# Importance of Population Genetics

Gene trees do not necessarily reflect phylogenetic relationships among species (species tree or population tree).

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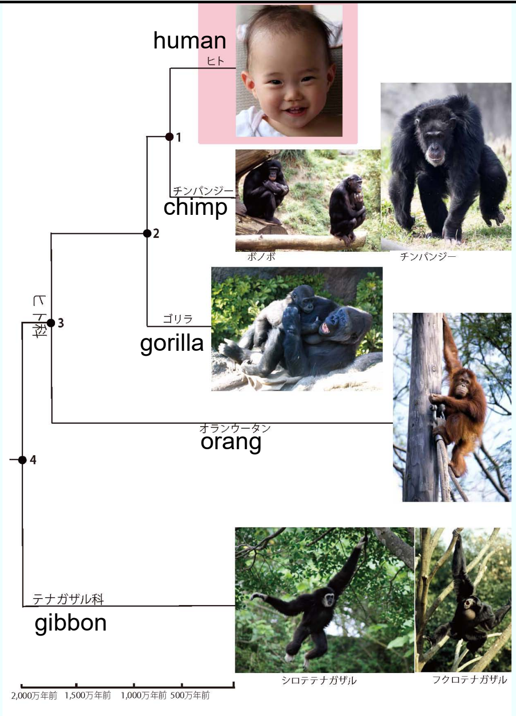
## Established Tree of Hominoidea

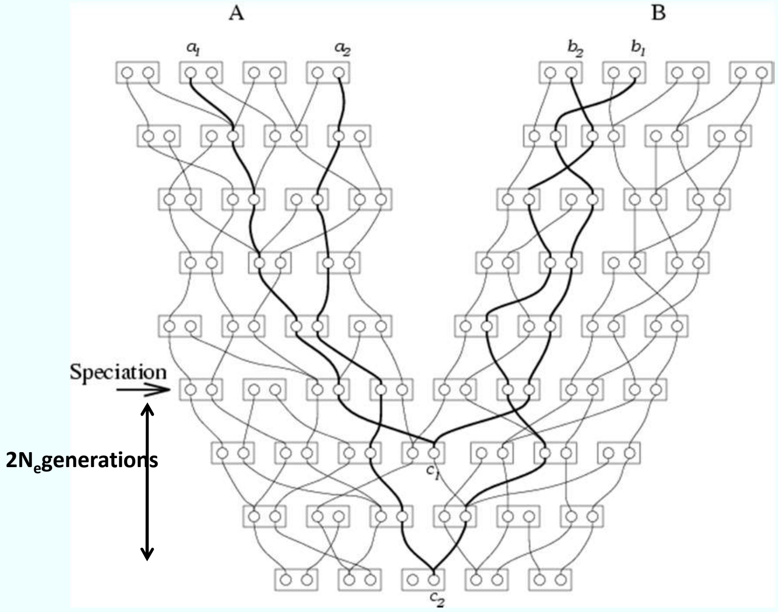


**Chimpanzees and bonobos are closer to humans than to gorillas . This relationship was established by Satoshi Horai in 1990's with the mitochondrial genome analysis, but …**

Number of genes significantly (PP>0.95) supporting the 3 topologies among human, chimp and gorilla

| | Gene | % |
|---|---|---|
| ((Human,Chimp),Gorilla) | 3,814 | 79.3 |
| ((Chimp,Gorilla),Human) | 504 | 10.5* |
| ((Human,Gorilla),Chimp) | 492 | 10.2* |

*: Incongruent trees (20.7%)
Modified from Table 3 of Ebersberger et al. (2007, Mol. Biol. Evol. 24, 2266-2276)



**2N$_e$ generations**

**Under the neutral evolution, a separation in a gene tree is expected to be older than the speciation time by 2N$_e$ generations .**

Hasegawa, Kishino & Yano (1989)
*J. Human Evol.* 18, 461-476

# Molecular evolution rate

**Evolution rate: v (substitutions/site/year)**
**Effective population size: $N_e$**
**Mutation rate: μ**
**Probability of fixation of the gene: u**
**$v = 2N_e\mu u = \mu$ : Under the neutral theory（$u = 1/2N_e$）**

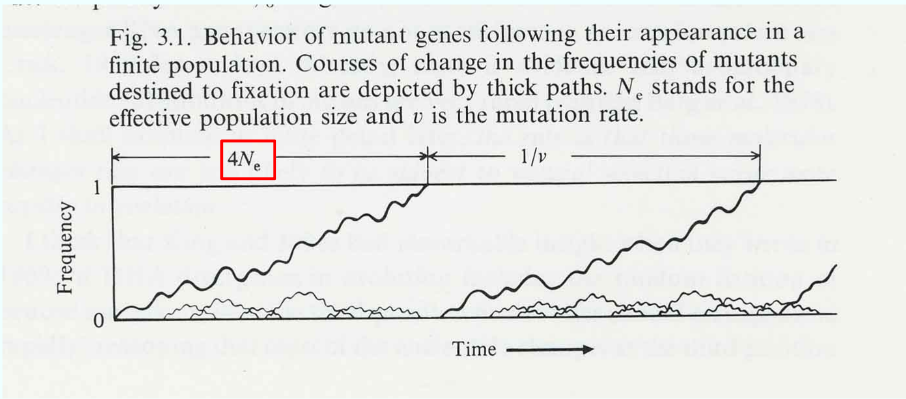
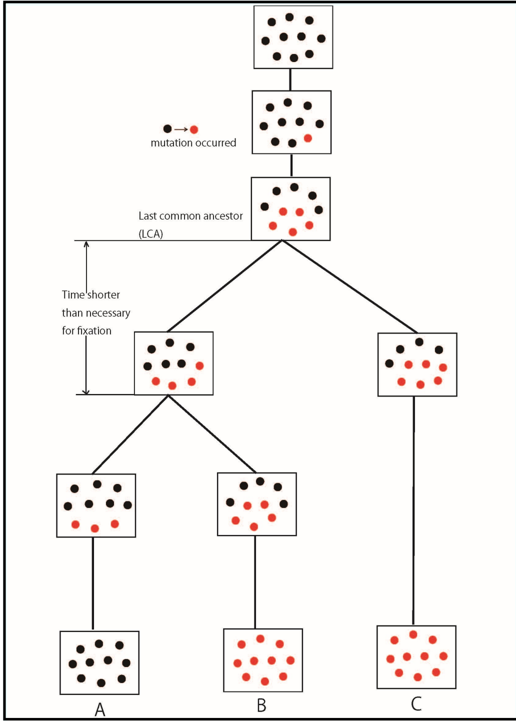


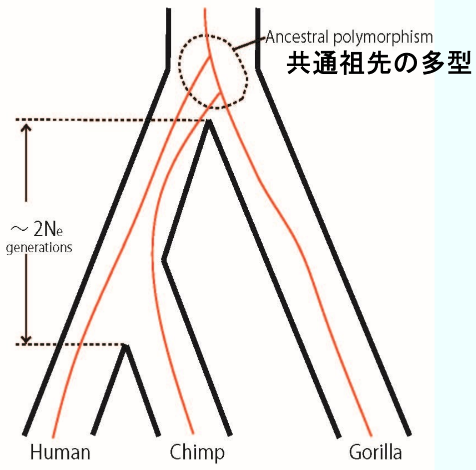
Fig. 3.1. Behavior of mutant genes following their appearance in a finite population. Courses of change in the frequencies of mutants destined to fixation are depicted by thick paths. $N_e$ stands for the effective population size and $v$ is the mutation rate.



Incomplete lineage sorting of ancestral polymorphism:

A/B clade in the species tree, but B can be closer to C in a gene tree.

