

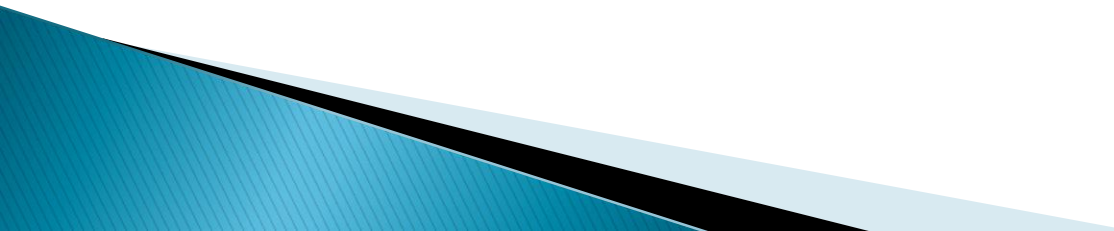
The Bioinformatic Analysis of Primates Bitter Taste Receptor **TAS2R16**

灵长类苦味受体**TAS2R16**的生物信息学
分析

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2013.11.22

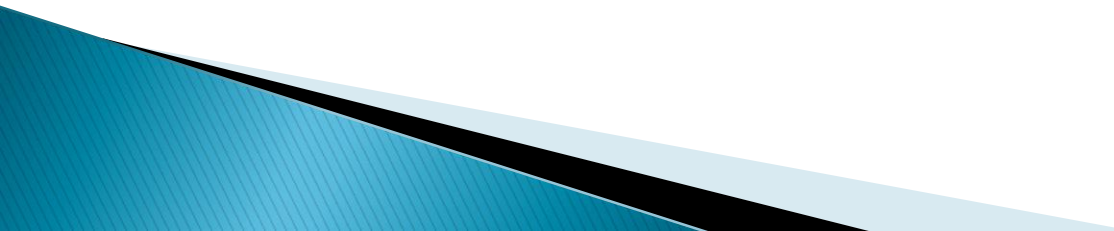
Outline

- Background
 - Research Purposes
 - Research Contents
 - Future Work
- 

Molecular Ecology

分子生态学

applying molecular population genetics, molecular phylogenetics, and more recently genomics to traditional ecological questions

- Population Structure
 - Phylogeography
 - Behavioral Ecology
 - Conservation Genetics
- 

白头叶猴 White-headed langur (*Trachypithecus leucocephalus*)

