

黑色素瘤抗原(MAGE)蛋白家 族序列及结构分析

Sequences and Structure Analysis of MAGE



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提 纲



- ◆ 研究背景
- ◆ 基因结构及序列分析
- ◆ 蛋白家族演化分析
- ◆ **MAGEA1**结构预测



黑色素瘤

Melanoma



黑色素瘤（Melanoma）：

- 黑色素细胞的恶性肿瘤，主要发生在白种人中。
- 主要出现在皮肤，还可以出现在人体的任何存在黑色素细胞的组织。
- 它占皮肤癌症的4%，但是死亡率占皮肤癌症的79%。

药物：

- **Yervoy**：2011年3月25日，美国FDA批准的第一个显示可让黑色素瘤患者延长寿命的药物。
- **Zelboraf (vemurafenib)**：2011年8月17日，美国FDA批准用于治疗晚期转移性或不能切除的黑色素瘤。

MAGE



黑色素瘤相关抗原（melanoma-associated antigen, MAGE）在睾丸、胎盘及许多肿瘤中有表达，是可能的肿瘤药物靶点。

MAGEA1，发现的第一个MAGE家族基因，于1991年发表在Science。

A gene encoding an antigen recognized by cytolytic T lymphocytes on a human melanoma

P van der Bruggen, C Traversari, P Chomez, C Lurquin, E De Plaen, B Van den Eynde, A Knuth, T Boon



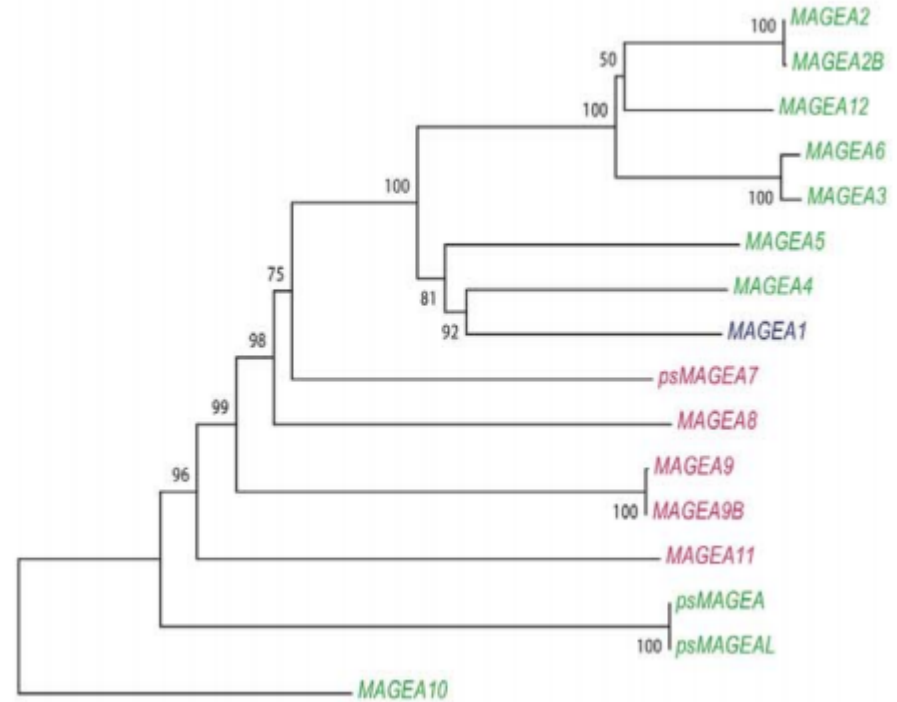
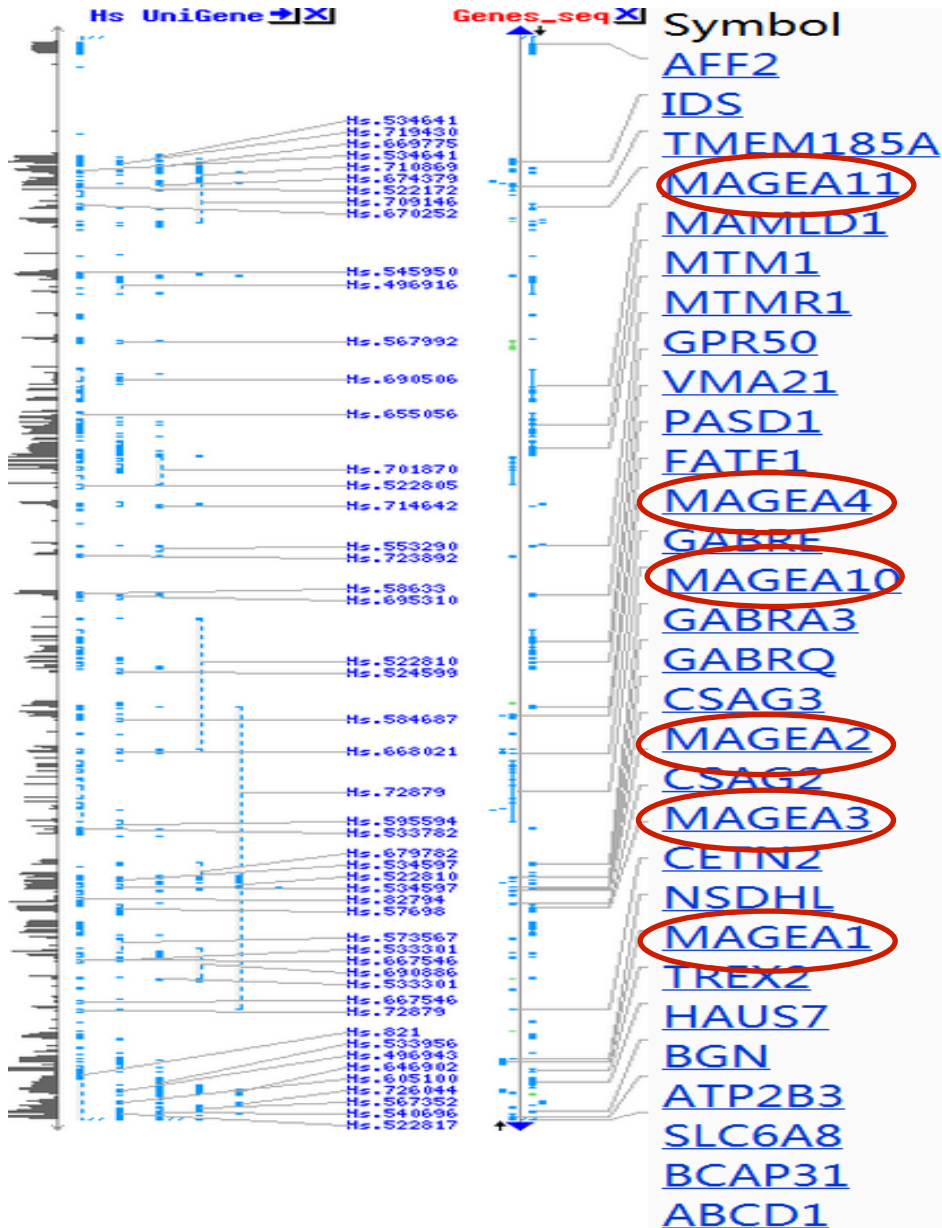
MAGE家族

