

表皮生长因子受体在肿瘤发生 中的作用及机制

柏庆然，丁淼，丁晓，郭文婷，李亚朴，张新新

表皮生长因子受体 (epidermal growth factor receptor, EGFR)

Isolation of a Mouse Submaxillary Gland Protein Accelerating Incisor Eruption and Eyelid Opening in the New-born Animal*

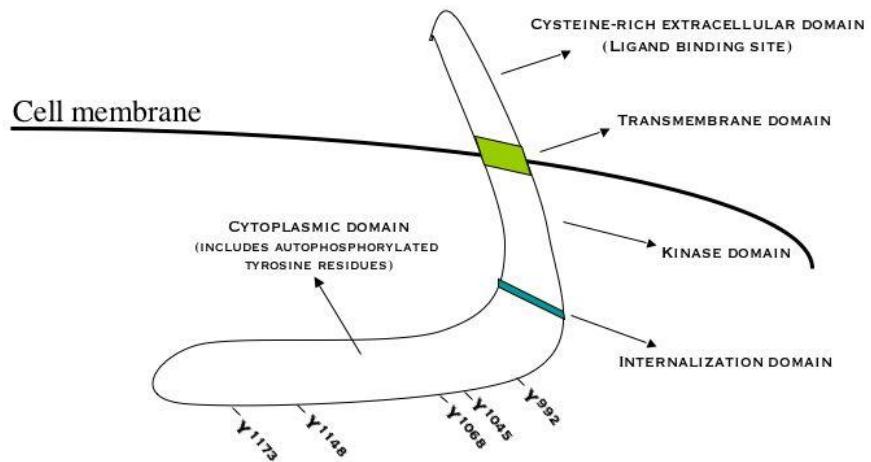
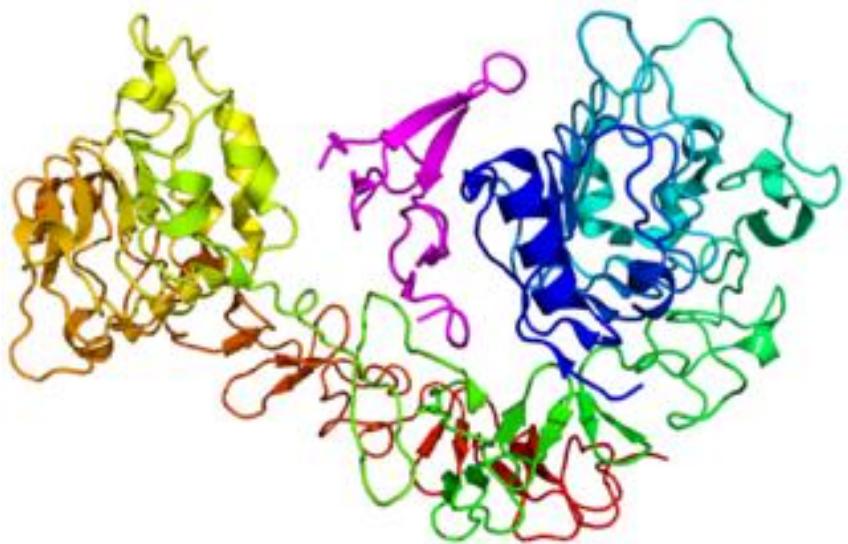
STANLEY COHEN†