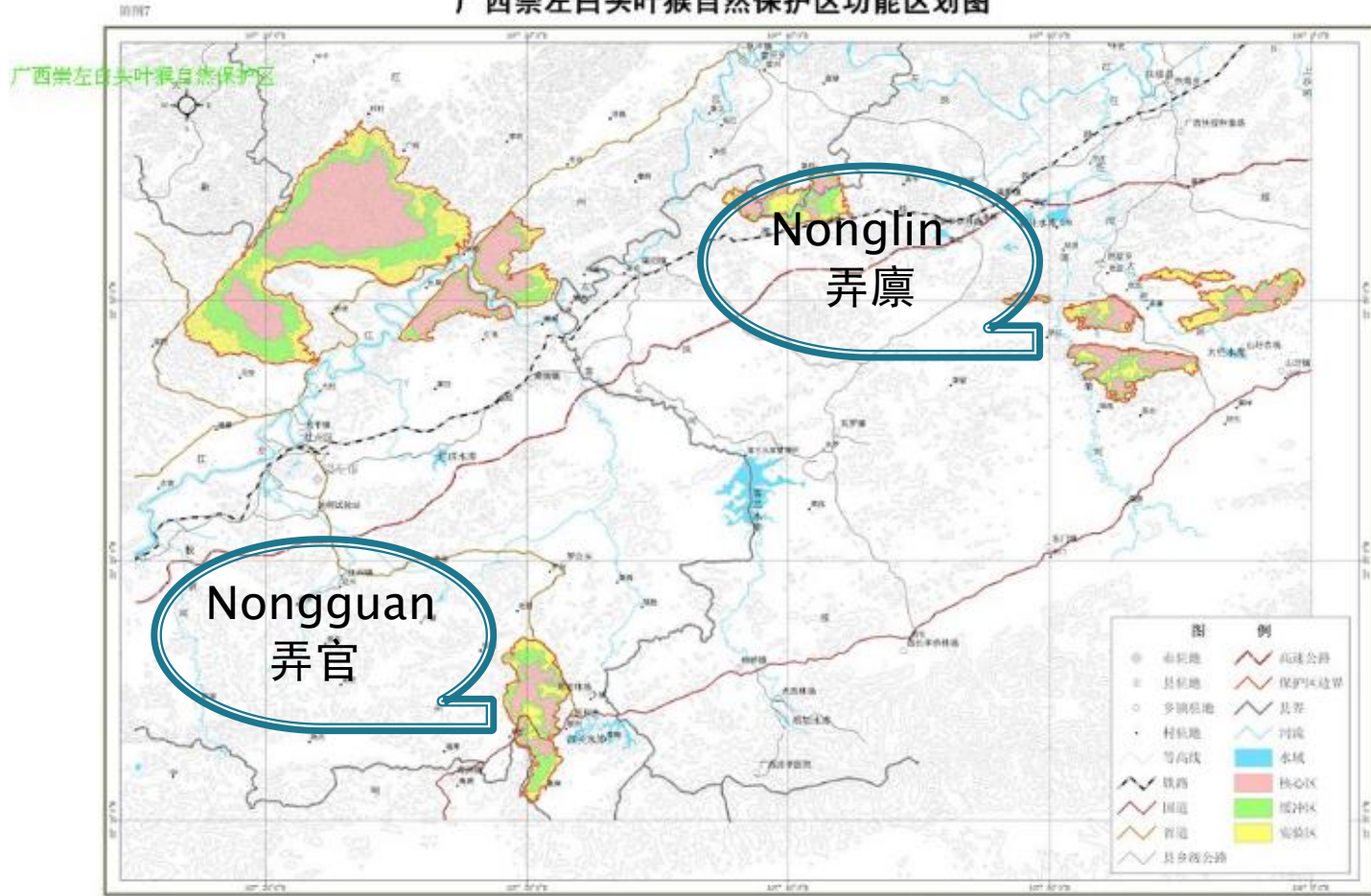


Population size: less than 1000

Diet: leafs, fruits, flowers

Habitat: Karst hills

广西崇左白头叶猴自然保护区功能区划图



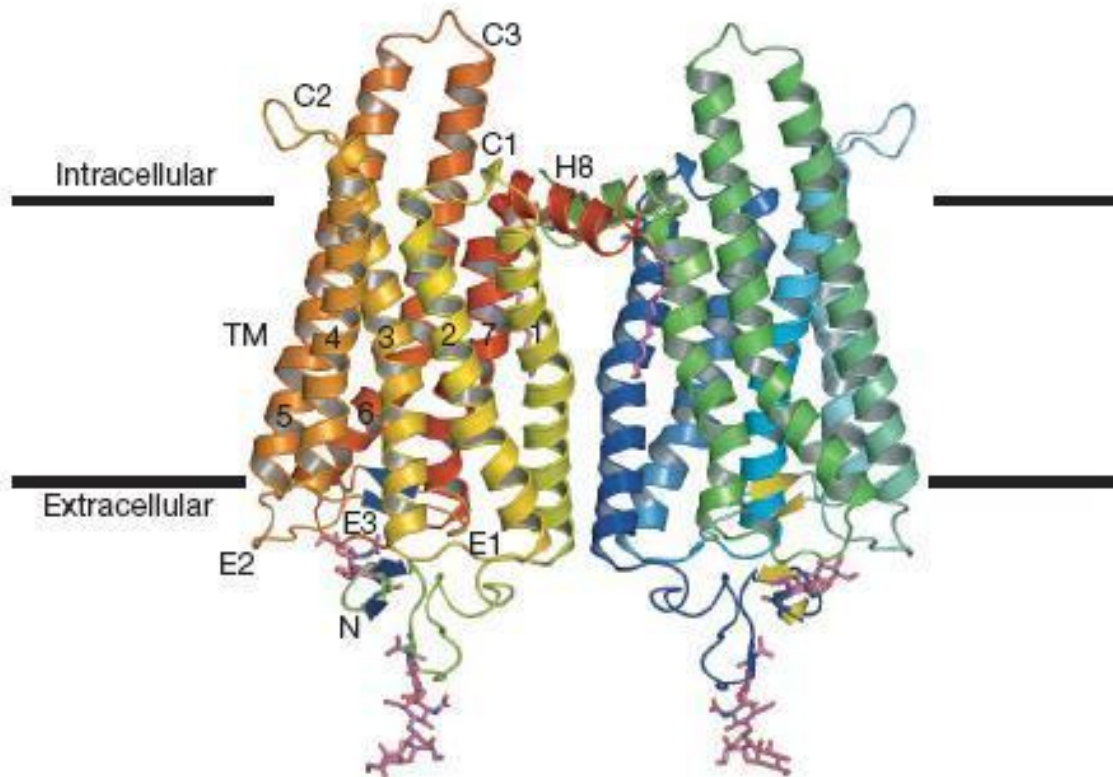
Background

- Different patterns of historical human disturbance in Nongguan and Nonglin habitats
- Different feeding choices between Nongguan and Nonglin populations

Nongguan: abundant or common plant species

Nonglin: less common plant species

G Protein-Coupled Receptors



integral membrane proteins that sense molecules outside and activate inside signal transduction

- 7 α -helical TM regions
- extracellular N-terminus, 3 extra- and 3 intra-cellular loops and intracellular C-terminus
- Interacting with G protein

Bovine Rhodopsin 2.8A
牛视紫红质2.8埃

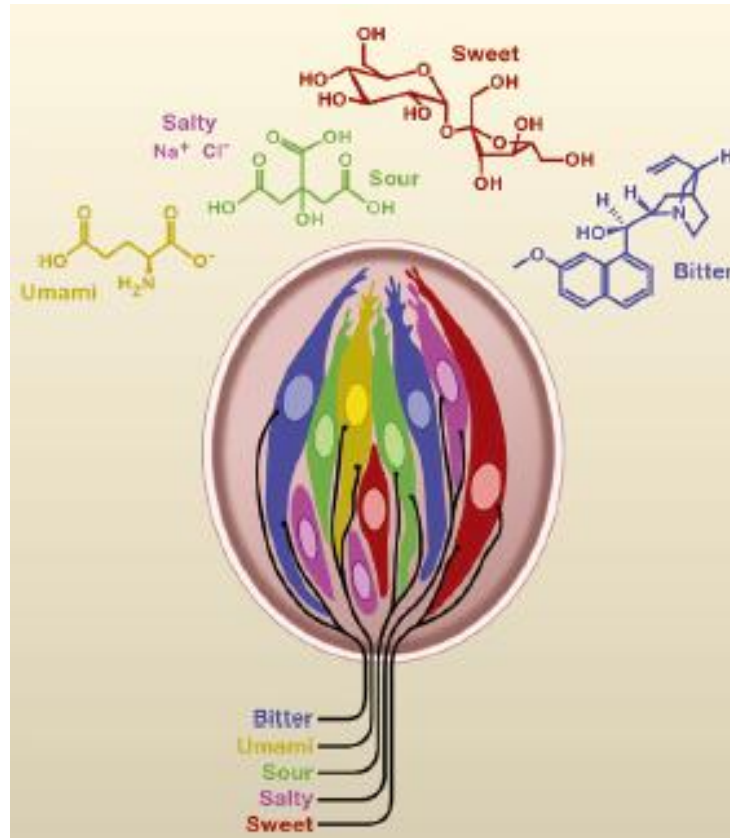
(Park *et al*, Nature, 2008)

Background

T2Rs: taste receptor, type 2 (bitter taste receptors)

Protein family: GPCR T2R family

Function: bitter recognition



Bitter

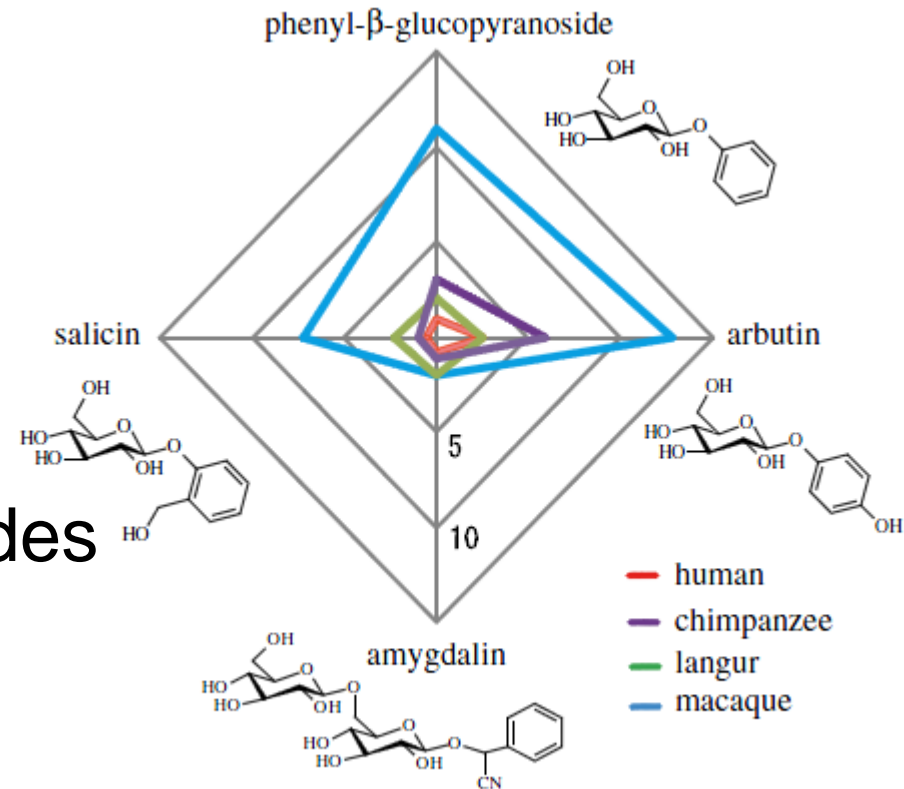
~30 T2Rs

- Cycloheximide** (mT2R5)
- Denatonium** (mT2R8, hT2R4)
- Salicin** (hT2R16)
- PTC** (hT2R38)
- Saccharin** (hT2R43, hT2R44)
- Quinine**
strychnine
atropine

