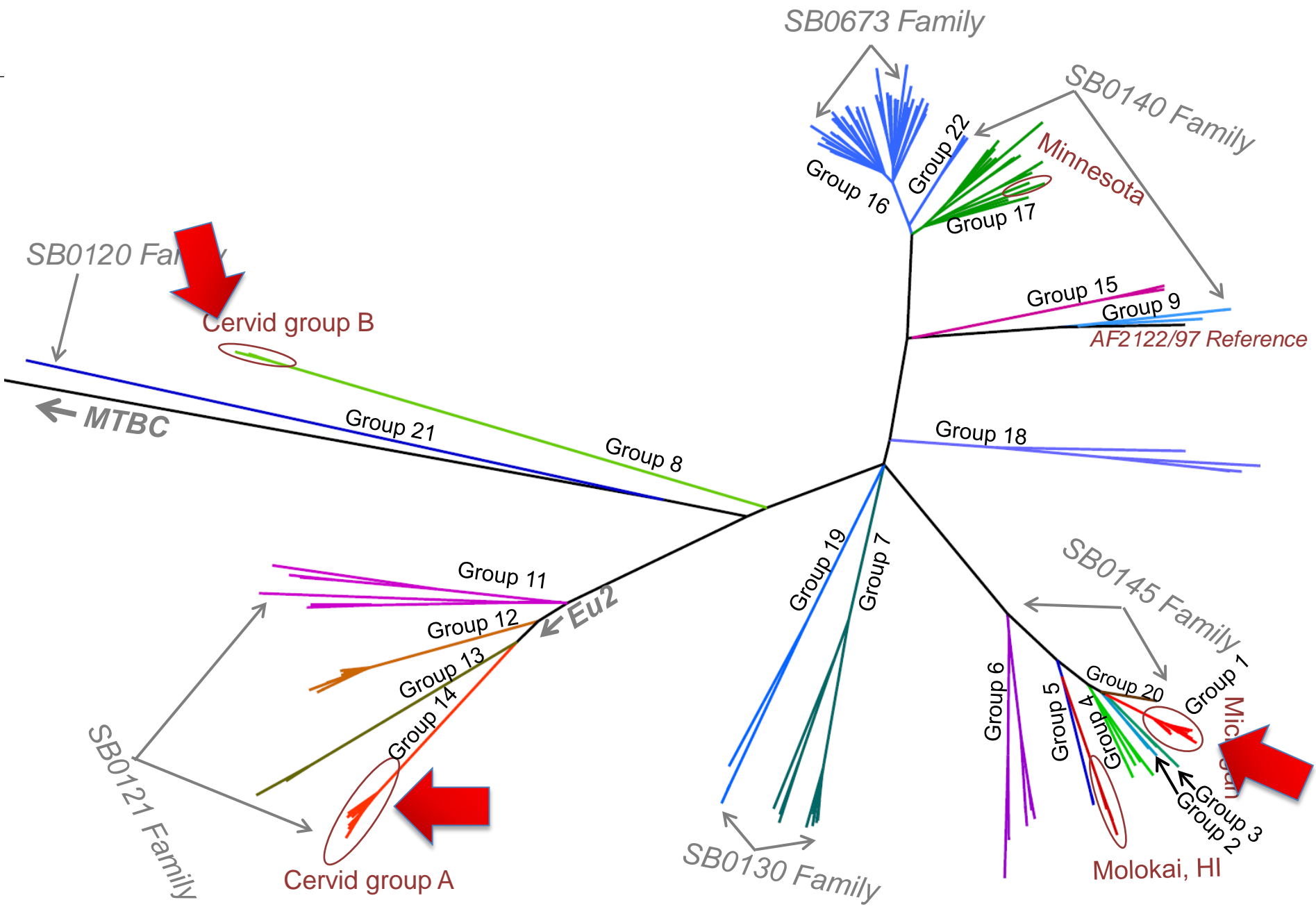
123/130 (94.6%) affected USA cattle/cervid herds sequenced since 1999.