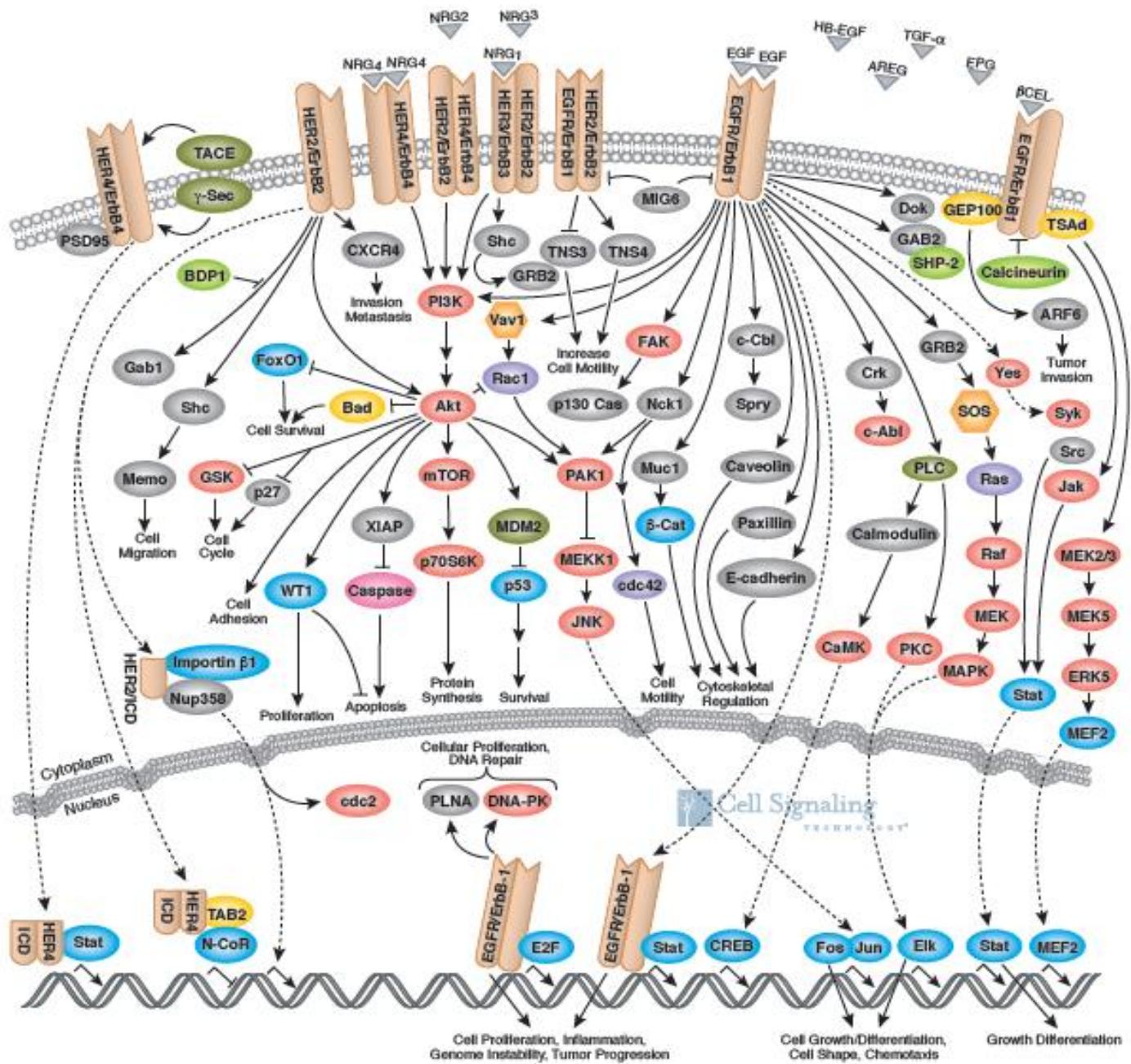
From the Department of Biochemistry, Vanderbilt University School of Medicine, Nashville 5, Tennessee

(Received for publication, November 20, 1961)



