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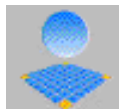
Minisatellite Markers Reveals Frequent Genetic Exchanges among House Mouse Subspecies

Eric Rivals

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LIRMM, CNRS, Université Montpellier 2

<http://www.lirmm.fr/~rivals>



Outline

1. Minisatellite data
2. Methods
 - 2.1 Protocol
 - 2.2 Molecular Divergence Estimation - Alignment
 - 2.3 Robustness and Confidence
3. Results
 - 3.1 Coalescence
 - 3.2 Intruders
4. Conclusion

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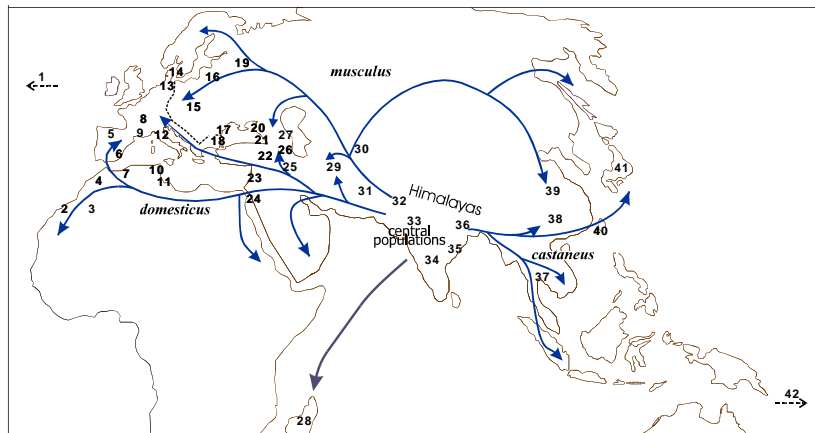
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- ▶ MS informative for intra-species evolution

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 (H_e) 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 = "aggagattcagttcaca**C**tatacagaagatggtgtcagc"

L = "aggagattcacttcaga**G**tatacagaagatggtgtcagc"

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Example of **maps** in wild mice

ID (species, location) map

SPR_FRAN_Ardeche KGKGLKHLKLLKYKG

CEN_INDE_Gauhati GKKKKWGGKKYKWKGWGHoGoKWKKKo**L**YY

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DOM_GEOR_Adjarie GYKKKWGKLYoWKGWKGKoGGYWYKKoK**Y**YYKG

DOM_OCEA_Tahiti GYKKKWGKLYoWKGWKGKoGGYWYKKoK**KK**YYYYKG

MUS_GEOR_Tbilissi GYYKGYKYKGYKKKWGKoKYoWKYYKG

Methods

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

Evolutionary model

- ▶ Substitution : WGY → WKY

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Evolutionary model

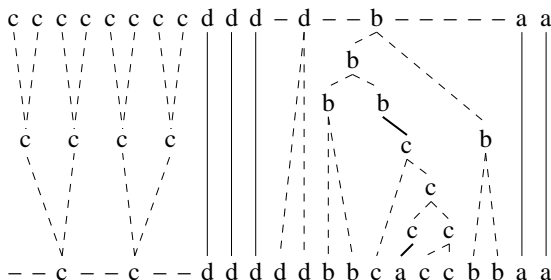
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\Rightarrow variation in their number of units

Example of an alignment of 2 maps



An alignment produced by *MS_Align* between maps *ccccccccdddbbaa* and *ccccccccdddbbaa* 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

