

对人癌胚抗原相关蛋白质的生物信息学工具分析

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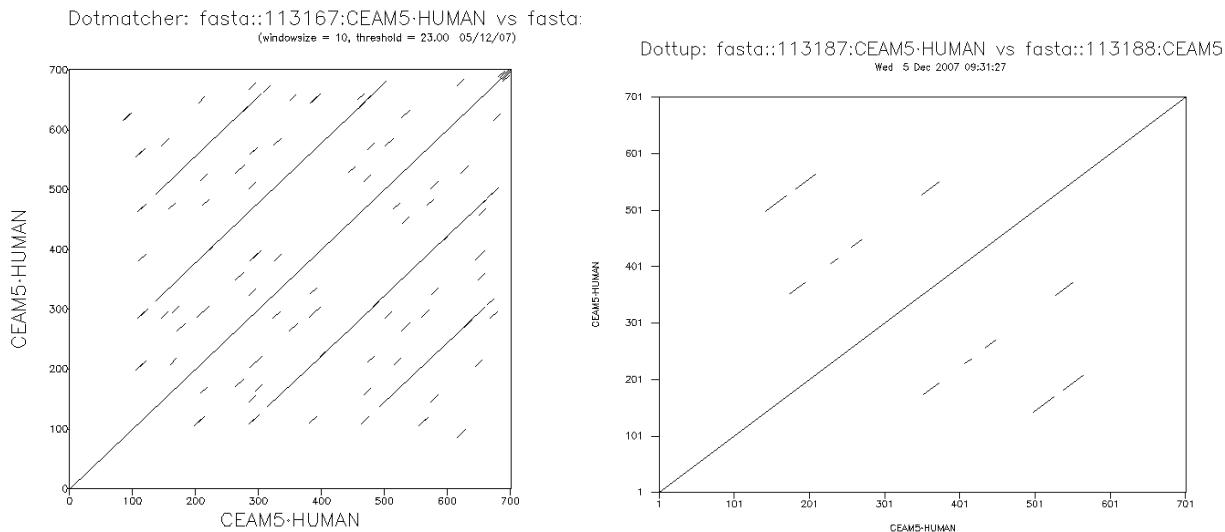
人癌胚抗原是一种富含多糖的蛋白复合物，主要存在于直、结肠癌组织和胎儿肠粘膜内，属性为膜表面蛋白质。在个体发育过程中，人癌胚抗原蛋白只在胎儿时期大量表达，随着发育过程的不断深入，许多人癌胚抗原的表达明显减少甚至停滞表达。成年细胞发生癌变后会出现去分化现象，导致原先被关闭表达的人癌胚抗原再次活跃起来，重新达到胎儿时期的表达状态。基于其生理功能的重要性，研究人癌胚抗原应该具有很强烈的现实意义。

分析之一：人癌胚抗原相关蛋白质的序列搜索与比对

通过 ExPASy 搜索获得 17 条与关键词“carcinoembryonic antigen”相关的蛋白质序列，分别是：CEA16_HUMAN (Q2WEN9)、CEA19_HUMAN (Q7Z692)、CEA20_HUMAN (Q6UY09)、CEA21_HUMAN (Q3KPI0)、CEAB_RAT (Q10753)、CEAM1_HUMAN (P13688)、CEAM1_MOUSE (P31809)、CEAM1_RAT (P16573)、CEAM2_MOUSE (Q925P2)、CEAM3_HUMAN (P40198)、CEAM3_RAT (Q63111)、CEAM5_HUMAN (P06731)、CEAM6_HUMAN (P40199)、CEAM7_HUMAN (Q14002)、CEAM8_HUMAN (P31997)、CEAMA_MOUSE (Q61400) 和 PSG3_HUMAN (Q16557)。其中 CEAB_RAT (Q10753) 只有部分序列，CEAM5_HUMAN (P06731) 为当前研究较为深入的蛋白质。

蛋白质序列比对的信息如下：

(1) CEAM5_HUMAN 自身序列的 Dotmatcher 和 Dottup 比对

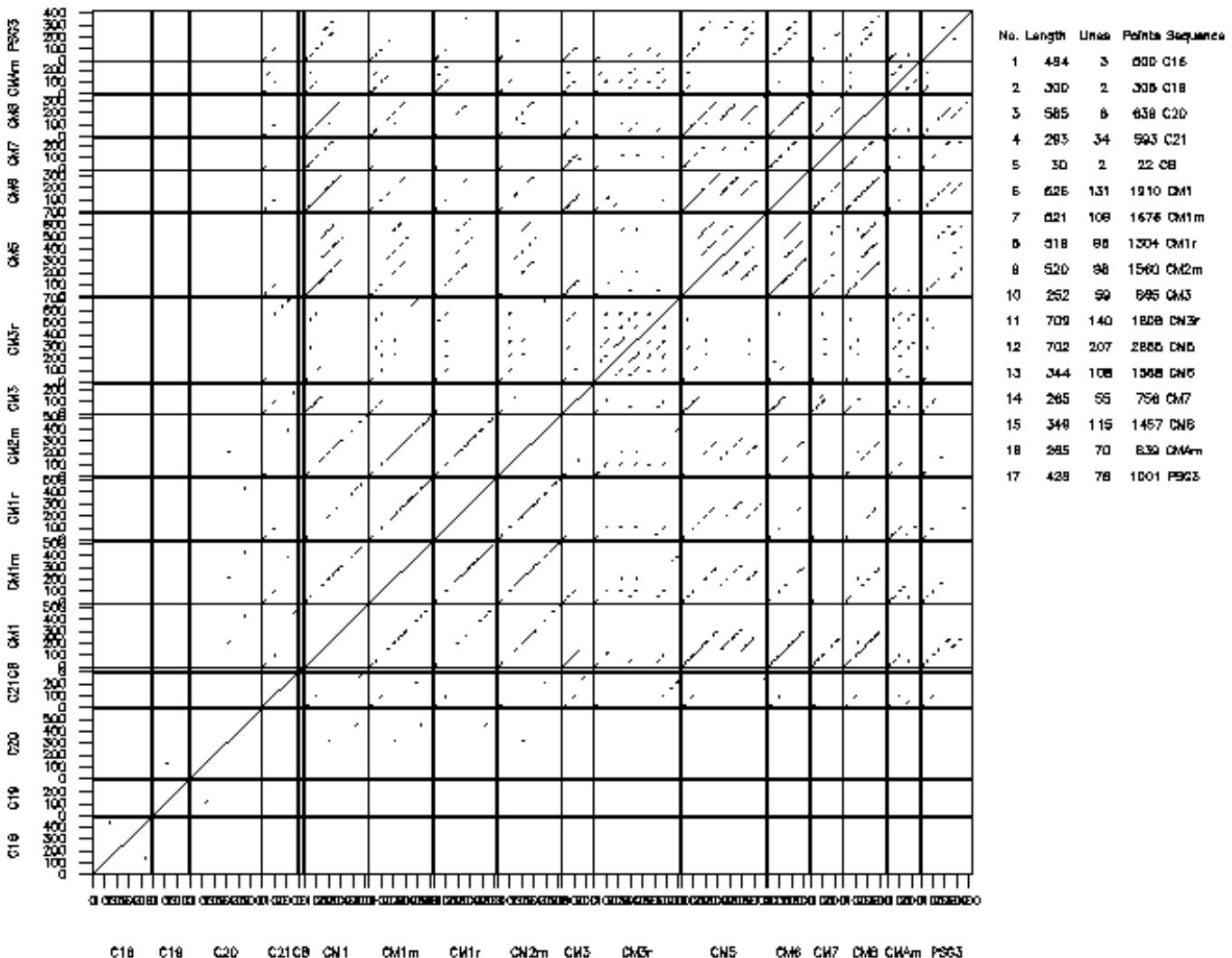


可以看出：CEAM5_HUMAN 自身序列内部存在不同程度的序列重复，这些重复序列与后面将要研究的免疫球蛋白结构域又有如何的关联呢？需要接下来的进一步工具分析。

(2) 17 条蛋白质信息的 Poly dotplot 比对:

Poly dotplot of 113178

Wed 5 Dec 2007 09:25:56



可以看出: CEA16_HUMAN (Q2WEN9)、CEA19_HUMAN (Q7Z692) 和 CEA20_HUMAN (Q6UY09)、三个序列之间以及与其它 14 个序列之间的序列差异很大, Poly dotplot 比对结果中几乎找不到重叠片段。发现序列 CEAM3_RAT 自身比对结果中有众多杂点区, 显示出该序列存在许多小片段的重复。还发现序列 CEAM5_HUMAN 与 CEAM1_HUMAN、CEAM6_HUMAN、CEAM8_HUMAN 三个序列间存在较大片段的重复。为了看一看它们相互之间的详细序列位点差异, 我们有必要进行以下初步蛋白质信息分析和 Clustalw 全序列信息比对分析。

(3) Showalign 和 emma 分析 17 条蛋白质信息:

10 20 30 40 50 60

Consensus MxxxxSxxHRxxVPWGQILLTASLLTFWNPPPTAQVTIEAxP*xNVAEGKxVLLLLVHNLPQ
 CEA16_HUMAN SDILsIVSAPV_VSTV_HmLOIRKLRLGRVHKLPRV1_VGNSGTMRSAYTFFF1RWSF
 CEA19_HUMAN EIFMGTQGFSKSILLSASILV_WMLQGQASALY1QK1PEOPOKNDL1SvQGVEDTF
 CEA20_HUMAN GPADsWG HWMGILLAS_CTVWSPPAAAQL_INANFLDATQSEDVVL_P.FGTPRTPQI
 CEA21_HUMAN GPP CP ECI A WIF_A A FE . eN H S VY . e
 CEAB_RAT PPEALNVQIYVEVXXXTNDKGEadXPGEIQ .
 CEA1_HUMAN GSP CP V
 CEA1_MOUSE ELA_HL_kGO_G
 CEA1_RAT ELA_RLL_kGOi_r
 CEA2_MOUSE ELA_HL_kGO_F
 CEA3_HUMAN GFP SP ECI
 CEA3_RAT ELS_VLPCKRCT_r
 CEA5_HUMAN GSP CP V
 CEA6_HUMAN GSP_EPC_LH_kEV
 CEA7_HUMAN GSP CPV
 CEA8_HUMAN GPI_PSC_WRI
 CEA9_MOUSE ELA_HL_kGO_V
 PSG3_HUMAN GPL_PPCTQRIT_k
 Consensus MxxxxSxxHRxxVPWGQILLTASLLTFWNPPPTAQVTIEAxP*xNVAEGKxVLLLLVHNLPQ