## Incongruent gene tree



$N_e$: Effective population size

**Incongruent gene tree from the species tree** by incomplete lineage sorting of ancestral polymorphism

The time separation the two speciation events is shorter than $2N_e$ generations

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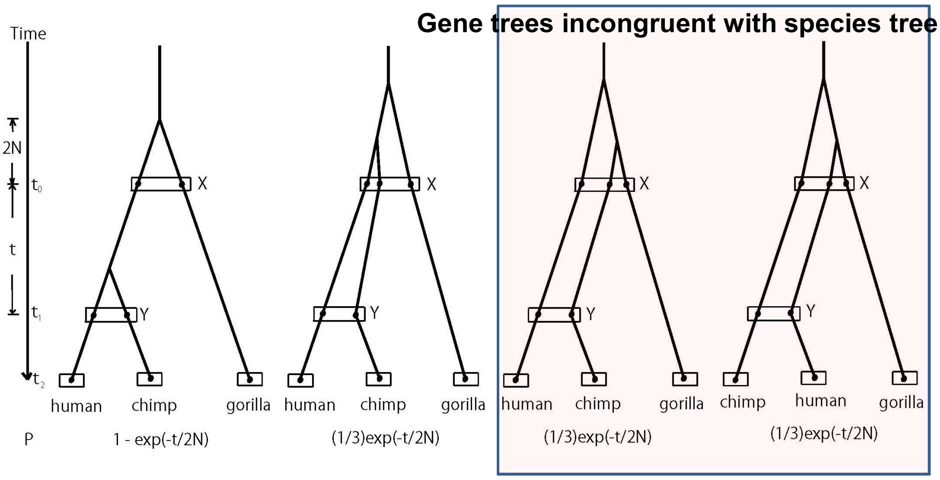
## Gene trees incongruent with species tree



Relationships between the species tree and the gene tree for the case of the three species of human, chimpanzee and gorilla. Redrawn from Pamilo and Nei (1988).

P：Probability of a gene tree under the neutral theory.

## Probabilities of gene trees

| $T/2N_e$ | ((human, chimp), gorilla) | (human,(chimp,gorilla) ) + ((human,gorilla),chimp) |
|---|---|---|
|  | $1-e^{-T/2N_e}$ | $(2/3)e^{-T/2N_e}$ |
| 0.5 | 59.6% | 40.4% |
| 1 | 75.5% | 24.5% |
| 2 | 91.0% | 9.0% |
| 4 | 98.8% | 1.2% |

Number of genes significantly (PP>0.95) supporting the 3 topologies among human, chimp and gorilla

|  | Gene | % |
|---|---|---|
| ((Human,Chimp),Gorilla) | 3,814 | 79.3 |
| ((Chimp,Gorilla),Human) | 504 | 10.5* |
| ((Human,Gorilla),Chimp) | 492 | 10.2* |

*: Incongruent trees (20.7%)
Modified from Table 3 of Ebersberger et al. (2007, *Mol. Biol. Evol.* 24, 2266-2276)

Ebersberger et al. (2007)

Human Genetic Ancestry 2271

% of gene trees rejecting the human/chimp clade

Estimated effective population size of the human/chimp common ancestor

**Effective population size of X-chromosome is ¾ of those of autosomes, …**

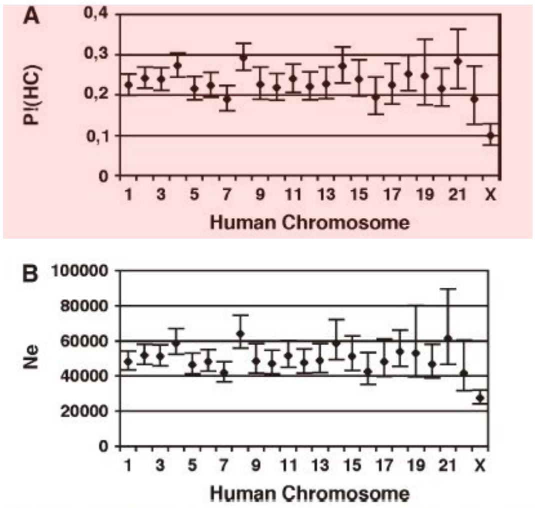


FIG. 3.—(*A*) Variation of the probability to observe a sequence tree significantly rejecting the human–chimp sister group (*P*!(HC)) among the human chromosomes. (*B*) Variation of the effective population size estimate of the human–chimp ancestral species among the human chromosomes. Bars denote the 95% CI.

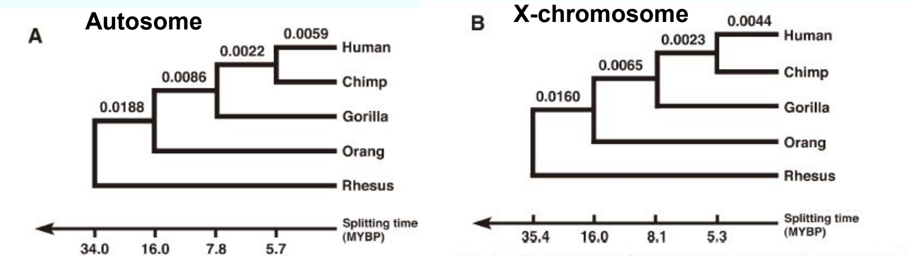
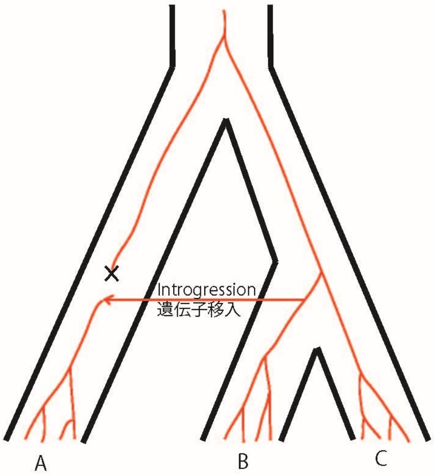


FIG. 4.—Sequence tree of the 5 species under study reconstructed from the autosomal sequences (*A*) and X chromosomal sequences (*B*), respectively. Splitting times were dated assuming the split of the orangutan lineage 16 MYBP. Trees are not drawn to scale.

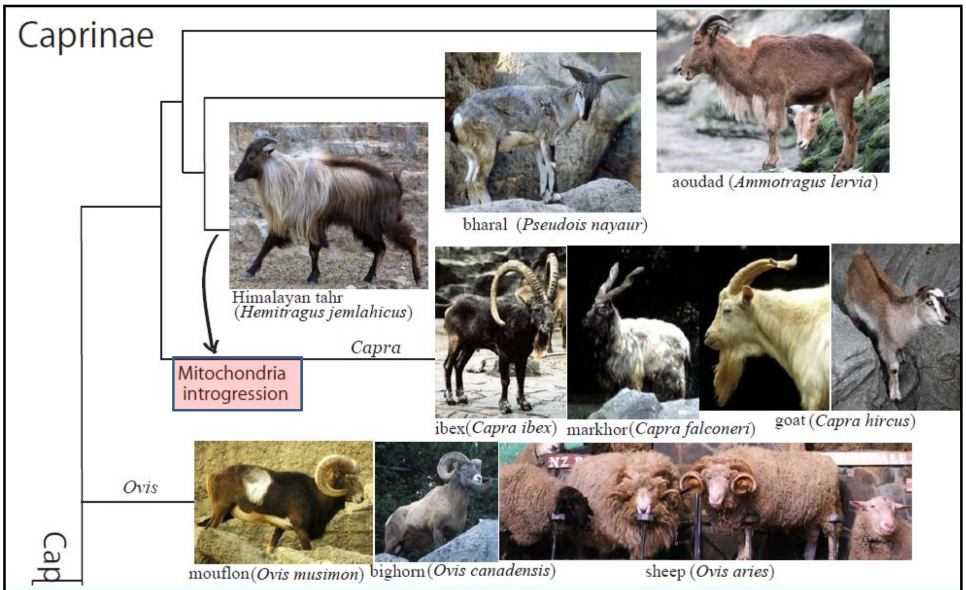
Ebersberger et al. (2007)

**The branching date estimated from X-chromosome is younger than that from autosomes (closer to species branching?)**
**→ Effective population size of mitochondria is ¼ of that of autosome, and therefore the branching date estimated from mitogenome may be closer to species divergence than those estimated from nuclear genes, but there is another problem…**

## Another possibility is introgression by hybridization



Effective population size of mitochondria is ¼ of autosomal genes, and therefore the introgressed haplotype lineage can be fixed more easily in mitochondrial genomes than in nuclear ones.