TAS2R16

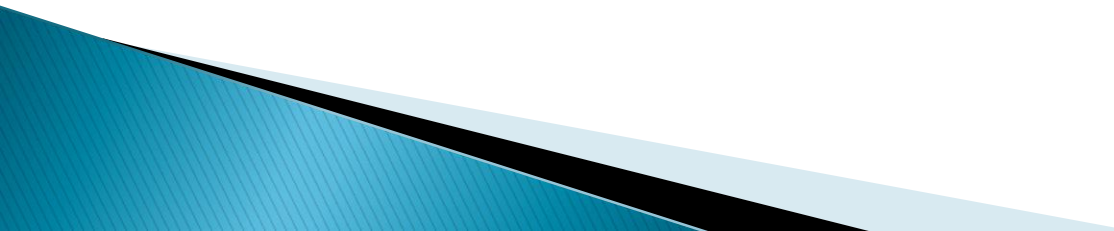
Length: 291aa (human)

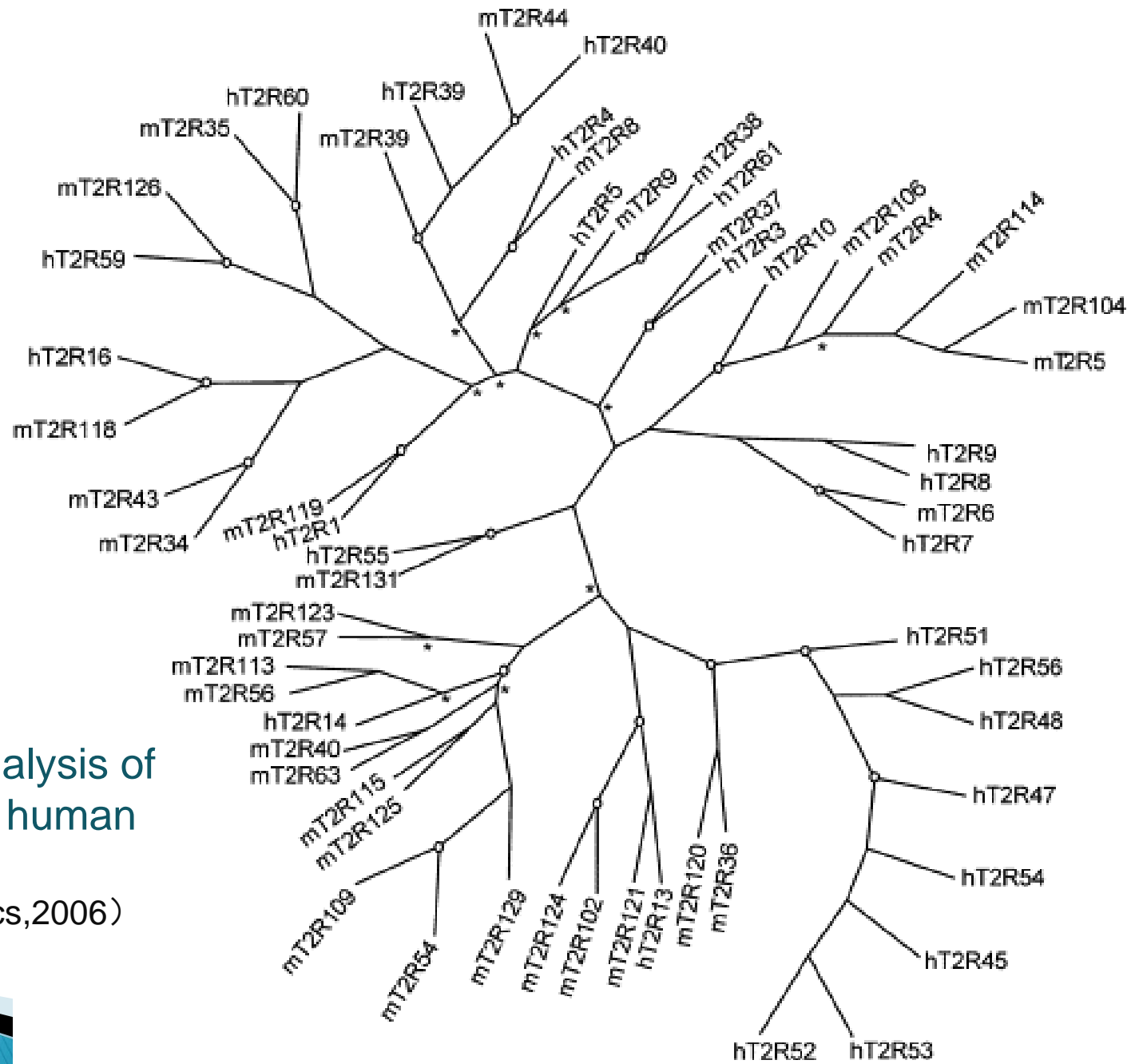
Ligand: β -glucopyranosides



According to the ligand, the sensitivities of TAS2R16 of different primate species varies.

