RIP1——决定细胞生死的关键激酶

RIP1,a kinase on the crossroads of a cell's decision to live or die.

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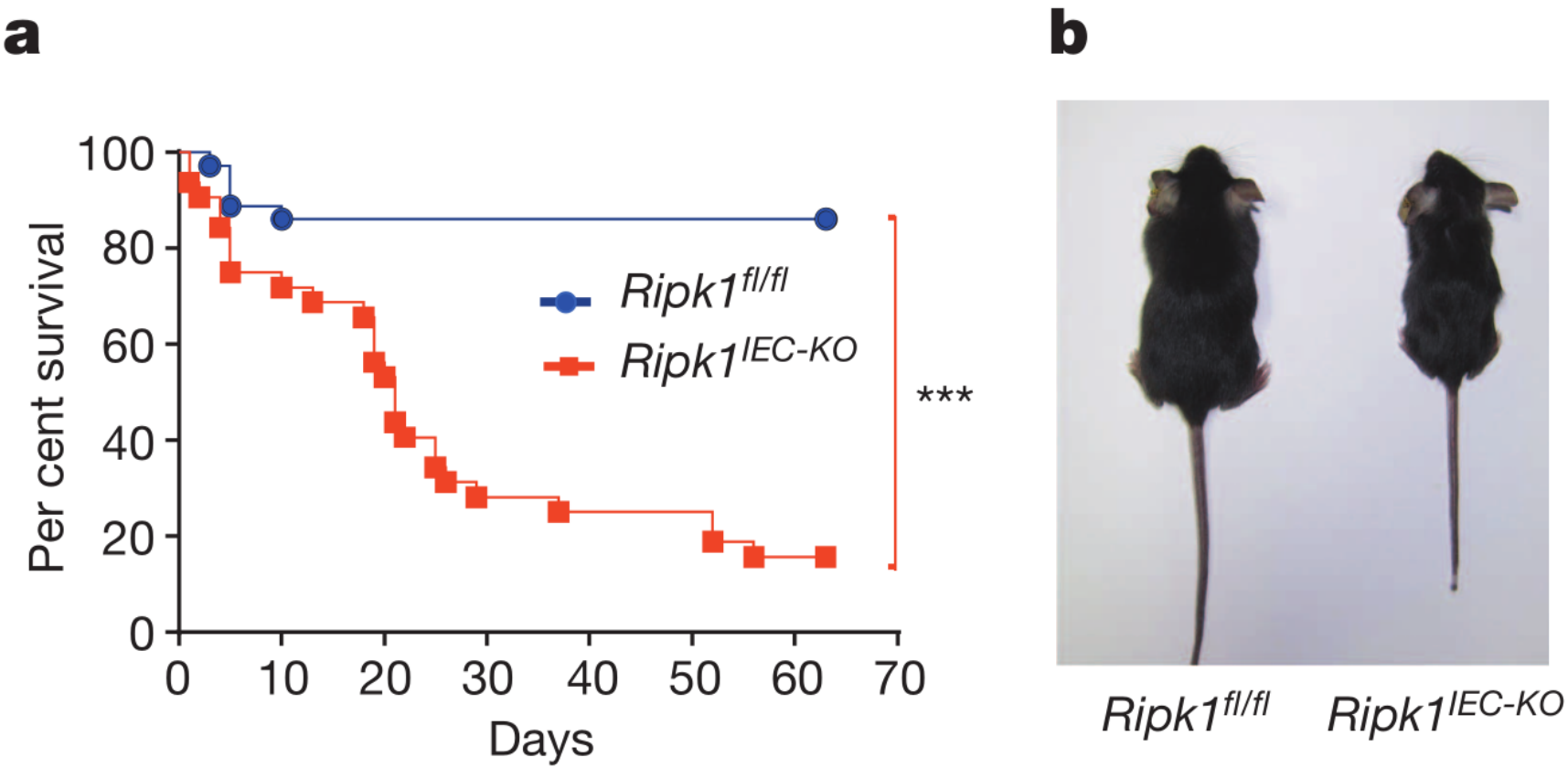
周钦超 袁野

主要内容

- 研究背景
- RIP1生物信息学分析
  - RIP1序列分析
  - RIP1基因表达
  - *RIP1*结构分析
  - *RIP1*信号通路及相互作用
- 小结
- 致谢

RIP1肠上皮特异性敲除的小鼠出生后四周内死亡



LETTER

doi:10.1038/nature13608

RIPK1 maintains epithelial homeostasis by inhibiting apoptosis and necroptosis

Marius Dannappel[1]*, Katerina Vlantis[1]*, Snehlata Kumari[1]*, Apostolos Polykratis[1]*, Chun Kim[1], Laurens Wachsmuth[1], Christina Eftychi[1], Juan Lin[1], Teresa Corona[1], Nicole Hermance[2], Matija Zelic[2], Petra Kirsch[3], Marijana Basic[4], Andre Bleich[4],