人类MAGE基因家族有10个亚家族。根据表达类型和功能，又可以分为两种类型。

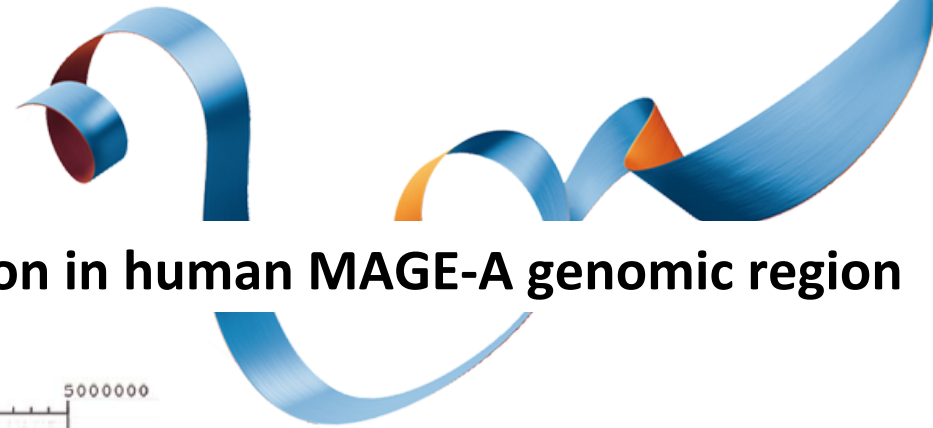
I型基因，定位于X染色体，编码癌症细胞里面的人体白细胞抗原（human leukocyte antigen, HLA)的抗原决定簇。包括MAGE-A, B, C三个亚家族。I型基因在高度增殖的细胞里表达，如肿瘤，胎盘，生殖细胞。

