

实用生物信息技术课程总结交流会

牛源口蹄疫病毒整联蛋白受体的 生物信息学分析

2011年12月25日

报告人：高闪电

其他组员：黄家兴 赵洪喜 李红娟

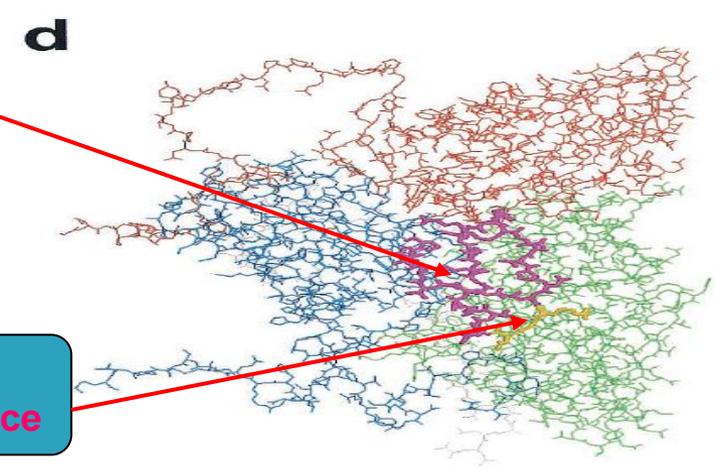
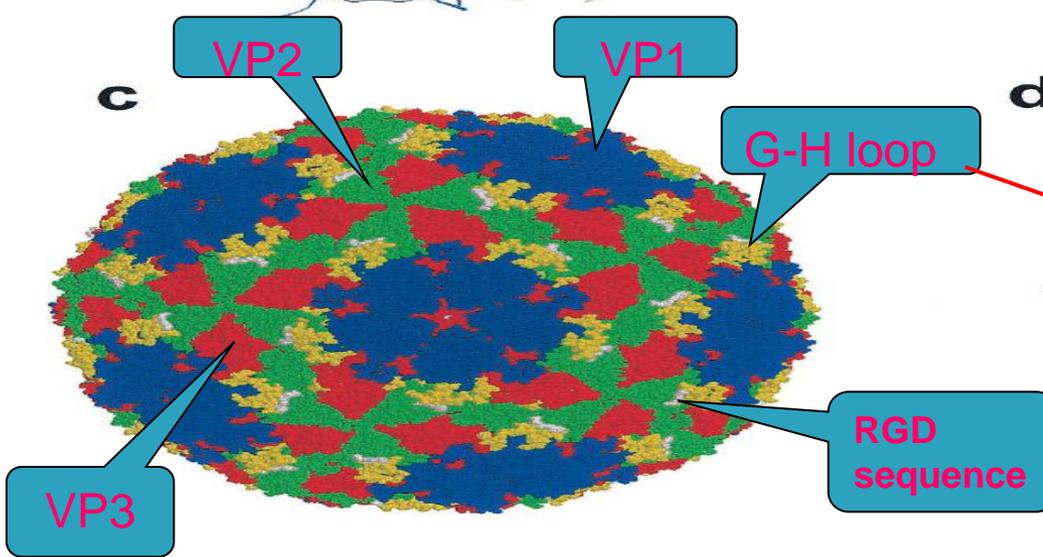
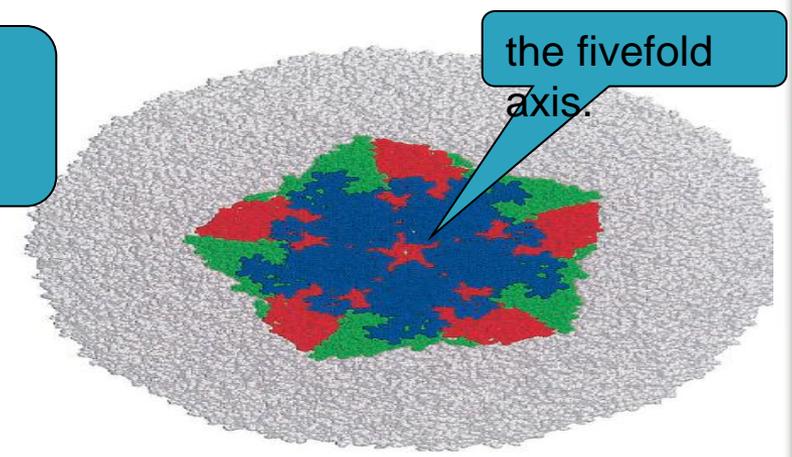
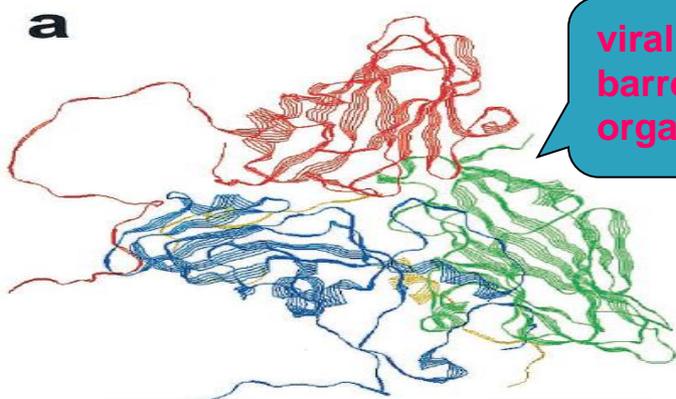
主要内容

