探究猫科动物毛色形成的遗传机制

——MC1R基因为例的生物信息学研究

Molecular genetic basis of coloration in cat family:

a case study of melanocortin receptor 1

实用生物信息学技术课程期末报告

Group 3: 郭生杰，宁小涵，杨晓彤，刘悦晨

汇报人：刘悦晨

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➤ **Evolutionary Genetics of the MC1R in Vertebrates**

- The molecular genetic basis of adaptive change in phenotype is a major outstanding issue in evolutionary biology.

- Evolutionary change in coat and plumage color is a promising system for making progress in this field.

- Several candidate genes are involved in evolutionary color change in mammals and birds.

- One such gene encodes the melanocortin-1 receptor (MC1R), which is one of the major regulators of eumelanin and pheomelanin content in hairs and feathers.
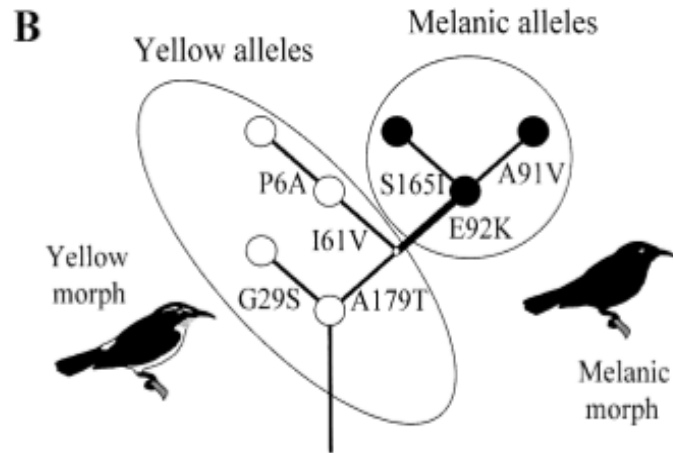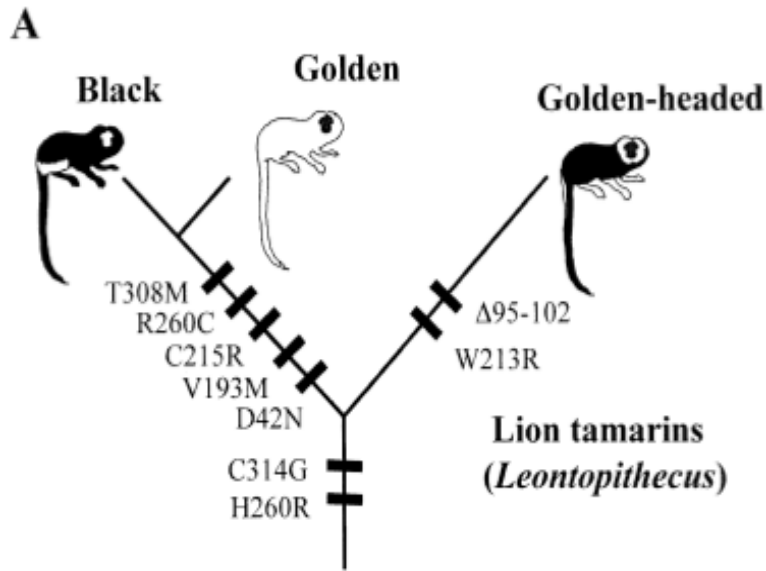
Mundy et al. (2006) Evolutionary genetics of the melanocortin-1 receptor in vertebrates.
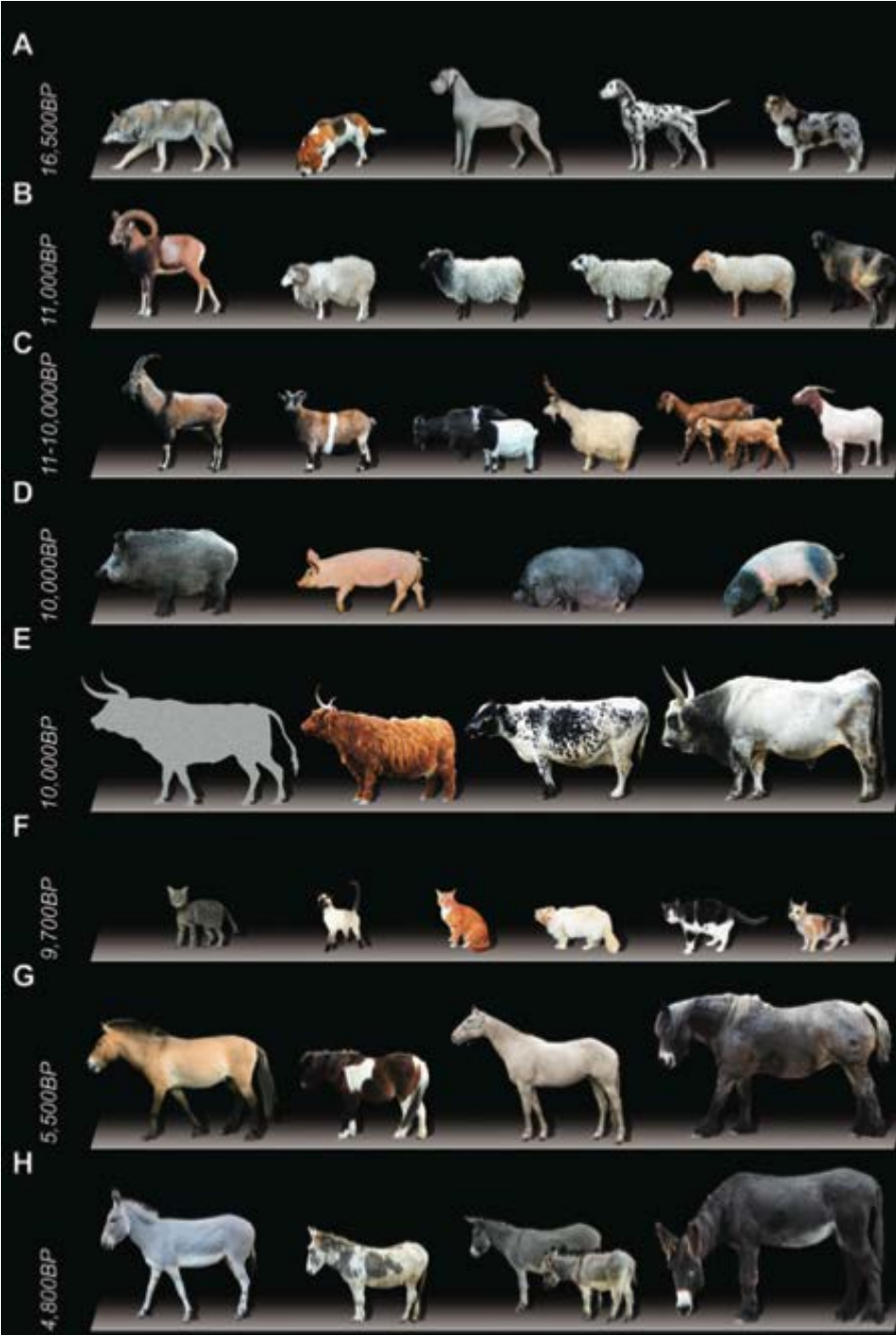
> **Coloration in domestication**

- In domestic mammals such as mice and cattle:

- Gain of function MC1R mutations lead to darkening in the coat

- Loss of function MC1Rmutations lead to yellow or red coat

- MC1R mutations lead to coloration changes in sheep, horses, pigs, dogs guinea pigs, foxes, chickens et al.