1986
Physiology or Medicine

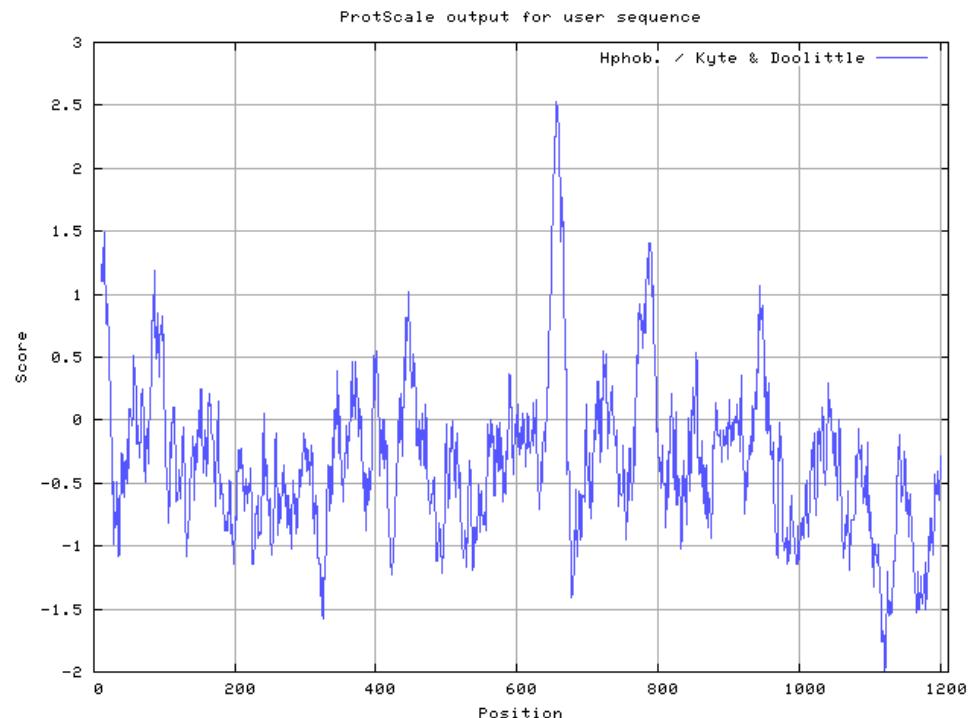




预测跨膜结构（疏水结构）

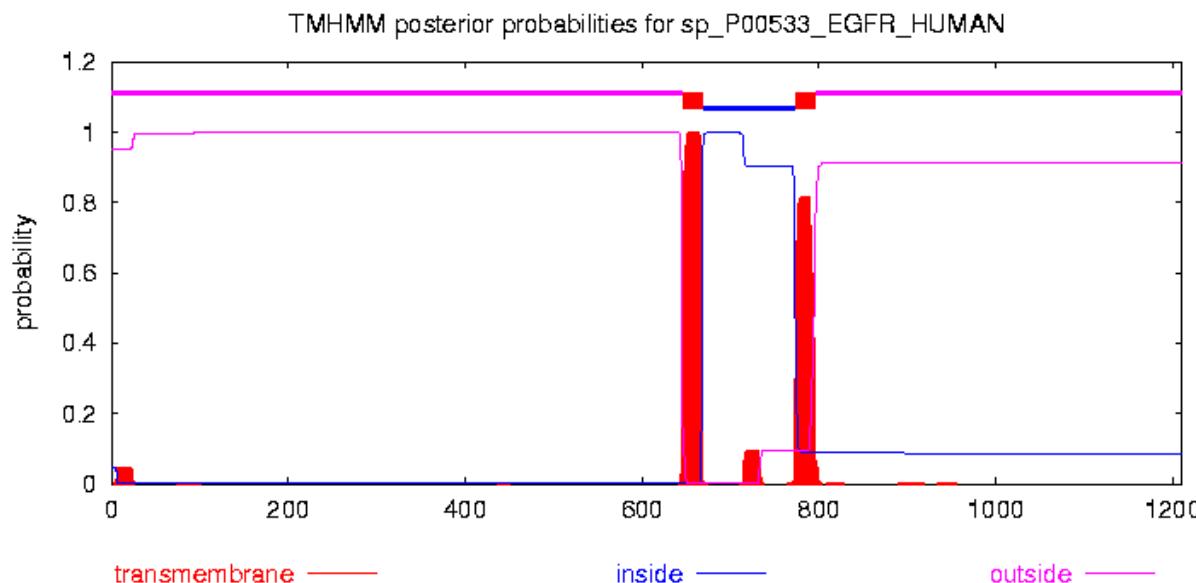
进入ExPASy的网站：

<http://expasy.org/tools/protscale.html>，选择
Hphob. / Kyte & Doolittle。将氨基酸序列输入



预测跨膜结构

- 使用TMHMM网站可预测蛋白的胞内区域和胞外区域:
- # sp_P00533_EGFR_HUMAN Length: 1210# sp_P00533_EGFR_HUMAN Number of predicted TMHs: 2# sp_P00533_EGFR_HUMAN Exp number of AAs in TMHs: 42.29864# sp_P00533_EGFR_HUMAN Exp number, first 60 AAs: 0.88712# sp_P00533_EGFR_HUMAN Total prob of N-in: 0.04662sp_P00533_EGFR_HUMAN TMHMM2.0 outside 1 645sp_P00533_EGFR_HUMAN TMHMM2.0 TMhelix 646 668sp_P00533_EGFR_HUMAN TMHMM2.0 inside 669 772sp_P00533_EGFR_HUMAN TMHMM2.0 TMhelix 773 795sp_P00533_EGFR_HUMAN TMHMM2.0 outside 796 1210