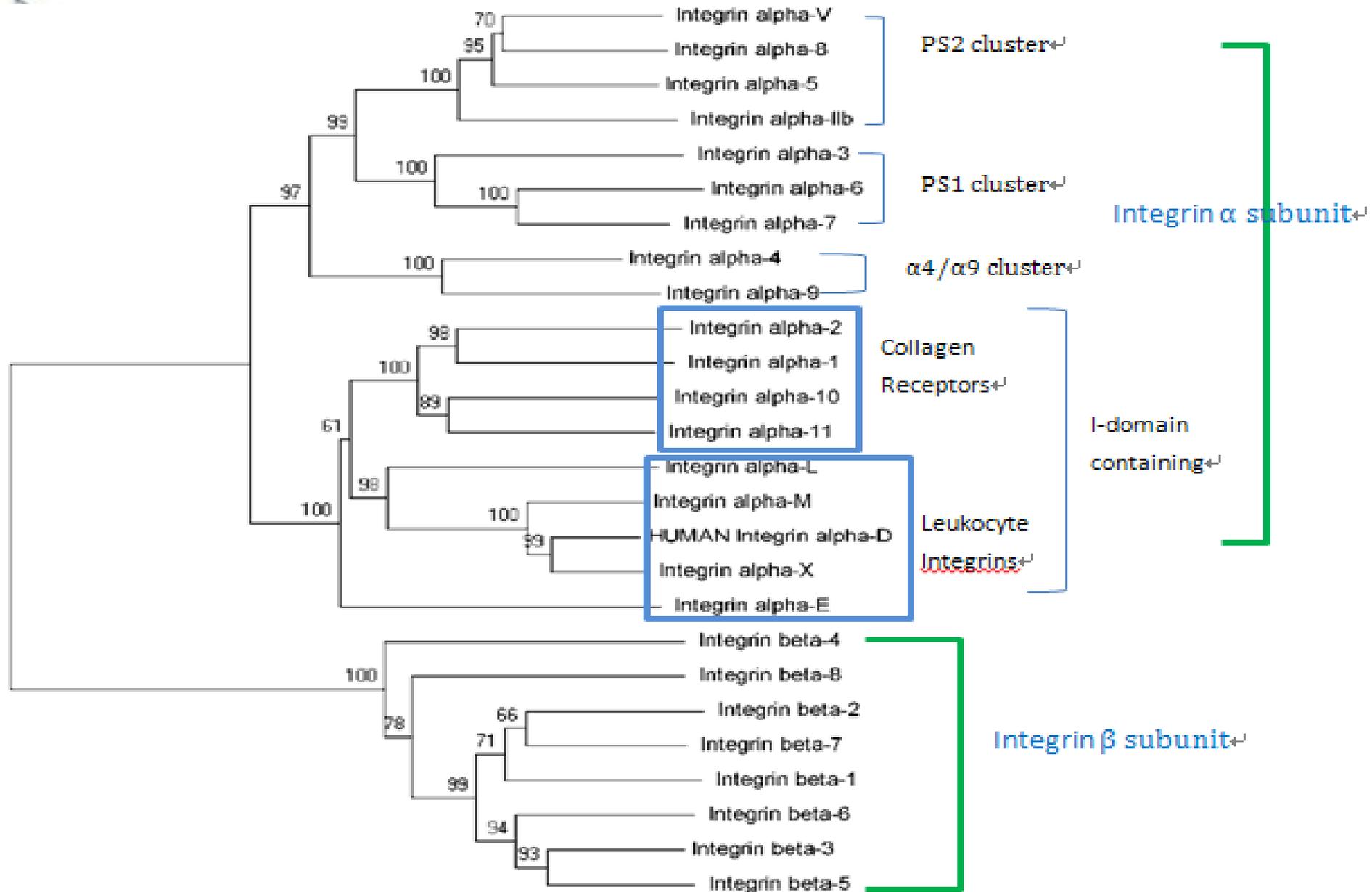
1. 口蹄疫病毒及其受体背景
2. 牛 α v家族整联蛋白的系统进化分析
3. 牛 α v家族整联蛋白的序列特征分析
4. 牛 α v家族整联蛋白的结构模拟
5. 结论与展望

口蹄疫病毒及其受体背景

口蹄疫病毒（FMDV）

- ▶ 小RNA病毒科(Picornaviridae)、口蹄疫病毒属(Aphthovirus) 成员，有A、O、C、SAT1、SAT2、SAT3以及Asia1型等7个血清型。
- ▶ 可导致牛、水牛、猪、绵羊、山羊和骆驼等20个科的70多种家养和野生偶蹄动物发病。
- ▶ 衣壳由VP1、VP2、VP3和VP4 4种结构蛋白各60分子组成，呈正二十面体立体结构。





人源整联蛋白家族系统发育分析

数据来源: [Uniprot](#); 建树方法: [Mega5](#), NJ tree, bootstrap=1000

Virus	Integrin receptor	Route	Kinase/ GTPase
Adenovirus	$\alpha v\beta 1$, $\alpha v\beta 3$, $\alpha v\beta 5$	Clathrin, microtubules	PI3K, CAS, PKA, p38/ Rab5, dynamin, Rac1, Cdc42
CoxsackievirusA9	$\alpha v\beta 3$, $\alpha v\beta 6$		
Echovirus	$\alpha v\beta 3$, $\alpha 2\beta 1$		/ dynamin
Foot and mouth disease virus	$\alpha v\beta 1$, $\alpha v\beta 3$, $\alpha v\beta 6$, $\alpha v\beta 8$	Clathrin	AKT deactivation, GSK3 dephosphorylation
Hantaan virus	$\alpha v\beta 3$, $\alpha II b\beta 3$		
Human parechovirus 1	$\alpha v\beta 3$		
Human immunodeficiency virus 1	$\alpha v\beta 3$		
Rotaviruses	$\alpha 2\beta 1$, $\alpha X\beta 2$, $\alpha v\beta 3$, $\alpha 4\beta 1$	Non-clathrin, non-caveolin	/ dynamin
KSHV/HHV-8	$\alpha 3\beta 1$, $\alpha 2\beta 1$	Clathrin microtubules	FAK, Src, PI3K, ERK, PKC ζ - MEK-ERK/ RhoA, Cdc42
Papillomavirus	$\alpha 6\beta 4$, $\alpha 6\beta 1$		
AAV-2	$\alpha v\beta 5(\alpha 5\beta 1)$		PI3K
Parechovirus 1	$\alpha v\beta 1$, $\alpha v\beta 3$		

牛 α v家族整联蛋白的系统进化分析

- ▶ Uniprot数据库中序列的提取
- ▶ ClustalW多序列比对
- ▶ Mega5系统发育分析

不同物种整联蛋白 αv 亚基序列信息

Entry name	Entry	Organisms	Length
ITAV_BOVIN	P80746	<u>Bos taurus</u> (Bovine)	1048
ITAV_HUMAN	P06756	Homo sapiens (Human)	1048
B0FY6_CAMBA	B0FY6	<u>Camelus bactrianus</u> (Bactrian camel)	1054
D2SYX8_CAMDR	D2SYX8	<u>Camelus dromedarius</u> (Dromedary) (Arabian camel)	1048
F6W3W7_HORSE	F6W3W7	<u>Equus caballus</u> (Horse)	1018
B0FY5_SHEEP	B0FY5	<u>Ovis aries</u> (Sheep)	1048
F7IJZ6_CALIA	F7IJZ6	<u>Callithrix jacchus</u> (White-tufted-ear marmoset)	1047
A2RQD8_PIG	A2RQD8	<u>Sus scrofa</u> (Pig)	1046
G3SU46_LOXAF	G3SU46	<u>Loxodonta africana</u> (African elephant)	1045
ITAV_MOUSE	P43406	<u>Mus musculus</u> (Mouse)	1044
F1LZX9_RAT	F1LZX9	<u>Rattus norvegicus</u> (Rat)	982
G3QQK9_GORGO	G3QQK9	Gorilla <u>gorilla gorilla</u> (Lowland gorilla)	1032
F6QSK2_MACMU	F6QSK2	<u>Macaca mulatta</u> (Rhesus macaque)	1048