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

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
GYKKKGWGKoGGYWYKKoKKKYYYKG

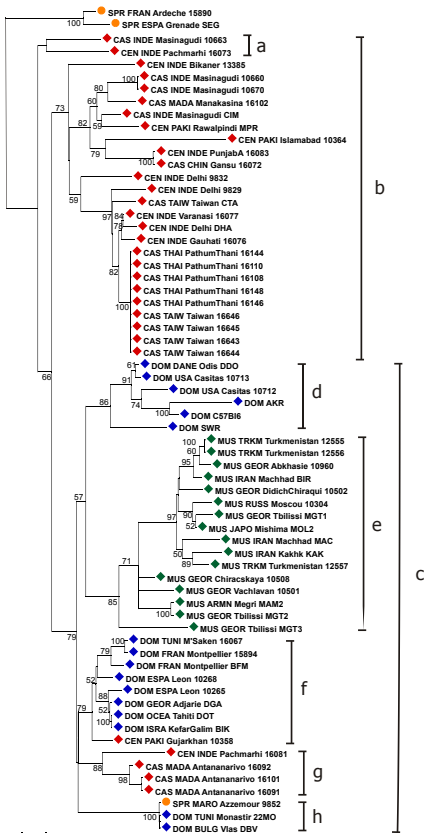
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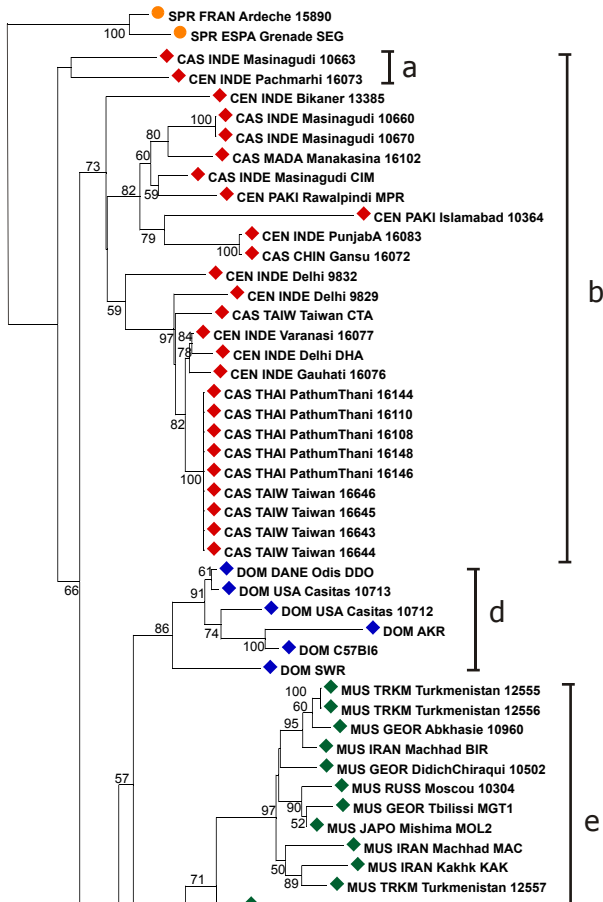
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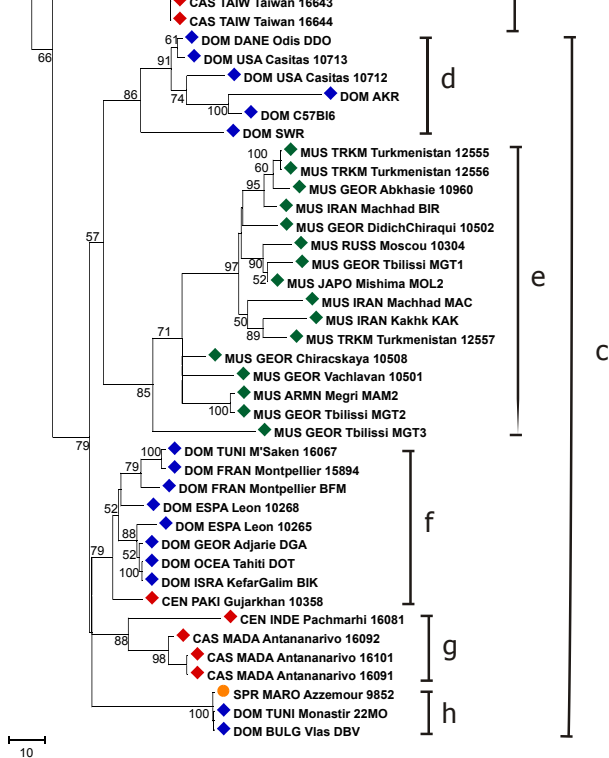
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GYKKKGWGK_oGGYWYKK_oKKKYYYKG