70 80 90 100 110 120

Consensus NLxxYSWYKGxxxxNxIxIVxYVxxxxQxxxxGxAYSGRETIYxNxSLLIQNVTOxDTGxY
 CEA16_HUMAN A_TG . LILSATL_VGAESI1TEPAQPSQEGDNVTLVWHGLsGE . AYSWYAGP_ISW
 CEA19_HUMAN QDFNwylGe . TTYGGTRLF_PQDQRPMSMGQDINGVGI_G_m_1rRAQfS= .
 CEA20_HUMAN hGROSRELAF_PCAVSGTAIEQKDwDwVwPCTKDwHITHWWS_NLSiPHERMOLsKDG
 CEA21_HUMAN Y.S.G . K1VEP_CIL_AA
 CEAB_RAT SPsGD_HF . LE . Y

CEAM1_HUMAN Q_FG . . ERVDG_RQ_G_AIGTO_ATP_P_N . . P_A . N_F
 CEA1_MOUSE A_Gafa . NTTAIDKE_ARF_PNSNNMF_Q . . V_SG . F_Mi_MK_M_V
 CEA1_RAT EFQVfY_VTTGTL_SE_AR_IRESNTSQTE
 CEA2_MOUSE Gvaf_f_h
 CEA3_HUMAN h_FG . . ERVDG_SI_G_IGTO_ATP_A . . I_S . R_MK_N_E_F
 CEA3_RAT I_AfV . . LTNMSLGLVALYS1TNYNTVITGPVHSGRETLVsNGSLW1QNVTOkDTGFYt
 CEA5_HUMAN h_FG . . ERVDG_RQ_IG_IGTO_ATP_P . . I_P_A . IIN_F
 CEA6_HUMAN RIG . . ERVDG_SI_G_IGTO_ATP_P . . P_A . N_F
 CEA7_HUMAN YG_n . . ERVHD_YR_IG_KNIS_EHAAPGPAHNGRETIYWPNGT . . IIONVTHnDAGf
 CEA8_HUMAN dPRA
 CEA9_MOUSE T_Avf . . NSGA_Ahne_GRF_TS1NPKM_Lh . . P_A . mr
 PSG3_HUMAN AG_I . . OMKDLYHRY_TS_VDGQIIIV_P . . V_S_A . xE_A_S
 Consensus NLxxYSWYKGxxxxNxIxIVxYVxxxxQxxxxGxAYSGRETIYxNxSLLIQNVTOxDTGxY

130 140 150 160 170 180

Consensus TLxViNxExTxQFvVYxLxKxxxSSNNSNxVxxxxVaxTxExxxxxx
 CEA16_HUMAN SYL_ASIVGSTGd_EFGPAHTGREAERPDCG_LdIQGILFRHSGTYILqTFNRQLOTEVGY
 CEA19_HUMAN QvAiTINsEWMTMKAKtEvQ_AEKNKELPStHLPt_AGILAAT1IGsLAAGALLISCIAYL
 CEA20_HUMAN KILT_LIVQREDTl_VCEARDA_ISQRSDPfIFld_VKYGPD_EIKL_SGVASGEVVEM
 CEA21_HUMAN Q_TYR_SQ1eqAsHHLR_EsvAqPSIqasstTVTEKGSV_LTCInNNTGTSFQWIFN
 CEAB_RAT
 CEA1_HUMAN Q_KSDLVNE_A_G_H . P_E_P_SI . . P_EDKA_F_C_PETQDTTLWWI
 CEA1_MOUSE DmTDE_XRRTqA_Vr_H_hPI_L_PnIt . . P_EGDDs_sL_CdSYTDPDNINYL
 CEA1_RAT S_DKQFNPIqT_v_R_PA_Q_PnVtG . . P_mEGEPF_sLMC_PYTNNNTSYLWSR
 CEA2_MOUSE iEmTDQ_YRRRVl_G . . hKl_L_SNI_t . . P_EGDDs_sL_CdSYTDPDNITYL
 CEA3_HUMAN Q_KSDLVNE_A_G_H . . QENAPGLPVGAvgI_TGVLVGVAlVALVCELLAKTG
 CEA3_RAT LRTiSNHGElVNTsLHLH . . FSTLTCGraatTsaoLsIESWPtisKGEsAllLahnLpe
 CEA5_HUMAN
 CEA6_HUMAN H_KSDLVNE_A_G_H . . P_E_P_SI . . K_P_E . P_C_PETQDTTLWW
 CEA7_HUMAN YTLhvIKENLVN_EVTRQFYVFSSEPPPKPSits . . NPVNPEVKNDiVVLTCOPETONTTLYWW
 CEA8_HUMAN Q_KL_1MSE_V_G_S_hPETP_PSI . . P_EDKA_F_C_PETQNTTLYWW
 CEA9_MOUSE YmlDQ_EEITPAiVr_H_hPS_LPSLSPPTTGTQVTEAVPPNVAEGENVILLVHNLP
 PSG3_HUMAN . . HivKRGDGTRGE_GH_TETLY_ETPKP_Iss . . LYFREDME_VsLTCDPETPDASYLW
 Consensus TLxViNxExTxQFvVYxLxKxxxSSNNSNxVxxxxVaxTxExxxxxx

190 200 210 220 230 240

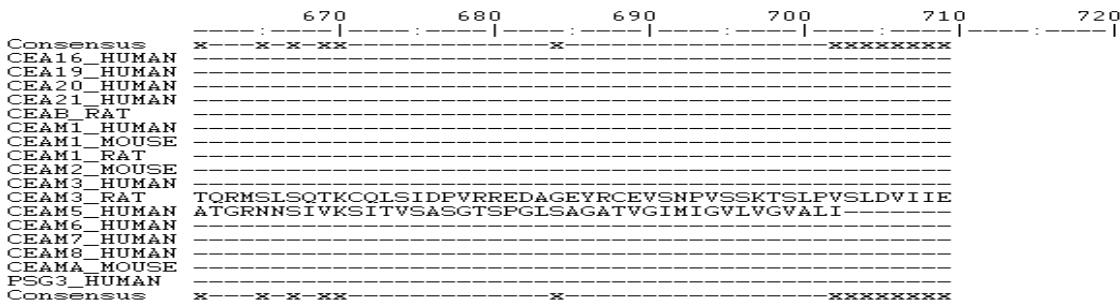
Consensus NxXXMxxxxxQlxNxNxTxLxxSxxxxxxNxSxxxxxVxxxxx
 CEA16_HUMAN GHVQVHEILQPTVIA_STALVERRDTLRLMCSSPSTAEVRUFFGCGALPVAlRIGLIS
 CEA19_HUMAN LVTNWRQGOSHr_PAFPGQGS_SILCSAVSPVSPVTPSTWMATTEKPELGPFAHDAGDNN
 CEA20_HUMAN EGSS_TFLATksSHPPCATWFLID . . ILSHTTRTETfIHAvSREhEGLYRCIVSNSATHL
 CEA21_HUMAN ORLQVTKRMKISWFN_hMLTIDPIQEDAGEyQCEVSNPVSNSRSDLKLTVKSDDNTLG
 CEAB_RAT
 CEA1_HUMAN NQS1PVSPRL_SNG_RTL . . LSvTRNDTGPYCECI_NPVWSA_R_DPVTLN_TYGPDTF
 CEA1_MOUSE SRNGESISEGDr_KLSEGMR . . TLLnVTRNDTGPVCeTRNPVsVn_RSDFPFs1N1YyGPD
 CEA1_RAT GES1SEGDRVPLSEG_RTI . . LNVRRTDKGYYCEArNPFAT_R_DPFNLD_IYGPDAF
 CEA2_MOUSE SRNGESISEGDr_KLSEGMR . . TLLnVTRNDTGPVCeTRNPVsVn_RSDFPFs1N1YyGPD
 CEA3_HUMAN RFLQDKEK_PALAKRGPPhs_APMSPMSQAE_PPNPRTsIYVEE1LKHDMNT
 CEA3_RAT LRA_FWYKGAI_vFKDLEVARYVIGt_NSSVPGPAHSGRETMYS_G_LLONVTRNDAGFy
 CEA5_HUMAN NQS1PVSPRL_SNG_RTI . . FNTvTRNDTASVYKCT_NPVWSA_R_DSVLN_LYGPDAF
 CEA6_HUMAN GQS1PVSPRL_SNG_MTL . . LSvKRNDAGSYCECI_NPASA_R_DPVTLN_LYGPDAF
 CEA7_HUMAN VNNQSLIVSPRI_IStDnRNLvLISsTaTKNDIgPYCEIOnPvVGASRSDPVTlNvRYESVQ
 CEA8_HUMAN GQS1PVSPRL_SNG_RTI . . LSvTRNDVGPYCECI_NPASA_F_DPVTLN_LYGPDAF
 PSG3_HUMAN TLRaiWYWRGTTAGER_EiARFiTA_NKiiLGPAsDriEiIYn_G_LFFQGVTKNDEGAY
 WMMNGQSLPMTHs_QLSKRNk_LFLGVTKYTAGPYEcIeIRNPVsA_RSDPVT1nLLPKL
 Consensus NxXXMxxxxxQlxNxNxTxLxxSxxxxxxNxSxxxxxVxxxxx

250 260 270 280 290 300

Consensus
 CEA16_HUMAN DGRVLARHGIRREAGAQCE_WNPVSVSRSEPInLTVYFGPERVAlLQDStTRTGCTIK
 CEA19_HUMAN DGRVMPSPVLIvSPFISdTRsNPrAFLPTPPFLHQAEPEHQNQYQD11NPDPAPyCQLVPTS
 CEA20_HUMAN S1GTLKVRVLET1LMPQVVPSSLNLVENARSvDLTCQVtNQsVNVQWFLSGOpLLPSeH
 CEA21_HUMAN 1IGVLVGSLLVAALvCFLNRLKTGRASDQSDfREQQFPAStTGPFGPSDSSIS
 CEAB_RAT
 CEA1_HUMAN T_SPSDTYYRPGANLsLSCYAA_NPPAQoWSWLNGTFOQSTQELF_PNITVNNNSGSYTC
 CEA1_MOUSE TPIISPSD1vLHPGs_LNLSChAA_NPPAQoFWLINEKPHASSQELF_PNITVNNNSGSYTC
 CEA1_RAT W_SPPDIvLHPGs_LNLSChAA_NPPAQoFWLINEKPHASSQELF_PNITVNNNSGSYTC
 CEA2_MOUSE TPIISPSD1vLHPGs_LNLSChAA_NPPAQoFWLINEKPHASSQELF_PNITVNNNSGSYTC
 CEA3_HUMAN TCRMDMhKAbVAS
 CEA3_RAT T_KT1LSTDkTIEIAVQVQDTCFMSYAGPPTsAQLTVEsAPSvAEGASVLLVHNLP
 CEA5_HUMAN T_SPLNTSYRSGEnLISChAA_NPPAQoWSVNGTFOQSTQELF_PNITVNNNSGSYTC
 CEA6_HUMAN T_SPSKANYRPGEnLISChAA_NPPAQoWSVINGTFOQSTQELF_PNITVNNNSGSYMC
 CEA7_HUMAN ASSPDILsAGTAVSIMIGVLAGMali
 CEA8_HUMAN T_SPSDTVYHAGVNL_ISChAA_NPPSQSYWSVNGTFOQYtQKLF_PNITTKNSGSYACH
 CEA9_MOUSE A1DMLFQNEdHTLMPQFnWHAkQ
 PSG3_HUMAN KPYITINNlNPRENkDvLAFTCEPKSENyTyIWWLNGQSLPVSPRvKRPIENRILILPSV
 Consensus

