Minisatellite Markers Reveals Frequent Genetic Exchanges among House Mouse Subspecies

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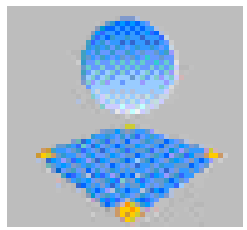

Outline

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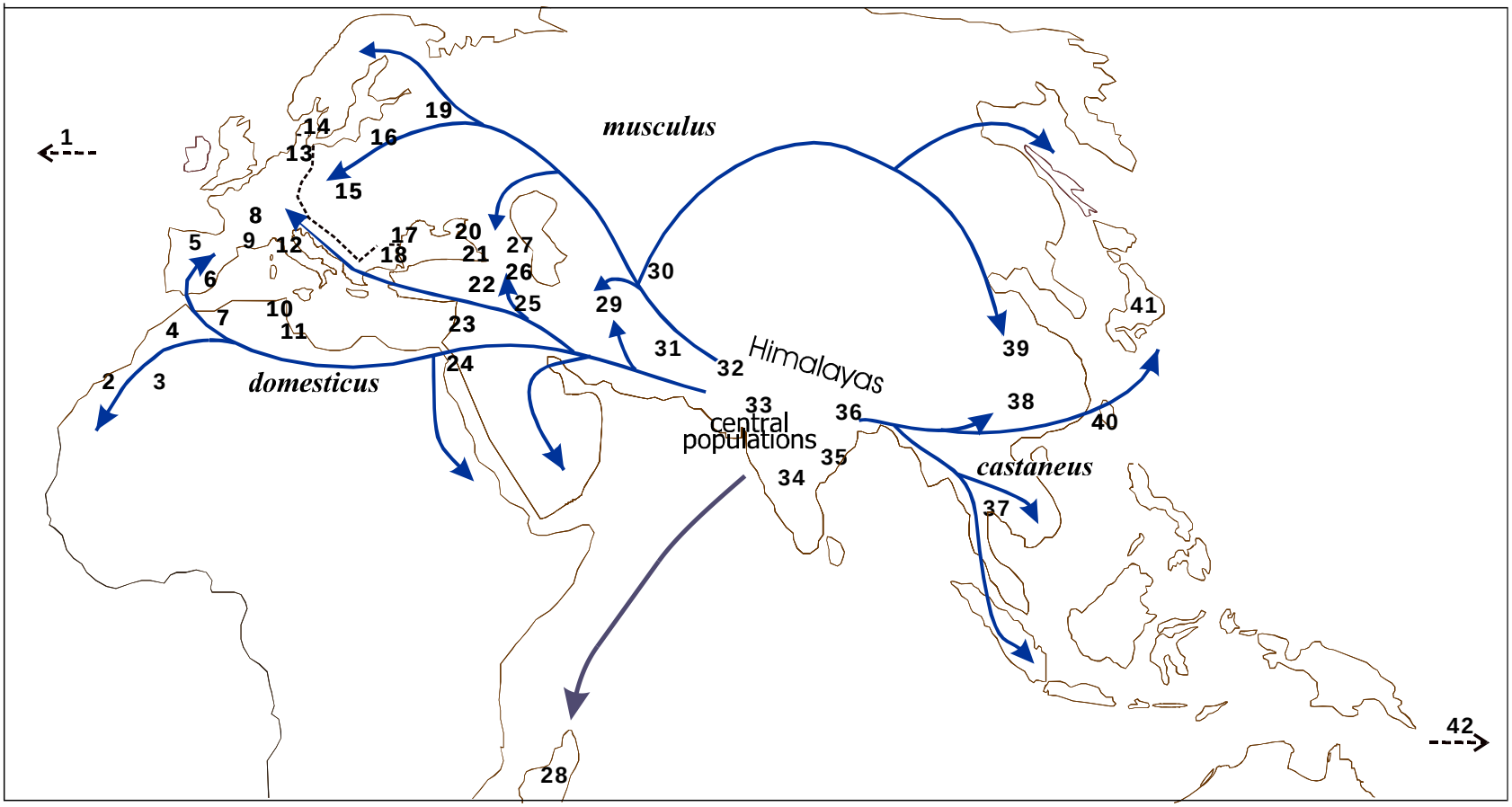
- MS informative for intra-species evolution

Minisatellite data

- Four minisatellite loci: MMS 24, 26, 80, and 30 respectively on chromosomes 7 (22 cM), 9 (68 cM and 79 cM), and X (43 cM)
- Panel of 116 individuals of various geographical origins
- Maps obtained by MVR-PCR as in [Bois et al., 2002]
- High diversity in length and array structure haplotypic diversity (He) in $[0.90, 0.99]$

Geographical origin of wild mice



Mouse minisatellite maps of MMS30 (X chr)

Repeat unit: 39 bps

Variant code		sequence
K	=	"aggagattcagttcacaCtatacagaagatggtgtcagc"
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Example of **maps** in wild mice

ID (species, location)	map
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CEN_INDE_Gauhati	GKKKKWGKKYKWKGWGHoGoKWKKKoLYY
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DOM_OCEA_Tahiti	GYKKKWGKLKYoWKGWGKoGGYWYKKoKKKYYYKG
MUS_GEOR_Tbilissi	GYYKGYKYKGYKKKWGKoKYoWKYYKG

Methods

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   Criterion: Rate of elementary well designed quartets (Re)
   Qualitree [Garreta, Guénoche, 2000]

Evolutionary model

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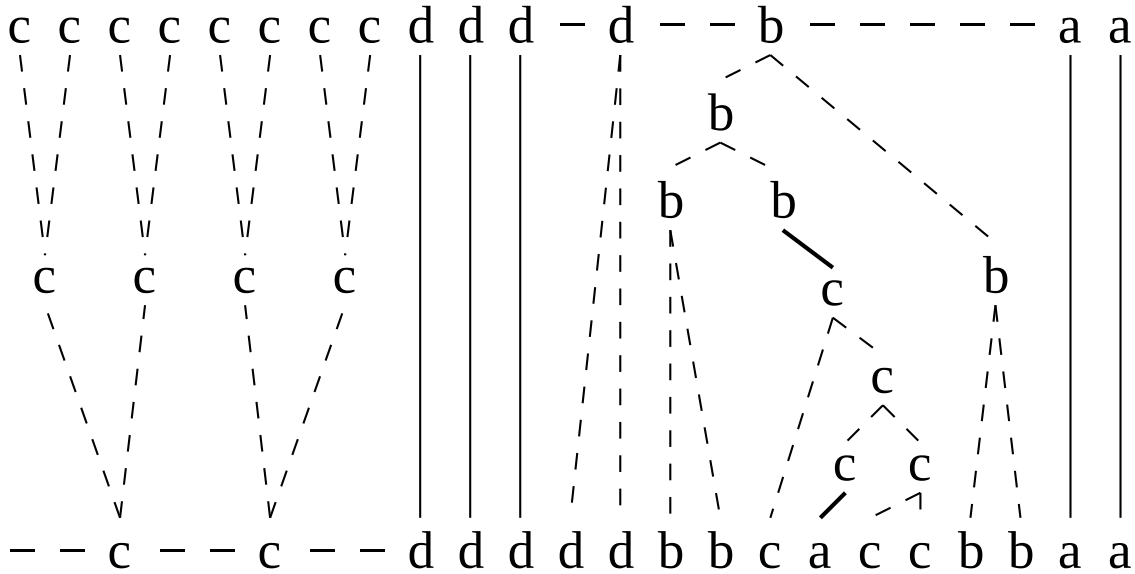
$\Rightarrow$ variation in their number of units

Example of an alignment of 2 maps



An alignment produced by *MS_Align* between maps *cccccccddddbaa* and *ccdddddbbcaccbbaa* with the costs $A = C = 1$, $I = D = 40$, $\mathcal{M}(a, b) = \mathcal{M}(a, d) = \mathcal{M}(b, d) = 20$, $\mathcal{M}(a, c) = \mathcal{M}(b, c) = \mathcal{M}(c, d) = 10$. Its cost is $14 \times A + \mathcal{M}(b, c) + \mathcal{M}(c, a) = 34$. Plain lines: matches, dashed lines: amplifications and contractions, bold lines: mutations.

