TRIM72:
Structure, Evolution & Function

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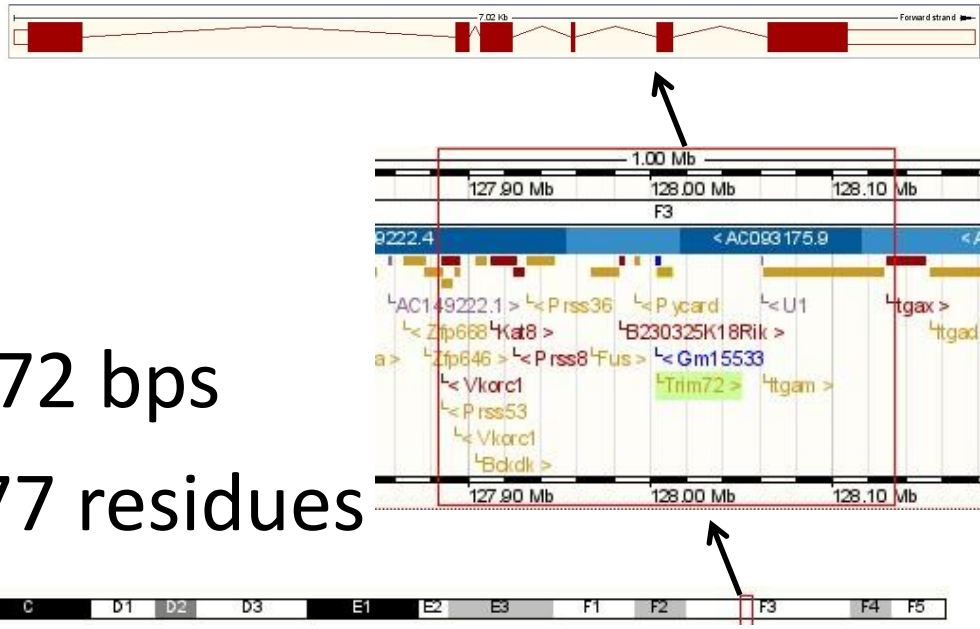
What is TRIM72?

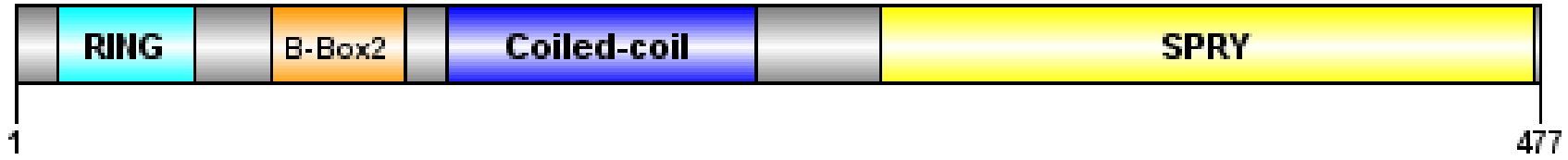
- TRIM72 is a striated muscle specific protein which located at Chromosome 7: 128,004,378-128,011,393.
- Transcripts: 2
- **Exons:** 6
- **Coding exons:** 6
- **Transcript length:** 2,472 bps
- **Translation length:** 477 residues



Schultz et al. (1998) *Proc. Natl. Acad. Sci. USA* **95**, 5857-5864
Letunic et al. (2012) *Nucleic Acids Res* , doi:10.1093/nar/gkr931

Primary Structure

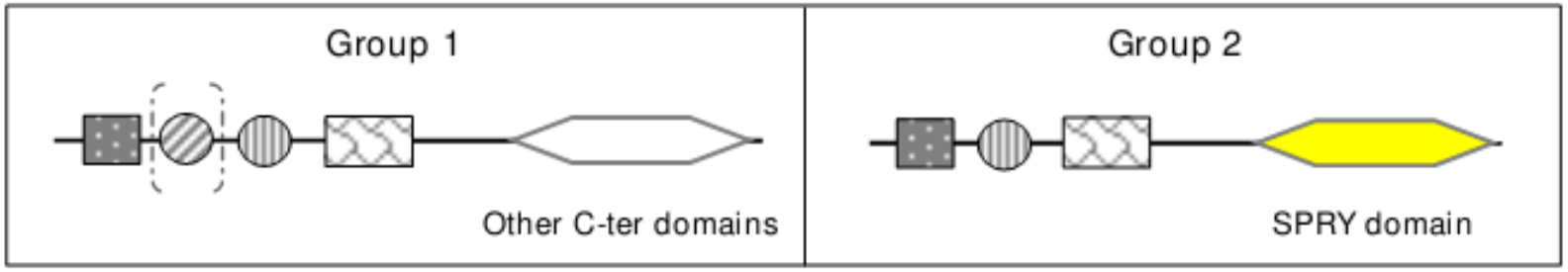
- RING(SM00184): Zinc-finger, E3 ubiquitin ligase activity.
- B-Box2(SM00336): Zinc-finger
- Coiled-coil(**PF05710**)
- SPRY(SM00449)