不同物种整联蛋白 $\beta 1$ 亚基序列信息

Entry name	Entry	Organisms	Length
ITB1_BOVIN	P53712	<u>Bos taurus</u> (Bovine)	798
ITB1_HUMAN	P05556	Homo sapiens (Human)	798
G3QTG8_GORGO	G3QTG8	Gorilla <u>gorilla gorilla</u> (Lowland gorilla)	798
E2RT52_CANFA	E2RT52	<u>Canis familiaris</u> (Dog) (<u>Canis lupus familiaris</u>)	805
F6UR46_HORSE	F6UR46	<u>Equus caballus</u> (Horse)	799
ITB1_CAMBA	A5Z1X6	<u>Camelus bactrianus</u> (Bactrian camel)	798
ITB1_FELCA	P53713	<u>Felis catus</u> (Cat) (<u>Felis silvestris catus</u>)	798
ITB1_PIG	Q9GLP0	<u>Sus scrofa</u> (Pig)	798
ITB1_SHEEP	B0FYY4	<u>Ovis aries</u> (Sheep)	798
C7AR57_CAMDR	C7AR57	<u>Camelus dromedarius</u> (Dromedary) (Arabian camel)	798
F6W202_CALJA	F6W202	<u>Callithrix jacchus</u> (White-tufted-ear marmoset)	798
G1MG66_AILME	G1MG66	<u>Ailuropoda melanoleuca</u> (Giant panda)	798
G1SK33_RABIT	G1SK33	<u>Oryctolagus cuniculus</u> (Rabbit)	798
G3TK94_LOXAF	G3TK94	<u>Loxodonta africana</u> (African elephant)	798

不同物种整联蛋白 $\beta 3$ 亚基序列信息

Entry name	Entry	Organisms	Length
F1MTN1_BOVIN	F1MTN1	<u>Bos taurus</u> (Bovine)	784
ITB3_HUMAN	P05106	Homo sapiens (Human)	788
G1M853_AILME	G1M853	<u>Ailuropoda melanoleuca</u> (Giant panda)	790
F6QIM6_CALJA	F6QIM6	<u>Callithrix jacchus</u> (White-tufted-ear marmoset)	788
G3QXN4_GORGO	G3QXN4	Gorilla <u>gorilla gorilla</u> (Lowland gorilla)	788
Q9TUN3_RABIT	Q9TUN3	<u>Oryctolagus cuniculus</u> (Rabbit)	788
F1PPG5_CANFA	F1PPG5	<u>Canis familiaris</u> (Dog) (<u>Canis lupus familiaris</u>)	787
Q52MQ6_HORSE	Q52MQ6	<u>Equus caballus</u> (Horse)	784
Q95JH1_PIG	Q95JH1	<u>Sus scrofa</u> (Pig)	784
G3TCQ0_LOXAF	G3TCQ0	<u>Loxodonta africana</u> (African elephant)	778
B5APS2_CAMBA	B5APS2	<u>Camelus bactrianus</u> (Bactrian camel)	762
D6BRG0_SHEEP	D6BRG0	<u>Ovis aries</u> (Sheep)	762

不同物种整联蛋白 $\beta 6$ 亚基序列信息

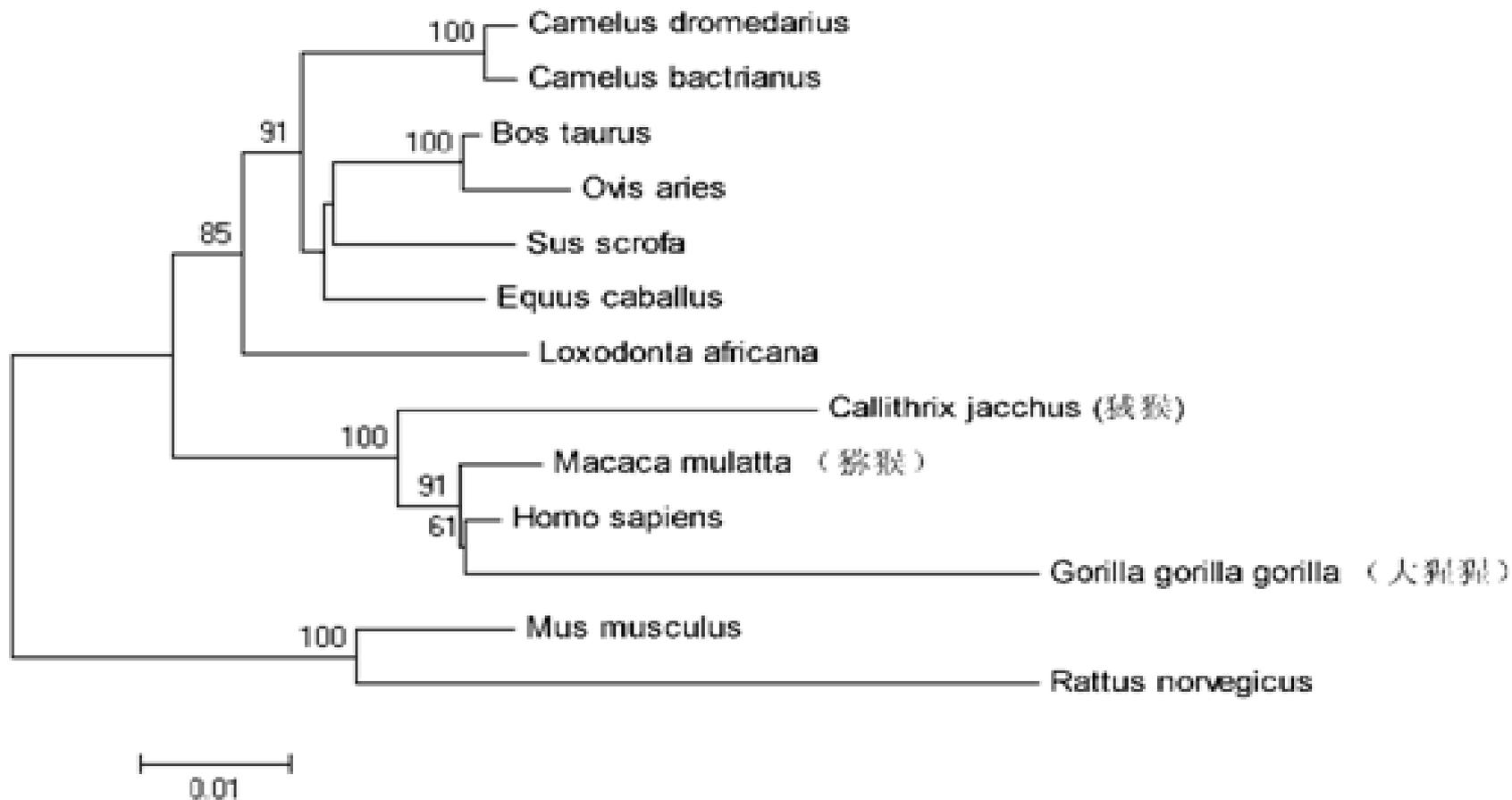
Entry name↕	Entry↕	Organisms↕	Length↕
ITB6_BOVIN↕	Q8SQB8 ↕	<u>Bos taurus</u> (Bovine)↕	788↕
ITB6_HUMAN↕	P18564 ↕	Homo sapiens (Human)↕	788↕
G1M1V6_AILME↕	G1M1V6 ↕	<u>Ailuropoda melanoleuca</u> (Giant panda)↕	788↕
E2RBL9_CANFA↕	E2RBL9 ↕	<u>Canis familiaris</u> (Dog) (<u>Canis lupus familiaris</u>)↕	788↕
ITB6_PIG↕	Q1RPR6 ↕	<u>Sus scrofa</u> (Pig)↕	788↕
A5Z1X7_CAMBA↕	A5Z1X7 ↕	<u>Camelus bactrianus</u> (Bactrian camel)↕	788↕
C9E0L7_CAMDR↕	C9E0L7 ↕	<u>Camelus dromedarius</u> (Dromedary) (Arabian camel)↕	788↕
ITB6_MOUSE↕	Q9Z0T9 ↕	<u>Mus musculus</u> (Mouse)↕	787↕
ITB6_RAT↕	Q6AYF4 ↕	<u>Rattus norvegicus</u> (Rat)↕	787↕
ITB6_SHEEP↕	Q863C4 ↕	<u>Ovis aries</u> (Sheep)↕	787↕
G1T891_RABIT↕	G1T891 ↕	<u>Oryctolagus cuniculus</u> (Rabbit)↕	786↕
F7B3K7_HORSE↕	F7B3K7 ↕	<u>Equus caballus</u> (Horse)↕	788↕
F7G573_CALJA↕	F7G573 ↕	<u>Callithrix jacchus</u> (White-tufted-ear marmoset)↕	788↕
G3R1W1_GORGO↕	G3R1W1 ↕	Gorilla <u>gorilla gorilla</u> (Lowland gorilla)↕	788↕
G3SPD2_LOXAF↕	G3SPD2 ↕	<u>Loxodonta africana</u> (African elephant)↕	788↕