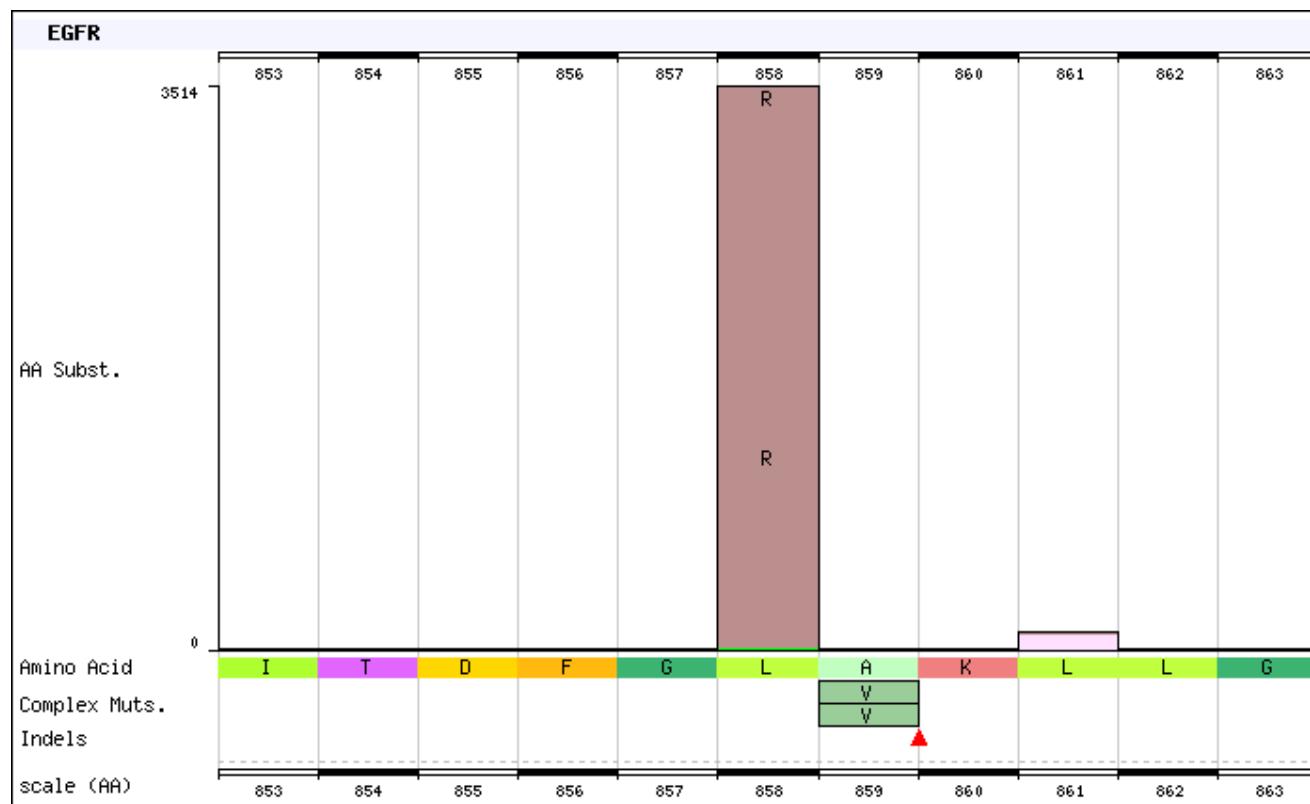


预测重复结构

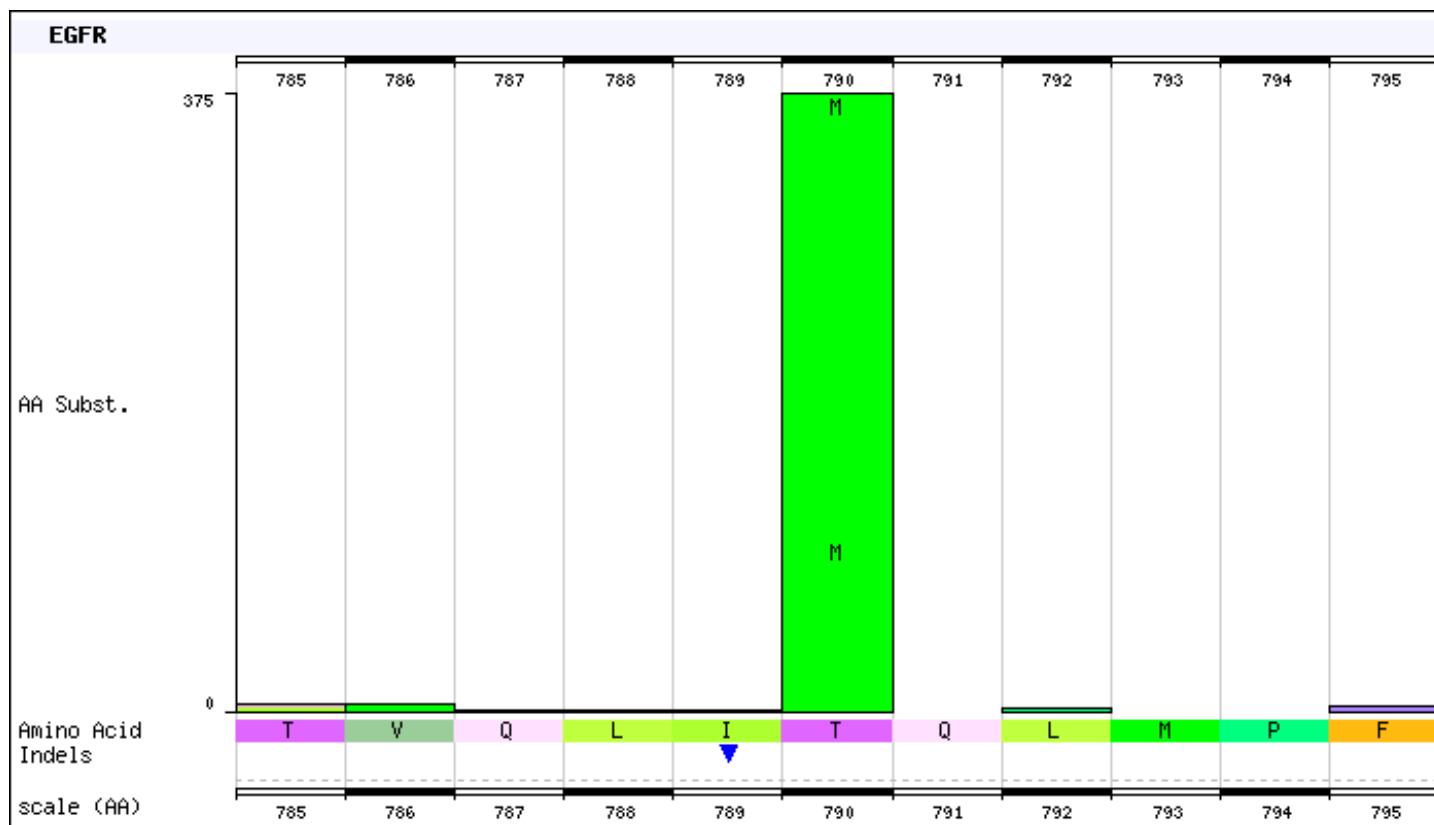
- 无重复结构

- COSMIC网站
- Catalogue of Somatic Mutations in Cancer - COSMIC
- www.sanger.ac.uk/genetics/CGP/cosmic
- 找出EGFR在癌细胞里的突变位点，分析这些突变为什么会引起癌症。
- 分别由三个位点在癌症中突变频率较高