Fig. 1 in **Cieslak et al. (2011) Colors of domestication. *Biol. Rev.***

MC1R Evolution Cases

Fig. 1. in Mundy et al. (2006) Evolutionary genetics of the melanocortin-1 receptor in vertebrates.
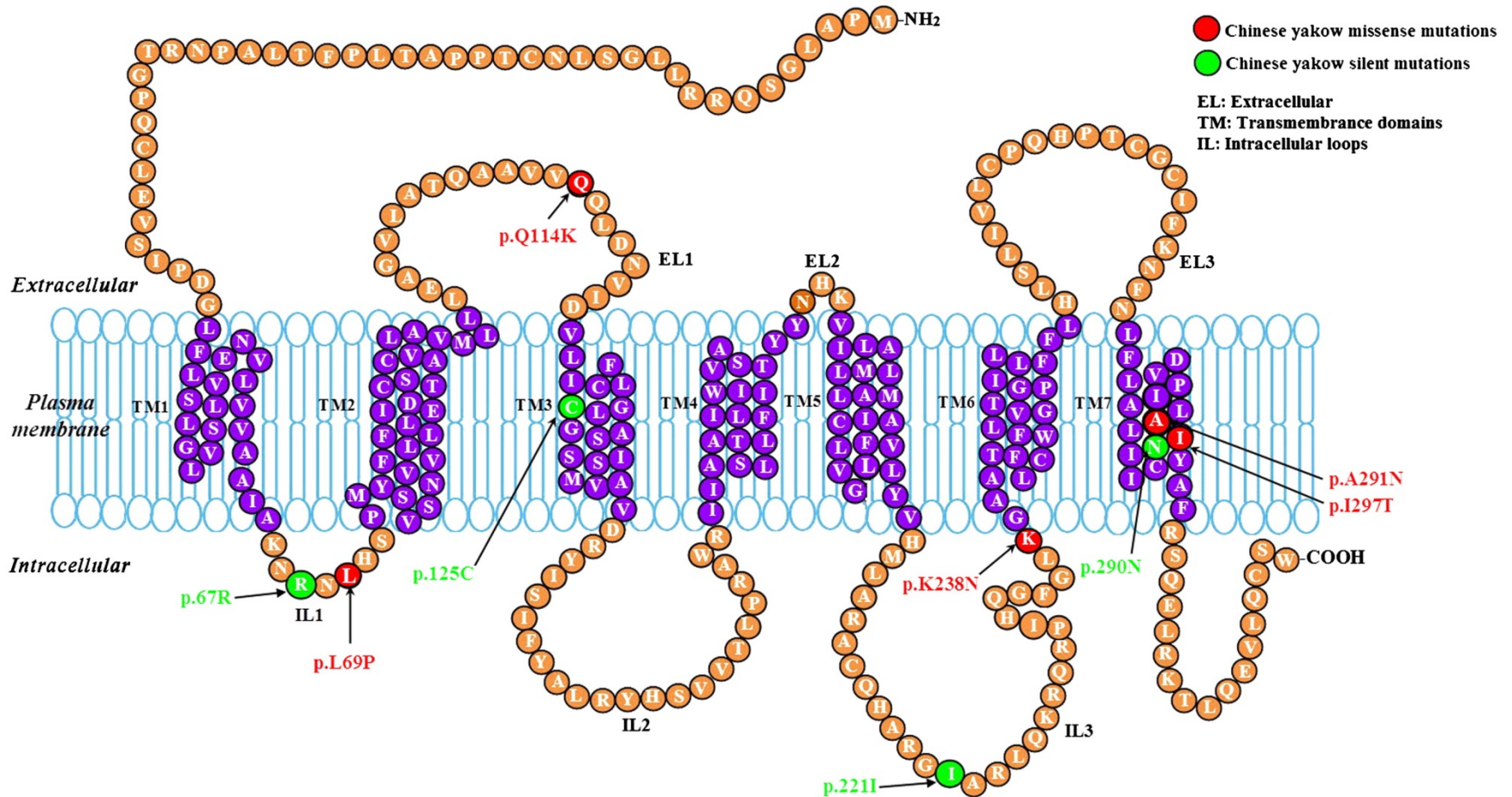
Two dimensional structure of the MC1R in Chinese yak

Fig. 5. in Xi et al. (2012) Isolation and characteristics of the melanocortin 1 receptor gene (MC1R) in the Chinese yakow. Gene

> # The MC1R locus

- A seven trans-membrane (TM) G-coupled receptor (GPCR)

- 1000 members account for more than 1% of mammalian genomes

- The MC1R belongs to class A, rhodopsin family

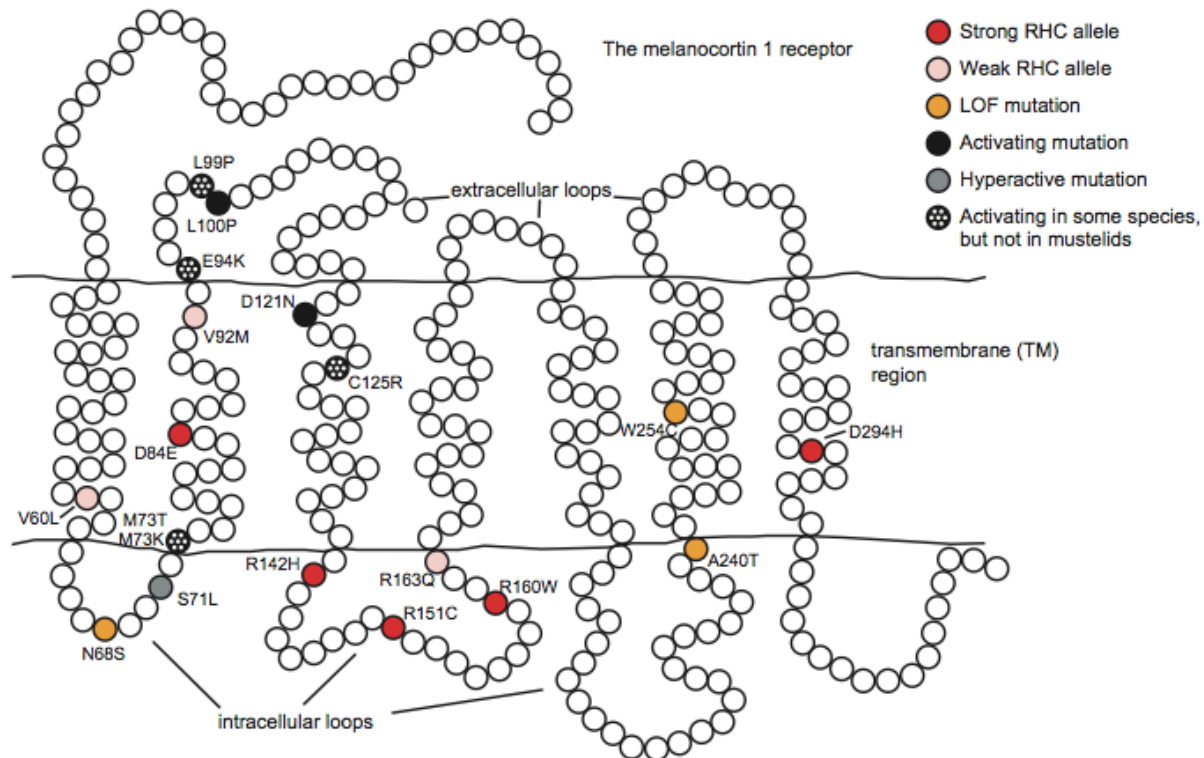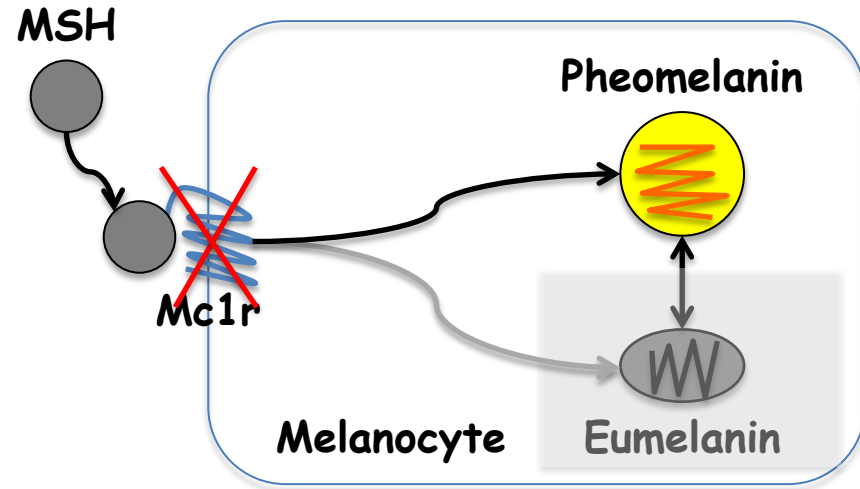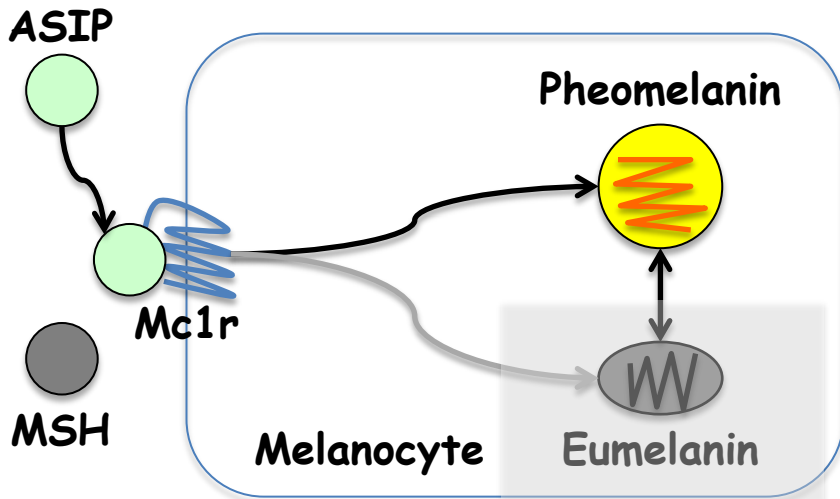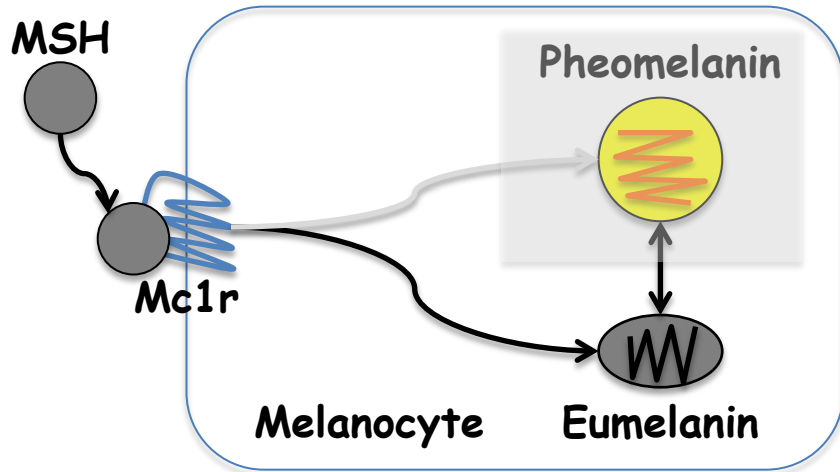- One of a five-member subfamily, the melanocortin (MC) receptors

