

# Beta-2 肾上腺素能受体激动剂在心血管疾病治疗 中的作用

## ——儿茶酚胺类药物筛选

陈杰、柳琳、李颖、黄颖、宋永飞、

宋颖、吴晓君、张晓玲、张立峰

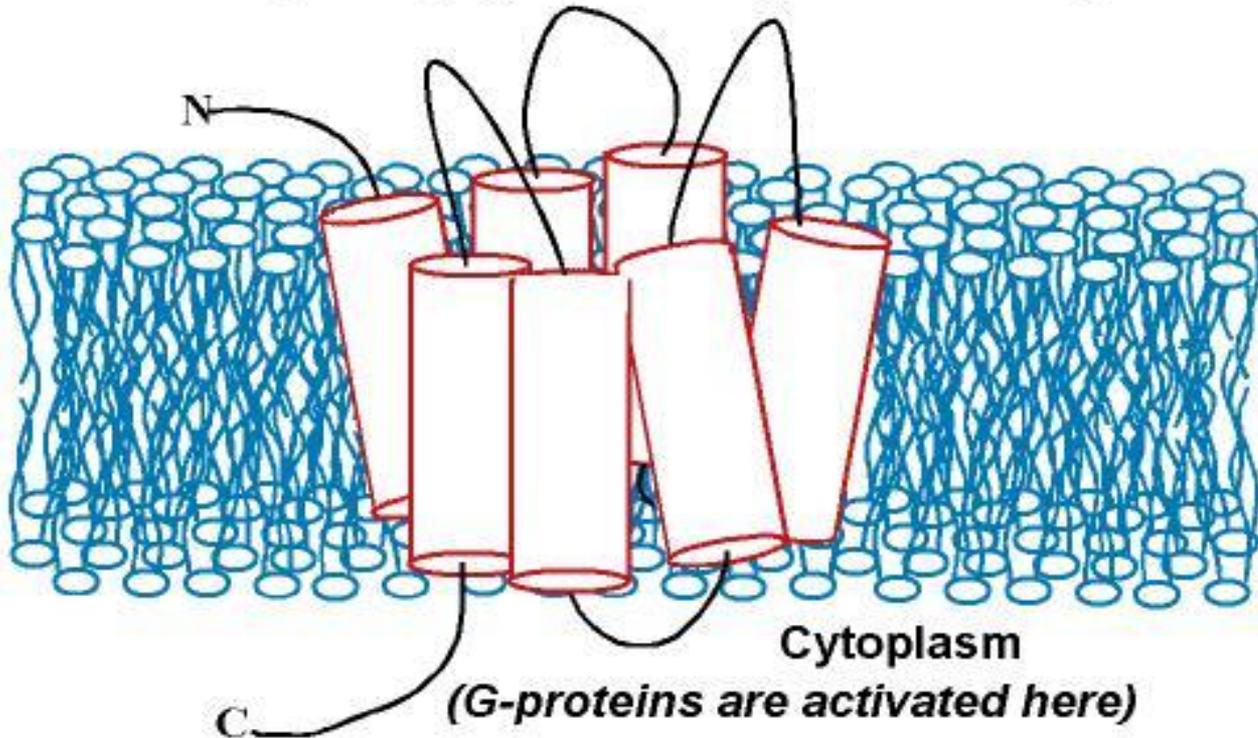
2011-12-23

# 大纲

- 研究背景
- 材料与amp;方法
- 结果与amp;讨论

# G Protein-Coupled Receptors

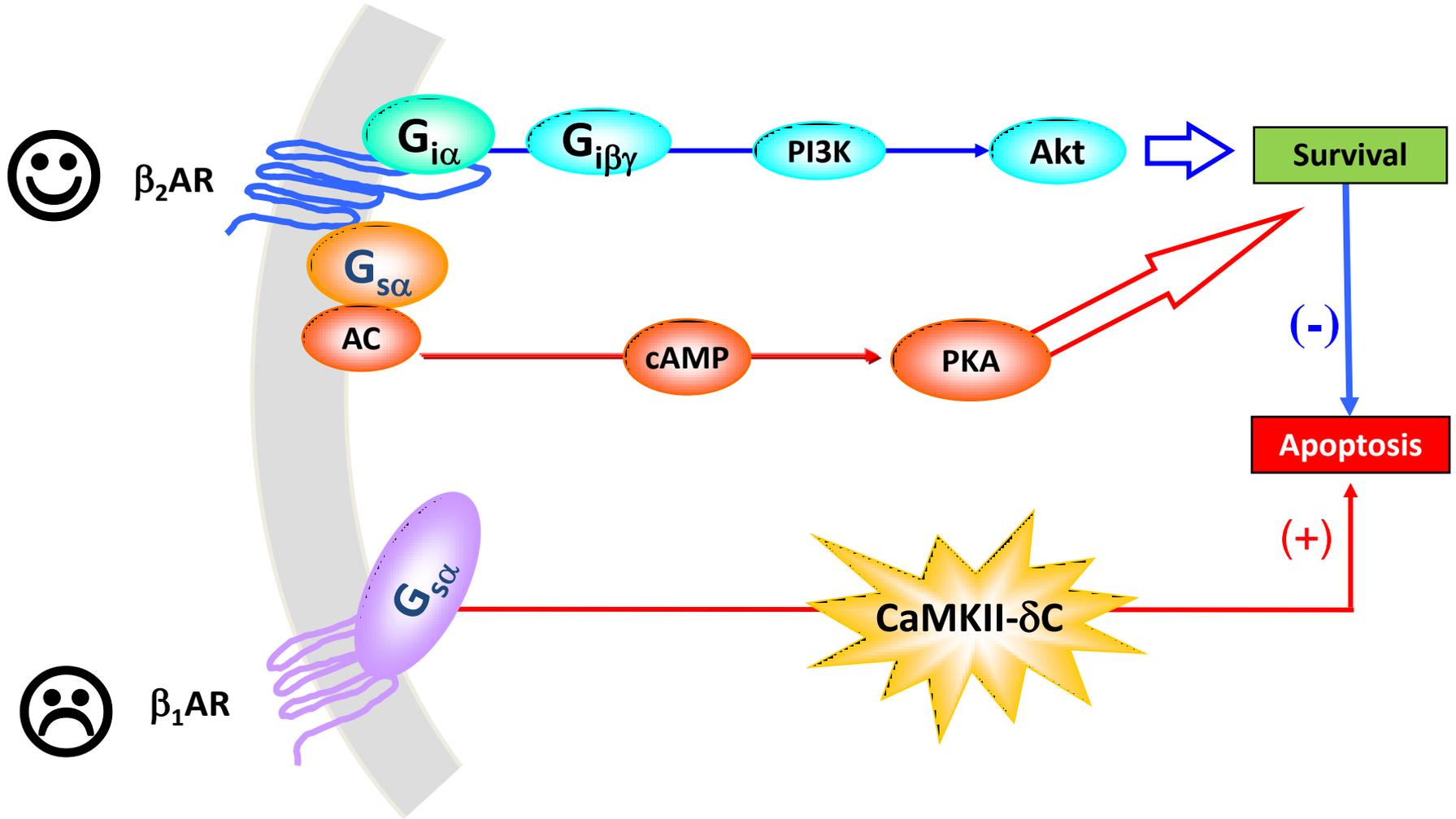
Ectoplasm (*Ligand Binding Occurs Here*)