Strain	# Herds	%	Where	# Years isolate	#Untraceable or fed	Wildlife
MI	63 (3)	51%	MI	15(1999)	2 (outside of MI)	Yes
MN	12	9%	MN	5	1 Fed	Yes
Cervid	11 (1)	9%	MULTI	23 (1991)	5 Untraceable	Yes
2010 CO	6 (1)		CO	2	0	No
2002/13 CA	3		CA	10	0	No
CA-08A, 08C	2		CA	1	0	No
CA-11B,11C	2		CA	1	0	No
TX/ND	2		TX/ND	2	0	No
NM/OH	2		NM/OH	2	0	No
AZ/NM	2		AZ/NM	2	0	No

– 24 sporadic- no WGS or epi links (2 not sequenced)

Affected USA cattle herds

- 123/130 (94.6%) affected USA cattle herds sequenced since 1999.
- 34 Strain types have been identified
 - Three strain types, MI and cervid A, B = 75/130. The index cases were prior to 1999.
 - 31 strain types unexplained (2 not sequenced)
 - Unknown residual infections?
 - New introductions?

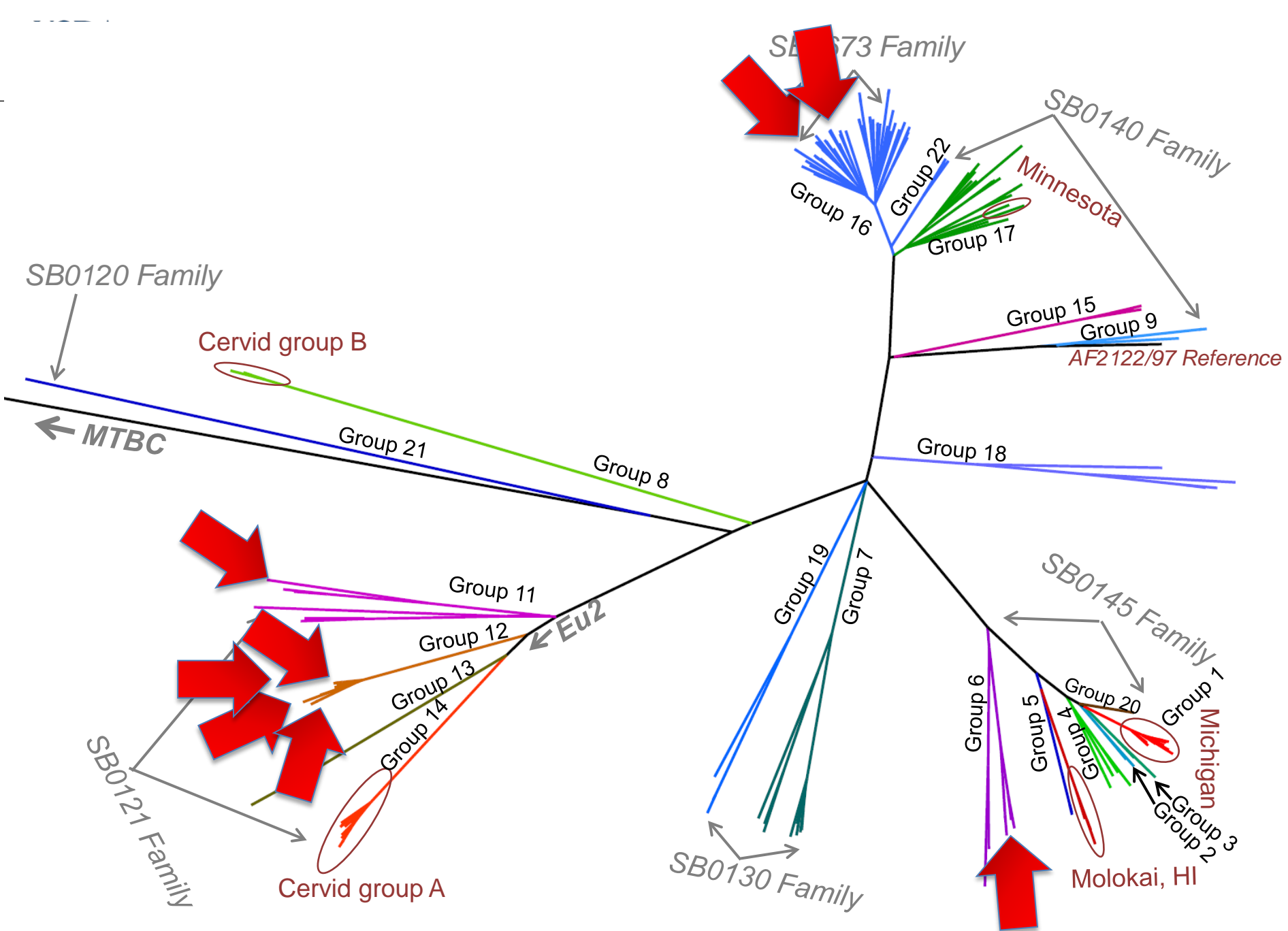




Where are USA bTB cases coming from?

Strain Types	Origin	# USA herds	Name
3	USA	75 (58%)	MI, Cervid A, Cervid B
8	Unknown	8 (6%)	Avg distance to MRCA = 32
21	Mexico	47 (46%)	Includes MN, CO, CA

- 99-0380_TX Dairy 90-A
- 99-1993_ND Dairy 99-A
- 01-5518_KS Beef 01-A
- 01-5950_TX Beef 01-A
- 03-1852_CA Dairy 02-A
