

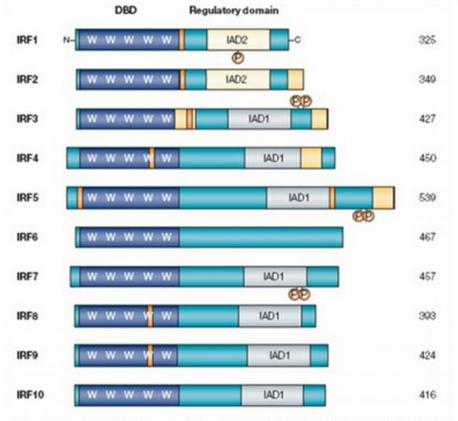
人IRF3(Interferon regulatory factor 3) 蛋白的生物信息学分析

G8: 巨艳 黄宁 李曾龙 管玉 坤

2012-6-11



The IRF family of transcription factors

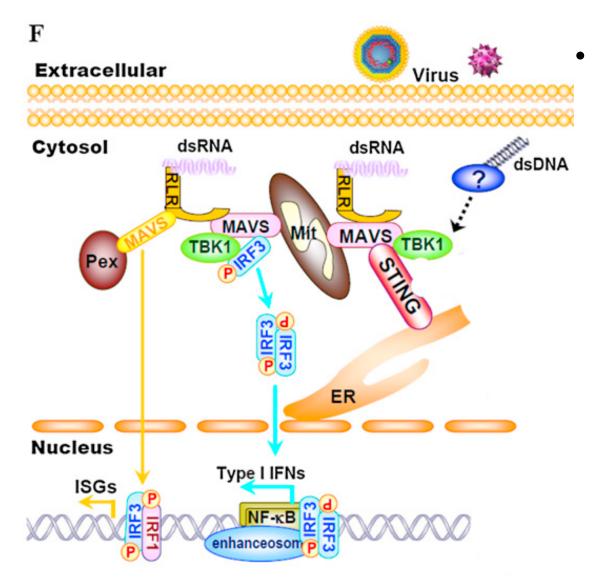


modified from: Lohoff & Mak Nat. Immunol. 2005

Figure 1 | Structure of Interferon-regulatory factors. All interferon-regulatory factors (IRFs) are composed of a DNA-binding domain (DBD; blue) and a regulatory domain (green). For all IRFs, the DBD is defined by 5 tryptophan (W) residues that are each separated by 10–18 amino acids. Most IRFs also contain an IRF-association domain (IAD) of either type 1 (grey) or type 2 (pale yellow). Some IRFs contain a repression domain(s) (yellow) and a nuclear-import signal(s) (orange). [AU:IRF5 has 2 orange domains, correct?] For IRF1, -3, -5 and -7, activity depends on phosphorylation, as shown. The size of each IRF in number of amino acids is also indicated. C, carboxyl terminus; N, amino terminus.



背景介绍



IRF3组成性表达在多 种细胞中, 主要存在 于细胞浆中,病毒感 染等因素可诱导IRF3 磷酸化,使IRF3形成 二聚体并移位至细胞 核,并与其他转录因 子如CBP/p300结合诱 导具有ISRE启动子序 列的基因表达,例如 IFN α / β, 在抗感染 免疫中发挥重要作用。



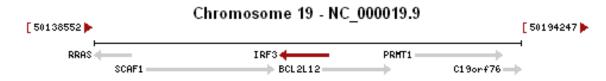
NCBI IRF3

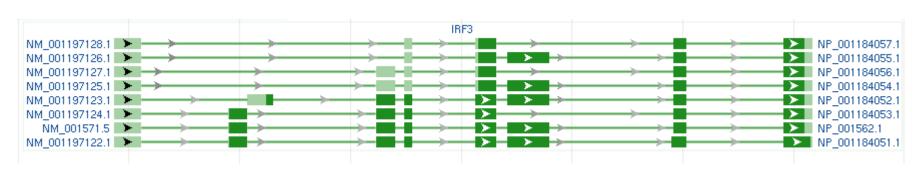
IRF3 interferon regulatory factor 3 [Homo sapiens]