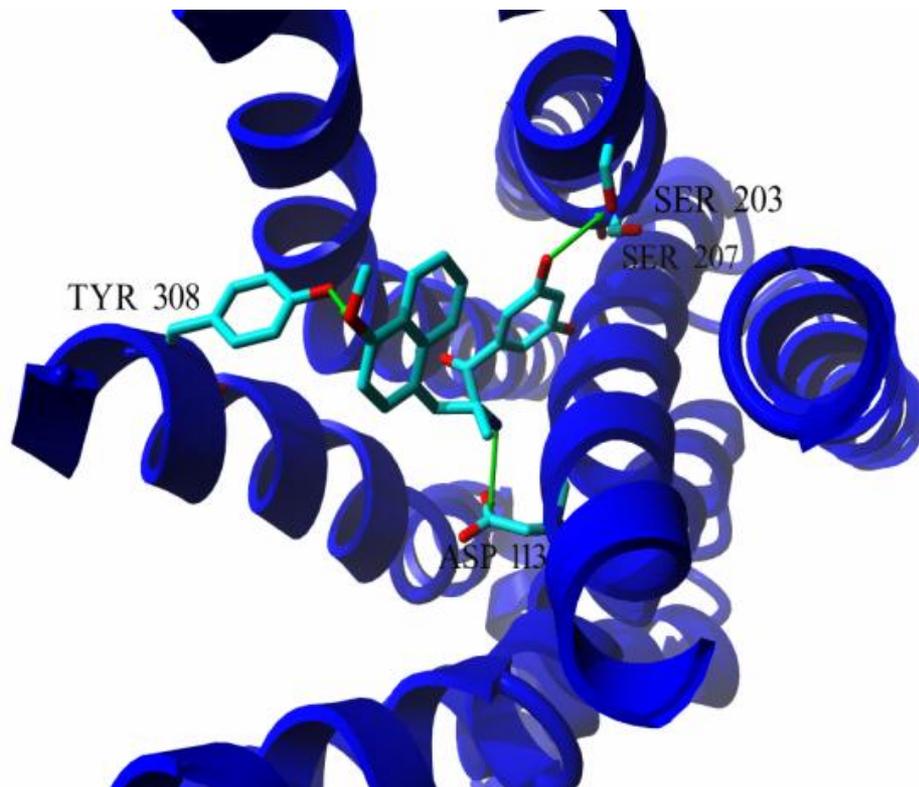
**Typical Molecular Weight: 40 kDa**

More than 50% of drug targets are GPCRs.

