

# GPR183简单生信分析

## 小组成员与分工

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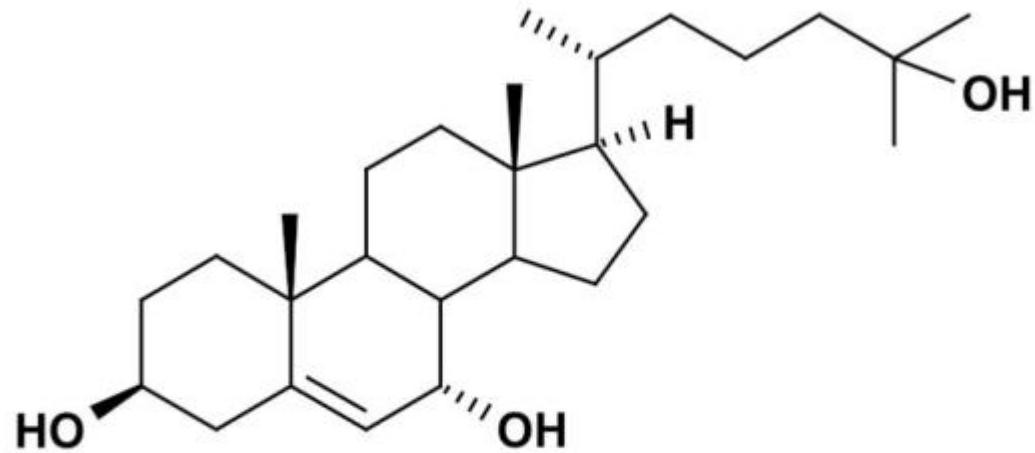
任务：GPR183基本背景以及简单分子演化和功能

第八组成员：史美程 张闻熙 盛开

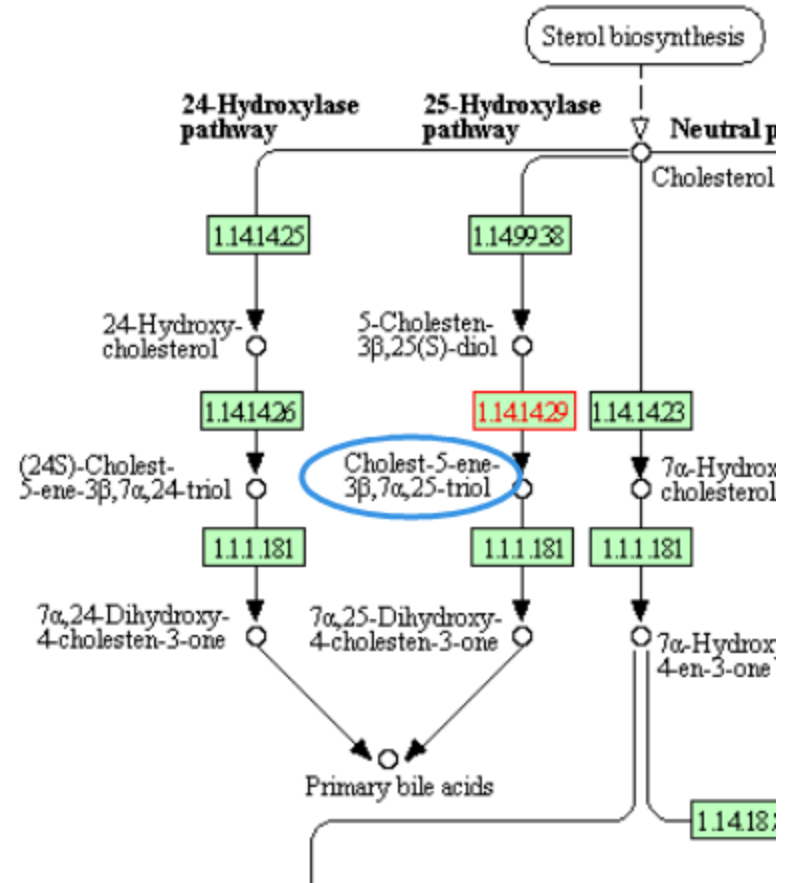
任务：GPR183简单结构与疾病分析

# GPR183背景

- Epstein-Barr Virus-Induced Molecule 2
- GPR183
- Gi coupled GPCR

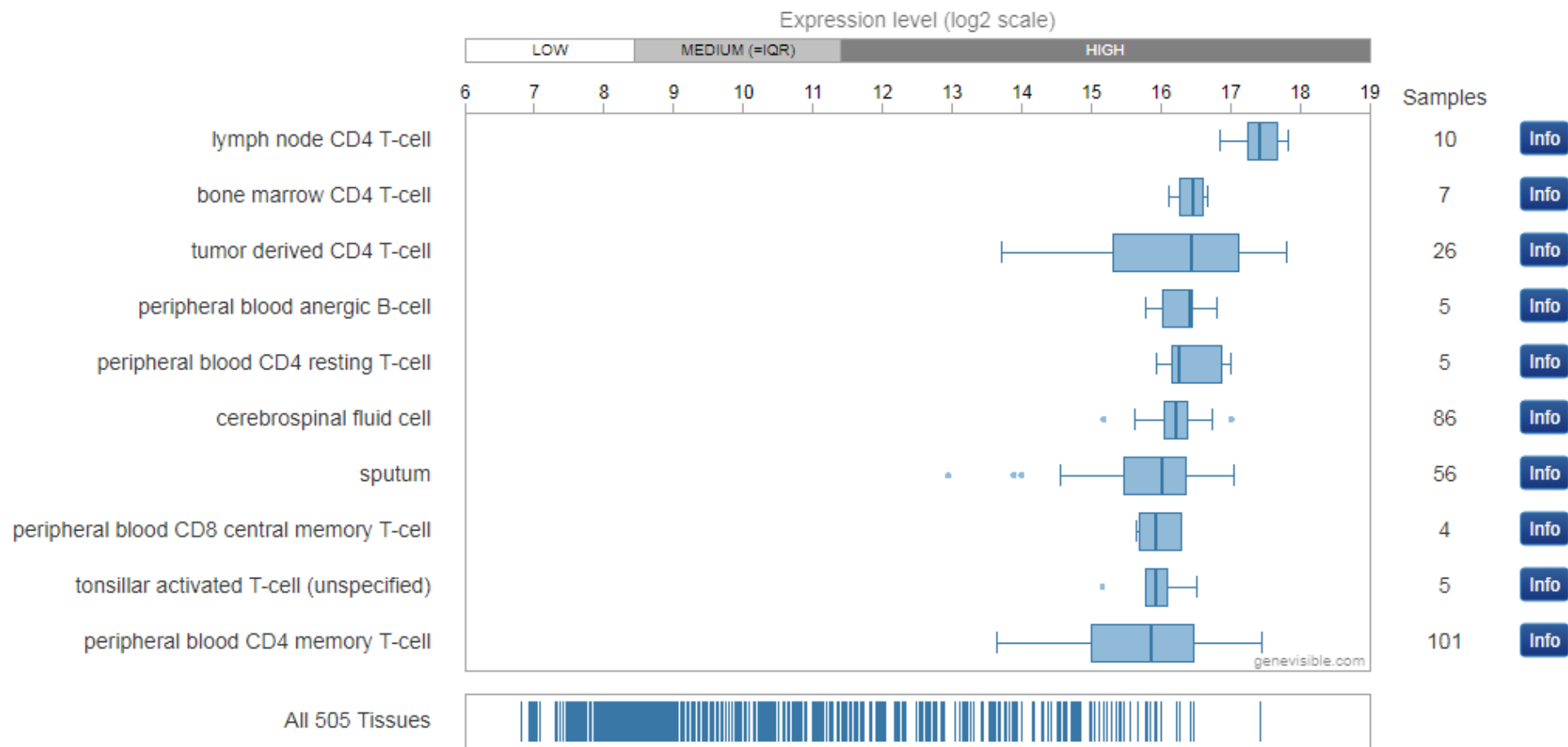


5-cholesten-3 $\beta$ , 7 $\alpha$ , 25-triol  
(7 $\alpha$ , 25-OHC)



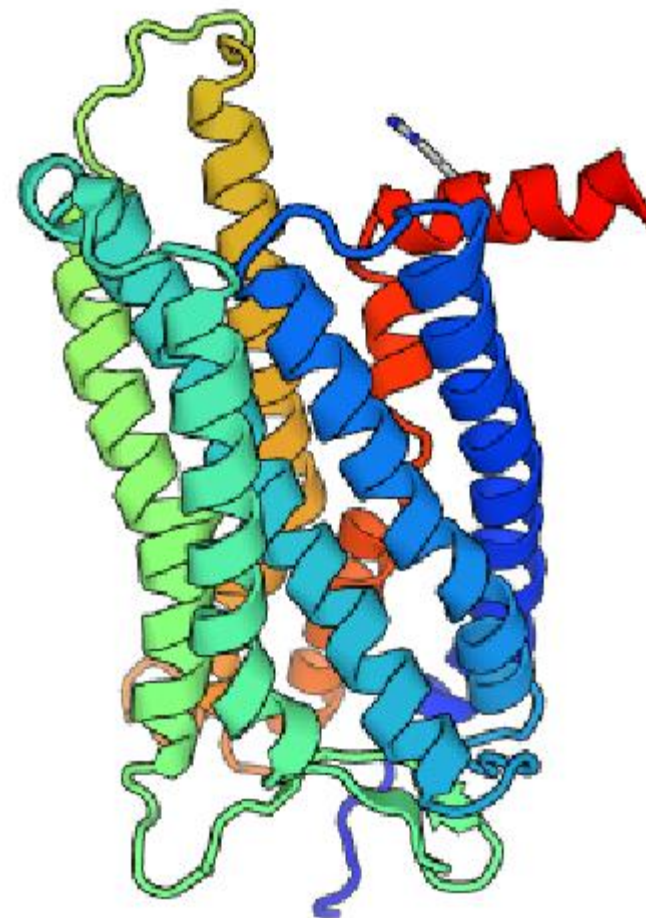
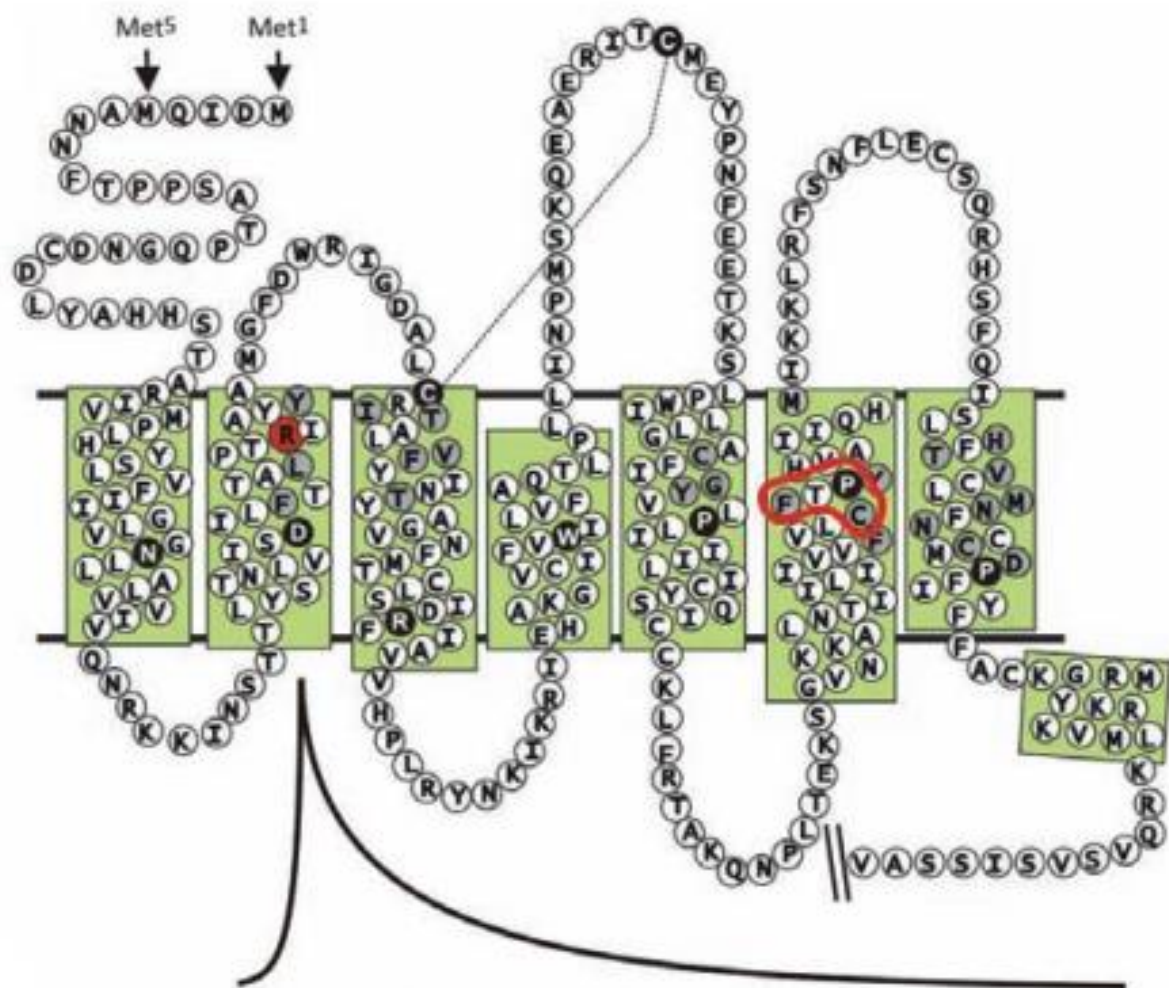
# GPR183背景

## TOP 10 TISSUES



Expression of P32249 (205419\_at)  
across 505 tissues tested by GENEVESTIGATOR

# GPR183序列及同源模型

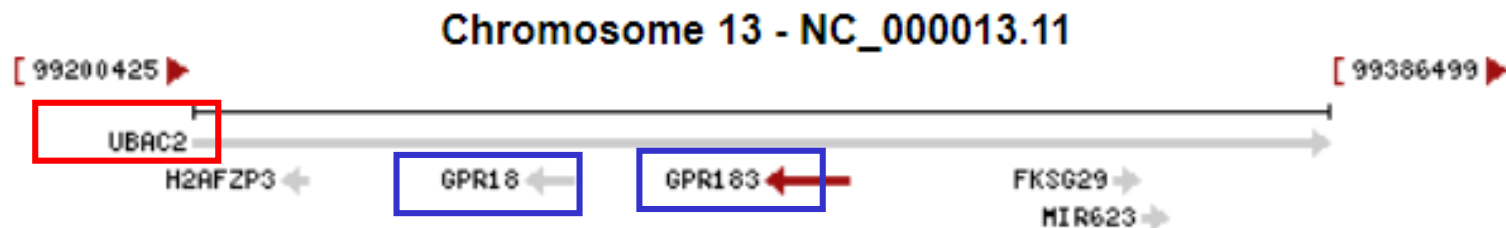


Homology models

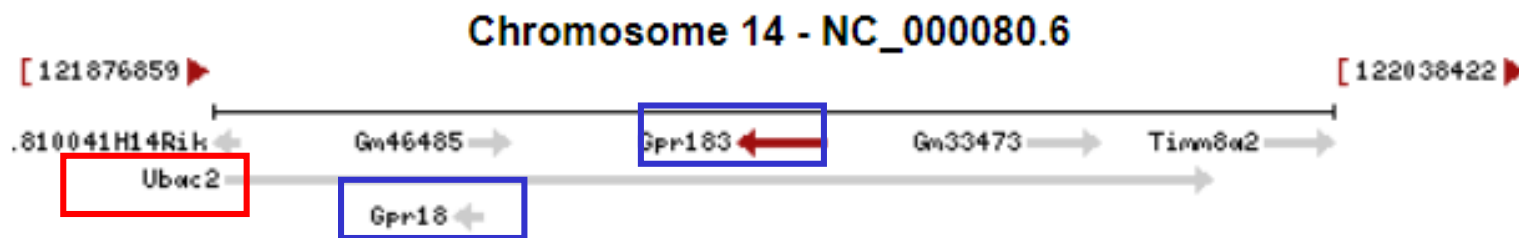
Oligo-state	Ligands	QMEAN	Template	Range	Seq id (%)	Report	Download
monomer		-3.93	5uiw.1.A	<div style="width: 100%; height: 10px; background-color: blue;"></div>	24.45		

