

Bioinformatics

Five

Case Study

The BIG Jaw

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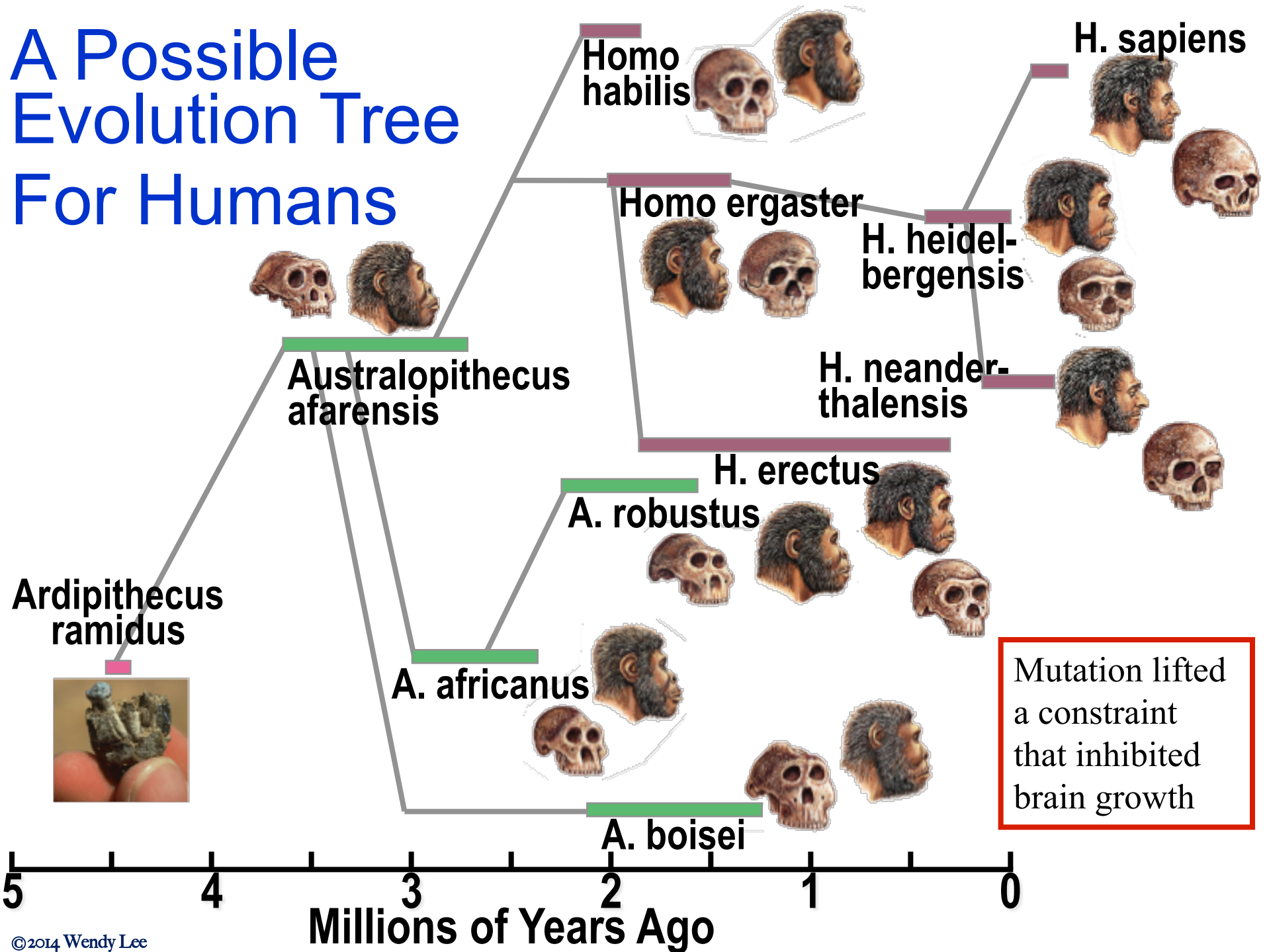
Biology/CS 123/SEA