- 04-2067_TX Dairy 04-A
- 08-1587_CA Dairy 08-A
- 09-5045_NE_Beef_09-A_1





21 Strain types anchor to Mexico

- Imported cattle
- Human
- Unknown



Imported cattle – 2 herds

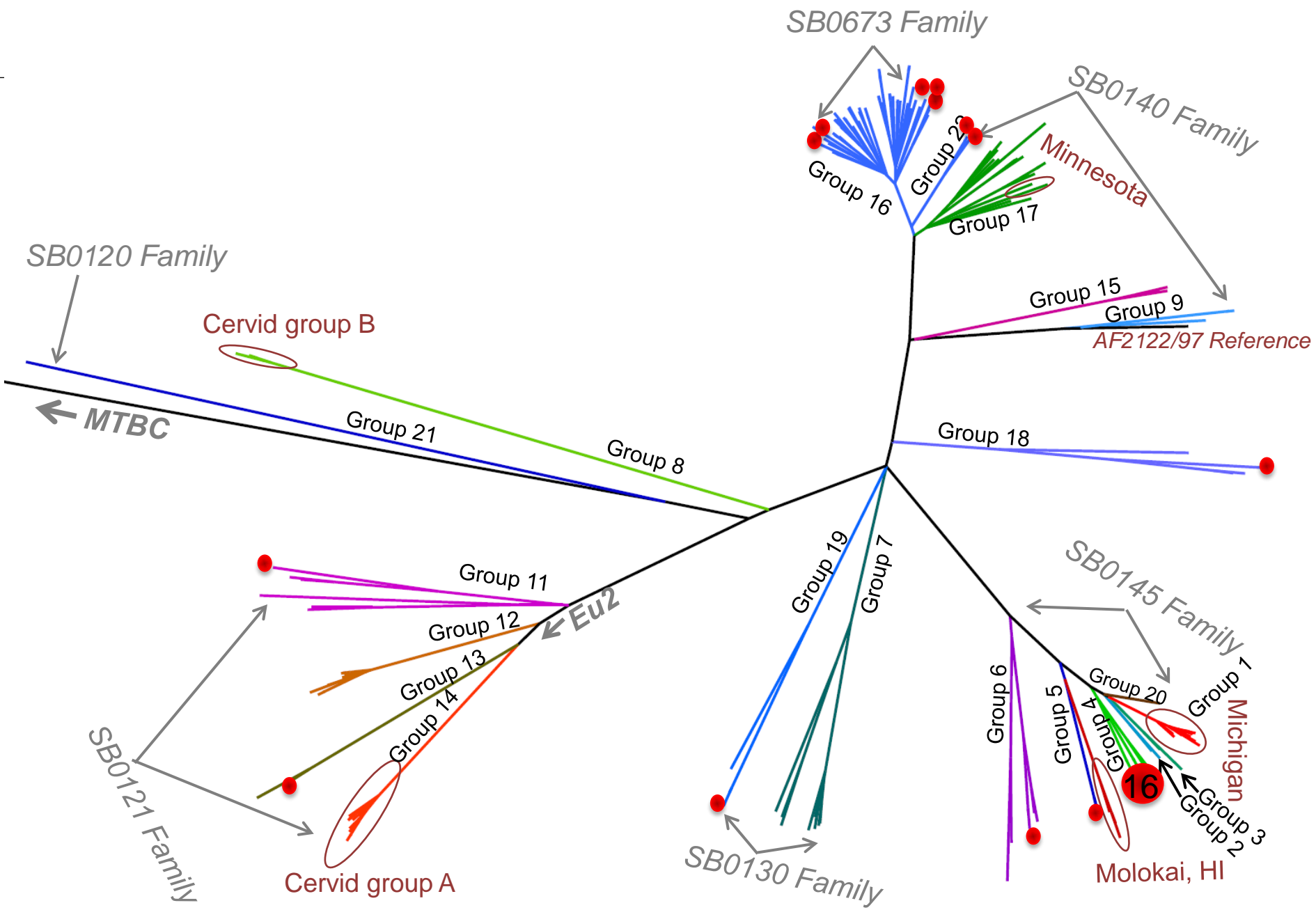
reference_pos	chrom1-3599454	chrom1-3608902	chrom1-3700845	chrom1-4148111	chrom1-424805	chrom1-4253845	chrom1-4340285	chrom1-49075	chrom1-532446	chrom1-602072	chrom1-638878	chrom1-72310	chrom1-3034685
reference_call	G	T	A	T	C	G	C	T	C	G	T	G	T
10-2758_UNK_MS_Event-Roping	A	C	G	C	T	A	T	C	T	C	C	A	T
10-4190_MS_Beef_10-A	A	C	G	C	T	A	T	C	T	C	C	A	C