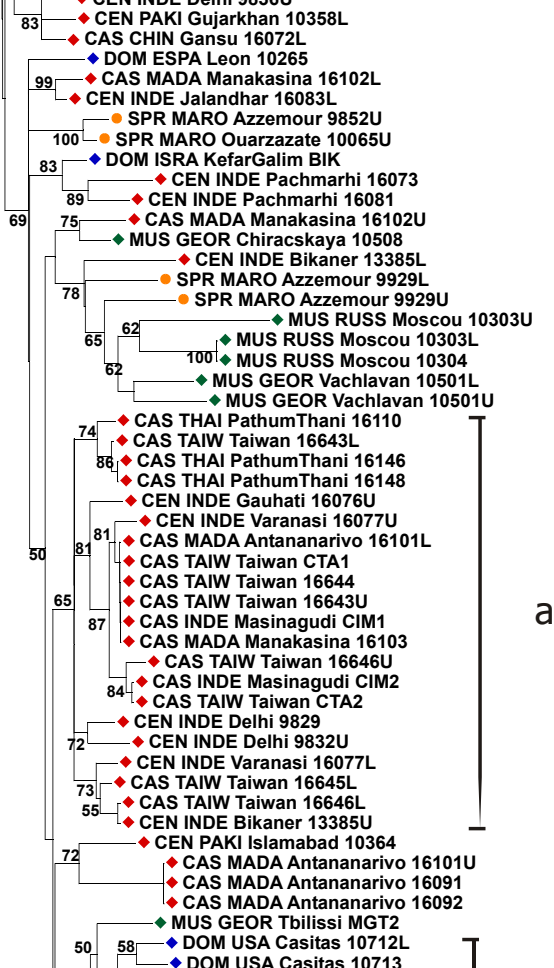
At MMS 26: CEN_INDE_Dehli_DHA; DOM_OCEA_Tahiti_DOT
YGGGGGGGGAGGGGAGAAGGYAAGGGGAAAAGAGAAGAAGGGG

