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

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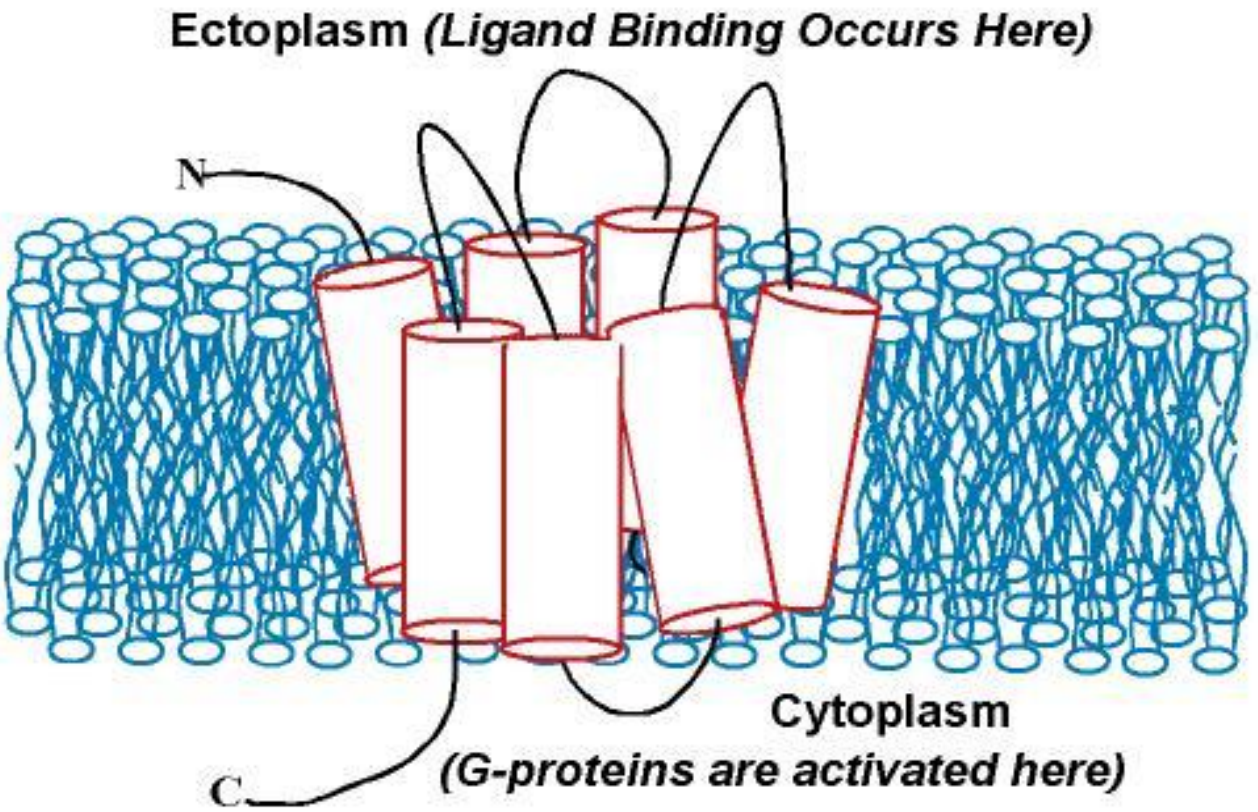
大纲