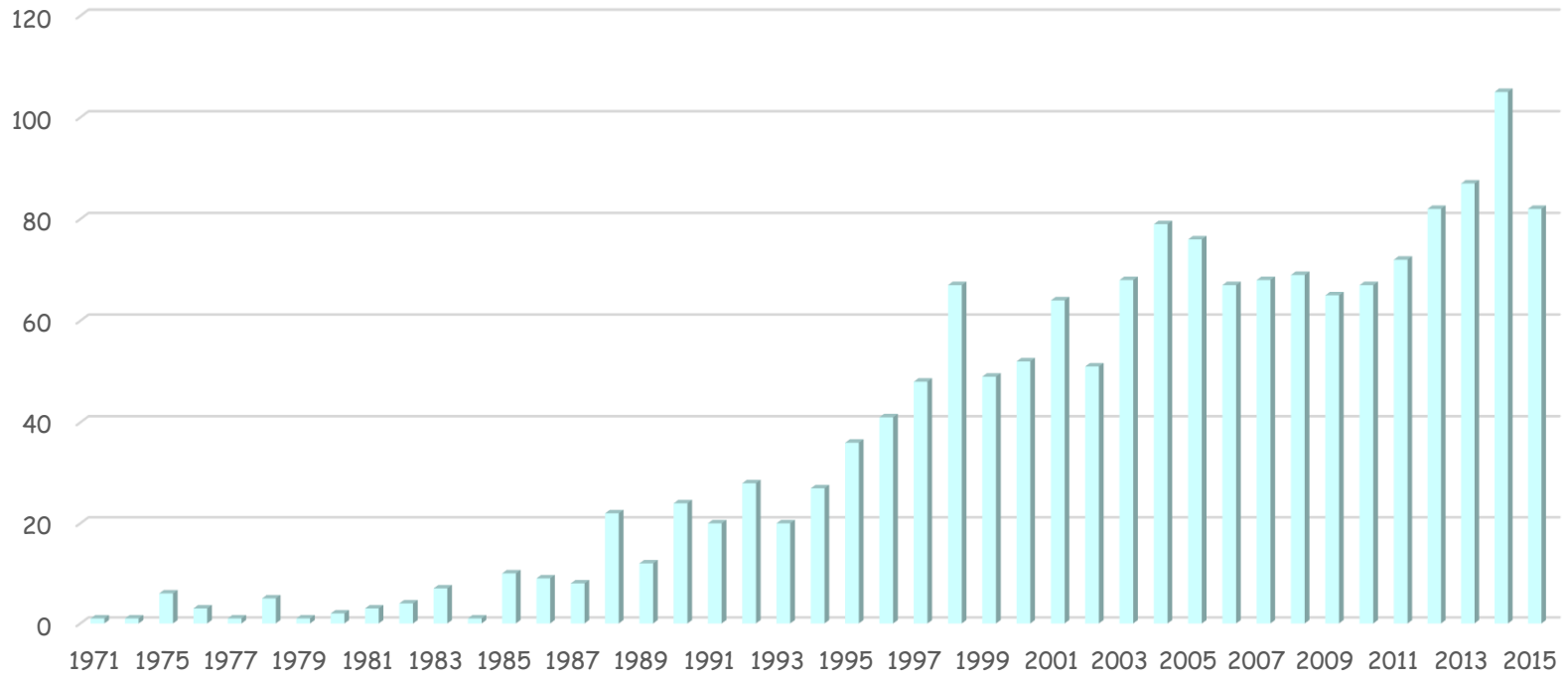
LETTER

doi:10.1038/nature13706

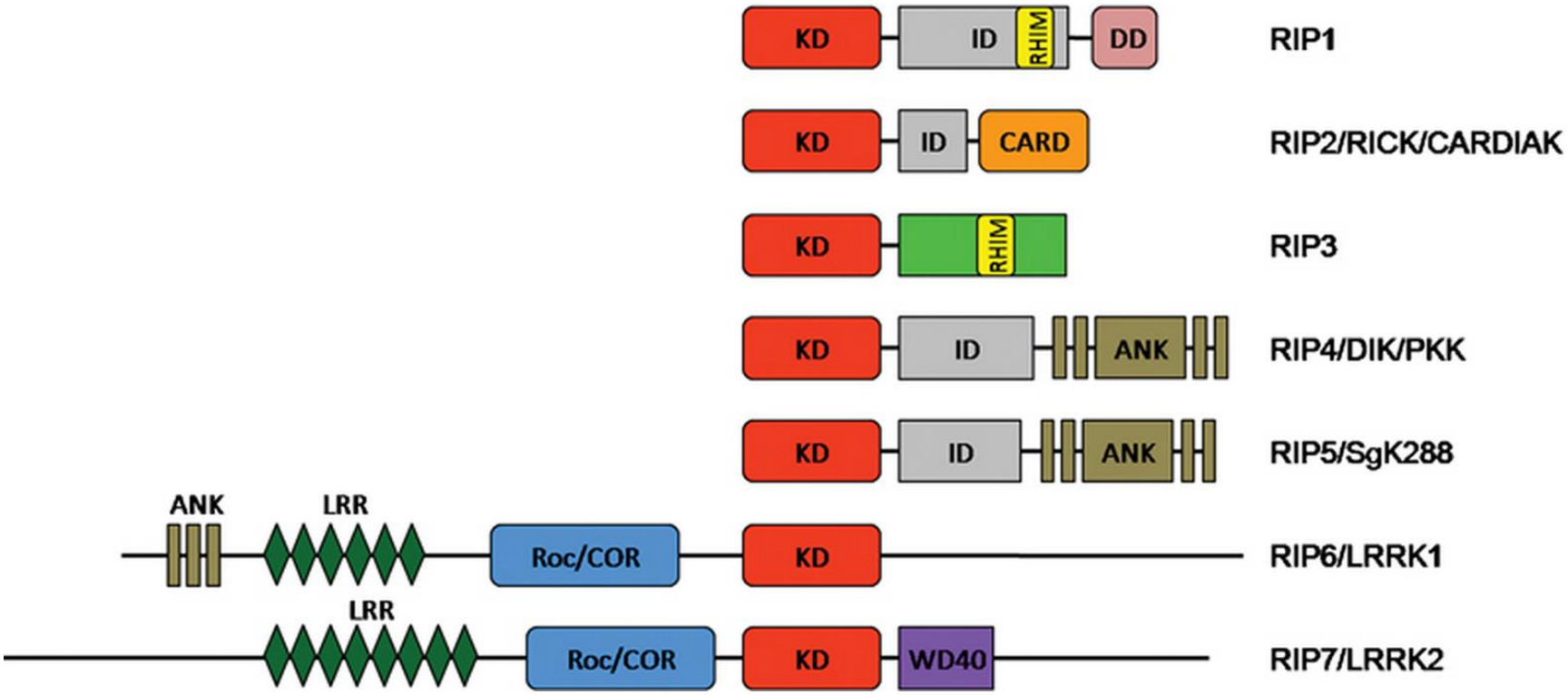
RIPK1 ensures intestinal homeostasis by protecting the epithelium against apoptosis