Percentage of explained variance (VAF)

$$\text{VAF} = 1 - \frac{\sum_{(i,j):i<j}(D(i,j) - T(i,j))^2}{\sum_{(i,j):i<j}(D(i,j) - D_m)^2}$$

where

$D(i,j)$: alignment distance between i and j

$T(i,j)$: tree distance between i and j

D_m : average alignment distance over all pairs (i,j)

Value in $[0,1]$

Rate of elementary well designed quartets (Re)

For an internal edge e, for all quartets (i, j, k, l)
s.t. e splits (i, j) and (k, l):

$R(e) =$ percentage of these quartets satisfying

$$(D(i,j) + D(k,l)) < \min\left(D(i,l) - D(j,k)\right), \left(D(i,k) - D(j,l)\right)$$

where
$D(i, j)$: alignment distance between i and j

Value in $[0, 1]$

Results

Identical alleles

Locus	2	3	≥ 4	Total	$\neq$ origin	$\neq$ subspecies
MMS 24	7	4	1	27	8 (18)	0 (1)
MMS 26	6	2	3	36	10 (26)	5 (1)
MMS 30	9	2	1	38	8 (18)	2 (0)
MMS 80	10	8	0	44	10 (22)	0 (0)

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Example

At MMS 30: DOM_BULG_Vlas_DBV, DOM_TUNI_Monastir_22MO, and SPR_MARO_Azzemour_9852
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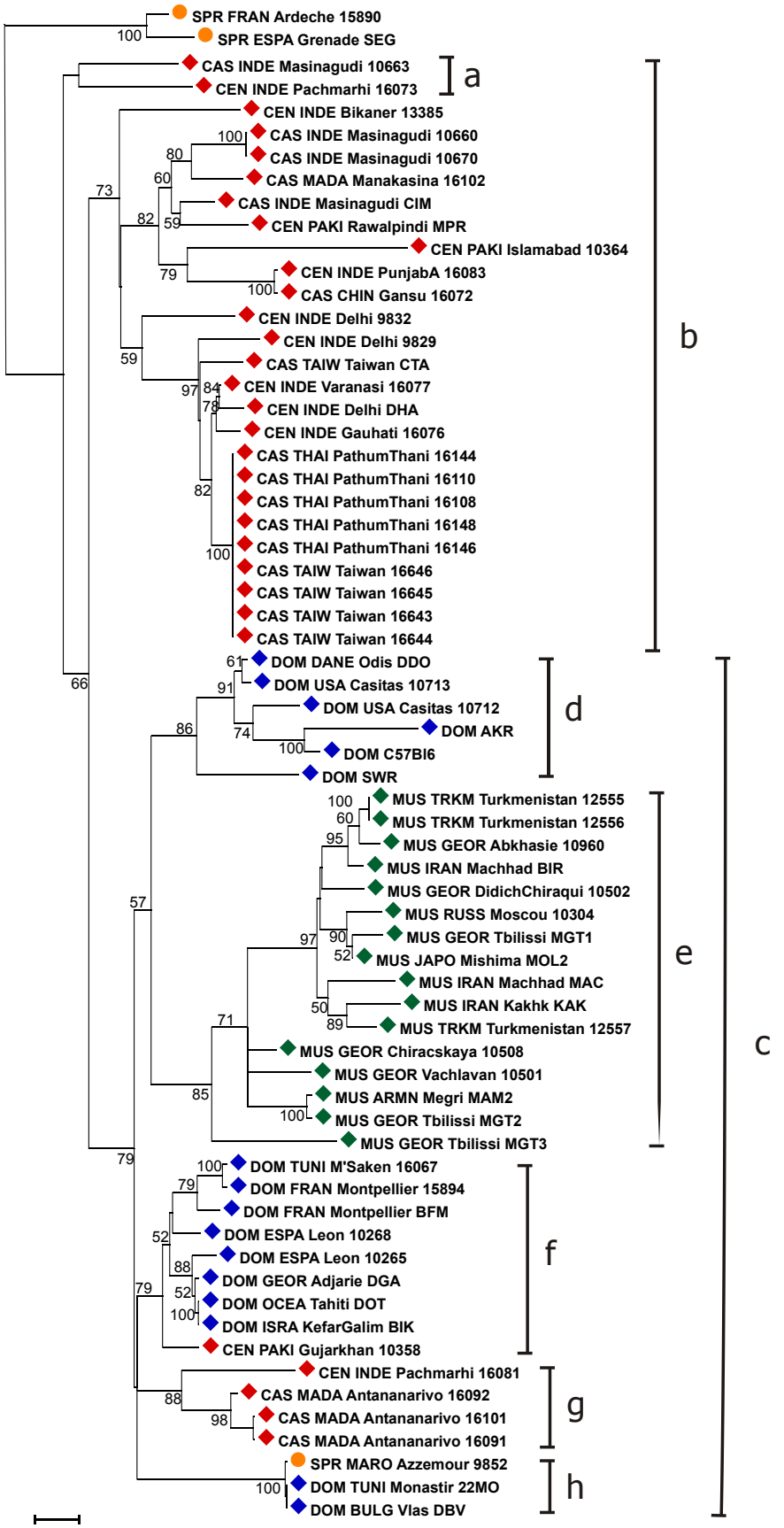
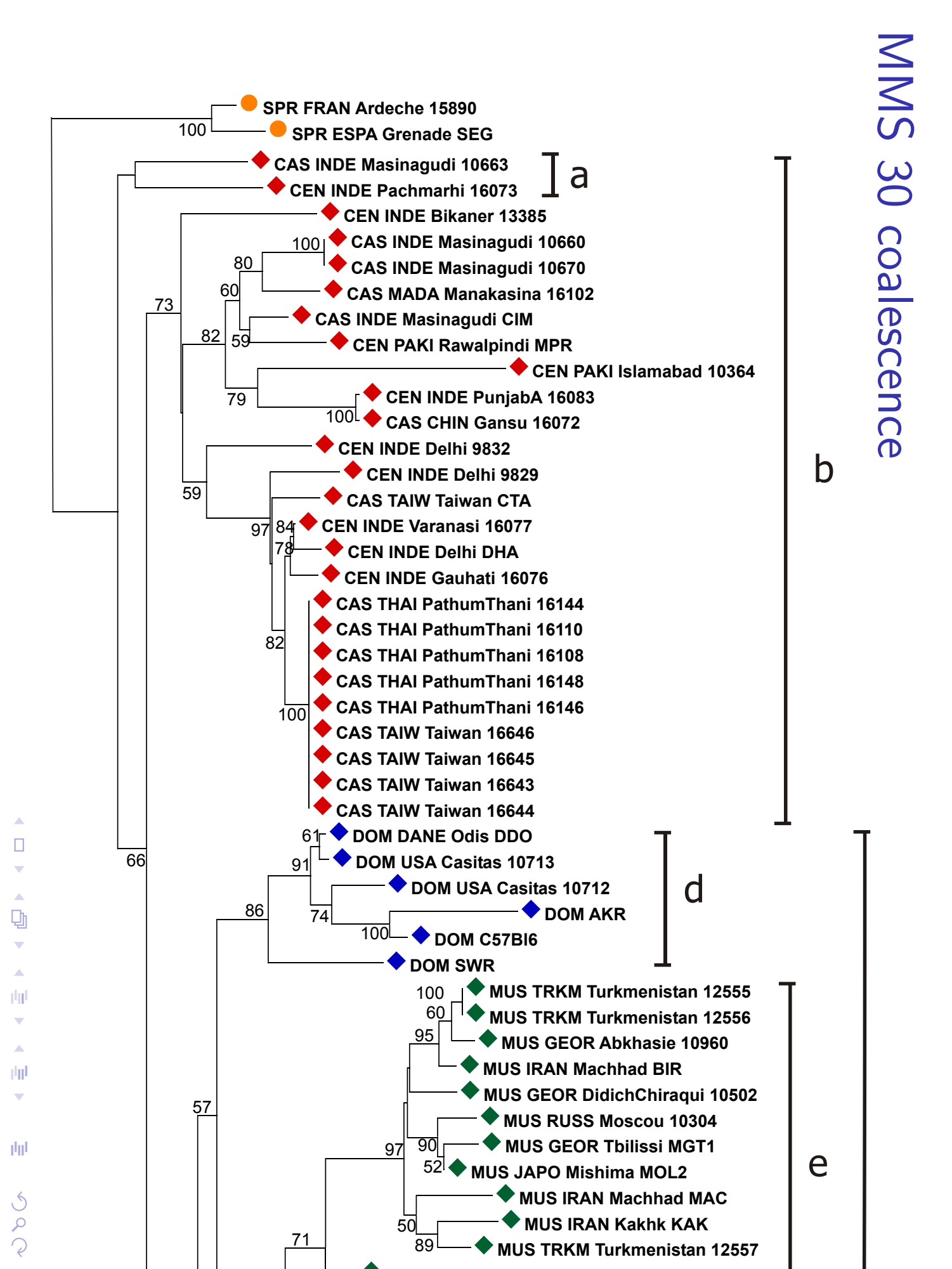
At MMS 26: CEN_INDE_Dehli_DHA; DOM_OCEA_Tahiti_DOT
YGGGGGGGGAGGGAGAAGGYAAGGGGAAAAGAGAAGAAGGGG