- 研究背景
- 材料与方法
- 结果与讨论

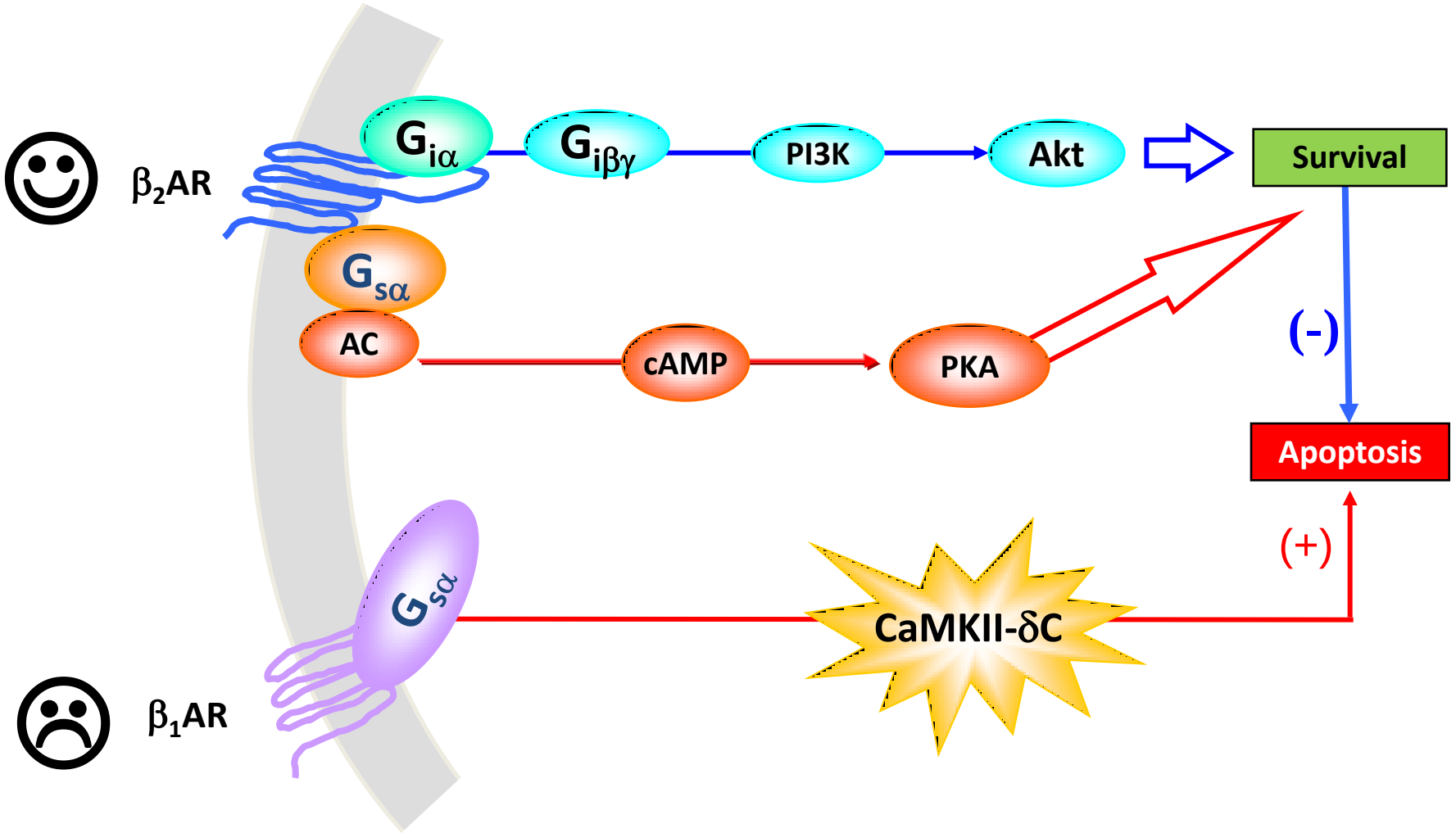
G Protein-Coupled Receptors



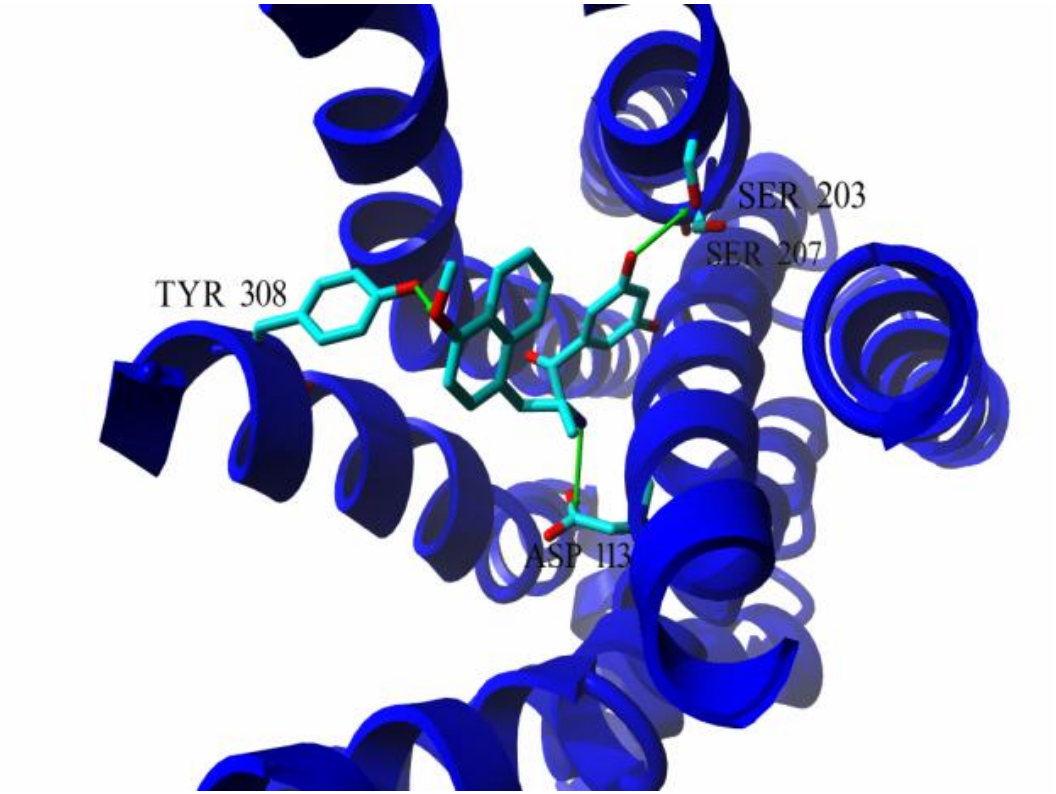
Typical Molecular Weight: 40 kDa

More than 50% of drug targets are GPCRs.