# $\beta$ AR Functional Selective Signal Transduction



## $\beta$ 2AR蛋白结构以及作用于它的配体药物化学结构



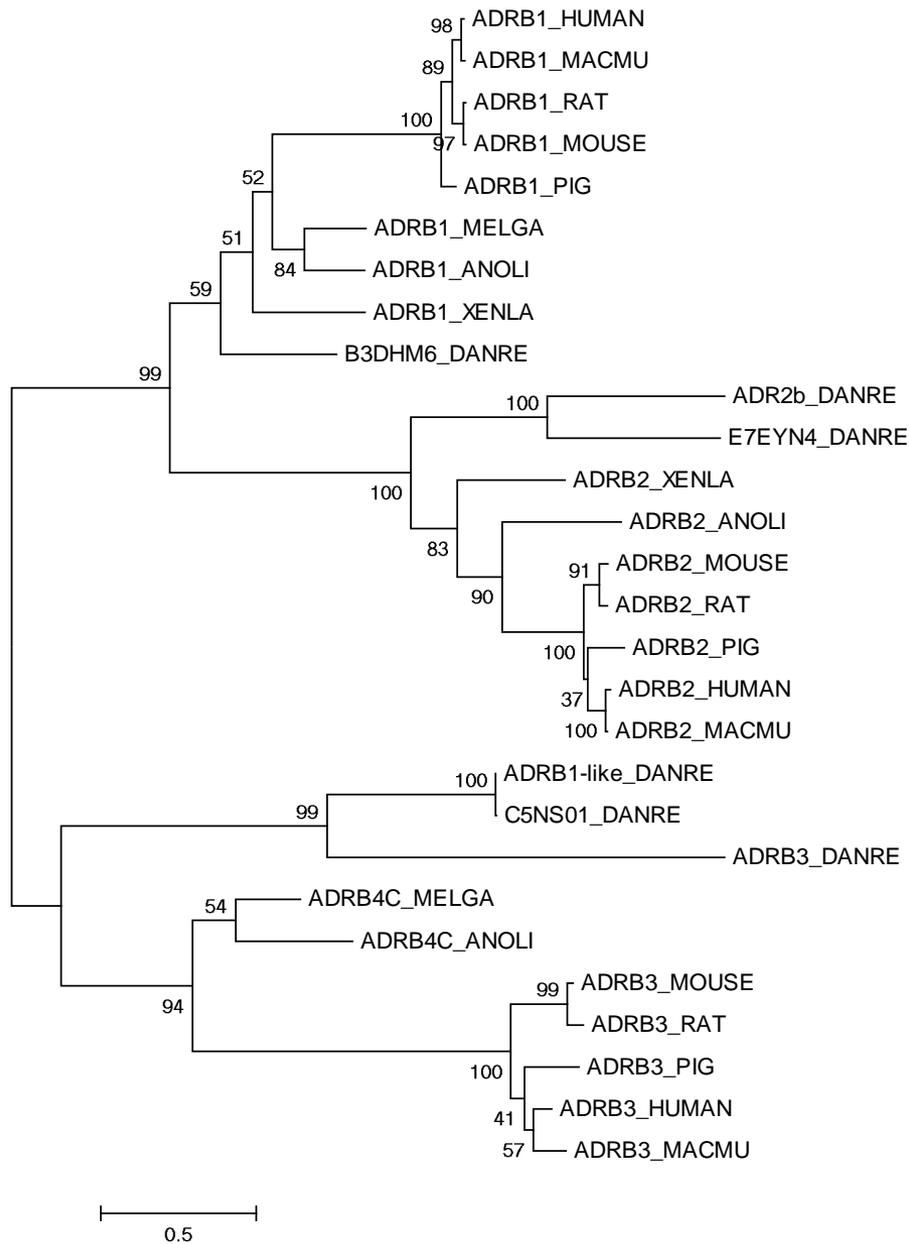
如何筛选选择性ADRB1阻滞和ADRB2激动联合治疗慢性心衰新药。