MMS 30 coalescence

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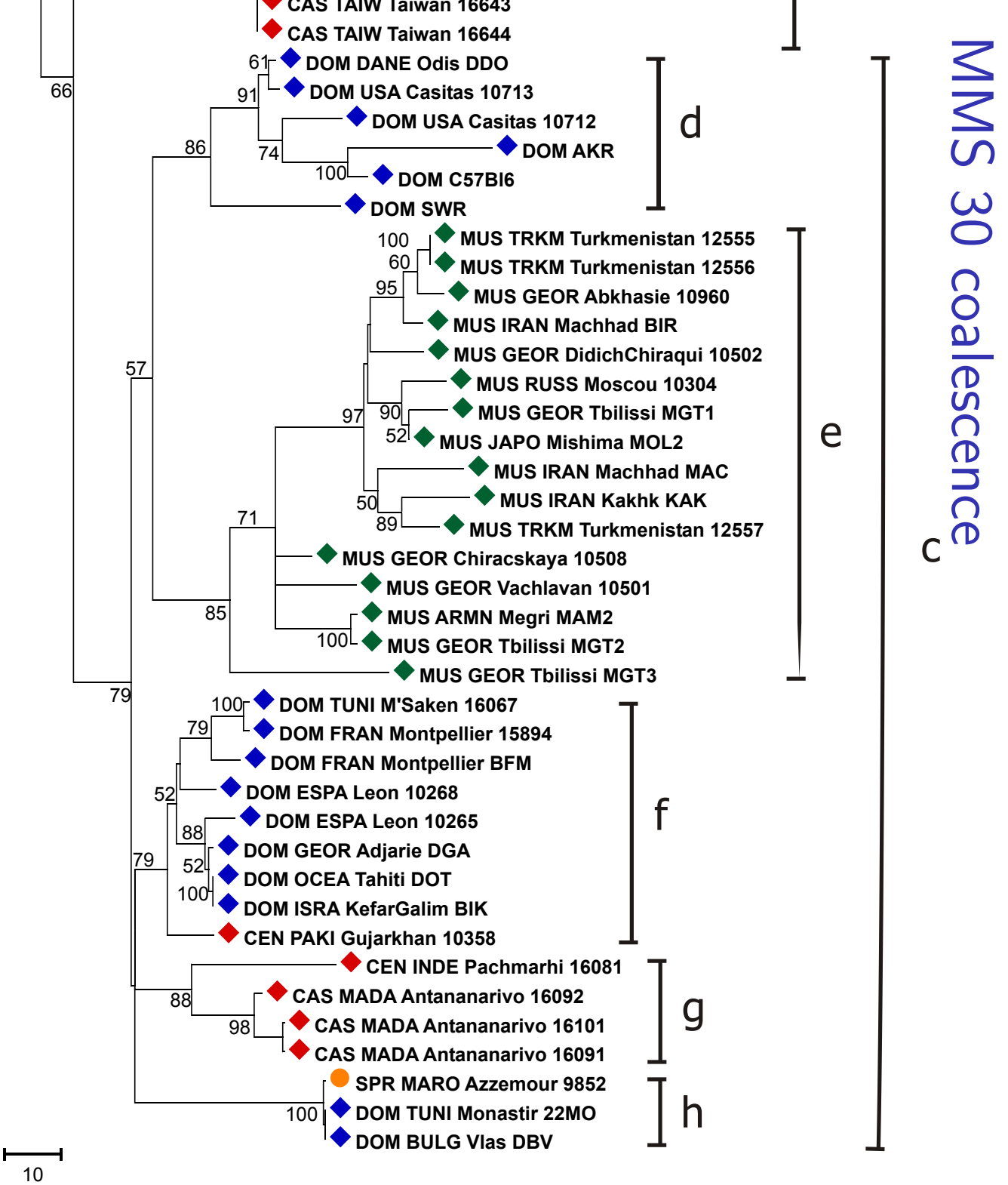
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MUS ARMN Megri MAM2
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MUS GEOR Tbilissi MGT3
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SPR MARO Azzemour 9852
DOM TUNI Monastir 22MO
DOM BULG Vlas DBV
d
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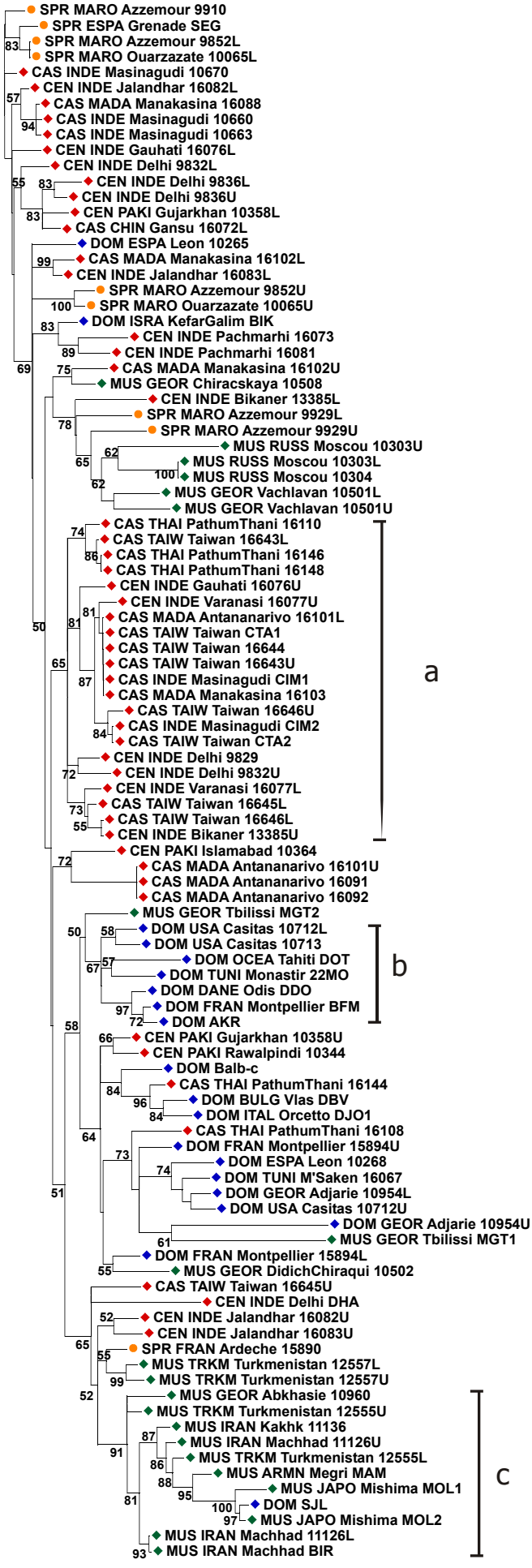
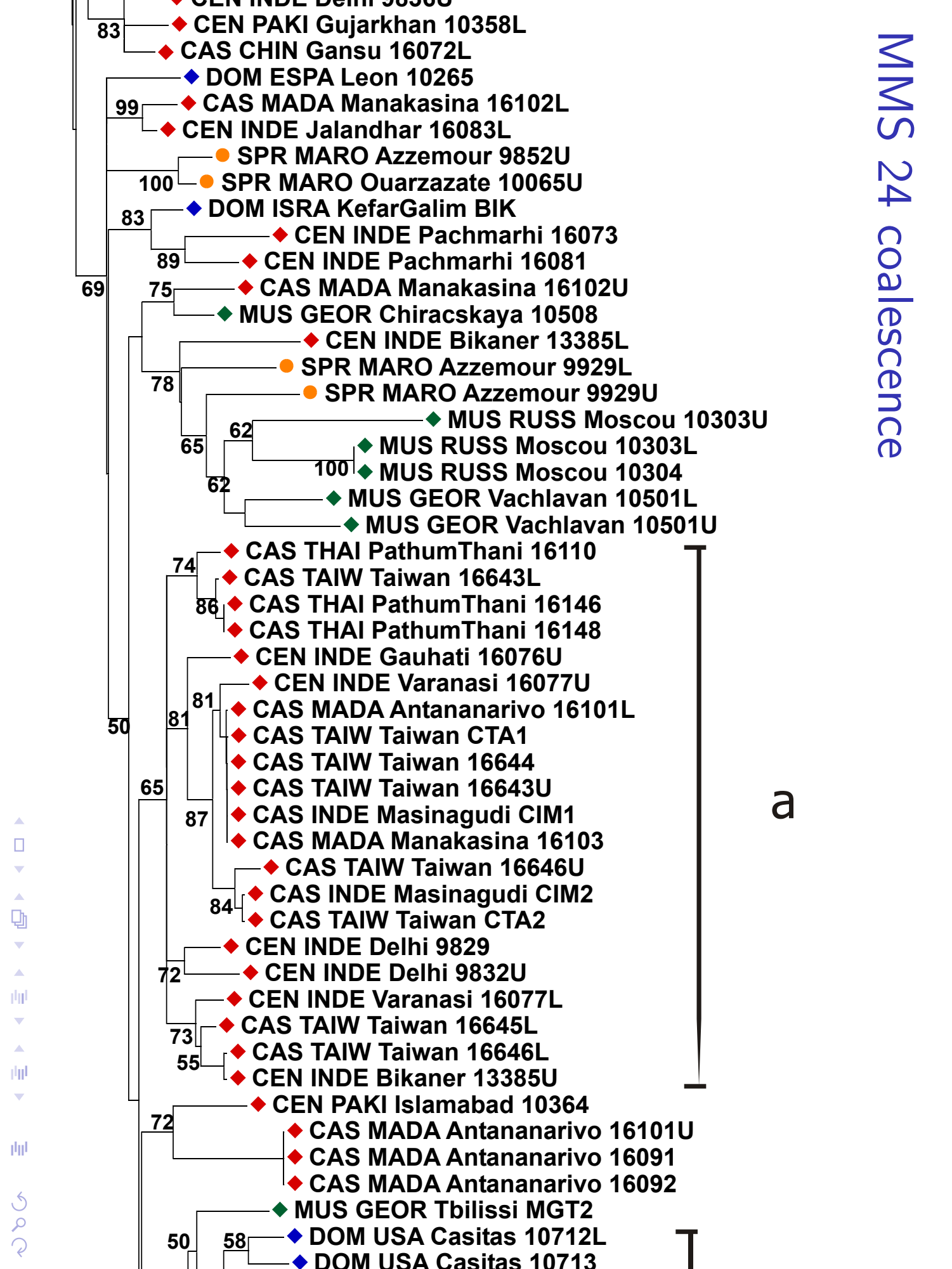
h
c
MMS 30 coalescence
10