Research purposes

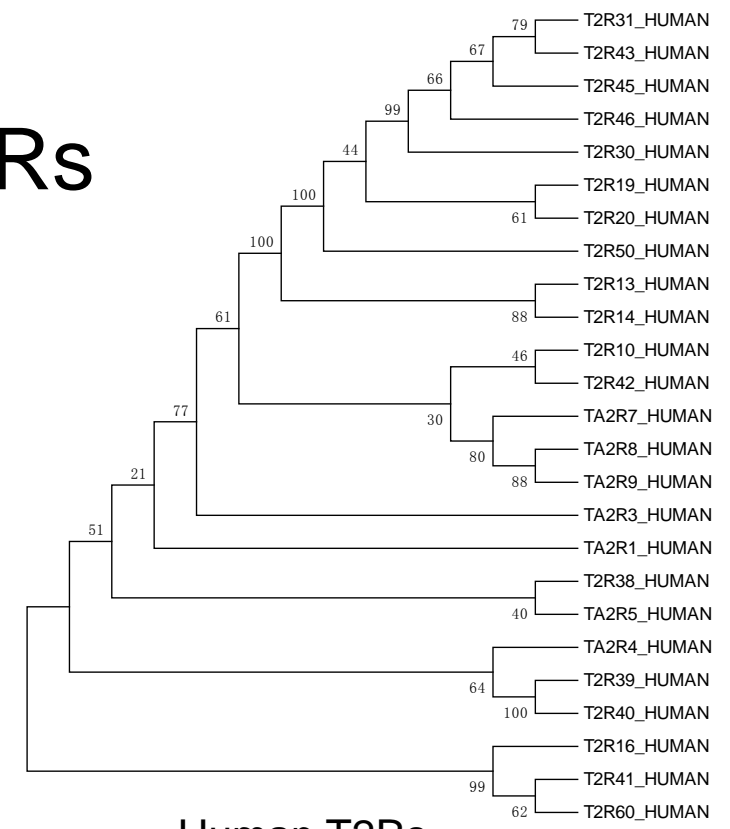
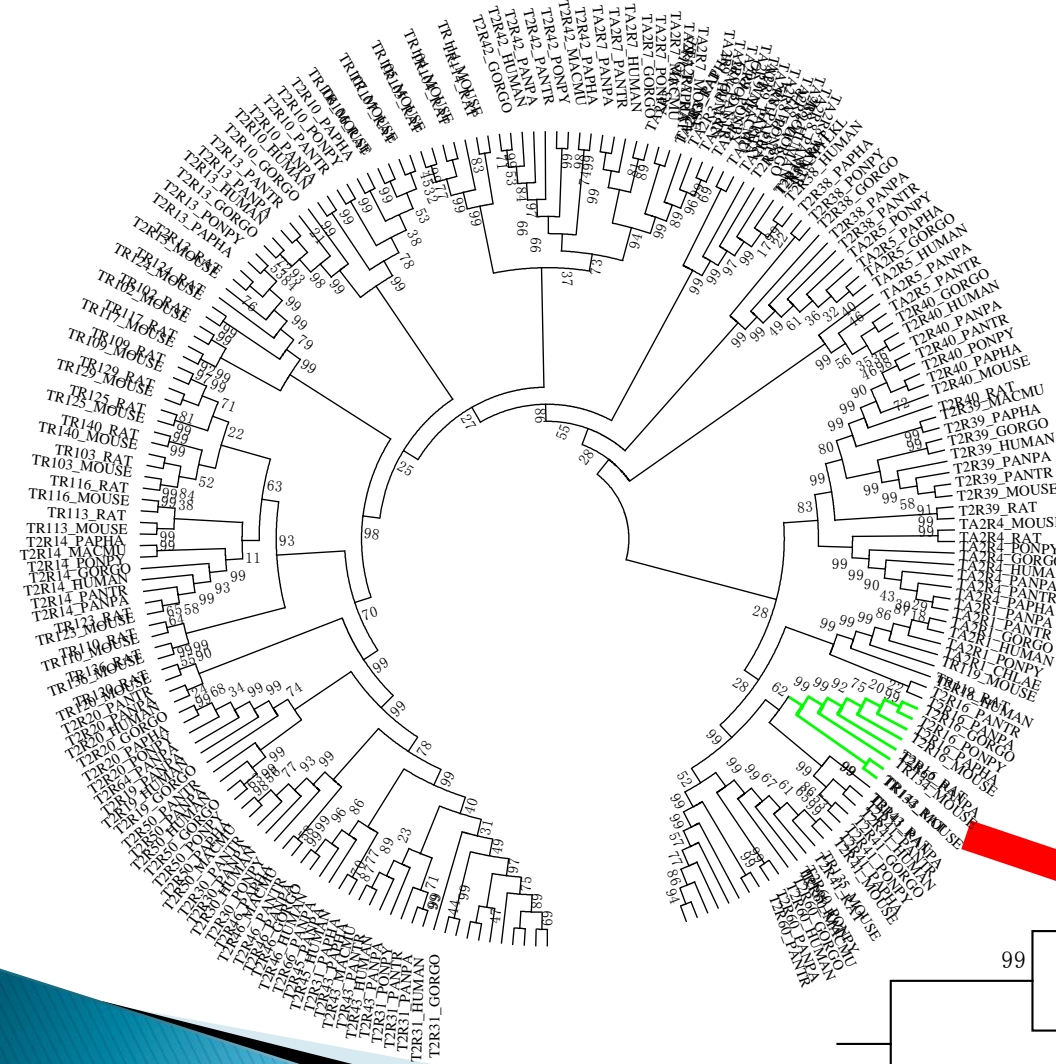
- Preliminary analysis the evolution, structure and function of primates TAS2R16
 - Examine inter-population variations of TAS2R16 in white-headed langurs
 - The relationship between food choices, genetics and environment
- 



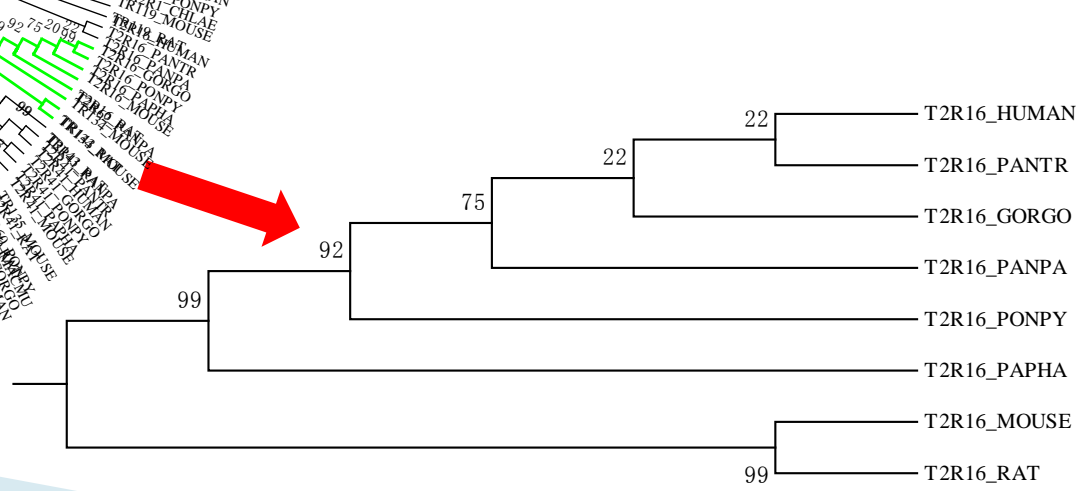
A phylogenetic analysis of
34 mouse and 25 human
Taste2 GPCRs

(Thóra *et al.*, Genomics, 2006)

Phylogeny Analysis of T2Rs



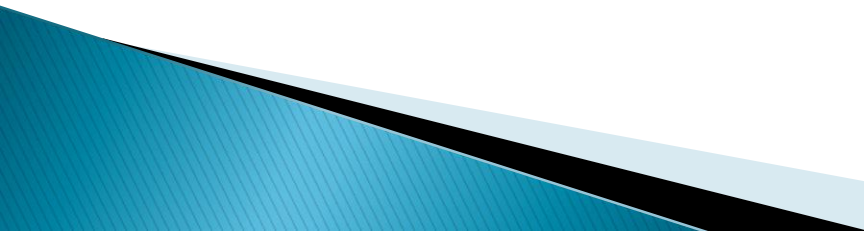
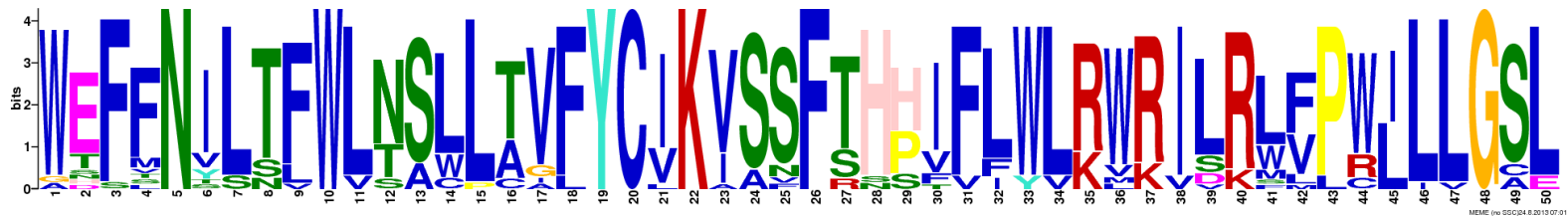
Human T2Rs