# GPR183和GPR18基因位置及基因结构

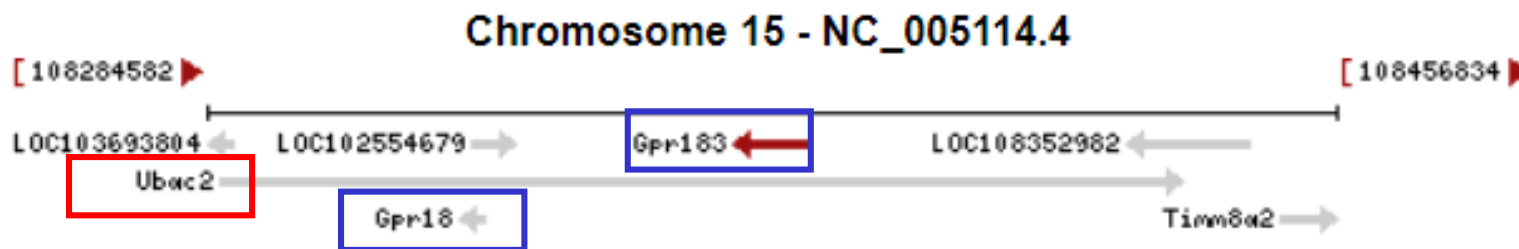
Human



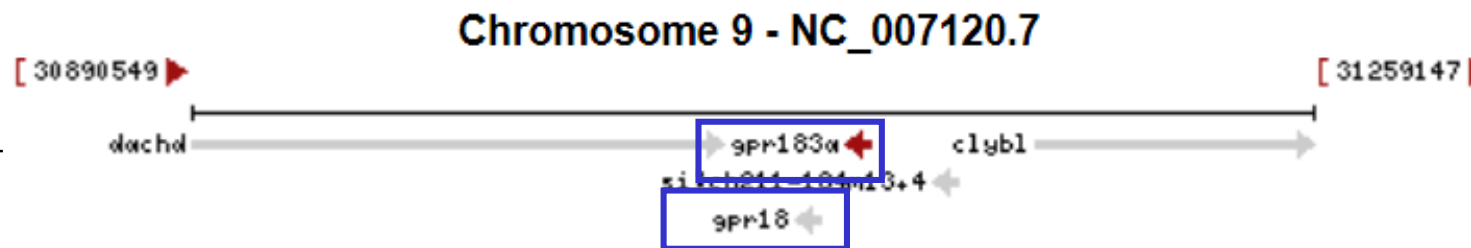
Mouse



Rat

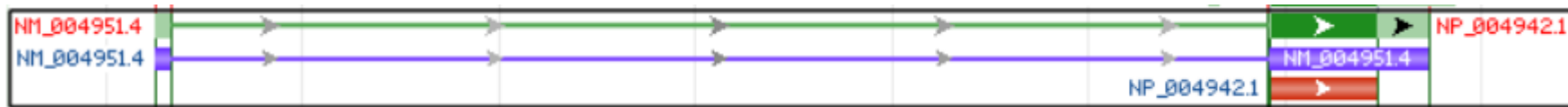


Zebrafish



# GPR183和GPR18基因位置及基因结构

Human

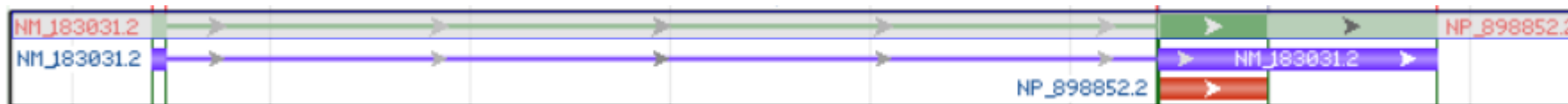


GPR183



GPR18

Mouse



GPR183



GPR18

Rat

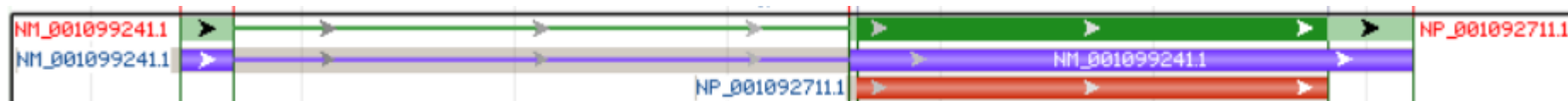


GPR183



GPR18

Zebrafish

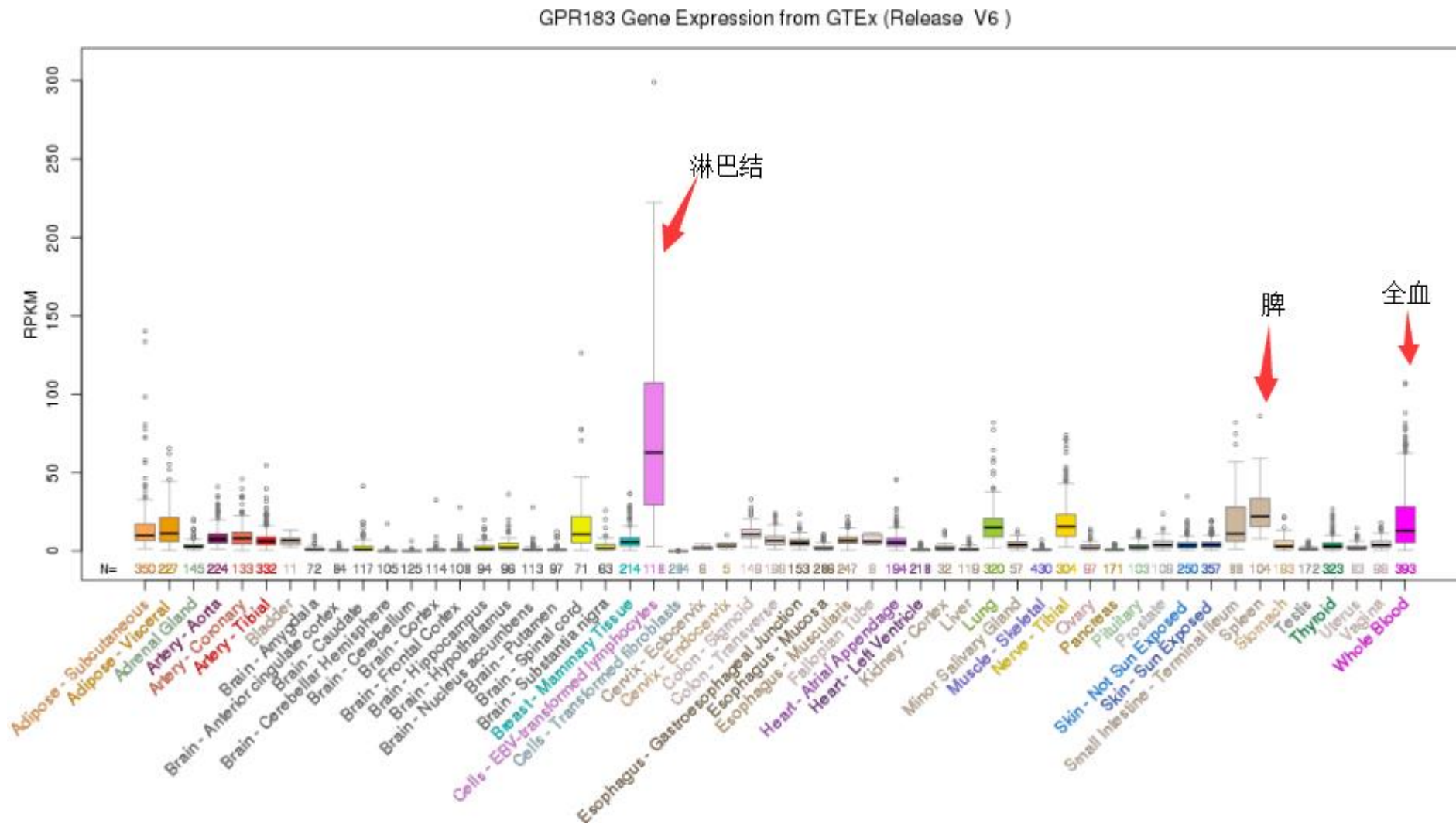


GPR183



GPR18

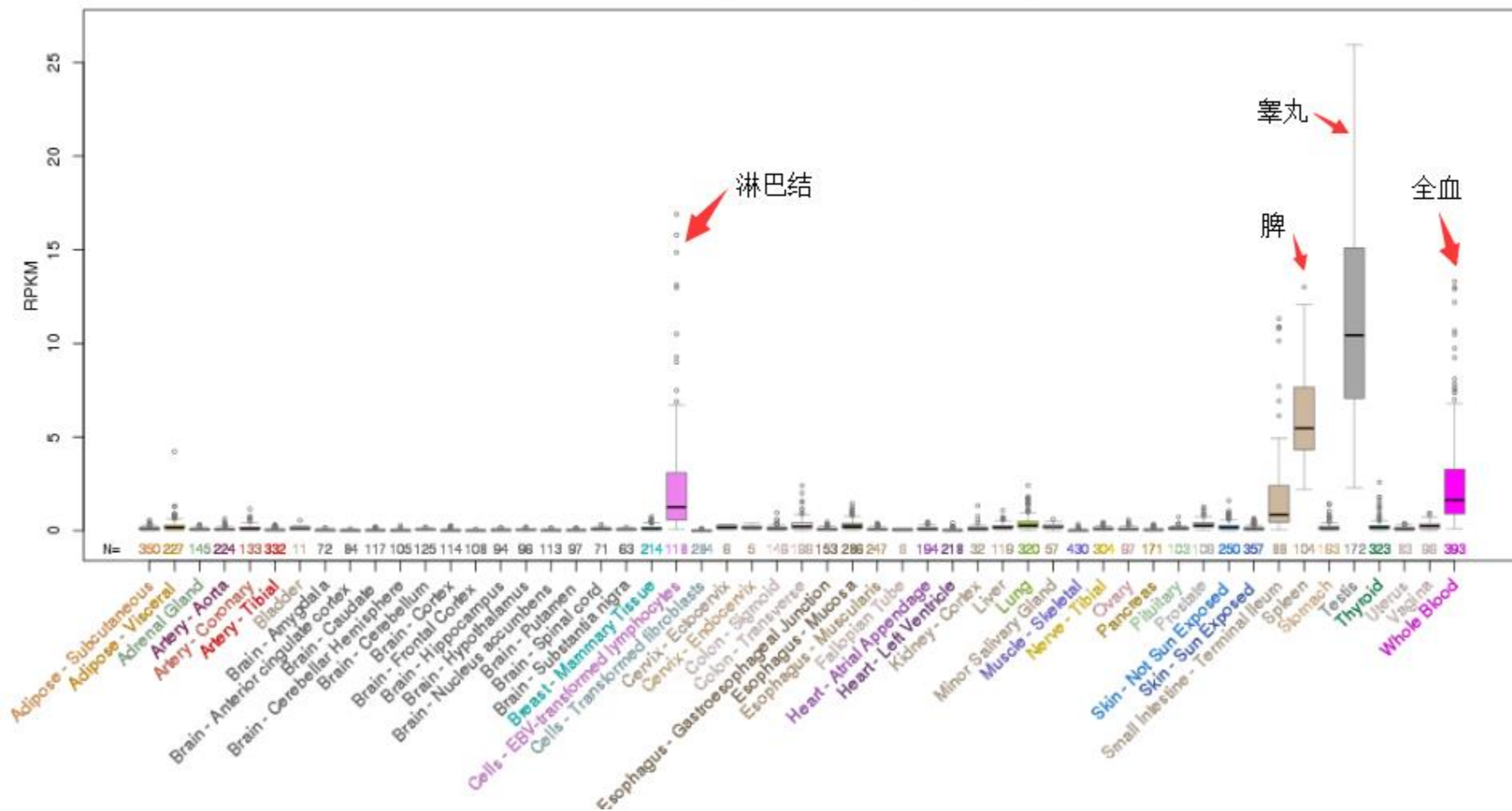
# 人GPR183基因表达谱





# 人GPR18基因表达谱

GPR18 Gene Expression from GTEx (Release V6)



# GO Biological process

## GPR183

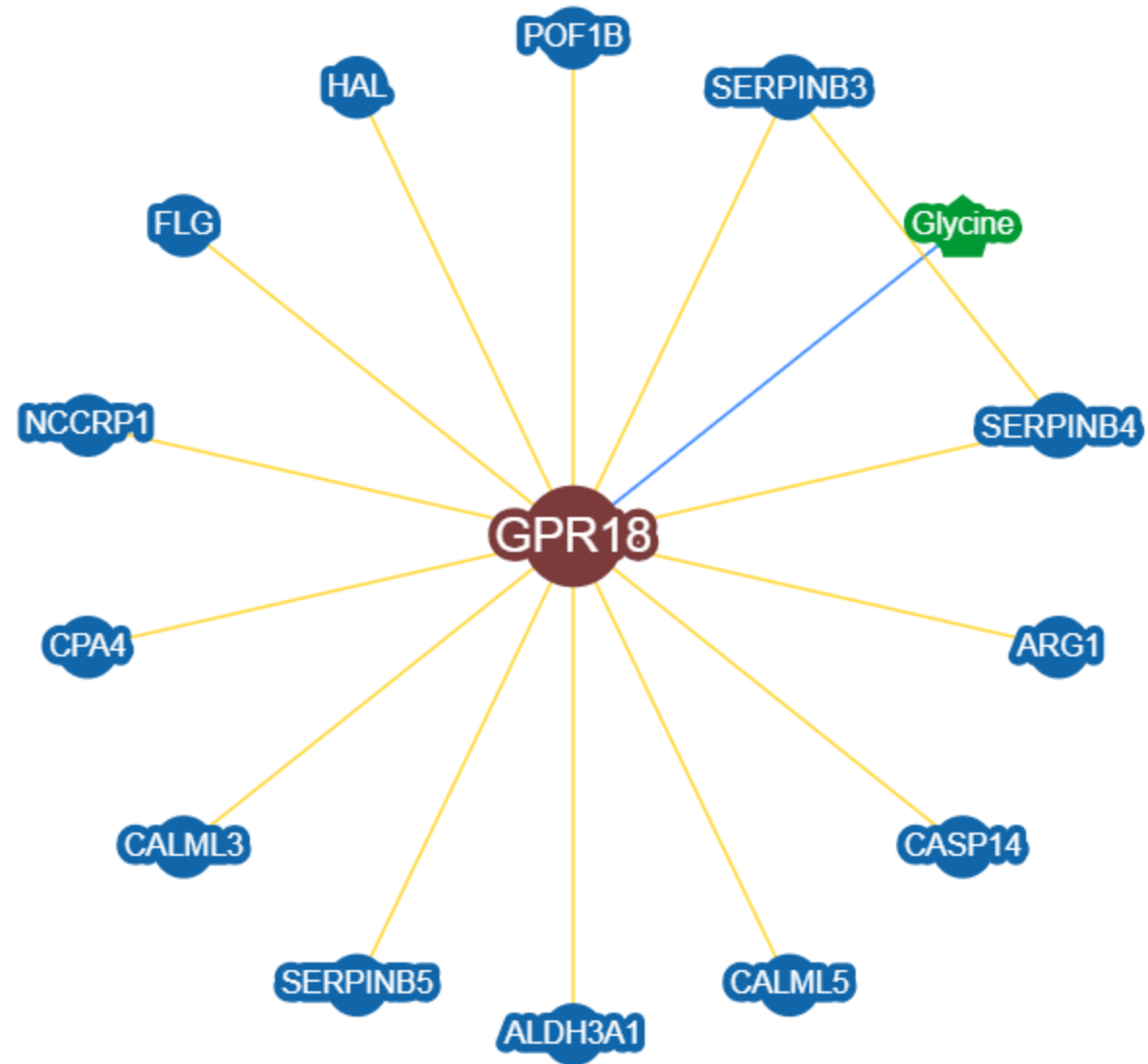
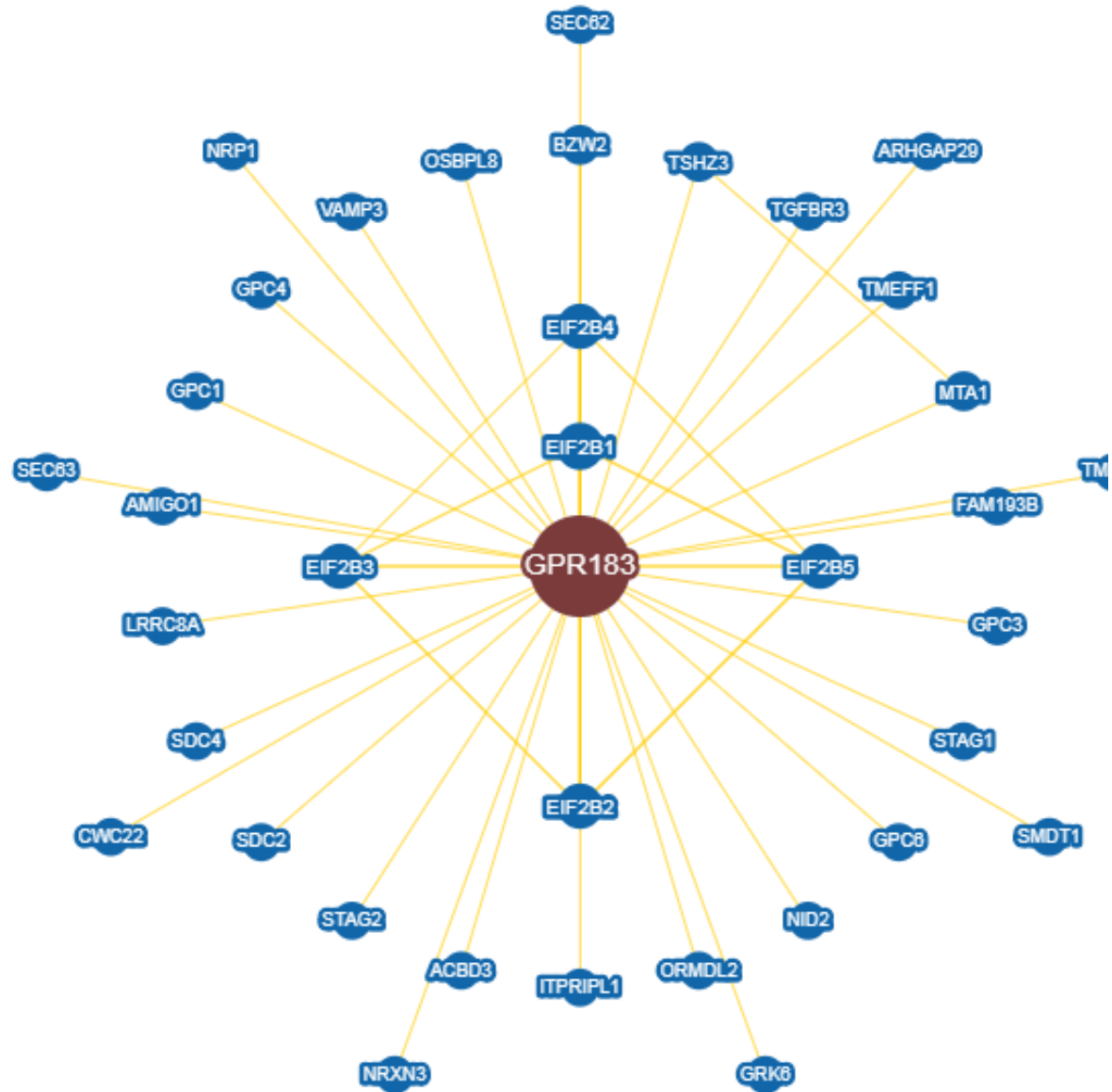
- adaptive immune response Source: UniProtKB
- B cell activation involved in immune response Source: GO\_Central
- dendritic cell chemotaxis Source: UniProtKB
- dendritic cell homeostasis Source: UniProtKB
- G-protein coupled receptor signaling pathway Source: UniProtKB
- humoral immune response Source: UniProtKB
- immune response Source: ProtInc
- leukocyte chemotaxis Source: UniProtKB
- mature B cell differentiation involved in immune response Source: UniProtKB
- osteoclast differentiation Source: UniProtKB
- positive regulation of B cell proliferation Source: UniProtKB
- positive regulation of ERK1 and ERK2 cascade Source: UniProtKB
- regulation of astrocyte chemotaxis Source: UniProtKB
- T cell chemotaxis Source: UniProtKB
- T follicular helper cell differentiation Source: UniProtKB