# 材料与amp;方法

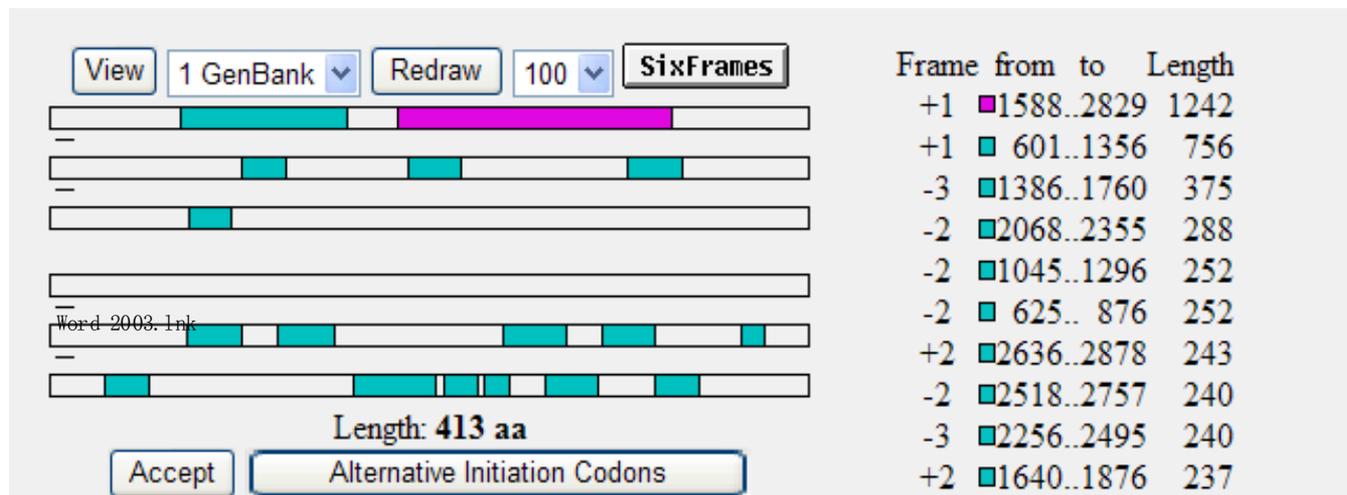
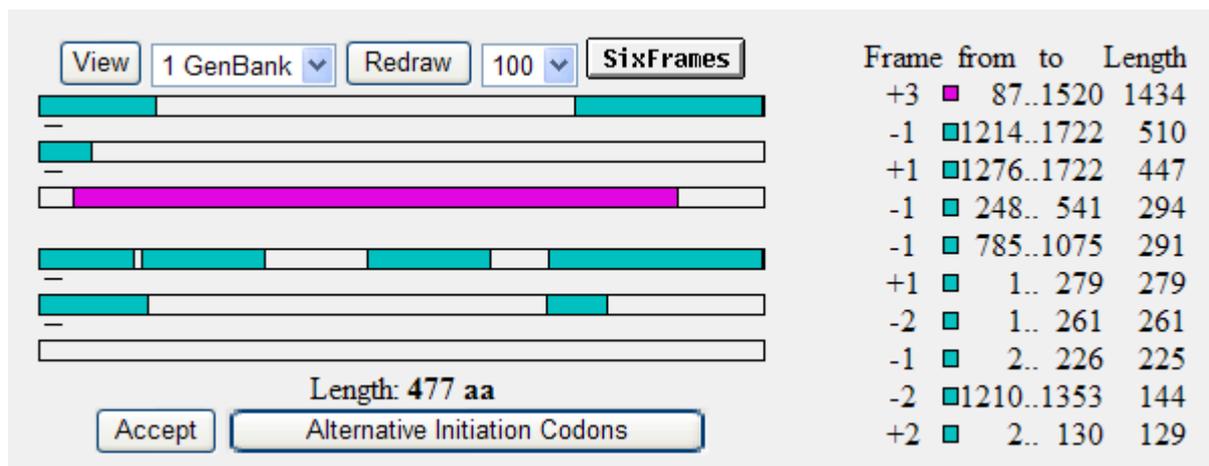
- 序列获得和系统发育分析
- ADRB1和ADRB2基因基因结构分析：ORF预测
- ADRB1和ADRB2基因氨基酸序列结构分析：信号肽、预测
- ADRB2三级结构与配体相互作用分析