Gene ID: 3661, updated on 2-Jun-2012

Location: 19q13.3-q13.4

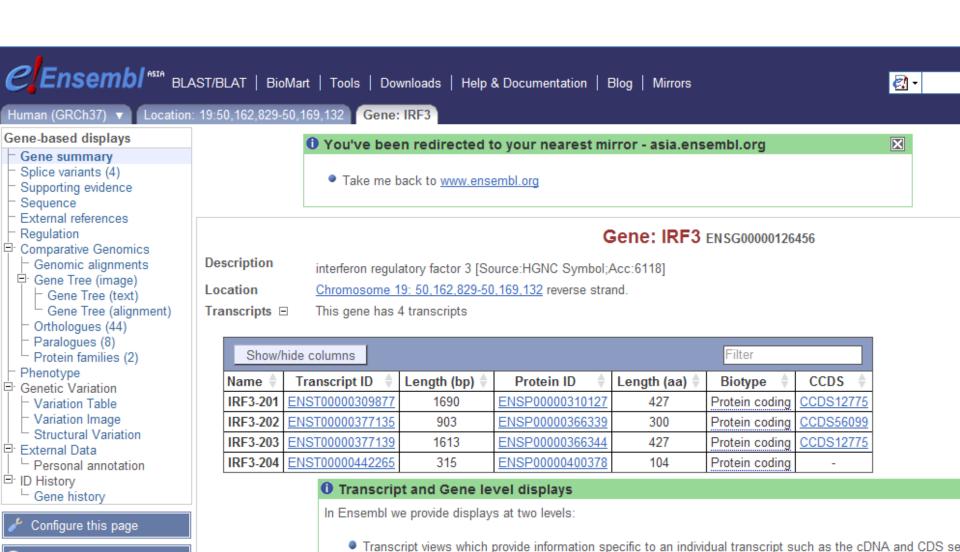
Sequence: Chromosome: 19; NC_000019.9 (50162826..50169132, complement)







Ensembl IRF3





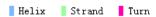
Uniprot IRF3

UniProt > UniProtKB	
Search Blast	
Protein Knowledgebase (UniPro	Query tKB) ✓ Search A
Q14653 (IRF3_HUMAN) ☆ Rev Last modified May 16, 2012. V	viewed, UniProtKB/Swiss-Prot Gersion 117. N History
Clusters with 100%, 90%,	50% identity 🗅 Documents (6) 📵 Third-party data
	eneral annotation · Ontologies · Interactions · Alt produc
Entry info · Documents (Customize order
Names and origin	
Protein names	Recommended name: Interferon regulatory factor 3 Short name=IRF-3
Gene names	Name: IRF3
Organism	Homo sapiens (Human)
Taxonomic identifier	9606 [NCBI]
Taxonomic lineage	Eukaryota > Metazoa > Chordata > Craniata > Vertebrata > Eutele Catarrhini > Hominidae > Homo
Protein attributes	
Sequence length	427 AA.
Sequence status	Complete.
Protein existence	Evidence at protein level



IRF3 结构域

Secondary structure



Molecule processing

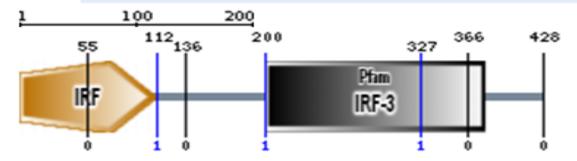
□ Chain	1 - 427	427	Interferon regulatory factor 3	

Regions

DNA binding	5 - 111	107	IRF tryptophan pentad repeat	
Region	200 - 360	161	Involved in HERC5 binding	
Motif	139 - 149	11	Nuclear export signal	
Compositional bias	151 - 191	41	Pro-rich	