310 320 330 340 350 360

Consensus
 CEA16_HUMAN xxxSxxxxxxVDFnTSILTlCVsRsCPEPEVYWTfNGQALKNGQDHlnISSMTAAQEGTYTCIAKNTKTL
 CEA19_HUMAN
 CEA20_HUMAN QLSaDNRTLIIHGLQRNDTGPYACEVWNWGSRARSEPLELTINYGPQVHITRESASEMI
 CEA21_HUMAN
 CEAB_RAT
 CEA1_HUMAN ANN_VTGCNRTTVKTIIVTELSPVVAkPQIKASKTTVTGDKDSvNLTCSTNDTGisIRWF
 CEA1_MOUSE CFVnNSVTGLsRTTVKNIITVLEPVTQFLOVNTTTVKELDSvTlTCLsNDIGANIQWLFn
 CEA1_RAT
 CEA2_MOUSE VNNtVTGIsRTTVKNIITVFEPTQPSQI1NTTtVKElGSvTlTcfsKDTGvsvRwlFn
 CEA3_HUMAN CLVnNSVTGLsRTTVKNIITVLEPVTQPSQI1NTTtVKElGSvTlTcfsKDTGvsvRwlFn
 CEA3_RAT NLRaIFWYKGVLFKDLEVARYVIGtNssVlGPAHSGRETMysSngslllQnVtrndagfY
 CEA5_HUMAN AHN_DTGLNRTTVTTITVVAEPKKPFITSNNNSNPVEdEADAVALTCEPEIQtNTTLYWW
 CEA6_HUMAN AHN_ATGLNRTTVTMITVSGSAPlvSAVATVGITGVLARVALI
 CEA7_HUMAN TTN_ATGRNRTTVRMITVSDALVQGSSPGlsARATVSiMIGVLARVALI
 CEA8_HUMAN TRNETGPYQCEIqdRYGGIRSYFPTLNVlyGPdLPRIyFpsFTyyHsgenlvLscfadsnp
 PSG3_HUMAN
 Consensus



Name	SeqLen	AlignLen	Gaps	GapLen	Ident	Similar	Differ	% Change	Weight	Description
CEAM1_MOUSE	CEAM1_MOUSE	521	545	7	24	159	26	336	70.825691	1.000000
CEAM2_MOUSE	CEAM2_MOUSE	520	545	7	25	155	32	333	71.559631	1.000000
CEAM1_RAT	CEAM1_RAT	519	545	8	26	154	24	341	71.743118	1.000000
CEAM5_HUMAN	CEAM5_HUMAN	702	723	6	21	190	11	501	73.720612	1.000000
CEAM6_HUMAN	CEAM6_HUMAN	344	365	6	21	193	11	140	47.123287	1.000000
CEAM8_HUMAN	CEAM8_HUMAN	349	370	6	21	192	10	147	48.108109	1.000000
CEAM1_HUMAN	CEAM1_HUMAN	526	545	6	19	196	12	318	64.036697	1.000000
CEAM7_HUMAN	CEAM7_HUMAN	265	273	3	8	144	17	104	47.252747	1.000000
PSG3_HUMAN	PSG3_HUMAN	428	435	3	7	130	36	262	70.114944	1.000000
CEA21_HUMAN	CEA21_HUMAN	293	303	4	10	111	26	156	63.366337	1.000000
CEAM3_HUMAN	CEAM3_HUMAN	252	264	5	12	100	12	140	62.121212	1.000000
CEAM3_RAT	CEAM3_RAT	709	715	3	6	76	33	600	89.370628	1.000000
CEAMA_MOUSE	CEAMA_MOUSE	265	271	3	6	78	23	164	71.217712	1.000000
CEA16_HUMAN	CEA16_HUMAN	484	494	5	10	81	47	356	83.603241	1.000000
CEA20_HUMAN	CEA20_HUMAN	585	589	3	4	70	37	478	88.115448	1.000000
CEA19_HUMAN	CEA19_HUMAN	300	305	2	5	34	40	226	88.852463	1.000000
CEAB_RAT	CEAB_RAT	30	30	0	0	6	1	23	80.000000	1.000000

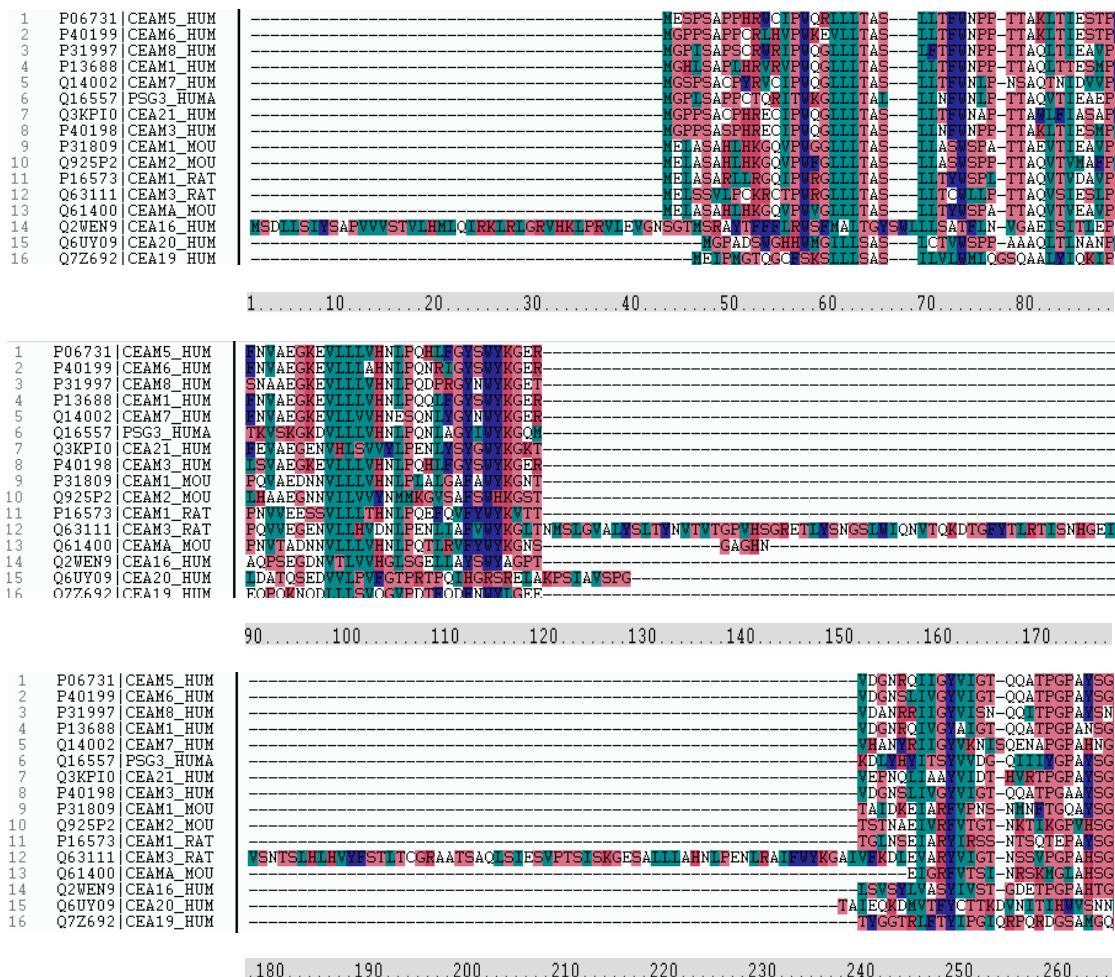
(4) Needle 和 Water 分析 17 条蛋白质信息:

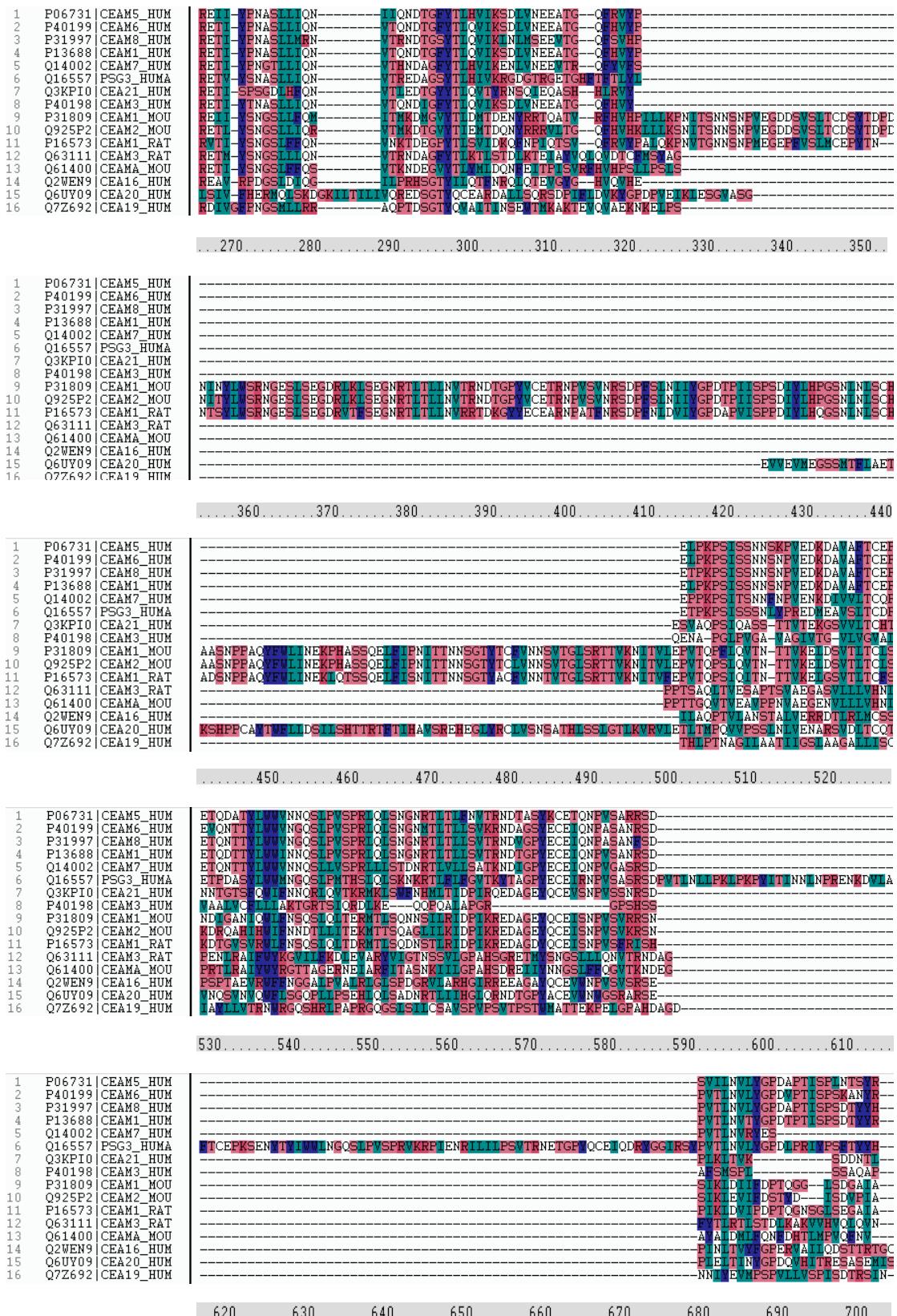
Alignment pairs	Alignment types	length	scope	identity	similarity	gaps
CEAM5&CEA16	needle	772	450.5	18.5%	28.1%	46.4%
	water	401	474.5	31.4%	46.9%	8.7%
CEAM5&CEA19	needle	723	148.5	11.8%	19.6%	61.4%
	water	395	157	20.3%	33.9%	34.7%
CEAM5&CEA20	needle	798	587	21.6%	33.6%	38.7%
	water	521	601	29.2%	45.5%	18.2%
CEAM5&CEA21	needle	722	551	17.6%	22.7%	62.2%
	water	254	564.5	46.5%	59.1%	6.7%
CEAM5&CEAM1	needle	722	1604.5	45.6%	52.2%	29.9%
	water	520	1612	62.7%	71.7%	5.0%
CEAM5&CEAM1-MO	needle	715	1025	33.3%	43.8%	29%
	water	555	1028.5	42.2%	54.8%	11.4%
CEAM5&CEAM1-RA	needle	706	974	32.2%	43.5%	27.1%
	water	567	975	40%	54.1%	9.5%
CEAM5&CEAM2-MO	needle	720	995.5	31.8%	43.1%	30.3%
	water	560	999	40.2%	53.8%	13.2%
CEAM5&CEAM3	needle	741	623	18.8%	20.9%	71.3%
	water	154	639.5	80.5%	84.4%	2.6%
CEAM5&CEAM3-RA	needle	904	500.5	21.2%	30.5%	43.9%
	water	792	503.5	24.2%	34.8%	36.2%
CEAM5&CEAM6	needle	702	1432	39%	40.9%	51%
	water	323	1443	83.9%	87.3%	0%
CEAM5&CEAM7	needle	711	825	23.2%	26.9%	64%
	water	245	832.5	65.7%	75.5%	2.9%

CEAM5 & CEAM8	needle	707	1255.5	34.9%	38.3%	51.3%
	water	314	1272	76.8%	82.8%	0%
CEAM5 & CEAMA-MO	needle	704	343.5	14.6%	20.3%	62.6%
	water	297	352	33%	45.8%	19.2%
CEAM5 & CEAPSG	needle	711	1135.5	33.6%	40.8%	41.1%
	water	496	1143	47.4%	57.7%	17.5%

可以看出,就全局比对而言,CEAM1_HUMAN与CEAM5_HUMAN的序列相似性最高,为52.2%;就局部比对而言,CEAM1_HUMAN、CEAM3_HUMAN、CEAM6_HUMAN、CEAM7_HUMAN、CEAM8_HUMAN都与CEAM5_HUMAN存在较高的序列相似性。就与CEAM5_HUMAN的整体比对效果而言,CEAM1_HUMAN综合成绩应该是最好的。同时我们还可以发现,尽管人和大、小鼠的形态差异较大,但是CEAM1_MOUSE、CEAM1_RAT和CEAM2_MOUSE三个蛋白质序列与人的CEAM5_HUMAN也存在较高的序列相似性。

(4) Clustalw 全序列分析 16 条蛋白质（除去了其中的 CEAB_RAT）信息：





1 P06731|CEAM5_HUM
 2 P40199|CEAM6_HUM
 3 P31997|CEAM8_HUM
 4 P13688|CEAM1_HUM
 5 Q14002|CEAM7_HUM
 6 Q16557|PSG3_HUMA
 7 Q3KPI0|CEA21_HUM
 8 P40198|CEAM3_HUM
 9 P31809|CEAM1_MOU
 10 Q925P2|CEAM2_MOU
 11 P16573|CEAM1_RAT
 12 Q63111|CEAM3_RAT
 13 Q61400|CEAMA_MOU
 14 Q2WEN9|CEA16_HUM
 15 Q6UY09|CEA20_HUM
 16 Q7Z692|CEA19_HUM

-----SGENINTSCHAASNPFAQSWEVNGTQOQSTQELIIPNITNNSGSVTCQAISDTGIRTTVTITVIAEPPKPFITSNS-----
 -----PGENINTSCHAASNPFAQSWEVNGTQOQSTQELIIPNITNNSGSVTCQAISDTGIRTTVTITVIAEPPKPFITSNS-----
 -----AGINNTSCHAASNPFAQSWEVNGTQOQSTQELIIPNITNNSGSVTCQAISDTGIRTTVTITVIAEPPKPFITSNS-----
 -----PGANTISCHAASNPFAQSWEVNGTQOQSTQELIIPNITNNSGSVTCQAISDTGIRTTVTITVIAEPPKPFITSNS-----
 -----SGENINTSCHAASNPFAQSWEVNGTQOQSTQELIIPNITNNSGSVTCQAISDTGIRTTVTITVIAEPPKPFITSNS-----
 -----GILIGLVGSLLVAALVCELLLRKTGRASDOSDREQQOPASTPGHGPDSSS-----
 -----LPNPTAASTIWEELKIDITNVRMDHKAEAS-----
 -----GIVIGVWAGVALIAGLAIPELSRKSGGGSDORDTEHKPSTSNNILAPSDDNSPNKWDDEAVATVILN-----
 -----VLTGAGAGVLLIAGLAIPELSRKSGGGSDORDTEHKPSTSNNILAPSDDNSPNKWDDEAVATVILN-----
 -----GIVIGVWAGVALIAGLAIPELSRKSGGGSDORDTEHKPSTSNNILAPSDDNSPNKWDDEAVATVILN-----
 -----TSSCCDILTFALITIDFVPRHAAKGEESVLDQWRNLFEDLRMIVWKSQIKRKAESRAIINVVERGAHSGREIVVING-----
 -----RAKIC-----
 -----TKPTEGQDVITIVQC-----
 -----AGIVIGIHAVAVASELG-----
 -----710.....720.....730.....740.....750.....760.....770.....780.....790-----
 -----NVEDEDAVALTCEPEAQNTTYLWVNQSLPVSPIQISNDNRITLTLISVTRNDVGFECGQNEISVDRISDFVILNVLYGPDDFT-----
 -----SILLQDATEKDTC-----
 -----TKPTEGQDVITIVQC-----
 -----AGIVIGIHAVAVASELG-----
 -----800.....810.....820.....830.....840.....850.....860.....870-----
 -----ISPSITVIRPGVNTSISCHAASNPFAQSWEVNGTQOQSTQELIIPNITNNSGSVTCQAANNSAAGHSRTTAKTITVSAELPKPSISS-----
 -----WAKPOIKA-----
 -----LTTQIIVRNPKETIAHIVSWSHTCHPSTTGOLVIES-----
 -----880.....890.....900.....910.....920.....930.....940.....950.....960.....
 -----SKPTEDKDATAITCEPEAQNTTYLWVNQSLPVSPIQISNCNRITLTLISVTRNDPAVCGQNSSANRSDEPTIDVLYGPDTPL-----
 -----TIVIGDDSNLTCSTINDTGISRUFKINOSIPSSERIKISQGNTTISINPKREDAGTVCEVINFISKNQSDPHINVN-N-AEQ-----
 -----ENWVEGGDWLLVNNPENIOSFSVKCVALVNREHISRNIIASNRSTLGPAGSGREIVSNGSLLLNATEEDNLVLTWNRHSE-----
 -----TFCIRNARRPSR-----
 -----970.....980.....990.....1000.....1010.....1020.....1030.....1040.....1050.....
 -----ISPPDGSVISGANINTSCHAASNPFAQSWEVNGTQOQSTQELIIPNNTNNSGSVTCQAISDTGIRTTVTITVIAEPPKPFITSNS-----
 -----SGSAP-----
 -----ENGLSPGAIACTIVIGVVALVAAIAAIAACIHLFGKTRASDORDTEHKPVSNSHTQDHNDPPNKHNEVTTISTNEAQOPTI-----
 -----TAASSI-----
 -----MESSKE-----
 -----INSQQPNRF-----
 -----INSQQPNRF-----
 -----INAQSKRF-----
 -----TOCIHVIIWKPVAQPFIRTESSVRKSSVLTCLSADTGTISQIILNNQNIRITORMISIOTKCOLSIDEVREDAEGYRCE-----
 -----VPKDILVAVVGRGASEPNRLISQPSGIVIAGPAHTGREGPNCSSIVVQINIDDTGRYVIL-----
 -----KTTEDPSHETSQTPKEEHPTEPSESISPECNTISQLOGRIRVELNQPPDPEETETKIPASRRGNSESPWKPPPFLMPPI-----
 -----1060.....1070.....1080.....1090.....1100.....1110.....1120.....1130.....1140-----

```

1 P06731|CEAM5_HUM |SAGATVGIIMIGVLVGVALI-
2 P40199|CEAM6_HUM |SARATVGIITIGVLARVALI-
3 P31997|CEAM8_HUM |SARATVSIIMIGVLARVALI-
4 P13688|CEAM1_HUM |SASPSSLTATEIIVSEVKKQ-
5 Q14002|CEAM7_HUM |SAGTAVSIMIGVLAGMALI-
6 Q16557|PSG3_HUMA |MTVKVSAPSGTGHLPGLNPTI-
7 Q3KPI0|CEA21_HUM |
8 P40198|CEAM3_HUM |
9 P31809|CEAM1_MOU |SAPSSSPRATEGVYSEVKKQ-
10 Q925P2|CEAM2_MOU |SAPSSSPRATEGVYSEVKKQ-
11 P16573|CEAM1_RAT |SASSSP--TETVYVSVVKKQ-
12 Q63111|CEAM3_RAT |SNPSSSKTSLPWSLDVVIE-
13 Q61400|CEAMA_MOU |
14 Q2WEN9|CEA16_HUM |TVTQGKTEITLEVLOVAPFG-
15 Q6UY09|CEA20_HUM |RLVSTWFKNMESIWEVLGMQQ-
16 Q7Z692|CEA19_HUM |

```

.....1150.....1160.....