Fig. 1. in Jean K. Lightner (2008) Genetics of coat color 1: the melanocortin 1 receptor (MC1R). *Answers Research Journal.*
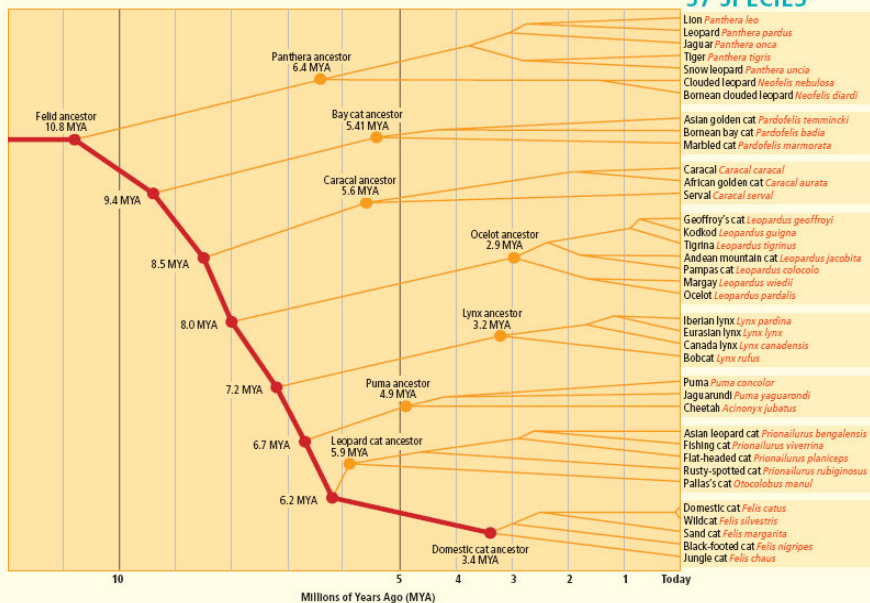
Pigment production controlled by MC1R and ASIP

> Melanistic coat coloration occurs as a common polymorphism in 13 of 37 felid species and reaches high population frequency in some cases but never achieves complete fixation. This mutant phenotype arose at least five times independently in the cat family. (Schneider *et al.* PLoS ONE 7(12), 2012)


THE CAT FAMILY TREE

Scientists compared DNA sequences in all 37 species of cats to determine the tree's branches. Fossils provided dates that indicate when major branching occurred.

37 SPECIES

Lion *Panthera leo*
Leopard *Panthera pardus*
Jaguar *Panthera onca*
Tiger *Panthera tigris*
Snow leopard *Panthera uncia*
Clouded leopard *Neofelis nebulosa*
Bornean clouded leopard *Neofelis diardi*

Asian golden cat *Pardofelis temminckii*
Bornean bay cat *Pardofelis badia*
Marbled cat *Pardofelis marmorata*

Caracal *Caracal caracal*
African golden cat *Caracal aurata*
Serval *Caracal serval*

Geoffroy's cat *Leopardus geoffroyi*
Kodkod *Leopardus guigna*
Tigrina *Leopardus tigrinus*
Andean mountain cat *Leopardus jacobita*
Pampas cat *Leopardus colocolo*
Margay *Leopardus wiedii*
Ocelot *Leopardus pardalis*

Iberian lynx *Lynx pardina*
Eurasian lynx *Lynx lynx*
Canada lynx *Lynx canadensis*
Bobcat *Lynx rufus*

Puma *Puma concolor*
Jaguarundi *Puma yaguarondi*
Cheetah *Acinonyx jubatus*

Asian leopard cat *Prionailurus bengalensis*
Fishing cat *Prionailurus viverrina*
Flat-headed cat *Prionailurus planiceps*
Rusty-spotted cat *Prionailurus rubiginosus*
Pallas's cat *Otocolobus manul*

Domestic cat *Felis catus*
Wildcat *Felis silvestris*
Sand cat *Felis margarita*
Black-footed cat *Felis nigripes*
Jungle cat *Felis chaus*

Felid ancestor 10.8 MYA
Panthera ancestor 6.4 MYA
Bay cat ancestor 5.41 MYA
Caracal ancestor 5.6 MYA
Ocelot ancestor 2.9 MYA
Lynx ancestor 3.2 MYA
Puma ancestor 4.9 MYA
Leopard cat ancestor 5.9 MYA
Domestic cat ancestor 3.4 MYA

9.4 MYA
8.5 MYA
8.0 MYA
7.2 MYA
6.7 MYA
6.2 MYA

Millions of Years Ago (MYA)

Middle Miocene | Late Miocene | Early Pliocene | Late Pliocene | Pleistocene

Sea Level (meters)

8 LINEAGES

1 PANTHERA
These medium- to large-size cats (15 to 350 kilograms) are found throughout the world. They are the dominant predators in the ecosystems and on the continents that they inhabit, often specializing on large ungulate species. The lion, tiger, jaguar, leopard and snow leopard have an incompletely ossified hyoid, which allows them to roar. The two clouded leopard species do not roar.
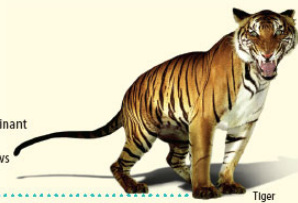
2 BAY CAT
This poorly known group of small- to medium-size cats (two to 16 kilograms) is restricted to forested habitats in tropical Southeast Asia. Before the authors' genetic analyses, taxonomists did not consistently group these species together.