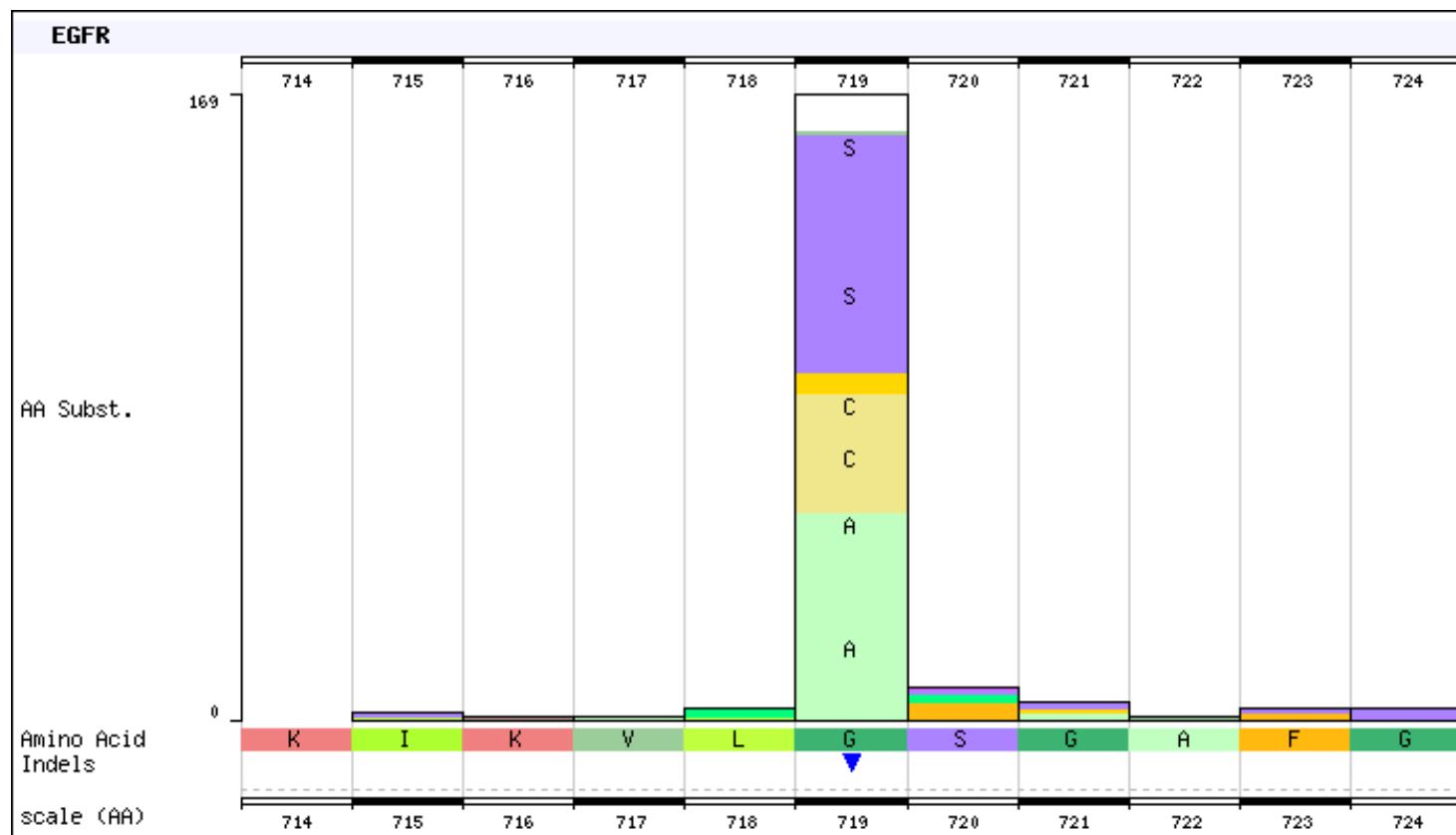
- 858 L>R、



- 790 T->M



- 719 G->SCA



EFGR 6个物种比较保守

Protein Acc.	Gene	Organism	
NP_005219.2	EGFR	H.sapiens	P_533073_2 1185 P_592211_2 772 P_533273_2 775 P_592211_3 785 P_113989_2 785 P_819405_2 784
XP_001156495.1	EGFR	P.troglodytes	P_005219_2 545 P_001156495_1 562 P_533073_2 1235 P_592211_2 522 P_897338_2 547 P_113989_2 546 P_819405_2 544
XP_533073.2	EGFR	C.lupus	P_005219_2 545 P_001156495_1 562 P_533073_2 1235 P_592211_2 572 P_897338_2 597 P_113989_2 596 P_819405_2 594
XP_592211.3	EGFR	B.taurus	P_005219_2 545 P_001156495_1 562 P_533073_2 1235 P_592211_2 522 P_897338_2 547 P_113989_2 546 P_819405_2 544
NP_997538.1	Egfr	M.musculus	P_005219_2 545 P_001156495_1 562 P_533073_2 1235 P_592211_2 522 P_897338_2 547 P_113989_2 546 P_819405_2 544
NP_113695.1	Egfr	R.norvegicus	P_005219_2 545 P_001156495_1 562 P_533073_2 1235 P_592211_2 522 P_897338_2 547 P_113989_2 546 P_819405_2 544
NP_919405.1	egfra	D.rerio	P_005219_2 545 P_001156495_1 562 P_533073_2 1235 P_592211_2 572 P_897338_2 597 P_113989_2 596 P_819405_2 594
			P_005219_2 1045 P_001156495_1 1022 P_533073_2 1235 P_592211_2 1022 P_897338_2 1022 P_113989_2 1046 P_819405_2 1043
			P_005219_2 1092 P_001156495_1 1109 P_533073_2 1475 P_592211_2 1287 P_897338_2 1282 P_113989_2 1281 P_819405_2 1286
			P_005219_2 1141 P_001156495_1 1155 P_533073_2 1237 P_592211_2 1116 P_897338_2 1141 P_113989_2 1140 P_819405_2 1137
			P_005219_2 1189 P_001156495_1 1208 P_533073_2 1274 P_592211_2 1164 P_897338_2 1189 P_113989_2 1185 P_819405_2 1177