βAR Functional Selective Signal Transduction



β2AR蛋白结构以及作用于它的配体药物化学结构



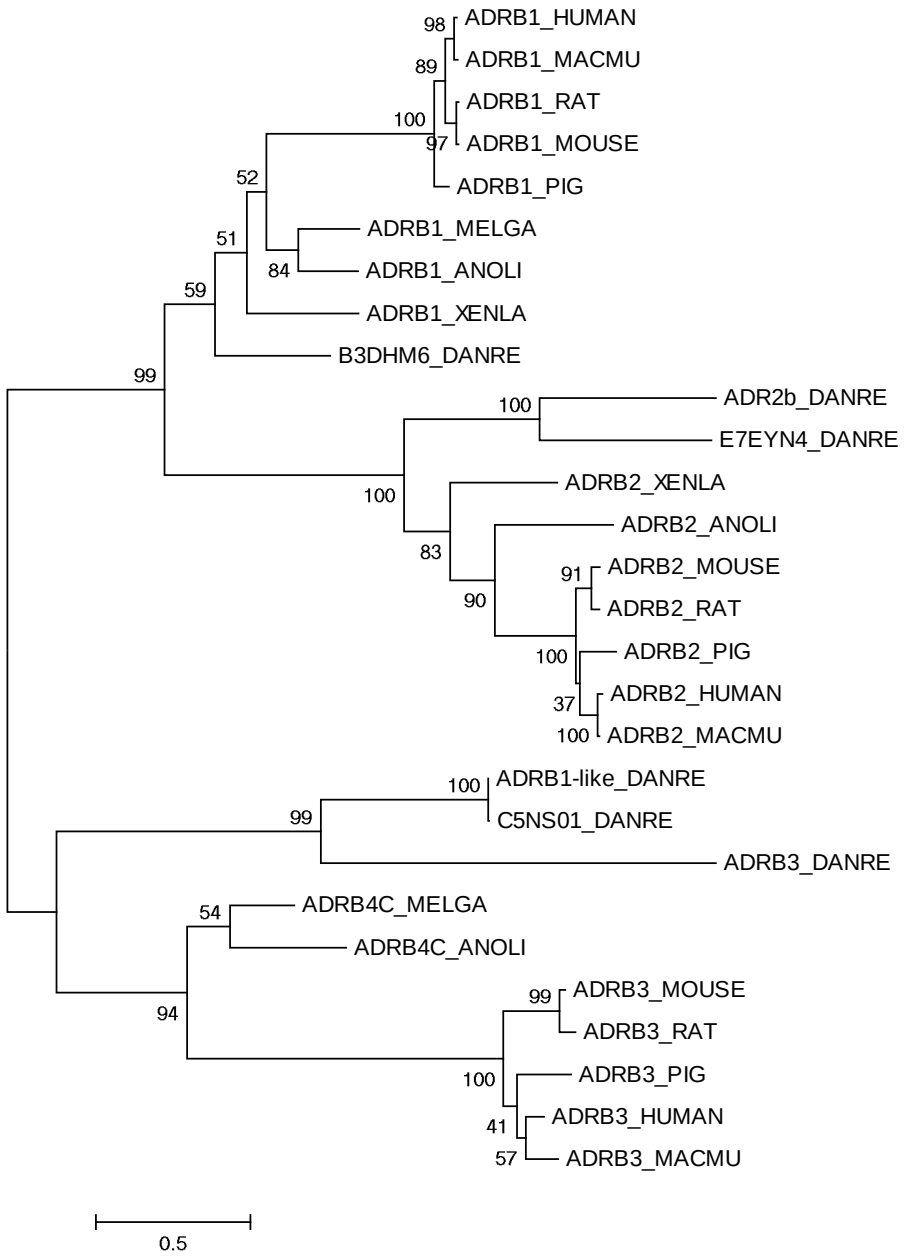
如何筛选选择性ADRB1阻滞和ADRB2激动联合治疗慢性心衰新药。

材料与方法

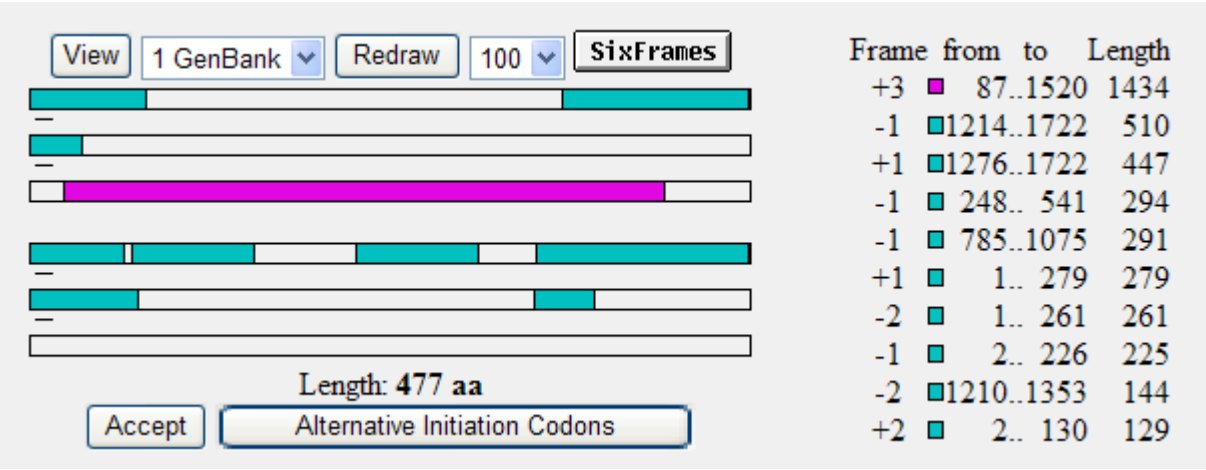
- 序列获得和系统发育分析
- ADRB1和ADRB2基因基因结构分析：ORF预测
- ADRB1和ADRB2基因氨基酸序列结构分析：信号肽、预测
- ADRB2三级结构与配体相互作用分析