## GO - Biological process<sup>i</sup>

## GPR18

- CD8-positive, alpha-beta intraepithelial T cell differentiation Source: Ensembl
- CD8-positive, gamma-delta intraepithelial T cell differentiation Source: Ensembl
- G-protein coupled receptor signaling pathway Source: Reactome
- negative regulation of leukocyte chemotaxis Source: Ensembl
- negative regulation of tumor necrosis factor production Source: Ensembl
- positive regulation of cytosolic calcium ion concentration involved in phospholipase C-activating G-protein coupled signaling pathway Source: GO\_Central
- positive regulation of Rho protein signal transduction Source: GO\_Central
- T cell differentiation Source: GO\_Central

# Interaction



# 问题与思考

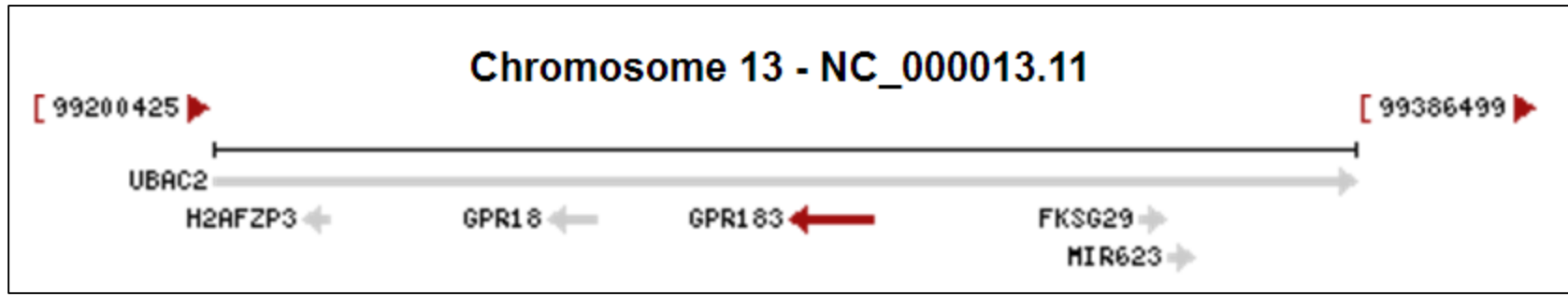
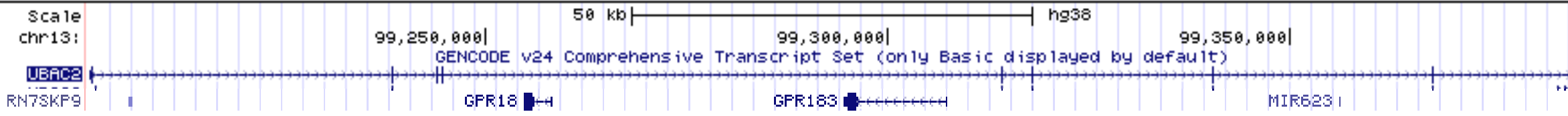
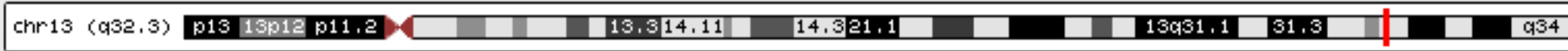
- GPR183和GPR18位置上很邻近，相距仅33Kb，而且都属于Class A（Rhodopsin-like receptors）型GPCR的subfamily A15。功能上都参与了免疫调节，而且表达谱也很相似。因此，GPR183与GPR18在结构和功能上是否协同或者拮抗？分子演化上又有什么关系？
- GPR183和GPR18基因座都UBAC2的第四个intron区，因此他们是否存在cis-regulation或者类似非编码RNA的调控作用？
- GPR183保守性以及疾病SNP分析。

# UCSC Genome Browser

## UCSC Genome Browser on Human Dec. 2013 (GRCh38/hg38) Assembly

move <<< << < > >> >>> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x 100x

chr13:99,200,774-99,385,540 184,767 bp. UBAC2 (Homo sapiens UBA domain containing 2 (UBAC2), transcr

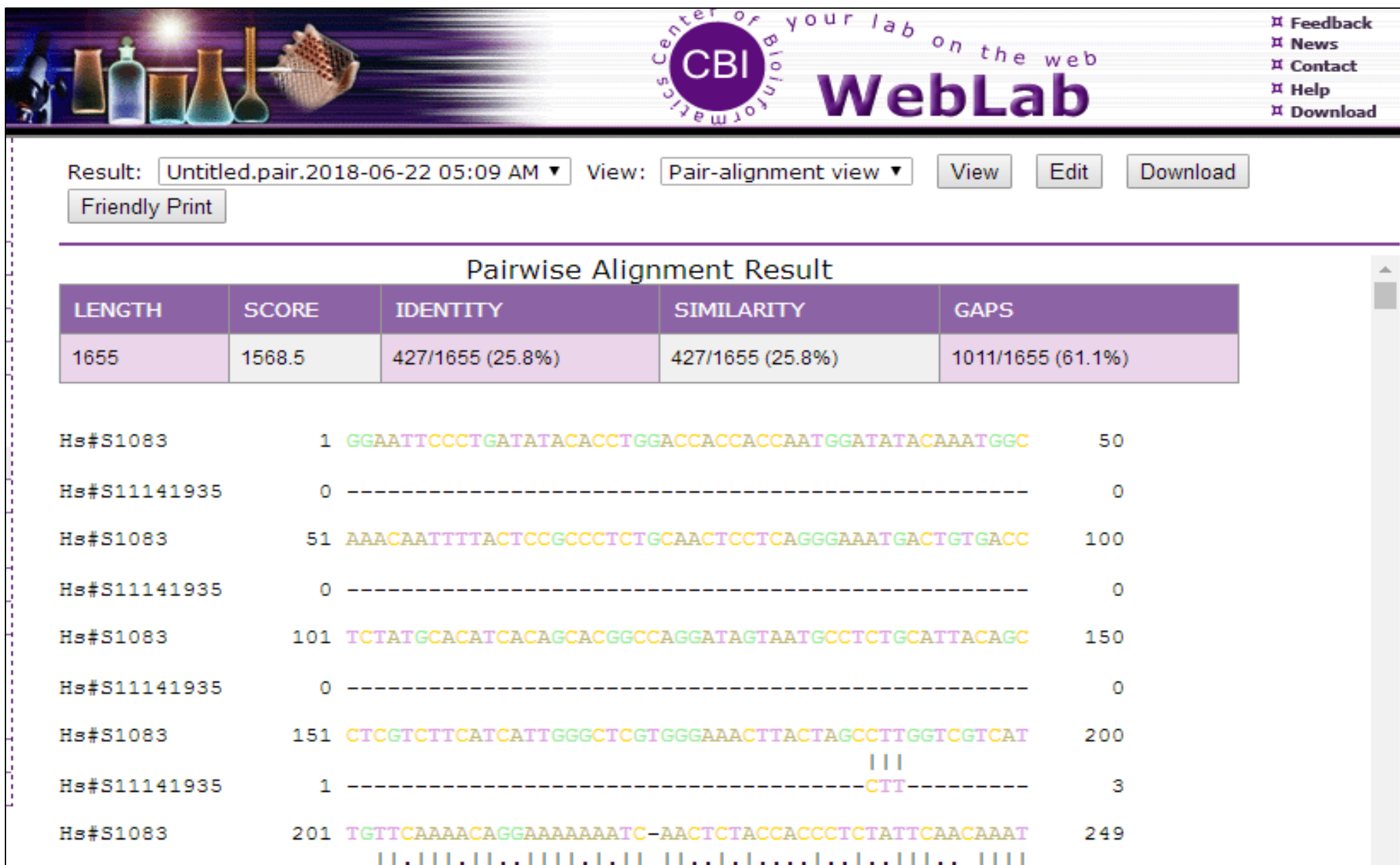


# Uniprot——GPR183 & GPR18蛋白序列比对

Q14330	GPR18_HUMAN	1	-MITLN-NQDQPVPF-----NSSHPDEYKIAALVFYSCIFIIGLFWNITALWVFSCTT	51
P32249	GP183_HUMAN	1	MDIQANMNETDPSATDQCNDLVAHISTARLWHLIKSLWELICLVGNLLALWYLVQNR	60
Q14330	GPR18_HUMAN			110
P32249	GP183_HUMAN			120
Q14330	GPR18_HUMAN			170
P32249	GP183_HUMAN			179
Q14330	GPR18_HUMAN			227
P32249	GP183_HUMAN			239
Q14330	GPR18_HUMAN			277
P32249	GP183_HUMAN			299
Q14330	GPR18_HUMAN			331
P32249	GP183_HUMAN			352
Q14330	GPR18_HUMAN	332	-----	331
P32249	GP183_HUMAN	353	IHSKSSNGK	361

Identical positions	87
Identity	23.577%
Similar positions	122

# WebLab ——GPR183 & GPR18 DNA序列比对 (needle)



The image shows the WebLab interface for a pairwise alignment. At the top, there is a navigation bar with the CBI logo and the text "Center of Bioinformatics your lab on the web". The main title "WebLab" is prominently displayed. On the right side of the navigation bar, there are links for Feedback, News, Contact, Help, and Download. Below the navigation bar, the result information is shown: "Result: Untitled.pair.2018-06-22 05:09 AM", "View: Pair-alignment view", and buttons for "View", "Edit", "Download", and "Friendly Print".

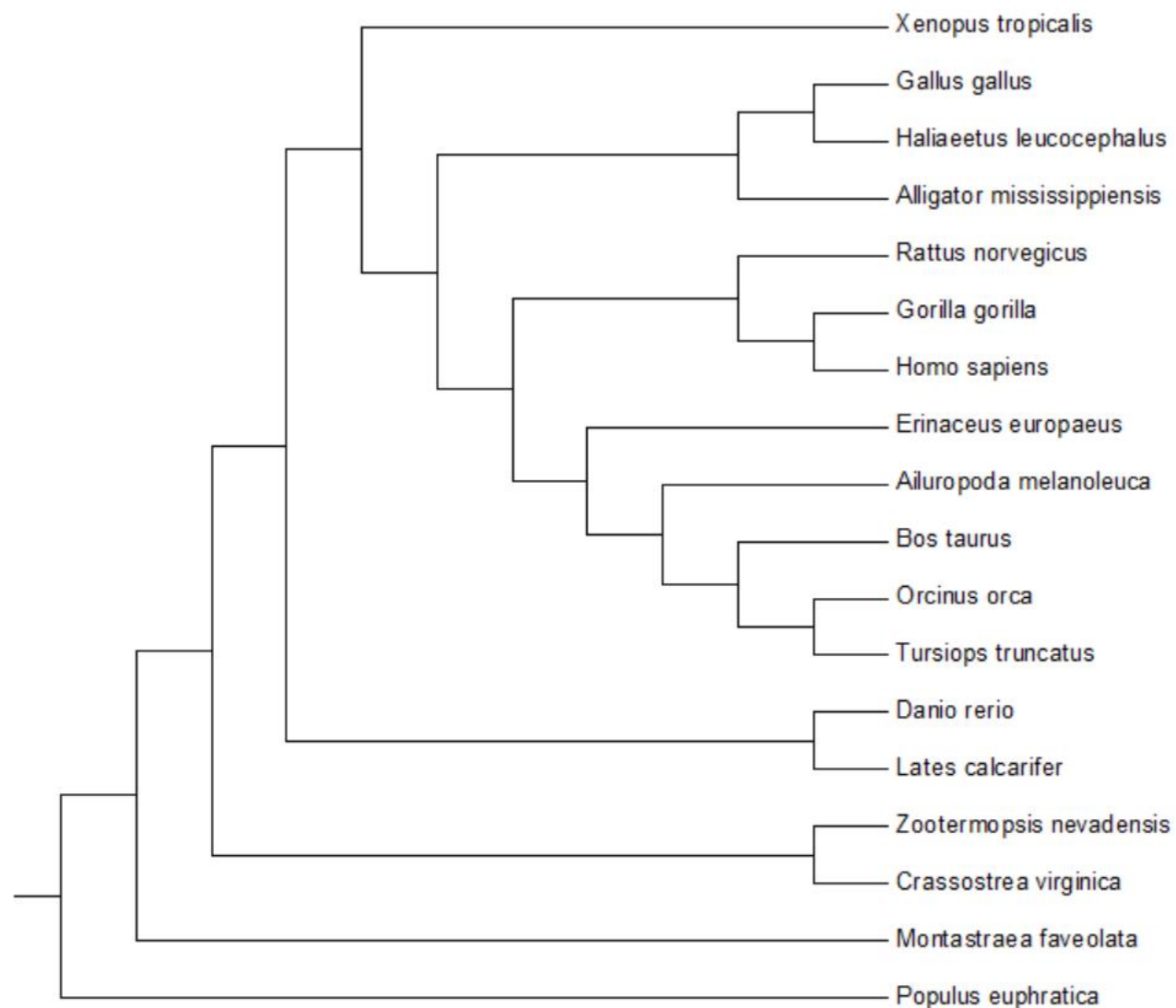
### Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
1655	1568.5	427/1655 (25.8%)	427/1655 (25.8%)	1011/1655 (61.1%)