II型基因，比较古老，某些的编码产物是与细胞增殖和凋亡相关的。包括7个亚家族。

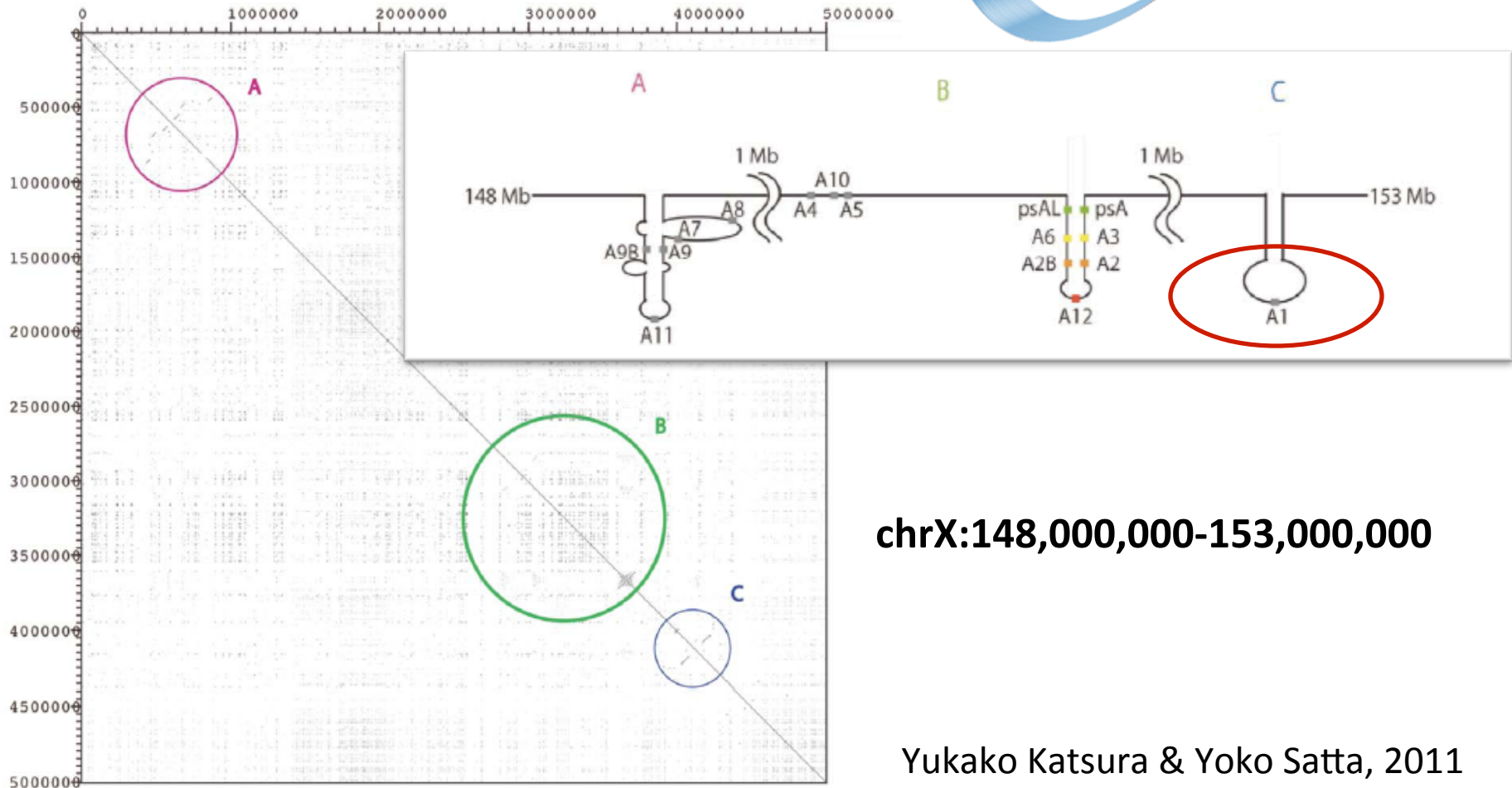
基因结构



基因结构



Genomic structure, palindrome prediction in human MAGE-A genomic region



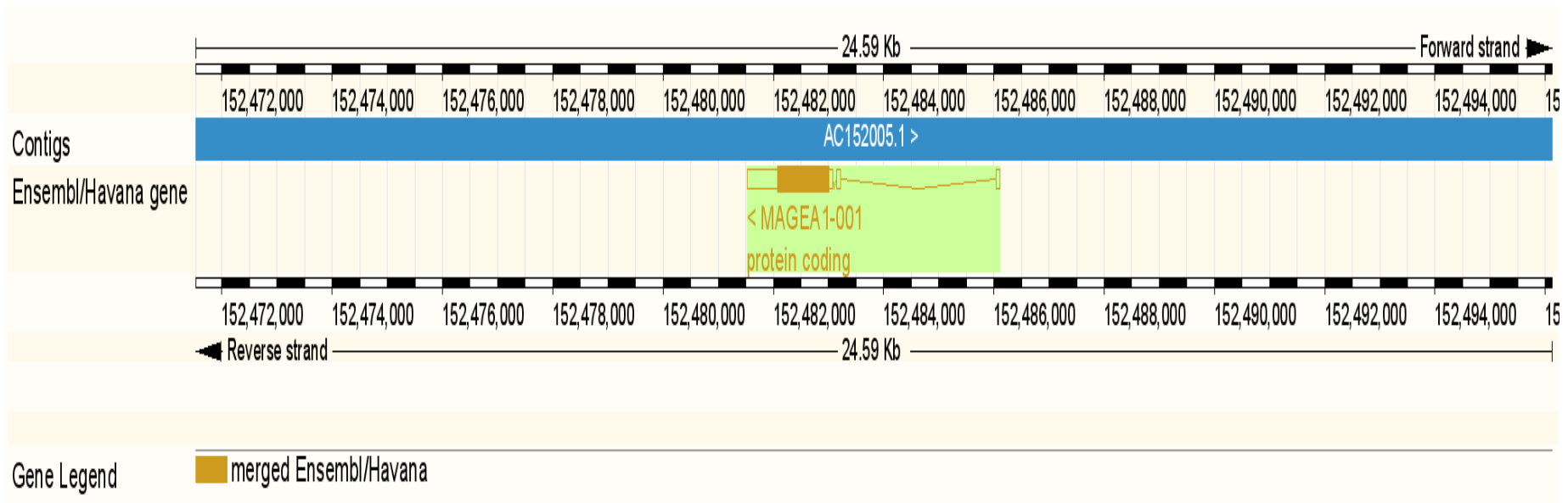
Yukako Katsura & Yoko Satta, 2011

MAGEA1

melanoma antigen family A, 1
[Homo sapiens]