结果与讨论

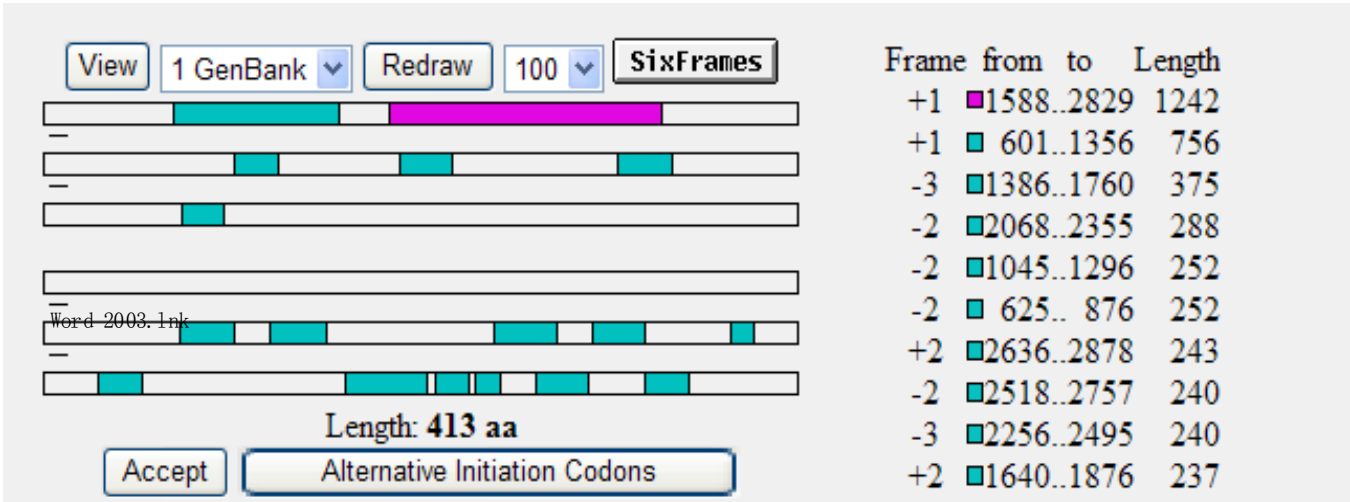
最大似然法重建ADRs系统发育树



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

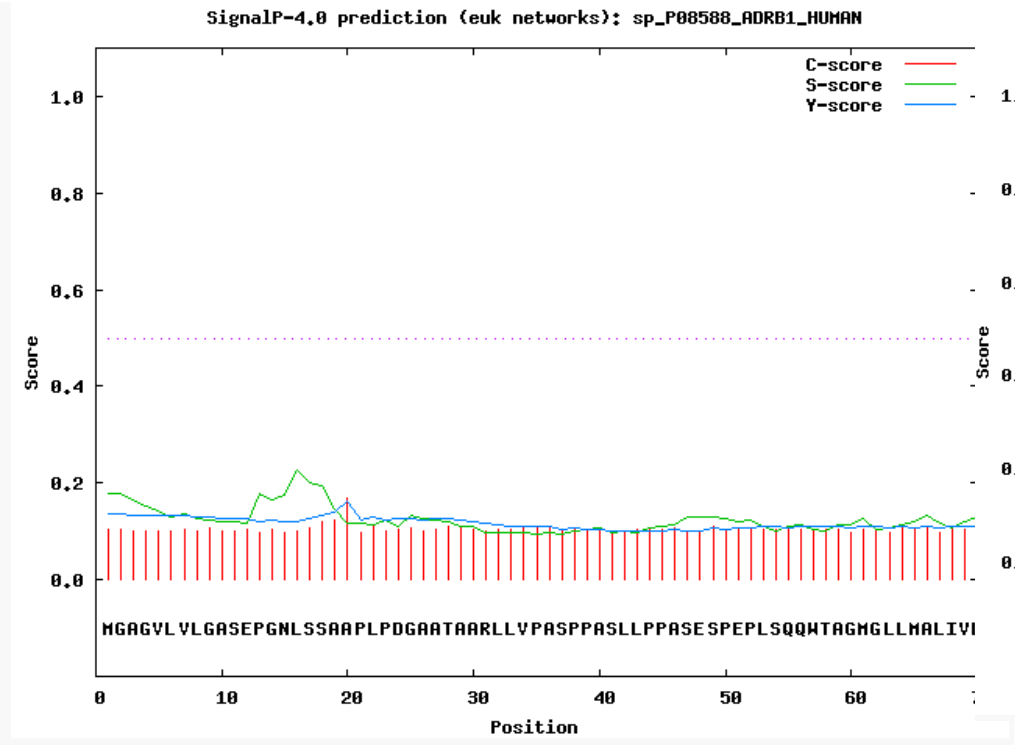


Frame	from	to	Length
+3	87	1520	1434
-1	1214	1722	510
+1	1276	1722	447
-1	248	541	294
-1	785	1075	291
+1	1	279	279