Hs#S1083	1	GGAATTCCTGATATACACCTGGACCACCACCAATGGATATACAAATGGC	50
Hs#S11141935	0	-----	0
Hs#S1083	51	AAACAATTTTACTCCGCCCTCTGCAACTCCTCAGGGAAATGACTGTGACC	100
Hs#S11141935	0	-----	0
Hs#S1083	101	TCTATGCACATCACAGCACGGCCAGGATAGTAATGCCTCTGCATTACAGC	150
Hs#S11141935	0	-----	0
Hs#S1083	151	CTCGTCTTCATCATTGGGCTCGTGGGAAACTTACTAGCCTTGGTCGTCAT	200
Hs#S11141935	1	-----CTT-----	3
Hs#S1083	201	TGTTCAAAACAGGAAAAAATC-AACTCTACCACCCTTATTCAACAAAT	249

# GPR18、GPR183进化推测



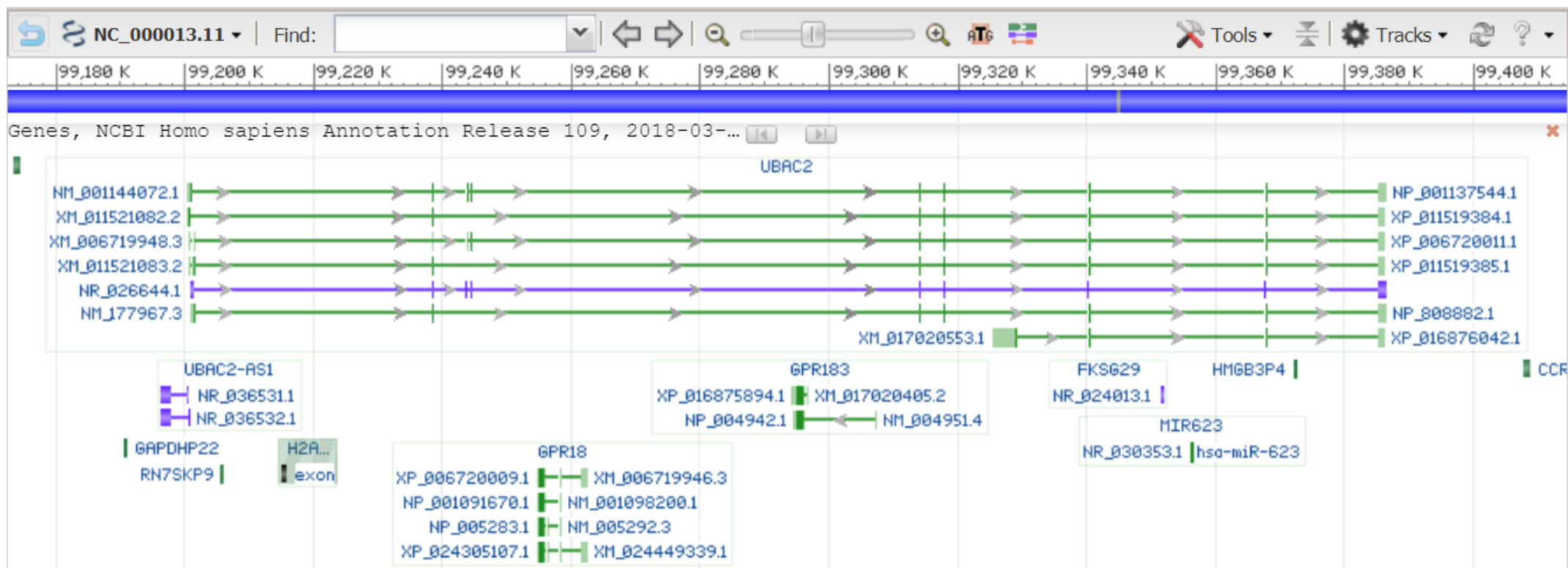
	UBAC2	GPR18	GPR183
非洲爪蟾	Yellow	Red	Blue
鸡	Yellow	Red	Blue
秃鹫	Yellow	Red	Blue
美洲短吻	Yellow	Red	Blue
大鼠	Yellow	Red	Blue
大猩猩	Yellow	Red	Blue
人	Yellow	Red	Blue
西欧刺猬	Yellow	Red	Blue
大熊猫	Yellow	Red	Blue
牛	Yellow	Red	Blue
虎鲸	Yellow	Red	Blue
宽吻海豚	Yellow	Red	Blue
斑马鱼	Yellow	White	Blue
尖吻鲈鱼	Yellow	White	White
湿木白蚁	Yellow	White	White
牡蛎	Yellow	White	White
珊瑚	Yellow	White	White
胡杨	Yellow	White	White

涂色代表基因存在



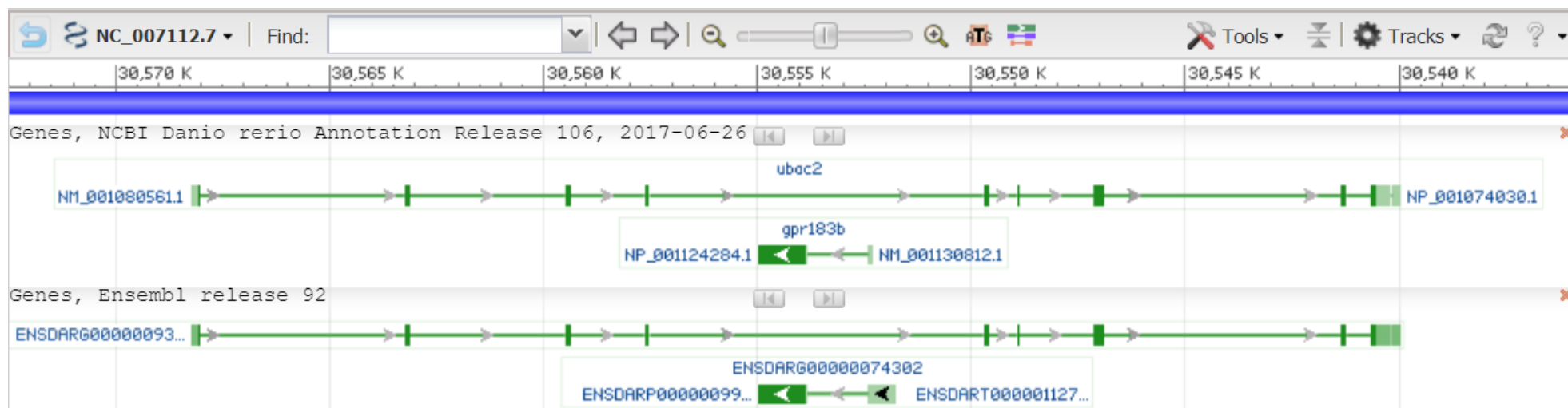
# 代表物种UBAC2基因结构

人UBAC2基因结构, GPR18/GPR183所在Intron长约60000bp

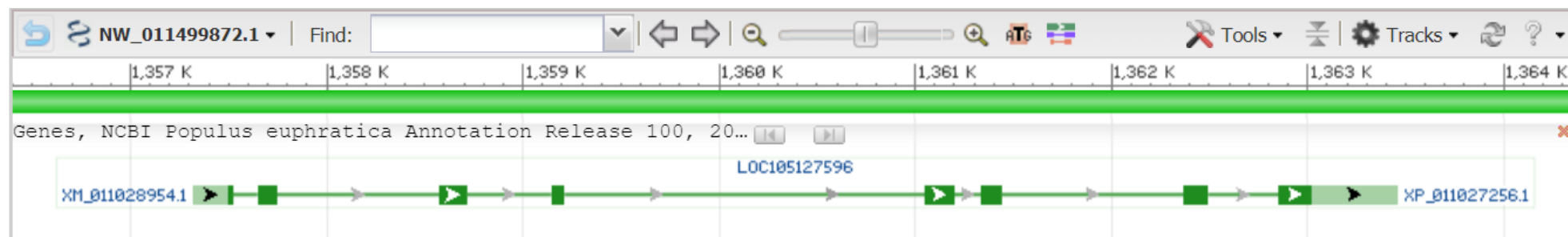


# 代表物种UBAC2基因结构

斑马鱼UBAC2基因结构， GPR183所在Intron长约8000bp



胡杨UBAC2基因结构， 相对应Intron长约1800bp

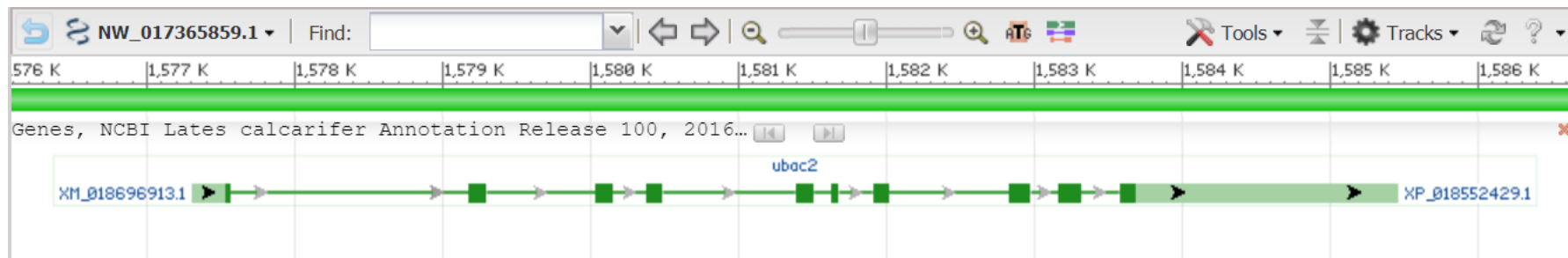


# UBAC2基因结构与GPR18/GPR183的关系

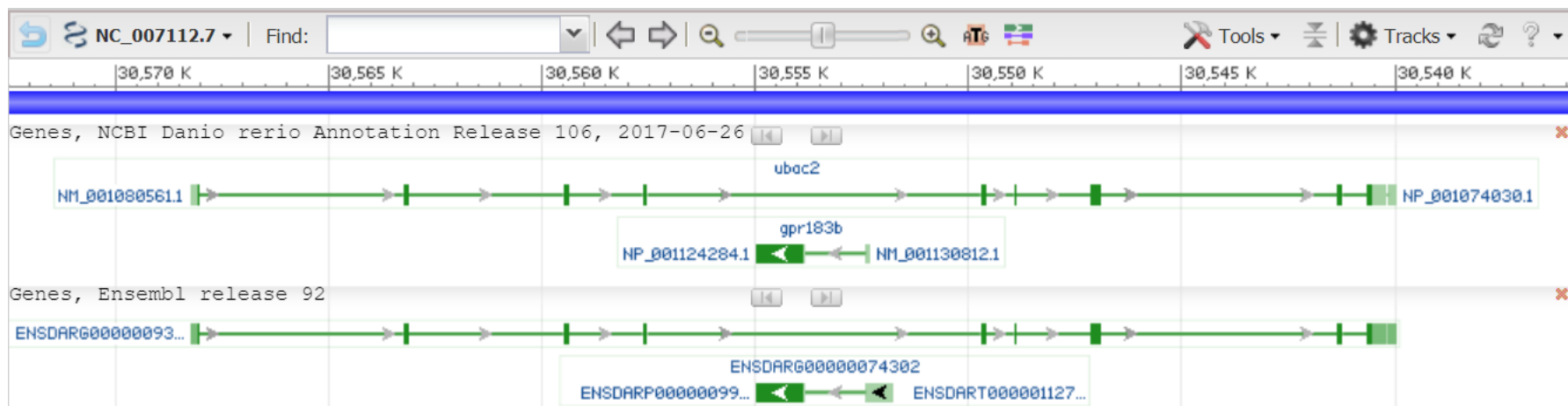
	UBAC2	GPR18	GPR183	UBAC2基因全长
非洲爪蟾				79041
鸡				101194
秃鹫				102679
美洲短吻				183188
大鼠				147125
大猩猩				192999
人				186075
西欧刺猬				198168
大熊猫				167501
牛				170469
虎鲸				151237
宽吻海豚				149494
斑马鱼				28249
尖吻鲈鱼				8151
湿木白蚁				12182
牡蛎				6038
珊瑚				7969
胡杨				6137