MMS 24 coalescence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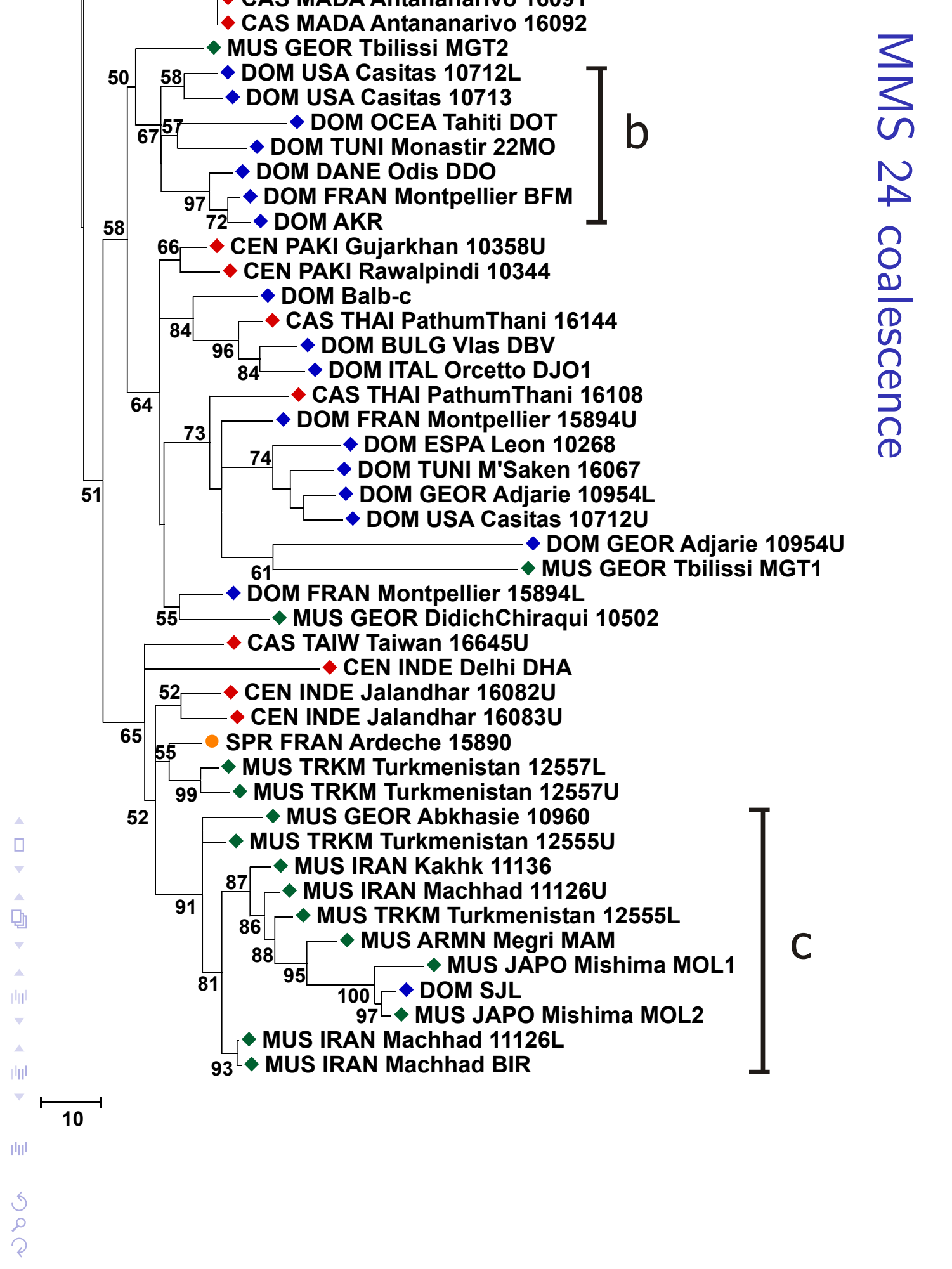
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