-2	1	261	261
-1	2	226	225
-2	1210	1353	144
+2	2	130	129

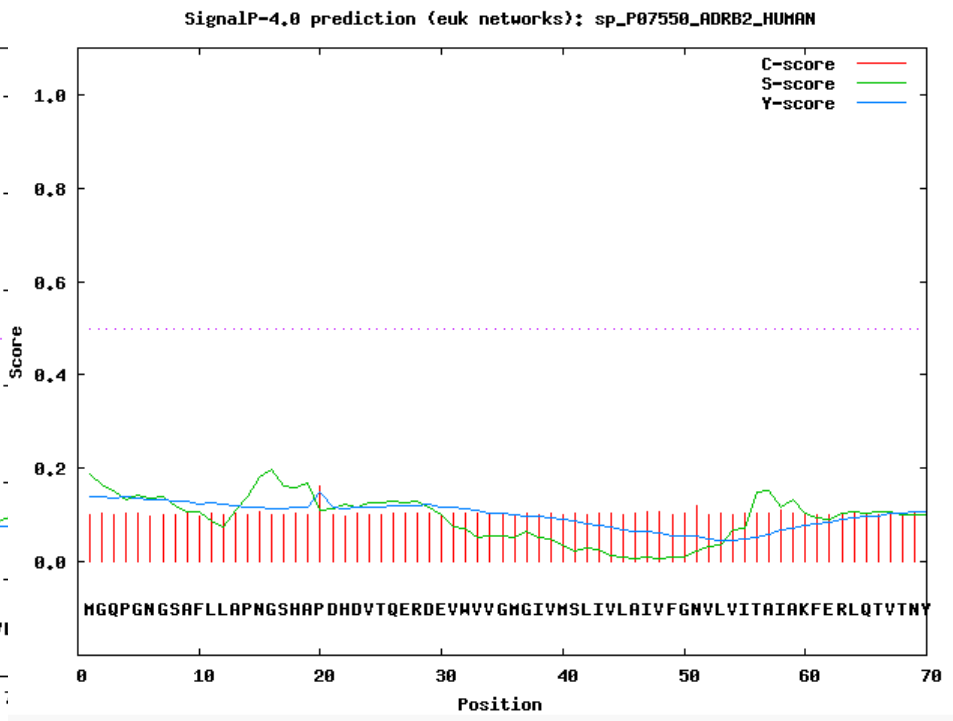


Frame	from	to	Length
+1	1588	2829	1242
+1	601	1356	756
-3	1386	1760	375
-2	2068	2355	288
-2	1045	1296	252
-2	625	876	252
+2	2636	2878	243
-2	2518	2757	240
-3	2256	2495	240
+2	1640	1876	237