Location: Xq28 152481522..152486116



MAGEA1核酸序列分析



BLAST

Chimpanzee (*Pan troglodytes*) 98.9%

Macaque (*Macaca mulatta*) 80.2%

Dog (*Canis lupus*) 56.7%

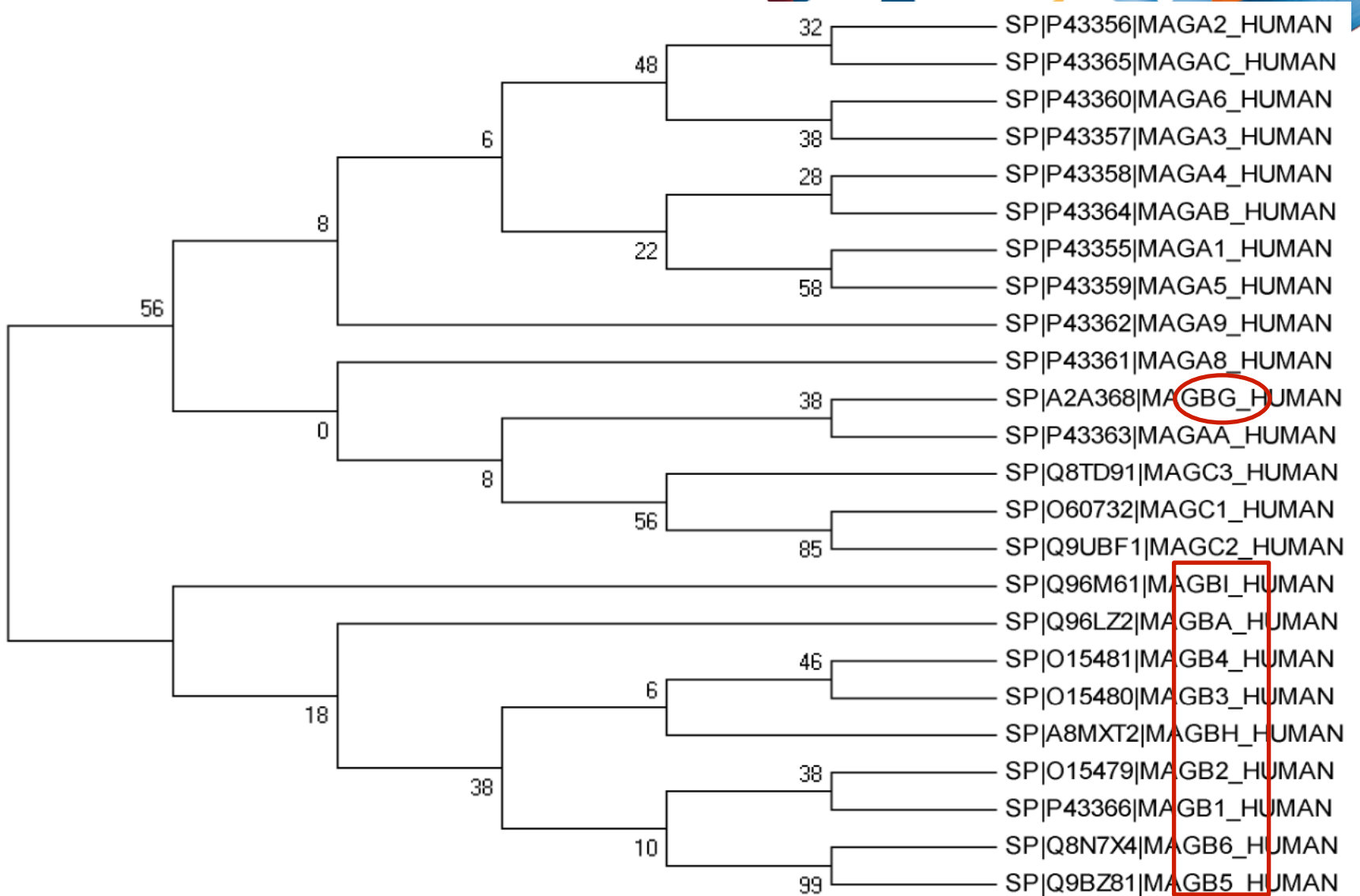
Mouse 52.4%



Human/Fly (CDS)