Fall 2014

**Myosin gene mutation
correlates with anatomical
changes in the human lineage by
Hansell H. Stedman et al.**

NATURE: VOL 428, 25 MARCH 2004

A Possible Evolution Tree For Humans



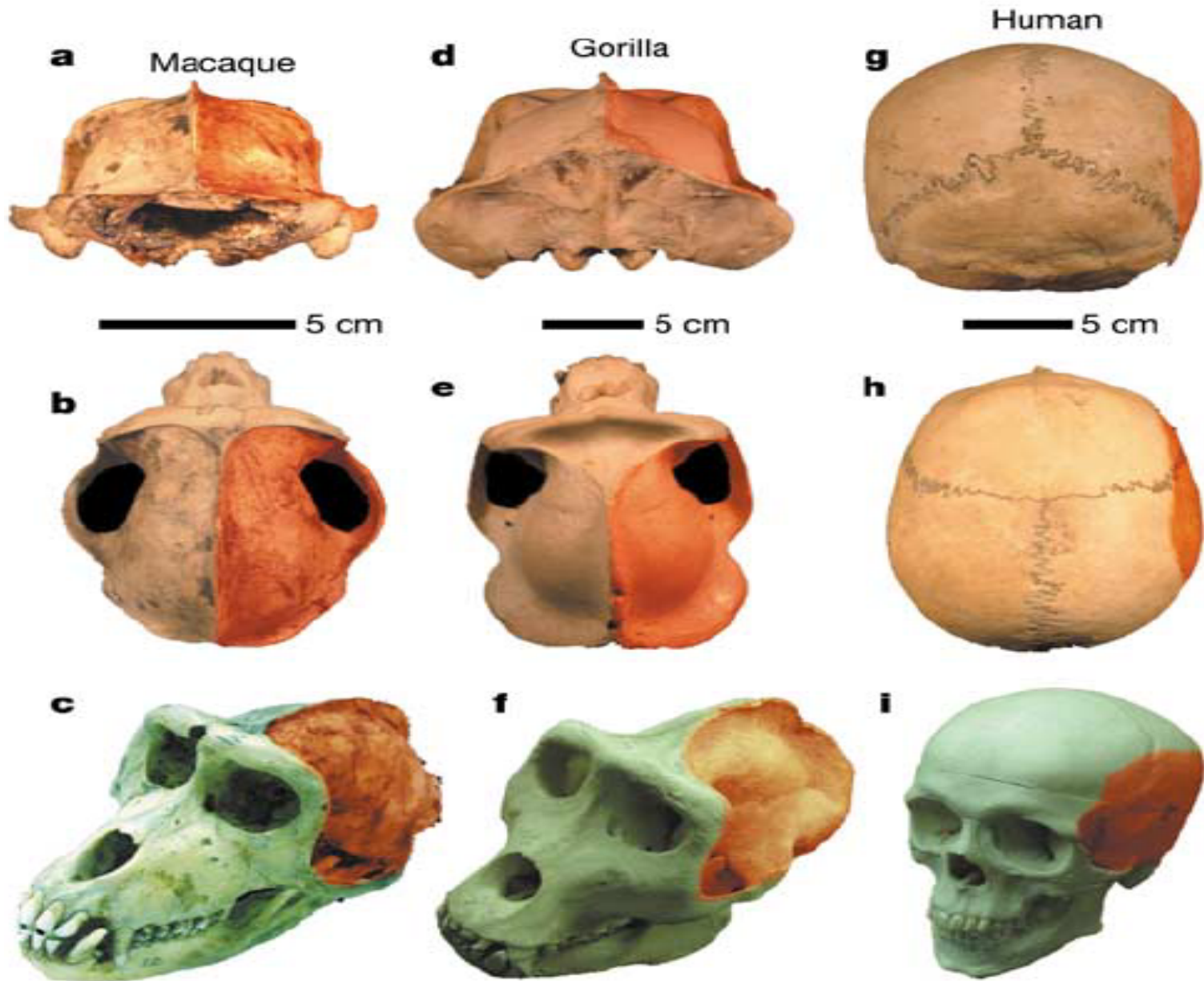
Powerful Masticatory Muscles

- Powerful masticatory muscles are found in most primates, including chimpanzees and gorillas, and also in *Australopithecus*.
- Masticatory muscles are considerably smaller in members of *Homo*.
- The gene encoding myosin heavy chain (MYH) expressed in these muscles was inactivated by a frameshifting mutation after the lineages leading to humans and chimpanzees diverged.



A decrease in jaw-muscle size, produced by inactivation of MYH16, removed a barrier to the remodelling of the hominid cranium which consequently allowed an increase in the size of the brain.