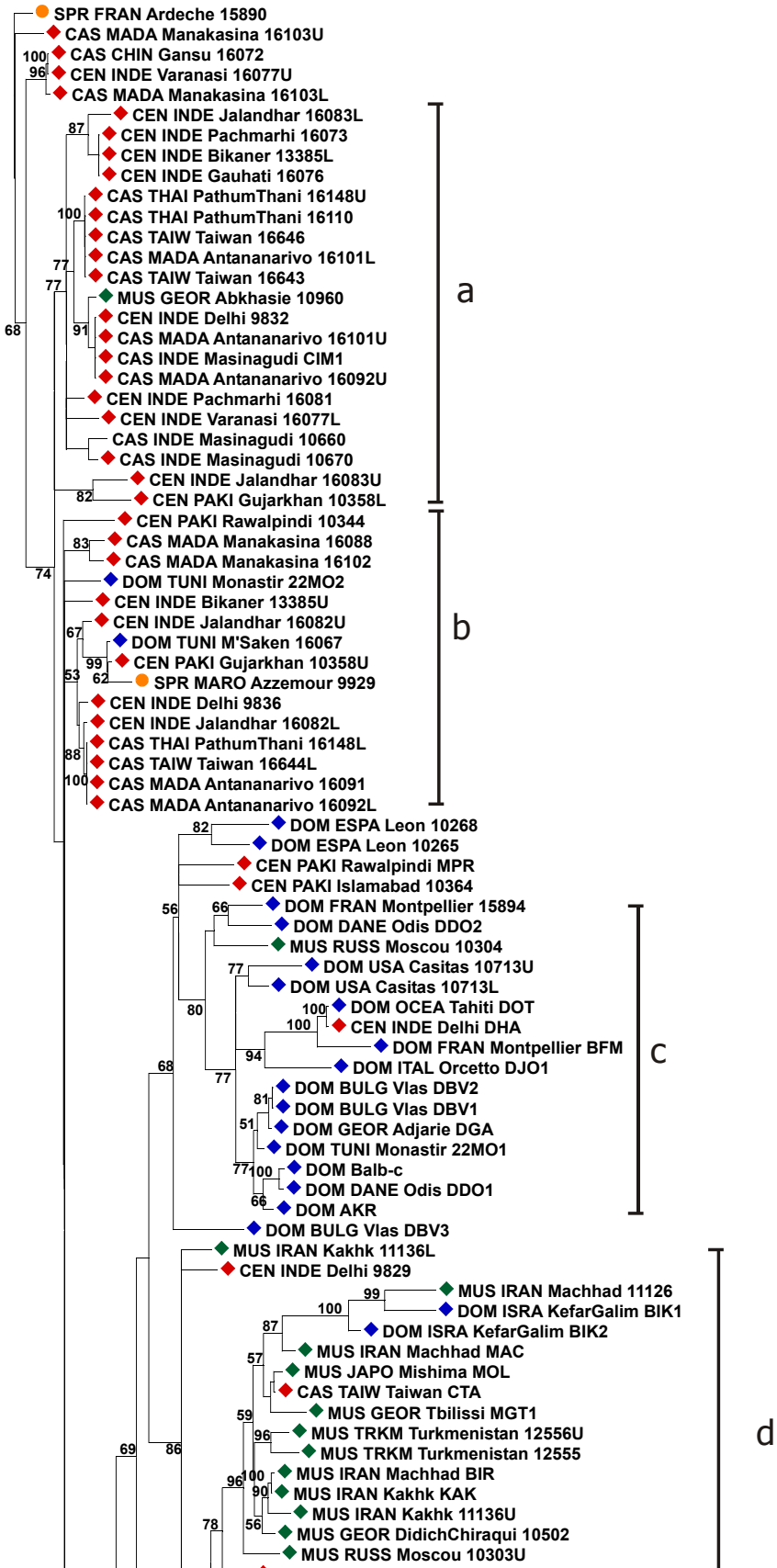
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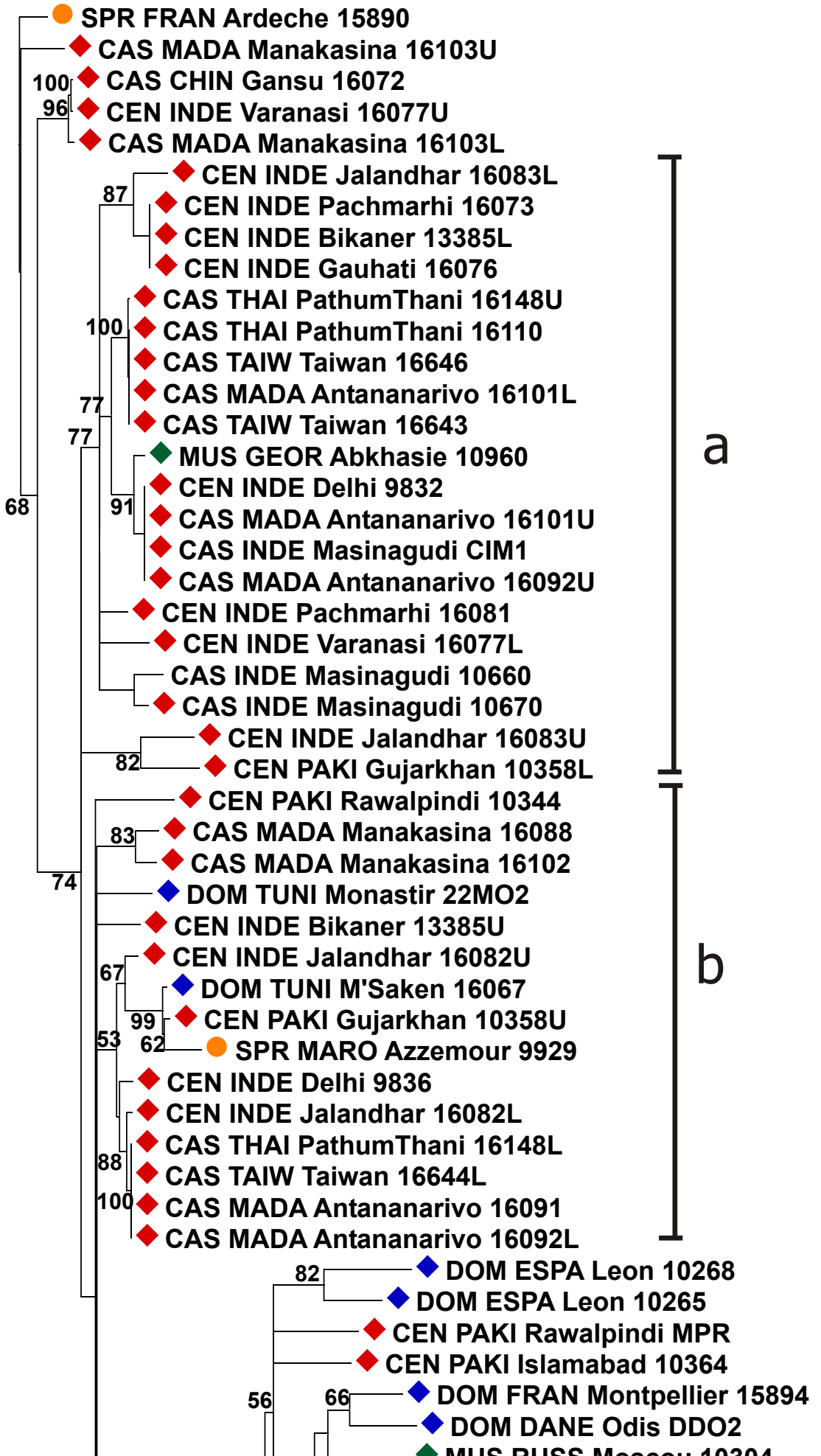
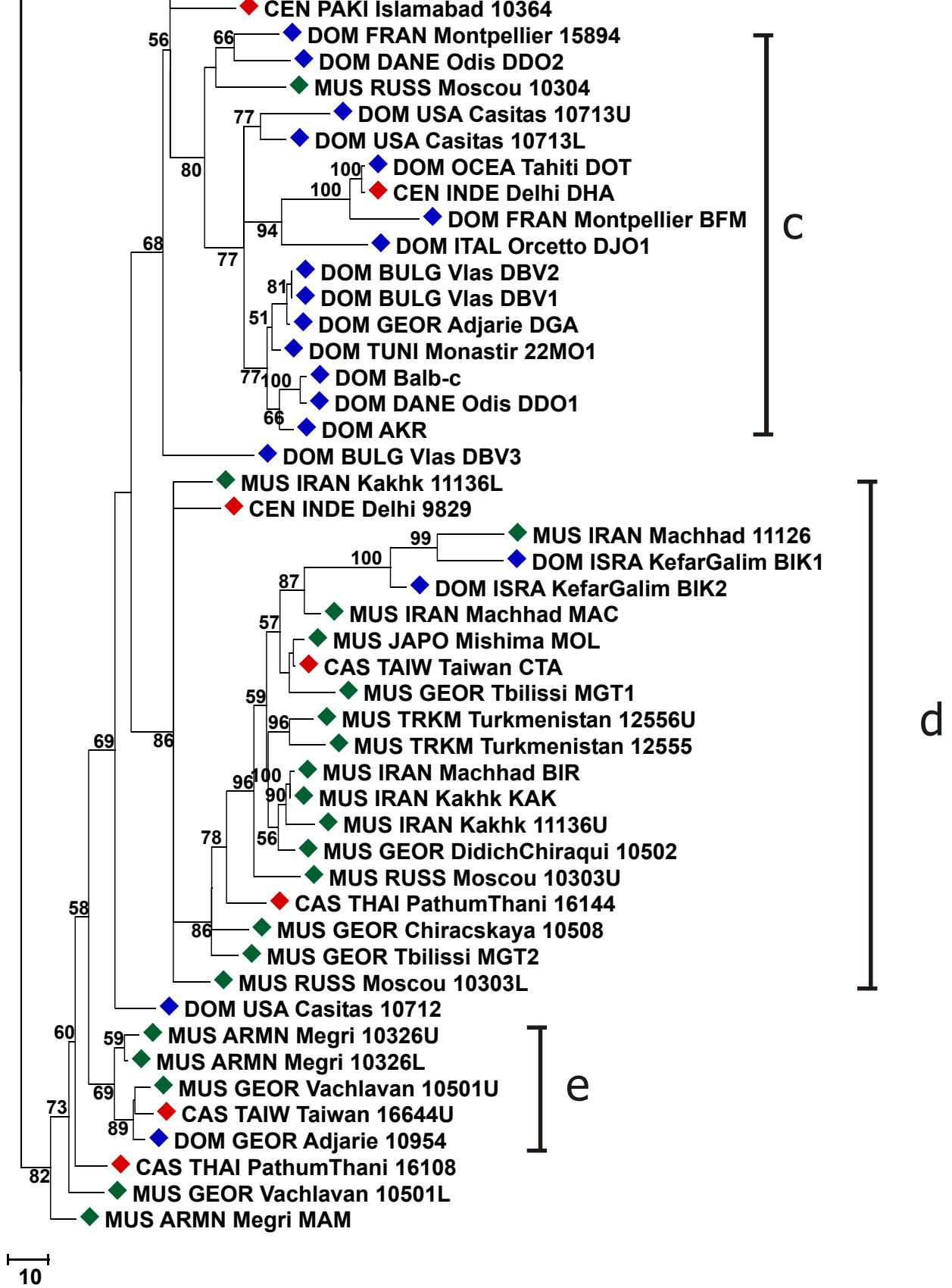