Nozomi Takahashi[1,2], Lars Vereecke[1,2], Mathieu J. M. Bertrand[1,2], Linde Duprez[1,2], Scott B. Berger[3], Tatyana Divert[1,2], Amanda Gonçalves[1,2,4], Mozes Sze[1,2], Barbara Gilbert[1,2], Stephanie Kourula[1,2], Vera Goossens[1,2], Sylvie Lefebvre[1,2], Claudia Günther[5], Christoph Becker[5], John Bertin[3], Peter J. Gough[3], Wim Declercq[1,2], Geert van Loo[1,2] & Peter Vandenabeele[1,2,6]

"RIP1"--Results by year-Pubmed

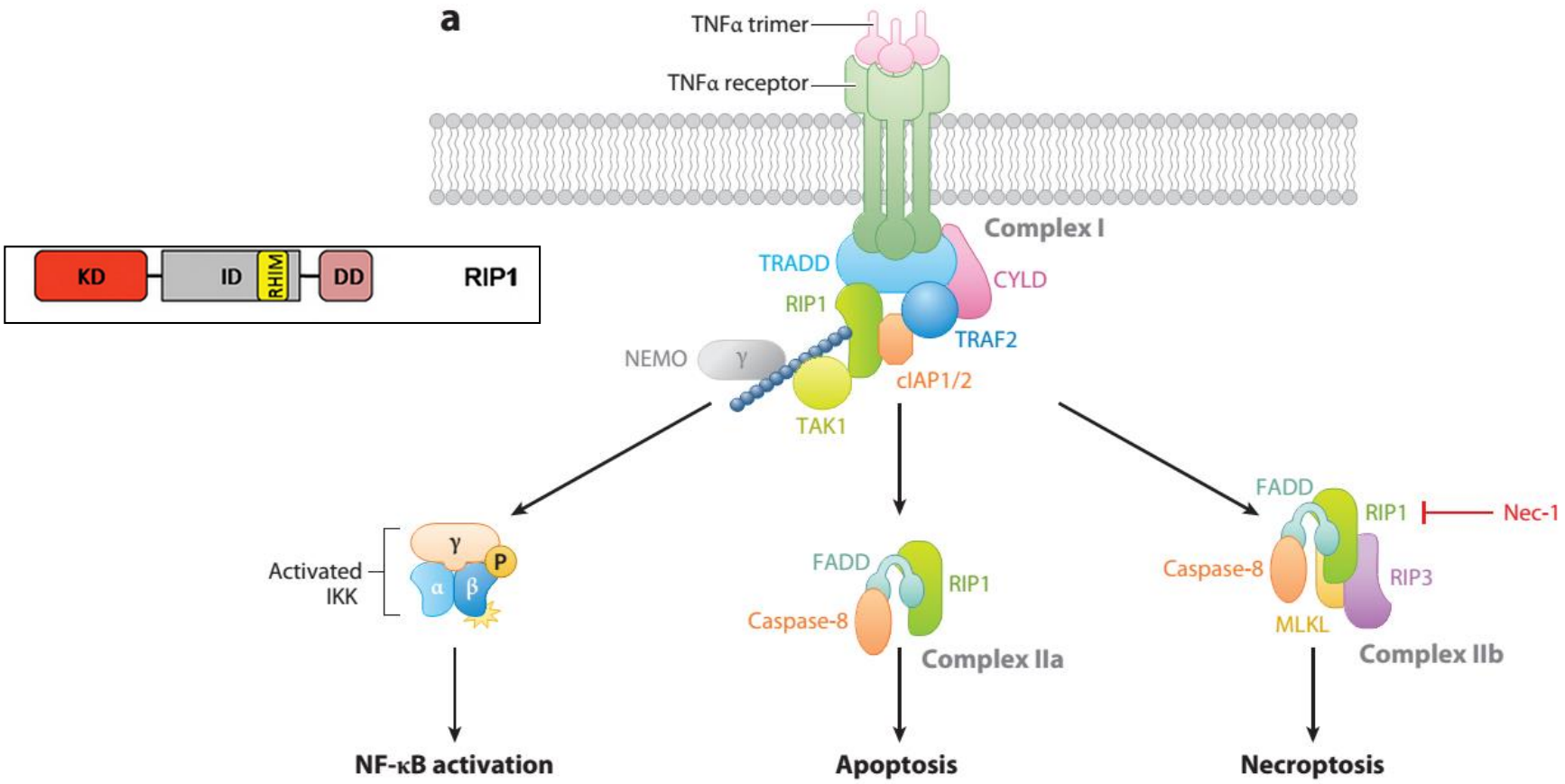


RIPs review



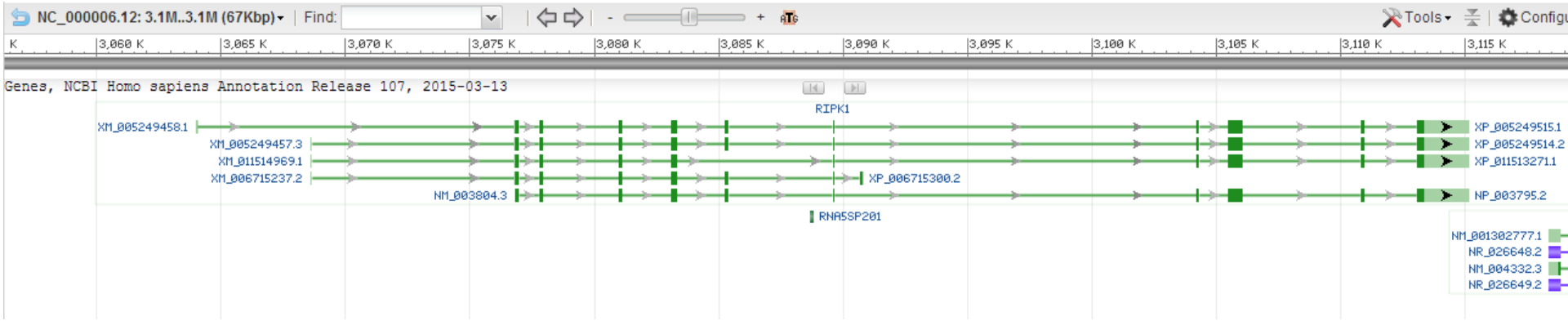
Domain organization of the RIP kinase family.