不同物种整联蛋白 $\beta 8$ 亚基序列信息

Entry name	Entry	Organisms	Length
F1MVW3_BOVIN	F1MVW3	<u>Bos taurus (Bovine)</u>	767
ITB8_HUMAN	P26012	Homo sapiens (Human)	769
F7I2K0_CALJA	F7I2K0	<u>Callithrix jacchus (White-tufted-ear marmoset)</u>	635
A9X6R3_PIG	A9X6R3	<u>Sus scrofa (Pig)</u>	767
E2R641_CANFA	E2R641	<u>Canis familiaris (Dog) (Canis lupus familiaris)</u>	767
D3ZGZ3_RAT	D3ZGZ3	<u>Rattus norvegicus (Rat)</u>	767
Q0VBDO_MOUSE	Q0VBDO	<u>Mus musculus (Mouse)</u>	767
ITB8_RABIT	P26013	<u>Oryctolagus cuniculus (Rabbit)</u>	768

不同物种整联蛋白 αv 亚基序列一致性分析

序列	牛	羊	双峰驼	单峰驼	猪	人	猕猴	狨猴	非洲象	小鼠	大猩猩	马
牛												
羊	0.986											
双峰驼	0.956	0.955										
单峰驼	0.961	0.96	0.99									
猪	0.969	0.967	0.957	0.962								
人	0.958	0.947	0.941	0.946	0.949							
猕猴	0.956	0.944	0.938	0.943	0.946	0.991						
狨猴	0.935	0.926	0.92	0.925	0.929	0.963	0.963					
非洲象	0.947	0.946	0.941	0.946	0.951	0.94	0.939	0.92				
小鼠	0.923	0.919	0.913	0.918	0.919	0.919	0.915	0.9	0.921			
大猩猩	0.905	0.894	0.889	0.894	0.896	0.941	0.938	0.91	0.89	0.867		
马	0.948	0.94	0.935	0.94	0.95	0.929	0.925	0.91	0.934	0.904	0.877	
大鼠	0.846	0.842	0.84	0.845	0.843	0.846	0.841	0.83	0.852	0.889	0.815	0.869

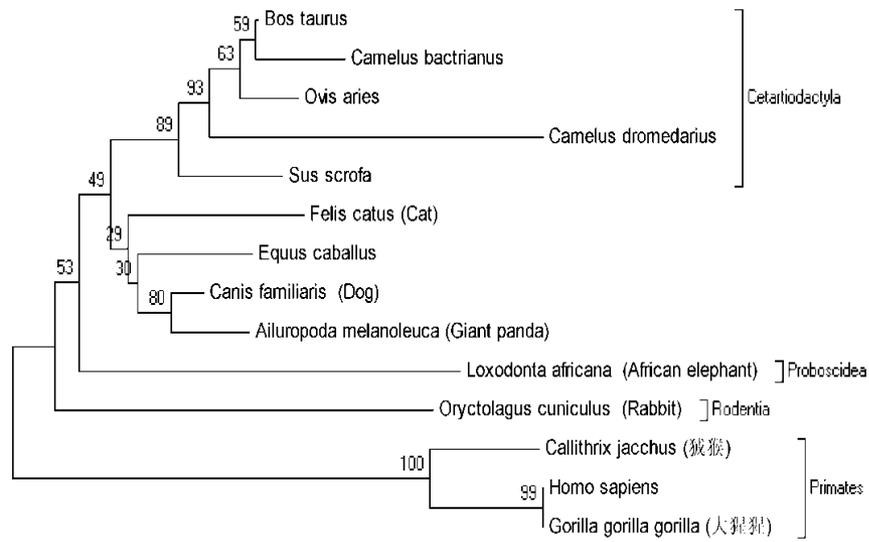


牛整联蛋白 $\alpha 2$ 亚基系统发育分析

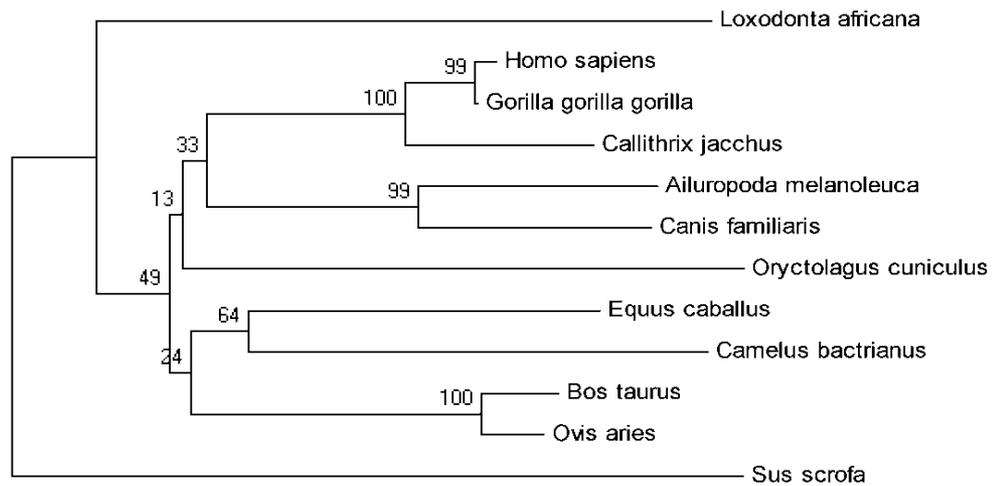
数据来源：Uniprot； 建树方法：Mega5， NJ tree， bootstrap=1000