6个物种比较保守序列进化



Erbb 蛋白家族保守结构域

重复序列比对 比较保守

59	UMGNLLEITLIGHNMADLSFLQNLNIRE/T/GVYLWVAMNEFSTILPPLNWLVR/VRG/TQYVGDGKFAIF	118	P21860	ERBB4_HUMAN
59	UMGNLLEITSIEHNRDLSFLR/SRE/T/GVYLWVALQMFRLYPLENLIRIIRGTGYEDRYVALA	118	Q15038	ERBB4_HUMAN
61	VGLNGLTYT/QRNLYLTSFLKUQTCAGVHQLLNLTRTPELENLQIIRGAMNTENSTALA	120	P00532	EGFR_HUMAN
61	VQGNLLETLTFLFINASLFLQDIEQGVGLVHANQVQVQLQRLARVTRGQLFDNVALA	115	P04626	ERBB2_HUMAN
	* AAAAA; * AAAAA; :AA AAAA; : :AAA :AA : : : : :			
119	VMLNYT-----NSHSALELTQLTQLTEILSLSGGVIIKEKDLKLCMHDITNDRDI	169	P21860	ERBB3_HUMAN
119	IFLVNRYK-----DGNGFLGELQGLGQNLNLINLGNGV/DWKQNLKTYCADIHNGQDVRIN	169	Q15038	ERBB4_HUMAN
121	LLENVY-----ANGTKELELBNMQLQEEHNGVAFSDNQFLNCEWSNTQDQDVSS	170	P00532	EGFR_HUMAN
116	VLDINGDPLNNTFVTGASPGLERIQJRLSLTEILKGGLVLRQNPQLCYQDILNODIFHK	175	P04626	ERBB2_HUMAN
	* : * :			
170	---RDAEVT/LKONGRSPPCPHCHEVNGC-RGCGFSGEDQCLWLTHTICAPQCNHGRCFGPNVNQ	225	P21860	ERBB3_HUMAN
170	FWFNSLTVLTVSTG33GSGCRCHSCIG-TFTENHCKVLIITRVCACDQGCKTCIGTFPS	225	Q15038	ERBB4_HUMAN
171	DPLNNSMDPQDNHLSQCGCPCPFCNGCSWQAGBEEQNCNKLTRICAKQGNCGKHSKPS	230	P00532	EGFR_HUMAN
176	NNQLALTIDINRNSRACHCFCSPMCUGKCGNCEG3ESDQSLSLRTVCAGCGCA-RKRGFLPTD	234	P04626	ERBB2_HUMAN
	* : * :			
226	CCHDEACCGGCGSPQDTDCFACRHNDPSGACVPRCPQBLVYMLKLTQFQLEPNPPTKQYQGGV	285	P21860	ERBB4_HUMAN
229	CCBRECACGGCGSPKUDTDCFACMFNDPSGACVTCQBPVYMPPTFOLHEHNAKTYTGF	285	Q15038	ERBB4_HUMAN
221	COHNCQACAGCTGPKHNSCLACLMHNHSGICELHCPALVINTIDTEFLMMNPMGGATITGAS	290	P00532	EGFR_HUMAN
235	CCHEQCAAGCTGPKHNSCLACLMHNHSGICELHCPALVINTIDTEFLMMNPMGGATITGAS	294	P04626	ERBB2_HUMAN
	* : * :			
286	CVACSPHNFVWQDQ-SCVACPPDMWTD-KNGLMCEPCCPGGLCPKACEGTGSGSRF--Q	341	P21860	ERBB3_HUMAN
289	CVKXCKHNFVWDS-S-CVACPPSMHEV-ENGIMKPCFKTDCICDG16TGSLLMSAQ	346	Q15038	ERBB4_HUMAN
291	CVTKHNFVWVTDHNSCCTVGRKADGASYME-CVACPPDMWTD-KNGLMCEPCCPGGLCPKACEGTGSGSRF	345	P00532	EGFR_HUMAN
295	CVTCACPFYVNLSTVDTCVLPCHLNQEVTAEDGTCRCECMKSKPCAVCYGLMCHLREVR	354	P04626	ERBB2_HUMAN