# 结果与讨论

最大似然法重建ADRs  
系统发育树

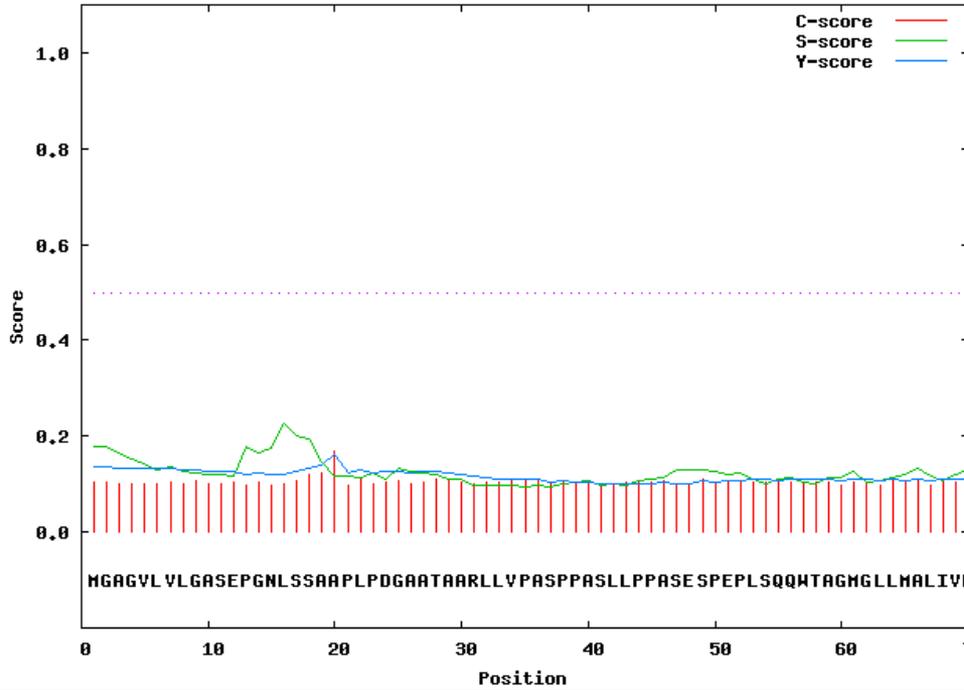


## 利用NCBI中的ORF Finder工具预测人ADRB1和ADRB2的ORF



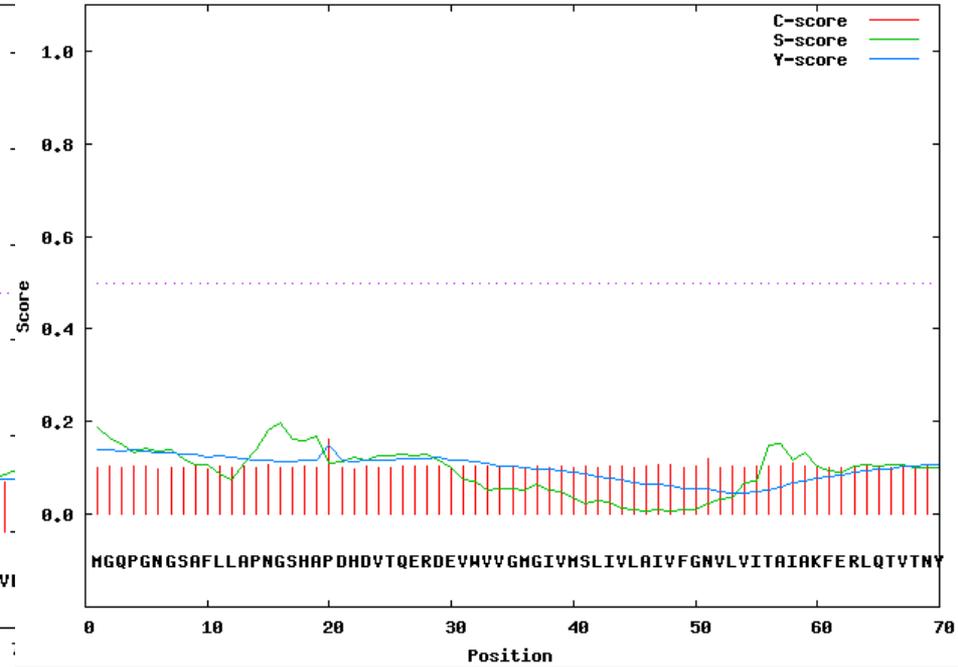
