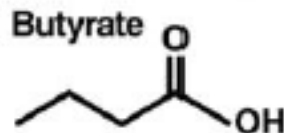


Apaf1的修饰可能参与丁酸钠 处理所诱导细胞凋亡

G06A 贲涛

丁酸钠

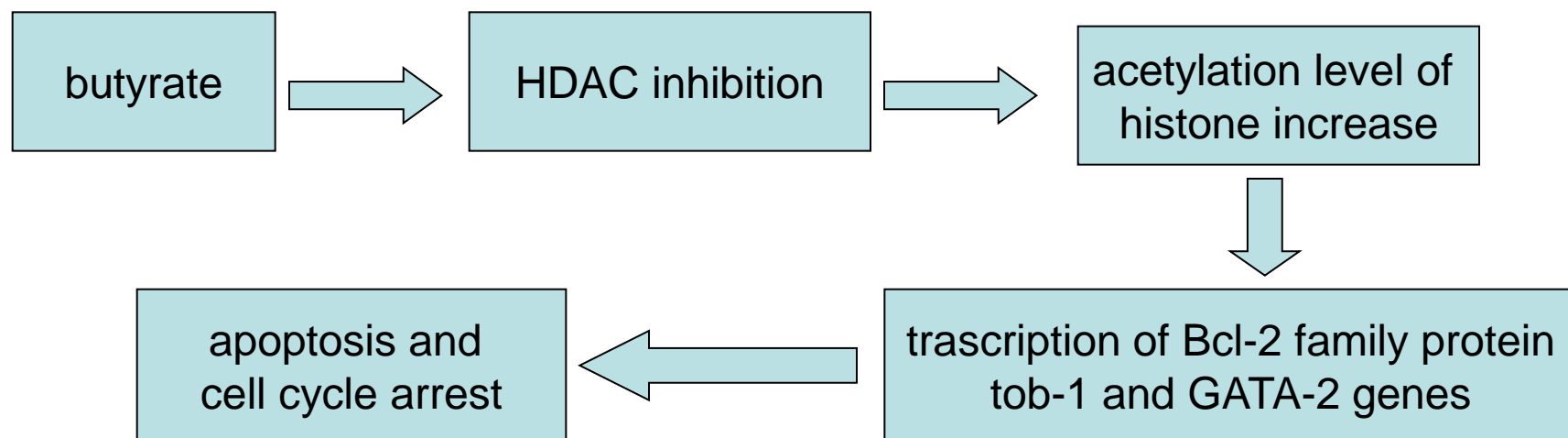
- 丁酸钠: Butyrate



- <http://www.ncbi.nlm.nih.gov/pubmed>
- Keyword:
butyrate(butyrate[Title/Abstract]) AND
apoptosis
- Filter: Free full text available; Humans
- 219 篇文章 10篇 review