单位: bp

## 尖吻鲈鱼UBAC2基因结构

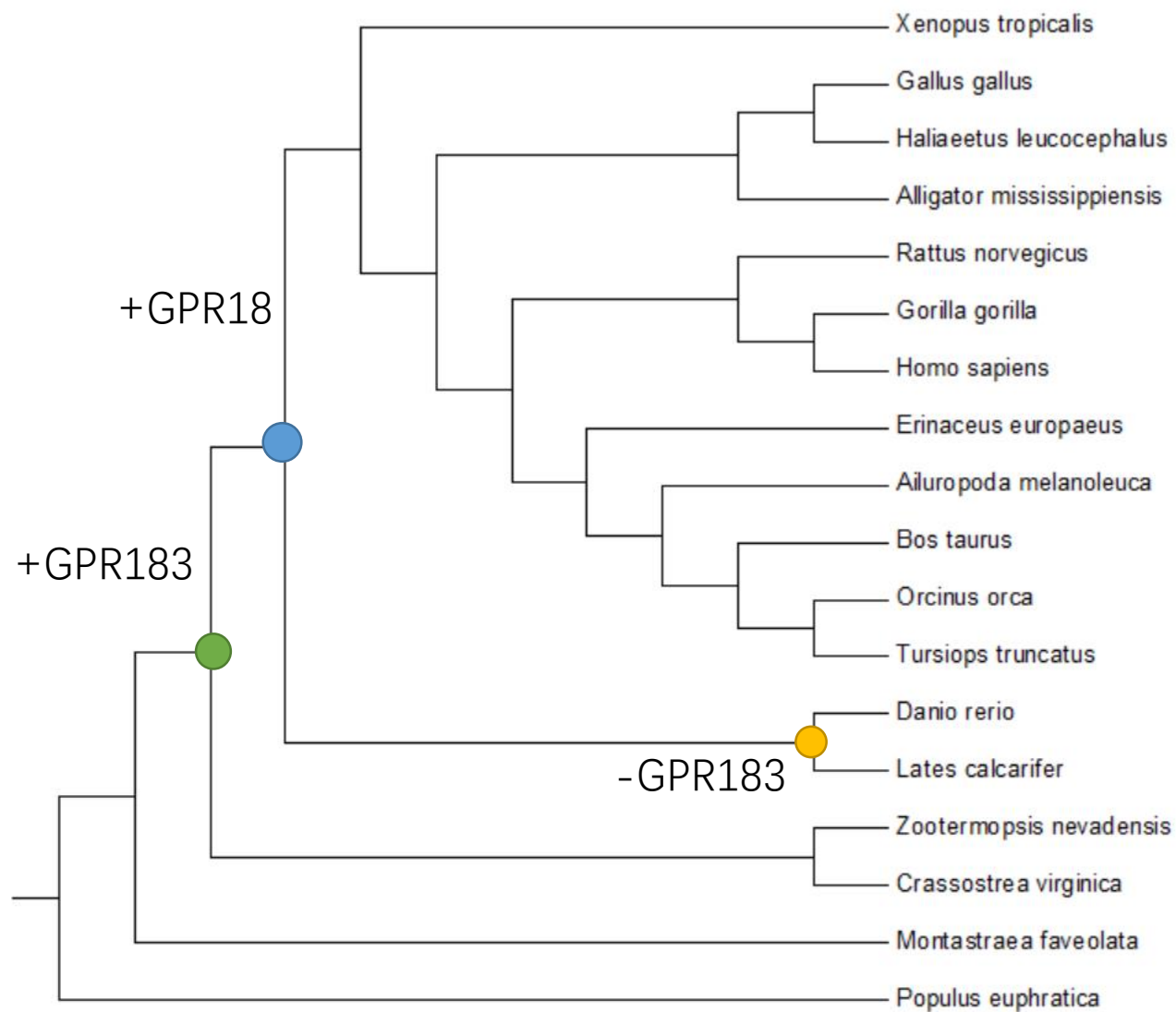


## 斑马鱼UBAC2基因结构



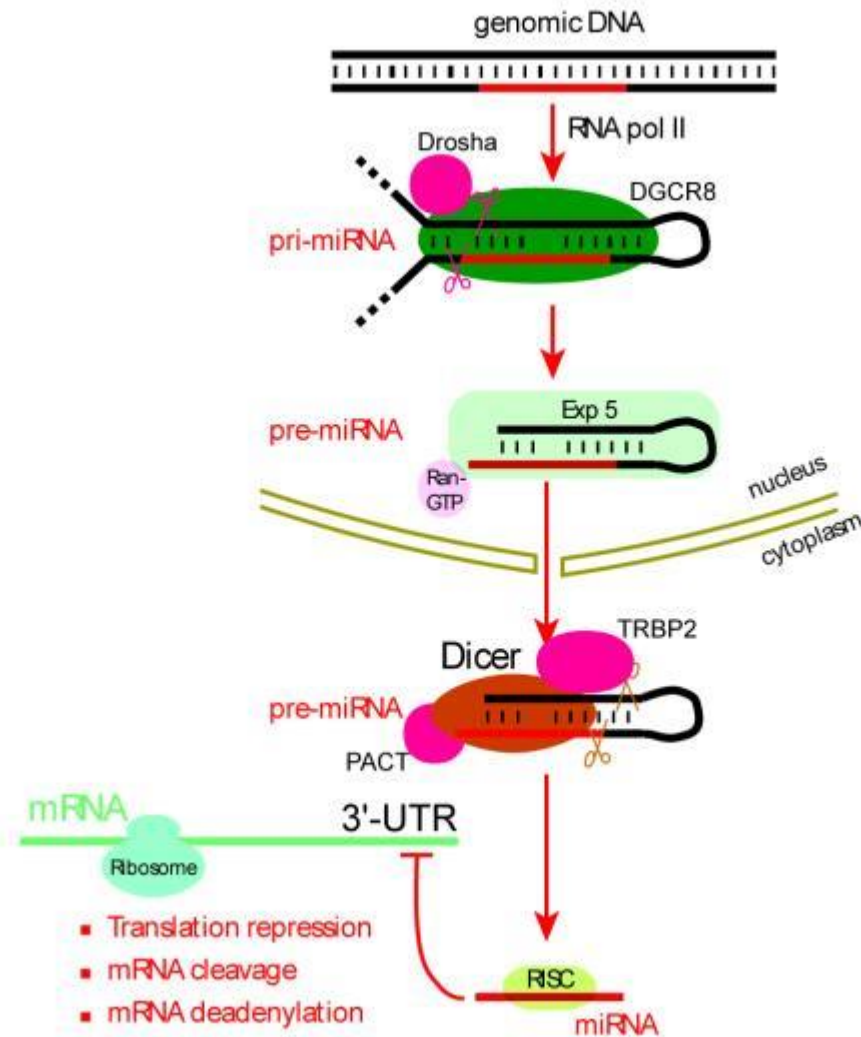
可以看到斑马鱼GPR183所在Intron长度明显更长 8000->1000

# GPR18、GPR183基因出现顺序

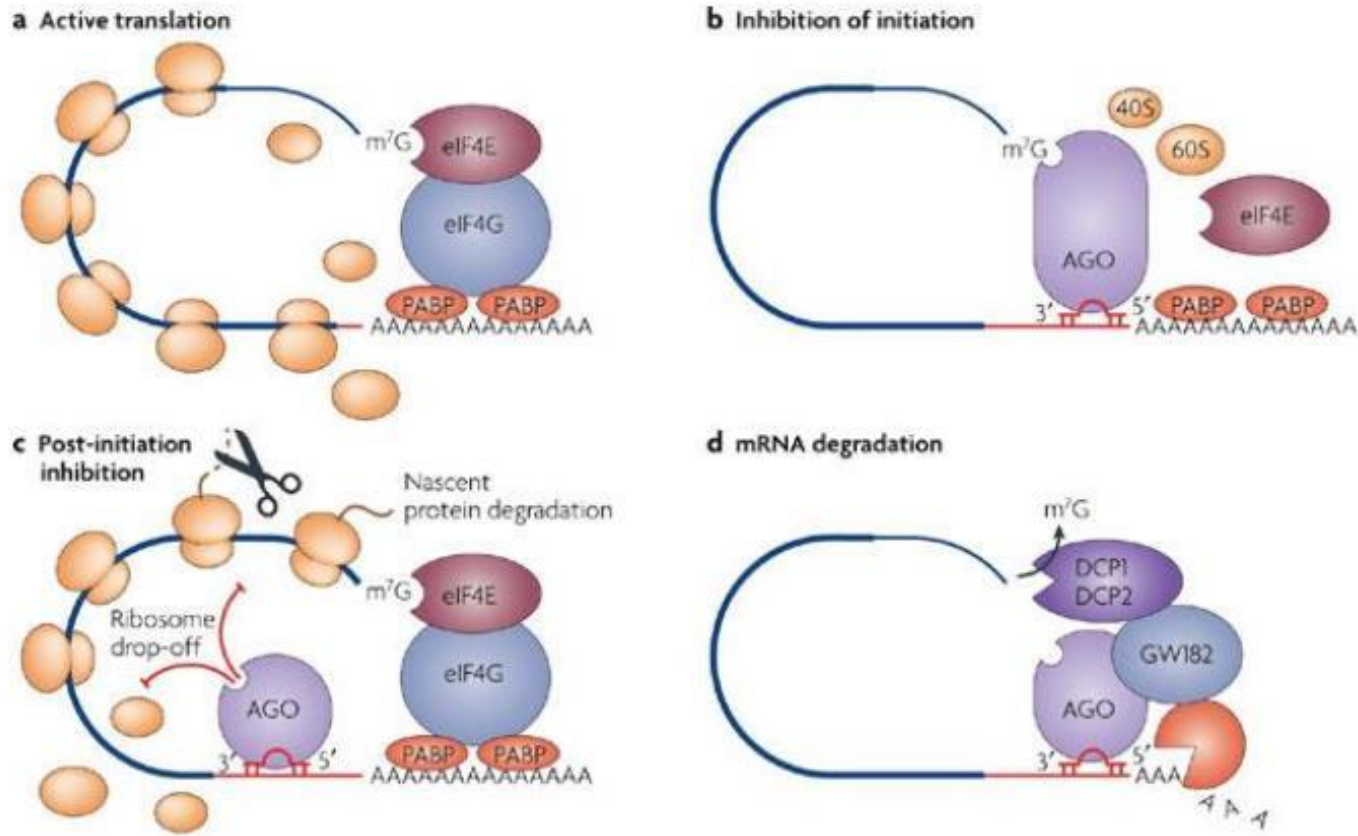


	UBAC2	GPR18	GPR183
非洲爪蟾			
鸡			
秃鹫			
美洲短吻			
大鼠			
大猩猩			
人			
西欧刺猬			
大熊猫			
牛			
虎鲸			
宽吻海豚			
斑马鱼			
尖吻鲈鱼			
湿木白蚁			
牡蛎			
珊瑚			
胡杨			

# miRNA biogenesis pathway

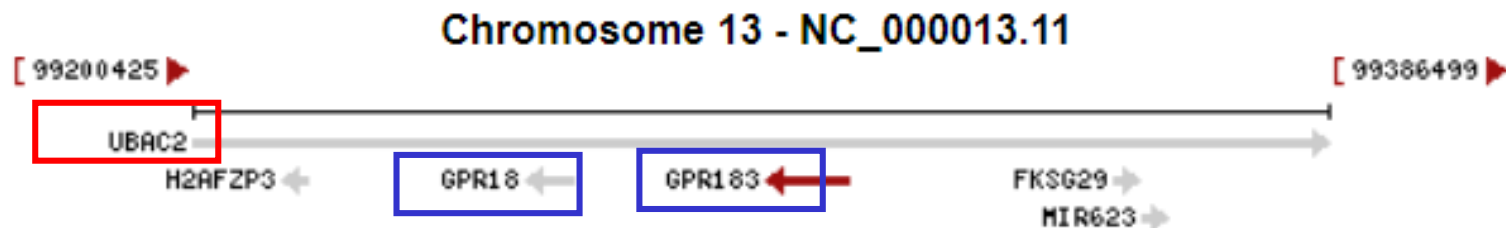


# The mechanism of miRNA regulated gene expression

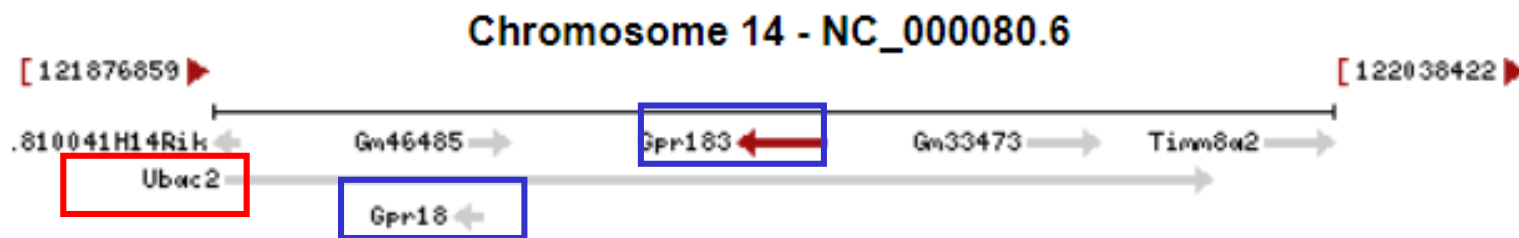


# GPR183和GPR18基因位置及基因结构

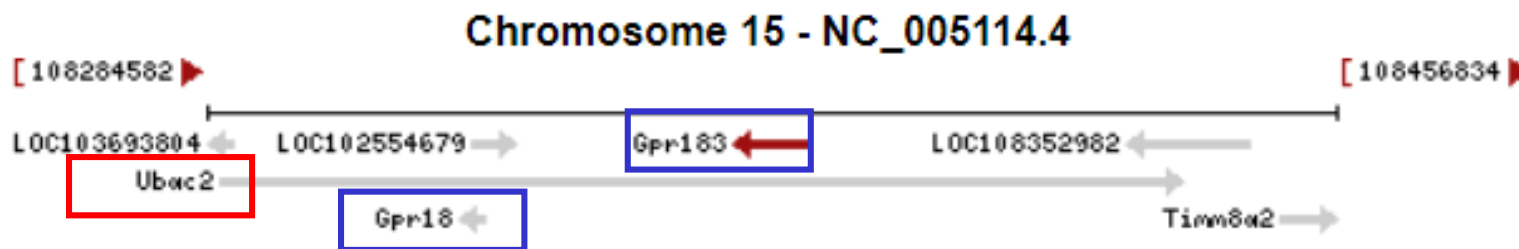
Human



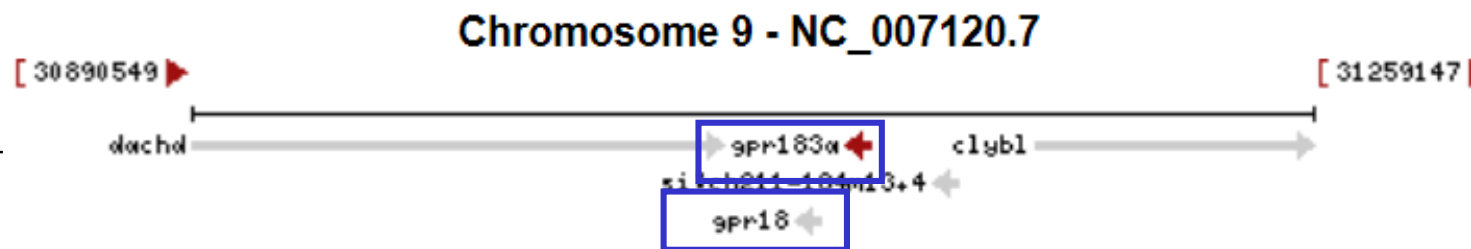
Mouse



Rat



Zebrafish





# miRNAs play important roles in disease

	MicroRNA	Status	Function	Target
<i>Lymphomas</i>				
HL	Mir-155	UR	OG	PU.1
	Let-7a	UR	OG	PRDM1/ BLIMP-1
	mir-9	UR	OG	PRDM1/ BLIMP-1
DLBCL	mir-155	UR in ABC	OG	PU.1, SHIP1
	mir-15a	DR	TSG	BCL-2
	mir-21	UR in ABC	OG	BCL-2
	mir-221	UR in ABC	OG	E2F1
	mir-17-92	UR	OG	
MCL	Mir-17-92	UR	OG	E2F1
	Mir-16-1	Binding site deleted	TSG	CCND1
<i>Leukemias</i>				
AML	Mir-181a	UR in M <sub>1</sub> , M <sub>2</sub> DR in M <sub>4</sub> , M <sub>5</sub>	OG/TSG	TCL-1
APL	Mir-15a, 16-1	UR *	TSG	BCL-2
	Mir-181b	DR		
ALL	mir-17-92	UR	OG	BIM
	mir-128b	UR		
	mir-204	UR		
CLL	mir-15a	DR	TSG	BCL-2
	mir-16-1	DR	TSG	BCL-2
	mir-29b	DR in poor prognosis CLL	TSG	TCL-1
	mir-181b	DR in poor prognosis CLL	TSG	TCL-1
	Mir-155	UR	OG	
CML	Mir-203	DR	TSG	ABL-1
	Mir-17-92	DR	OG	
MM	Mir-15a,16	DR	TSG	

# EBI2保守区域分析及突变分析

2.1 基于少数序列的多序列比对

2.2 利用Psi-BLAST分析其保守区域

2.3 利用同源模建分析其保守区域

2.4 疾病相关突变分析



# 基于Psi-BLAST的保守区域分析

1000条  $E\text{value} < e^{-41}$  基本上都是GPCR

80% Consensus

G-protein coupled receptor ...	257	6e-67
PREDICTED: galanin receptor...	255	2e-66
Leucokinin receptor protein...	255	3e-66
Neuropeptide receptor A23 n...	254	3e-66
Neuropeptide Y2/7 receptor ...	253	7e-66
Neuropeptide GnIHR3 n=3 Tax...	253	8e-66
Neuropeptide FF receptor 2 ...	253	9e-66
Alpha-1B adrenergic recepto...	252	2e-65
Neuropeptide FF receptor 1 ...	251	2e-65
Putative uncharacterized pr...	251	3e-65
Putative uncharacterized pr...	250	4e-65
Putative uncharacterized pr...	248	3e-64
Putative uncharacterized pr...	248	3e-64
Melanopsin n=2 Tax=Branchio...	247	4e-64
Tachykinin-like peptides re...	247	5e-64
Neuropeptide Y receptor n=1...	247	7e-64
class A rhodopsin-like G-pr...	246	1e-63
Galanin receptor type 2 n=3...	246	1e-63
Orexin receptor type 2 n=64...	246	1e-63
PREDICTED: similar to type ...	245	1e-63
Dopamine D1/beta receptor n...	245	1e-63
Somatostatin receptor type ...	245	1e-63
Octopamine receptor beta-2R...	245	2e-63
Apelin receptor n=22 Tax=Am...	245	2e-63
Somatostatin receptor type ...	245	3e-63
Pyrokinin-like receptor 2 n...	244	3e-63

MDIQMANNFTPPSATPQGNDLCDLYAHHSTARIVMPLHYSLVFII  
GLVGNLLALVVIVQNRKKINSTTLYSTNLVISDILFTTALPTRIAYY  
AMGFDWRIGDALCRITALVFIINTYAGVNFMTCLSIDRFIAVVH  
PLRYNKIKRIEHAKGVCIFVWILVFAQTLPLLINPMSKQEAERITC  
MEYPNFEETKSLPWILLGACFIGYVPLIILICYSQICCKLFRITAKQ  
NPLTEKSGVNNKALNTIILIVVFLCFTPYHVAIIQHMIKKLRFSNF  
LECSQRHSFQISLHFTVCLMNFNCCMDPFIYFFACKGYKRKVMR  
MLKRQVSVSISAVKSAPEENSREMTETQMMIHSKSSNGK

Gly48 Asn49 Leu73 Val74 Asp77 Trp97 Gly100 Cys104  
Gly118 Arg129 Trp156 Pro165 Cys181 Pro208 Tyr216  
Pro259 Pro305 Tyr308