SMART

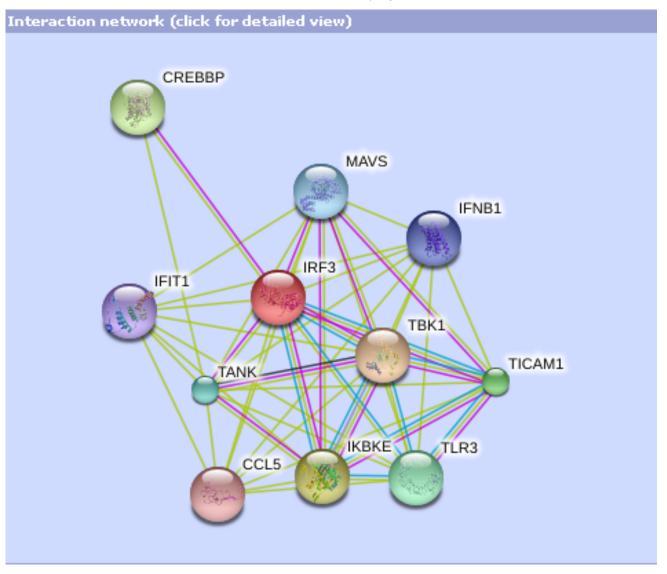
Interferon regulatory factor 3



Name	Begin	End	E-value
IRF	1	112	1.49e-54
Pfam:IRF-3	201	380	7.60e-47



TRF3 相互作用蛋白





PDB IRF3 结构





Alignment

Learn how to print this alignment in color

1	MGTPKPRILPWLVSQLDLGQLEGVAWVNKSRTRFRIPWKHGLRQDAQQEDFGIFQAWAEA	60	Q14653	IRF3_HUMAN
1	MGTQKPRILPWLISQLDRGELEGVAWLGESRTRFRIPWKHGLRQDAQQEDFGIFQAWAVA	60	Q4JF28	IRF3_BOVIN
1	MGTPKPLILPWLVSQLDLGQLKGVAWLDESRTKFRIPWKHGLRQDAQMADFGIFQAWAEA	60	Q5XIBO	Q5XIBO_RAT
1	MGTQKPRILPWLISQLNQGQLEGVAWLDEGHTRFRIPWKHGLRQDAQQEDFGIFQAWAEA	60	Q764M6	IRF3_PIG
1	METPKPRILPWLVSQLDLGQLEGVAWLDESRTRFRIPWKHGLRQDAQMADFGIFQAWAEA	60	P70671	IRF3_MOUSE
	$*\ *\ *o $			
61	TGAYVPGRDKPDLPTWKRNFRSALNRKEGLRLAEDRSKDPHDPHKIYEFVNSG-VGDFSQ	119	Q14653	IRF3_HUMAN
61	SGAYTPGKDKPDLPTWKRNFRSALNRKEVLRLAEDHSKDSQDPHKIYEFVNSG-VRDIPE	119	Q4JF28	IRF3_BOVIN
61	SGAYTPGKDKPDLSTWKRNFRSALNRKEVLRLAEDRSKDPFDPHKVYEFVTPGGARDFVH	120	Q5XIBO	Q5XIBO_RAT
61	SGAYTPGKDKPDLPTWKRNFRSALNRKEALRLAEDHSKDPHDPHKIYEFVTSG-VGDFPE	119	Q764M6	IRF3_PIG
61	SGAYTPGKDKPDVSTWKRNFRSALNRKEVLRLAADNSKDPYDPHKVYEFVTPG-ARDFVH	119	P70671	IRF3_MOUSE
	; work, work; workers acceptated acceptation of the contraction of the			25/25/2

Guide tree

QSXIBO	Q5XIBO RAT
P70671	Q5XIBO_RAT IRF3_MOUSE IRF3_HUMAN IRF3_BOVIN IRF3_PIG
Q14653	IRF3_HUMAN
Q4JF28	IRF3_BOVIN
Q764M6	IRF3_PIG