丁酸钠

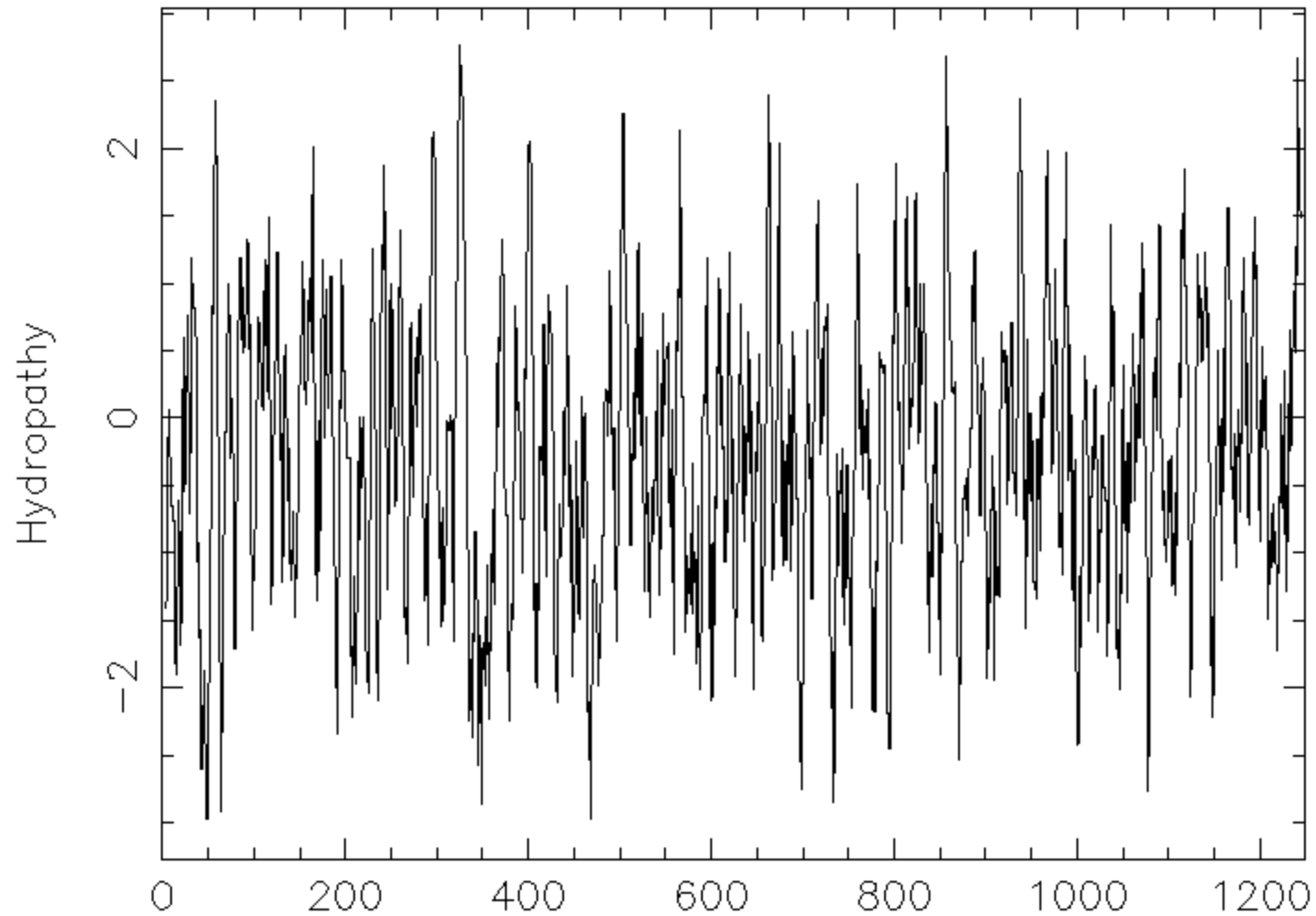
- 在肠道（结肠）中由细菌的无氧发酵产生
- 生物功能：可以诱导细胞凋亡
- 已经广泛研究的机制：组蛋白去乙酰化酶抑制剂(HDAC inhibitor)



Apaf1

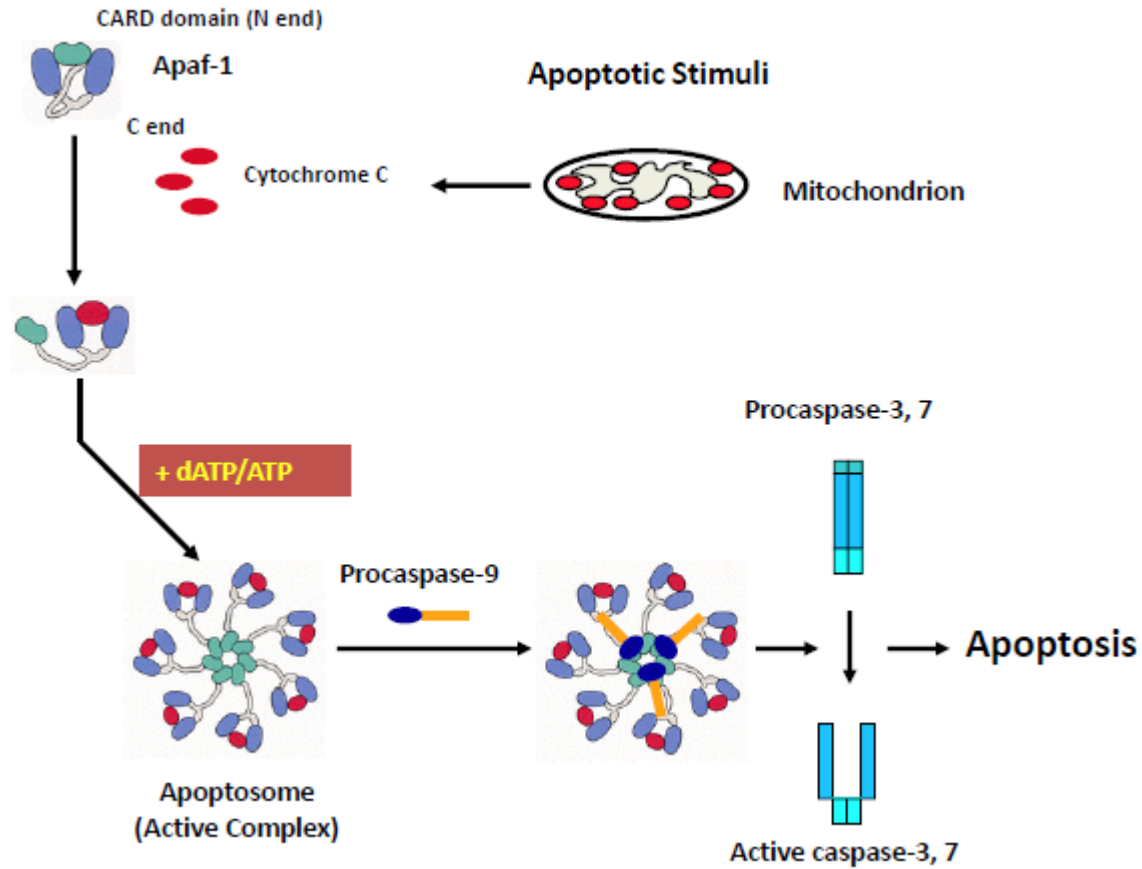
- Apaf1 (apoptotic proteases-activating factor 1)
- <http://www.uniprot.org/uniprot/O14727>
- <http://www.ncbi.nlm.nih.gov/pubmed>
- Gene RIF: 166篇报道, 3篇综述
- 1248 aa 定位: 细胞质
- 三个结构域: CARD domain
NB-ARC domain
WD repeats