	* : * :			
342	TVDSSNIDGFCANTIKLWGLNQFLITGLNGDPWNSKALPDPEKLN/FRTV/REITGVNLNIQS	401	P21860	ERBB3_HUMAN
347	TVDSSNIDKPIINCTKINGNLNLFITVGHGDPYNAIEADPEKLN/FRTV/REITGVNLNIQS	406	Q15038	ERBB4_HUMAN
350	SINATINHKKWNCITSIGDHLILPWFAGFDSTPHTFLDFP/DELIDLTIVKREITGVNLNIQS	409	P00532	EGFR_HUMAN
355	AVTSAMIGEFAQGKMKIIGSLLAFPLPSDFGDPASNTIAQFPLPQQVFTEELEYGHLYIIS	414	P04626	ERBB2_HUMAN
	* : * :			
402	WPFHMNFSV/FSNLNTIIGGRSLYNNRGFSLLIMHNLNVTSLGFRLSLWEIASGRGIYISANRQ	461	P21860	ERBB3_HUMAN
407	WPFHMNFS/FSNLNTIIGGRSLYNNRGFSLLIMHNLNVTSLGFRLSLWEIASGRGIYISANRQ	465	Q15038	ERBB4_HUMAN
410	WPFHMNFS/FSNLNTIIGGRSLYNNRGFSLLIMHNLNVTSLGFRLSLWEIASGRGIYISANRQ	468	P00532	EGFR_HUMAN
415	WEDSLPDLTS/FPQNLYVIRGRIHLNGAYSLTLQG-LG15WGLRSLRELGSGLALIHNTN	473	P04626	ERBB2_HUMAN
	* : * :			
462	LCTHRSNLNTWV/LRGPTEERLDRDINHMRFRDPLA2VAGKWCDFPLC3S2GGCNGPFGPQFLCLSCR	521	P21860	ERBB3_HUMAN
466	LCTHSYLNTWTFPS-TINGRIVLDRNMRKAENCTAGMVWNLHSDGCGNGPFGPQFLCLSCR	524	Q15038	ERBB4_HUMAN
469	LCVANTINWHLR-NFSQGLKIIISNRGNSCAGTQVWHALCSEPGCGVTPEDCNU	527	P00532	EGFR_HUMAN
474	LCVHTVPMWQLR-NFHQLALLNTARPEDECVGEGLGLCARHGCHNGPFGCQCNCS	532	P04626	ERBB2_HUMAN
	* : * :			
522	NV3RGGVWVTHCNFLNGEPREFAHAEACFSCHPCPQEMG-TATCNGSGDTCACQHCFR	580	P21860	ERBB3_HUMAN
525	RSEFRGICIESCNLYDEFREFPENSICTECQDCQEWEMDGLLTCGKQHGDINCTKSHPK	584	Q15038	ERBB4_HUMAN
528	WSEFRGICIESCNLYDEFREFPENSICQCPHCLPQML-WITTCRGEFRMTCQACNT	586	P00532	EGFR_HUMAN
533	QFLRG-CEVLCRVLQSLPREFVYARHCLCPHCBCQFQNG-STICPGEFQDGCYACANTK	591	P04626	ERBB2_HUMAN
	* : * :			
581	DGPHCVC3CPHGVGLV--AKGPIIYKPD/VQECRCHCENCTQGCKGCPFLQCL----GQT	633	P21860	ERBB3_HUMAN
585	DGFCVNCFLDGLQG---AMSIPIFYAD-FDRECHCPHCNCCTQGCPGTSFIIYCFPWTGHS	642	Q15038	ERBB4_HUMAN
587	DGPHCVC3CPHGVGLV----GNTML-WVTKADYAGHCHLNCNCTQGCKGCPFLQCL---	687	P00532	EGFR_HUMAN
592	DGPHCVC3CPHGVGLV----GNTML-WVTKADYAGHCHLNCNCTQGCKGCPFLQCL----	643	P04626	ERBB2_HUMAN
	* : * :			

与其他激酶家族结构域比对 保守区域