# 信号肽分析

SignalP-4.0 prediction (euk networks): sp\_P08588\_ADRB1\_HUMAN



ADRB1

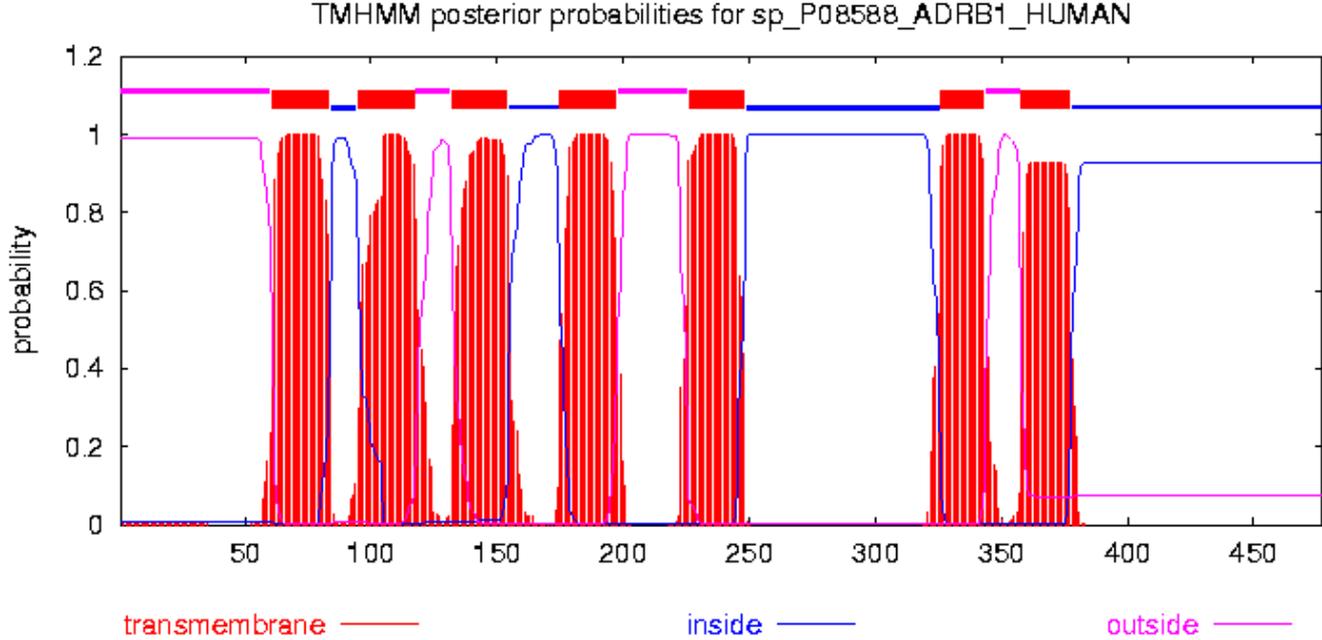
SignalP-4.0 prediction (euk networks): sp\_P07550\_ADRB2\_HUMAN