Kyte-Doolittle Plot



non-polar	(A+C+F+G+I+L+M+P+T+V+Y+W) 623	50.000
Polar	(D+E+H+K+N+Q+R+S+T+Z) 623	49.920
Charged	(B+D+E+H+K+R+Z) 348	27.885
Basic	(H+K+R) 184	14.744
Acidic	(B+D+E+Z) 164	13.141

Apaf1



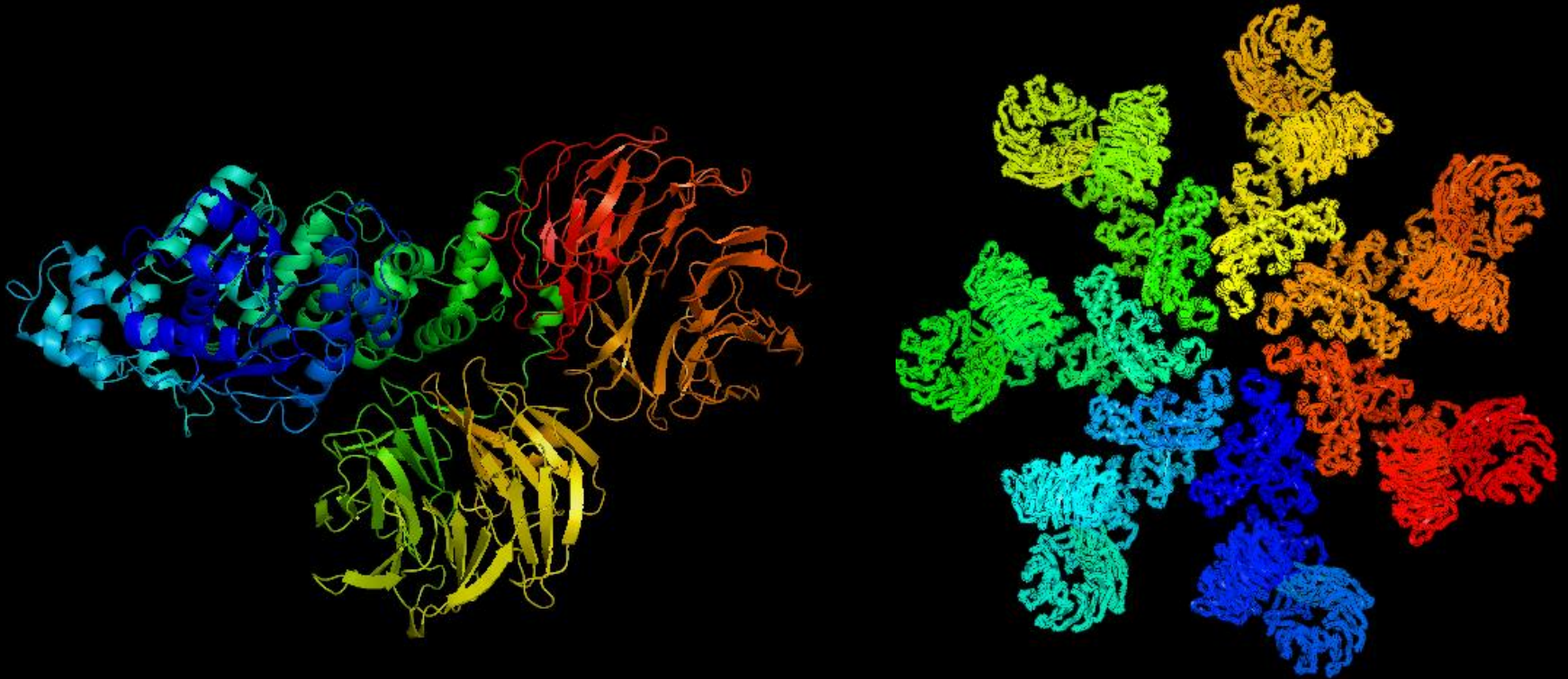
红色：细胞色素c

墨绿色：WD重复 结构域

蓝色：CARD 结构域

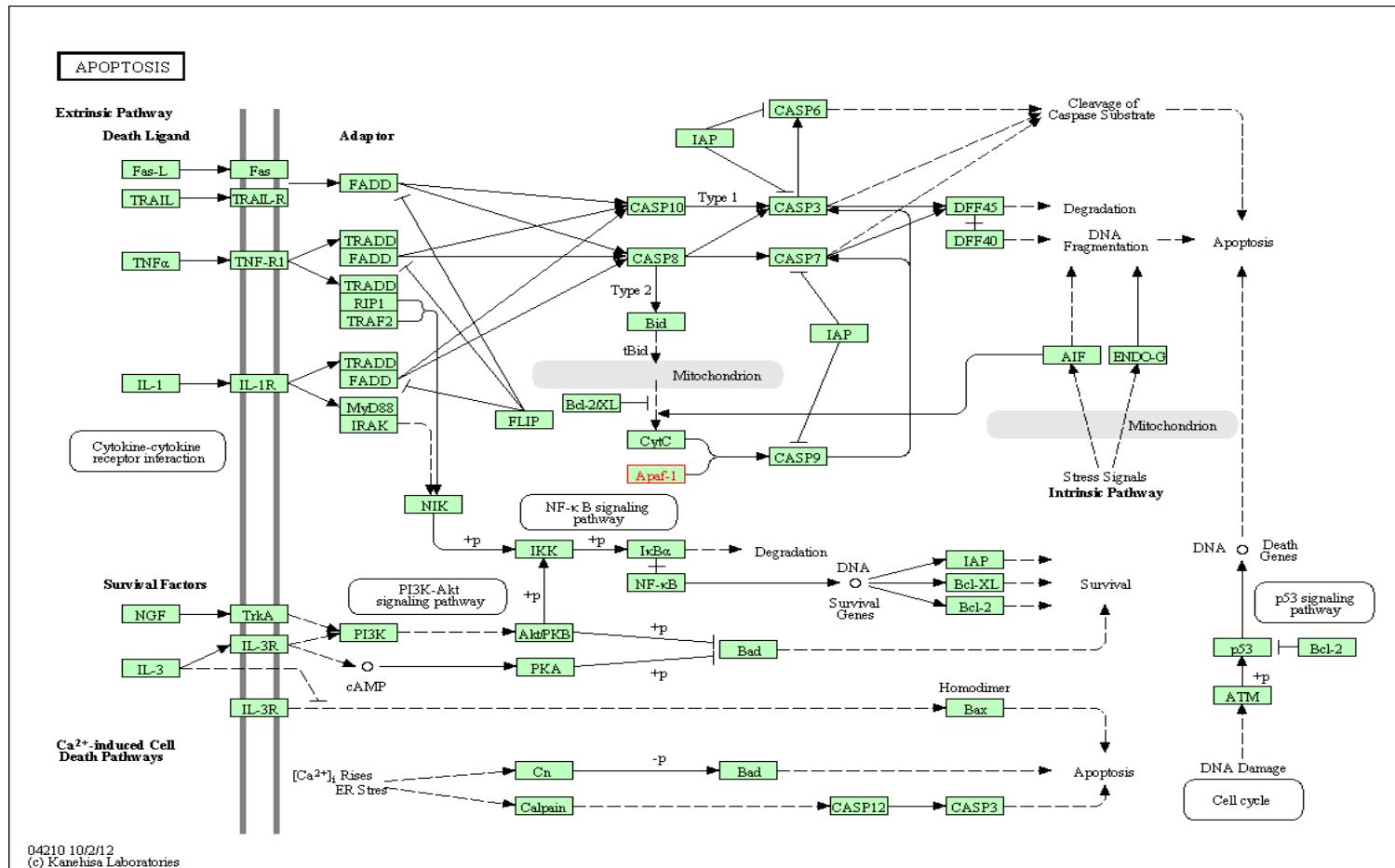
Apaf1

- 3SFZ and 3IZA in PyMol



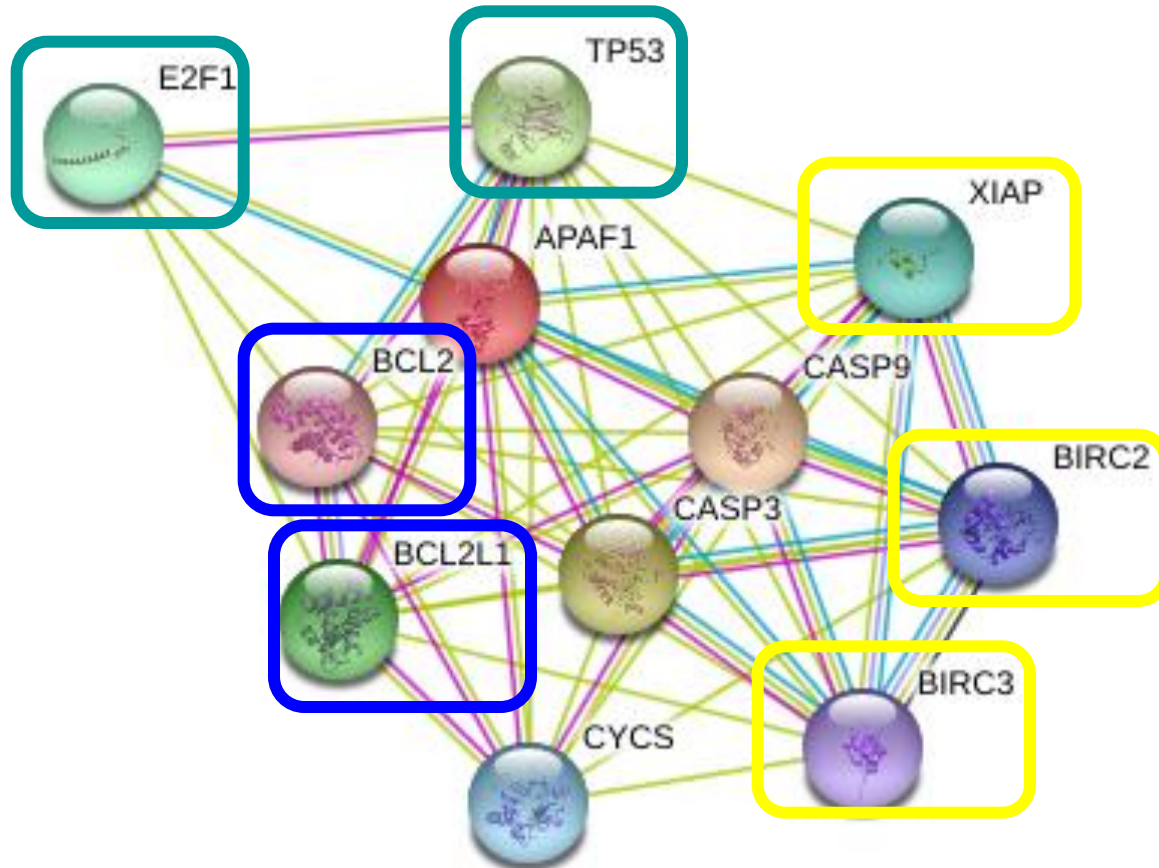
Apaf1

- In KEGG database:



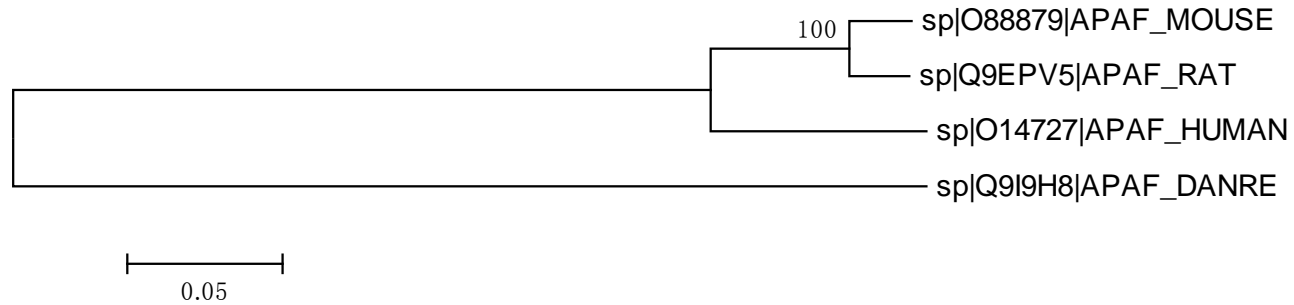
Apaf1

- STRING database



Apaf1

- phylogenetic tree of Apaf1

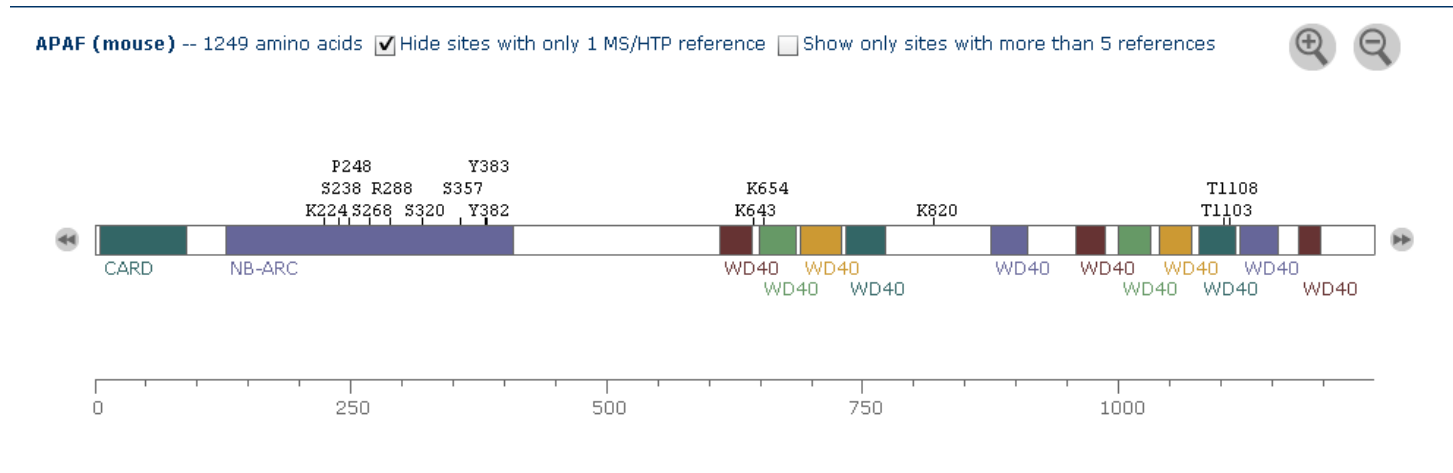


Apaf1与丁酸钠

- 丁酸钠处理后发现，Apaf1 在柱子上的行为发生了明显变化。
- 可能有修饰的出现--使得在分子量、电荷、亲疏水性性质上发生了变化。
- 假说：丁酸钠处理后，Apaf1发生了翻译后修饰，这种修饰参与到了丁酸钠介导的细胞凋亡途径。

Apaf1 的翻译后修饰

- Uniprot 中的链接:
- PTM database中只有磷酸化信息
- <http://www.phosphosite.org/>



Apaf1的翻译后修饰

Experimental Post-Translational Modification Sites						Download	
Locations (AA)	Modification	Substrate Sites	Secondary Structure	Accessible Surface Area (%)	Resource	Pubmed ID	Orthologous Protein Cluster
204	Phosphothreonine	QNLCTRLDQ	HHHHHHHHH	37.12	HPRD 9.0	17081983	show
204	Phosphothreonine	QNLCTRLDQ	HHHHHHHHH	37.12	PhosphoELM.10011	17081983	show
204	Phosphothreonine	QNLCTRLDQ	HHHHHHHHH	37.12	SysPTM 1.1	17081983	show
204	Phosphothreonine.	QNLCTRLDQ	HHHHHHHHH	37.12	Swiss-Prot 1010711	17081983	show
224	Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in ubiquitin)	IEEAKDRLR	CHHHHHHHH	46.81	Phosphositeplus.1010730	21906983	show
238	Phosphoserine	KHPRSLIL	CCCCEEEE	31.79	HPRD 9.0	17081983 20068231	show
238	Phosphoserine	KHPRSLIL	CCCCEEEE	31.79	PhosphoELM.10011	17081983	show
238	Phosphoserine	KHPRSLIL	CCCCEEEE	31.79	Phosphositeplus.1010730	17081983 20068231 21406692	show
238	Phosphoserine	KHPRSLIL	CCCCEEEE	31.79	SysPTM 1.1	17081983	show
238	Phosphoserine.	KHPRSLIL	CCCCEEEE	31.79	Swiss-Prot 1010711	17081983	show
248	Phosphoserine	DVWDSWVLK	CCCCHHHH	11.90	HPRD 9.0	17081983 20068231	show
248	Phosphoserine	DVWDSWVLK	CCCCHHHH	11.90	PhosphoELM.10011	17081983	show
248	Phosphoserine	DVWDSWVLK	CCCCHHHH	11.90	Phosphositeplus.1010730	17081983 20068231 21406692	show
248	Phosphoserine	DVWDSWVLK	CCCCHHHH	11.90	SysPTM 1.1	17081983	show
248	Phosphoserine.	DVWDSWVLK	CCCCHHHH	11.90	Swiss-Prot 1010711	17081983	show
268	Phosphoserine	TRDKSVTDS	ECCHHHCC	34.24	Phosphositeplus.1010730	22246185	show
288	Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in ubiquitin)	SSLGKEKGL	CCCCHHHH	62.64	Phosphositeplus.1010730	21906983	show
357	Phosphoserine	IRKSSSYDY	CCCCCCHH	35.63	Phosphositeplus.1010730	22246185	show