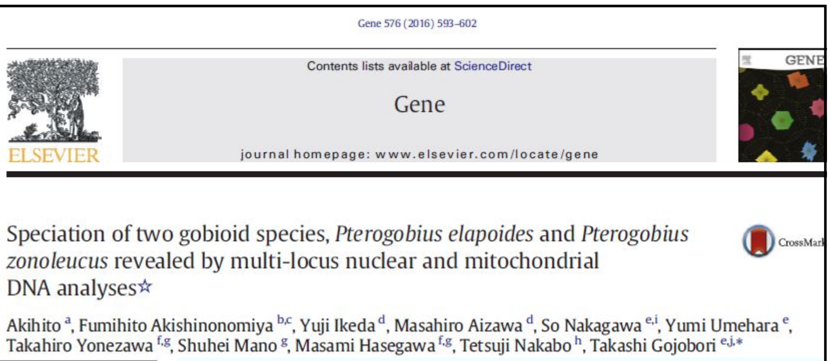
While Himalayan tahr is a sister-group to *Capra* in the mtDNA tree, it is close to bharal in the nuclear gene tree.

# Merit and demerit of mitochondrial tree

- Effective population size of mtDNA is ¼ of those of nuclear autosomal genes (haploid and maternal inheritance)

→Incomplete lineage sorting of ancestral polymorphism is less of a concern for mtDNA tree than for nuclear gene trees.

- On the other hand, small effective population size of mtDNA may facilitate fixation of introgressed haplotype lineage.



Gene 576 (2016) 593–602

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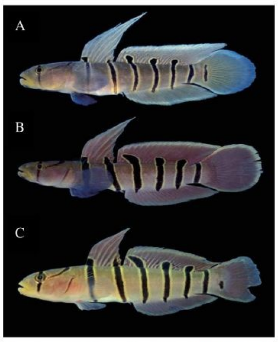
journal homepage: www.elsevier.com/locate/gene

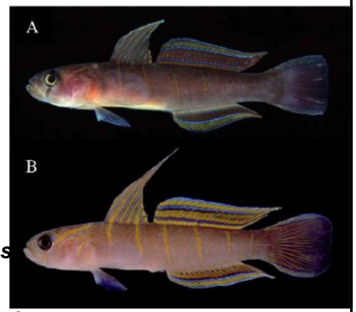
Speciation of two gobioid species, *Pterogobius elapoides* and *Pterogobius zonoleucus* revealed by multi-locus nuclear and mitochondrial DNA analyses☆

Akihito [a], Fumihito Akishinonomiya [b,c], Yuji Ikeda [d], Masahiro Aizawa [d], So Nakagawa [e,i], Yumi Umehara [e], Takahiro Yonezawa [f,g], Shuhei Mano [g], Masami Hasegawa [f,g], Tetsuji Nakabo [h], Takashi Gojobori [e,j,*]



**_Pterogobius elapoides_**
キヌバリ

Fig. 1. *Pterogobius elapoides*: (A) The Sea of Japan, Ishikawa Prefecture (BLIH20020439); (B) The Pacific Ocean, Chiba Prefecture (BLIH20030467); (C) The Inland Sea, Ehime



**_Pterogobius zonoleucus_**
チャガラ

**_Pterogobius zonoleucus:_**
チャガラ

Fig. 2. *Pterogobius zonoleucus*: (A) The Sea of Japan, Ishikawa Prefecture (BLIH200505
(B) The Pacific Ocean, Chiba Prefecture (BLIH20060883).

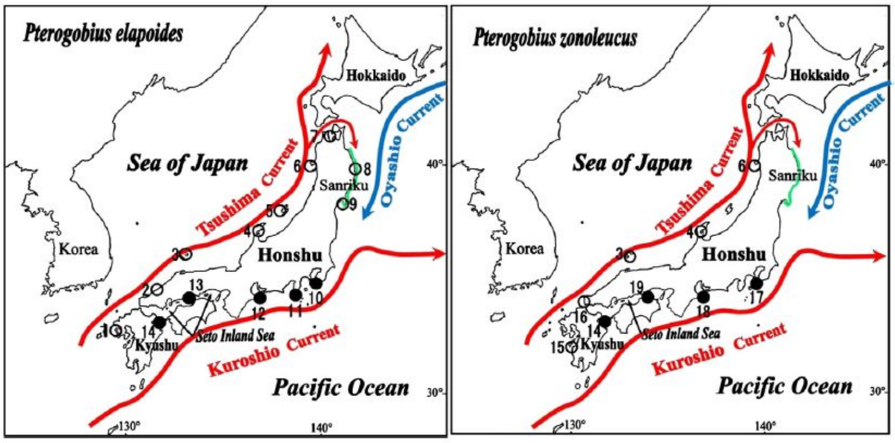
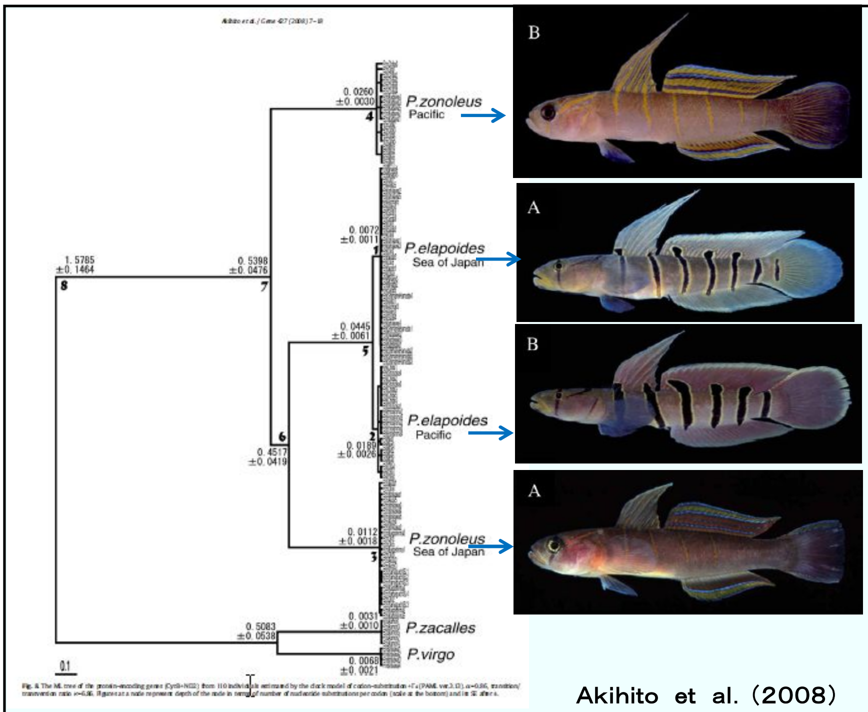


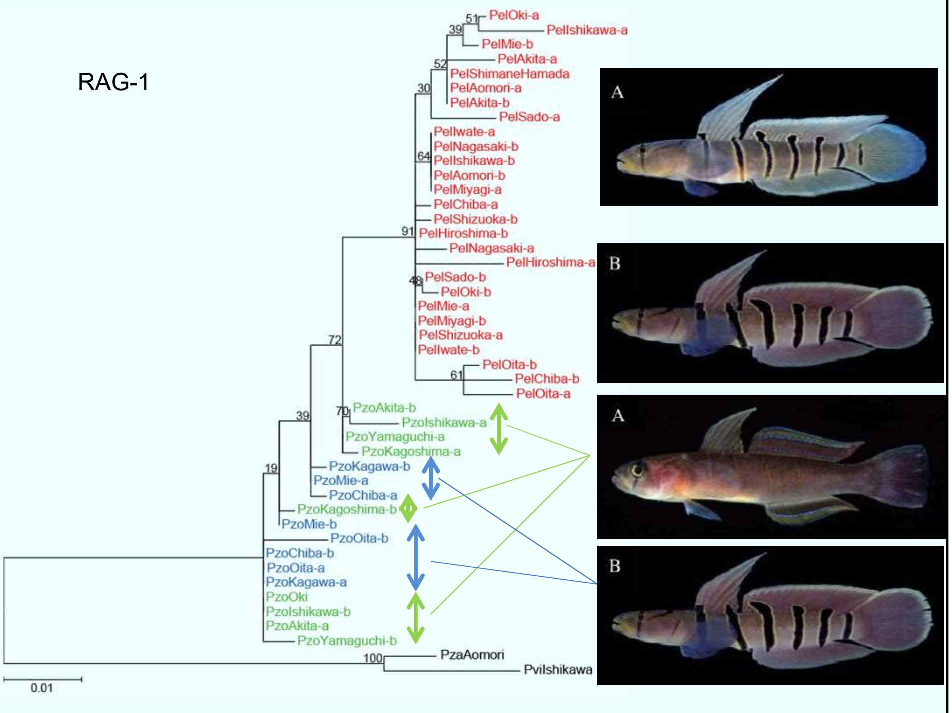
**Fig. 4.** The sampling localities of *Pterogobius elapoides* and *Pterogobius zonoleucus*: The Sea of Japan population(○), The Pacific Ocean population (●); each number of localities are shown in Table 1. 🟩 shows the coast of the Sanriku District; 🟥 show the warm currents, 🟦 shows the cold current.