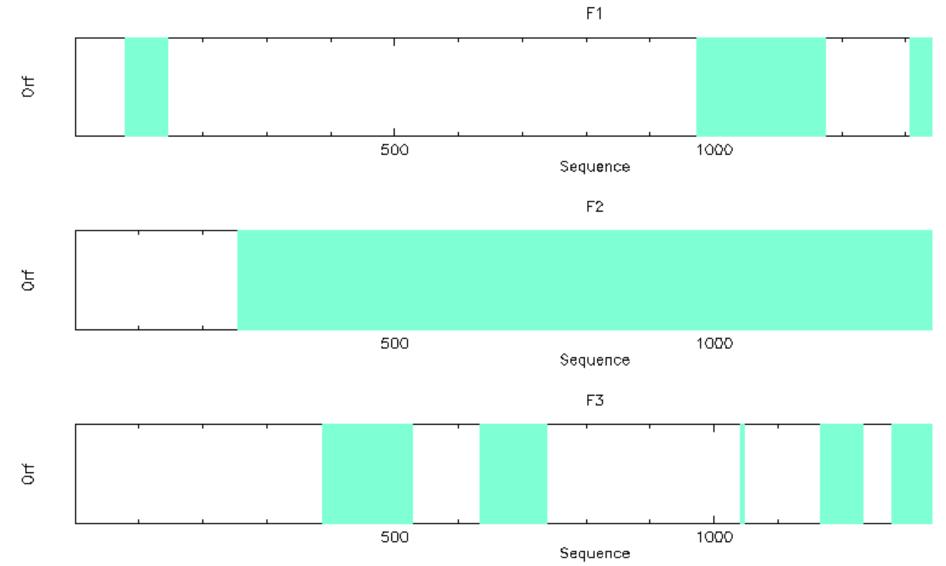


北京大学 PEKING UNIVERSITY IRF3 酶切位点分析

161 161	XhoI Bsi	TGTCCCCACCCAAGGTCGAC CRI BslI Nla mII XemI HKAI BbvI 286I	GGGCGTGCGGGGCTGGAAGGTA	
241	CGTAGGCCGGACCATGGGAACCCCAAAGCCACGGATCC	TGCCCTGGCTGTCTCGCAG	CTGGACCTGGGGCAACTGGAGG	320
241	GCATCCGGCCTGGTACCCTTGGGGTTTCGGTGCCTAGC			
	BsaJI NlaIV AlwI	NlaIV TspGWI	MspA1I BbvI	BsrI
	BtgI BsaJI	•	oI PvuII MnlI	
	NcoI BtgI		pyF10VI BsaJI	14411
	StyI Ban		pyrrovi bsaji	
	BslI Bs			
	Hin4I	.11		
	Hin4I			
	MINT			
321	GCGTGGCCTGGGTGAACAAGAGCCGCACGCGCTTCCGG	ATCCCTTGGAAGCACGGCCT	'ACGGCAGGATGCACAGCAGGAG	400
321	CGCACCGGACCCACTTGTTCTCGGCGTGCGCGAAGGCC	TAGGGAACCTTCGTGCCGGA	TGCCGTCCTACGTGTCGTCCTC	400
	BsaJI Hpy8I HphI HpyF10	VI Bsa∏	SfaNI BceAI	BceAI
	BpmI FokI	BstF5I SfaNI	EcoNI Bst	F5I
	Eco57MI Cac8I	StyI	BslI MmlI	FokI
	MwoI	-		