MMS 26 coalescence



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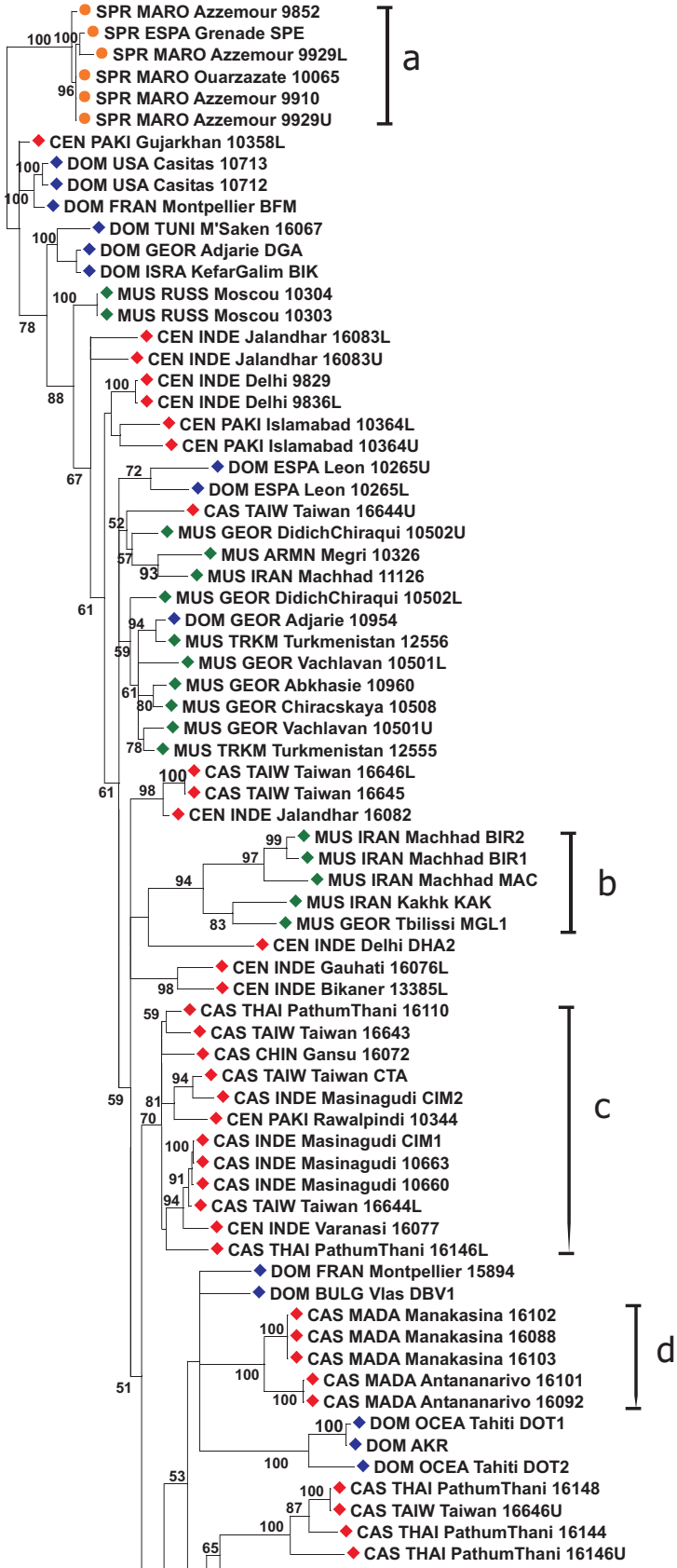
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DOM ESPA Leon 10265L
CAS TAIW Taiwan 16644U
MUS GEOR DidichChiraqui 10502U
MUS ARMN Megri 10326
MUS IRAN Machhad 11126
MUS GEOR DidichChiraqui 10502L
DOM GEOR Adjarie 10954
MUS TRKM Turkmenistan 12556
MUS GEOR Vachlavan 10501L
MUS GEOR Abkhasie 10960
MUS GEOR Chiracskaya 10508
MUS GEOR Vachlavan 10501U
MUS TRKM Turkmenistan 12555
CAS TAIW Taiwan 16646L
CAS TAIW Taiwan 16645
CEN INDE Jalandhar 16082
MUS IRAN Machhad BIR2
MUS IRAN Machhad BIR1
MUS IRAN Machhad MAC
MUS IRAN Kakhk KAK
MUS GEOR Tbilissi MGL1
b
CEN INDE Delhi DHA2
CEN INDE Gauhati 16076L
CEN INDE Bikaner 13385L
CAS THAI PathumThani 16110
CAS TAIW Taiwan 16643
CAS CHIN Gansu 16072
CAS TAIW Taiwan CTA
CAS INDE Masinagudi CIM2
CEN PAKI Rawalpindi 10344
CAS INDE Masinagudi CIM1
CAS INDE Masinagudi 10663
CAS INDE Masinagudi 10660
CAS TAIW Taiwan 16644L
CEN INDE Varanasi 16077
CAS THAI PathumThani 16146L
c
DOM FRAN Montpellier 15894
DOM BULG Vlas DBV1
CAS MADA Manakasina 16102
CAS MADA Manakasina 16088
CAS MADA Manakasina 16103
CAS MADA Antananarivo 16101
CAS MADA Antananarivo 16092
d
DOM OCEA Tahiti DOT1
DOM AKR
DOM OCEA Tahiti DOT2
CAS THAI PathumThani 16148