3 CARACAL
These medium-size cats (five to 25 kilograms), which are restricted to Africa, are distinctive and recognizable but were not typically grouped together before the authors' genetic work.

4 OCELOT
These small- to medium-size cats (1.5 to 16 kilograms) live in a broad range of habitats throughout Central and South America. They have a different number of chromosomes than other Felidae species do (36 instead of 38).

5 LYNX
These medium-size cats (six to 20 kilograms) all have short tails and pointed ears. They live in temperate climates of North America and Eurasia and tend to specialize on hare and rabbit. With the exception of the Iberian lynx, these species have been among the most widely exploited for their fur.

6 PUMA
These diverse cats, from the small jaguarundi (three to 10 kilograms) to the large African cheetah (21 to 65 kilograms), originated in North America but have spread widely across four continents and remain broadly distributed. Pumas can be locally common and are legally hunted in parts of their range.
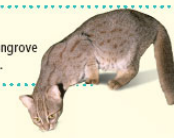
7 ASIAN LEOPARD CAT
These small cats (two to 12 kilograms) occupy a wide range of habitats in Asia, from mangrove forest to Mongolian steppe. The Asian leopard cat is the most common small cat in Asia.
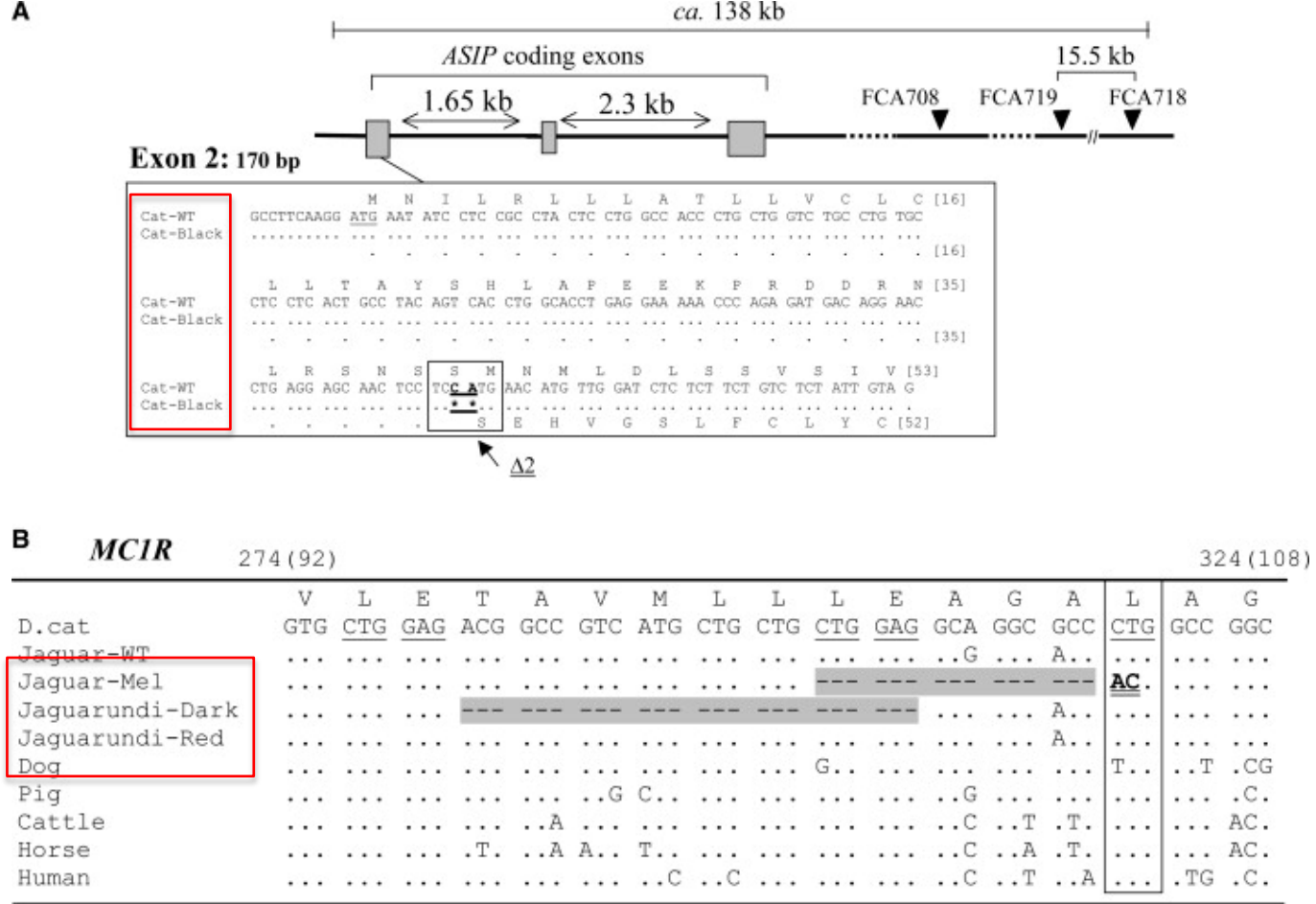
8 DOMESTIC CAT
These small cats (one to 10 kilograms), with the exception of the domestic cat, which is worldwide, have African and Eurasian distribution.

Tiger
Asian golden cat
Serval
Ocelot
Bobcat
Puma (mountain lion)
Rusty-spotted cat
Domestic cat

Stephen J. O'Brien and Warren E. Johnson, 2007. The Evolutionary of Cats. *Scientific American*

Table 1. Available information on the occurrence of melanism in felid species.

Species	Strongest evidence and original references	Proposed mode of Inheritance	No. of offspring analyzed in the original literature source
Felis catus	**Visual** [30,31]	**Recessive** [5,30,31]	**1 black offspring from a pair of wild type parents** [30,31]
Felis chaus	**Photograph** [32]	**Dominant** [32]	**1 wild-type offspring from a pair of melanistic parents** [32]
Felis silvestris, F. lybica	Anecdotal [32,33]	-	-
Prionailurus bengalensis	Anecdotal [34,35]	-	-
Panthera pardus	**Visual** [36,37]	**Recessive** [36,37]	**Total of 439 offspring** [36,37]
Panthera onca	**Visual** [32]	**Dominant** [5,32]	**Total of 81 offspring** [32]
Panthera leo	Anecdotal [32]	-	-
Panthera tigris	Anecdotal [34,38]	-	-
Panthera uncia	Anecdotal [39]	-	-
Neofelis nebulosa	Anecdotal [40,41]	-	-
Lynx rufus	**Photograph** [34]	-	-
Leopardus geoffroyi	**Visual** [42]	-	-
Leopardus guigna	**Photograph** [32,43,44,45]	-	-
Leopardus tigrinus	**Visual** [32,46]	-	-
Leopardus colocolo	**Photograph** [32]	**Recessive** [32]	**2 black offspring from a pair of wild-type parents** [32]
Acinonyx jubatus	Anecdotal [40,47]*	-	-
Puma concolor	Anecdotal [48]	-	-
Puma yagouaroundi	**Visual** [5]	**Co-dominant** [5]	-
Leptailurus serval	**Video** [33,34,39]	-	-
Caracal caracal	Anecdotal [34]	-	-
Caracal aurata	Anecdotal [49]	-	-
Pardofelis temminckii	**Photograph** [34,35]	**Recessive****	-
Pardofelis marmorata	**Photograph** [50]	-	-

(A) Nucleotide sequence of domestic cat *ASIP* exon 2, shown for a wild type and a black individual homozygous for the *ASIP*-Δ2 allele.