Akihito et al. (2008)

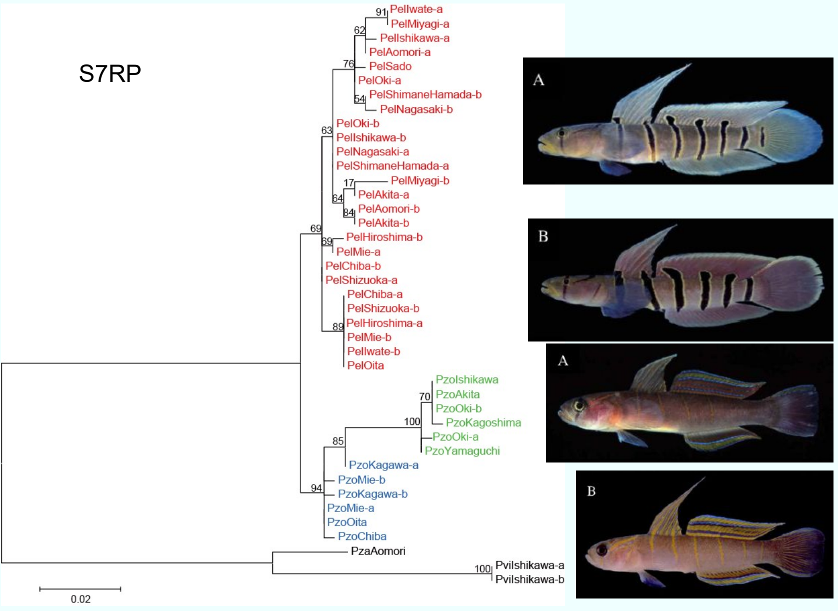


Akihito et al. (2008)

## RAG-1


51
PelOki-a
39
PelIshikawa-a
PelMie-b
52
PelAkita-a
PelShimaneHamada
30
PelAomori-a
PelAkita-b
PelSado-a
PelIwate-a
PelNagasaki-b
64
PelIshikawa-b
PelAomori-b
PelMiyagi-a
PelChiba-a
PelShizuoka-b
91
PelHiroshima-b
PelNagasaki-a
PelHiroshima-a
48
PelSado-b
PelOki-b
PelMie-a
PelMiyagi-b
PelShizuoka-a
PelIwate-b
72
PelOita-b
61
PelChiba-b
PelOita-a
70
PzoAkita-b
PzoIshikawa-a
39
PzoYamaguchi-a
PzoKagoshima-a
PzoKagawa-b
19
PzoMie-a
PzoChiba-a
PzoKagoshima-b
PzoMie-b
PzoOita-b
PzoChiba-b
PzoOita-a
PzoKagawa-a
PzoOki
PzoIshikawa-b
PzoAkita-a
PzoYamaguchi-b
100
PzaAomori
PvIshikawa
0.01
A
B
A
B

## S7RP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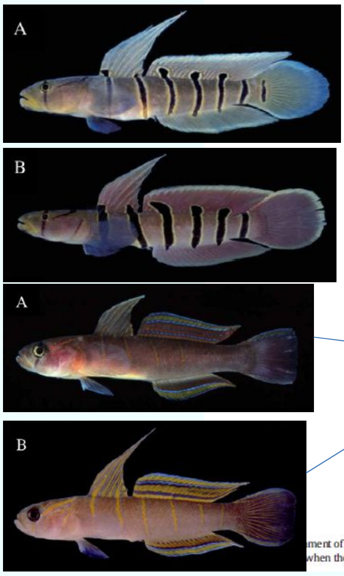
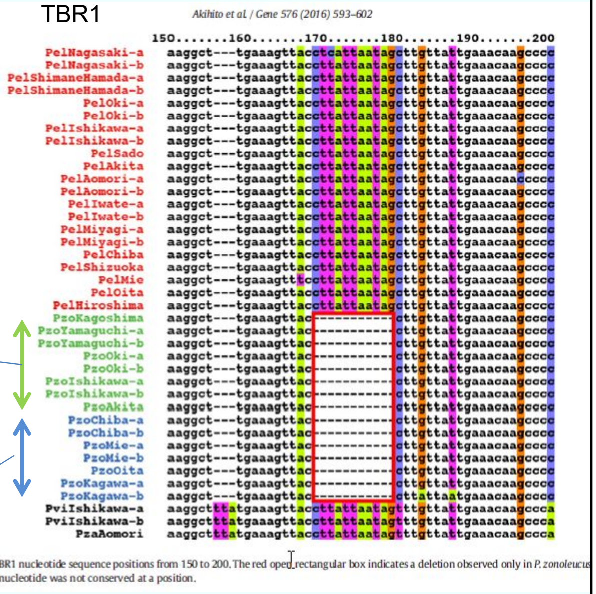
PelIwate-a
PelMiyagi-a
62
PelIshikawa-a
PelAomori-a
76
PelSado
PelOki-a
54
PelShimaneHamada-b
PelNagasaki-b
PelOki-b
63
PelIshikawa-b
PelNagasaki-a
PelShimaneHamada-a
17
PelMiyagi-b
64
PelAkita-a
84
PelAomori-b
PelAkita-b
69
69
PelHiroshima-b
PelMie-a
PelChiba-b
PelShizuoka-a
PelChiba-a
PelShizuoka-b
89
PelHiroshima-a
PelMie-b
PelIwate-b
PelOita
PzoIshikawa
70
PzoAkita
PzoOki-b
100
PzoKagoshima
85
PzoOki-a
PzoYamaguchi
PzoKagawa-a
PzoMie-b
94
PzoKagawa-b
PzoMie-a
PzoOita
PzoChiba
PzaAomori
100
PvIshikawa-a
PvIshikawa-b
0.02
A
B
A
B