# 基于Psi-BLAST的保守区域分析

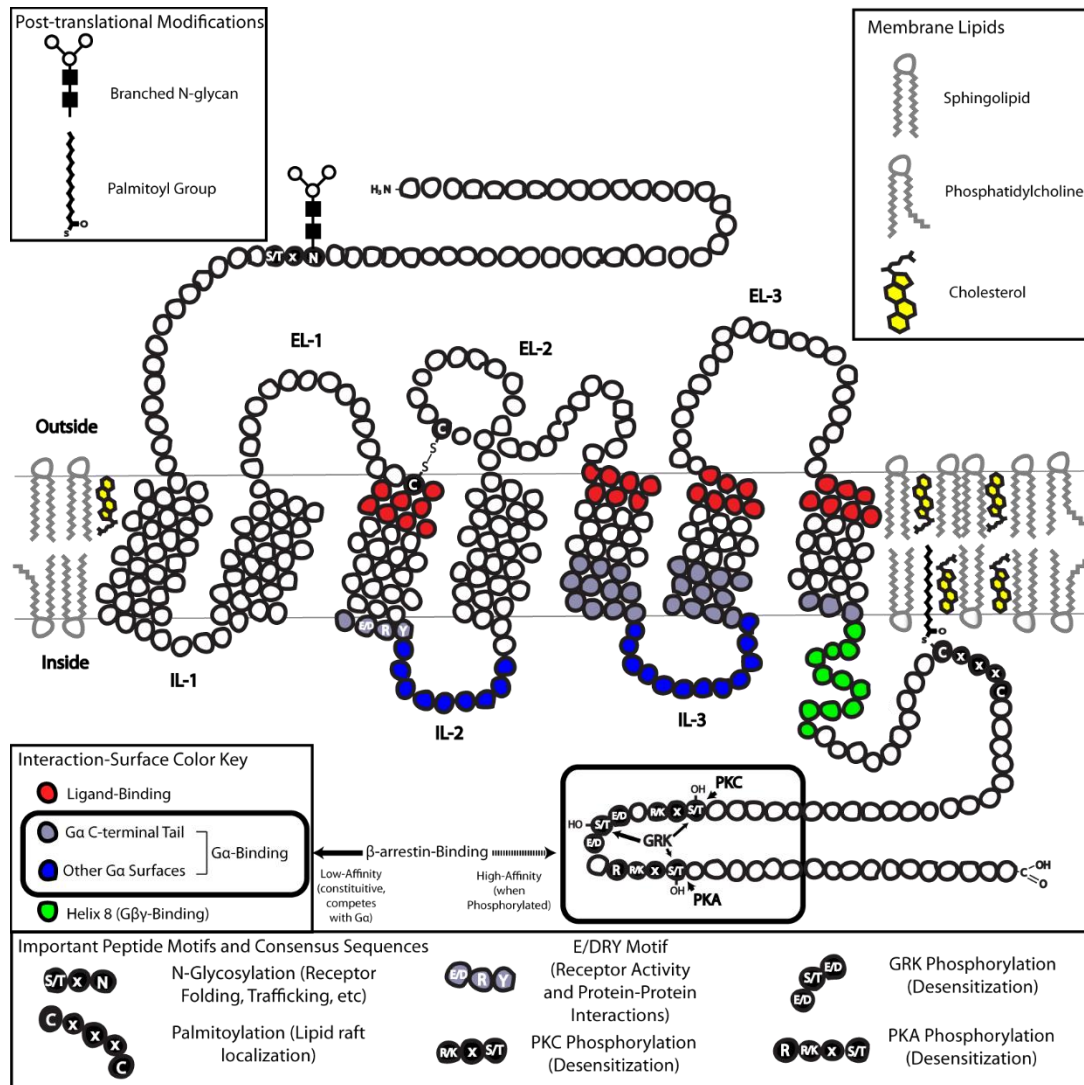
## GPCR: 7次跨膜

```
1 ----MANNFTTPLATSHGNNCDLYAHHSTARVLMPLHYSLVFIIGLVGNLLALVVIVQNR 56
1 MDIQMANNFTPPSATPQGNDCLDYAHHSTARIVMPLHYSLVFIIGLVGNLLALVVIVQNR 60
1 ----MANNFTTPLAASHGNNCDLYAHHSTARILMPLHYSLVFIIGLVGNLLALVVIVQNR 56
***** * * : ** : ***** : ***** : ***** : ***** : *****
57 KKINSTTLYSMNLVISDILFTTALPTRIAYYALGFDWRIGDALCRVTALVFIINTYAGVN 116
61 KKINSTTLYSTNLVISDILFTTALPTRIAYYAMGFDWRIGDALCRITALVFIINTYAGVN 120
57 KKINSTTLYSMNLVISDILFTTALPTRIVVYALGFDWRIGDALCRITALVFIINTYAGVN 116
***** ***** . *** : ***** : ** : *****
117 FMTCLSIDRFFAVVHPLRYNKIKRIEYAKGVCISVWILVFAQTLPLLLTPMSKEEGDKTT 176
121 FMTCLSIDRFFAVVHPLRYNKIKRIEHAKGVCIFVWILVFAQTLPLLLNPMSKQEAERIT 180
117 FMTCLSIDRFFAVVHPLRYNKIKRIEYAKGICVFWILVFAQTLPLLLKPMKQEAADKTT 176
***** : ***** : ** : ***** : ***** : ***** : *
177 CMEYPNFEGTASLPWILLGACLLGYVLPITVILLQYSQICCKLFRTAKQNPLTEKSGVNK 236
181 CMEYPNFEETKSLPWILLGACFIGYVLPILIIILICYSQICCKLFRTAKQNPLTEKSGVNK 240
177 CMEYPNFEGTASLPWILLGACLLGYVLPILAIILLCYSQICCKLFRTAKQNPLTEKSGVNK 236
***** * ***** : ***** : ** : ***** : ***** : *****
237 KALNTIILIIIVVFLCFTPYHVAVIIQHMIKMLCSPGALECGARHSFQISLHFTVCLMNFN 296
241 KALNTIILIIIVVFLCFTPYHVAVIIQHMIKMLRFSNFLECSQRHSFQISLHFTVCLMNFN 300
237 KALNTIILIIIVVFLCFTPYHVAVIIMQHMVKTLYAPGALCGVRHSFQISLHFTVCLMNFN 296
***** ** : ***** : ** : * * . * * . *****
297 CCMDPFIYFFACKGYKRKVMKMLKRQVSVSISAVRSAPENSREMTESQMMIHSKASNG 356
301 CCMDPFIYFFACKGYKRKVMRMLKRQVSVSISAVKSAPENSREMTETQMMIHSKSSNG 360
297 CCMDPFIYFFACKGYKRKVMKMLKRQVSVSISAVRSAPENSREMTESQMMIHSKASNG 356
***** : ***** : ***** : ***** : ***** : **
357 R 357
361 K 361
357 R 357
:
```

## 跨膜螺旋:

```
MDIQMANNFTPPSATPQGNDCLDYAHHSTAR
IVMPLHYSLVFIIGLVGNLLALVVIV
QNRKKINSTTLYSTNLVISD
ILFTTALPTRIAYYAMGF
DWRIGDALCR
ITALVFIINTYAGVNFMTCLSI
DRFFIAVVHPLRYNKIKRIEHAK
GVCIFVWILVFAQTLPLLI
NPMKQEAERITCMEYPNFEETKS
LPWILLGACFIGYVLPILIIILIC
YSQICCKLFRTAKQNPLTEKSGVNKK
ALNTIILIIIVVFLCFTPYHVAVII
QHMIKMLRFSNFLECSQRHSFQ
ISLHFTVCLMNFNCCMDPFIYFFAC
KGYKRKVMRMLKRQVSVSISAVKSAPENSREMTETQMMIHS
KSSNGK
```

# 基于Psi-BLAST的保守区域分析



跨膜螺旋:

MDIQMANNFTPPSATPQGNDLCDLYAHHSTAR

IVMPLHYSLVFIIGLVGNLLALVVIV

QNRKKINSTTLYSTNLVISED (IL-1)

ILFTTALPTRIAYYAMGF

DWRIGDALCR (EL-1)

ITALVFIINTYAGVNFMTCLSI

DRFIAVVHPLRYNKIKRIEHAK (IL-2)

GVCIFVWILVFAQTLPLLI

NPMSKQEAERITCMEYPNFEETKS (EL-2)

LPWILLGACFIGYVLPILIIIC

YSQICCKLFRRTAKQNPLTEKSGVNKK (IL-3)

ALNTIILIVFVLCFTPYHVAII

QHMIKKLRFSNFLECSQRHSFQ (EL-3)

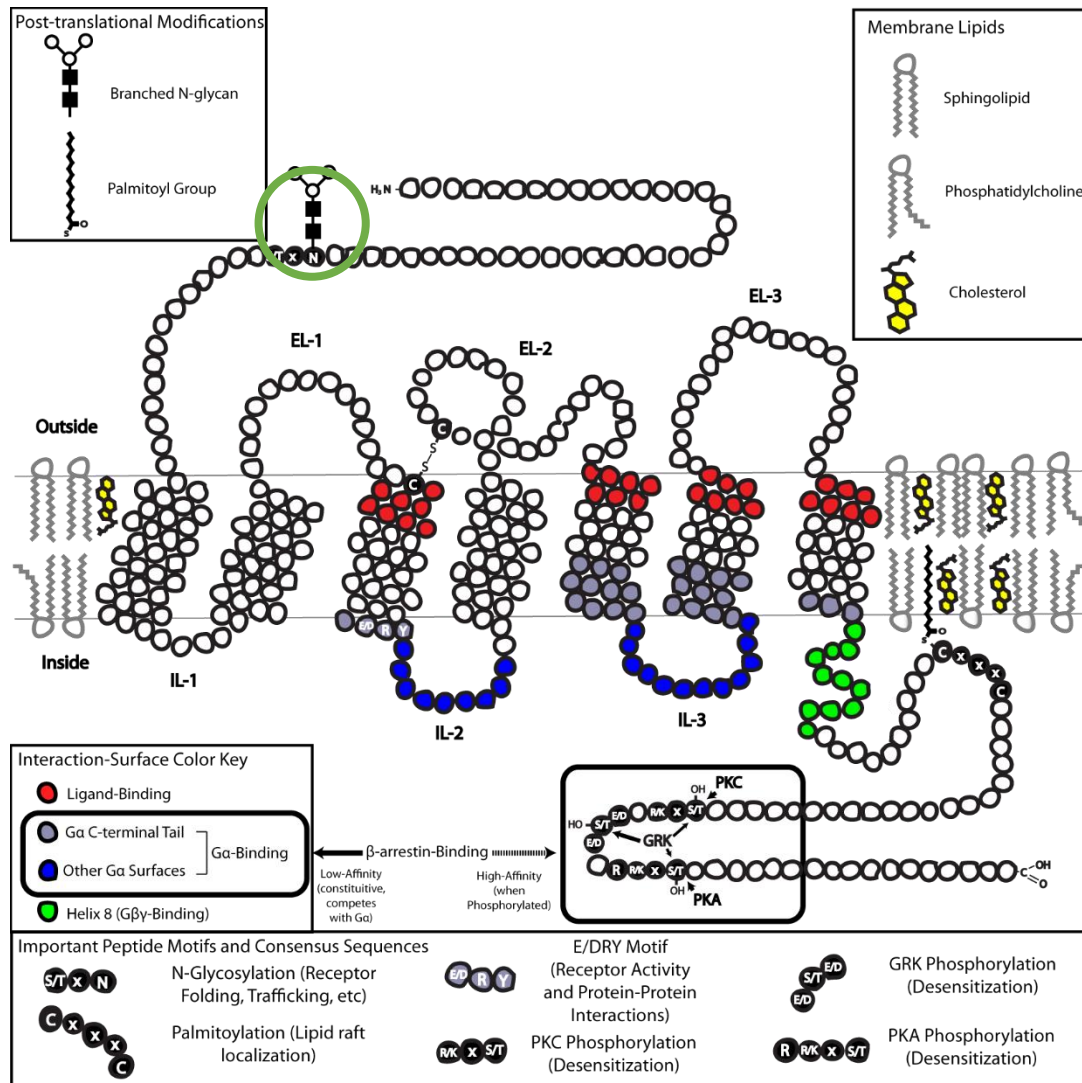
ISLHFTVCLMNFNCCMDPFIYFFAC

KGYKRKVMRMLKRQVSVSISAVKSAPEENSREMTETQMMIHS

KSSNGK

图1 GPCR结构示意图

# 基于Psi-BLAST的保守区域分析

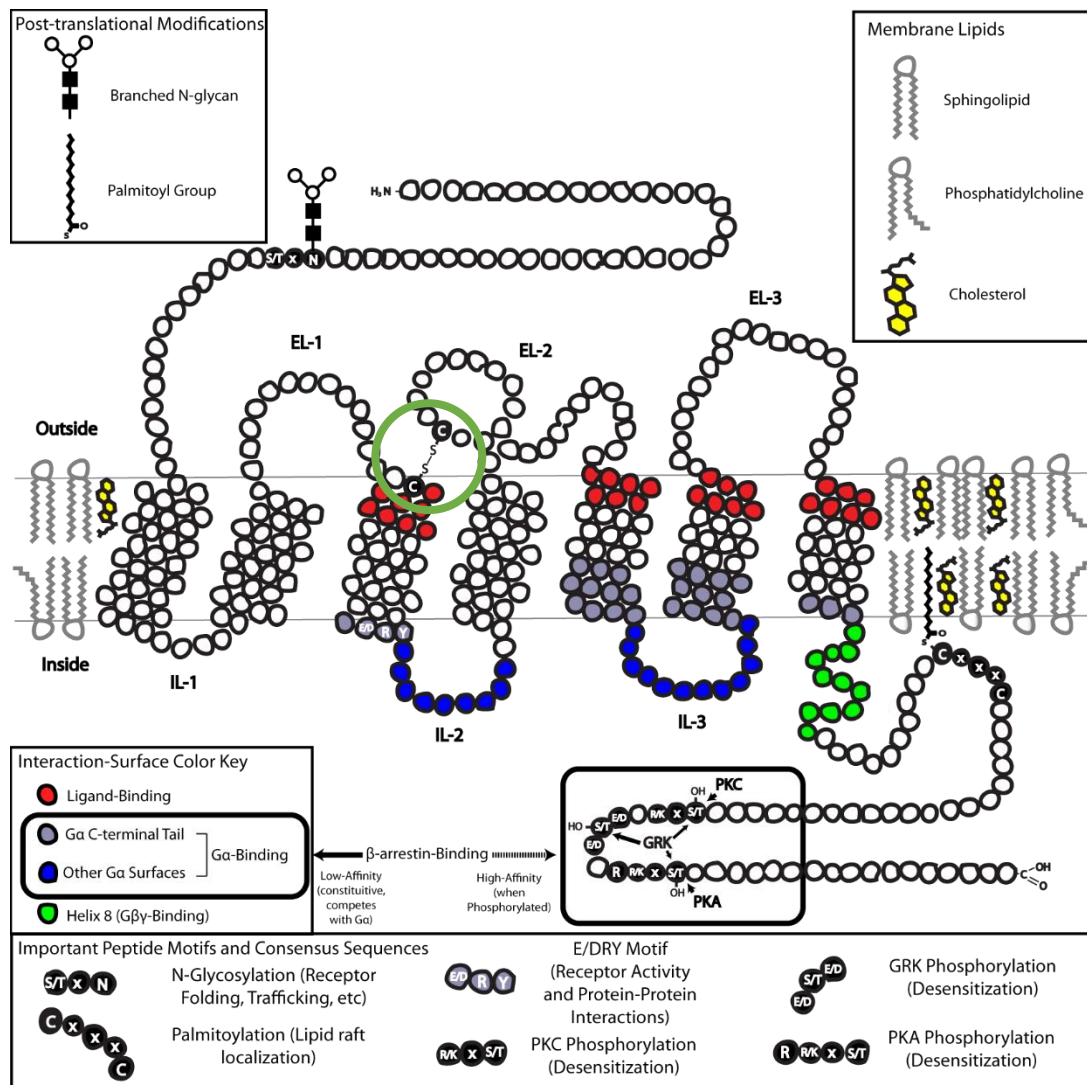


跨膜螺旋: 糖基化

MDIQMANNTPPSATPQGNDLCDLYAHHSTAR  
 IVMPLHYSLVFIIGLVGNLLALVVIV  
 QNRKKINSTTLYSTNLVISED (IL-1)  
 ILFTTALPTRIAYYAMGF  
 DWRIGDALCR (EL-1)  
 ITALVFIINTYAGVNFMTCLSI  
 DRFIAVVHPLRYNKIKRIEHAK (IL-2)  
 GVCIFVWILVFAQTLPLLI  
 NPMSKQEAERITCMEYPNFEETKS (EL-2)  
 LPWILLGACFIGYVLP LIILIC  
 YSQICCKLFRRTAKQNPLTEKSGVNKK (IL-3)  
 ALNTIILIVFVLCFTPYHVAIL  
 QHMIKKLRFSNFLECSQRHSFQ (EL-3)  
 ISLHFTVCLMNFNCCMDPFIYFFAC  
 KGYKRKVMRMLKRQVSVSISAVKSAPEENSREMTETQMMIHS  
 KSSNGK