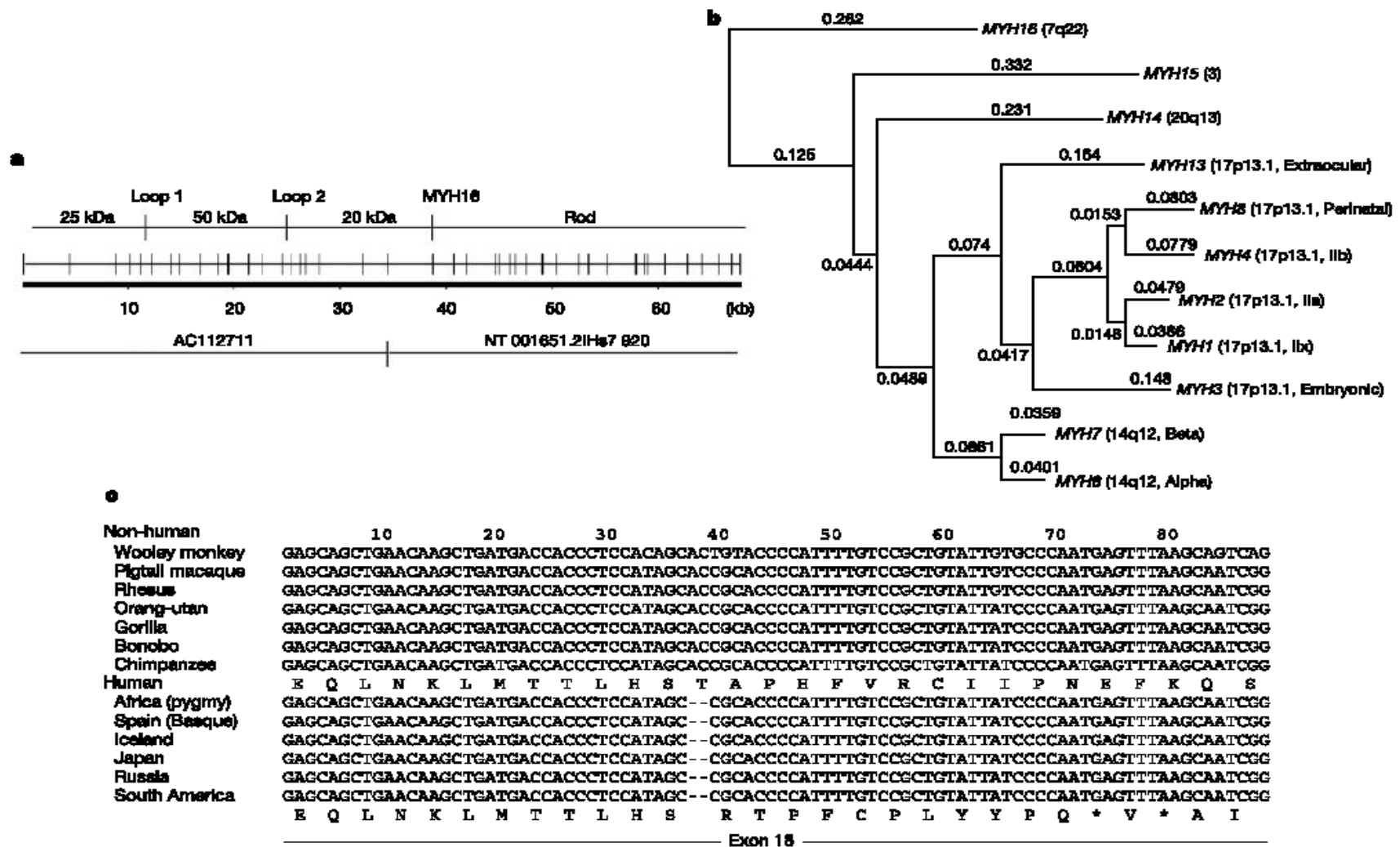


Figure 1 Molecular evolution of *MYH16*. **a**, Distribution of 42 predicted coding exons spanning 67,983 base pairs (bp) in the region of human chromosome 7q22 flanked 5' by *SMURF1* and 3' by *ARPC1A*. **b**, Phylogenetic reconstruction for all human sarcomeric myosin genes (heavy chain), showing early divergence of *MYH16* from others. Branch lengths shown are derived from a maximum likelihood analysis of the aligned cDNAs, beginning