TBR1




Akihito et al. / Gene 576 (2016) 593–602

```
                    150.......160.......170.......180.......190.......200
     PelNagasaki-a  aaggct---tgaaagttacctcattaatagcttgttattgaaacaagcccc
     PelNagasaki-b  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
PelShimaneHamada-a  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
PelShimaneHamada-b  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
          PelOki-a  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
          PelOki-b  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
     PelIshikawa-a  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
     PelIshikawa-b  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
           PelSado  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
          PelAkita  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
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            PelMie  aaggct---tgaaagtttccttattaatagcttgttattgaaacaagcccc
          PelOita   aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
      PelHiroshima  aaggct---tgaaagttaccttattaatagcttgttattgaaacaagcccc
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    PzoYamaguchi-a  aaggct---tgaaagttac-----------cttgttattgaaacaagcccc
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        PzoChiba-b  aaggct---tgaaagttac-----------cttgttattgaaacaagcccc
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           PzoOita  aaggct---tgaaagttac-----------cttgttattgaaacaagcccc
       PzoKagawa-a  aaggct---tgaaagttac-----------cttgttattgaaacaagcccc
       PzoKagawa-b  aaggct---tgaaagttac-----------cttattaatgaaacaagcccc
     PviIshikawa-a  aaggctttatgaaagttaccttattaatagtttgttattgaaacaagcccca
     PviIshikawa-b  aaggctttatgaaagttaccttattaatagtttgttattgaaacaagcccca
          PzaAomori  aaggctttatgaaagttaccttattaatagtttgttattgaaacaagcccca
```
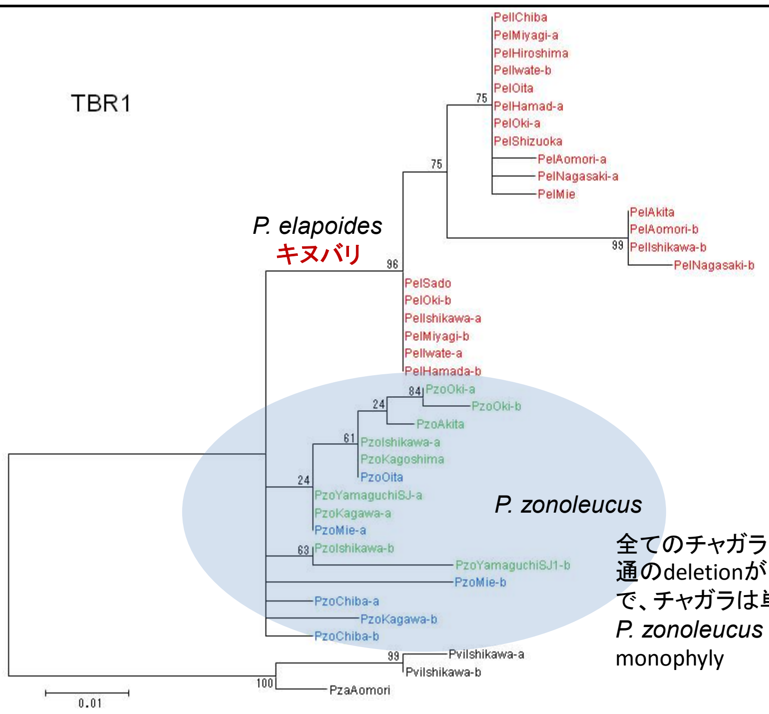

ment of TBR1 nucleotide sequence positions from 150 to 200. The red open rectangular box indicates a deletion observed only in *P. zonoleucus*
when the nucleotide was not conserved at a position.

TBR1



*P. elapoides*
キヌバリ

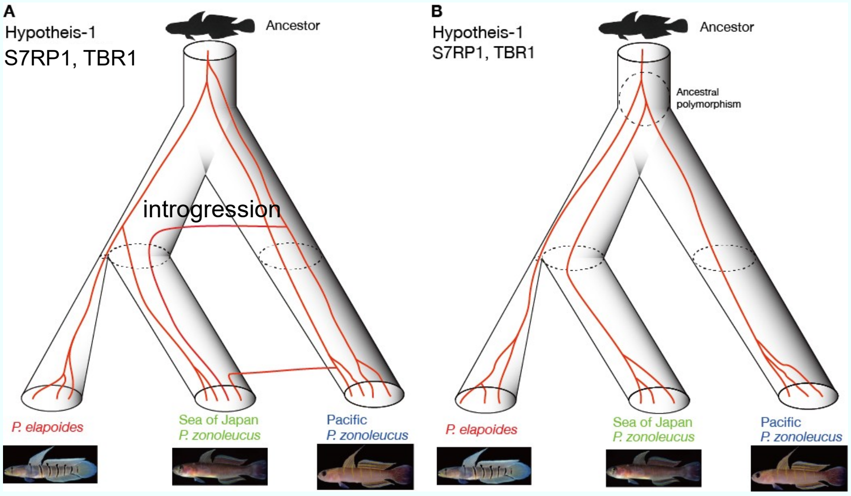
*P. zonoleucus*

全てのチャガラに共
通のdeletionがあるの
で、チャガラは単系統
*P. zonoleucus*
monophyly

# Two possible hypotheses

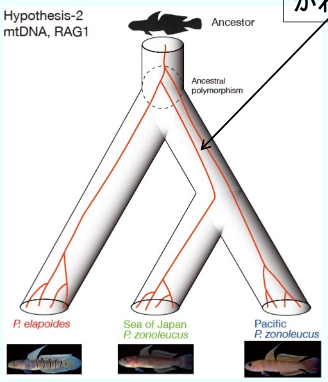
- Hypothesis-1: In the population tree, *P. elapoides* evolved from the Japan Sea population of *P. zonoleucus*.
- Hypothesis-2: In the population tree, the two populations (Sea of Japan & Pacific) of *P. zonoleucus* are monphyletic, and *P. elapoides* is a sister-group of these two.

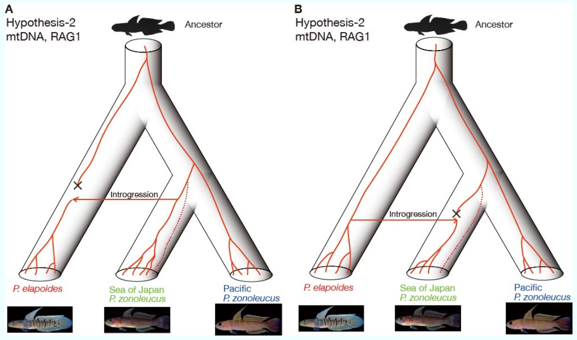
How the incongruence of the gene trees can be explained by these hypotheses?



If Hypothesis-1 is true, it is expected that the population size of *P. elapoides* was expected to be smaller than that of Sea of Japan *P. zonoleucus*, because a new species usually evolve from a local population of the mother species.

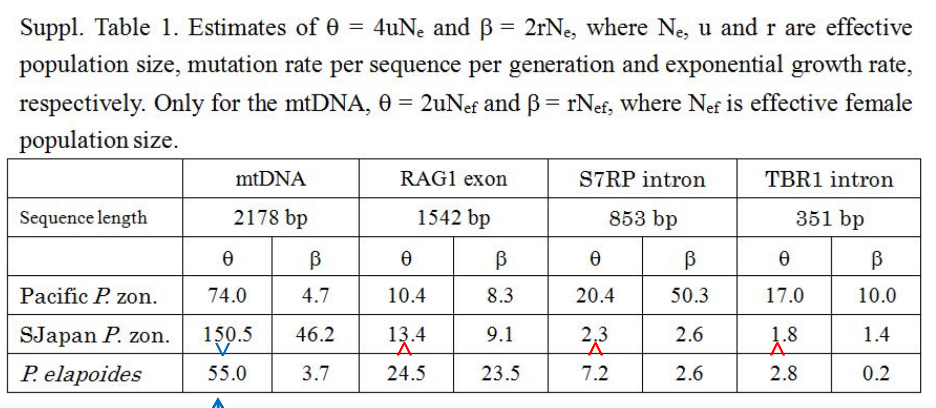
共通祖先集団の多型が日本海チャガラと太平洋チャガラが分かれるまで存続した。





ミトコンドリアのeffective population sizeは核の1/4だから、そんなに長く多型が存続する可能性は低い。

仮説2が正しいとすれば、ミトコンドリアはintrogressionを起した可能性が高い。

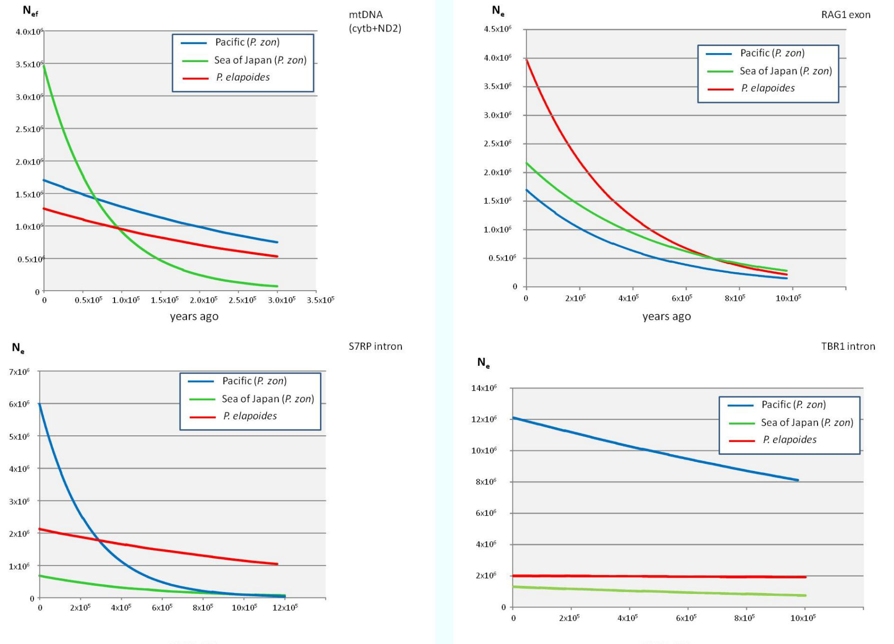


Suppl. Table 1. Estimates of $\theta = 4uN_e$ and $\beta = 2rN_e$, where $N_e$, u and r are effective population size, mutation rate per sequence per generation and exponential growth rate, respectively. Only for the mtDNA, $\theta = 2uN_{ef}$ and $\beta = rN_{ef}$, where $N_{ef}$ is effective female population size.