reference_pos	chrom1-440678	chrom1-1513131	chrom1-1836082	chrom1-3649648	chrom1-4222294	chrom1-896450	chrom1-3708596	chrom1-1880321	chrom1-2670266	chrom1-2952201	chrom1-3128143	chrom1-3602841	chrom1-3826561	chrom1-865535	chrom1-651065	chrom1-1865074	chrom1-4261657	chrom1-727832
reference_call	G	A	G	A	G	A	T	C	G	C	C	G	G	G	C	A	T	T
06-10752_COA_TX_Fed	C	G	A	G	C	A	T	C	G	C	C	G	G	G	C	A	T	T
04-5382_COA_TX_Fed	C	G	A	G	C	G	T	C	G	C	C	G	G	G	C	A	T	T
02-6203_UNK_OK_Fed	C	A	G	A	G	A	C	T	A	A	T	A	C	A	T	A	T	T
02-0419_TX_Dairy_01-A-Val	C	A	G	A	G	A	C	T	A	A	T	A	C	A	C	C	C	C



21 Strain types anchor to Mexico

- Imported cattle – 2 cases
- Human
- Unknown

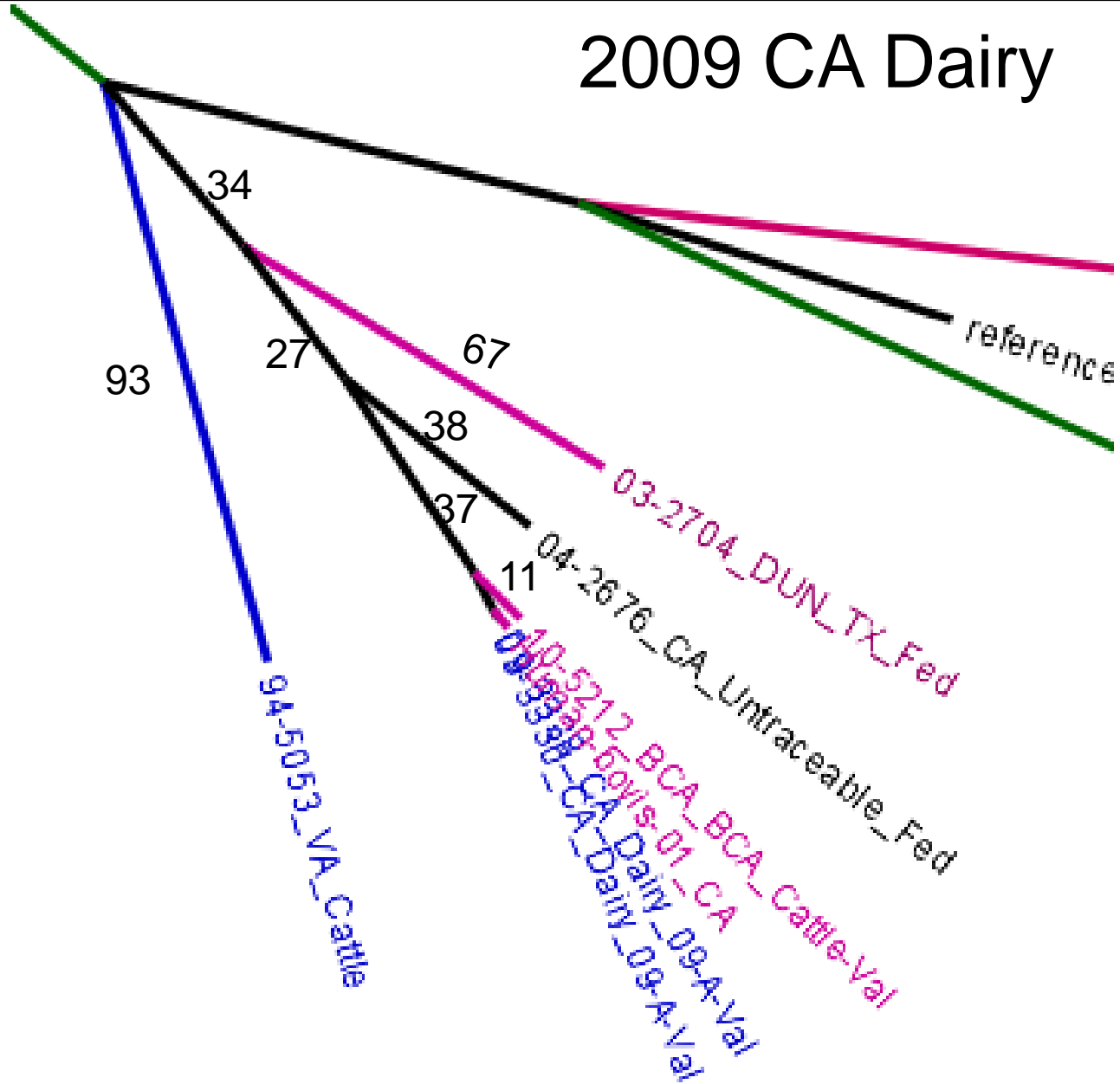




2013 ND Dairy

reference_pos	chrom1-4091785	chrom1-448360	chrom1-656454	chrom1-900162	chrom1-1672787	chrom1-3385556	chrom1-3538852	chrom1-3556472	chrom1-3704598	chrom1-1356338	chrom1-2155436	chrom1-2660087	chrom1-1793953	chrom1-2489986	chrom1-3156770	chrom1-3211069	chrom1-3437658	chrom1-3517522	chrom1-695360	chrom1-452237	chrom1-4098003	chrom1-4098004	chrom1-1264009	chrom1-1448183	chrom1-1547971	chrom1-2857242	chrom1-3535374	chrom1-4033086	chrom1-681583	chrom1-1729140	chrom1-1782100	chrom1-18848	chrom1-2954614	chrom1-3432760	chrom1-4092258	chrom1-517735		
reference_call	A	A	C	T	G	C	A	G	A	C	G	G	G	G	G	C	C	G	C	A	G	C	G	T	T	T	G	C	A	A	C	G	G	G	A	C		
03-5160_TAM_TAM_Cattle	G	G	T	C	A	A	C	A	C	C	G	G	G	G	G	C	C	G	C	A	G	C	G	T	T	T	G	C	A	A	C	G	G	G	A	C		
03-5158_TAM_TAM_Cattle	G	G	T	C	A	A	C	A	C	T	A	A	G	G	G	C	C	G	C	A	G	C	G	T	T	T	G	C	A	A	C	G	G	G	A	C		