RIP1 review


a
TNFα trimer
TNFα receptor
Complex I
TRADD
CYLD
RIP1
TRAF2
NEMO
γ
cIAP1/2
TAK1
KD
ID
RHIM
DD
RIP1
Activated IKK
γ
P
α
β
FADD
RIP1
Caspase-8
Complex IIa
FADD
RIP1
Nec-1
Caspase-8
RIP3
MLKL
Complex IIb
NF-κB activation
Apoptosis
Necroptosis

RIPK1--receptor (TNFRSF)-interacting serine-threonine kinase 1

- Location：6p25.2；Exons: 13

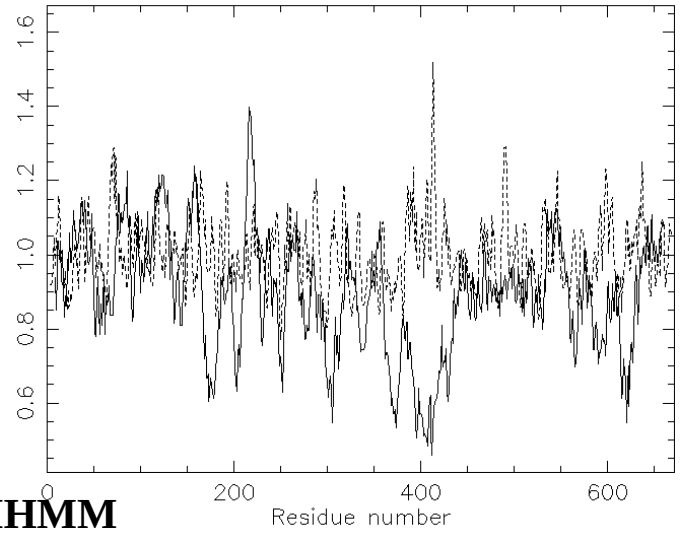


蛋白序列比对

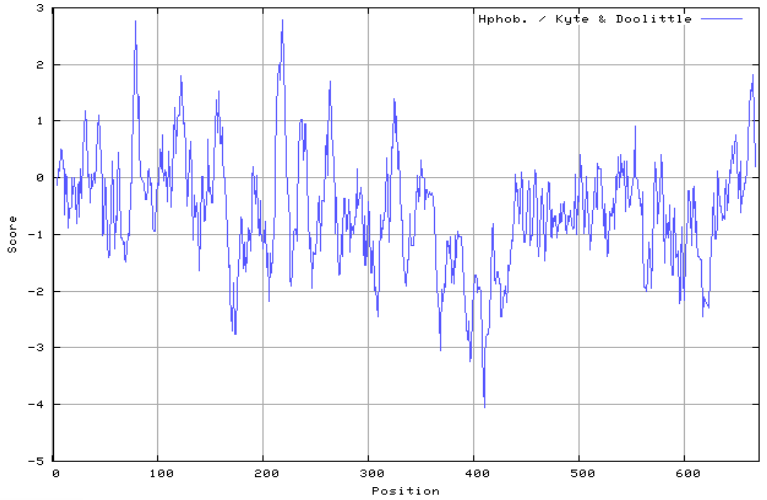
NO	Accession	Name	Species	Total Score	Query cover	E-value	Identity
1	NP_003795.2	RIP1	*Homo sapiens*	1477	100%	0.0	100%
2	NP_001030184.1	Rip1	*Bos taurus*	1069	99%	0.0	75%
3	NP_001100820.1	Rip1	*Rattus orvegicus*	1006	100%	0.0	70%
4	NP_033094.3	Rip1	*Mus musculus*	996	100%	0.0	70%
5	NP_006862.2	RIP3	*Homo sapiens*	145	39%	7e-37	32%
6	NP_001029782.1	Rip2	*Bos taurus*	141	36%	2e-35	33%
7	NP_001100573.1	Rip4	*Rattus orvegicus*	143	36%	3e-35	36%
8	NP_076152.2	Rip4	*Mus musculus*	143	36%	3e-35	36%
9	NP_620402.1	Rip2	*Mus musculus*	138	36%	1e-34	32%
10	NP_001178794.1	Rip2	*Rattus orvegicus*	136	36%	6e-34	32%
11	NP_065690.2	RIP4	*Homo sapiens*	139	39%	7e-34	34%
12	NP_003812.1	RIP2	*Homo sapiens*	134	36%	4e-33	32%