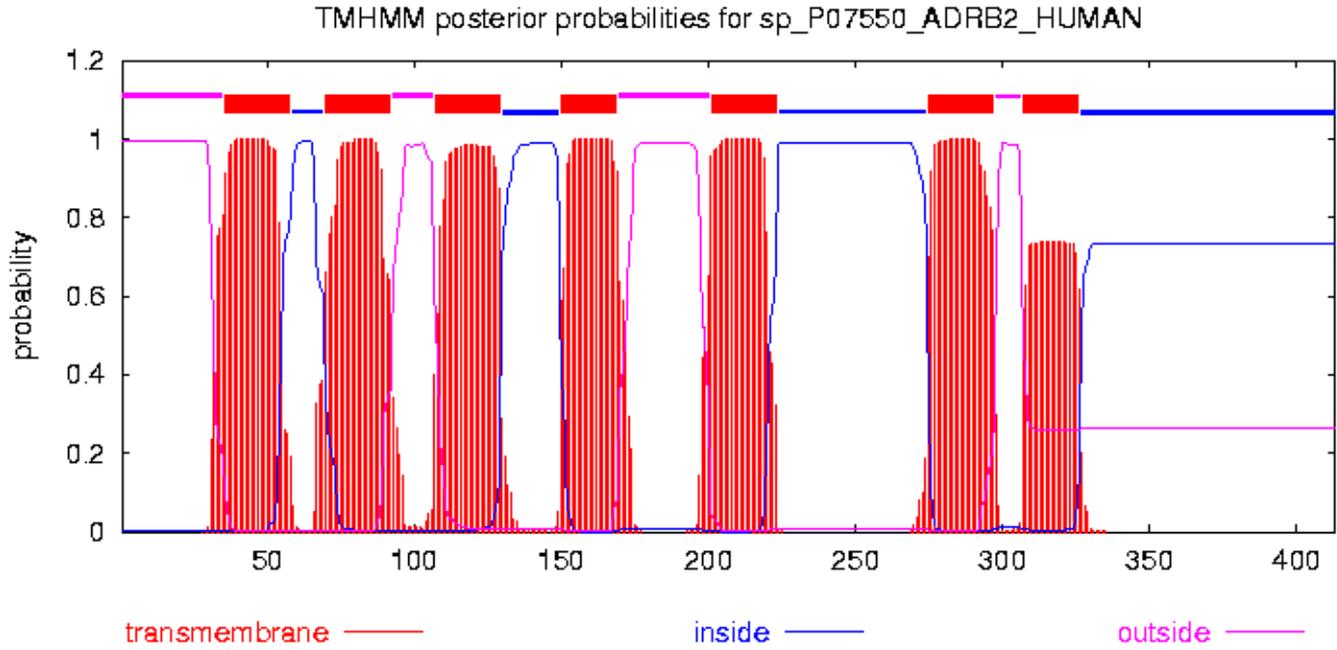
ADRB2



# 利用TMHMM 软件预测ADRB1跨膜结构



# 利用TMHMM 软件预测ADRB2跨膜结构



# 利用ScanPROSITE 软件预测结构域

hits by profiles: [1 hit (by 1 profile) on 1 sequence]

Hits by PS50262 G\_PROTEIN\_RECEP\_F1\_2 G-protein coupled receptors family 1 profile :

sp-P08588-ADR  
B1\_HUMAN  (477 aa)