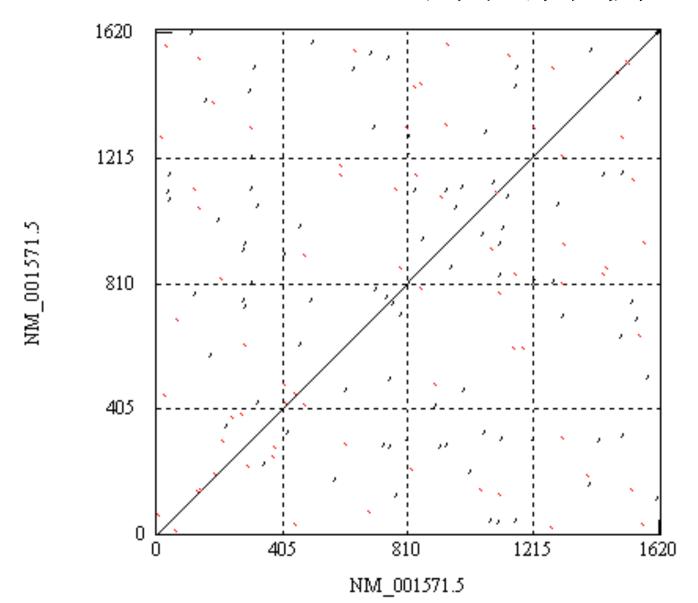


IRF3 ORF分析





TRF3 mRNA点阵图分析





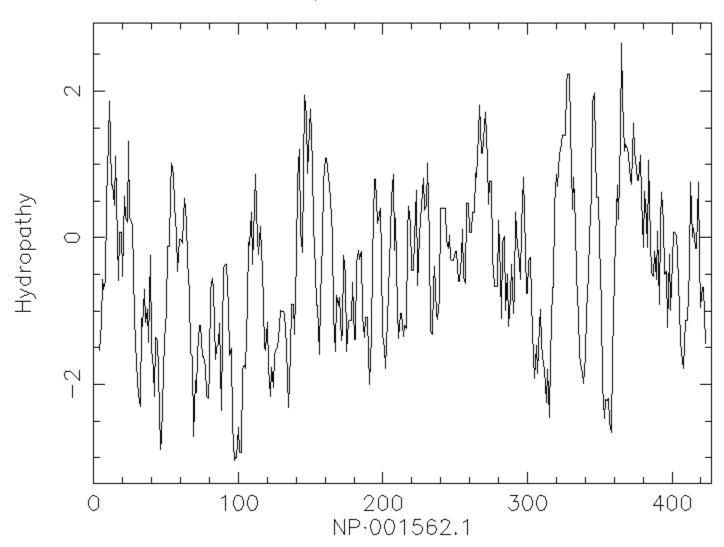
北京大学 PEKING UNIVERSITY IRF3 氨基酸组成分析

Residue		Number	Mole%		DayhoffS	tat
A = Ala		21	4.918		0.572	
B = Asx		0	0.000		0.000	
C = Cys		6	1.405		0.485	
D = Asp		28	6.557		1.192	
E = Glu		26	6.089		1.015	
F = Phe		15	3.513		0.976	
G = Gly		43	10.070		1.199	
H = His		9	2.108		1.054	
I = Ile		9	2.108		0.468	
J =		0	0.000		0.000	
K = Lys		14	3.279		0.497	
L = Leu		47	11.007		1.487	
M = Met		7	1.639		0.964	
N = Asn		12	2.810		0.654	
0 =		0	0.000		0.000	
P = Pro		42	9.836		1.892	
Q = Gln		19	4. 450		1.141	
R = Arg		26	6.089		1.243	
S = Ser		30	7. 026		1.004	
T = Thr		21	4. 918		0.806	
v =		0	0.000		0.000	
V = Val		30	7.026		1.065	
W = Trp		14	3, 279		2.522	
X = Xaa		0	0.000		0.000	
Y = Tyr		8	1.874		0.551	
Z = Glx		0	0.000		0.000	
Property	Resi dues	Numb	er	Mole%		
Tiny		(A+C+G+S+T)		121		28.337
Small		(A+B+C+D+G+N+P+	S+T+V) 233		54, 567	
Aliphatic	(A+I+L+V)	107		25, 059		
Aromatic	(F+H+W+Y)	46		10.773		
Non-polar	(A+C+F+G+I	+ <u>L</u> +M+P+V+W+Y)	242		56.674	
Polar		(D+E+H+K+N+Q+R+	S+T+Z) 185		43.326	
Charged		(B+D+E+H+K+R+Z)	l	103		24.122
Basic		(H+K+R)		49		11.475



IRF3 疏水性分析

Kyte-Doolittle Plot





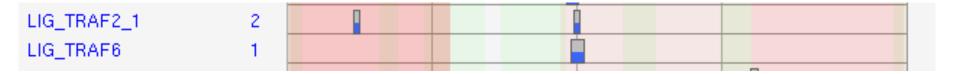
TRF3 二级结构分析

20 . 30 . 40 . 10 . MGTPKPRILPWLVSQLDLGQLEGVAWVNKSRTRFRIPWKHGLRQDAQQED жж helix EEEEEEEE E E sheet turns T T TTTTTT TT coil CCCCC CCCC C c cccccccc . 60 . 70 . 80 . 90 . 100 FGIFQAWAEATGAYVPGRDKPDLPTWKRNFRSALNRKEGLRLAEDRSKDP helix ИННИН жини sheet EE turns TT TTTT TTT TT TTTTT T TTTT T coil C C C CC C CCCC . 110 . 120 . 130 . 140 . 150 HDPHKIYEFVNSGVGDFSQPDTSPDTNGGGSTSDTQEDILDELLGNMVLA жининин Е Е helix sheet EEEEEE EE T T TT T TT TT turns . 160 . 170 . 180 . 190 . 200 PLPDPGPPSLAVAPEPCPOPLRSPSLDNPTPFPNLGPSENPLKRLLVPGE helix sheet E EEEE E EE EE EEEE TTT TT TTTT T turns coil CCCCCCC CC cccc cccccc CCC . 210 . 220 . 230 . 240 . 250 EWEFEVTAFYRGROVFQQTISCPEGLRLVGSEVGDRTLPGWPVTLPDPGM helix HOHHHHHH EEEE EEEE EE sheet turns TTTTT TT TTT TTT TT coil CC C CC C . 260 . 270 . 280 . 290 . 300 CT TIDAMICVIADUA CAT ACAT AT WOACOUT WAODT AUGUSTWAIJCOUT T