信号肽分析

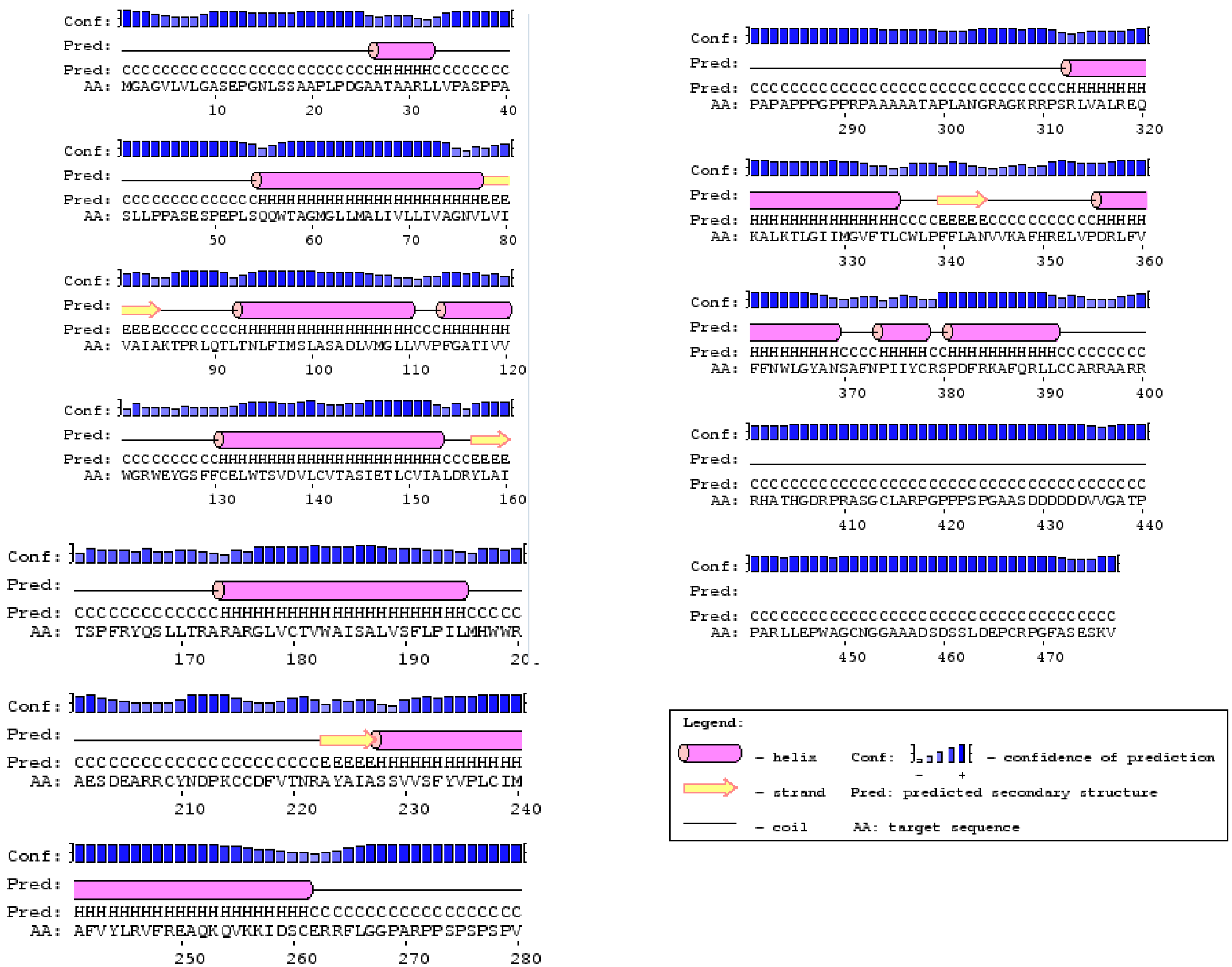


ADRB1

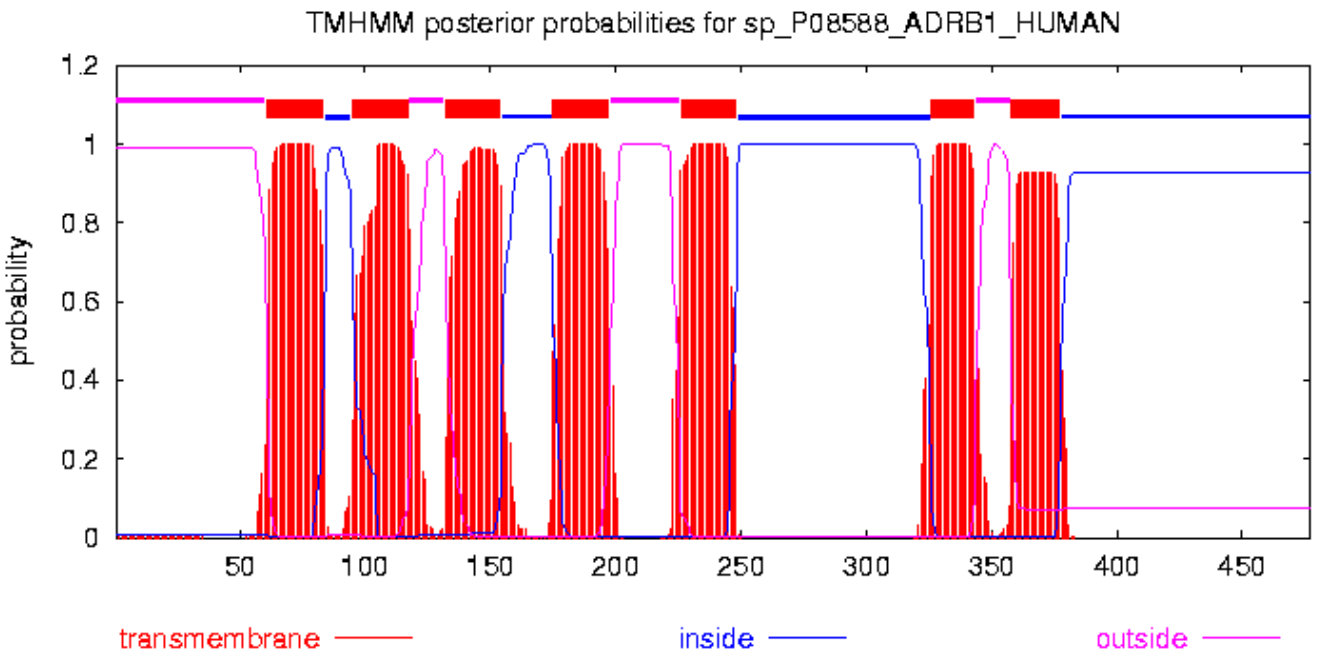


ADRB2

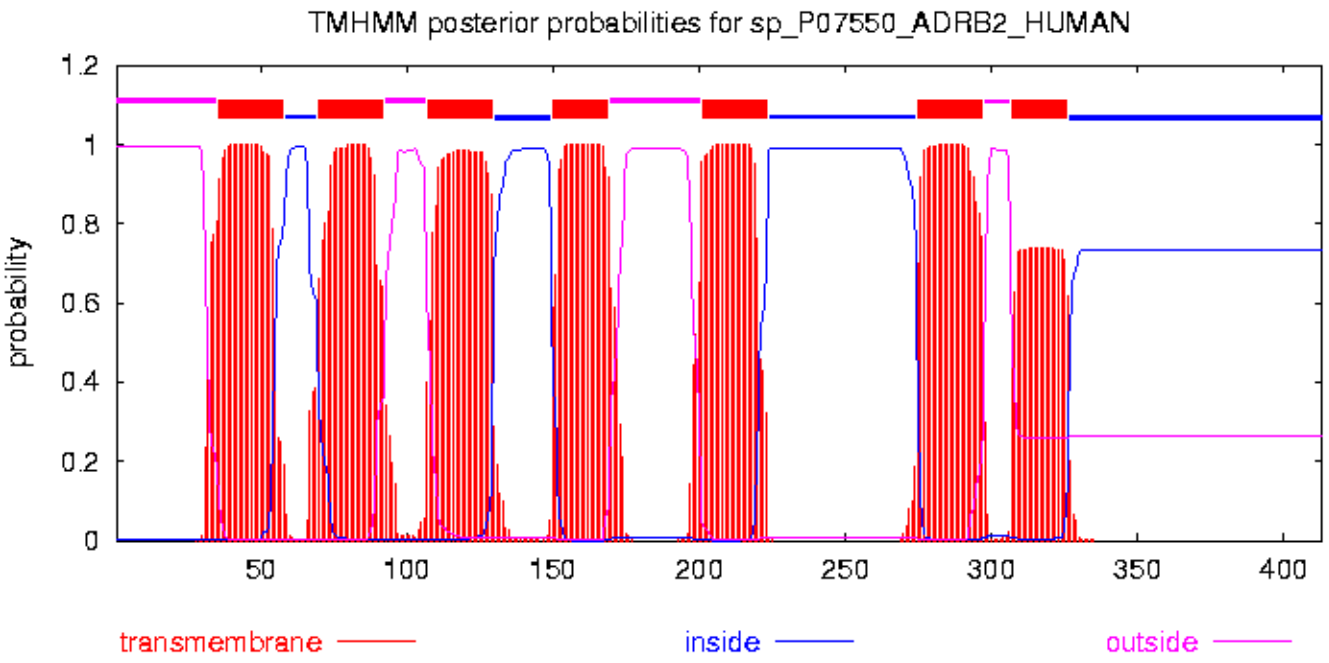
基于PSIpred软件的ADRB1蛋白二级结构分析



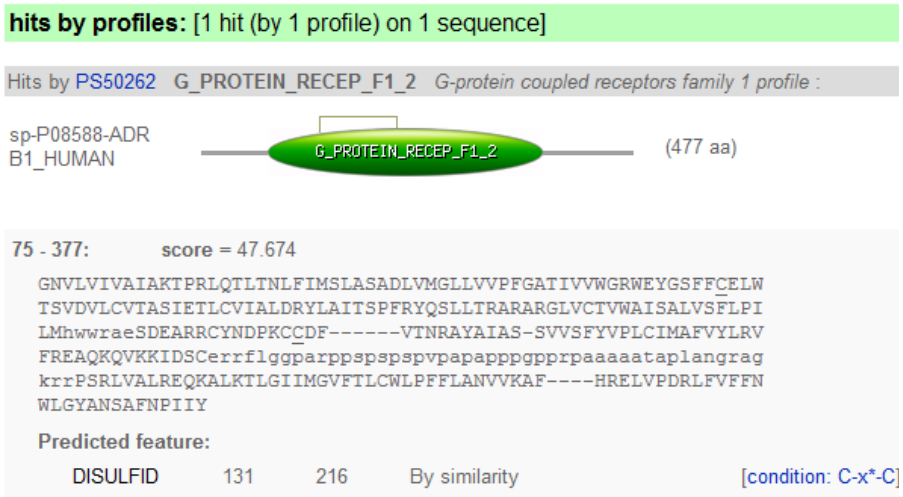