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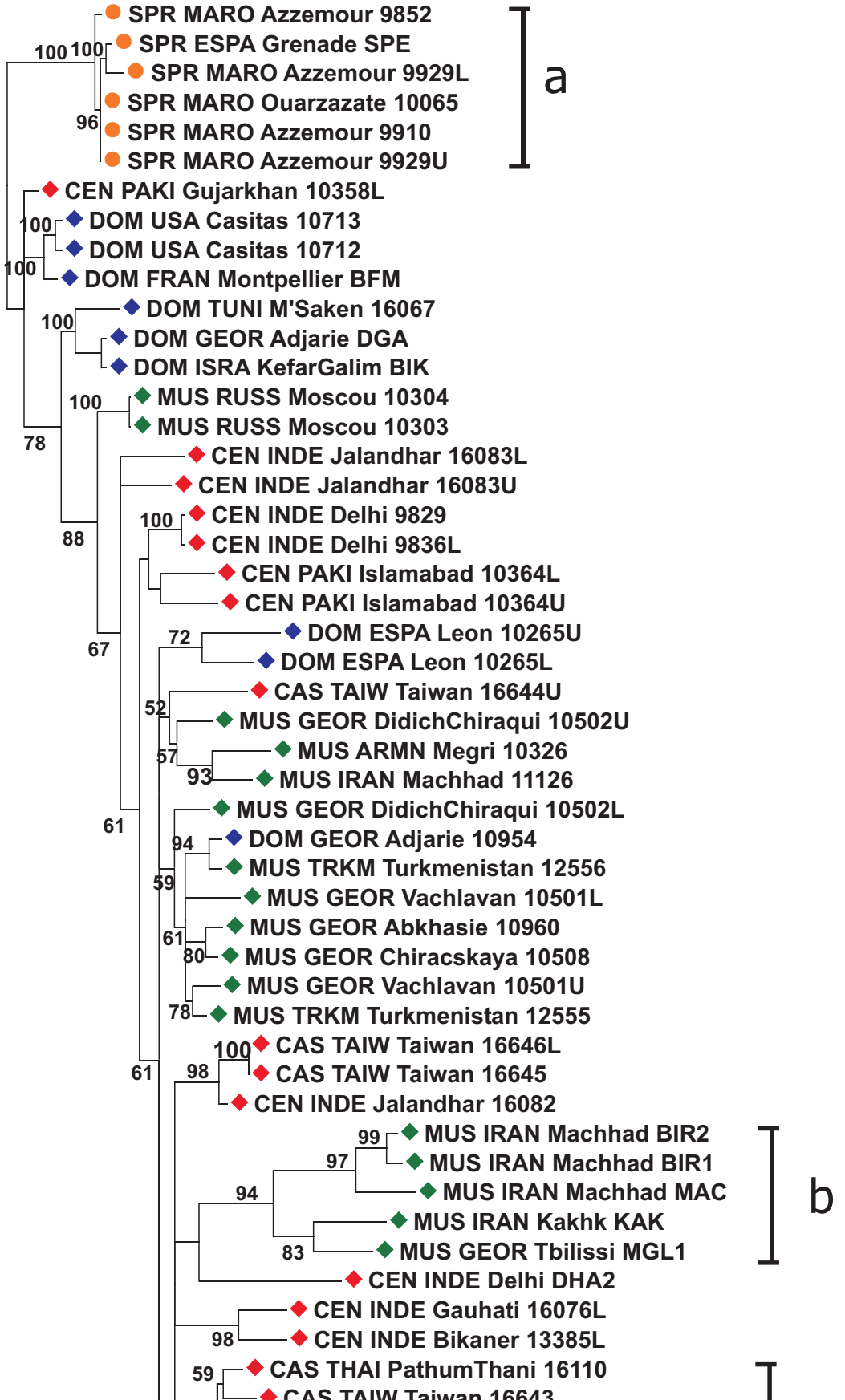
CAS THAI PathumThani 16144
CAS THAI PathumThani 16146U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SPR MARO Ouarzazate 10065
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SPR MARO Azzemour 9929U
a
CEN PAKI Gujarkhan 10358L
DOM USA Casitas 10713
DOM USA Casitas 10712
DOM FRAN Montpellier BFM
DOM TUNI M'Saken 16067
DOM GEOR Adjarie DGA
DOM ISRA KefarGalim BIK
MUS RUSS Moscou 10304
MUS RUSS Moscou 10303
CEN INDE Jalandhar 16083L
CEN INDE Jalandhar 16083U
CEN INDE Delhi 9829
CEN INDE Delhi 9836L
CEN PAKI Islamabad 10364L
CEN PAKI Islamabad 10364U
DOM ESPA Leon 10265U
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CAS TAIW Taiwan 16644U
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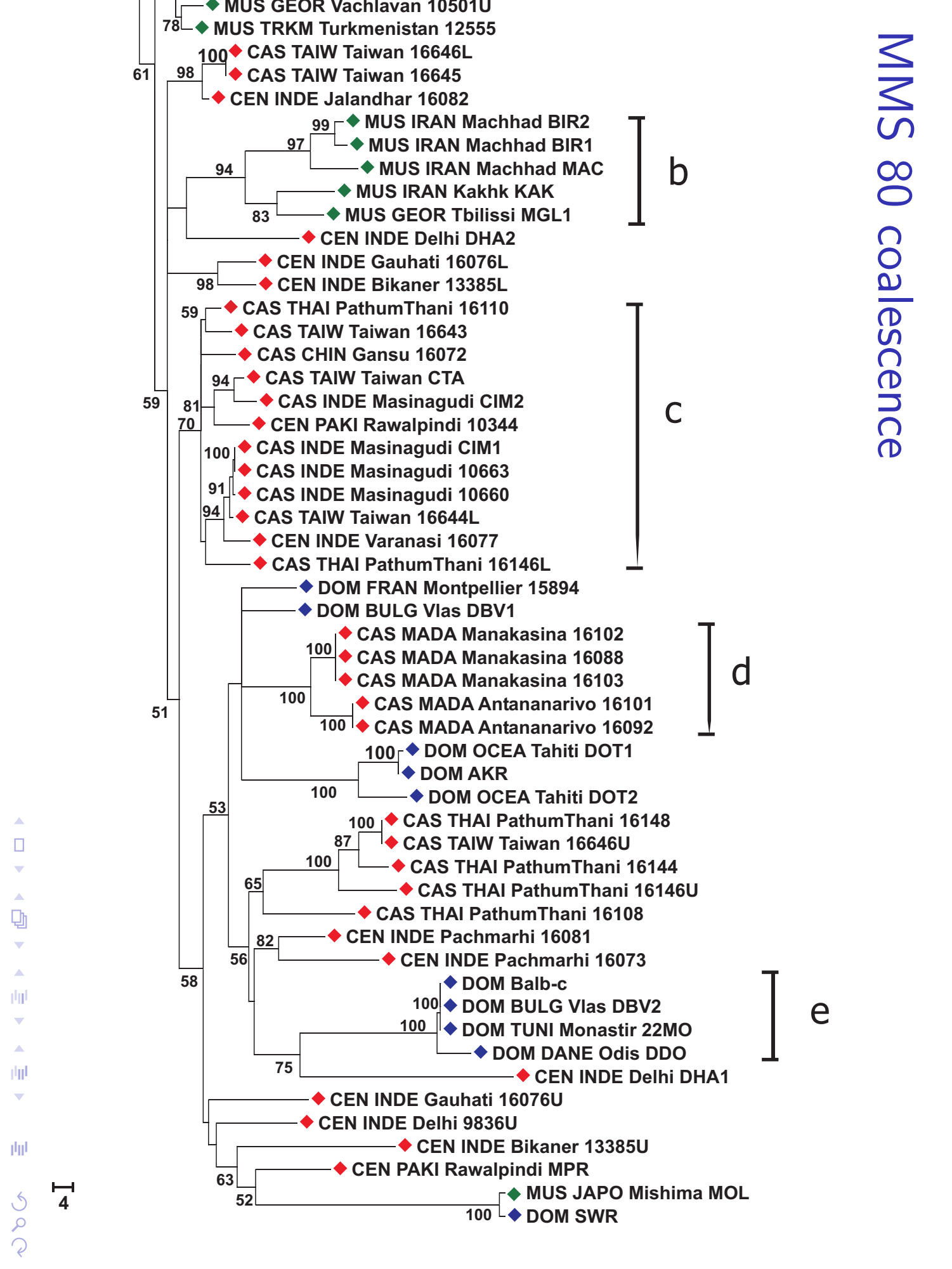
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MUS TRKM Turkmenistan 12555
CAS TAIW Taiwan 16646L
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CEN INDE Pachmarhi 16081
CEN INDE Pachmarhi 16073
DOM Balb-c
DOM BULG Vlas DBV2
DOM TUNI Monastir 22MO
DOM DANE Odis DDO
CEN INDE Delhi DHA1
CEN INDE Gauhati 16076U
CEN INDE Delhi 9836U
CEN INDE Bikaner 13385U
CEN PAKI Rawalpindi MPR
MUS JAPO Mishima MOL
DOM SWR
b
c
d
e
4