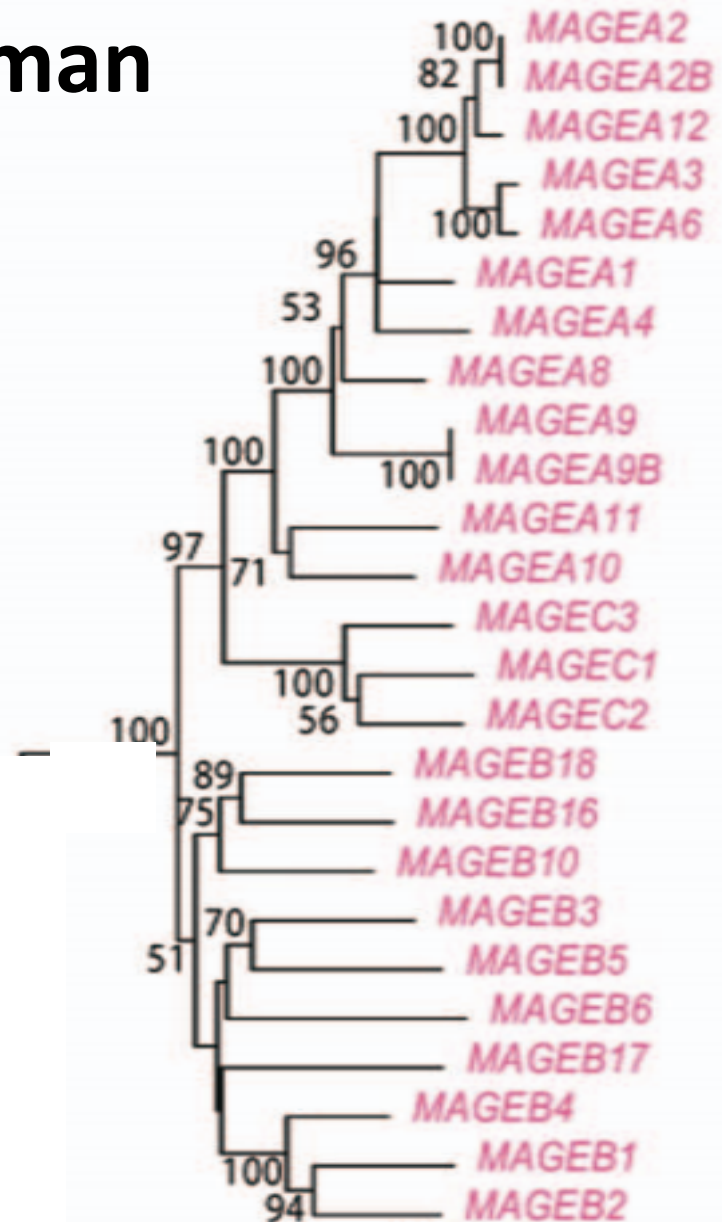
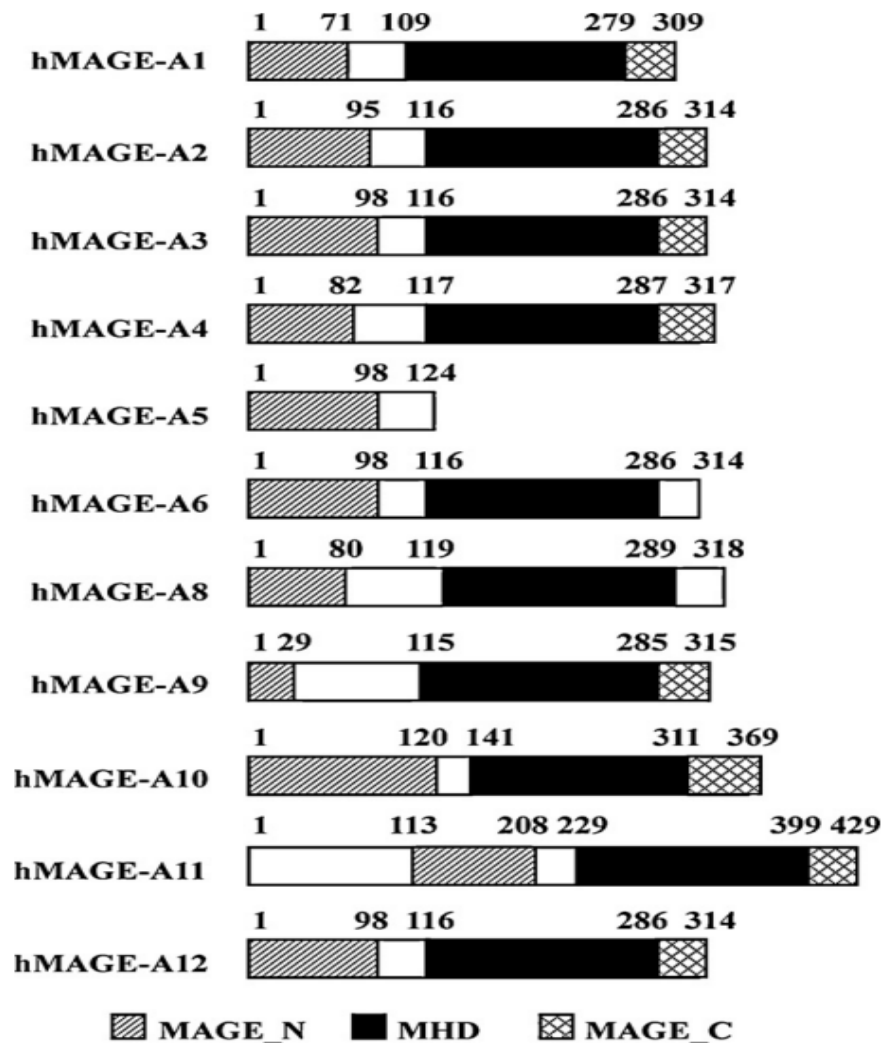
LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
1045	672.5	442/1045 (42.3%)	442/1045 (42.3%)	467/1045 (44.7%)

Phylogeny



MAGE family A, B, C Phylogenetic Tree

Phylogeny of MHD in human MAGE genes



MAGEA1序列分析

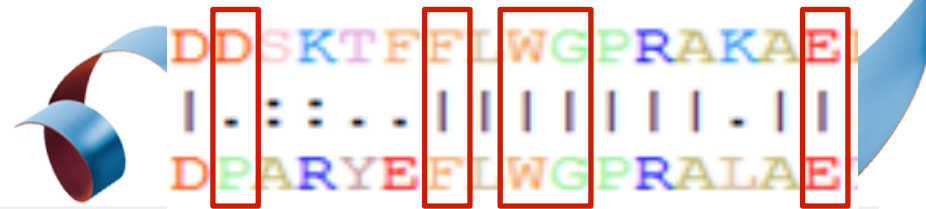


Human/Fly

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
226	148.0	50/226 (22.1%)	102/226 (45.1%)	38/226 (16.8%)