预测的Apaf1翻译后修饰

Predicted Post-Translational Modification Sites by profile HMM							Download						
Locations (AA)	Modification	Substrate Sites	Secondary Structure	Accessible Surface Area (%)	Resource	Orthologous Protein Cluster							
65	N-linked_Aspargine	LKKD N SYV	HHCCCEEE	49.35	HMM Predicted	show	602	N-linked_Aspargine	IN KK NITNL	CCCCCCCC	48.18	HMM Predicted	show
68	Phosphotyrosine(EGFR)	D N DSY V SFY	CCCEEEEEE	11.72	HMM Predicted	show	605	N-linked_Aspargine	KNIT N SRL	CCCCCEEE	32.02	HMM Predicted	show
68	Phosphotyrosine(INSR)	D N DSY V SFY	CCCEEEEEE	11.72	HMM Predicted	show	624	Phosphoserine(CK1)	HAC F SE D GQ	EEEECCCC	34.36	HMM Predicted	show
80	Phosphotyrosine(Syk)	LHEGY K DLA	HHHHHHHH	9.80	HMM Predicted	show	709	N-linked_Aspargine	CH F T N SSHH	EEEECCCE	40.34	HMM Predicted	show
96	Phosphoserine(CDC2)	P V V S SSGK	CEECCECCC	19.53	HMM Predicted	show	891	Phosphoserine(ATM)	G V M F SPDGS	EEEECCCC	12.18	HMM Predicted	show
193	Phosphoserine(IKK)	K Q D K S G L L M	CCCCGHHH	42.85	HMM Predicted	show	896	Phosphoserine(IKK)	P D G SS F L T S	CCCCEEEEE	29.79	HMM Predicted	show
213	Phosphoserine(ATM)	DE S F S Q R L P	HCCCCCCC	24.54	HMM Predicted	show	899	O-linked_Threonine_Man	SS F L T SSDD	CEEEEECC	24.95	HMM Predicted	show
268	Phosphoserine(IKK)	TR D K S V T D S	ECCHHHCC	34.24	HMM Predicted	show	967	S-palmitoyl_cysteine	Q V S C C L S P	CEEEEECC	1.72	HMM Predicted	show
268	Phosphoserine(PKB)	TR D K S V T D S	ECCHHHCC	34.24	HMM Predicted	show	968	S-palmitoyl_cysteine	V S C C L S PH	EEEEEECC	5.03	HMM Predicted	show
272	Phosphoserine(IKK)	S V T D S V M G P	HHCCCCCC	12.49	HMM Predicted	show	975	Phosphotyrosine(Jak)	P H L Q Y I A F G	CCCCEEEEE	10.69	HMM Predicted	show
320	Phosphoserine(CDC2)	E C K G S P L V V	HHCCCHHH	10.68	HMM Predicted	show	1060	Phosphoserine(CAMK2)	S R L L S W S F D	CEEEEECC	25.85	HMM Predicted	show
361	Phosphotyrosine(Syk)	SS V D Y E A L D	CCCHHHHH	8.55	HMM Predicted	show	1062	Phosphoserine(IKK)	L L S W S F D G T	EEEECCCE	15.30	HMM Predicted	show
361	Sulfonyltyrosine	SS V D Y E A L D	CCCHHHHH	8.55	HMM Predicted	show	1103	O-linked_Threonine_Man	K F S T S A D K	EEEEEECC	27.08	HMM Predicted	show
369	Phosphoserine(CK1)	DE A M S I S VE	HHHHHHHC	20.82	HMM Predicted	show	1186	Phosphoserine(CDC2)	D L C F S P D G K	EEEECCCC	22.53	HMM Predicted	show
420	N-linked_Aspargine	Q E F V N K S L L	HHHCCEEE	33.25	HMM Predicted	show	1216	N-linked_Aspargine	T F Y T N G T N L	EEECCEEE	43.86	HMM Predicted	show
449	N-linked_Aspargine	L T E K N C S Q L	HHHHHHHH	25.17	HMM Predicted	show	1219	N-linked_Aspargine	T N G T N L K K I	CCCCEEEEE	51.79	HMM Predicted	show
451	Phosphoserine(ATM)	E K N C S Q L D	HHHHHHHH	43.23	HMM Predicted	show	1226	Phosphoserine(CDK)	K I H V S P D F K	EEEECCCC	12.46	HMM Predicted	show
577	Phosphotyrosine(SRC)	T S E V Y Q A K	CCCCCCCC	7.28	HMM Predicted	show	1232	Phosphotyrosine(INSR)	D F K T Y V T V D	CCCEEEEEE	8.50	HMM Predicted	show