12-0173_ZAC_TX_Fed-Val	G	G	T	C	A	C	A	G	A	C	G	G	A	A	A	T	G	A	T	G	G	C	G	T	T	T	G	C	A	A	C	G	G	G	A	C		
12-3660_ZAC_NE_Fed-Val	G	G	T	C	A	C	A	G	A	C	G	G	A	A	A	T	G	A	T	A	A	T	G	T	T	T	G	C	A	A	C	G	G	G	A	C		
13-7506_ND_Dairy_13-A-Val	G	G	T	C	G	C	A	G	A	C	G	G	G	G	G	C	C	G	C	A	G	C	A	G	C	A	G	C	C	A	G	G	A	C	G	G	A	C
13-7994_MEX_ND_Human	G	G	T	C	G	C	A	G	A	C	G	G	G	G	G	C	C	G	C	A	G	C	A	G	C	A	G	C	A	A	C	G	G	G	A	C		
13-8046_ND_Dairy_13-A	G	G	T	C	G	C	A	G	A	C	G	G	G	G	G	C	C	G	C	A	G	C	G	T	T	T	G	C	A	G	T	A	A	T	G	T		

2009 CA Dairy





United States Department of Agriculture

reference_pos	chrom1-993746	chrom1-117851	chrom1-1401165	chrom1-1533593	chrom1-1573609	chrom1-2326349	chrom1-2371298	chrom1-2817372	chrom1-3255546	chrom1-3394713	chrom1-3834751	chrom1-4342720	chrom1-1446356	chrom1-2429487	chrom1-2645331	chrom1-4276944	chrom1-4290091	chrom1-4329490	chrom1-438422	chrom1-1852730	chrom1-1922825	chrom1-3447778	chrom1-3554832	chrom1-782731	chrom1-789954
reference_call	G	G	G	G	A	G	G	A	C	G	G	G	A	T	A	G	G	G	C	C	G	G	C	A	G
04-2676_CA_Untraceable_Fed	G	G	G	G	A	G	G	A	C	G	G	G	A	T	A	G	G	G	C	C	G	G	C	A	G
10-5212_BCA_BCA_Cattle-Val	A	C	A	C	G	A	A	G	T	A	A	A	A	T	A	G	G	G	C	C	G	G	C	A	G
Human-bovis-01_CA	A	G	G	G	A	G	G	A	C	G	G	G	G	C	C	A	C	A	T	T	C	C	A	A	G
09-3328_CA_Dairy_09-A-Val	A	G	G	G	A	G	G	A	C	G	G	G	G	C	C	A	C	A	T	C	G	G	C	C	A
09-3330_CA_Dairy_09-A-Val	A	G	G	G	A	G	G	A	C	G	G	G	G	C	C	A	C	A	T	C	G	G	C	C	A

93

27

67

38

37

11

reference

09-5053_VA_Cattle

09-3328_CA_Dairy_09-A-Val
09-3330_CA_Dairy_09-A-Val
10-5212_BCA_BCA_Cattle-Val
04-2676_CA_Untraceable_Fed