图1 GPCR结构示意图

# 基于Psi-BLAST的保守区域分析



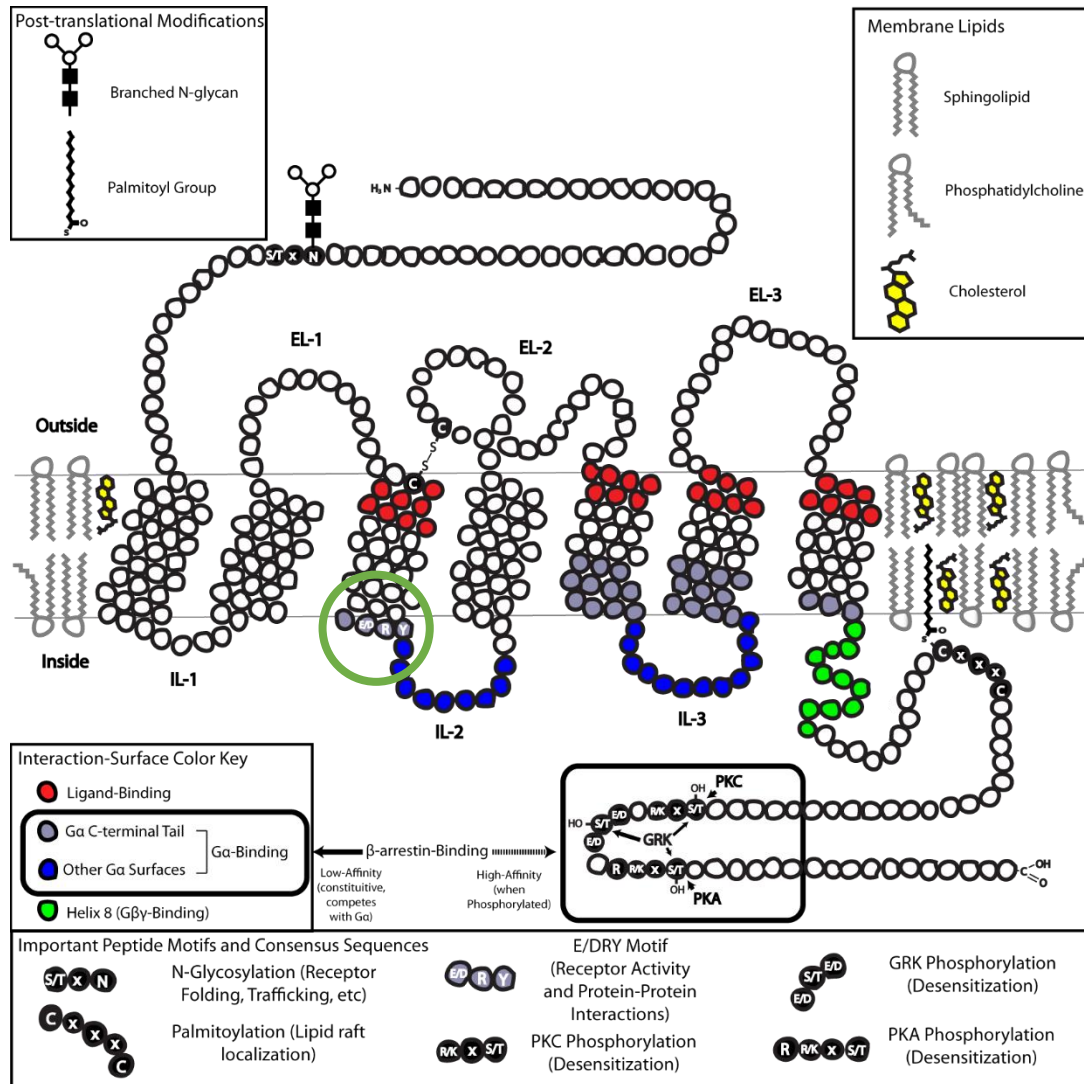
跨膜螺旋:

MDIQMANNFTPPSATPQGNDLCDLYAHHSTAR  
 IVMPLHYSLVFIIGLVGNLLALVVIV  
 QNRKKINSTTLYSTNLVISED (IL-1)  
 ILFTTALPTRIAYYAMGF  
 DWRI**G**DAL**C**R (EL-1) 二硫键  
 ITALVFIINTYAGVNFMTCLSI  
 DRFI<sup>R</sup>AVVHPLRYNKIKRIEHAK (IL-2)  
 GVCIFV**W**ILVFAQTL**P**LLI  
 NPMSKQEAERIT**C**MEYPNFEETKS (EL-2)  
 LPWILLGACFIGYVLP**L**IILIC  
 YSQICCKLFR**T**AKQNPLTEKSGVNKK (IL-3)  
 ALNTIILIVVFLCFT**P**YHVAIL  
 QHMIKKLRFSNFLECSQRHSFQ (EL-3)  
 ISLHFTVCLMNFNCCMD**P**FIYFFAC  
 KGYKRKVMRMLKRQVSVSISAVKSAPEENSREMTETQMMIHS  
 KSSNGK

图1 GPCR结构示意图



# 基于Psi-BLAST的保守区域分析



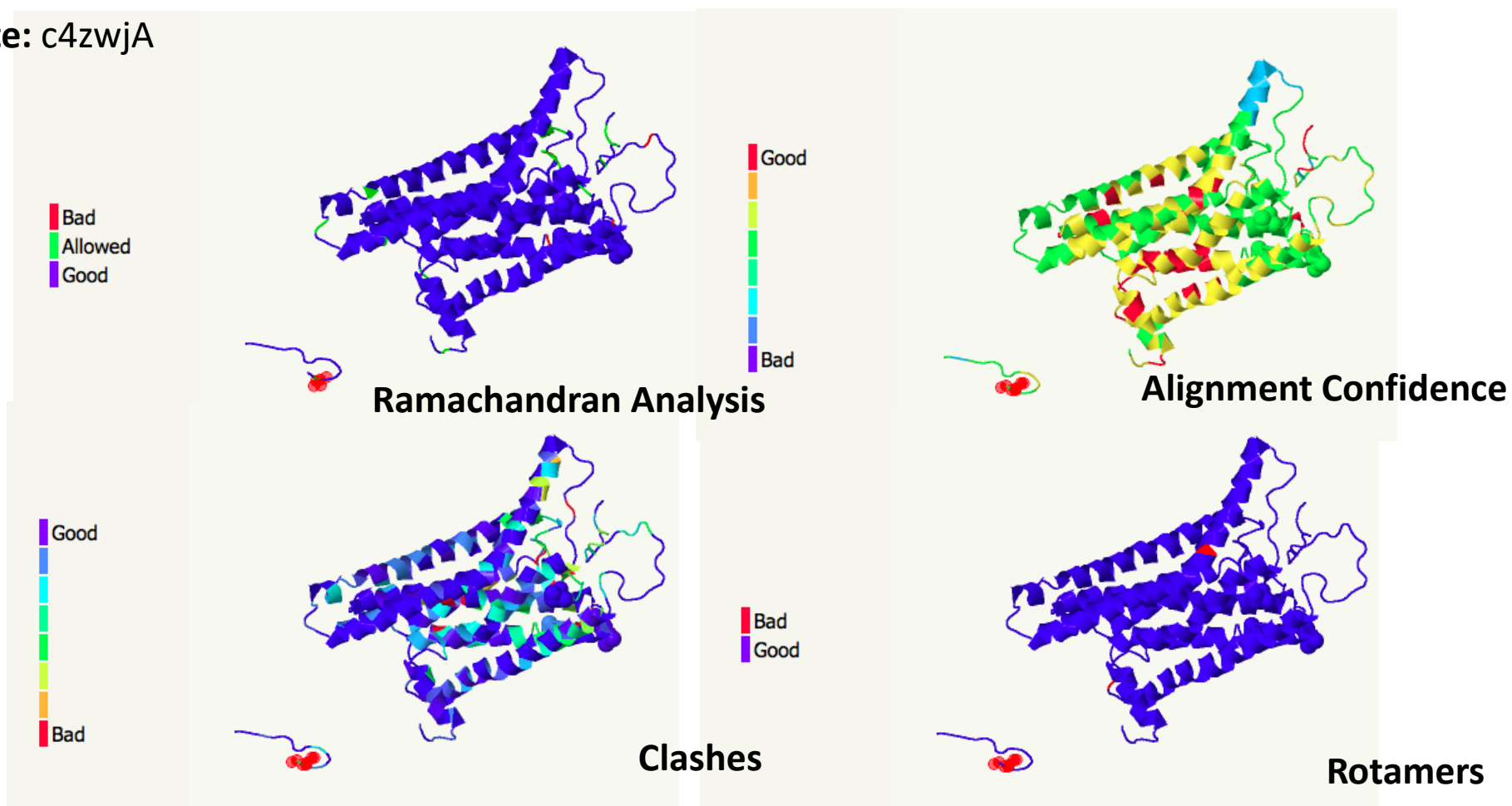
跨膜螺旋:

MDIQMANNFTPPSATPQGNDLCDLYAHHSTAR  
 IVMPLHYSLVFIIGLVGNLLALVVIV  
 QNRKKINSTTLYSTNLVISED (IL-1)  
 ILFTTALPTRIAYYAMGF  
 DWRI<sup>G</sup>DAL<sup>C</sup>R (EL-1) E/DRY motif  
 ITALVFIINTYAGVNFMTCLSI  
 D<sup>R</sup>FAVVHPLRYNKIKRIEHAK (IL-2)  
 GVCIFV<sup>W</sup>ILVFAQTL<sup>P</sup>LLI  
 NPMSKQEAERIT<sup>C</sup>MEYPNFEETKS (EL-2)  
 LPWILLGACFIGYVLP<sup>L</sup>IIILIC  
 YSQICCKLFR<sup>T</sup>AKQNPLTEKSGV<sup>N</sup>KK (IL-3)  
 ALNTIILIVFVLCFT<sup>P</sup>YHVAIL  
 QHMIKKLRFSNFLECSQRHSFQ (EL-3)  
 ISLHFTVCLMNFNCCMD<sup>P</sup>FIYFFAC  
 KGYKRKVMRMLKRQVSVSISAVKSAPEENSREMTETQMMIHS  
 KSSNGK