不同物种整联蛋白 β 亚基序列一致性分析

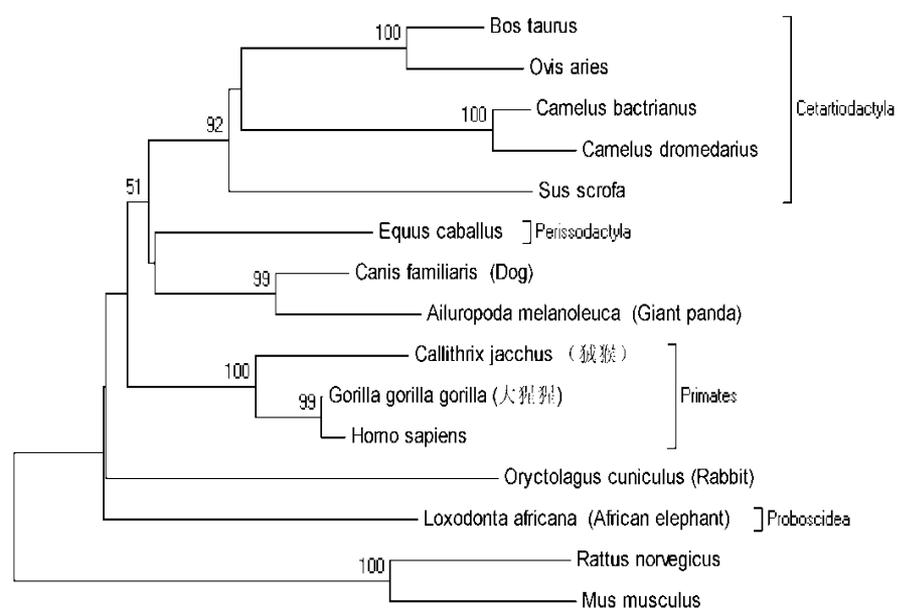
序列	$\beta 1$	$\beta 3$	$\beta 6$	$\beta 8$
双峰驼	0.993	0.923	0.944	-
羊	0.994	0.964	0.977	-
单峰驼	0.974	-	0.94	-
猪	0.987	0.934	0.94	0.947
人	0.947	0.947	0.934	0.911
狨猴	0.948	0.94	0.932	0.739
猩猩	0.947	0.946	0.936	-
犬	0.975	0.932	0.94	0.93
猫	0.979	-	-	-
大熊猫	0.981	0.924	0.934	-
兔	0.958	0.936	0.916	0.856
大鼠	-	-	0.895	0.858
小鼠	-	-	0.897	0.851
非洲象	0.961	0.932	0.923	-
马	0.977	0.955	0.942	-



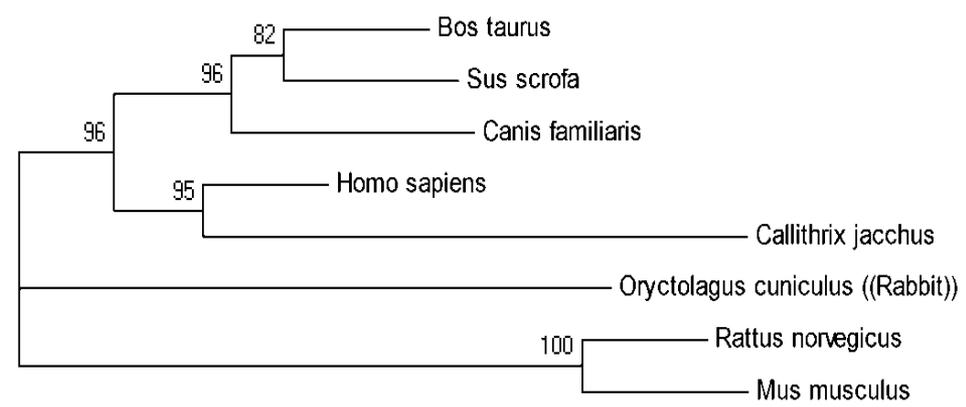
A



B



C



D

牛整联蛋白β亚基系统发育分析

A: β1; B: β3; C: β6; D: β8

数据来源: Uniprot; 建树方法: Mega5, NJ tree, bootstrap=1000

牛 α v家族整联蛋白的序列特征分析

▶ 跨膜分析

利用WebLab跨膜蛋白预测工具Tmap工具、TMHMM、SOSUI、Expasy ProtScale里面Hphob. / Kyte & Doolittle方法、MEMSAT3