Intruders

Locus	ID	clade	Average distance to CAS	CEN	DOM	MUS
24	CAS THAI Pathumtani 16108	DOM	52	53	40	61
24	CAS THAI Pathumtani 16144	DOM	45	47	37	60
24	DOM SJL	MUS	71	74	74	53
26	MUS GEOR Abkhasie 10960	CAS	23	34	84	72
26	CEN INDE Dehli DHA	DOM	99	96	58	91
26	MUS RUSS Moscou 10304	DOM	69	62	60	92
26	CAS TAIW Taiwan CTA	MUS	77	80	73	42
80	DOM GEOR Adjarie 10954	MUS	37	39	56	28
80	DOM BULG Vlas DBV1	CAS	40	50	50	51
80	DOM FRAN Montpellier 15894	CAS	42	49	51	50

MMS24 intruders alignments

```
DOM_ESPA_Leon     CTCCC~CCT~~oTCTTCoTC~oTCToT~~oTTCCCC~~
DOM_USA_Casit     CTCCo~CCo~oo~CTTCoTC~oTCTo~~ooTTCCCC~~
DOM_GEOR_Adja     CTCCT~CCTT~o~CTTCoTCCoTCTo~~ooTTCCCC~~
DOM_TUNI_M'Sa     CTCCT~CCT~~oTCTTCoTC~oTCTo~~ooTTC~~~~~
DOM_FRAN_Mont     CTCCT~CCT~~oTCTTC~~~~oTCTT~~~oTTCCCC~~
CAS_THAI_Path     CTCCT~CCT~~oTCTTC~~~~oTCoT~~~CT~~~~~~~
CAS_THAI_Path     CTCCT~CCTT~~TCTTCTTC~TTCTTTT~~TTC~~~~~
DOM_BULG_Vlas     CTCCTTC~TT~~TCTTCTTC~TTCTTTT~~TTCCCCTC
DOM_ITAL_Orce     CTCCT~CCTT~~TCTTCTTC~TTCTTT~~oTTCCCCT~
                  ****  *..    ****     **.     *..
```

MMS30 intruders alignments

```
DOM ESPA   GYKKKWGKLKYLWKGWGKoGGYWYKKoKKK~YYY~KG
DOM TURQ   GYKKKWGKWKYoWKGWGKoGGYLYKKoKKK~YYY~KG
DOM TURQ   GYKKKWGKWKYoWKGWGKoGGYLYKKoK~~~YYY~KG
DOM GEOR   GYKKKWGKLKYoWKGWGKoGGYWYKKoK~~~YYY~KG
DOM ISRA   GYKKKWGKLKYoWKGWGKoGGYWYKKoKKK~YYY~KG
DOM ESPA   GYKKKWGKLKWoWKGWGKoGGYWYKKoKKK~YYY~KG
DOM FRAN   GYKKKWGKLKYLWKGWGKWGGYWYKKoKKK~YY~~~G
DOM FRAN   GYKKKWGKLKYoWKGWGKWGGYYYKKoKKK~YY~~~G
DOM ITAL   GYKKKWGKLKYoWKGWGKoGGYWYKKoKKK~YY~~~G
DOM TURQ   GYKKKWGKLKYoWKGWGLWGGYWYKKoKKK~YYY~KG
CEN PAKI   GYKKKWGKoKYKWKGWGKoGGYWYKKoKKK~YYY~KG
CEN INDE   GYKKKWGLWKYooKoWGLWGGYWYKKoKKKKYY~~KG
CAS MADA   GYKKK-GLLKYLoKGWGLoGGKWKKKoKKKKYY~~KG
CAS MADA   GYKKKWGLLKYLoKGWGLoGGKWKKKoKKKKYY~~KG
           *****...  ..  .*.**  .**.     **    **   .*
```

MMS30 intruders alignments

```
DOM ESPA   GYKKKWGKLKYLWKGWGKoGGYWYKKoKKK~YYY~KG
DOM TURQ   GYKKKWGKWKYoWKGWGKoGGYLYKKoKKK~YYY~KG
DOM TURQ   GYKKKWGKWKYoWKGWGKoGGYLYKKoK~~~YYY~KG
DOM GEOR   GYKKKWGKLKYoWKGWGKoGGYWYKKoK~~~YYY~KG
DOM ISRA   GYKKKWGKLKYoWKGWGKoGGYWYKKoKKK~YYY~KG
DOM ESPA   GYKKKWGKLKWoWKGWGKoGGYWYKKoKKK~YYY~KG
DOM FRAN   GYKKKWGKLKYLWKGWGKWGGYWYKKoKKK~YY~~~G
DOM FRAN   GYKKKWGKLKYoWKGWGKWGGYYYKKoKKK~YY~~~G
DOM ITAL   GYKKKWGKLKYoWKGWGKoGGYWYKKoKKK~YY~~~G
DOM TURQ   GYKKKWGKLKYoWKGWGLWGGYWYKKoKKK~YYY~KG
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           *****...  ..  .*.**  .**.     **    **   .*
```

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DOM ESPA   GYKKKWGKLKYLWKGWGKoGGYWYKKoKKK~YYY~KG
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DOM ISRA   GYKKKWGKLKYoWKGWGKoGGYWYKKoKKK~YYY~KG
DOM ESPA   GYKKKWGKLKWoWKGWGKoGGYWYKKoKKK~YYY~KG
DOM FRAN   GYKKKWGKLKYLWKGWGKWGGYWYKKoKKK~YY~~~G
DOM FRAN   GYKKKWGKLKYoWKGWGKWGGYYYKKoKKK~YY~~~G
DOM ITAL   GYKKKWGKLKYoWKGWGKoGGYWYKKoKKK~YY~~~G
DOM TURQ   GYKKKWGKLKYoWKGWGLWGGYWYKKoKKK~YYY~KG
CEN PAKI   GYKKKWGKoKYKWKGWGKoGGYWYKKoKKK~YYY~KG
CEN INDE   GYKKKWGLWKYooKoWGLWGGYWYKKoKKKKYY~~KG
CAS MADA   GYKKK-GLLKYLoKGWGLoGGKWKKKoKKKKYY~~KG
CAS MADA   GYKKKWGLLKYLoKGWGLoGGKWKKKoKKKKYY~~KG
           *****... .. .*.** .**.    **   **   .*
```

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  2. past and present exchanges within the species range
- when handled with appropriate comparison algorithms [Bérard, Rivals, 2003]
- MS versus SNPs and micro-satellites
- Mice genomes: set of interrelated gene pools, still able to exchange genes, even on chromosome X
- Difficult to find genes important for speciation

Publications and algorithms

- S. Bérard, E. Rivals, *Comparison of Minisatellites*, *J. of Computational Biology*, p. 357-372, vol. 10(3-4), 2003.

- S. Bérard, F. Nicolas, J. Buard, O. Gascuel, E. Rivals, *A Fast and Specific Alignment Method for Minisatellite Maps*, *Evolutionary Bioinformatics Online*, 2:327–344, 2006.

  MS_Align http://atgc.lirmm.fr/

- F. Bonhomme, E. Rivals, A. Orth, G.R. Grant, A. J. Jeffreys, P.R.J. Bois
  Species wide distribution of highly polymorphic minisatellite markers reveals long range gene flow and frequent genetic exchanges among House Mouse subspecies submitted

Credits and collaborators

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- Dpt Genetics, Univ. Leicester, GB
  - G. Grant
  - A.J. Jeffreys
- St Jude Childrens Research Hospital, Memphis, USA:
  - P. Bois
- Support: ACI IMPBIO REPEVOL, BioSTIC LR, Génopole LR.

ACI IMPBIO REPEVOL

http://www.lirmm.fr/~rivals/RESEARCH/REPEVOL/