可以看出，16个序列内部存在一定的氨基酸残基位点，是哪一些具体的位点保守呢？这些位点的变异范围又如何呢？这些疑问又需要依赖下面的相关蛋白质的保守基序和进化树分析结果来予以说明。

分析之二：人癌胚抗原相关蛋白质的保守基序和进化树分析

(1) MEME 分析：

MOTIFS ./meme.html (peptide)

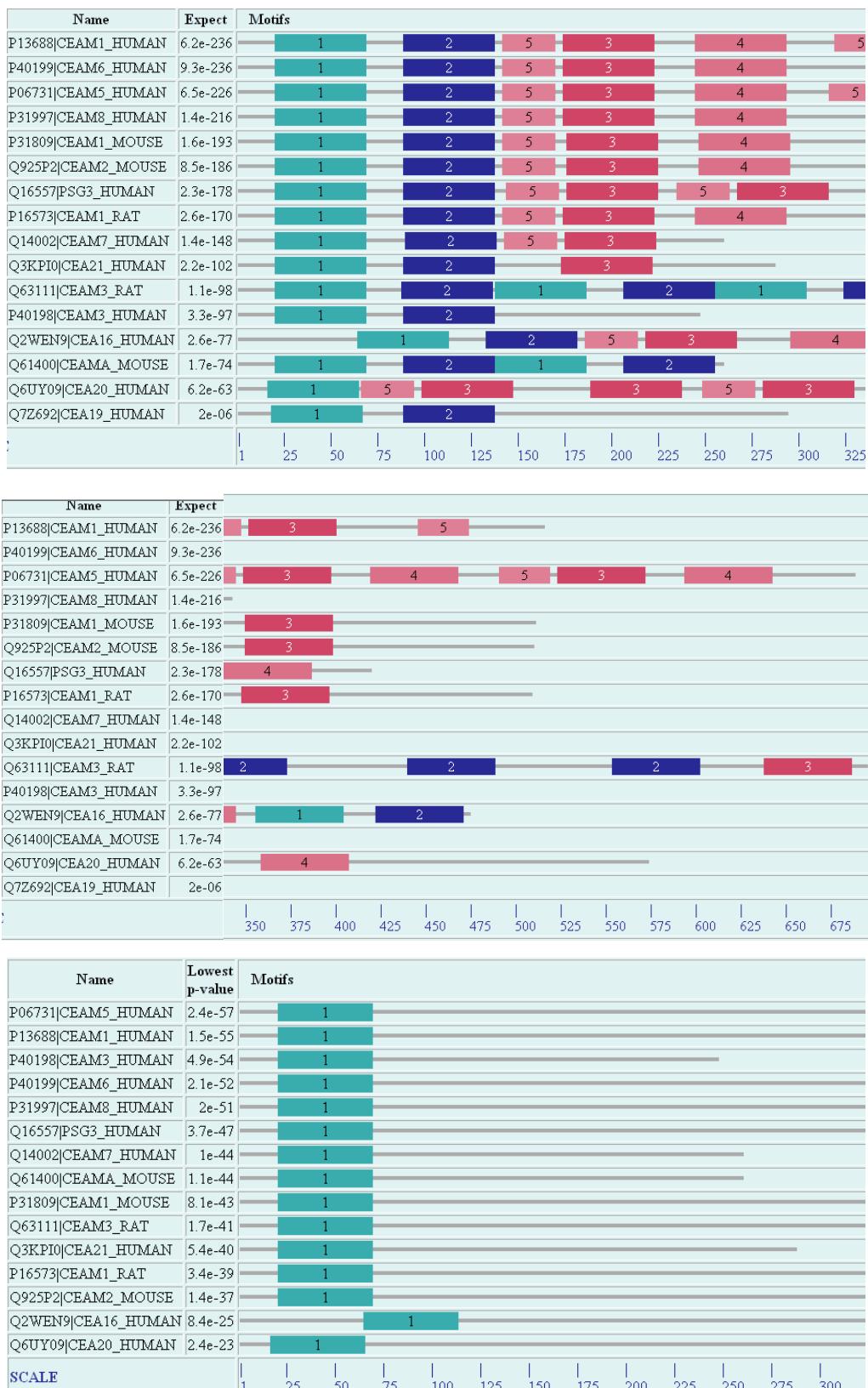
MOTIF WIDTH BEST POSSIBLE MATCH

```

----- -----
1   50   TASLLTFWNPPPTAQVTIEAMPNVAEGKEVLLLVHNLPQHLFGYSWYKG
2   50   PGPAYSGRETIYPNGSLLFQNVTMNDTGFYTLHMIKRDFKNEEATGQFHV
3   50   WWFNGQSLPVSDRLQLSEGRTLTFNVRRNDAGPYCEIWNPVANSRSD
4   50   HPGENLNLSCHAASNPPAQYFWFINGKFQQSTQELFIPNITTNNSGSYMC
5   29   PKPSITSNNNSNPVEDKDAVFTCEPETQN

```

Sequence Name	Description	E-value	Length
P13688 CEAM1_HUMAN	Carcinoembryonic antigen-...	6.2e-236	526
P40199 CEAM6_HUMAN	Carcinoembryonic antigen-...	9.3e-236	344
P06731 CEAM5_HUMAN	Carcinoembryonic antigen-...	6.5e-226	702
P31997 CEAM8_HUMAN	Carcinoembryonic antigen-...	1.4e-216	349
P31809 CEAM1_MOUSE	Carcinoembryonic antigen-...	1.6e-193	521
Q925P2 CEAM2_MOUSE	Carcinoembryonic antigen-...	8.5e-186	520
Q16557 PSG3_HUMAN	Pregnancy-specific beta-1...	2.3e-178	428
P16573 CEAM1_RAT	Carcinoembryonic antigen-...	2.6e-170	519
Q14002 CEAM7_HUMAN	Carcinoembryonic antigen-...	1.4e-148	265
Q3KPI0 CEA21_HUMAN	Carcinoembryonic antigen-...	2.2e-102	293
Q63111 CEAM3_RAT	Carcinoembryonic antigen-...	1.1e-98	709
P40198 CEAM3_HUMAN	Carcinoembryonic antigen-...	3.3e-97	252
Q2WEN9 CEA16_HUMAN	Carcinoembryonic antigen-...	2.6e-77	484
Q61400 CEAMA_MOUSE	Carcinoembryonic antigen-...	1.7e-74	265
Q6UY09 CEA20_HUMAN	Carcinoembryonic antigen-...	6.2e-63	585
Q7Z692 CEA19_HUMAN	Carcinoembryonic antigen-...	2e-06	300



>P06731|CEAM5_HUMAN(start=21)TASLLTFWNPPPTAKLTIESPFNVAEGKEVLLLvhNLPQHLFGYSWYKG
>P13688|CEAM1_HUMAN(start= 21)TASLLTFWNPPTTAQLTIESMPFNVAEGKEVLLLvhNLPQQLFGYSWYKG
>P40198|CEAM3_HUMAN(start= 21)TASLLNFWNPPTTAKLTIESMPLSVAEGKEVLLLvhNLPQHLFGYSWYKG
>P40199|CEAM6_HUMAN(start= 21)TASLLTFWNPPTTAKLTIESPFNVAEGKEVLLLahNLPQRIGYSWYKG
>P31997|CEAM8_HUMAN(start= 21)TASLFTFWNPPTTAQLTIEAVPSNAAEGKEVLLLvhNLPQDPRGYNWYKG
>Q16557|PSG3_HUMAN(start= 21)TALLNFWNLPTTAQVTIEAEPKVSKGKDVLVLLvhNLPQNLAGYIWYKG