跨膜结构及疏水性预测

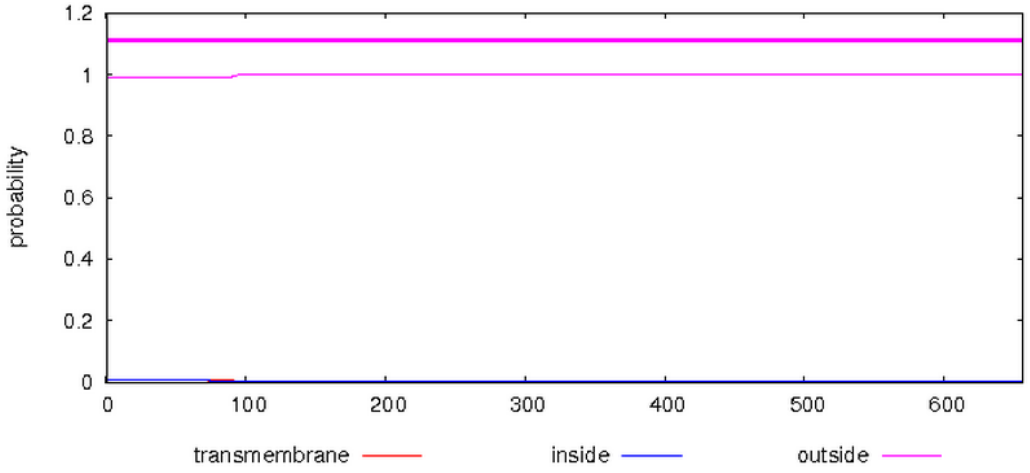
Tmap



ProtScale

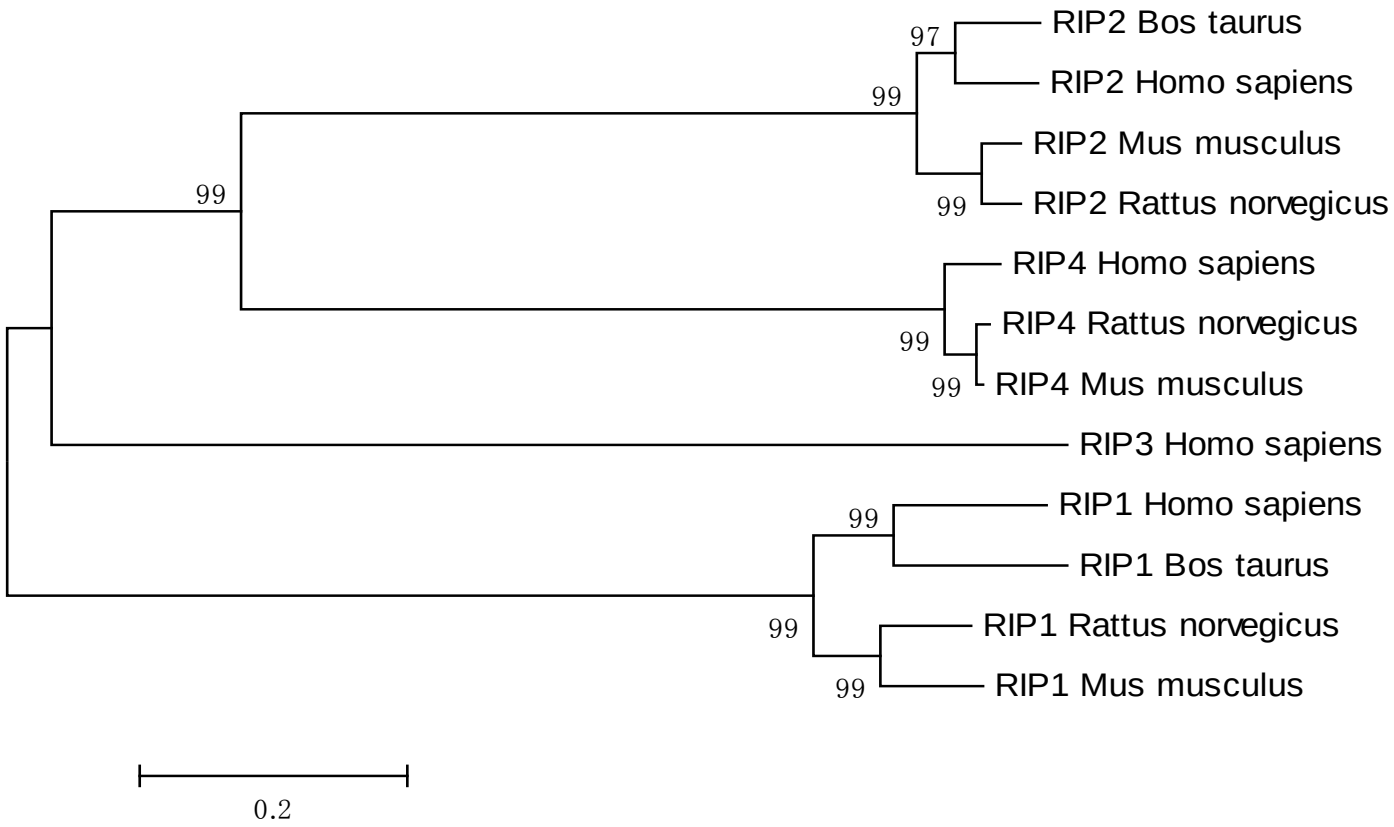


TMHMM

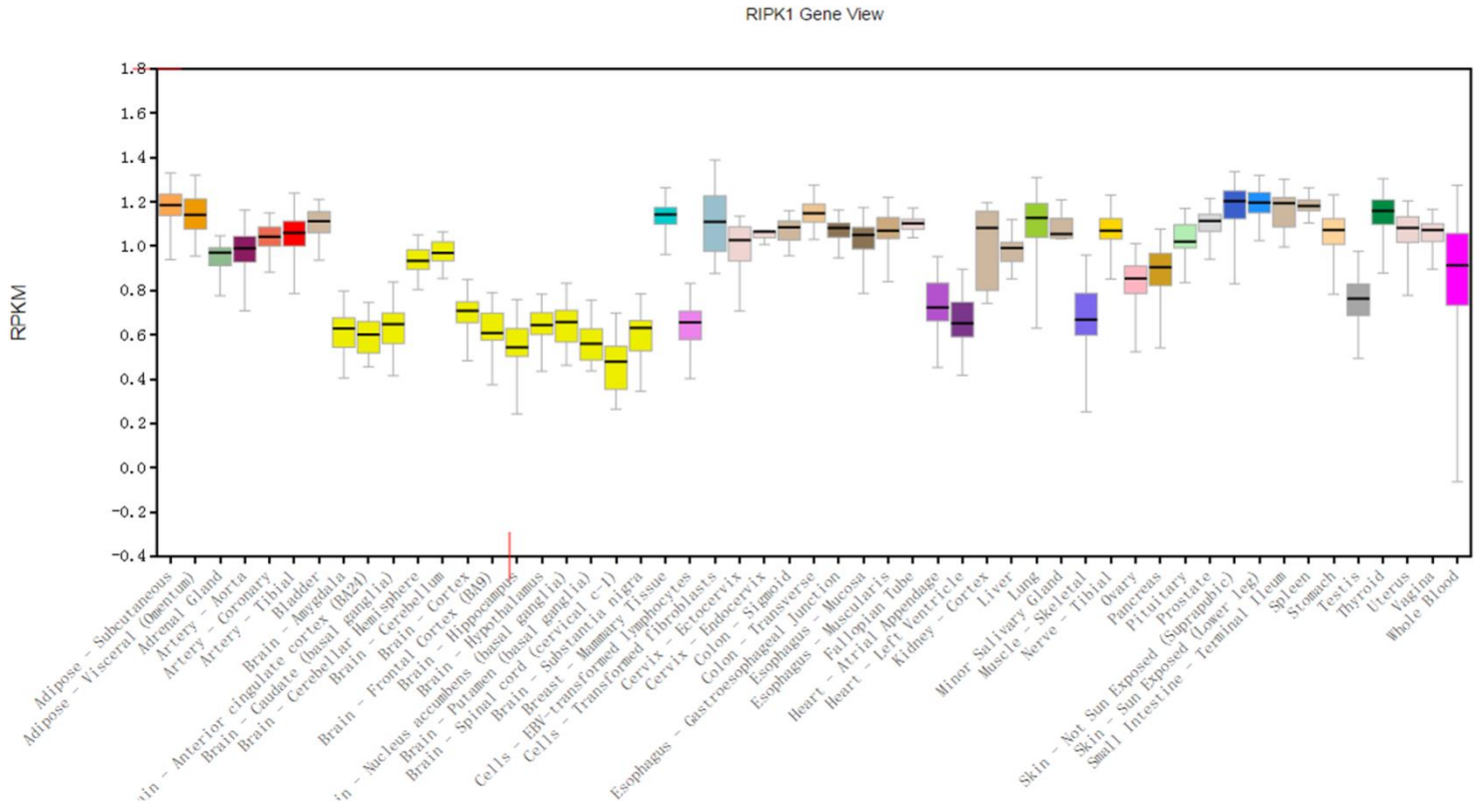


系统发育树