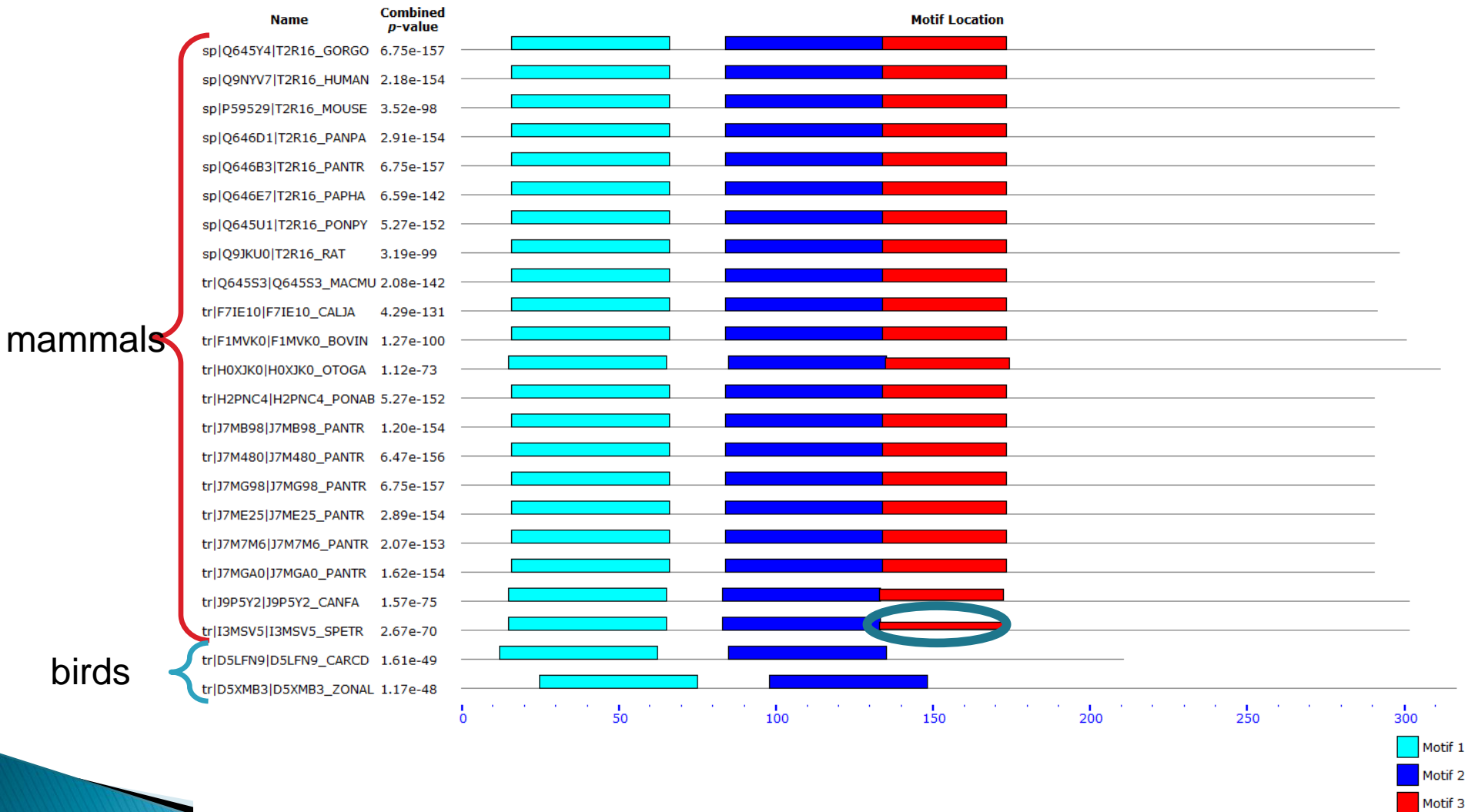
TAS2R16



Conserved Motifs in TAS2R16



Conserved Motifs in TAS2R16



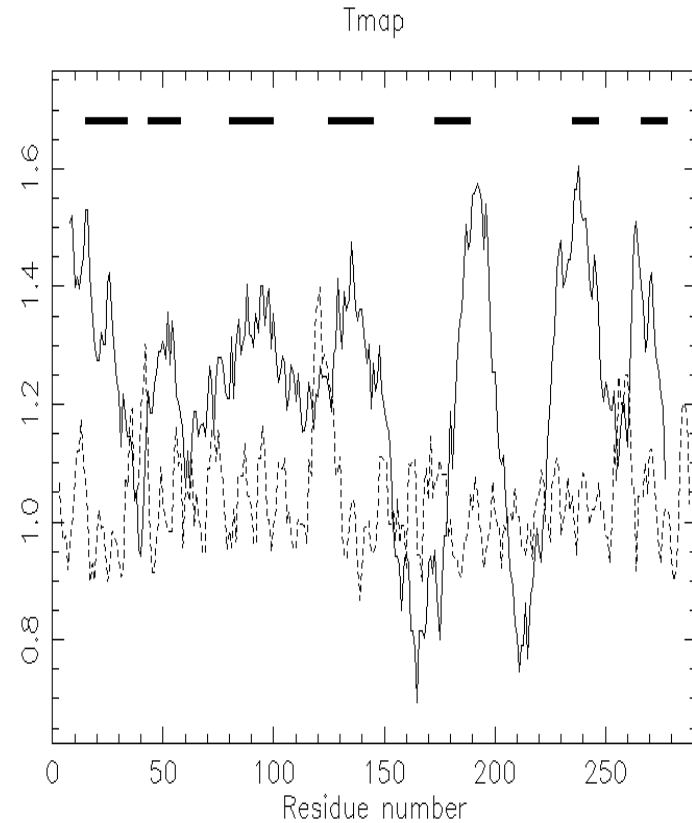
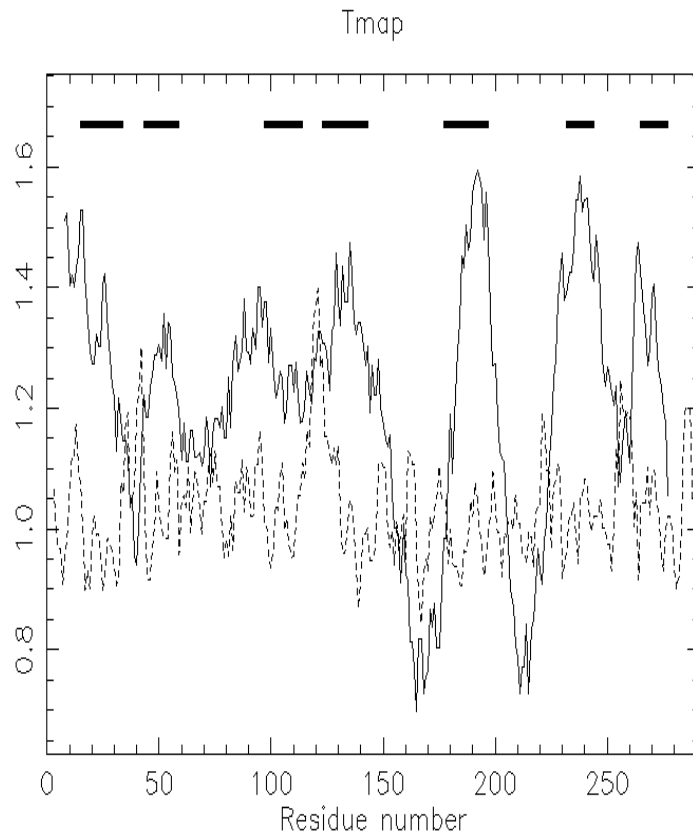
■ Motif 1
■ Motif 2
■ Motif 3

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
291	1376.0	261/291 (89.7%)	270/291 (92.8%)	0/291 (0.0%)