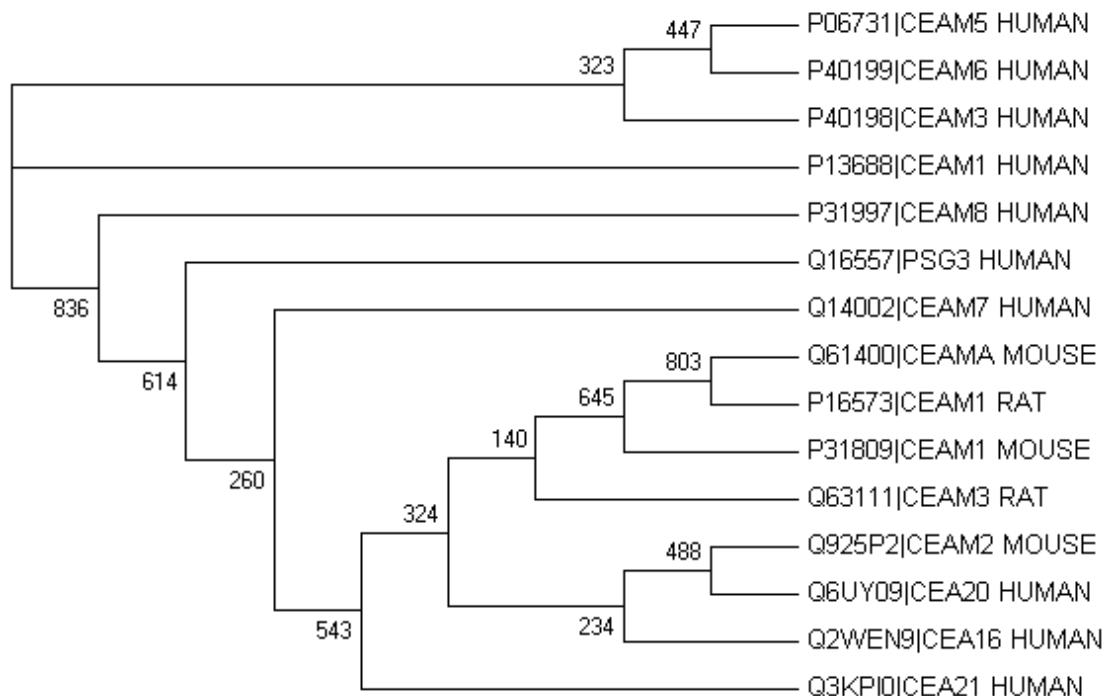
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>Q14002|CEAM7_HUMAN( start= 21 )TASLLTFWNLPNSAQTNIDVVPFNVAEGKEVLLVHNESQNLYGYNWYKG
>Q61400|CEAMA_MOUSE( start= 21 )TASLLTYWSPATTAQVTVEAVPPNVTADNNVLLVHNLPLQLRWFYWK
>P31809|CEAM1_MOUSE( start= 21 )TASLLASWSPATTAEVTEAVPPQVAEDENNVLLVHNLPLALGAFAWYKG
>Q63111|CEAM3_RAT( start= 21 )TASLLTCWLLPTTAQVSIESLPPQVVEGENVLLHVNDLPLNIAFVWYKG
>Q3KPIO|CEA21_HUMAN( start= 21 )TASLLTFWNAPTTAWLFIASAPFEVAEGENVHLSVVYLPENLYSYGWFYKG
>P16573|CEAM1_RAT( start= 21 )TASLLTYWSPLTTAQVTVDVAPPNVVEESSVLLTHNLPQEFLQVFYWKV
>Q925P2|CEAM2_MOUSE( start= 21 )TASLLASWSPPTTAQVTMPLHAAEGNNVILVYNNMMKGVSASFWSHKG
>Q2WEN9|CEA16_HUMAN( start= 66 )SWLLLSATFLNVGAEISITLEPAQPSEGDNVTLVHGLSGELLAWSYAG
>Q6UY09|CEA20_HUMAN( start= 17 )SASLCTVWSPPAAAQLTLNANPLDATQSEDVVLVFGTPRTPQIHGRSRE
```

(2) Weblog 分析:



可以看出在这些蛋白质序列中存在着部分位点的氨基酸残基的不同程度的保守性，如上图中的 4 位的 P、14 位的 A、22 位的 P、31 位的 V 和 33 位的 L。这些保守氨基酸残基对于该类蛋白的功能表现的作用如何，有赖于从上述蛋白质的三维结构中得到些许证实，可惜，当前该类蛋白的结构研究很少。

(3) 进化树分析:

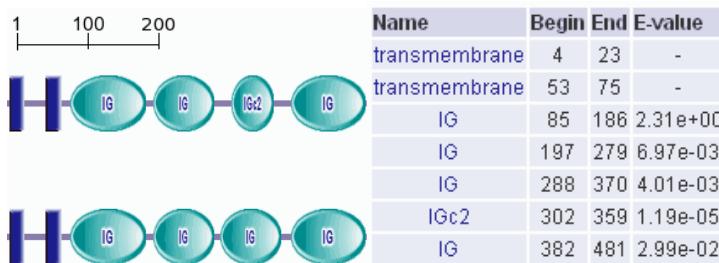


由此对基序 1 进行的进化树分析图可以初步得出上述几种蛋白之间的进化关系，结果与前面进行的序列比对结果差异较大，不仅说明比对与进化树构建两种分析途径的不同，也说明 CEA 家族成员内部之间的明显差异性，研究 CEA 家族面临的困难可能要超过以往。

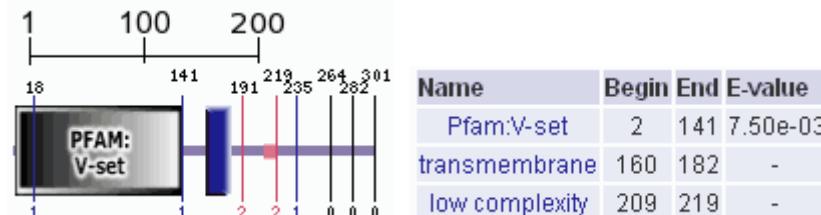
分析之三：人癌胚抗原相关蛋白质的结构域和跨膜分析

(1) SMART 分析：

>Q2WEN9|CEA16_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 16 - Homo sapiens (Human).

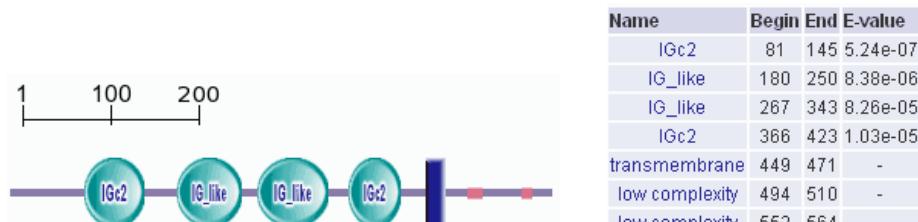


>Q7Z692|CEA19_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 19 - Homo sapiens (Human).

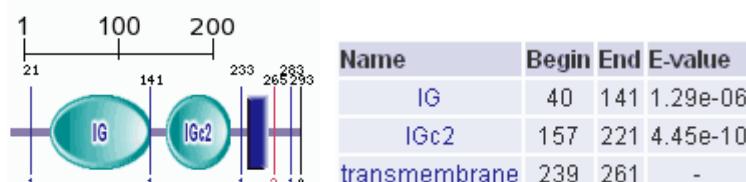