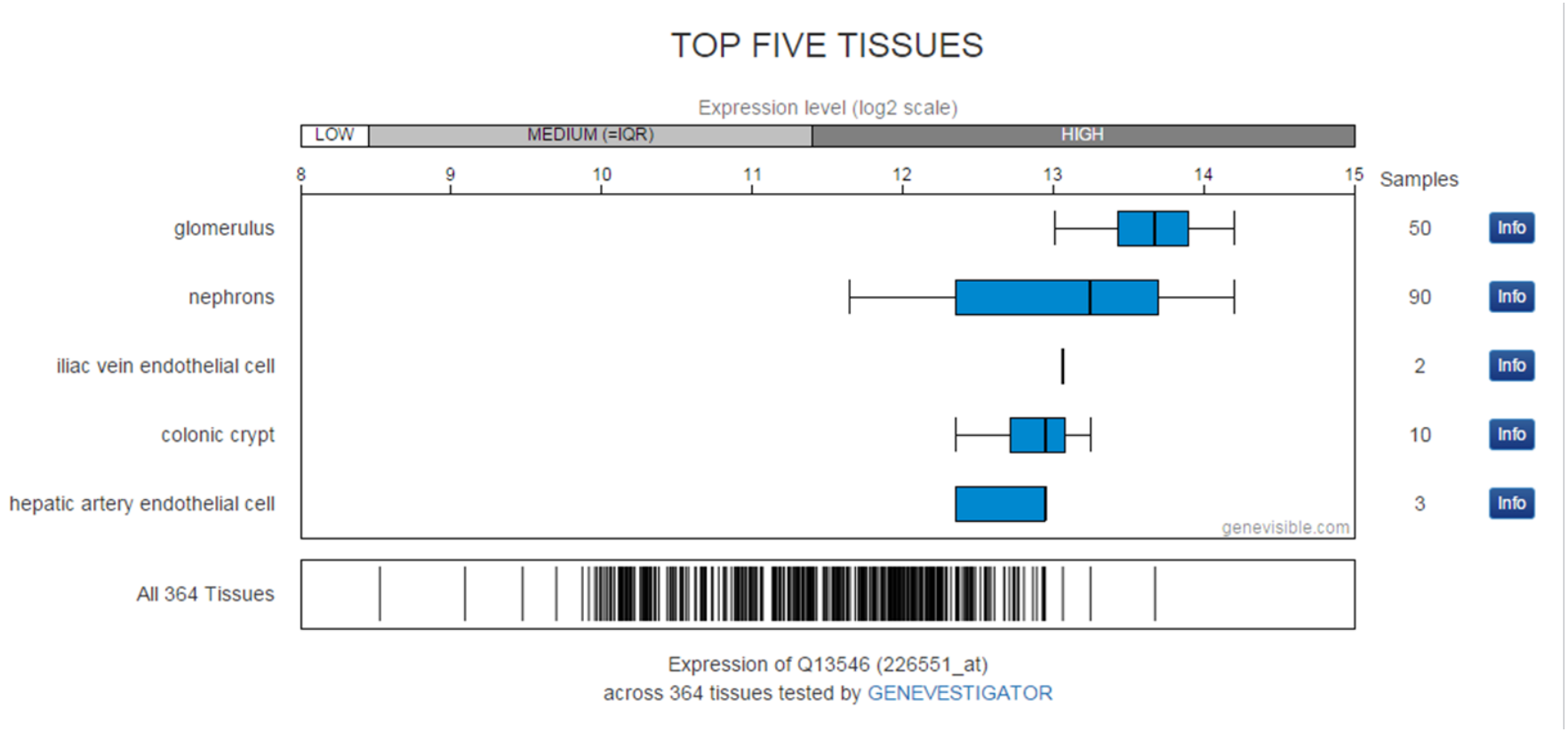
Neighbor-joining method



RIP1在不同组织中的表达

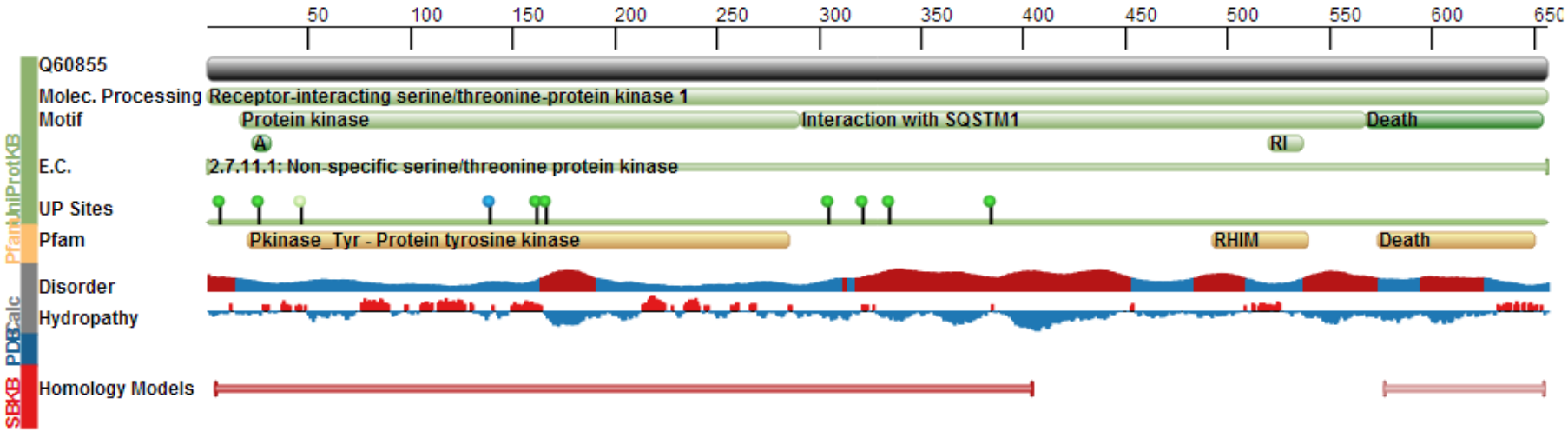


RIP1高表达的五个组织

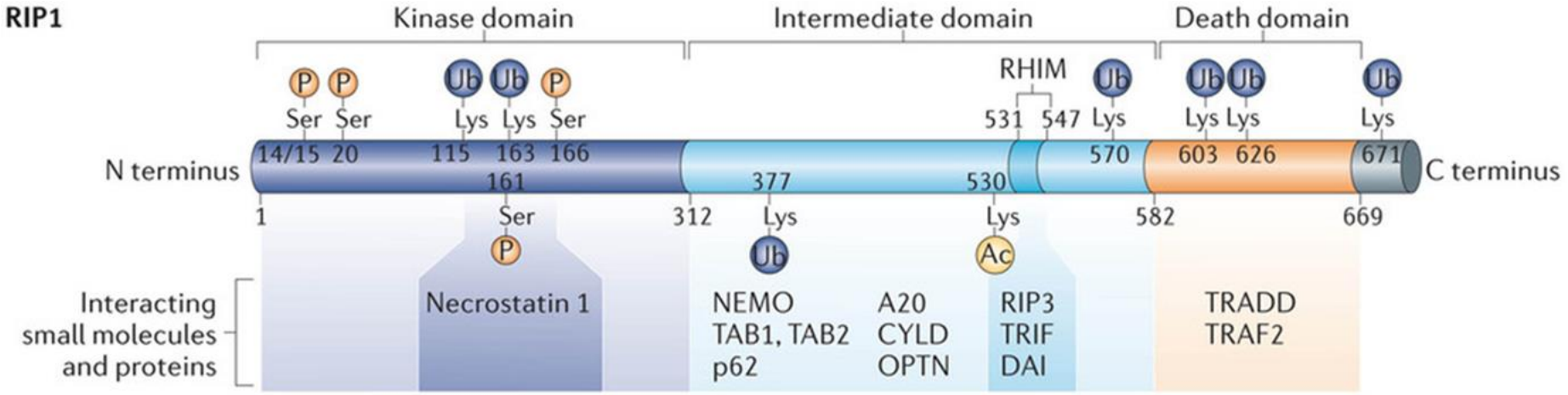