利用TMHMM 软件预测ADRB1跨膜结构

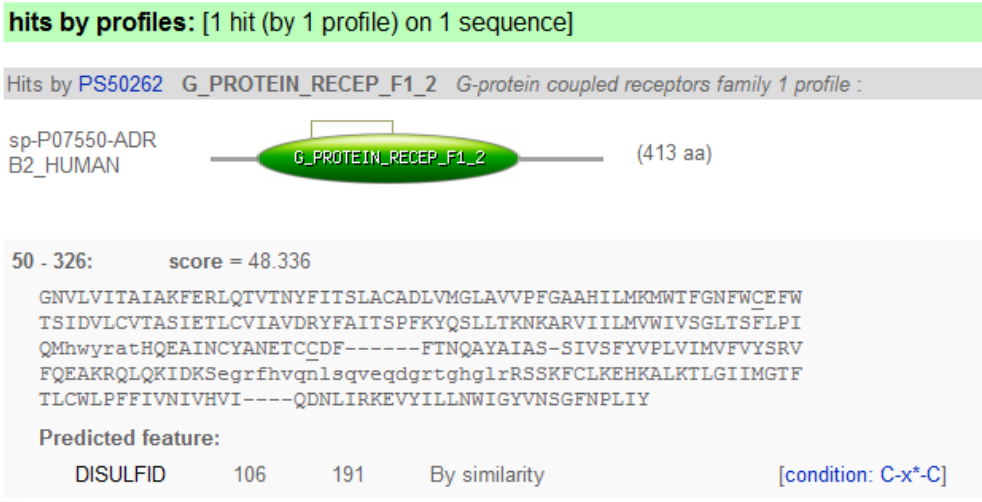


利用TMHMM 软件预测ADRB2跨膜结构



利用ScanPROSITE 软件预测结构域

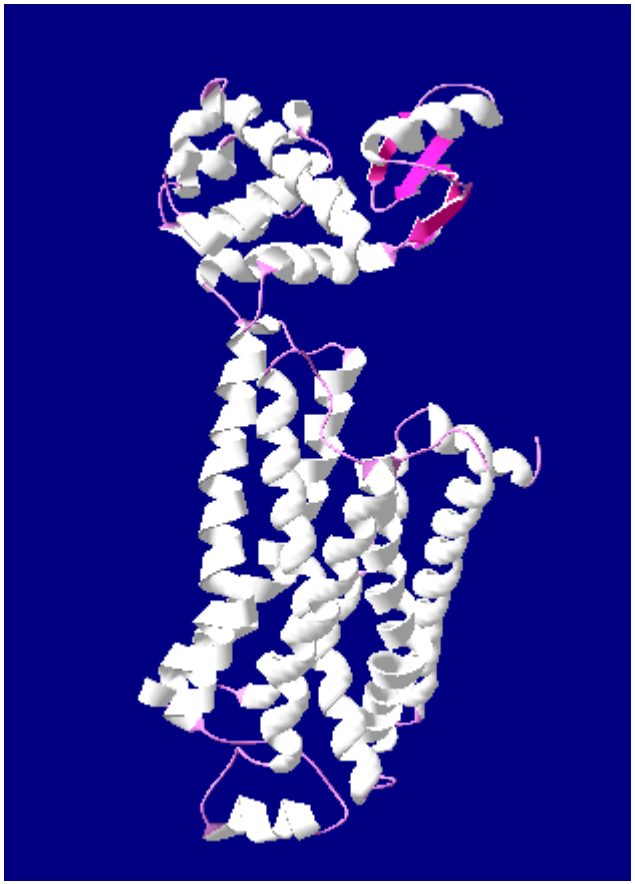




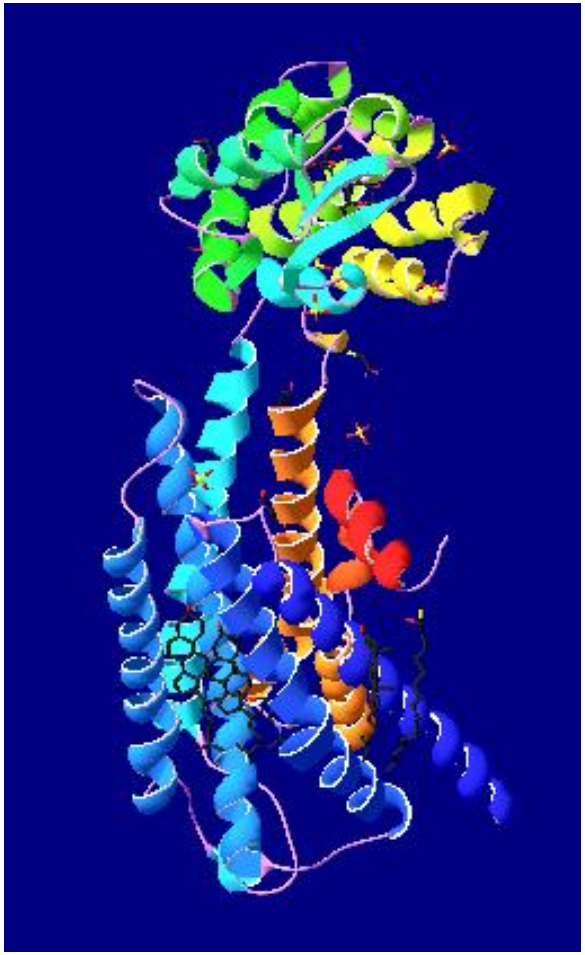
ADRB1：结构域位于75-377 氨基酸位点。且在131和216 存在二硫键

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-异丙胺基-2-羟基丙氧基)咔唑（CAU）、胆固醇（cholesterol）、麦芽糖（maltose）、软脂酸（palmitic acid）、硫酸根离子（SO4）

麦芽糖配体结构空间