03-2704_DUN_TX_Fed
04-2676_CA_Untraceable_Fed
10-5212_BCA_BCA_Cattle-Val

21 Strain types anchor to Mexico

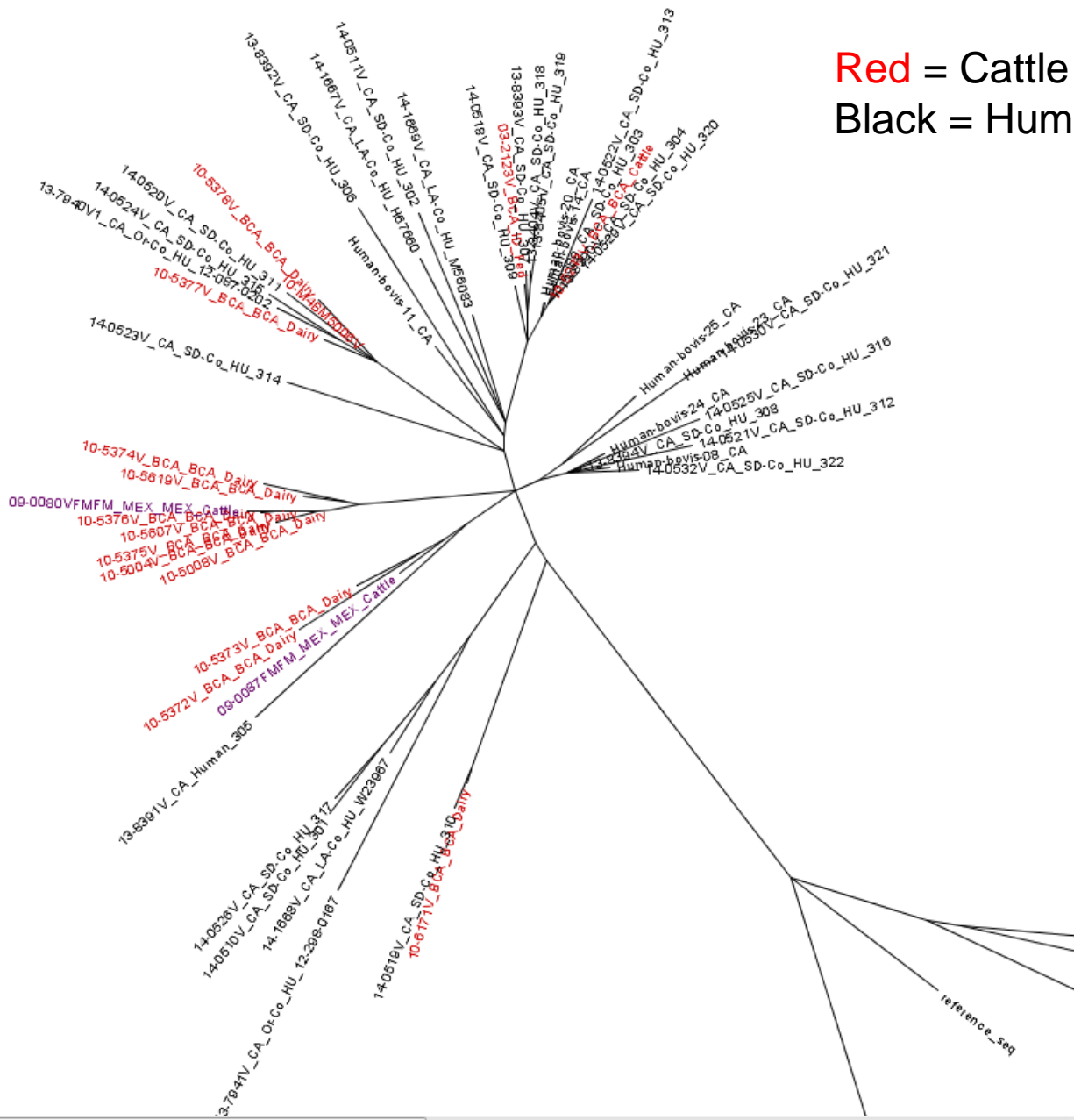
- Imported cattle – 2 cases
- Human – 2 cases
- Unknown