SLTDRGVMSYVRHVLSCLGGGLALWRAGQWLWAQRLGHCHTYWAVSEELL нннн helix sheet EEEE EEEEEEEEE EEEE TT TTT T TTTTTTT T turns TTT cc cc coil CC . 310 . 320 . 330 . 340 . 350 PNSGHGPDGEVPKDKEGGVFDLGPFIVDLITFTEGSGRSPRYALWFCVGE helix HH sheet EE EEE EEEEEEE turns TTTT T T TT T TTTT TTTT coil CCC C C CCC C CC . 360 . 370 . 380 . 390 . 400 SWPQDQPWTKRLVMVKVVPTCLRALVEMARVGGASSLENTVDLHISNSHP helix X HOHHHHHHHH ининин sheet EEEEEEEE turns T TT TT Т coil CC C C CCCCCC CC CCC . 410 . 420 LSLTSDQYKAYLQDLVEGMDFQGPGES helix sheet EE EEEEEEEE turns T TTT TTT coil C C # Residue totals: H: 67 E:114 T:123 C:123 # percent: H: 16.3 E: 27.7 T: 29.9 C: 29.9 # Total sequences: 1 # Total hitcount: 142



TRAF结合位点



LIG_TRAF2_1

(Probability: 0.0042998)

<< LIG_TPR << Menu >> LIG_TRAF2_2 >>

Functional Site Class: TRAF2 binding site

Functional site

description:

Endogenous TRAF2 is a cytosolic protein that is recruited to membrane associated receptors.

ELMs: LIG_TRAF2_1 LIG_TRAF2_2

Description: Major TRAF2-binding consensus motif. Members of the tumor necrosis factor receptor (TNFR) superfamily initiate intracellular signaling by recruiting

the C-domain of the TNFR-associated factors (TRAFs) through their cytoplasmic tails.

Pattern: [PSAT].[QE]E

Present in taxons: Eukaryota

Interaction Domain: MATH (PF00917)

MATH domain (Stochiometry: 1 : 1)

■ See 14 Instances for LIG_TRAF2_1



TRAF结合位点

Menu

LIG_TRAF6

>> LIG_TRFH_1 >>

(Probability: 0.0017147)

<< LIG_TRAF2_2 <<

Functional Site Class: Functional site

description:

TRAF6 protein acts as intracellular adaptor that is recruited to different receptors through its C-terminal TRAF domain.

ELMs: LIG_TRAF6

Description: TRAF6 binding site. Members of the tumor necrosis factor receptor (TNFR) superfamily initiate intracellular signaling by recruiting the C-domain of the

TNFR-associated factors (TRAFs) through their cytoplasmatic tails.

Pattern: ..p.E..[FYWHDE].

Present in taxons: Vertebrata

Interaction Domain: MATH (PF00917)

MATH domain

TRAF6 binding site

(Stochiometry: 1:1)

■ See 20 Instances for LIG_TRAF6



磷酸化位点预测

Home PhosphoBlast Contribute Download Help Links About

Substrate: IRF3 (Transcription factor)

Seq-ID: Q14653 [Homo sapiens]

Interaction Network(s): STRING NetworkIN

External Source(s):

PhosphoSitePlus*

MINT Interaction(s): [show]
GO-Terms: [show]

Conservation:

Click on table h

Res. \$	Pos. \$	Sequence \$	Kinase \$	PMID \$	Src \$	Cons. \$	ELM \$	Binding Domain	SMART/Pfam \$	IUPRED score	PDB \$	P3D Acc. \$
S	385	LVEMARVGGASSLENTVDLHI	-	9463386	LTP	1.00		-	-	0.32	1QWT	40.98%
S	385	LVEMARVGGASSLENTVDLHI	-	14703513	LTP	1.00		-	-	0.32	1QWT	40.98%
S	385	LVEMARVGGASSLENTVDLHI	TBK1	17526488	LTP	1.00		-	-	0.32	1QWT	40.98%
S	386	VEMARVGGASSLENTVDLHIS	-	9463386	LTP	0.99		-	-	0.35	1QWT	111.48%
S	386	VEMARVGGASSLENTVDLHIS	IKK_epsilon	14703513	LTP	0.99		-	-	0.35	1QWT	111.48%
S	386	VEMARVGGASSLENTVDLHIS	TBK1	14703513	LTP	0.99		-	-	0.35	1QWT	111.48%
S	386	VEMARVGGASSLENTVDLHIS	TBK1	17526488	LTP	0.99		-	-	0.35	1QWT	111.48%
S	396	SLENTVDLHISNSHPLSLTSD	-	12524442	LTP	1.00		-	-	0.40	1QWT	23.77%
S	396	SLENTVDLHISNSHPLSLTSD	-	17526488	LTP	1.00		-	-	0.40	1QWT	23.77%
S	398	ENTVDLHISNSHPLSLTSDQY	-	9566918	LTP	0.31		-	-	0.36	1QWT	40.16%
S	402	DLHISNSHPLSLTSDQYKAYL	-	9566918	LTP	0.20		-	-	0.26	1QWT	46.72%
Т	404	HISNSHPLSLTSDQYKAYLQD	-	9566918	LTP	0.16		-	-	0.25	1QWT	35.62%
S	405	ISNSHPLSLTSDQYKAYLQDL	-	9566918	LTP	0.09		-	-	0.26	1QWT	33.61%
S	405	ISNSHPLSLTSDQYKAYLQDL	-	17526488	LTP	0.09		-	-	0.26	1QWT	33.61%



IRF 家族

		V-			V	V-				
	Search	Blast		Align	Retrieve	ID Mapping *				
Searc	:h in		C	Query						
Protein Knowledgebase (UniProtKB) organism:human AND family:irf AND reviewed:yes										
result	ts for organ i	ism:human⊠ AN[) family:ir	f⊠ AND revie	ewed:yes⊠ in UniPı	rotKB sorted by scor	e descei	nding ⊠		
2 5		y, keyword, gene o			r pathway					Download
0)	ooquonoo .	outmumby to rear	, 0070 07							Page 1 of
	Columns: Pro	nize otein families								
	Entry	[‡] Entry name	Status	[‡] Protein na	ames		>1			[‡] Length
~	Q14653	IRF3_HUMAN	*	Interferon r	egulatory factor 3			IRF3	Homo sapiens (Human)	427
~	O14896	IRF6_HUMAN	*	Interferon r	egulatory factor 6			IRF6	Homo sapiens (Human)	467
~	Q92985	IRF7_HUMAN	*	Interferon r	egulatory factor 7			IRF7	Homo sapiens (Human)	503
v	P10914	IRF1_HUMAN	*	Interferon r	egulatory factor 1			IRF1	Homo sapiens (Human)	325
v	P14316	IRF2_HUMAN	*	Interferon r	egulatory factor 2			IRF2	Homo sapiens (Human)	349
~	Q15306	IRF4_HUMAN	*	Interferon r	egulatory factor 4			IRF4 MUM1	Homo sapiens (Human)	451

IRF5

IRF8 ICSBP1

IRF9 ISGF3G

IRF2BP1

IRF2BP2

IRF2BPL C14orf4 EAP1 KIAA1865 My039

. 16

Q13568

Q9H1B7

Q02556

Q8IU81

Q7Z5L9

Q00978

Page 1 of 1

498

796

426

584

587

393

Homo sapiens (Human)

IRF5_HUMAN

I2BPL_HUMAN

IRF8_HUMAN

I2BP1_HUMAN

I2BP2_HUMAN

IRF9_HUMAN

Interferon regulatory factor 5

Interferon regulatory factor 8

Interferon regulatory factor 9

Interferon regulatory factor 2-binding protei...

Interferon regulatory factor 2-binding protei...

Interferon regulatory factor 2-binding protei...