NP_058641.1	1	MIP I Q L T V F F M I I Y V L E S L T I I V Q S S L I V A V L G R E W L Q V R R L M P V D M I L I	50
NP_001074228.	1	MIP I Q L S V F F M I I Y V L E S L T I I V Q S S L I V A V L G R E W L Q V R R L M P V D M I L I	50
NP_058641.1	51	S L G I S R F C L Q W A S M L N N F C S Y F N L N V L C N L T I T W E F F N I L T F W L N S L L T	100
NP_001074228.	51	S L G I S R F C L Q W T S M L N D F C F Y F N F N V L C N L T I T W T F F N V L T F W L N S L L T	100
NP_058641.1	101	V F Y C I K V S S F T H H I F L W L R R I L R L F P W I L L G S L M I T C V T I I P S A I G N Y I	150
NP_001074228.	101	I F Y C I K V S S F T H P I V L W L R R I L R W L P W L L L G C L M I T C V T I I P S A I G N Y I	150
NP_058641.1	151	Q I Q L L T M E H L P R N S T V T D K L E N F H Q Y Q F Q A H T V A L V I P F I L F L A S T I F L M	200
NP_001074228.	151	Q I Q F L T M E H P P R N S T V I D R L Q K F H Q Y L H Q A H T V A L V I P F I L F L A S T I L L M	200
NP_058641.1	201	A S L T K Q I Q H H S T G H C N P S M K A R F T A L R S L A V L F I V F T S Y F L T I L I T I I G T	250
NP_001074228.	201	A S L T K Q I Q H H G T G H C N P S M K A H F T A L R S L A I L F I V F T S Y F L T I L I T M I G T	250
NP_058641.1	251	L F D K R C W L W V W E A F V Y A F I L M H S T S L M L S S P T L K R I L K G K C	291
NP_001074228.	251	L F D K R C W L W F W E A F V Y A F I F M H S T S L M L S S P T L K R I L N G K C	291

Alignment of human and macaca TAS2R16 proteins by needle
NP_0.58641.1,hTAS2R16; NP_001074228,mTAS2R16

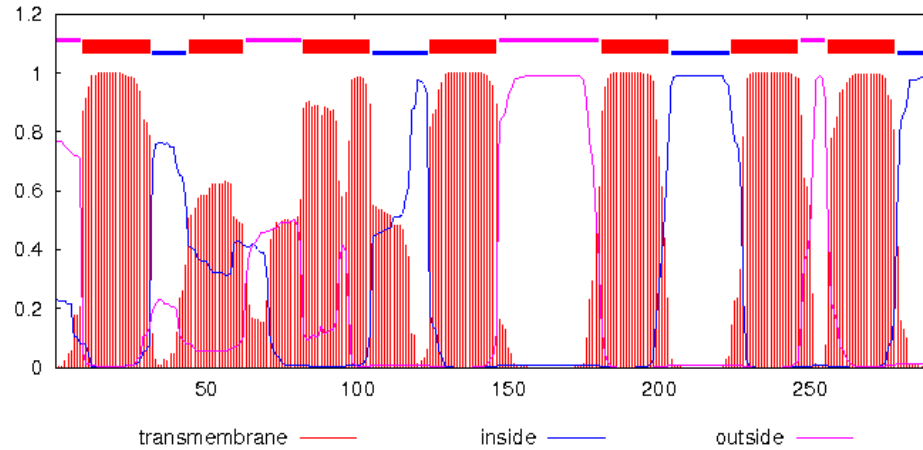
Transmembrane Structure Prediction



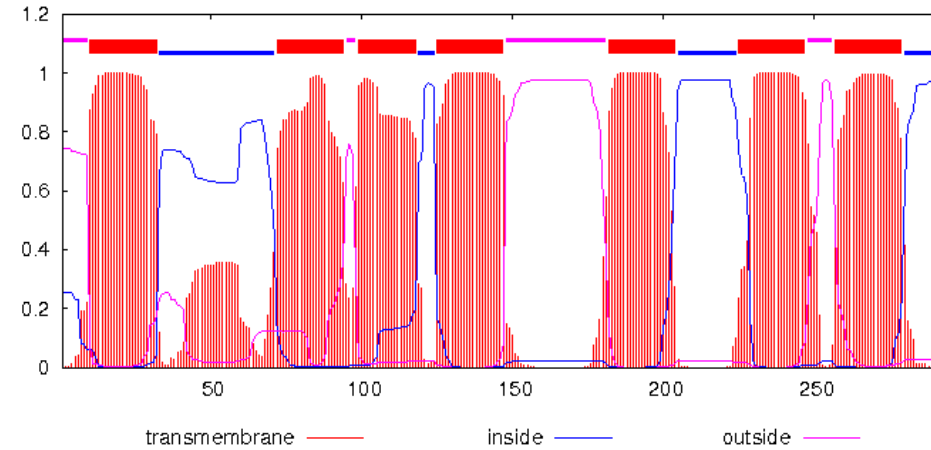
Transmembrane Structure Prediction by Tmap
left, hTAS2R16; right, mTAS2R16

Transmembrane Structure Prediction

TMHMM posterior probabilities for gj|8394395|ref|NP_058641.1|

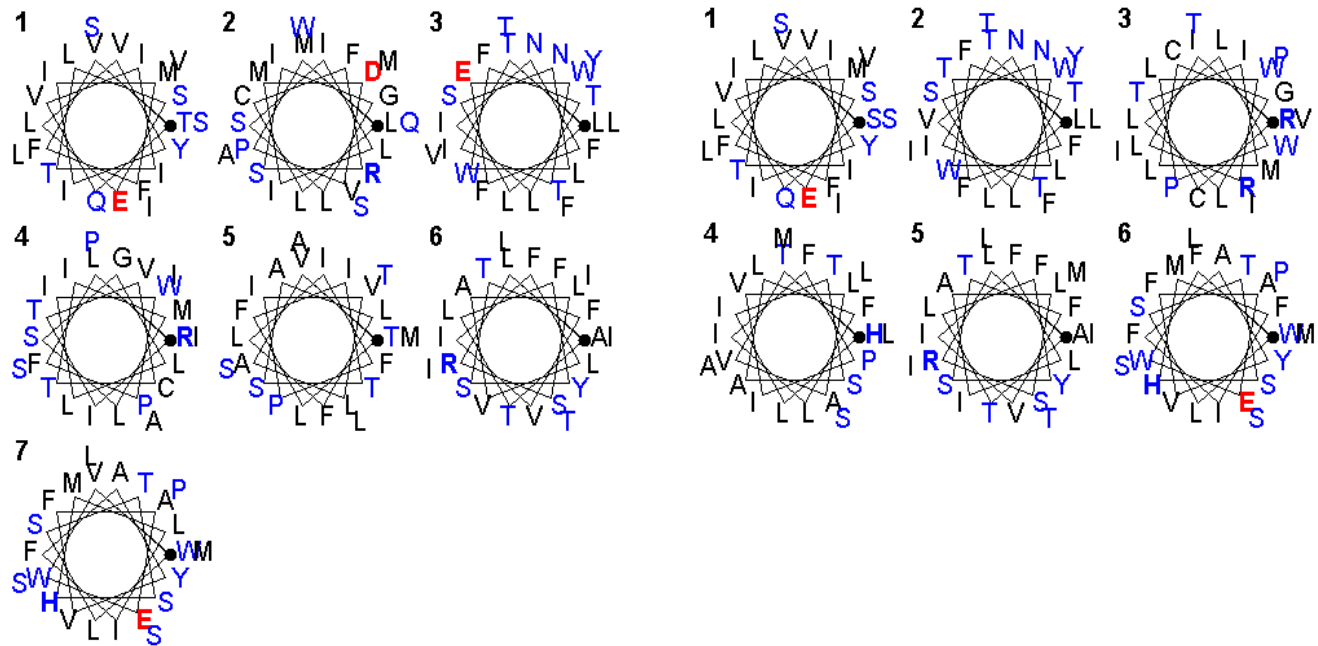


TMHMM posterior probabilities for gj|189303547|ref|NP_001074228.1|



Transmembrane Structure Prediction by TMHMM
left, hTAS2R16; right, mTAS2R16

Transmembrane Structure Prediction



Transmembrane Structure Prediction by SOUSI
left, hTAS2R16; right, mTAS2R16

Subcellular Localization

Number of query sequences: 1
 Cleavage site predictions included.
 Using NON-PLANT networks.