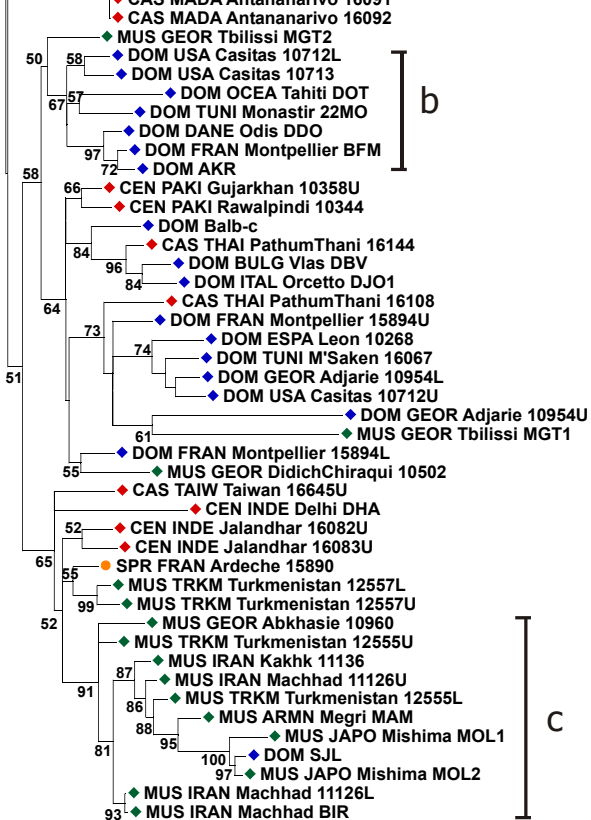


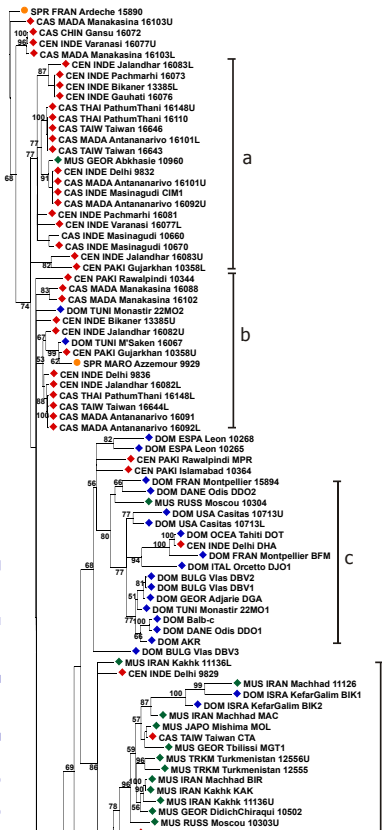


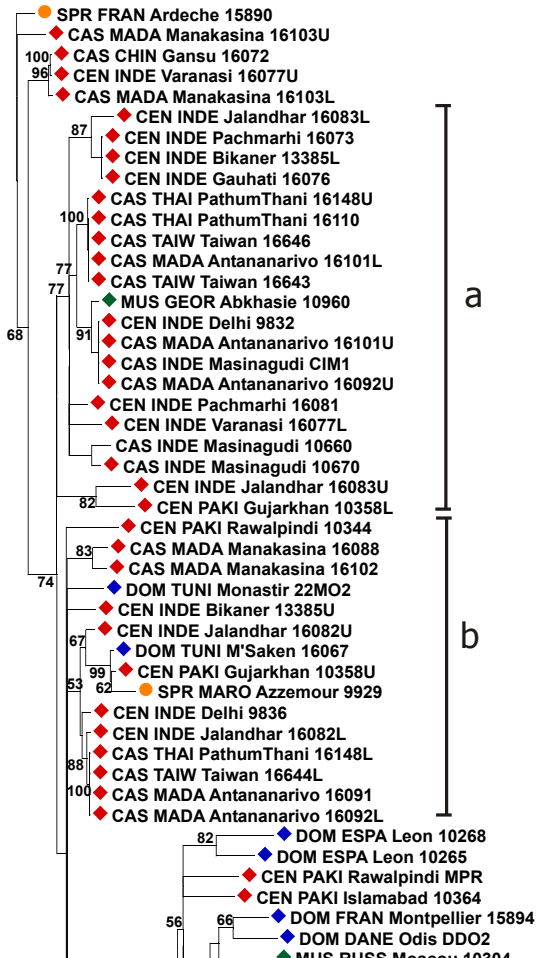
MMS 30 coalescence



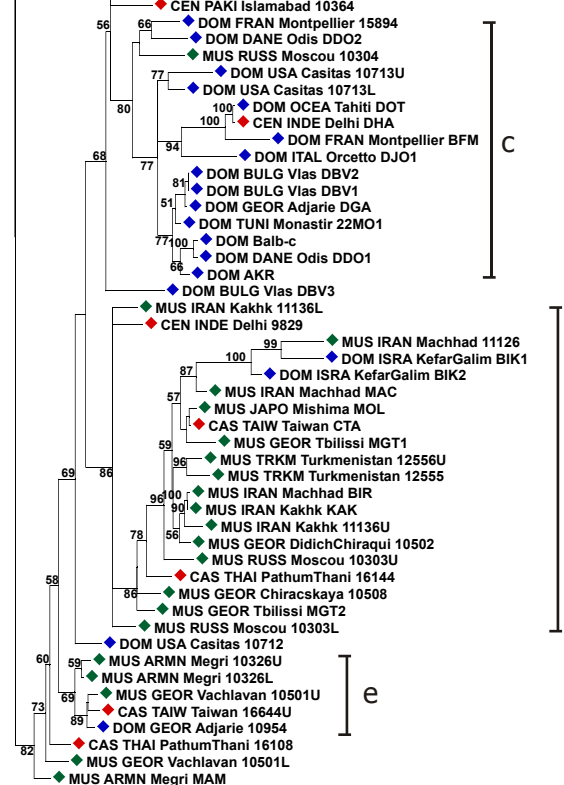


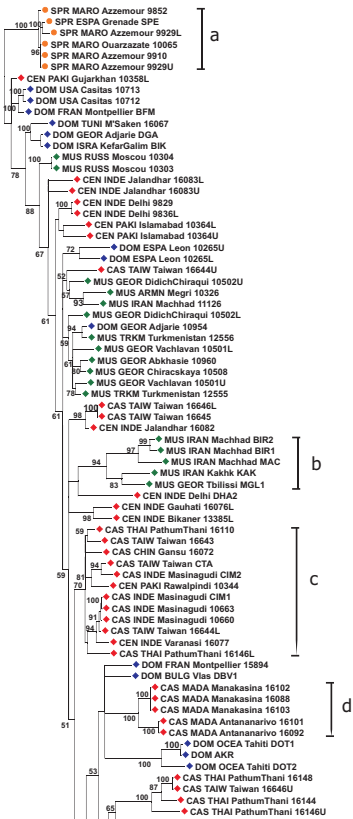


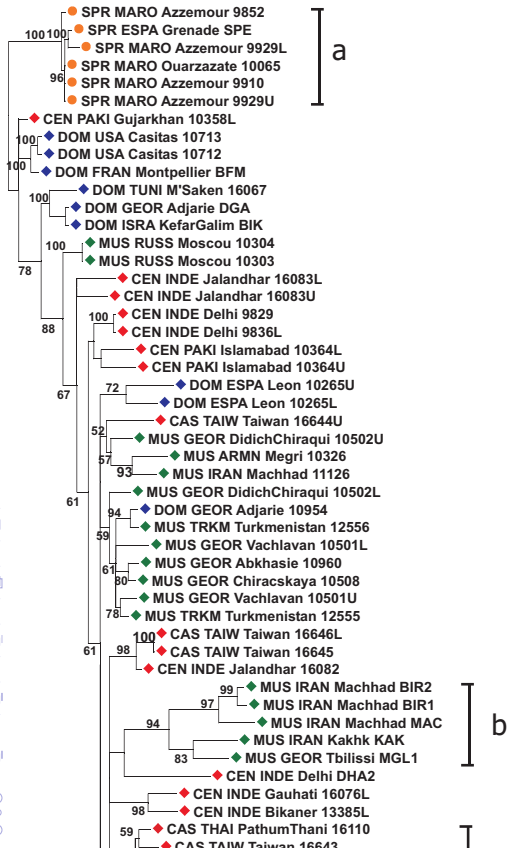


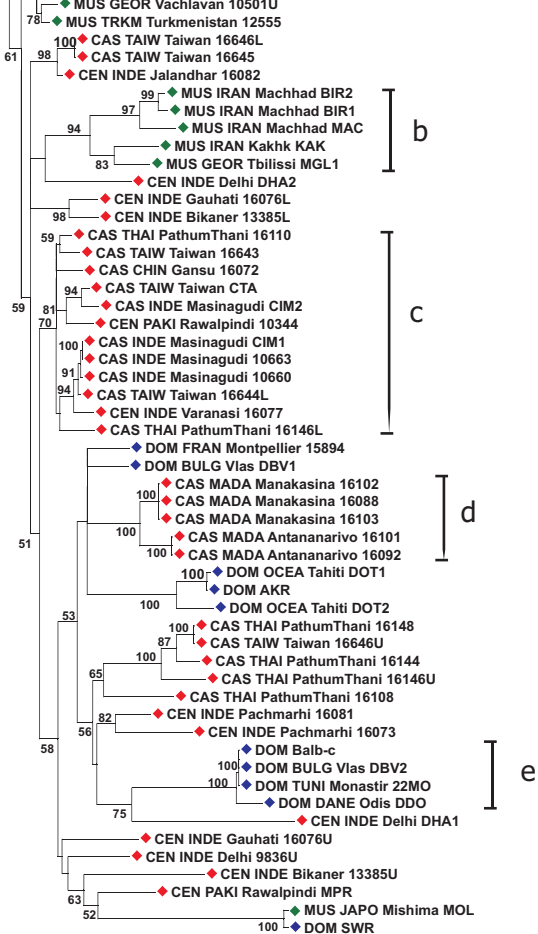


MMS 26 coalescence









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  GYKKKWGK LKYLWKGWGK oGGYWYKK oKKK~YYY~KG
DOM TURQ  GYKKKWGK WKY oWKGWGK oGGYLYKK oKKK~YYY~KG
DOM TURQ  GYKKKWGK WKY oWKGWGK oGGYLYKK oK~~~YYY~KG
DOM GEOR  GYKKKWGK LKY oWKGWGK oGGYWYKK oK~~~YYY~KG
DOM ISRA  GYKKKWGK LKY oWKGWGK oGGYWYKK oKKK~YYY~KG
DOM ESPA  GYKKKWGK LKW oWKGWGK oGGYWYKK oKKK~YYY~KG
DOM FRAN  GYKKKWGK LKYLWKGWGK WGGYWYKK oKKK~YY~~~G
DOM FRAN  GYKKKWGK LKY oWKGWGK WGGY Y Y K K oKKK~YY~~~G