MAGEA1_Human	101	VITKKVADLVGFLLLKYRAREPVTKAEMLESVIKNYKHCFFEIFGKASE-	149
MAGE_Fly	25	VVDAKVRAILNLYILDHTAQKIPKDKDLI-----AVAGDKSEL	62
MAGEA1_Human	150	--SLQLV-----FGIDVKEADPTGHSYVLVTCLGLSYDGLLGDNQI--	188
MAGE_Fly	63	KKRLPLVTNLLAETFGIILTPLDATTKTFICT-----AEEPVASIHELTP	107
MAGEA1_Human	189	--MPKTGFLIIIVLVMIAMEGGHAPEEEIWEELSVMEVYDGREHSAYG-EP	235
MAGE_Fly	108	AQRQFTILLYIILMYIFLRGNRIEDSKLYVMLEMLNIYPDEEHGYFGPNL	157
MAGEA1_Human	236	RKLLTQDLVQEKYL--EYRQVPDSDPAPFEFLWGFPRALAEISYVKVLEYV	283
MAGE_Fly	158	RKQIEETFVKQQYLKRERSQLSAYDDSYTFFLWGFPRAKAEFEQMVQFA	207
MAGEA1_Human	284	IKVSARVRFPPSLREAAALREEEEGV	309
MAGE_Fly	208	SKLLNQ----HPKVFGHHL SMAQEGV	229

MAGEA1序列分析



6 MA13P_HL	V	Q	E	K	Y	L	E	C	C	Q	V	S	N	S	D	P	P	R	Y	K	F	P	W	G	P	R	A	H	A	E	T
5 MAGA1_HL	V	Q	E	K	Y	L	E	Y	R	Q	V	P	D	S	D	P	A	R	Y	E	F	L	W	G	P	R	A	L	A	E	T
8 MAGA2_HL	V	Q	E	N	Y	L	E	Y	R	Q	V	P	G	S	D	P	A	C	Y	E	F	L	W	G	P	R	A	L	I	E	T
7 MAGA3_HL	V	Q	E	N	Y	L	E	Y	R	Q	V	P	G	S	D	P	A	C	Y	E	F	L	W	G	P	R	A	L	V	E	T
8 MAGA4_HL	V	Q	E	N	Y	L	E	Y	R	Q	V	P	G	S	N	P	A	R	Y	E	F	L	W	G	P	R	A	L	A	E	T
9 MAGA5_HL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
0 MAGA6_HL	V	Q	E	N	Y	L	E	Y	R	Q	V	P	G	S	D	P	A	C	Y	E	F	L	W	G	P	R	A	L	I	E	T
1 MAGA8_HL	V	Q	E	N	Y	L	E	Y	R	Q	A	P	G	S	D	P	V	R	Y	E	F	L	W	G	P	R	A	L	A	E	T
2 MAGA9_HL	V	Q	E	N	Y	L	E	Y	R	Q	V	P	G	S	D	P	A	H	Y	E	F	L	W	G	S	K	A	H	A	E	T
3 MAGAA_HL	V	Q	E	N	Y	L	E	Y	R	Q	V	P	G	S	D	P	A	R	Y	E	F	L	W	G	P	R	A	H	A	E	I
4 MAGAB_HL	V	Q	E	K	Y	L	V	Y	R	Q	V	P	G	T	D	P	A	C	Y	E	F	L	W	G	P	R	A	H	A	E	T
5 MAGAC_HL	V	Q	E	N	Y	L	E	Y	R	Q	V	P	G	S	D	P	A	C	Y	E	F	L	W	G	P	R	A	L	V	E	T
6 MAGB1_HL	V	Q	E	K	Y	L	K	Y	E	Q	V	P	N	S	D	P	P	R	Y	Q	F	L	W	G	P	R	A	Y	A	E	T
79 MAGB2_HL	V	Q	E	K	Y	L	E	Y	K	Q	V	P	S	S	D	P	P	R	F	Q	F	L	W	G	P	R	A	Y	A	E	T
80 MAGB3_HL	V	K	L	K	Y	L	E	Y	R	Q	V	P	N	S	N	P	A	R	Y	E	F	L	W	G	P	R	A	H	A	E	T
81 MAGB4_HL	V	Q	E	K	Y	L	E	Y	Q	Q	V	P	N	S	D	P	P	R	Y	Q	F	L	W	G	P	R	A	H	A	E	T
81 MAGB5_HL	V	R	L	T	Y	L	E	Y	H	Q	V	P	C	S	Y	P	A	H	Y	Q	F	L	W	G	P	R	A	Y	T	E	T
X4 MAGB6_HL	V	Q	D	K	Y	V	V	Y	R	Q	V	C	N	S	D	P	P	C	Y	E	F	L	W	G	P	R	A	Y	A	E	T
Z2 MAGBA_HL	V	K	E	N	Y	L	E	Y	Q	Q	V	P	N	S	D	P	P	R	Y	Q	F	L	W	G	P	R	A	H	A	E	T
68 MAGBG_HL	V	K	E	K	Y	L	E	Y	Q	Q	V	A	N	S	D	P	A	R	Y	E	F	L	W	G	P	R	A	K	A	E	T
161 MAGBI_HL	V	Q	L	K	Y	L	E	Y	Q	Q	V	P	N	S	D	P	P	R	Y	E	F	L	W	G	P	R	A	H	A	E	T
32 MAGC1_HL	V	Q	E	H	Y	L	E	Y	R	E	V	P	N	S	S	P	P	R	Y	E	F	L	W	G	P	R	A	H	S	E	V
IF1 MAGC2_HL	V	Q	G	H	Y	L	E	Y	R	E	V	P	H	S	S	P	P	Y	Y	E	F	L	W	G	P	R	A	H	S	E	S
91 MAGC3_HL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
V3 MAGD1_HL	V	K	Q	K	Y	L	D	Y	R	R	V	P	N	S	N	P	P	E	Y	E	F	L	W	G	L	R	S	Y	H	E	T
IF1 MAGD2_HL	V	K	Q	K	Y	L	D	Y	A	R	V	P	N	S	N	P	P	E	Y	E	F	F	W	G	L	R	S	Y	Y	E	T
G8 MAGD4_HL	V	K	Q	K	Y	L	E	Y	K	K	I	P	N	S	N	P	P	E	Y	E	F	L	W	G	L	R	A	R	H	E	T
15 MAGE1_HL	V	W	Q	R	Y	L	D	Y	R	P	V	T	D	C	K	P	V	E	Y	E	F	F	W	G	P	R	S	H	L	E	T
90 MAGE2_HL	V	C	M	R	F	L	E	Y	W	P	V	Y	G	T	N	P	L	E	F	E	F	L	W	G	S	R	A	H	R	E	I
V2 MAGF1_HL	V	Q	Q	R	Y	L	S	Y	R	R	V	P	H	T	N	P	P	E	Y	E	F	S	W	G	P	R	S	N	L	E	I
1G7 MAGG1_HL	V	R	Q	R	Y	L	E	Y	R	R	I	P	H	T	D	P	V	D	Y	E	F	Q	W	G	P	R	T	N	L	E	T
13 MAGH1_HL	V	R	R	G	Y	L	I	Y	K	P	V	P	R	S	S	P	V	E	Y	E	F	F	W	G	P	R	A	H	V	E	S
55 MAGL2_HL	V	R	Q	K	Y	L	E	Y	R	R	I	P	Y	T	E	P	A	E	Y	E	F	L	W	G	P	R	A	F	L	E	T
16 TROP_HL	V	K	Q	K	Y	L	E	Y	K	R	V	P	N	S	R	P	P	E	Y	E	F	F	W	G	L	R	S	Y	H	E	T