IRF 家族

```
-----MALAPERAAPRVLFGEWLLGEISSGCYEGLQWLDEARTCFRVPWKHFARK
                                                                  50
                                                                      Q92985
                                                                               IRF7_HUMAN
 1
      -----MNQSIPVAPTPPRRVRLKPWLVAQVNSCQYPGLQWVNGEKKLFCIPWRHATRH
                                                                  53
                                                                      Q13568
                                                                               IRF5 HUMAN
                                                                      Q15306
                                                                               IRF4_HUMAN
      MNLEGGGRGGEFGMSAVSCGNGKLRQWLIDQIDSGKYPGLVWENEEKSIFRIPWKHAGKQ
                                                                   60
             -----MCDRNGGRRLRQWLIEQIDSSMYPGLIWENEEKSMFRIPWKHAGKQ
                                                                      902556
                                                                               IRF8_HUMAN
            -----MASGRARCTRKLRNWVVEQVESGQFPGVCWDDTAKTMFRIPWKHAGKQ
                                                                  48
                                                                      Q00978
                                                                               IRF9_HUMAN
             -----MALHPRRVRLKPWLVAQVDSGLYPGLIWLHRDSKRFQIPWKHATRH
                                                                  46
                                                                      014896
                                                                               IRF6 HUMAN
                                                                  44 P10914
                                                                               IRF1 HUMAN
            -----MPITRMRMRPWLEMQINSNQIPGLIWINKEEMIFQIPWKHAAKH
                -----MPVERMRMRPWLEEQINSNTIPGLKWLNKEKKIFQIPWMHAARH
                                                                   44 P14316
                                                                               IRF2 HUMAN
                                                                  44 Q14653
                                                                               IRF3_HUMAN
                ----MGTPKPRILPWLVSQLDLGQLEGVAWVNKSRTRFRIPWKHGLRQ
                            : *: ::.
                                          *: * .
                                                     * (** * ))
 51
      DLSE-ADARIFKAWAVARGRWPPSSRGGGPPPEAETAERAGWKTNFRCALRSTRRFVMLR
                                                                  109
                                                                      Q92985
                                                                               IRF7_HUMAN
 54
                                                                      013568
                                                                               IRF5_HUMAN
      GPSQDGDNTIFKAWAKETGKYTEGVD-----EADPAKWKANLRCALNKSRDFRLIY
                                                                  104
                                                                      Q15306
                                                                               IRF4 HUMAN
 61
      DYNREEDAALFKAWALFKGKFREGID-----KPDPPTWKTRLRCALNKSNDFEELV
                                                                  111
 47
      DYNQEVDASIFKAWAVFKGKFKEG-D-----KAEPATWKTRLRCALNKSPDFEEVT
                                                                      Q02556
                                                                               IRF8 HUMAN
 49
      DFREDQDAAFFKAWAIFKGKYKEG-D----TGGPAVWKTRLRCALNKSSEFKEVP
                                                                  98
                                                                      Q00978
                                                                               IRF9_HUMAN
 47
                                                                      014896
                                                                               IRF6_HUMAN
      SPQQEEENTIFKAWAVETGKYQEGVD-----DPDPAKWKAQLRCALNKSREFNLMY
                                                                      P10914
 45
      GWDINKDACLFRSWAIHTGRYKAGEK-----EPDPKTWKANFRCAMNSLPDIEEVK
                                                                               IRF1 HUMAN
 45
      GWDVEKDAPLFRNWAIHTGKHQPGVD-----KPDPKTWKANFRCAMNSLPDIEEVK
                                                                  95
                                                                      P14316
                                                                               IRF2 HUMAN
1 45
      DAQQ-EDFGIFQAWAEATGAYVPGRD-----KPDLPTWKRNFRSALNRKEGLRLAE
                                                                      Q14653
                                                                               IRF3 HUMAN
                                                                   94
            : :*: **
                                             ** . (*, *).
                                                                            IRF7 HUMAN
                                                                .92985
                                                                P10914
                                                                            IRF1 HUMAN
                                                                .P14316
                                                                            IRF2 HUMAN
                                                                            IRF3 HUMAN
                                                                .014653
                                                                            IRF5 HUMAN
                                                                .013568
                                                                .014896
                                                                            IRF6 HUMAN
                                                                .015306
                                                                            IRF4 HUMAN
                                                                Q02556
                                                                            IRF8 HUMAN
                                                                .000978
                                                                            IRF9 HUMAN
```



小结

- 利用实用生物信息学课上所学到数据库和软件对IRF 3蛋白及其家族进行了初步分析,得到的结论和文献 的结论是基本一致的。
- IRF3是非常保守的转录因子,在抗感染免疫中发挥重要作用。在小鼠、大鼠、猪、牛和人这五个物种中分析表明IRF3的氨基酸序列几乎一致,保守性很高。同时对其磷酸化位点进行了预测,和文献报道一致。

• IRF家族中,均含有非常保守的DNA-binding区域。



敬请各位老师同学批评指正

谢谢大家!