(B) Sequences are shown from a domestic cat, wild-type jaguar allele, melanistic jaguar allele *MC1R*-Δ15, dark-brown jaguarundi allele *MC1R*-Δ24, and a reddish jaguarundi.

Fig. 1. in Eizirik et al. (2003) *Current Biology*.

	Signal peptide		'Mature' N-terminus		Basic central domain	
Cat	MNILRLLLAT LLVCLCLLTA YS	HLAPEEKP RDDRNLRSNS	SMNMLDLSSV SIVALN	KKSK KISRKEAEK-	KRSSKKKASM [80]
Ppa	....S...... ..	....M....	...L...P..	....-	.... [80]
Ppa-M	....S...... ..	....M....	...L...P..	....-	.... [80]
Pte	....S...... ..	....	...L...P..	....-	.... [80]
Pte-M	....S...... ..	....	...L...P..	....-	.... [80]
Dog	...F..... ...S..F... ..	...-.... K...S....	.V.L..FP..	....-	.... [80]
Fox	...F..... ...S..F... ..	...-.... K...S....	.V.L..FP..	....-	.... [80]
Horse	.DVIH.F... ...S..F... ..	...S..... K...S..N...	...L..SP.. ..M...	....K	.... [80]
Cow	.DVS...... ......F... ..	....E...KN..	...L..FP..	....N...K	..P..R..P. [80]
Pig	.DVT...... ....FF.. S.	.......S K.E.S....	...L..FP..	....-	-......... [80]
Human	.DVT...... ...F..FF.. N.	..P....L ....S....	.V.L..VP..	.... Q.G..A...-	......E... [80]
Mouse	.DVT...... .VSF..FF.V H.	...L..TL G...S....	...S..F...	....R	.... [80]
Rat	.DVT...... .VGF..F..V H.	..VF..TL G...S.K...	.I.S..F...	....R	.........I [80]

			1	2	34 5 6 7		8 9	10	
Cat	KNVAQ	PRRPR	PPPPAP	CVAT	RDSCKPPAPA	CCDPCASCQC	RFFRSSCSCR	VLNPTC	[136]
Ppa	....R	.....	......	....	.N....	....	....	......	[136]
Ppa-M	....R	.....	......	....	.N....	....	....	......	[136]
Pte	....R	.....	......	....	....	....	....	......	[136]
Pte-M	....R	.....	......	....	....	....	....	.W.	[136]
Dog	....R	---..	....T.	....	.N...S....	....	..A.T.. ..S.R.	[136]
Fox	....R	---..	....N.	....	.N...S....	....	..A.T.. ..S.S.	[136]
Horse	TK..R	---..	LLQ...	....	....	....	..A.... ..TR..	[136]
Cow	....R	---T.	....T.	....	....	....F....	..A....	[136]
Pig	.K...	---..	..R...	...N	.........L.	....F....	..A....	[136]
Human	.K.VR	---..	T.LS..	...N	....	....	..A.... ..SLN.	[136]
Mouse	.K..R	-----	....S.	....	....	....	...G.A.T.. ....N.	[136]
Rat	.K..R	-----	....S.	....	..N.....	....	...G.A.T.. ....N.	[136]

Proline-rich domain   **Cysteine-rich C-terminal domain**

Amino acid alignment of ASIP. Wild-type and melanistic sequences of each wild cat species are shown. Vertical lines demarcate the boundaries among the five functional domains proposed for ASIP, named above or below the sequences. Numbers 1–10 refer to the 10 conserved cysteine residues present in the C-terminal domain.

Fig. 1, 2 in Schneider *et al*. 2012 PLoS ONE 7(12)

What do we care about?

➤ Genetic basis of reddish and grey coloration in Asiatic Golden Cats

• Asiatic Golden Cat (*Pardofelis temminckii*)

• Carnivora Felidae

• NT (Near Threatened) in the IUCN Red List & Appendix I of CITES

• Geographic Range: from the Himalayan foothills into China and Southeast Asia.

• Habitat and Ecology: primarily found in forest habitats

Pardofelis temminckii

NOT EVALUATED	DATA DEFICIENT	LEAST CONCERN	NEAR THREATENED	VULNERABLE	ENDANGERED	CRITICALLY ENDANGERED	EXTINCT IN THE WILD	EXTINCT
NE	DD	LC	NT	VU	EN	CR	EW	EX

Materials Specificity: ancient DNA procedure

TABLE 1   Overview over different types of damage in ancient DNA

Type of damage	Process	Effects on DNA	Possible solutions
Strand breaks	Degradation by microorganisms Nucleases in the postmortem cell Other chemical processes	Reduction of overall DNA amounts Size reduction	PCR of overlapping fragments of short length
Oxidative lesions	Damage to bases	Base fragmentation	PCR of overlapping fragments of short length
	Damage to deoxyribose residues	Sugar fragmentation	
		Nucleotide modification	Multiple independent PCRs Cloning and sequencing of several clones
DNA crosslinks	Reactions between DNAs as well as DNA and other biomolecules	e.g., Maillard products	PTB (N-phenylacyl thiazolium bromide)
Hydrolytic lesions	Loss of amino groups 1. adenine $\Rightarrow$ hypoxanthine 2. cytosine $\Rightarrow$ uracil 3. 5-methyl-cytosine $\Rightarrow$ thymine 4. guanine $\Rightarrow$ xanthine	Change of coding potential	Multiple independent PCRs Cloning and sequencing of several clones

Paabo et al. (2004)

Copyright: Photos taken by Yuechen Liu in Shanghai Science and Technology Museum

Phylogenetic tree construction (MEGA)