75 - 377: score = 47.674

```
GNVLVIVIAIAKT PRLQTLTNLFIMSLASADLVMGLLVVFPGATIVVWGRWEYGSFFCELW  
TSVDVLCVTASIEITLCVIALDRYLAITSPFRYQSLLTRARARGLVCTVWVAISALVSLPI  
LMhwraeSDEARRCYNDPKCCDF-----VINRAYAIAS-SVVSFYVPLCIMAFAVYLRV  
FREAQKQVKKIDSCerflgpparppspspvpapppppppraaaaaataplragrag  
krrPSRLVALREQKALKTLGIIMGVFTLCWLPFFLANVVKAF----HRELVPDRLFVFFN  
WLGYSANSAFNPIIY
```

Predicted feature:

DISULFID 131 216 By similarity [condition: C-x\*-C]

hits by profiles: [1 hit (by 1 profile) on 1 sequence]

Hits by PS50262 G\_PROTEIN\_RECEP\_F1\_2 G-protein coupled receptors family 1 profile :

sp-P07550-ADR  
B2\_HUMAN  (413 aa)

50 - 326: score = 48.336

```
GNVLVITAIKFERLQVTNYFITSLACADLVMGLAVVFPGAHILMKMWTFGNFWCFEWF  
TSIDVLCVTASIEITLCVIAVDRYFAITSPFKYQSLTKNKARVILMVWIVSGLTSFLPI  
QMhwyraHQEAINCYNANETCCDF-----FTNQAYAIAS-SIVSFYVPLVIMVFVYSRV  
FQEAKRQLQKIDKSegrfhvqnlsqveqdgtrtghglrRSSKFCLKEHKALKTLGIIMGT  
TLCWLPFFIVNIVHVI----QDNLIRKEVYILLNWIGYVNSGFNPLIY
```

Predicted feature:

DISULFID 106 191 By similarity [condition: C-x\*-C]

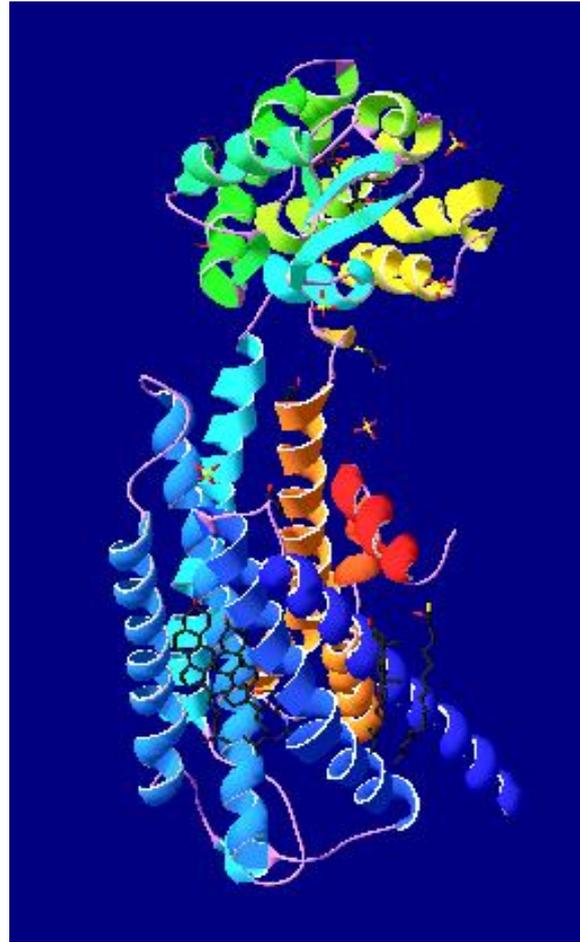
ADRB1: 结构域位于75-377 氨基酸位点。且在131和216 存在二硫键

ADRB1: 结构域位于50-326 氨基酸位点。且在106和191 存在二硫键

# 人ADRB2的结构分析- 2RH1.pdb



# 配体结合位点



十二甘醇 (dodecaethylene glycol)、乙酰胺 (acetamide)、1,4-丁二醇 (1,4-butanediol)、4-(3-异丙氨基-2-羟基丙氧基) 咪唑 (CAU)、胆固醇 (cholesterol)、麦芽糖 (maltose)、软脂酸 (palmitic acid)、硫酸根离子 (SO<sub>4</sub>)

# 麦芽糖配体结构空间