with the conserved proline at the head-rod junction. Non-sarcomeric class II

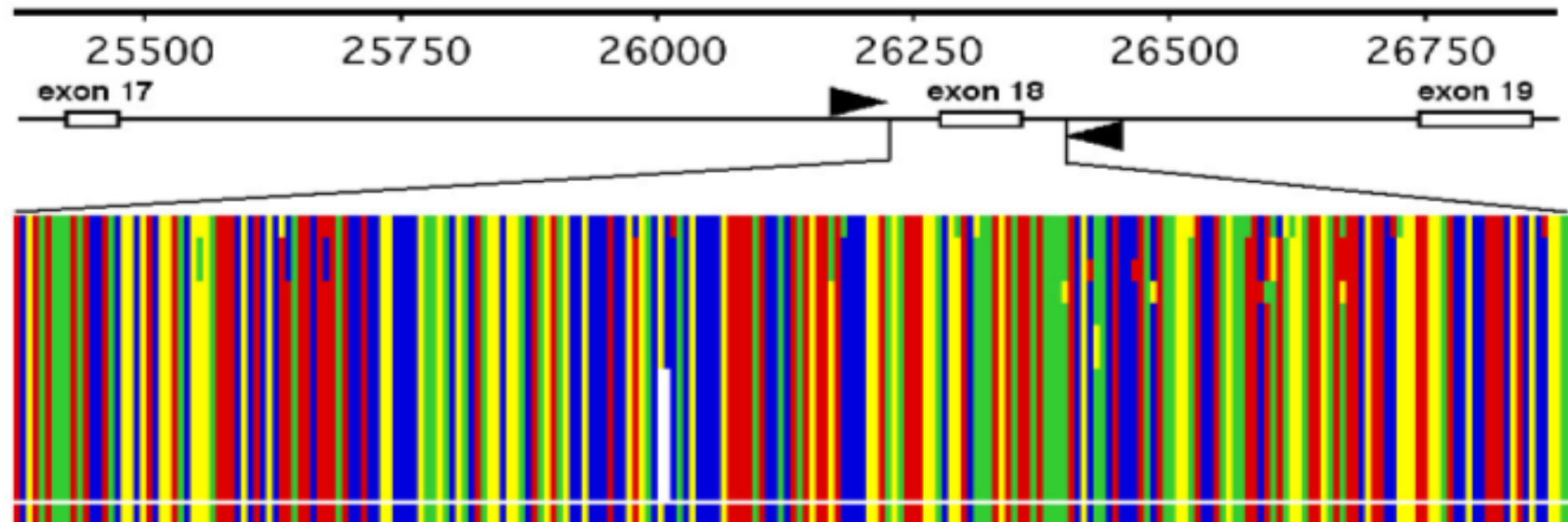
myosins (designated *MYH9*, -10 and -11; data not shown) are used to root the tree. **c**, Aligned DNA sequences for *MYH16* exon 18 representing seven non-human primate species and six geographically dispersed human populations, revealing the effect of frameshift on reading frame and deduced amino acid sequence. Note stop codon at position 72-74.