Acquire the MC1R nucleotides sequence from UCSC

Acquire the MC1R nucleotides sequence from UCSC

Acquire the MC1R nucleotides sequence from UCSC

MC1R nucleotide sequences alignment (ClustalW2)

```
HUMAN  MAVQGSQRRLLGSLNSTPTAIPQLGLA---ANQTGARCLEVSISDGLFLSLGLVSLVENA  [60]
HORSE  .PL..P...............LPT.Y...T---T...EPP......P..............V  [60]
MOUSE  .ST.EP.KS.........N--TSH.......---T..SEPW..Y...P.............V  [60]
PIG    .P.L.PE....A..S.A.P.A.R.....ANQT....PQ......P...............V  [60]
FELCA  .S...P...........SP.A.R.........P...L.VP........G......V...V  [60]
CHICK  .SMLAPL.LVREPW.ASEGNQSNATAG-----AG..W.QGLD.PNE...T...........L  [60]

HUMAN  LVVATIAKNRNLHSPMYCFICCLASDLLVSGSNVLETAVILLLEAGALVARAAVLQQLD  [120]
HORSE  ...TA.................Y......V.....M......M.IL......V.ATQ.S......  [120]
MOUSE  ...IA.T...............Y......V.....M.V.I....TI......I....V.LV....  [120]
PIG    ....A.................Y.V....V......V......L........A.Q...V....  [120]
FELCA  ....A.................Y......V......V.S....M........AG.....V.R..  [120]
CHICK  ....A.L...........T.Y......V..M...V..LAK.LFM...M.H.V...I..SIVRHM.  [120]

HUMAN  NVIDVITCSSMLSSLCFLGAIAVDRYISIFYALRYHSIVTLPRARRAVAAIWVASVVFST  [180]
HORSE  .I....LI.G..V...........SI.............MM...VW..IV....V..LS.  [180]
MOUSE  .L....LI.G..V..........I...I..............VG...MV.I.S.  [180]
PIG    ..M...LI.G..V..............V.............G..I.....AG..LS.  [180]
FELCA  DI....LV.GA.V.................W..IS........LS.  [180]
CHICK  ....MLI...VV...S.....V...........T........M..Q..VVTM.SV.L..T.S.  [180]

HUMAN  LFIAYYDHVAVLLCLVVFFLAMLVLMAVLYVHMLARACQHAQGIARLHKRQRPVHQGFGL  [240]
HORSE  .......N.T.........T...V...............R........H.I.....  [240]
MOUSE  ...T..K.T......T......A....I.A.FT.......Q....R.SIR...C.  [240]
PIG    ....H.T...G...S..V..A............GRH.....T.H.TR..C.  [240]
FELCA  ........T.......S..V............R...............L.  [240]
CHICK  VL.T..RNN.I....IG...F.....L...I..F.L..H.VRS..SSQQ.-..PTIYRTSS.  [240]

HUMAN  KGAVTLTILLGIFFLCWGPFFLHLTLIVLCPEHPTCGCIFKNFNLFLALIICNAIIDPLI  [300]
HORSE  ..A.........V..........S..LI..Q.....V......K...T..L.S..V...  [300]
MOUSE  ..A...........L....Q.....S.....L..VLSSTV..  [300]
PIG    ..A.....V.L..A.....S.V....Q.....V.....V.....S..V...  [300]
FELCA  ..A.........S..M....R..I...V........T.....S..V..F.  [300]
CHICK  ....V..I.......F...I...T.TN.F.T.F.SY......I....S.VV.  [300]

HUMAN  YAFHSQELRRTLKEVLTCSW  [320]
HORSE  ...R......K..Q....L..  [320]
MOUSE  ...R......M.......L..  [320]
PIG    ...R......K..Q...Q..  [320]
FELCA  ...R......K..Q....L..  [320]
CHICK  ...R..........R..VL..  [320]
```

Prediction of trans-membrane helices in proteins (TMHMM)

TMHMM posterior probabilities for sp|Q865E9|MSHR_FELCA

TMHMM Server v. 2.0

UniProtKB
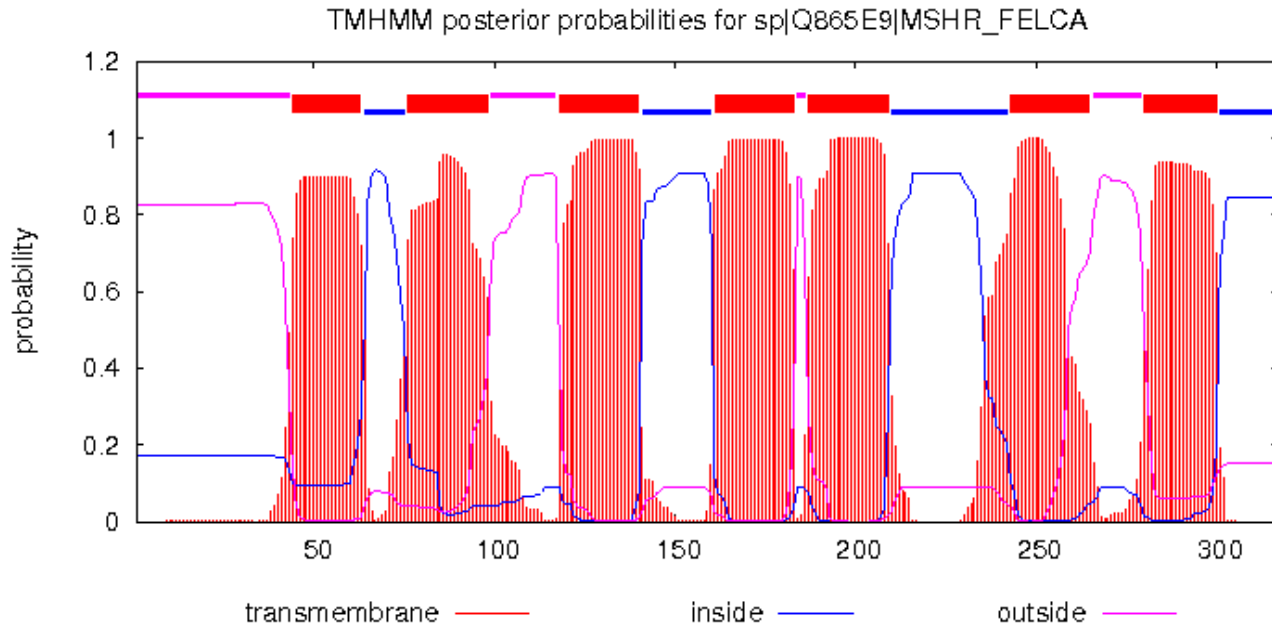
Regions

|					
☐	Topological domain	1 – 37	37	Extracellular (Potential)	
☐	Transmembrane	38 – 63	26	Helical; Name=1; (Potential)	
☐	Topological domain	64 – 72	9	Cytoplasmic (Potential)	
☐	Transmembrane	73 – 93	21	Helical; Name=2; (Potential)	
☐	Topological domain	94 – 118	25	Extracellular (Potential)	
☐	Transmembrane	119 – 140	22	Helical; Name=3; (Potential)	
☐	Topological domain	141 – 163	23	Cytoplasmic (Potential)	
☐	Transmembrane	164 – 183	20	Helical; Name=4; (Potential)	
☐	Topological domain	184 – 191	8	Extracellular (Potential)	
☐	Transmembrane	192 – 211	20	Helical; Name=5; (Potential)	
☐	Topological domain	212 – 240	29	Cytoplasmic (Potential)	
☐	Transmembrane	241 – 266	26	Helical; Name=6; (Potential)	
☐	Topological domain	267 – 279	13	Extracellular (Potential)	
☐	Transmembrane	280 – 300	21	Helical; Name=7; (Potential)	
☐	Topological domain	301 – 317	17	Cytoplasmic (Potential)	

Domains within *Felis catus* protein MSHR_FELCA (Q865E9)
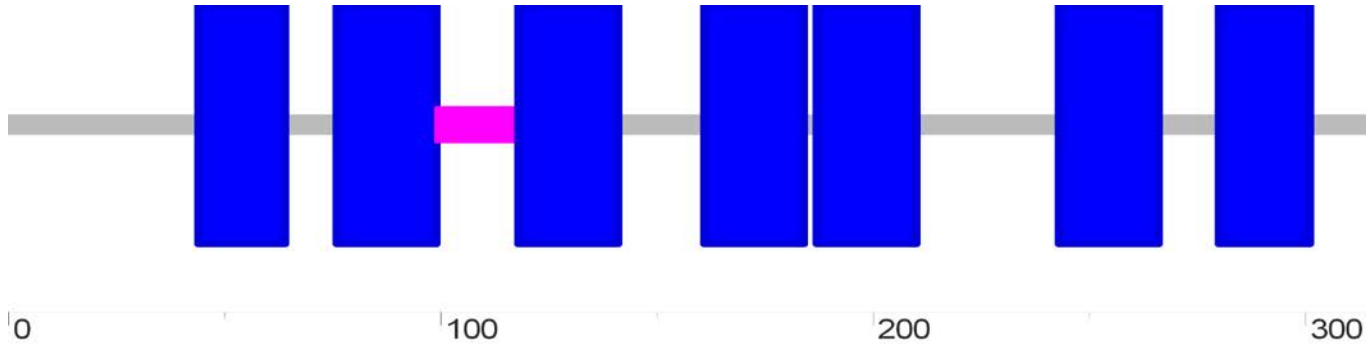
Confidently predicted domains, repeats, motifs and features:

Name	Start ▲	End	E-value
transmembrane region	44	63	N/A
transmembrane region	76	98	N/A
low complexity	99	116	N/A
transmembrane region	118	140	N/A
transmembrane region	161	183	N/A
transmembrane region	187	209	N/A
transmembrane region	243	265	N/A
transmembrane region	280	300	N/A