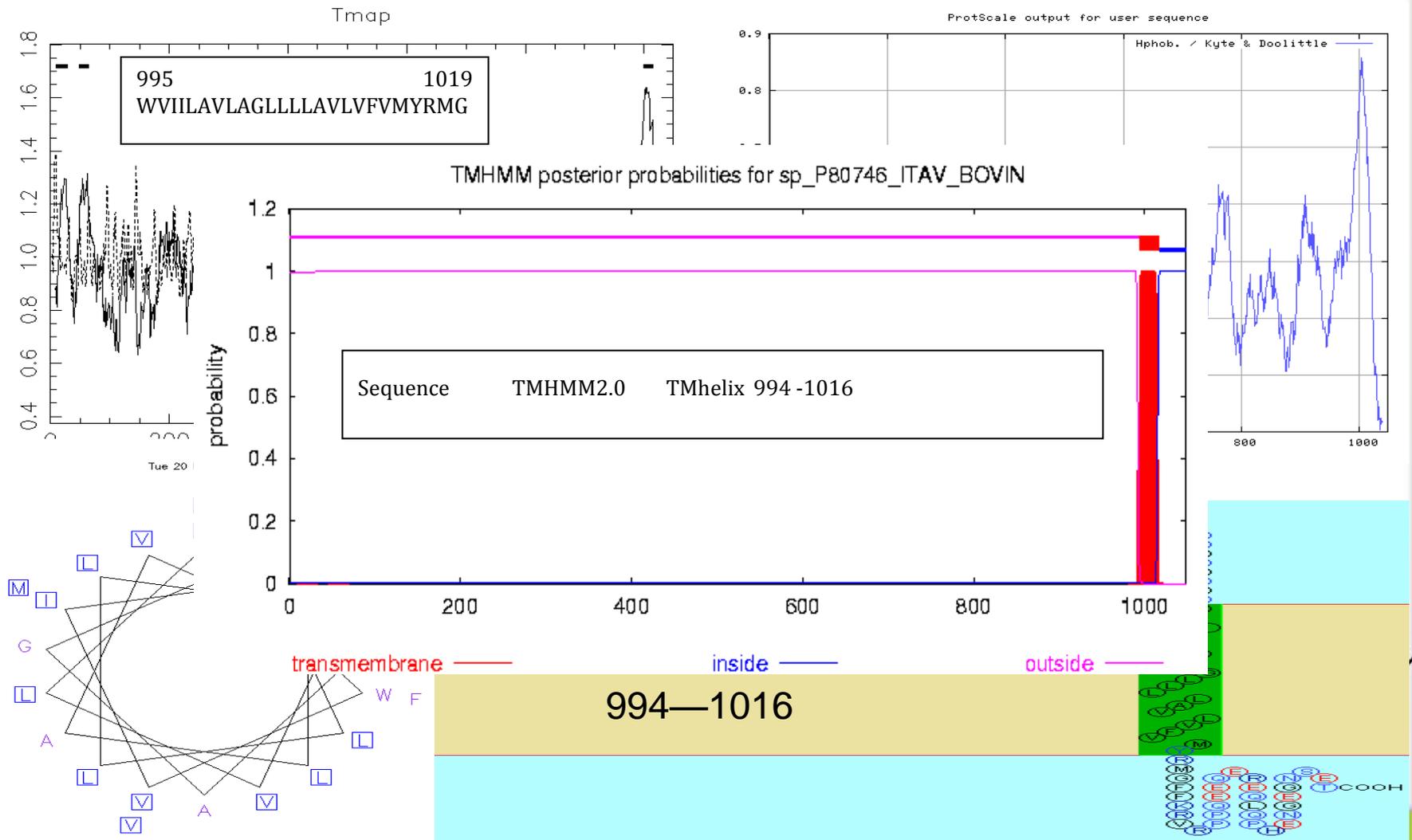
▶ 信号肽分析

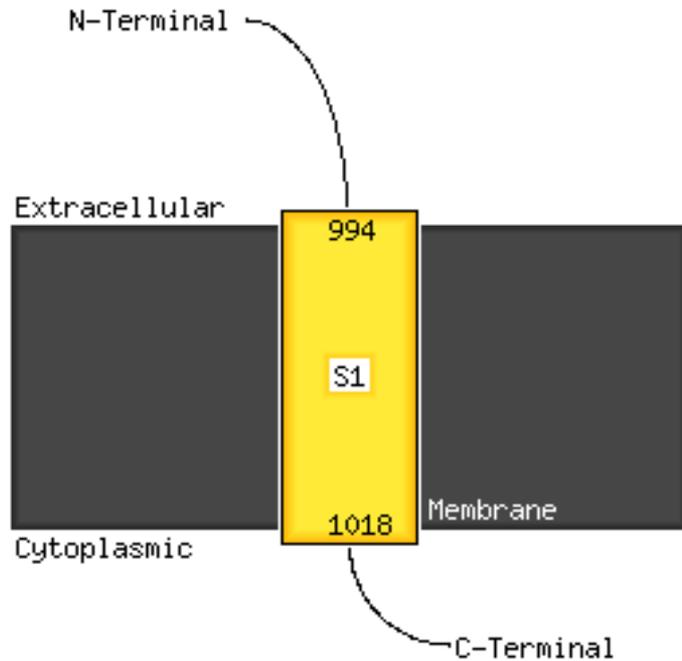
SOSUISignal、SignalP 4.0

▶ 蛋白结构域、功能位点

PROSITE

α v亚基的分析

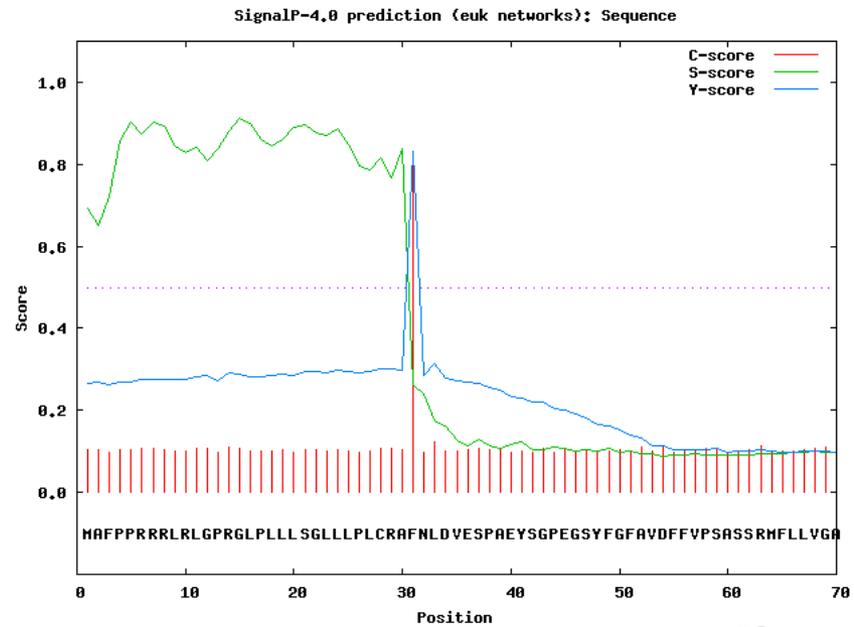




MEMSAT3 result

No.	N terminal	transmembrane region ^o	C terminal	type ^o	length
0 ^o	1 ^o	MAFP RRRLRLGPRGLPLLLSGLLLPLCRAFNLD	34 ^o	SignalPeptide (Secondary)	34 ^o
1 ^o	994 ^o	VWVILAVLAGLLLLAVLVFVMY ^o	1016 ^o	Primary	23 ^o

SOSUisignal result

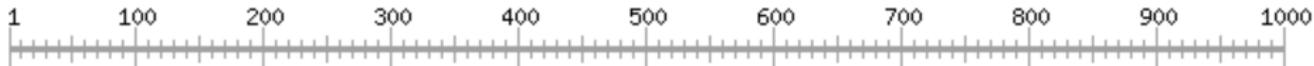


结果

▶ 牛 α v家族整联蛋白各亚基组成

序列	α v	β 1	β 3	β 6	β 8
信号肽	1-30	1-20	1-22	1 - 21	1-21
胞外区	31 - 992	21 - 728	23-714	22 - 709	22-679
跨膜区	993 - 1016	729 - 749	715—737	710 - 730	680-702
胞内区	1017 - 1048	750 - 798	738-784	731 - 788	703-767

ruler:



hits by profiles: [7 hits (by 1 profile) on 1 sequence]

Hits by PS51470 FG_GAP FG-GAP repeat profile :