MAGEA1_HUMAN结构预测



Swiss Model

Template: MAGEA4

Modeled residue range: 95 to 304

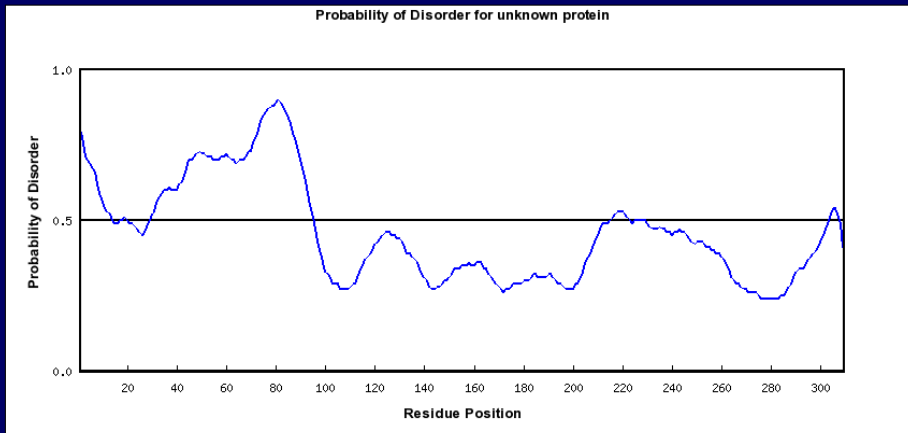
Workunit: P000002 Title: MAGEA1_HUMAN



Disordered regions

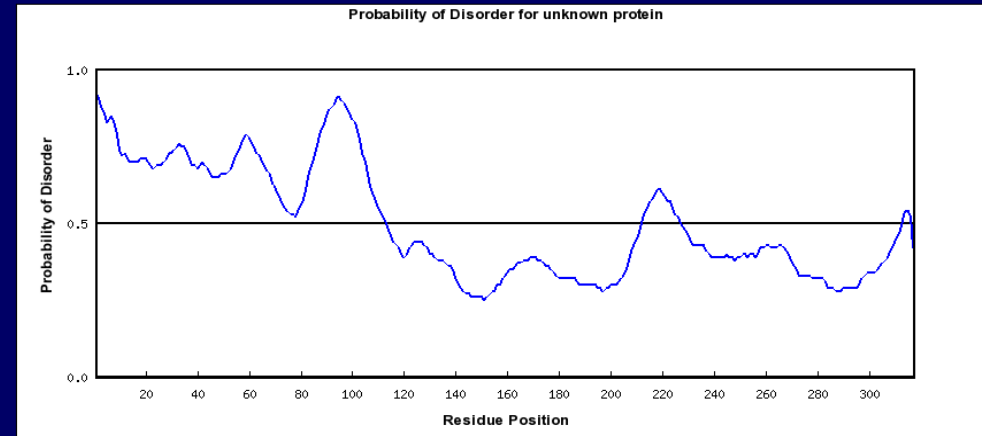


Disordered regions:
1 - 13, 19 - 19, 30 - 95, 216 - 222, 304 - 307