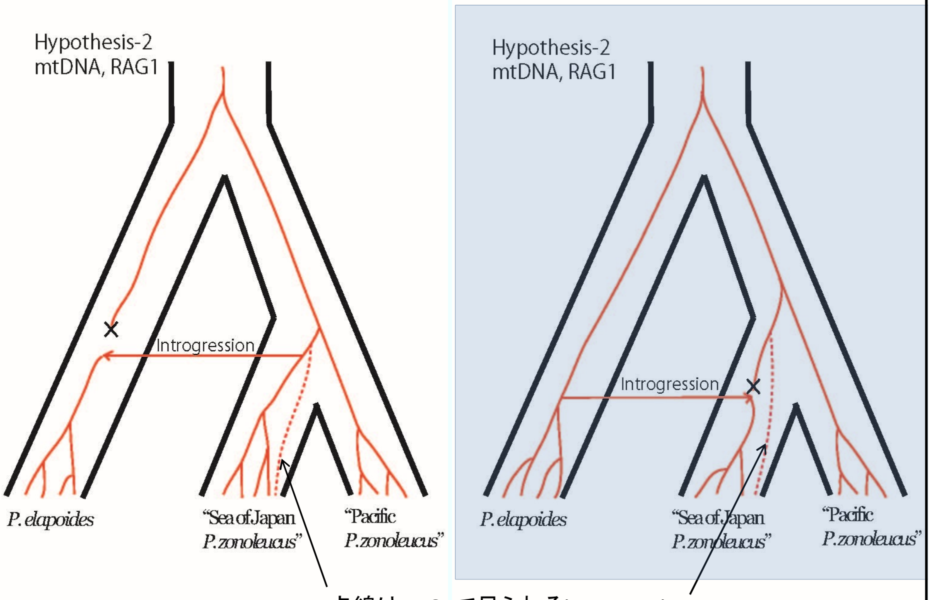
| | mtDNA | | RAG1 exon | | S7RP intron | | TBR1 intron | |
|---|---|---|---|---|---|---|---|---|
| Sequence length | 2178 bp | | 1542 bp | | 853 bp | | 351 bp | |
| | θ | β | θ | β | θ | β | θ | β |
| Pacific *P.* zon. | 74.0 | 4.7 | 10.4 | 8.3 | 20.4 | 50.3 | 17.0 | 10.0 |
| SJapan *P.* zon. | 150.5 | 46.2 | 13.4 | 9.1 | 2.3 | 2.6 | 1.8 | 1.4 |
| *P. elapoides* | 55.0 | 3.7 | 24.5 | 23.5 | 7.2 | 2.6 | 2.8 | 0.2 |

↑

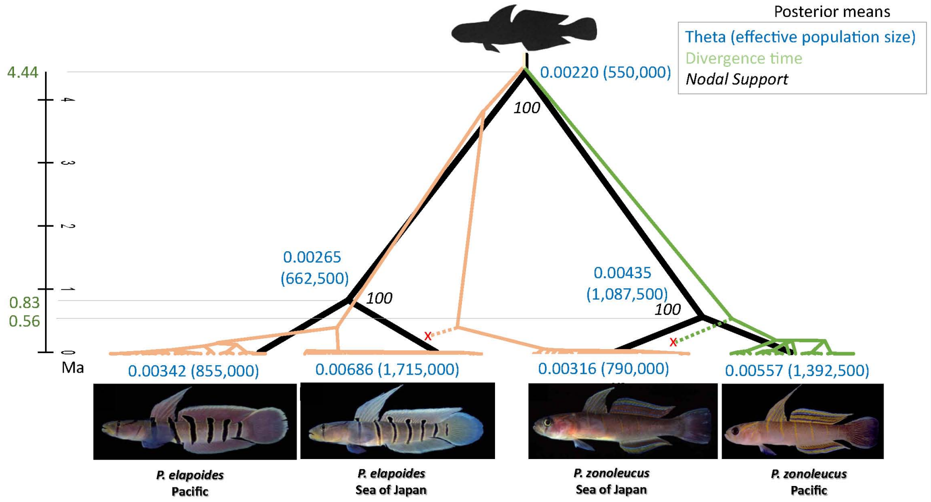
現存集団では日本海チャガラのNeはキヌバリのものよりも大きいが、種分化直後では逆転していた。



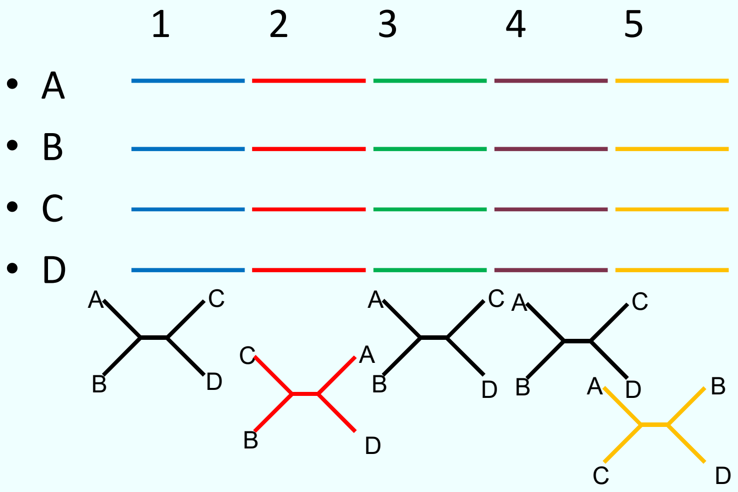
キヌバリのNeが小さかったとは考えられない→仮説２



点線はRAG1で見られるintrogression
以前のbasal lineageを示す。



# Analysis of concatenated sequences



**Since gene trees can be incongruent among different genes, it cannot be justified to analyze concatenated sequences.**

## Problems of the "concatenated sequence" analyses

- Each gene has its own history, and gene trees can be different among different genes.
- Concatenation of different genes ignores this.
- Gene tree vs. Species tree

  Importance of population genetics

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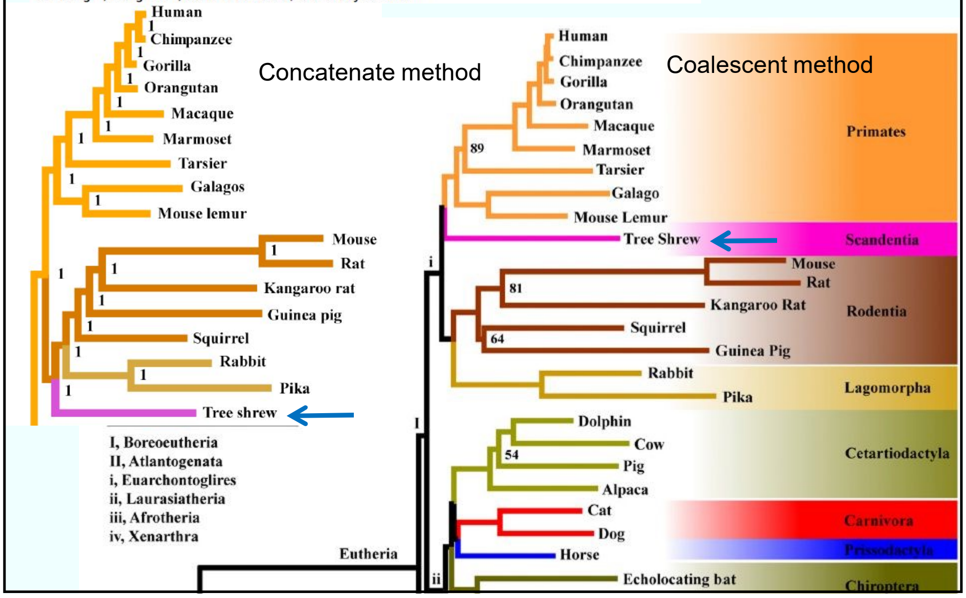
### Resolving conflict in eutherian mammal phylogeny using phylogenomics and the multispecies coalescent model