Immunoglobulin V-set domain

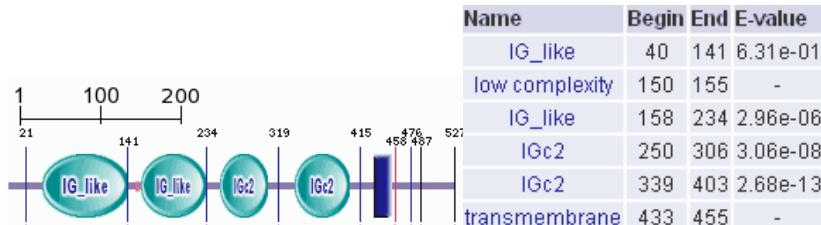
>Q6UY09|CEA20_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 20 - Homo sapiens (Human).



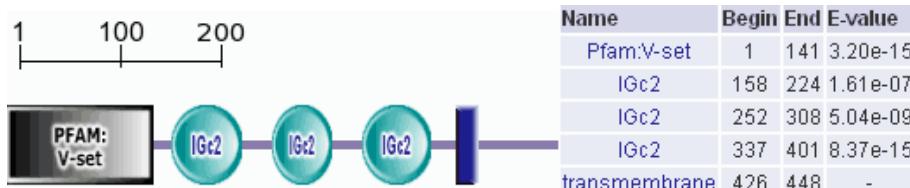
>Q3KPI0|CEA21_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 21 - Homo sapiens (Human).



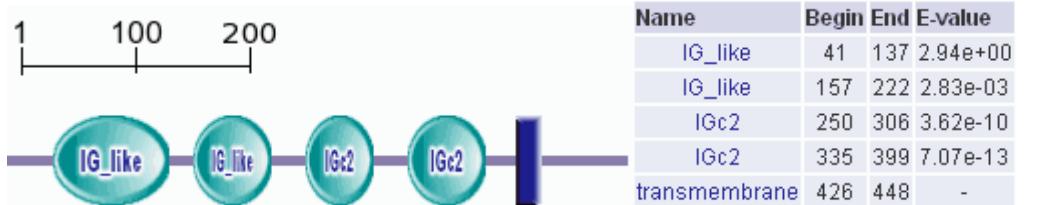
>P13688|CEAM1_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 1 - Homo sapiens (Human).



>P31809|CEAM1_MOUSE Carcinoembryonic antigen-related cell adhesion molecule 1 - Mus musculus (Mouse).



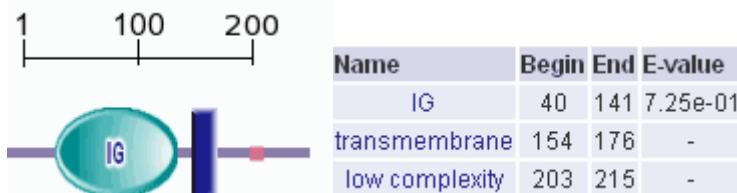
>P16573|CEAM1_RAT Carcinoembryonic antigen-related cell adhesion molecule 1 - Rattus norvegicus (Rat)



>Q925P2|CEAM2_MOUSE Carcinoembryonic antigen-related cell adhesion molecule 2 - Mus musculus (Mouse).



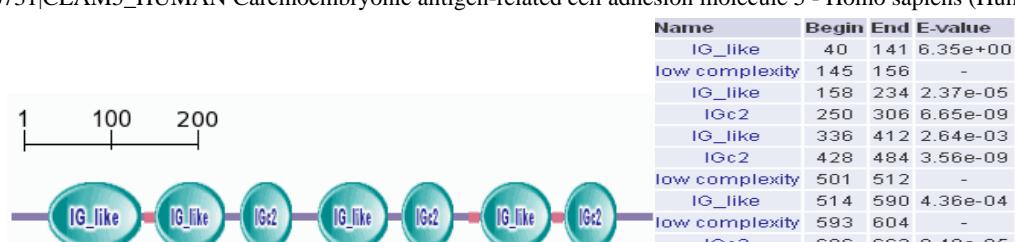
>P40198|CEAM3_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 3 - Homo sapiens (Human).



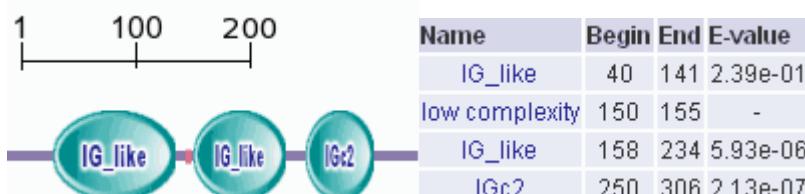
>Q63111|CEAM3_RAT Carcinoembryonic antigen-related cell adhesion molecule 3 - Rattus norvegicus (Rat).



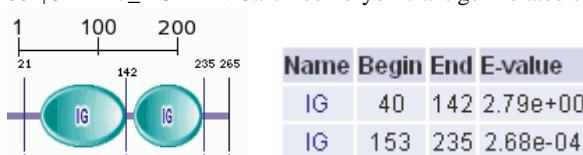
>P06731|CEAM5_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 5 - Homo sapiens (Human).



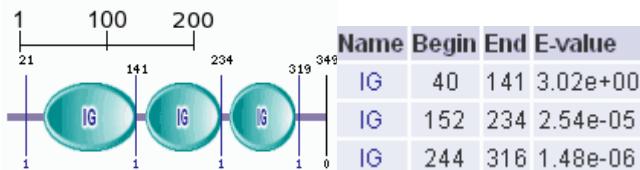
>P40199|CEAM6_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 6 - Homo sapiens (Human).



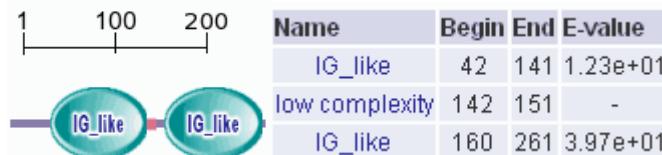
>Q14002|CEAM7_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 7 - Homo sapiens (Human).



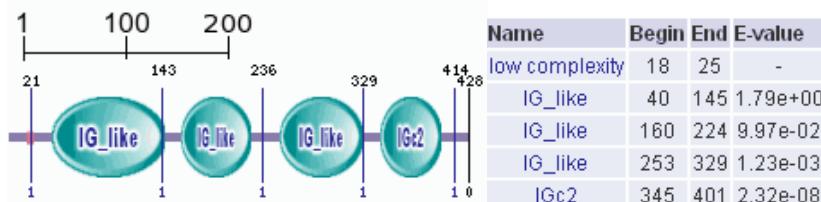