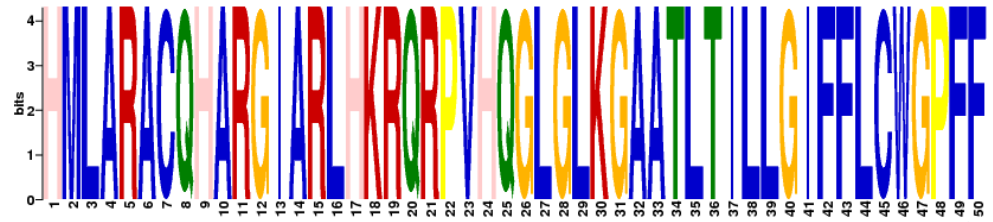# Motifs within Felidae protein MSHR (Q865E9, Q865E5, Q865E8)
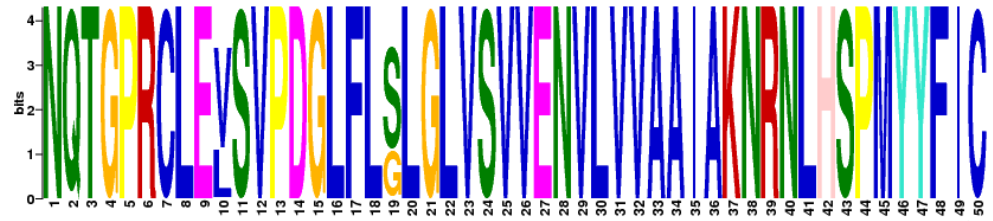

Motif 1
- 2.2e-060
- 3 sites
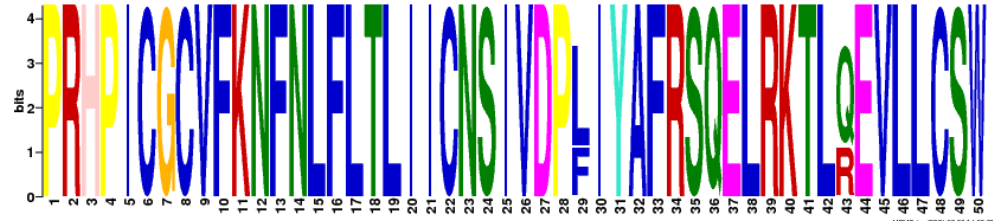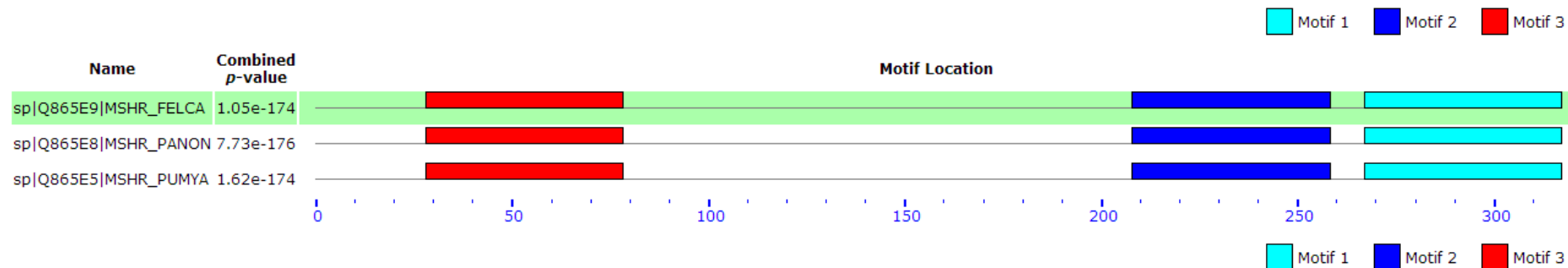
Motif 2
- 3.6e-054
- 3 sites

Motif 3
- 5.2e-050
- 3 sites

ALL MOTIFS

Top

Combined Block Diagrams ❓

Non-overlapping sites with a *p*-value better than 0.0001.
The height of the motif "block" is proportional to -log(p-value), truncated at the height for a motif with a p-value of 1e-10.
Click on any row to highlight sequence in all motifs. The motif blocks have tool tips with more information.

	Motif 1 ▢	Motif 2 ▢	Motif 3 ▢

Name	Combined *p*-value	Motif Location
sp|Q865E9|MSHR_FELCA	1.05e-174	
sp|Q865E8|MSHR_PANON	7.73e-176	
sp|Q865E5|MSHR_PUMYA	1.62e-174	

0   50   100   150   200   250   300

	Motif 1 ▢	Motif 2 ▢	Motif 3 ▢

Swiss model structure prediction

Model-Template Alignment

|		
Model_01	MSVQGPQRRLLGSLNSTSPAAPRLGLAANQTGPRCLELSVPDGLFLGLGLVSVVENVLVVAAIAKNRNLHSPMYYFICCL	80
2rh1.1.A	--------------------------------------GMGIVMSLIVLAIVFGNVLVITAIAKFERLQTVTNYFITSL	82
Model_01	AVSDLLVSVSSVLETAVMLLLEAGALAGRAAVVQRLDDIIDVLVCGAMVSSLCFLGAIAVDRYISIFYALRYHSIVTLPR	160
2rh1.1.A	ACADLVMGLAVVPFGAAHILM--KM-WTFGNFWCEFW---TSIDVLCVTASIETLCVIAVDRYFAITSPFKYQSLLTKNK	156
Model_01	AWRAISAIWVAS-VLSSTLFIA-YYD-----------------------HTAVLLCLVSFFVAMLVLMAVLYVHMLARACQH	217
2rh1.1.A	ARVIILMVWIVSGLTSFLPIQMHWYRATHQEAINCYAEETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQ	236
Model_01	ARGIARLHK--	226
2rh1.1.A	LNIFEMLRIDEGLRLKIYDTEGYYTIGIGHLLTKSPSLNAAKSELDKAIGRNTNGVITKDEAEKLFNQDVDAAVRGILR	316
Model_01	---RQRP-------------VH	232
2rh1.1.A	NAKLKPVYDSLDAVRRAALINMVFQMGETGVAGFTNSLRMLQQKRWDEAAVNLAKSRWYNQTPNRAKRVITTFRTGTWDA	396
Model_01	QG---LGLKGAATLTILLGIFFLCWGPFFLHLSLMVLCPRHPICGCVFKNFNLFLTLIICNSIVDPFIYAFRSQELRKTL	309
2rh1.1.A	YKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNL----IRKEVYILLNWIGYVNSGFNPLIY-CRSPDFRIAF	471
Model_01	QEVLLCSW	317
2rh1.1.A	QELLCLR-	478