Name	Len	mTP	SP	other	Loc	RC	TPlen
gi_8394395_ref_NP_05	291	0.012	0.994	0.033	S	1	18
cutoff		0.000	0.000	0.000			

hTAS2R16

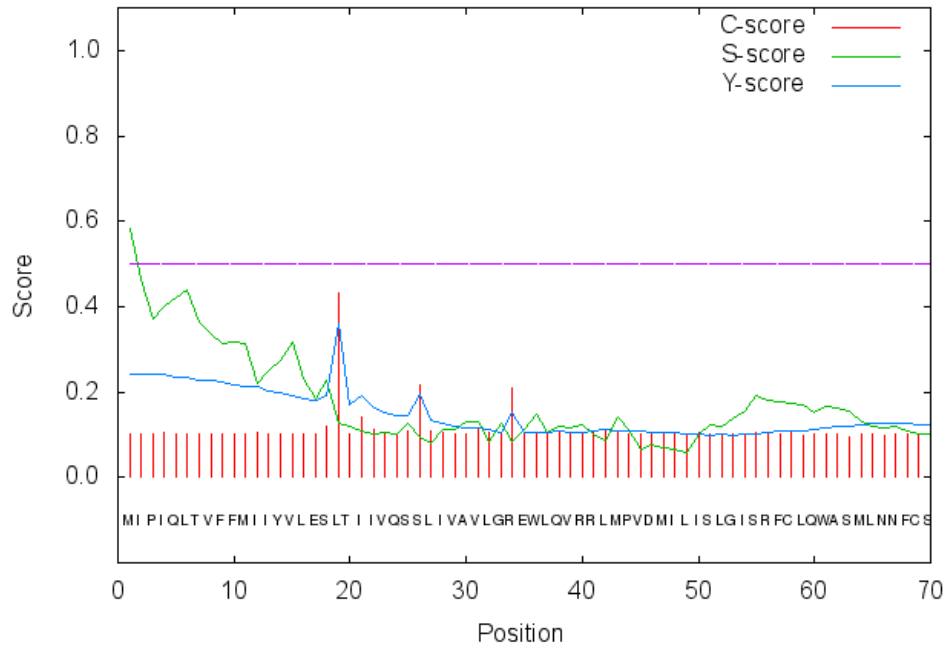
Number of query sequences: 1
 Cleavage site predictions included.
 Using NON-PLANT networks.

Name	Len	mTP	SP	other	Loc	RC	TPlen
gi_189303547_ref_NP_	291	0.010	0.994	0.037	S	1	18
cutoff		0.000	0.000	0.000			

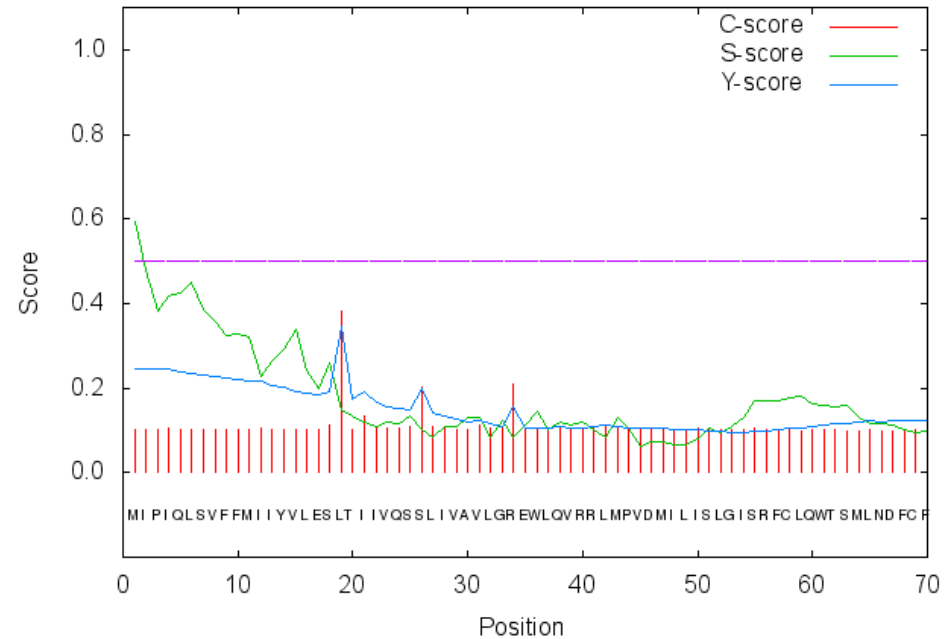
mTAS2R16

Signal Peptide Prediction

SignalP-4.1 prediction (euk networks): gi_8394395_ref_NP_058641.1_



SignalP-4.1 prediction (euk networks): gi_189303547_ref_NP_001074228.1_



left, hTAS2R16; right, mTAS2R16

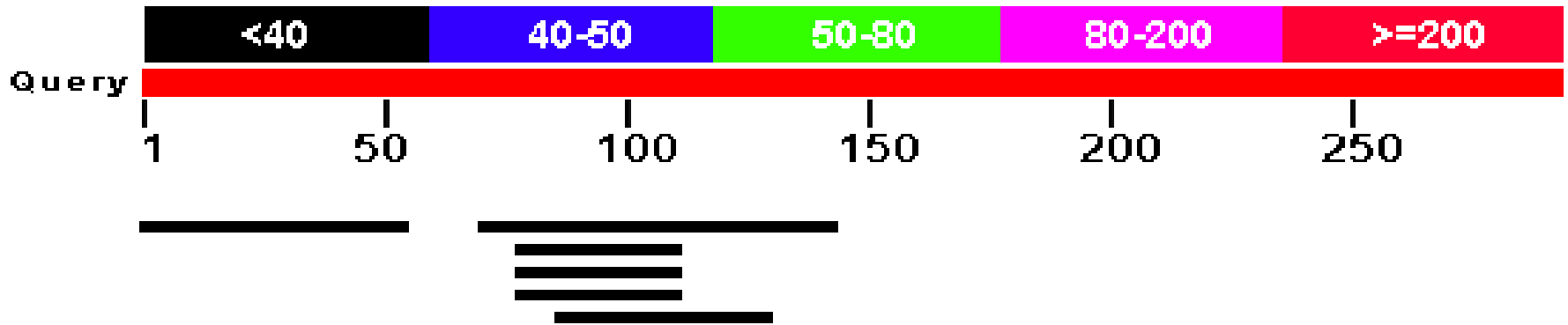
Conclusion: transmembrane protein without signal peptide

Structure Prediction

- Homology Modeling: identity > 30%
Swiss model, Modeller
- Protein threading: fold recognition
Phyre2
- *Ab initio* protein modelling: energy minimization
Rossetta

Homology Modeling?