Sen Song[a,1], Liang Liu[b,1], Scott V. Edwards[c], and Shaoyuan Wu[b,d,2]

PNAS 2012


Concatenate method

Coalescent method

Molecular Phylogenetics and Evolution
Vol. 15, No. 2, May, pp. 319–326, 2000
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# Phylogeography of Mitochondrial DNA Variation in Brown Bears and Polar Bears

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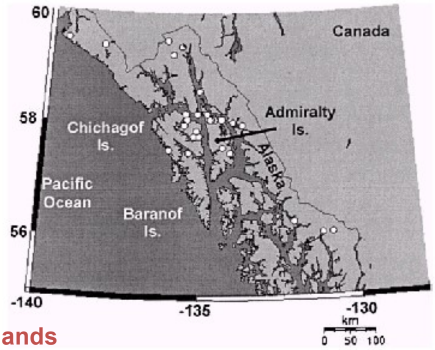

**ABC Islands**

FIG. 1. Locations (open circles) on Admiralty, Baranof, and Chichagof islands and on the coastal mainland of southeast Alaska where tissues of brown bears were obtained.

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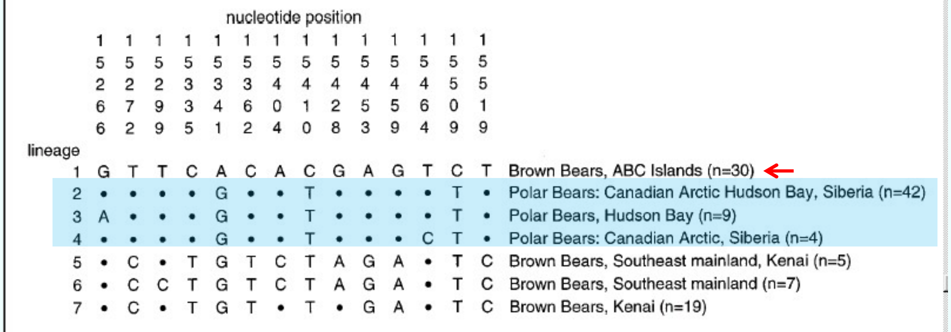

| lineage | 15266 | 15272 | 15299 | 15335 | 15341 | 15362 | 15404 | 15410 | 15428 | 15453 | 15459 | 15464 | 15509 | 15519 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | G | T | T | C | A | C | A | C | G | A | G | T | C | T | Brown Bears, ABC Islands (n=30) ← |
| 2 | • | • | • | • | G | • | • | T | • | • | • | • | T | • | Polar Bears: Canadian Arctic Hudson Bay, Siberia (n=42) |
| 3 | A | • | • | • | G | • | • | T | • | • | • | • | T | • | Polar Bears, Hudson Bay (n=9) |
| 4 | • | • | • | • | G | • | • | T | • | • | • | C | T | • | Polar Bears: Canadian Arctic, Siberia (n=4) |
| 5 | • | C | • | T | G | T | C | T | A | G | A | • | T | C | Brown Bears, Southeast mainland, Kenai (n=5) |
| 6 | • | C | C | T | G | T | C | T | A | G | A | • | T | C | Brown Bears, Southeast mainland (n=7) |
| 7 | • | C | • | T | G | T | • | T | • | G | A | • | T | C | Brown Bears, Kenai (n=19) |

**FIG. 7.** Condensed dot matrix of variable nucleotide positions among 286 nucleotides (15243 to 15529) of the middle portion of the cytochrome *b* gene of bears of this study.

MtDNA of brown bear from ABC Islands is closer to those of polar bears than to those of brown bears from other areas.

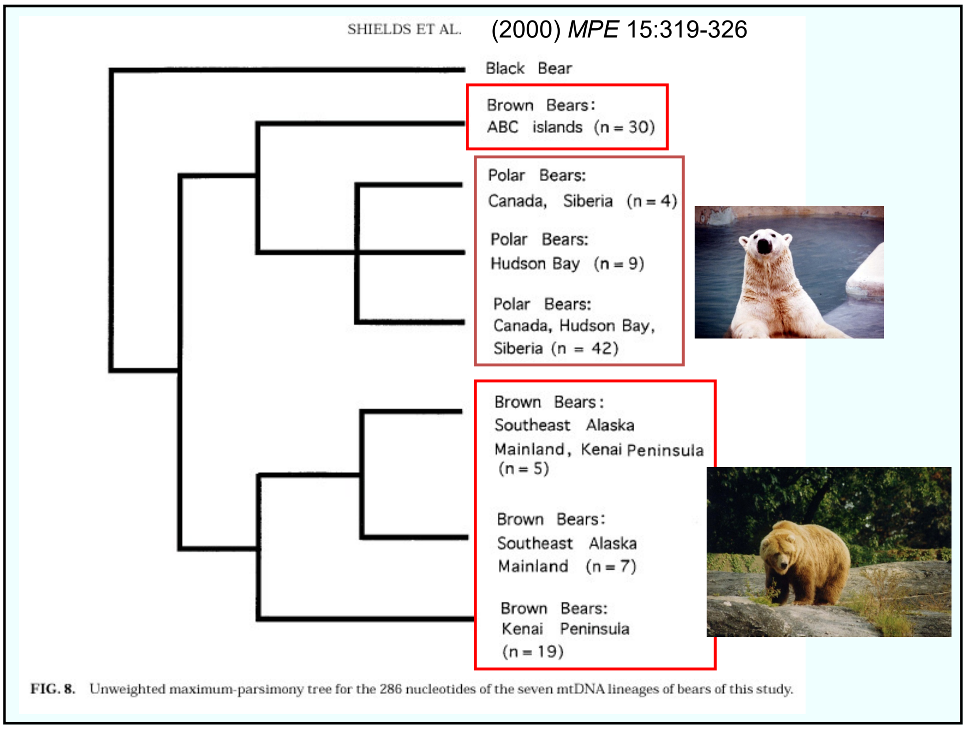

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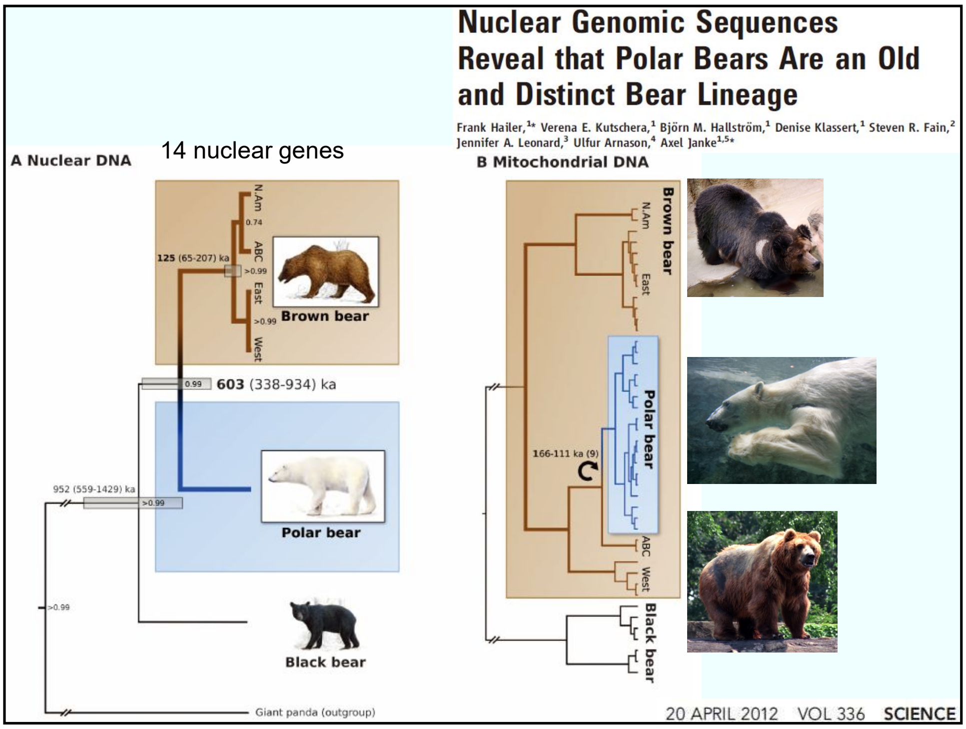
**FIG. 8.** Unweighted maximum-parsimony tree for the 286 nucleotides of the seven mtDNA lineages of bears of this study.