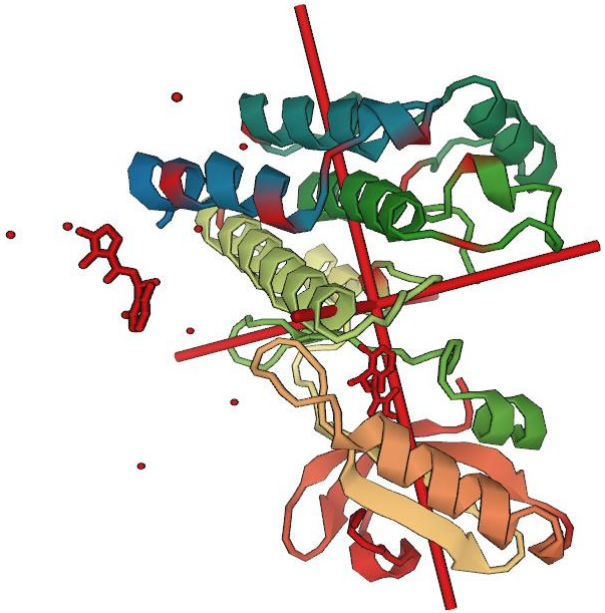
小鼠RIP1蛋白质模体和结构域

- RIP homotypic interaction motif (RHIM)
- C末端是一段死亡结构域(death domain, DD)序列，介导含有死亡结构域蛋白的相互作用