	10	20	30	40	50	60	70	80
Non-human								
Woolly monkey	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	ACTGTACCCCATTTTGTCCGCTGTATTGTCCCAATGAGTTTAAGCAATCGG						
Pigtail macaque	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	ACCGCAGCCCATTTTGTCCGCTGTATTGTCCCAATGAGTTTAAGCAATCGG						
Rhesus	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	ACCGCAGCCCATTTTGTCCGCTGTATTGTCCCAATGAGTTTAAGCAATCGG						
Orang-utan	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	ACCGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Gorilla	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	ACCGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Bonobo	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	ACCGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Chimpanzee	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	ACCGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Human	E Q L N K L M T T L H S	T A P H F V R C I I P N E F K Q S						
Africa (pygmy)	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	-CGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Spain (Baque)	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	-CGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Iceland	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	-CGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Japan	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	-CGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
Russia	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	-CGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
South America	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC	-CGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG						
	E Q L N K L M T T L H S	R T P F C P L Y Y P Q	*	V	*	A	I	
				Exon 18				

MYH16: Myosin Heavy Gene

Accession Number: BK001410 at NCBI (exon 19)

MYH 16, Position relative to start codon



	20										30										40										50										60									
Woolly/Monkey	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	C	R	G	C	R	C	T	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Pigtail/Mac	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	R	C	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Rhesus	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	R	C	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Orangutan	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	R	C	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Gorilla	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	R	C	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Bonobo	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	R	C	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Chimpanzee	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	R	C	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
African Pygmy	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	-	-	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Besque	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	-	-	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Icelandic	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	-	-	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Japanese	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	-	-	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Russian	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	-	-	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Amerindian	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	-	-	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
consensus	R	R	G	C	T	G	R	T	G	R	C	C	R	C	C	C	T	C	C	A	T	R	G	C	C	C	G	C	A	C	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T	

	10	20	30	40	50	60	70	80
CHIMPANZEE	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGCACCGCACCCCATTTTGTCCGCTGTATTATCCCCCAATGAGTTTAAGCAATCGG							
	E Q L N K L M T T L H S T A P H F V R C I I P N E F K Q S							
HUMAN	GAGCAGCTGAACAAGCTGATGACCACCCCTCCATAGC--CGCACCCCATTTTGTCCGCTGTATTATCCCCCAATGAGTTTAAGCAATCGG							

WoolleyMonkey	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	T	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
PigtailMac	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Rhesus	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Orangutan	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Gorilla	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Bonobo	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Chimpanzee	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
African Pygmy	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	-	-	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Beaque	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	-	-	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Icelandic	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	-	-	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Japanese	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	-	-	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
Russian	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	-	-	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
AmerIndian	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	-	-	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T
consensus	A	A	G	C	T	G	A	T	G	A	G	C	A	C	C	C	T	C	C	A	T	A	G	C	A	C	C	G	C	A	C	C	C	A	T	T	T	T	G	T	C	C	G	C	T	G	T	A	T

10 20 30 40 50 60 70 80

CHIMPANZEE GAGCAGCTGAACAAGCTGATGACCACCCTCCATAGCACCAGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG
E Q L N K L M T T L H S T A P H F V R C I I P N E F K Q S

HUMAN GAGCAGCTGAACAAGCTGATGACCACCCTCCATAGC--CGCAGCCCATTTTGTCCGCTGTATTATCCCAATGAGTTTAAGCAATCGG