>P31997|CEAM8_HUMAN Carcinoembryonic antigen-related cell adhesion molecule 8 - Homo sapiens (Human).



>Q61400|CEAMA_MOUSE Carcinoembryonic antigen-related cell adhesion molecule 10 - Mus musculus (Mouse).

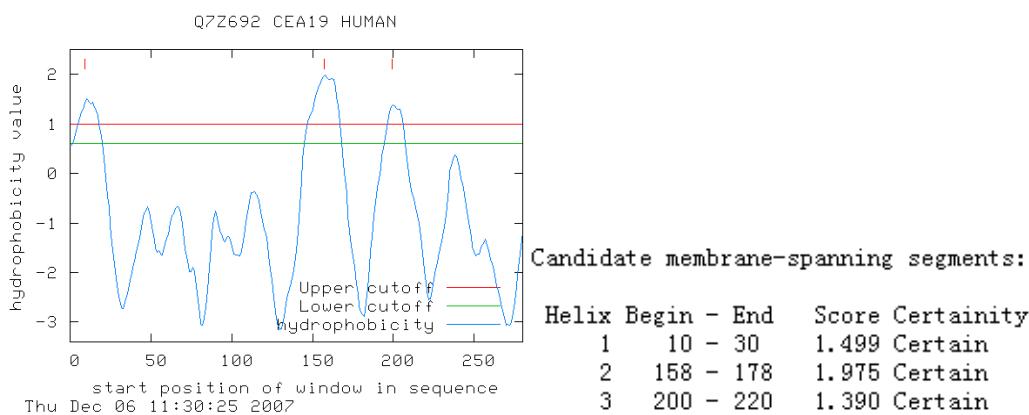
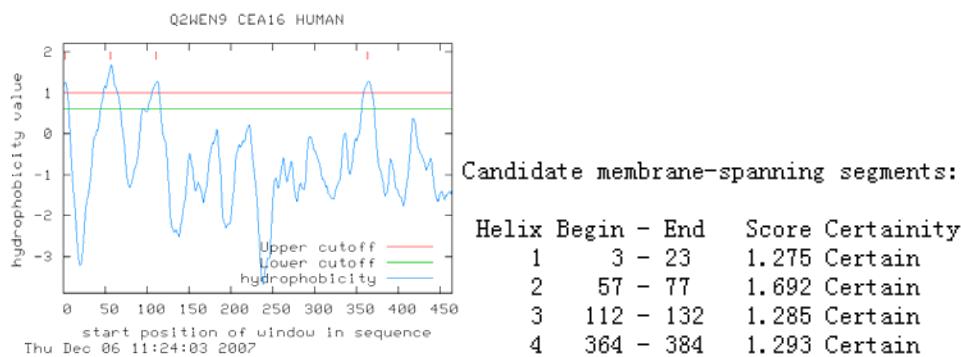


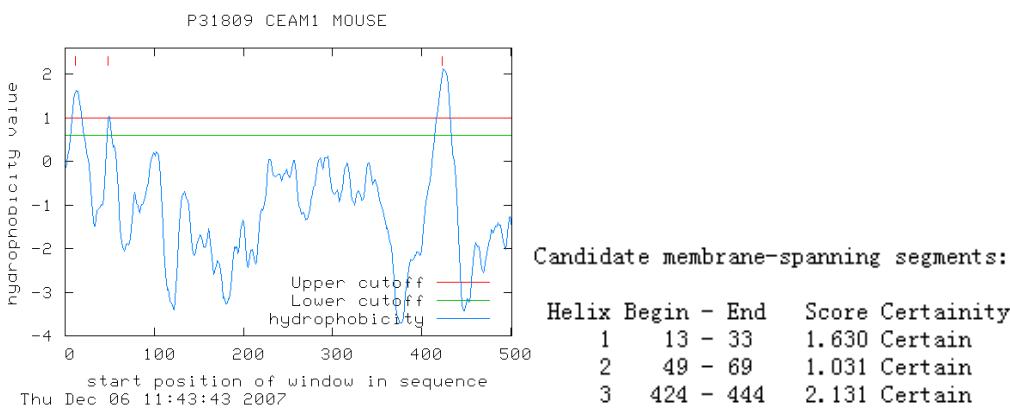
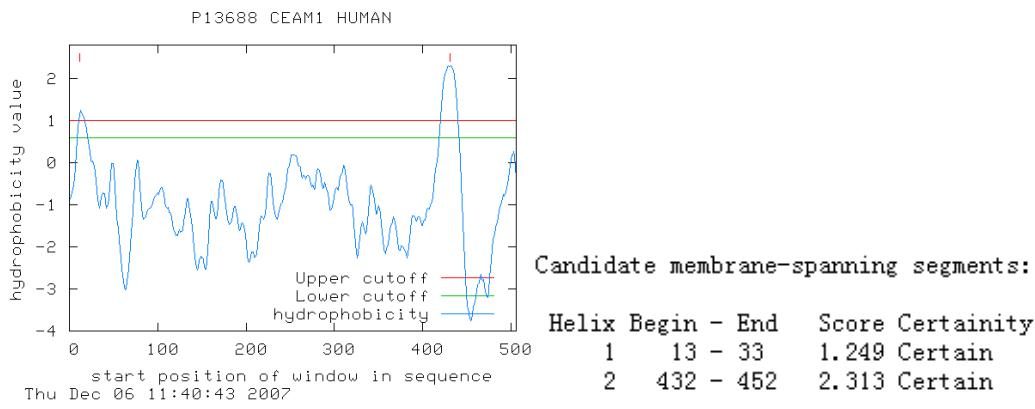
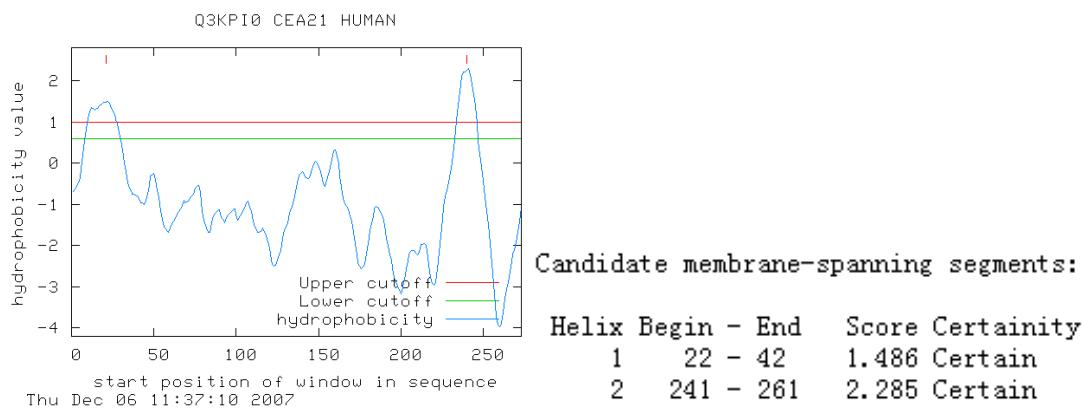
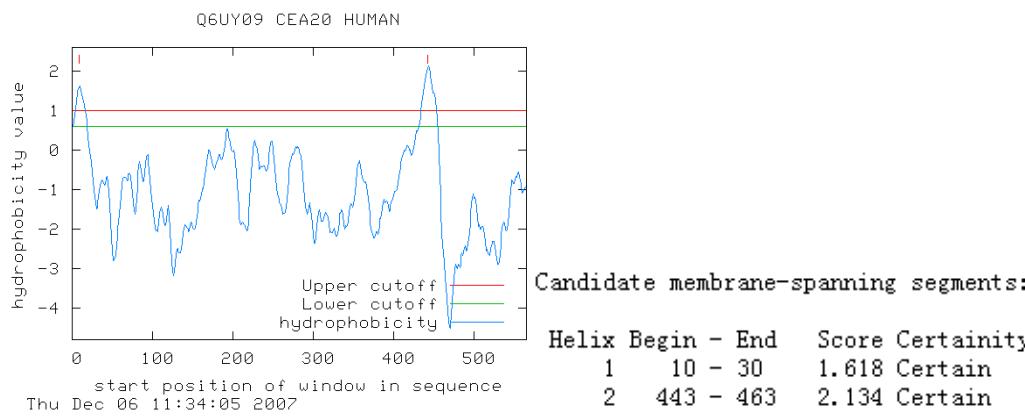
>Q16557|PSG3_HUMAN Pregnancy-specific beta-1-glycoprotein 3 - Homo sapiens (Human).

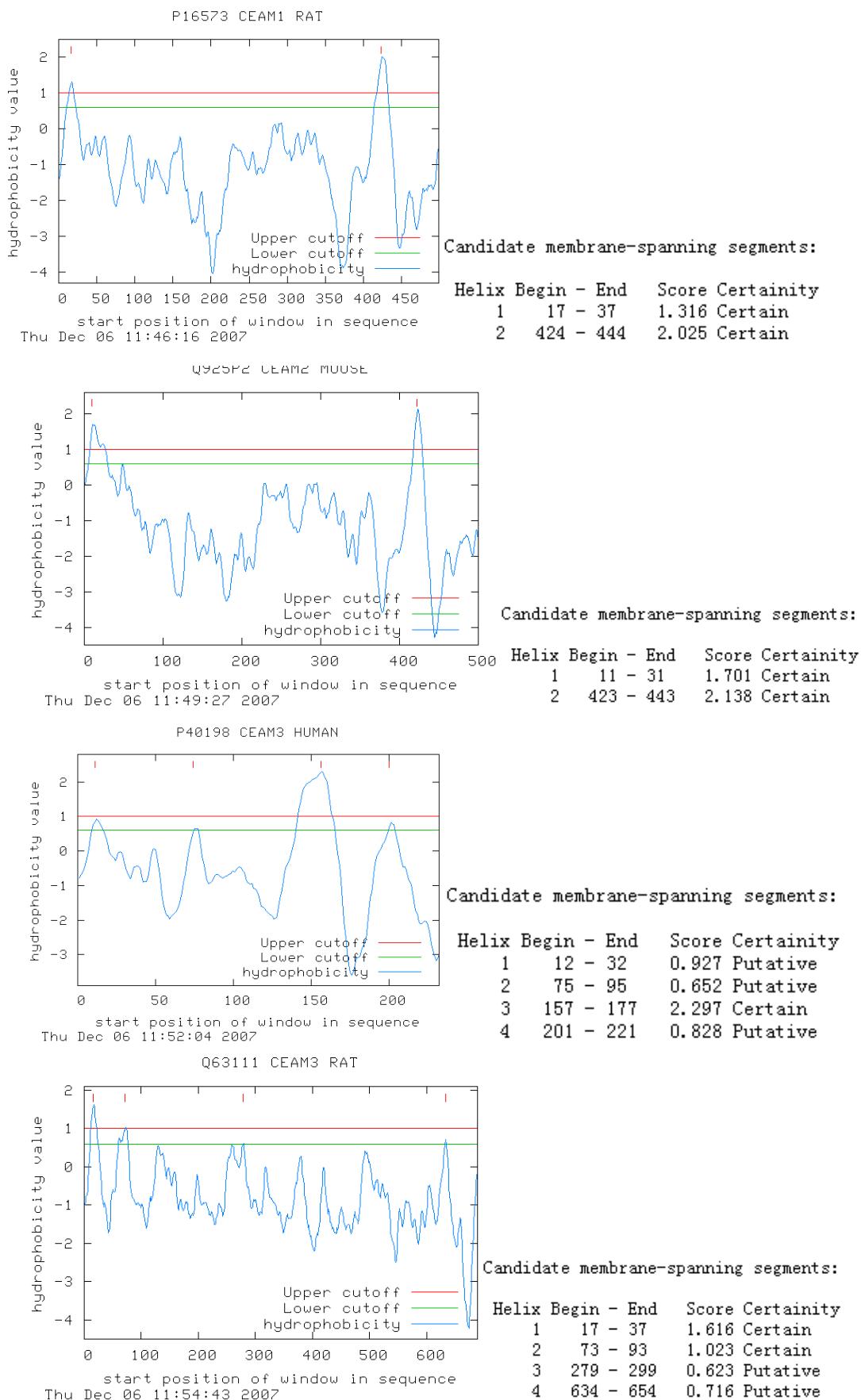


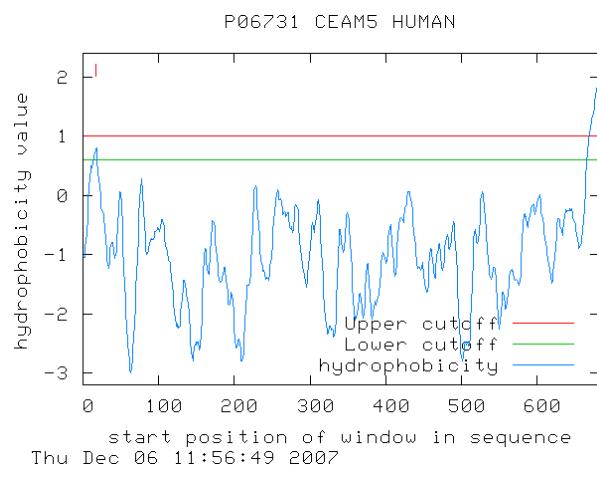
SMART 分析可以初步解释在前面序列比对中出现的重复点阵区应该是免疫球蛋白结构域区，也可以一定程度上解释出 CEA5 与 CEA3 的综合相似程度高，还可以看出 CEA 家族成员普遍具有免疫球蛋白结构域，从这一点出发，可以利用已知的免疫球蛋白三维结构来推测未知结构的 CEA 家族蛋白。

(2) TopPred 分析:



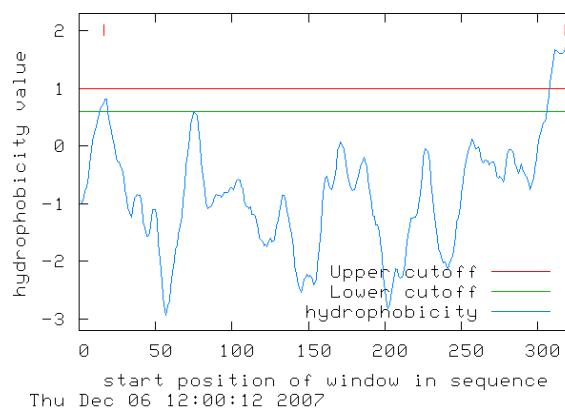






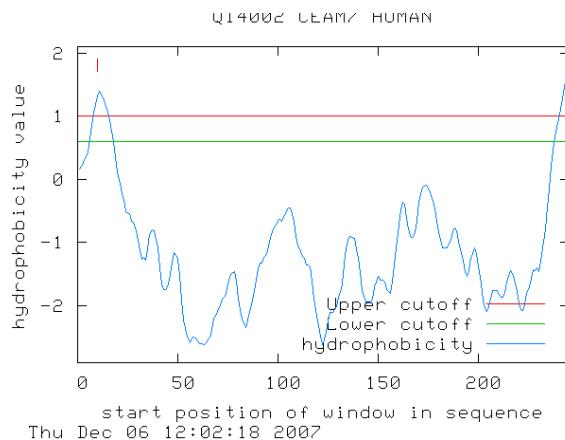
Candidate membrane-spanning segments:

Helix	Begin - End	Score	Certainty
1	18 - 38	0.807	Putative
2	682 - 702	2.070	Certain



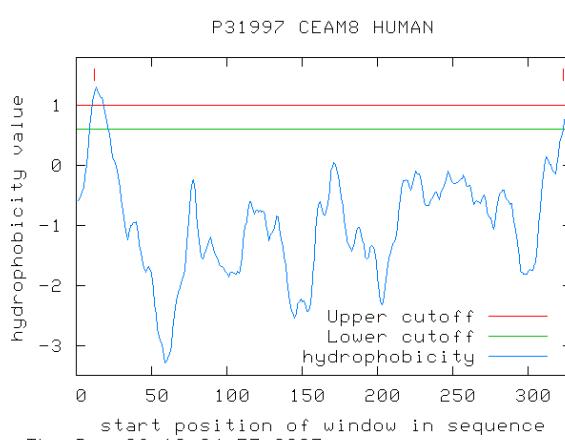
Candidate membrane-spanning segments:

Helix	Begin - End	Score	Certainty
1	17 - 37	0.823	Putative
2	319 - 339	1.768	Certain



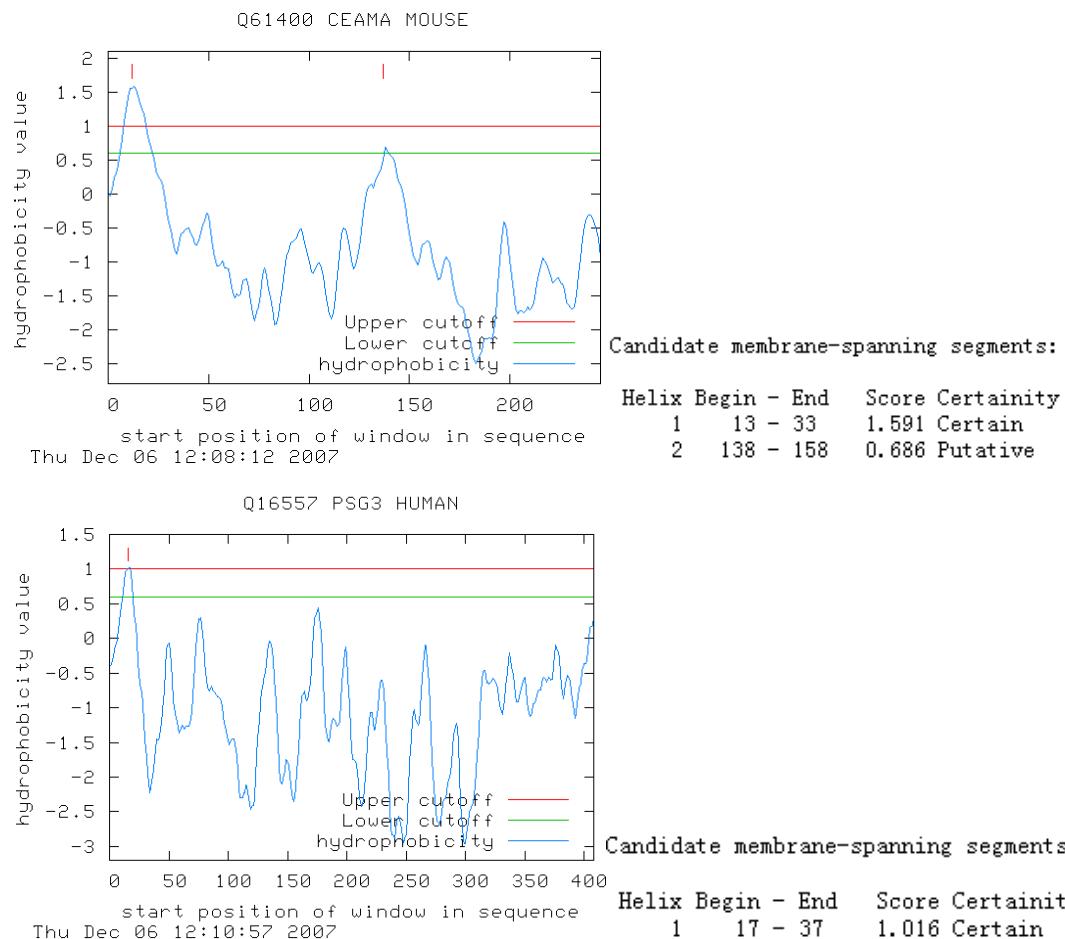
Candidate membrane-spanning segments:

Helix	Begin - End	Score	Certainty
1	11 - 31	1.403	Certain
2	245 - 265	1.909	Certain



Candidate membrane-spanning segments:

Helix	Begin - End	Score	Certainty
1	13 - 33	1.310	Certain
2	324 - 344	0.758	Putative



结果表明上述蛋白质都存在非常明显的跨膜区域，这些特点对于研究相关抗原蛋白的详细功能应该有用。下一步，可以考虑参照免疫球蛋白结构来预测人癌胚抗原蛋白的三维结构，具体分析还有待于本小组成员的进一步学习。