USERSEQ1



(1048

FG-GAP repeat of α subunit

VYNAIPIIMGSSV	GALLLLALITATLYK	GFFKRYKEMLEDKPEDTATFSGDDFSCVAPNVPLS-----	1161	Q13349	ITAD_HUMAN
VHNP TPLIVGSS	IGL LLLALITAVLYK	VGFFKROYKEMMEEANGQIAPENG TQTP SPPSEK-----	1163	P20702	ITAX_HUMAN
VPNPLPLIVGSS	VGGL LLLALITAALYK	LGFFKROYKDMSEGGPPGAEPQ-----	1152	P11215	ITAM_HUMAN
AEVPTGVIIIGSI	IAG I L L L L A L V A I L W K	LGFFKRYEKMTKNPDEIDETTELSS-----	1181	P17301	ITA2_HUMAN
SRVPLWVILL	SAFAG L L L L M L L I L A L W K	IGFFKRLK K K M E K-----	1179	P56199	ITA1_HUMAN
ILISLWILIGSV	LGGL L L L A L L V F C L W K	LGFFAHKK IPEEEKREEKLEQ-----	1167	O75578	ITA10_HUMAN
#QVPIWIIIVGST	LGGL L L L A L L V L A L W K	LGFFRSARRRREPGLDPTPKVLE-----	1188	Q9UKX5	ITA11_HUMAN
MPVPVWVILAV	LAG L L L L A V L V F V M Y R	MGFFKRYRPPQEEQ-EREQLQPHENGE GNSET-----	1048	P06756	ITAV_HUMAN
MPVPVWVILAV	LAG L L L L A V L V F V M Y R	MGFFKRYRPPQEEQ-EREQLQPHENGE GNSET-----	1048	P80746	ITAV_BOVIN
?SIPLWVILAI	LLGL L V L A I L T L A L W K	CGFFDRARPPQEDMTDREQL TNDK TPEA-----	1063	P53708	ITA8_HUMAN
YGVPLWIIILAI	LFGL L L L G L L I Y I L Y K	LGFFKRLPYGTAM-EKAQLKPPATSDA-----	1049	P08648	ITA5_HUMAN
-AIP I W V L V G V	LGGL L L L T I L V L A M W K	VGFFKRYRPPLEEDDEEGE-----	1039	P08514	ITA2B_HUMAN
SGVPWVWIIILVAI	LAG I L M L A L L V F I L W K	CGFFKRYRY-DSVPRYHAVRIRKEEREIKDEKYIDNLEKKQWI	1120	P23229	ITA6_HUMAN
EGVPWVVILLAV	LAG L L V L A L L V L L L W K	MGFFKRAKHPEATVPQYHAVK IPREDRQQFKEEKTGTILRNNWG	1149	Q13683	ITA7_HUMAN
-YFTIWIISSSL	LLGL I V L L L I S Y V M W K	AGFFKROYKSILQEENRR----DSWSYINSKSNDD-----	1032	P13612	ITA4_HUMAN
-YVVGWIIAISL	LVG I L I F L L L A V L L W K	MGFFRRYKEIEAEKNRKENEDSWDWWQKNQ-----	1035	Q13797	ITA9_HUMAN
AEIELWLVLVA	VGAG L L L L G L I I L L L W K	CGFFKRYRTRALYEAQRQAEMK SQPSETERL TDDY-----	1051	P26006	ITA3_HUMAN
EKQMLYLYVLSG	IGL L L L L L I F I V L Y K	VGFFKRYLKEKMEAGRGVPNG IPAEDSEQLASGQEAGDPGLCP	1157	P20701	ITAL_HUMAN
KYHSLPIIIKGS	VGGL L V L I V I L V I L F K	CGFFKRYQQLNLESIRKAQLKSENLL EEN-----	1179	P38570	ITAE_HUMAN

牛 α v家族整联蛋白的结构预测

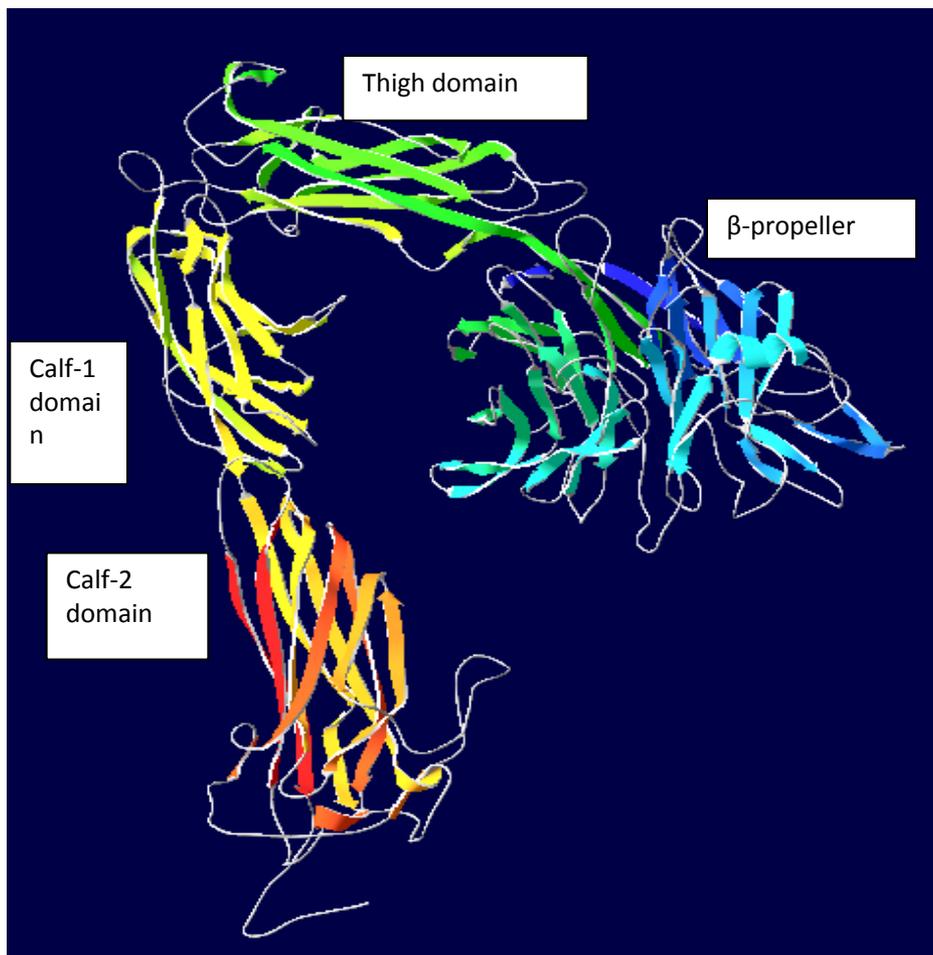
- ▶ 利用Swissmodel同源建模的方法对牛整联蛋白 α v、 β 3亚基进行了结构预测。
- ▶ 模板[3ijeA]、 [3ijeB]

Model information:

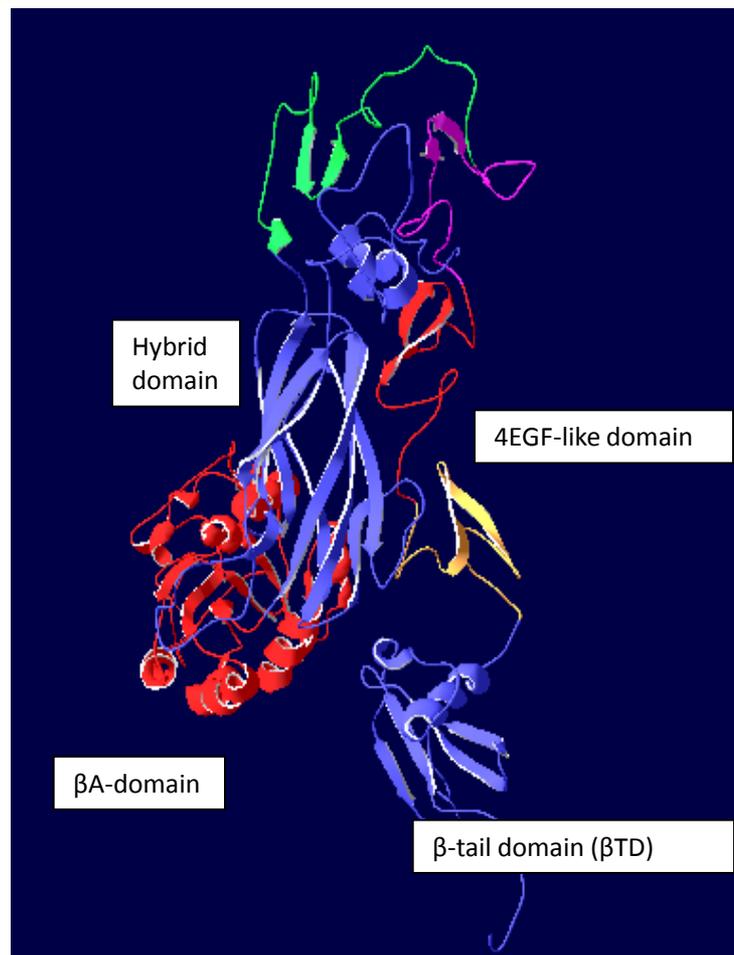
Modelled residue range: 31 to 997
Based on template: [3ijeA]* (2.90 Å)
Sequence Identity [%]: 93.18
Evaluate: 0.00e-1

Model information:

Modelled residue range: 23 to 717
Based on template: [3ijeB]* (2.90 Å)
Sequence Identity [%]: 95.68
Evaluate: 0.00e-1

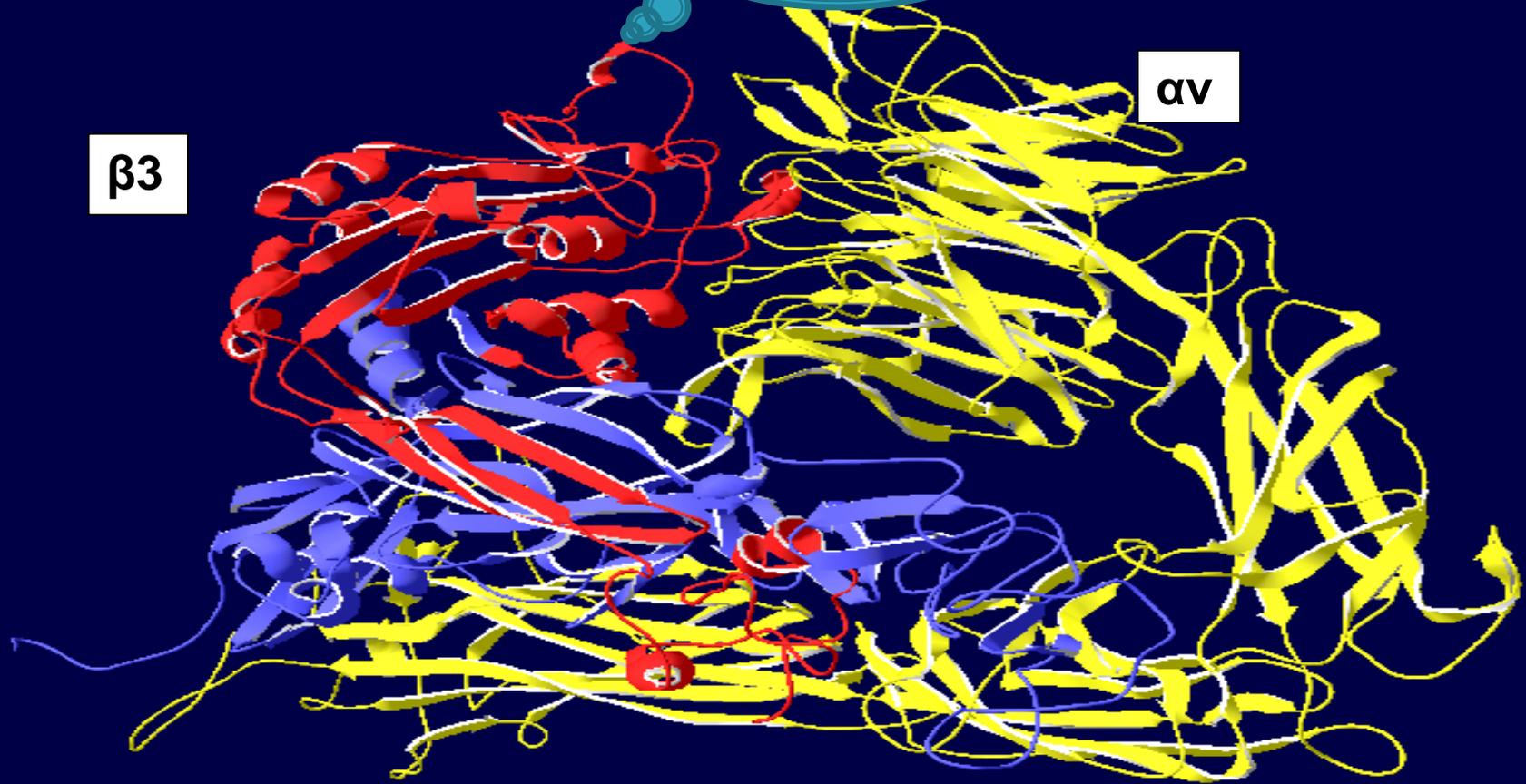


牛整合蛋白 α V亚基的结构



牛整合蛋白 β 3亚基的结构

β -propeller与 β A-domain形成配体结合区



牛整联蛋白 $\alpha v \beta 3$

结论与展望

- ▶ 牛FMDV受体整联蛋白各亚基均与偶蹄家畜羊、猪等相应亚基氨基酸序列呈现较高的一致性，可能是决定FMDV宿主嗜性的重要因素。
- ▶ 整联主要通过信号转导来发挥其蛋白功能，是否出现于FMDV感染过程中，还需证实。



请罗老师和各位同学
批评指正

聖誕快樂 新年進步

Merry Christmas & Happy New Year