小鼠RIP1 3D结构

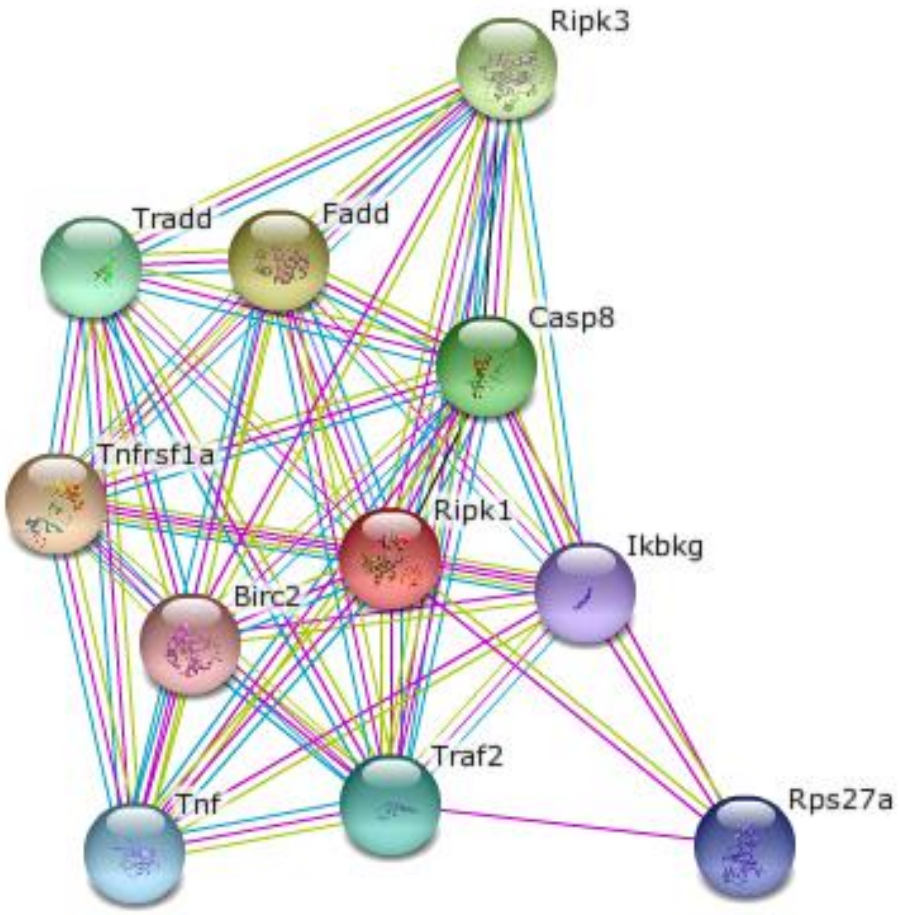




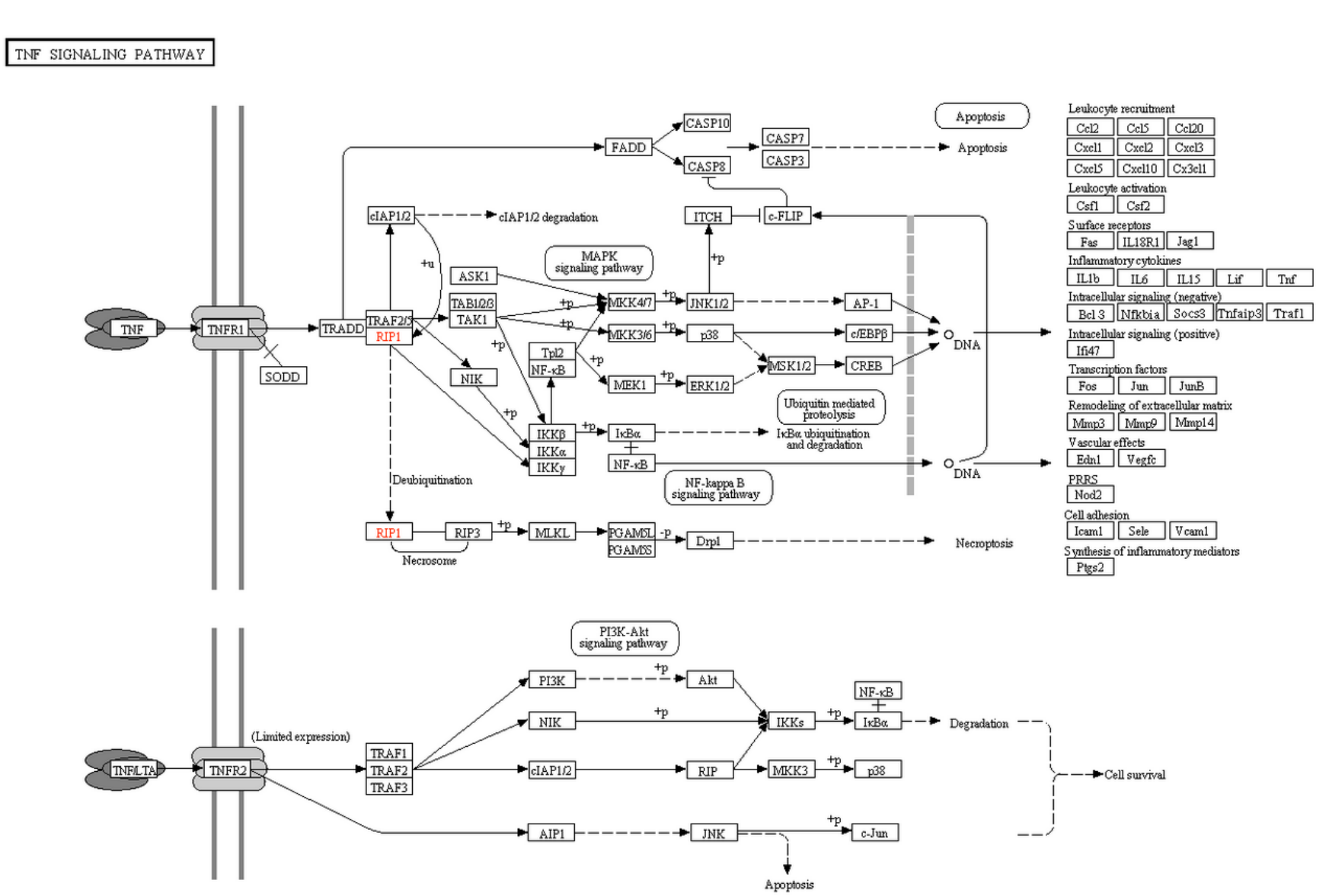
Ofengeim D1, Yuan J. Nat Rev Mol Cell Biol. 2013

Xie, T et.al, 2013, Structure 21: 493-499

蛋白蛋白相互作用


Ripk3
Tradd
Fadd
Casp8
Tnfrsf1a
Ripk1
Ikbkg
Birc2
Traf2
Tnf
Rps27a

RIP1参与的信号通路



致谢

- 感谢罗老师一学期以来的辛苦付出和对我们的悉心指导
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- 感谢G09组队友的互相帮助
- 感谢ABC课程的所有同学

谢 谢