# Nuclear Genomic Sequences Reveal that Polar Bears Are an Old and Distinct Bear Lineage

Frank Hailer,[1*] Verena E. Kutschera,[1] Björn M. Hallström,[1] Denise Klassert,[1] Steven R. Fain,[2] Jennifer A. Leonard,[3] Ulfur Arnason,[4] Axel Janke[1,5*]

14 nuclear genes

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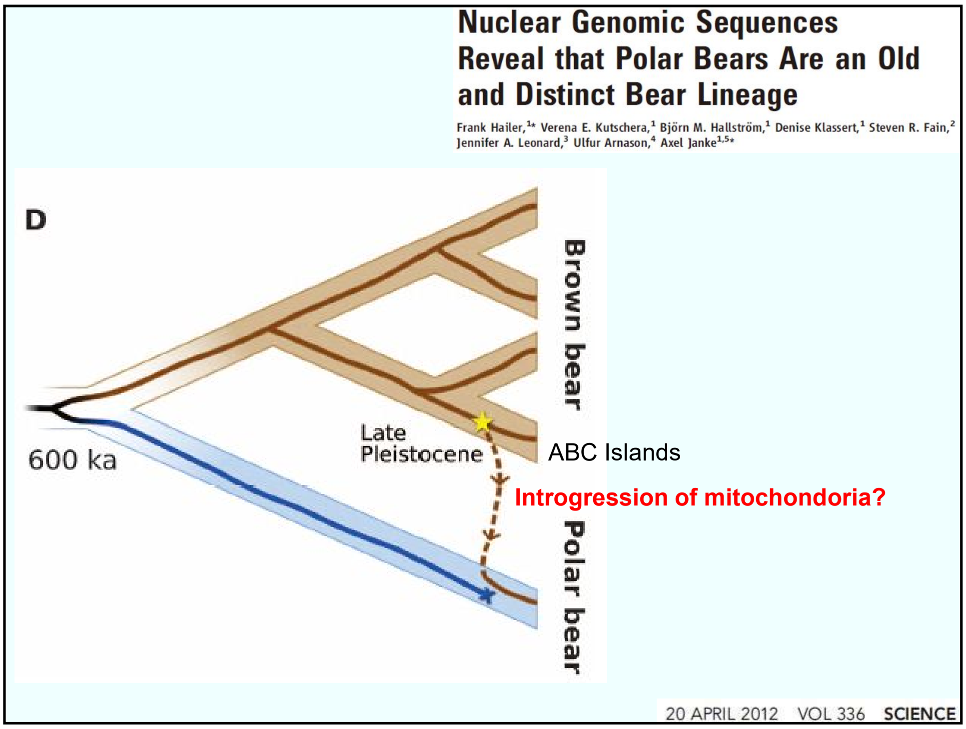

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ABC Islands

**Introgression of mitochondoria?**

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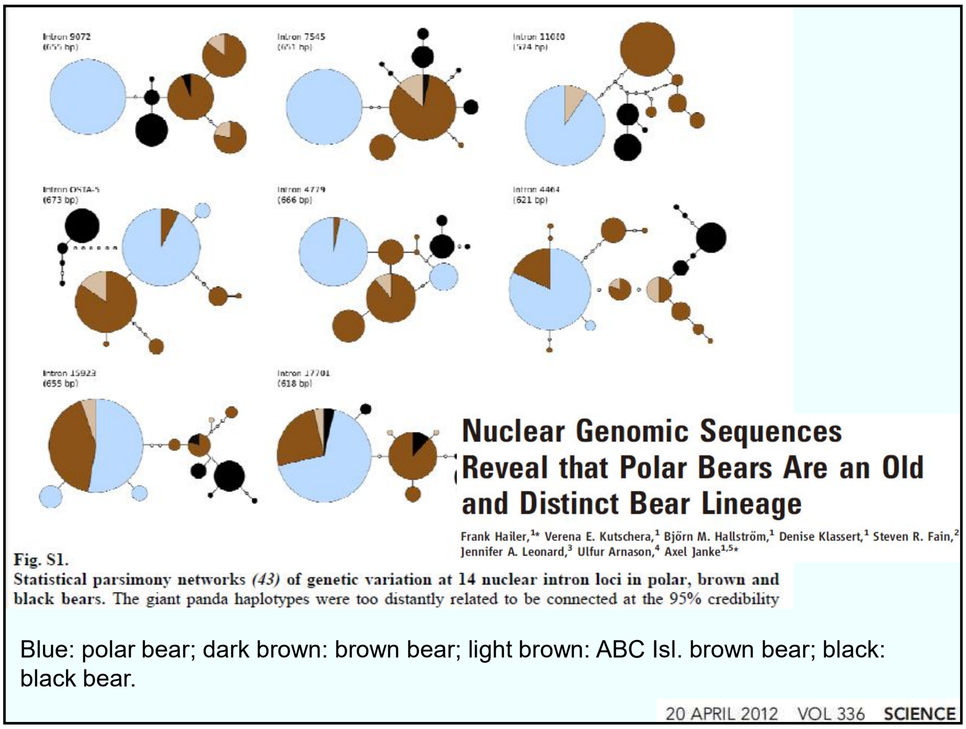

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**Fig. S1.**
**Statistical parsimony networks** *(43)* **of genetic variation at 14 nuclear intron loci in polar, brown and black bears.** The giant panda haplotypes were too distantly related to be connected at the 95% credibility

Blue: polar bear; dark brown: brown bear; light brown: ABC Isl. brown bear; black: black bear.

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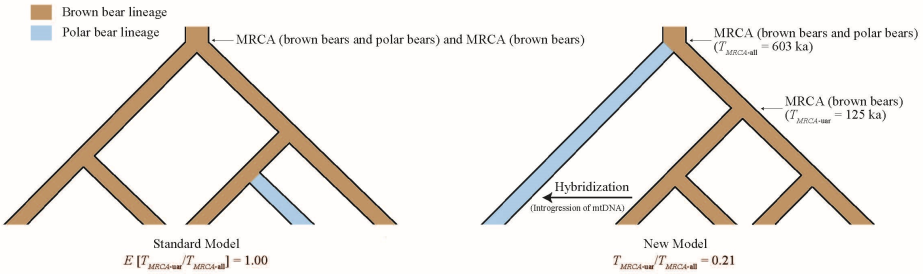
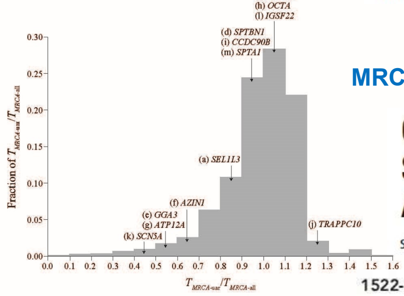
Figure 1

(A) Two evolutionary models



(B) Histogram of $T_{MRCA\text{-uar}}/T_{MRCA\text{-all}}$ under the "Standard Model."



$T_{\text{MRCA-uar}}/T_{\text{MRCA-all}}$ : **Test statistics which discriminates two models**

**MRCA: Most Recent Common Ancestor**

## Comment on "Nuclear Genomic Sequences Reveal that Polar Bears Are an Old and Distinct Bear Lineage"

Shigeki Nakagome,[1*] Shuhei Mano,[1] Masami Hasegawa[1,2]

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