Cluster of *M. bovis* human cases in San Diego County, CA

- SB1040
- CDC flagged

Red = Cattle isolates
Black = Human isolates





reference_pos	chrom1-779595	chrom1-947102	chrom1-309448:	chrom1-529163	chrom1-293967:	chrom1-173660:	chrom1-374243:	chrom1-428139:	chrom1-92640	chrom1-131816:	chrom1-213117:	chrom1-278450:	chrom1-281178:	chrom1-349851	chrom1-592576	chrom1-702522	chrom1-7511
reference_call	A	G	G	C	C	G	C	G	C	A	A	C	G	G	A	A	C
Human-bovis-20_CA-Val	G	T	A	C	C	G	C	G	C	A	A	C	G	G	A	A	C
Human-bovis-14_CA-Val	G	T	G	T	C	G	C	G	C	A	A	C	G	G	A	A	C
13-8389_CA_SD-Co_HU_303	G	T	G	C	T	G	C	G	C	A	A	C	G	G	A	A	C
10-5243_BCA_BCA_Cattle-Val	G	T	G	C	T	G	C	G	C	A	A	C	G	G	A	A	C
13-8390_CA_SD-Co_HU_304-Val	G	T	G	C	T	A	C	G	C	A	A	C	G	G	A	A	C
14-0529_CA_SD-Co_HU_320-Val	G	T	G	C	T	G	T	A	T	A	A	C	G	G	A	A	C
14-0522_CA_SD-Co_HU_313-Val	G	T	G	C	T	G	C	G	C	G	G	G	A	A	G	G	T

reference_pos	chrom1-3436165	chrom1-464117	chrom1-2377773	chrom1-3213480	chrom1-3984594	chrom1-4276450	chrom1-2199658	chrom1-1489766	chrom1-1784093	chrom1-1990236	chrom1-2014774	chrom1-2301718	chrom1-1052635	chrom1-121337	chrom1-1517792	chrom1-1552503	chrom1-2086064	chrom1-3328546	chrom1-4085695	chrom1-1107474	chrom1-160676	chrom1-2027406	chrom1-2142597	chrom1-2251420	chrom1-2290953	chrom1-2475291	chrom1-3250265	chrom1-3314259	chrom1-1821744	chrom1-2633925	chrom1-2729687	chrom1-3202988	chrom1-467793	chrom1-118677	chrom1-2910859	chrom1-2952439	chrom1-3506543	chrom1-3921707	chrom1-4029369		
reference_call	G	C	C	G	G	A	C	G	G	A	C	G	G	C	A	T	G	C	C	C	G	C	C	C	G	G	G	G	G	A	A	T	C	C	G	G	G	C	C	G	C
10-5377_BCA_BCA_Dairy-Val	A	T	T	A	A	C	C	G	G	A	C	G	G	C	A	T	G	C	C	C	G	C	C	C	G	G	G	G	G	A	A	T	C	G	G	G	C	C	G	G	C
09-0119FM_MEX_MEX_Dairy	A	T	C	G	G	A	A	A	A	C	T	A	G	C	A	T	G	C	C	G	C	C	C	C	G	G	G	G	G	A	A	T	C	G	G	G	C	C	G	G	C
14-0520_CA_SD-Co_HU_311-Val	A	T	C	G	G	A	A	G	G	A	C	G	A	T	G	Y	A	A	Y	G	C	C	C	C	G	G	G	G	G	A	A	T	C	G	G	G	C	C	G	G	C
10-5378_BCA_BCA_Dairy-Val	A	T	C	G	G	A	C	G	G	A	C	G	G	C	A	T	G	C	C	C	Y	G	T	T	C	A	G	G	A	A	T	C	G	G	G	C	C	G	G	C	
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14-0524_CA_SD-Co_HU_315-Val	A	T	C	G	G	A	C	G	G	A	C	G	G	C	A	T	G	C	C	G	C	C	C	C	G	G	A	A	G	A	T	C	G	G	A	T	A	T	A	T	

21 Strain types anchor to Mexico

- Imported cattle – 2 cases
- Human – 2 cases
- Unknown – 17 cases

Summary

- *M. bovis* affected herds 58% endemic 6% unknown, 46% Mexican strains.
- Only 2 (9%) can be explained by imported cattle.
 - Why?
- NVSL's database is still small and limited in scope.
 - Work with public health to submit strains.
 - NVSL will continue to partner with Mexico