Z-score

QMEAN4	-6.10
CBeta	-4.41
All Atom	-3.07
Solvation	-2.89
Torsion	-4.55
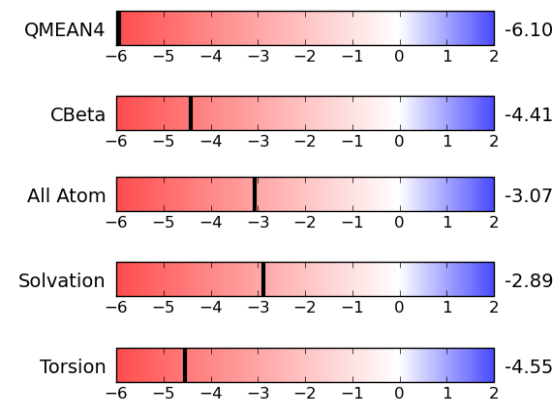
Local Quality Estimate
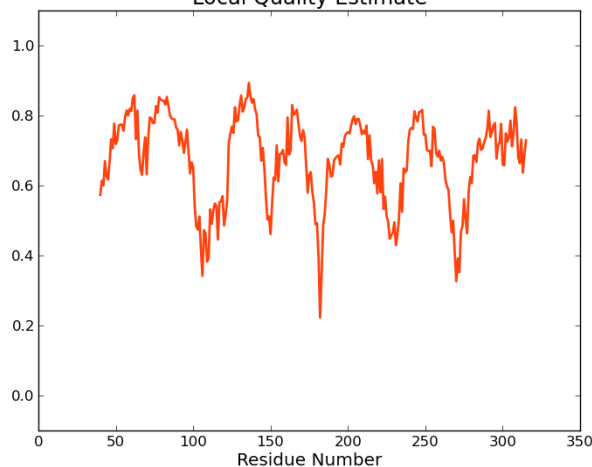
Comparison with Non-redundant Set of PDB Structures
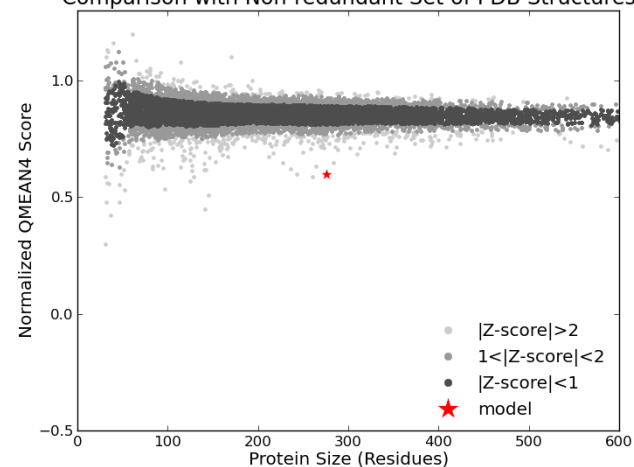
Protein interaction:
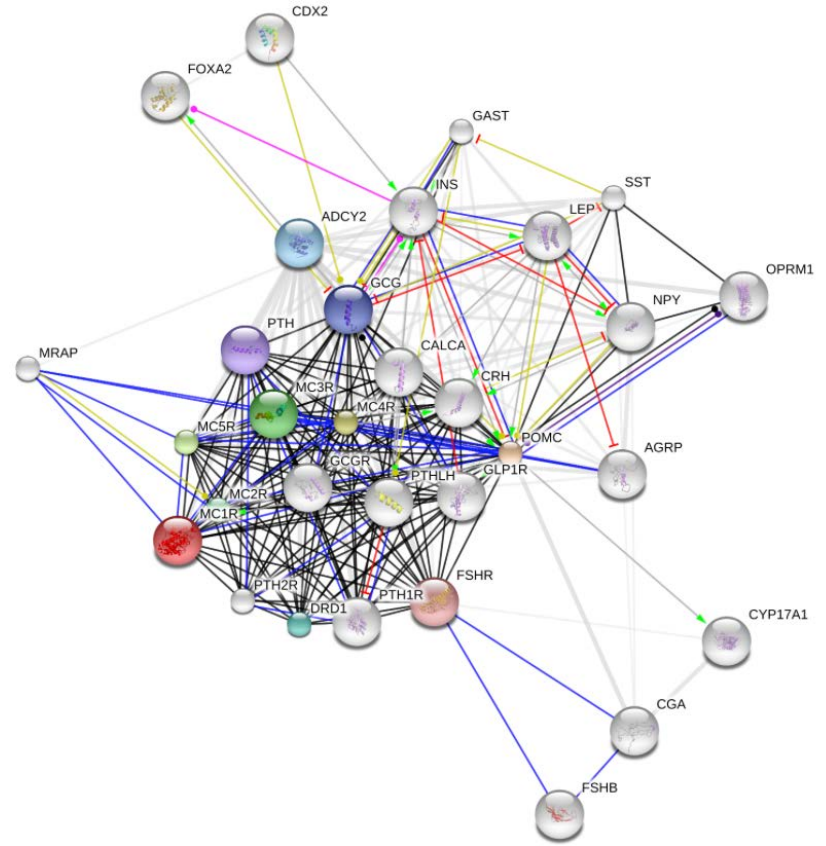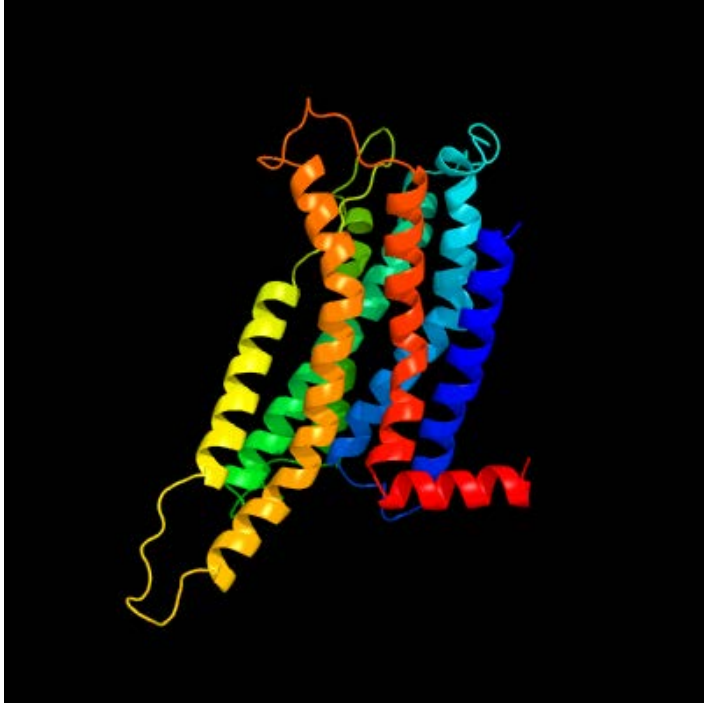
🔴	**MC1R**	melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor); Tubulin is the major constituent of microtubules. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha-chain (By similarity) (450 aa) *(Homo sapiens)*								

Predicted Functional Partners:

		Activation	Inhibition	Binding	Phenotype	Catalysis	Post-transl. m	Reaction	Expression	Score
🟤 POMC	proopiomelanocortin; ACTH stimulates the adrenal glands to release cortisol (267 aa)			●				●		0.998
🟡 MC4R	melanocortin 4 receptor; Receptor specific to the heptapeptide core common to adrenocorticotrop [...] (332 aa)			●				●		0.983
🟢 MC5R	melanocortin 5 receptor; Receptor for MSH (alpha, beta and gamma) and ACTH. The activity of thi [...] (325 aa)			●				●		0.963
🟢 MC3R	melanocortin 3 receptor; Receptor for MSH (alpha, beta and gamma) and ACTH. This receptor is me [...] (323 aa)			●				●		0.958
🟢 MC2R	melanocortin 2 receptor (adrenocorticotropic hormone); Receptor for ACTH. This receptor is medi [...] (297 aa)							●		0.948
🔵 DRD1	dopamine receptor D1; This is one of the five types (D1 to D5) of receptors for dopamine. The a [...] (446 aa)							●		0.915
🔵 ADCY2	adenylate cyclase 2 (brain); This is a membrane-bound, calmodulin-insensitive adenylyl cyclase (1091 aa)									0.914
🔵 GCG	glucagon; Glicentin may modulate gastric acid secretion and the gastro-pyloro-duodenal activity [...] (180 aa)							●		0.913
🟣 PTH	parathyroid hormone; PTH elevates calcium level by dissolving the salts in bone and preventing [...] (115 aa)							●		0.913
🔴 FSHR	follicle stimulating hormone receptor; Receptor for follicle-stimulating hormone. The activity [...] (695 aa)							●		0.912

Summary

➢ The molecular genetic basis of adaptive change in phenotype is a major out-standing issue in evolutionary biology;

➢ Evolutionary change in coat and plumage color is a promising system for making progress in this field;

➢ MC1R is an critical important candidate gene in coloration of mammals;

➢ MC1R is a kind of G-protein coupled receptor activated by α-MSH;

➢ Bioinformatics analyses are useful for deeply acquiring the sequence characteristics, phylogenetic relationships, structures, and protein interactions.

Acknowledgements