图1 GPCR结构示意图

# 基于同源模建的保守区域分析

Phyre2: Template: c4zwjA

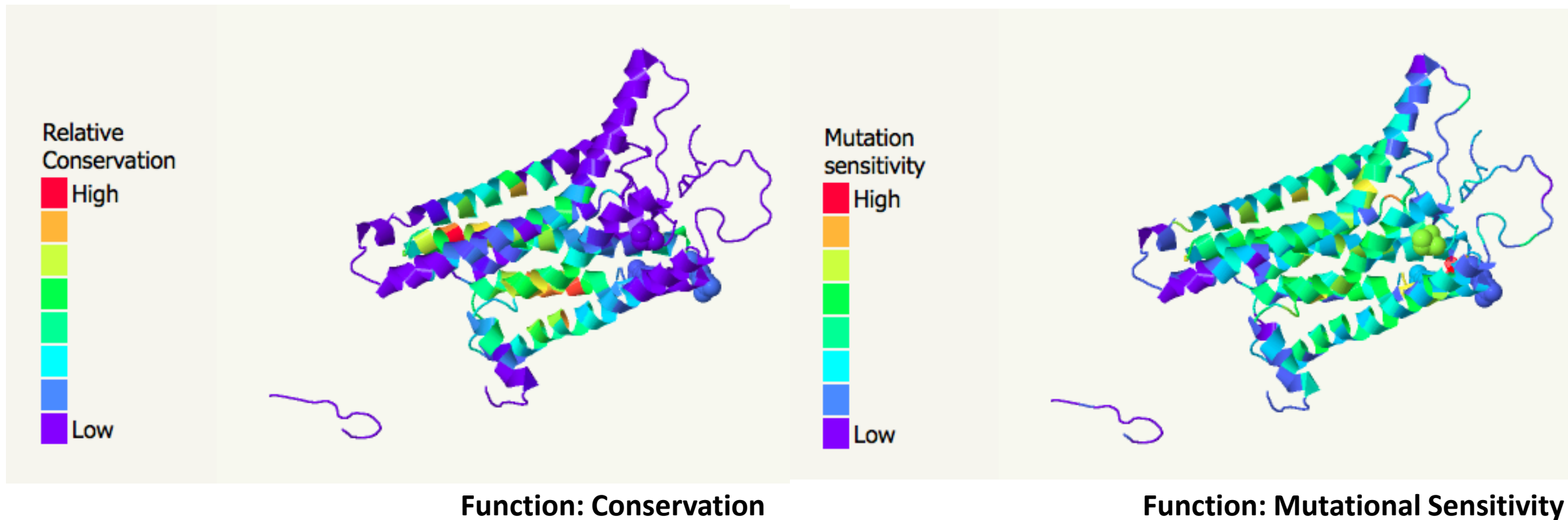


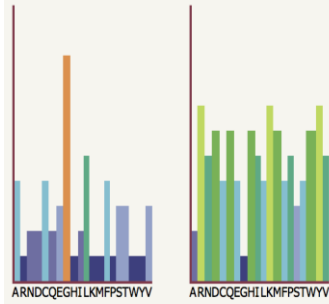
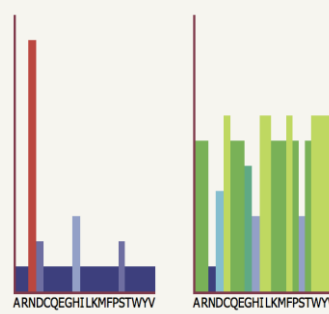
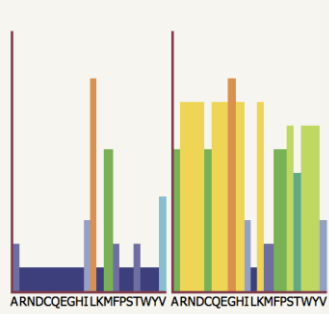
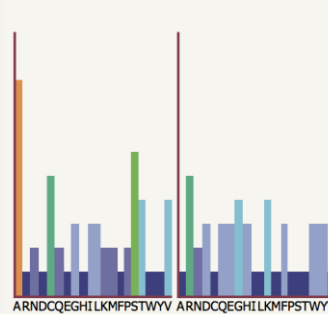
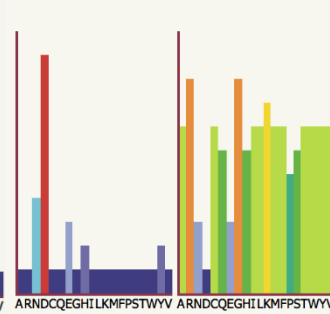
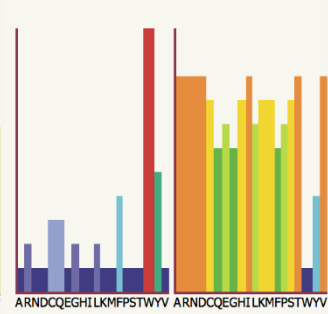
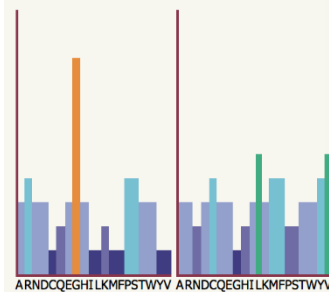
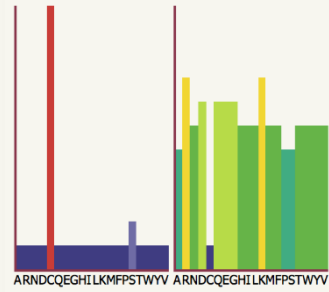
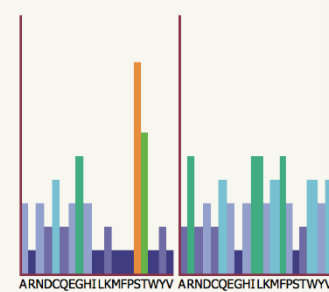
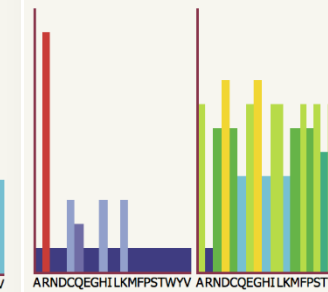
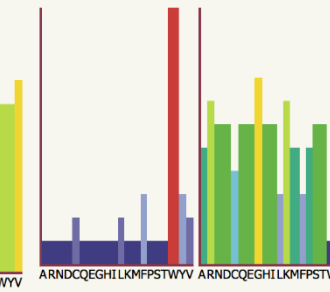
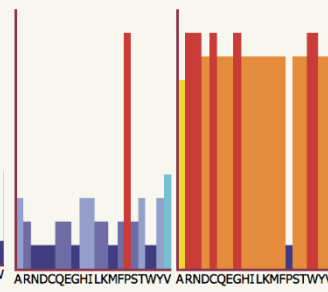
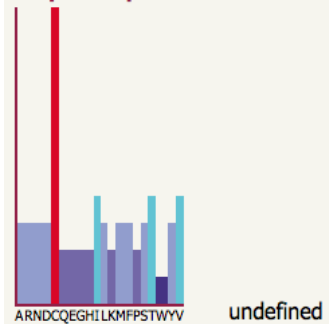
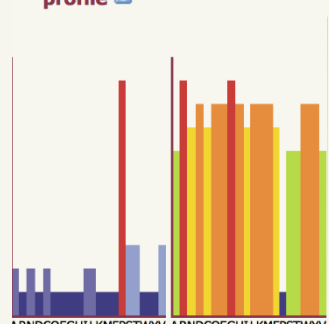
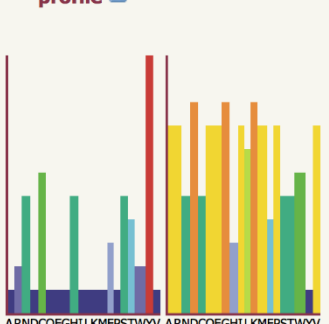
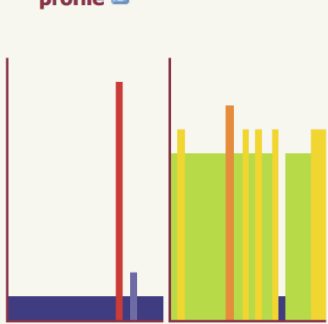
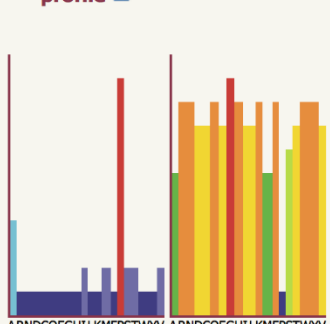
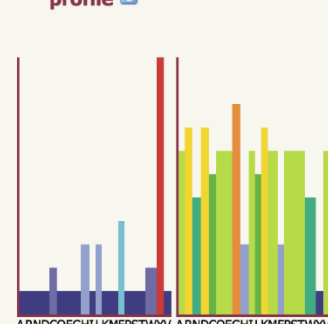
**PDB Molecule:** chimera protein of human rhodopsin, mouse s-arrestin

**Confidence:** 100.0%

**Coverage:** 91%

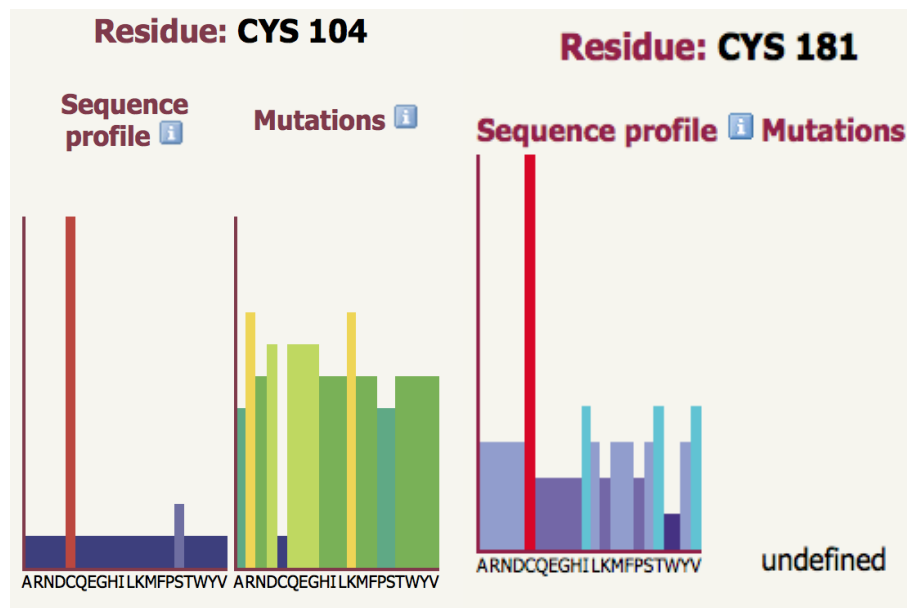
# 基于同源模建的保守区域分析



**Residue: GLY 48**Sequence profile [?](#) Mutations [?](#)**Residue: ASN 49**Sequence profile [?](#) Mutations [?](#)**Residue: LEU 73**Sequence profile [?](#) Mutations [?](#)**Residue: VAL 74**Sequence profile [?](#) Mutations [?](#)**Residue: ASP 77**Sequence profile [?](#) Mutations [?](#)**Residue: TRP 97**Sequence profile [?](#) Mutations [?](#)**Residue: GLY 100**Sequence profile [?](#) Mutations [?](#)**Residue: CYS 104**Sequence profile [?](#) Mutations [?](#)**Residue: GLY 118**Sequence profile [?](#) Mutations [?](#)**Residue: ARG 129**Sequence profile [?](#) Mutations [?](#)**Residue: TRP 156**Sequence profile [?](#) Mutations [?](#)**Residue: PRO 165**Sequence profile [?](#) Mutations [?](#)**Residue: CYS 181**Sequence profile [?](#) Mutations [?](#)**Residue: PRO 208**Sequence profile [?](#) Mutations [?](#)**Residue: TYR 216**Sequence profile [?](#) Mutations [?](#)**Residue: PRO 259**Sequence profile [?](#) Mutations [?](#)**Residue: PRO 305**Sequence profile [?](#) Mutations [?](#)**Residue: TYR 308**Sequence profile [?](#) Mutations [?](#)

undefined

# 疾病相关突变分析



绝大多数GPCR均有这个二硫键

在体外如果将这两个位点任意Cys- > Ala

1. 膜上表达量降低
2. 丧失配体的结合能力

Region of Residue Changed	Mutation	Receptor Expression		[ <sup>35</sup> S]GTPγS Binding		Specific Radioligand Binding
		Surface	Total	EC <sub>50</sub>	E <sub>max</sub>	
		% of WT level		nM	% of WT response	% of WT level
WT EBI2		100.00	100.00	0.11 ± 0.03	100	100.00
N terminus	C21A	20.68	59.97	2.29 ± 0.82	23.36 ± 1.21	5.42 ± 3.39
ECL1	C104A	2.75	90.22	N.A.	N.A.	N.A.
ECL2	C181A	5.49	79.51	N.A.	N.A.	N.A.
	E183A	59.82	74.26	5.46 ± 2.00	53.90 ± 2.07	11.33 ± 1.47
ECL3	C280A	32.60	53.24	0.93 ± 0.07	50.26 ± 2.00	16.56 ± 3.29

# 疾病相关突变分析

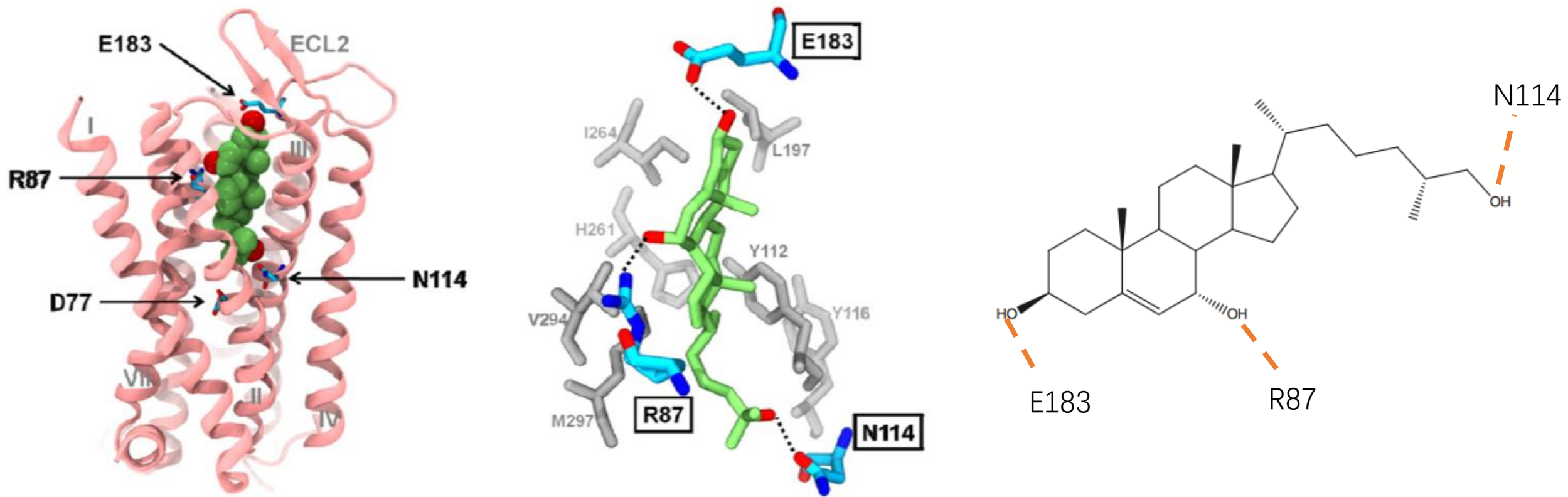
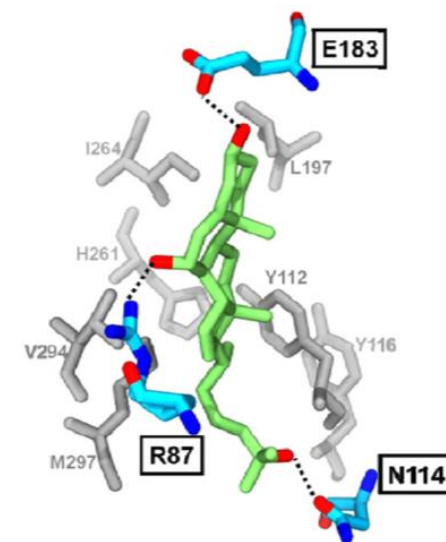
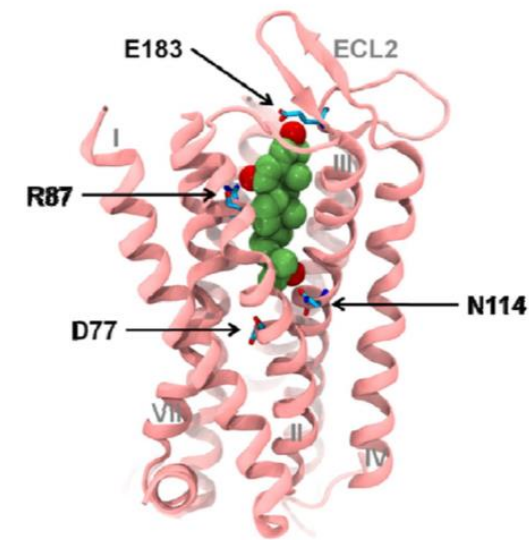


图2 利用CXCR4模拟的EB12与配体的对接模拟

# 疾病相关突变分析

Region of Residue Changed	Mutation	Receptor Expression		[ <sup>35</sup> S]GTPγS Binding		Specific Radioligand Binding
		Surface	Total	EC <sub>50</sub>	E <sub>max</sub>	
		% of WT level		nM	% of WT response	% of WT level
WT EBI2		100.00	100.00	0.11 ± 0.03	100	100.00
N terminus	C21A	20.68	59.97	2.29 ± 0.82	23.36 ± 1.21	5.42 ± 3.39
ECL1	C104A	2.75	90.22	N.A.	N.A.	N.A.
ECL2	C181A	5.49	79.51	N.A.	N.A.	N.A.
	E183A	59.82	74.26	5.46 ± 2.00	53.90 ± 2.07	11.33 ± 1.47
ECL3	C280A	32.60	53.24	0.93 ± 0.07	50.26 ± 2.00	16.56 ± 3.29
TM2	P85A	17.44	62.42	2.16 ± 1.67	27.28 ± 8.37	6.37 ± 1.43
	Y90A	23.56	80.78	23.74 ± 3.25	39.74 ± 1.81	N.A.
	D77A	86.97	78.50	N.A.	N.A.	99.31 ± 5.86
	R87A	110.84	117.04	49.04 ± 7.72	49.97 ± 1.01	N.A.
	R87W	77.13	144.55	64.01 ± 4.01	76.17 ± 0.86	17.59 ± 8.72
	R87K	75.63	78.64	3.99 ± 0.36	78.21 ± 1.43	78.02 ± 9.35
TM3	N114A	47.63	77.51	N.A.	N.A.	15.98 ± 5.04
	Y112A	91.83	89.34	11.42 ± 2.49	96.01 ± 3.22	9.39 ± 4.04
	Y116A	118.08	110.49	9.13 ± 0.92	51.71 ± 4.99	N.A.
TM5	L197A	105.57	116.52	11.78 ± 0.76	87.93 ± 3.36	20.21 ± 1.77
TM6	F257A	35.86	45.06	0.11 ± 0.21	36.74 ± 3.43	15.85 ± 2.26
	Y260A	114.07	125.93	140.50 ± 6.87	125.90 ± 2.15	N.A.
	H261A	79.95	97.96	63.71 ± 17.19	44.81 ± 3.68	4.65 ± 1.54
	I264A	112.03	104.26	1.72 ± 0.49	73.30 ± 7.87	10.84 ± 3.48
TM7	V294A	74.29	137.79	3.11 ± 4.60	80.37 ± 4.42	47.65 ± 2.24
	M297I	105.34	90.98	4.09 ± 0.42	92.88 ± 2.09	36.95 ± 3.71
	M297A	110.75	142.23	0.68 ± 0.04	158.5 ± 4.63	93.55 ± 5.05

WT, wild-type; N.A., not applicable, because no receptor stimulation by 7α,25-OHC or specific binding was observed.



# 疾病相关突变分析

·急性髓细胞样白血病

A338V

·炎症性肠道疾病

SNP 13:99304368 T->C (Intron)

Phenotype, disease and trait	Source(s)	Mapped Terms	Ontology Accessions	Study	Reported gene(s)	Associated allele	Statistics
<a href="#">Inflammatory bowel disease</a>	<a href="#">NHGRI-EBI GWAS catalog</a>	Inflammation of the large intestine, inflammatory bowel disease	<a href="#">EFO:0003767</a> , <a href="#">HP:0002037</a>	<a href="#">PMID:28067908</a>	<a href="#">GPR18</a> , <a href="#">GPR183</a> , <a href="#">UBAC2</a>	-	<b>p-value:</b> 1.00e-6
<a href="#">Inflammatory bowel disease</a>	<a href="#">NHGRI-EBI GWAS catalog</a>	Inflammation of the large intestine, inflammatory bowel disease	<a href="#">EFO:0003767</a> , <a href="#">HP:0002037</a>	<a href="#">PMID:23128233</a>	<a href="#">GPR183</a> , <a href="#">GPR18</a> <a href="#">T</a>		<b>p-value:</b> 2.00e-14 <b>odds ratio:</b> 1.112

Ley T J, *et al*, *Nature*, **2008**, 456(7218):66-72.

de Lange K M, *et al*, *Nature Genetics*, **2017**, 49(2):256-261.



# 总结

- 初步探究GPR183与GPR18存在一定的相似性，进化树分析显示其可能存在同源性。
- GPR183与GPR18各自的互作蛋白中没有交叉，是否存在结构功能互作仍需进一步分析。
- GPR183保守位点突变参与可各种疾病而且也存在疾病相关SNP，疾病相关SNP如何致病需进一步分析。