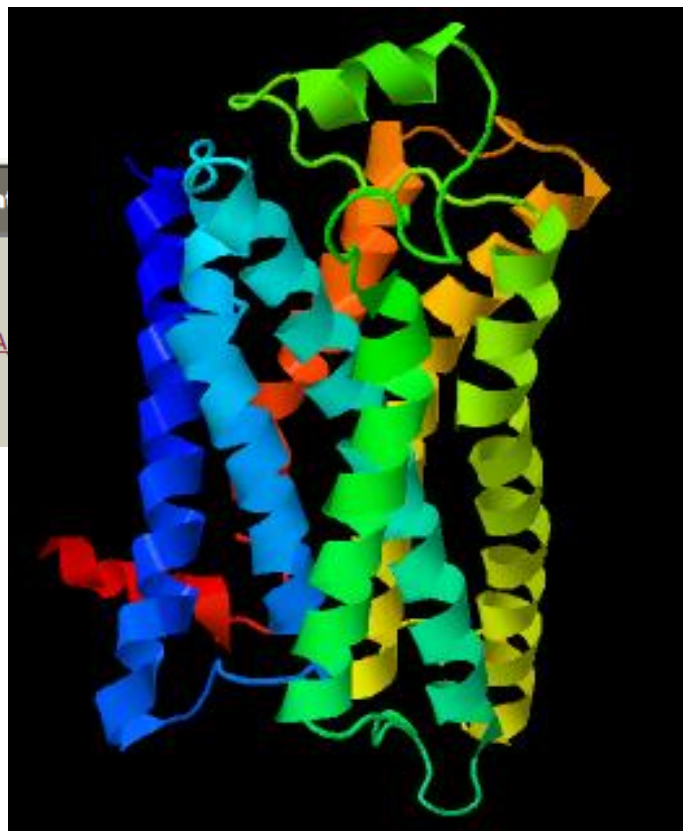
Color key for alignment scores



PSI-BLAST → no homologous protein with known structure



Structure Prediction



hTAS2R16

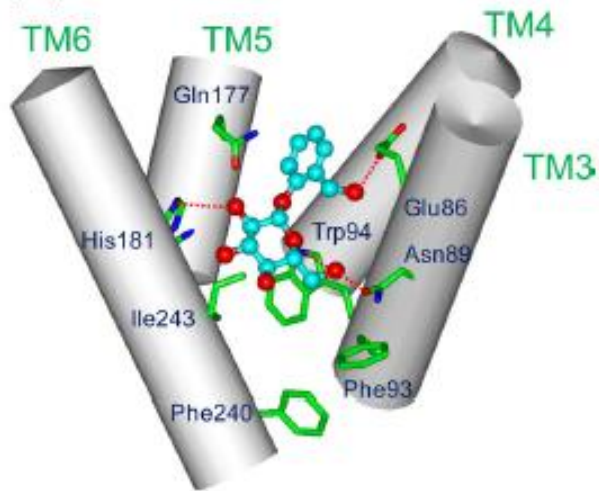
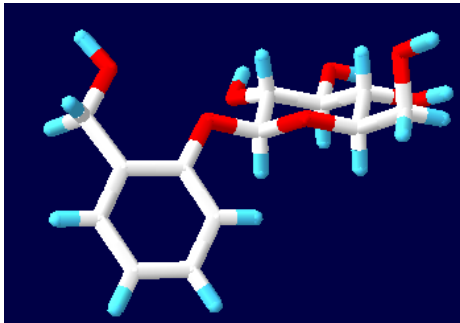


mTAS2R16

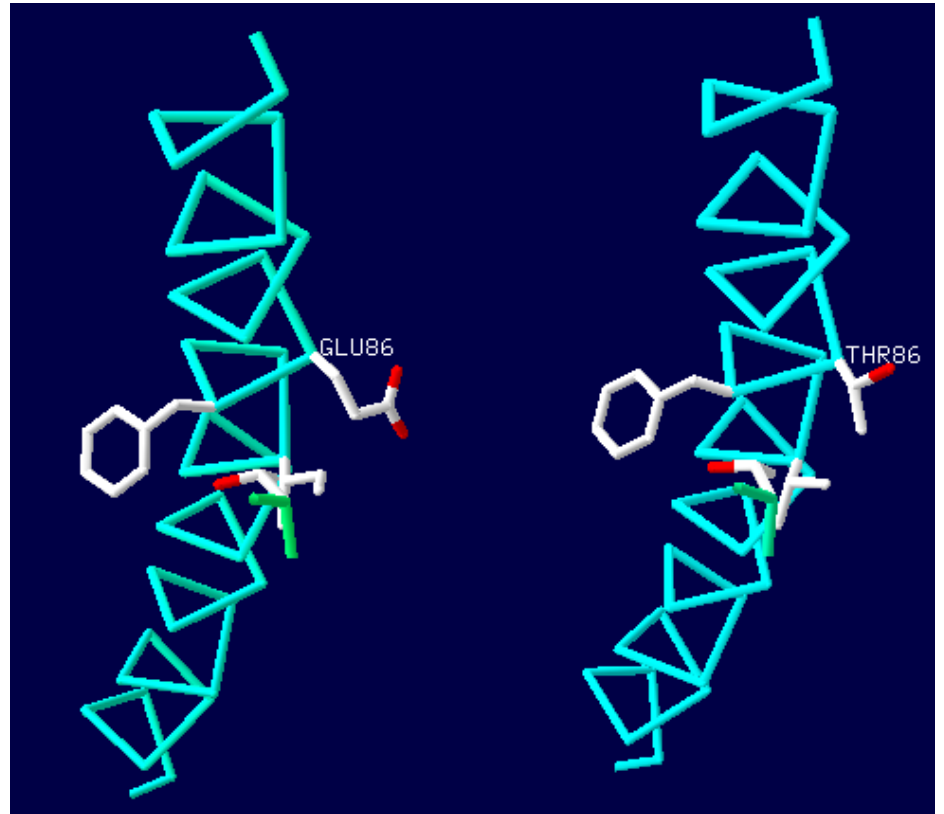
#	Template	Confidence	
1	c2rh1A	100.0	ceptor/t4-lysozyme uman b2-adrenergic

Binding site

salicin



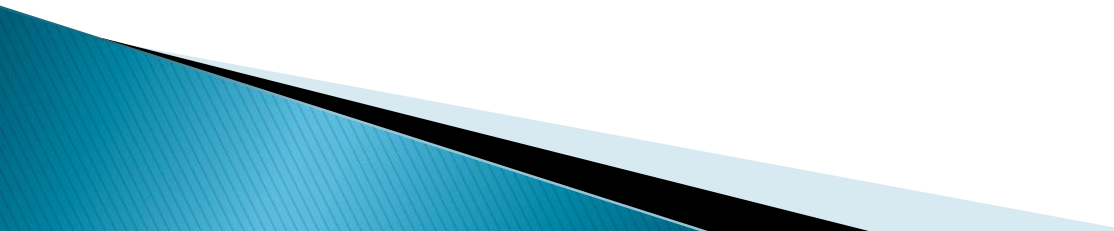
Sakurai *et al.* 2010



hTAS2R16

mTAS2R16

Future work

- Get *TAS2R16* gene sequences from different langur populations
 - Structure prediction
 - Protein–ligand docking
- 

References

Imai H, Suzuki N, Ishimaru Y, Sakurai T, Yin L, Pan W, Abe K, Misaka T, Hirai H. 2012. Functional diversity of bitter taste receptor TAS2R16 in primates. *Biol Lett.* 23, 8(4):652-6.

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Yarmolinsky, D. A., Zuker, C. S. & Ryba, N. J. 2009 Common sense about taste: from mammals to insects. *Cell* 139, 234–244.

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Thanks