MAGEA1

Disordered regions:
1 - 112, 213 - 226, 313 - 316



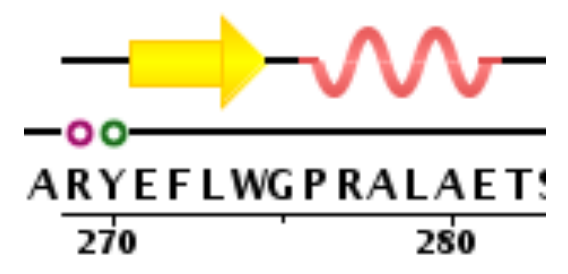
MAGEA4

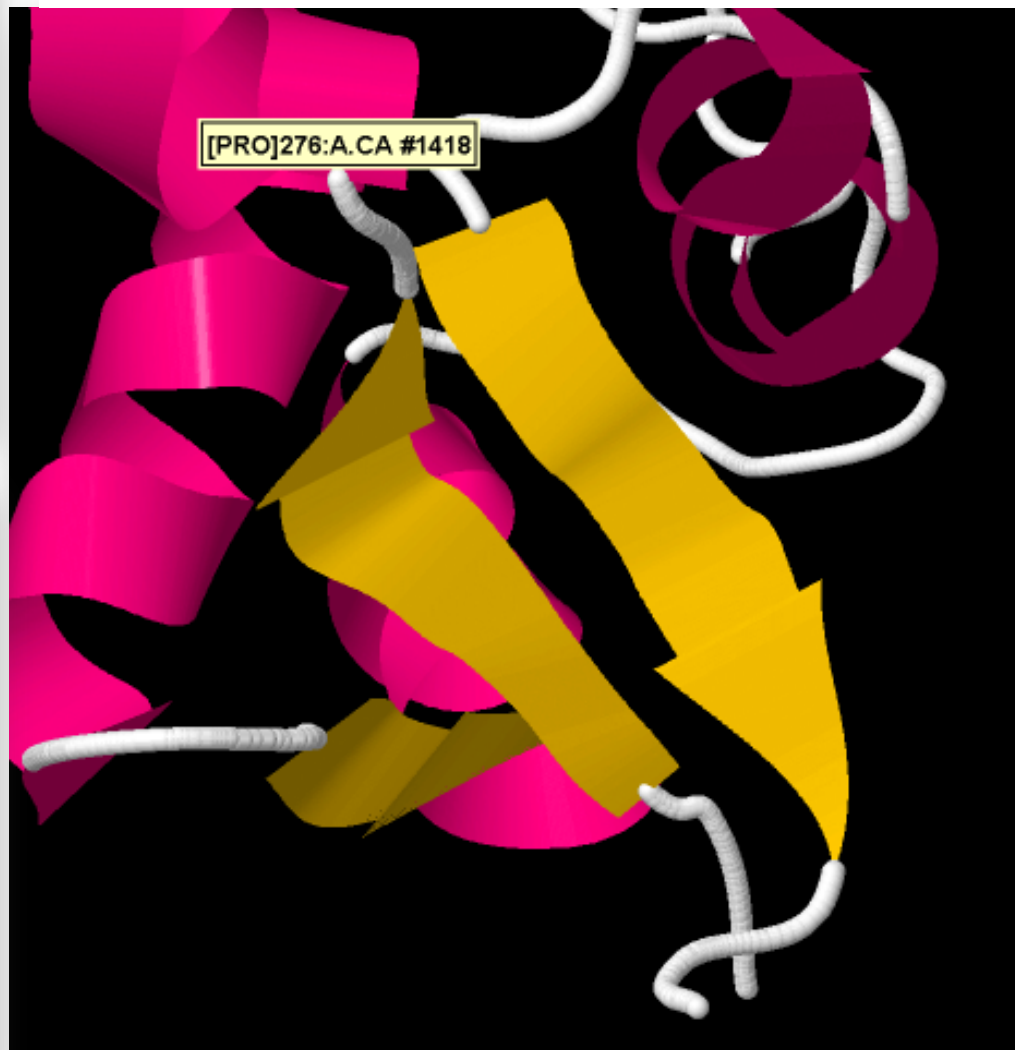
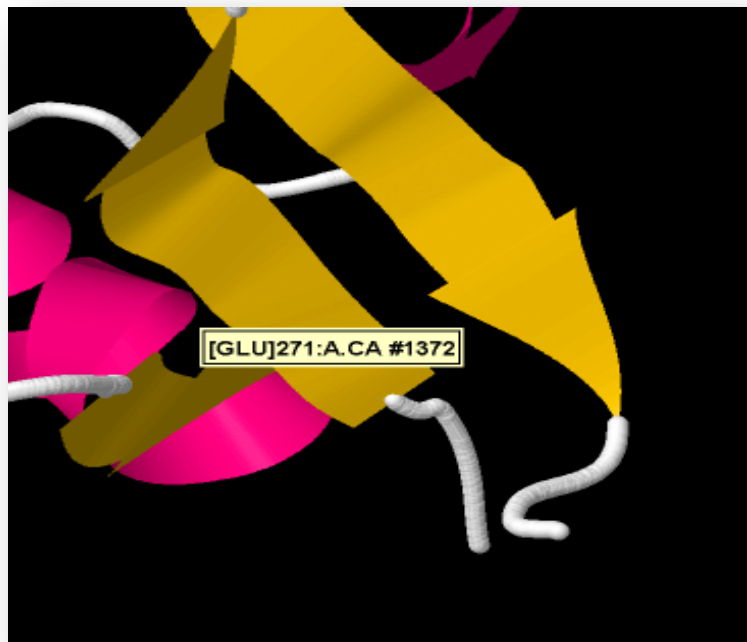


MAGEA1 (Predict)



MAGEA4







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Thanks !