DOM ITAL  GYKKKWGK LKY oWKGWGK oGGYWYKK oKKK~YY~~~G
DOM TURQ  GYKKKWGK LKY oWKGWGL WGGYWYKK oKKK~YYY~KG
CEN PAKI  GYKKKWGK oKYKWKWGK oGGYWYKK oKKK~YYY~KG
CEN INDE  GYKKKWGL WKY o o K oWGL WGGYWYKK oKKKKYY~~KG
CAS MADA  GYKKK-GL LKYL oKGWGL oGGKWKKK oKKKKYY~~KG
CAS MADA  GYKKKWGL LKYL oKGWGL oGGKWKKK oKKKKYY~~KG
***** . . . . * . ** . ** .      **   **   .*
```

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DOM FRAN  GYKKKWGK LKYLWKGWGK WGGYWYKK oKKK~YY~~~G
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DOM ESPA  GYKKKWGK LKYLWKGWGK o GGYWYKK o KKK~YYY~KG
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DOM TURQ  GYKKKWGK WKY o WKGWGK o GGYLYKK o K~YY~YYY~KG
DOM GEOR  GYKKKWGK LKY o WKGWGK o GGYWYKK o K~YY~YYY~KG
DOM ISRA  GYKKKWGK LKY o WKGWGK o GGYWYKK o KKK~YYY~KG
DOM ESPA  GYKKKWGK LKW o WKGWGK o GGYWYKK o KKK~YYY~KG
DOM FRAN  GYKKKWGK LKYLWKGWGK WGGYWYKK o KKK~YY~YY~G
DOM FRAN  GYKKKWGK LKY o WKGWGK WGGY WYKK o KKK~YY~YY~G
DOM ITAL  GYKKKWGK LKY o WKGWGK o GGYWYKK o KKK~YY~YY~G
DOM TURQ  GYKKKWGK LKY o WKGWGL WGGY WYKK o KKK~YYY~KG
CEN PAKI  GYKKKWGK o KYKWKWGK o GGYWYKK o KKK~YYY~KG
CEN INDE  GYKKKWGL WKY o o K o WGL WGGY WYKK o KKKKYY~KG
CAS MADA  GYKKK-GL LKYL o KGWGL o GGKWKKK o KKKKYY~KG
CAS MADA  GYKKKWGL LKYL o KGWGL o GGKWKKK o KKKKYY~KG
***** . . . . * . ** . ** .      **   **   . *
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- ▶ 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

- ▶ ISEM, Montpellier, France
 - F. Bonhomme
 - A. Orth
- ▶ 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/>