<http://dbptm.mbc.nctu.edu.tw/>

最有可能的机制?

人类中的组蛋白去乙酰化酶 HDAC 家族

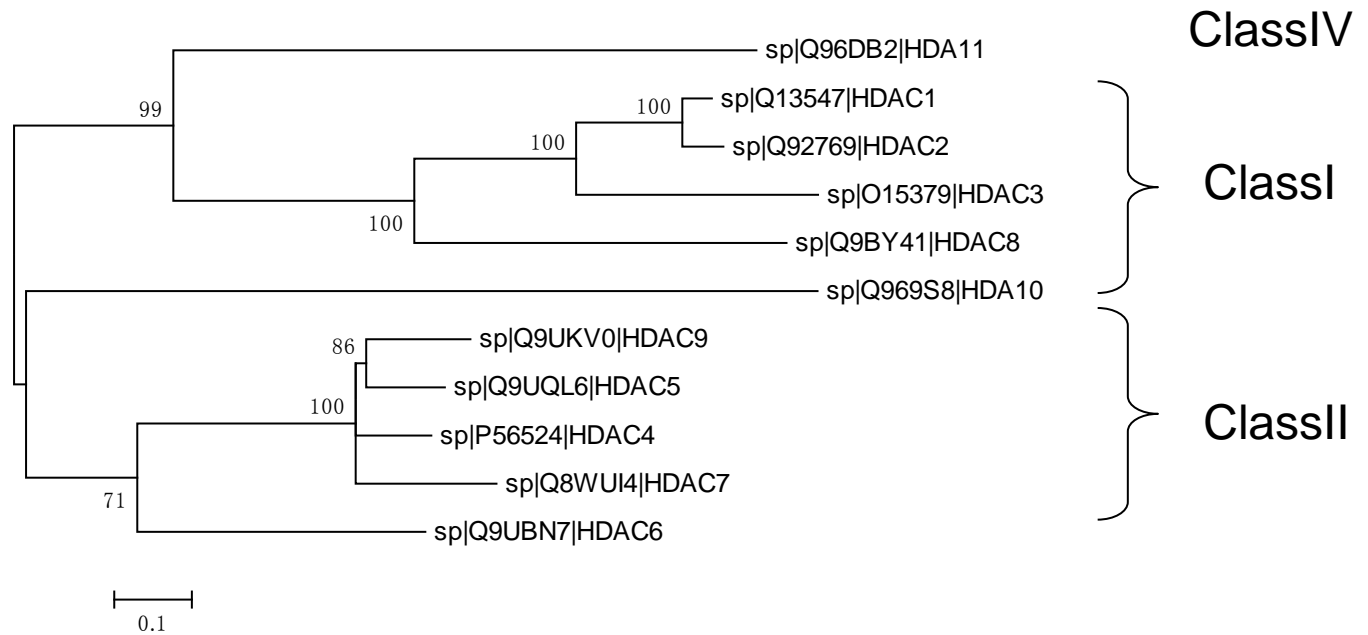
- 在Uniprot中检索(HDAC AND organism:"Human [9606]") AND reviewed:yes AND gene:HDAC

- 发现HDAC1-11,共11个成员。

- 阅读文献发现，组蛋白去乙酰化酶分为四个Classes:

ClassI(HDAC1,2,3,8);ClassII(HDAC4,5,6,7,9,10);ClassIII(Sirtuins);ClassIV(HDAC11).

HDACs的分析



- 因为butyrate只对Class I/II的HDACs其抑制作用。

HDACs的分析

- 查询Uniprot
class I/II的HDACs的亚细胞定位发现
HDAC4/5/6/7/8/10 在细胞核细胞质双定位
即推测可能影响Apaf1乙酰化水平

致谢

- 感谢罗静初老师
- 感谢G06的杨佳怡、周悦欣和徐昌强
- 希望大家多多交流，多提建议。