drawn by DOG 2.0

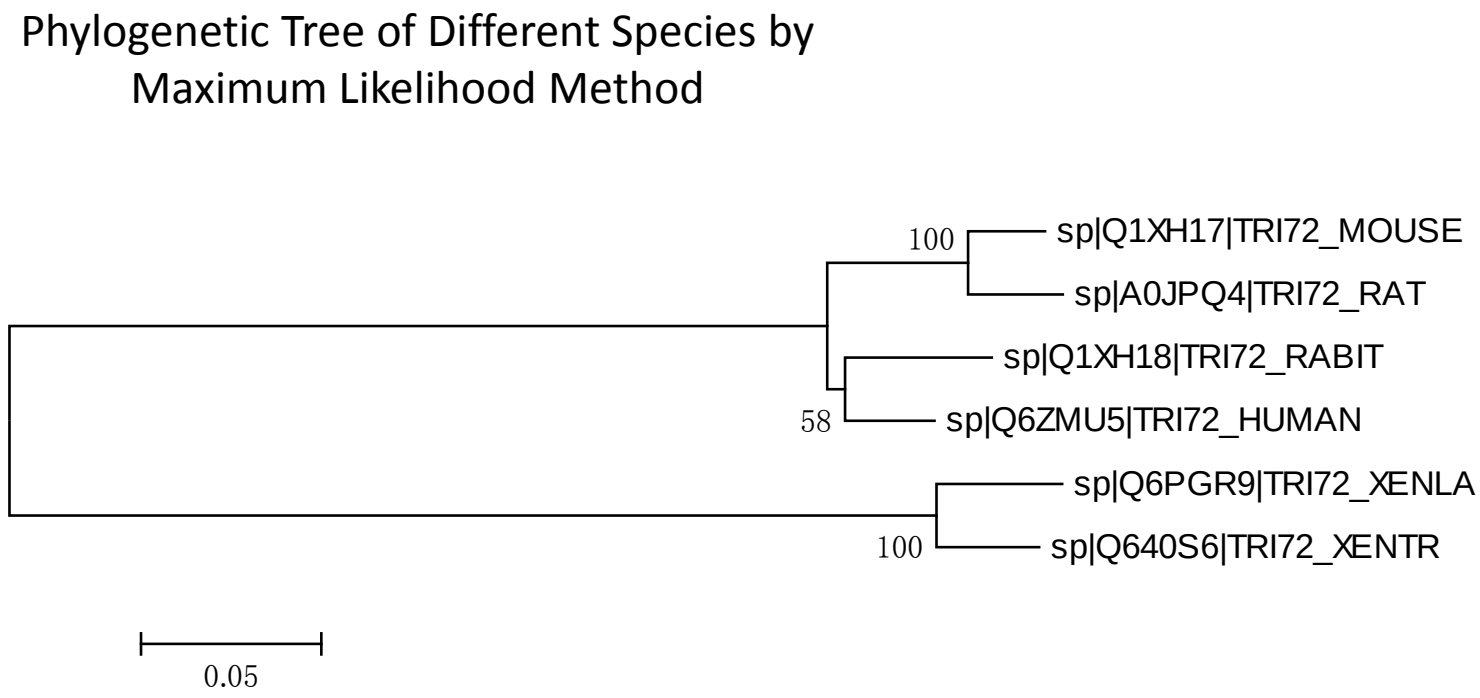
TRIM family (tripartite motif family)

- The TRIM motif includes the following three domains: RING, B-Box, Coiled-coil.
- According to the C-teminus, TRIM proteins could be divided into two groups.
- Group 2 proteins: **a SPRY C-terminal domain.**
- Group 1 proteins: **a NHL/PHD/MATH/… C-terminal domain.**

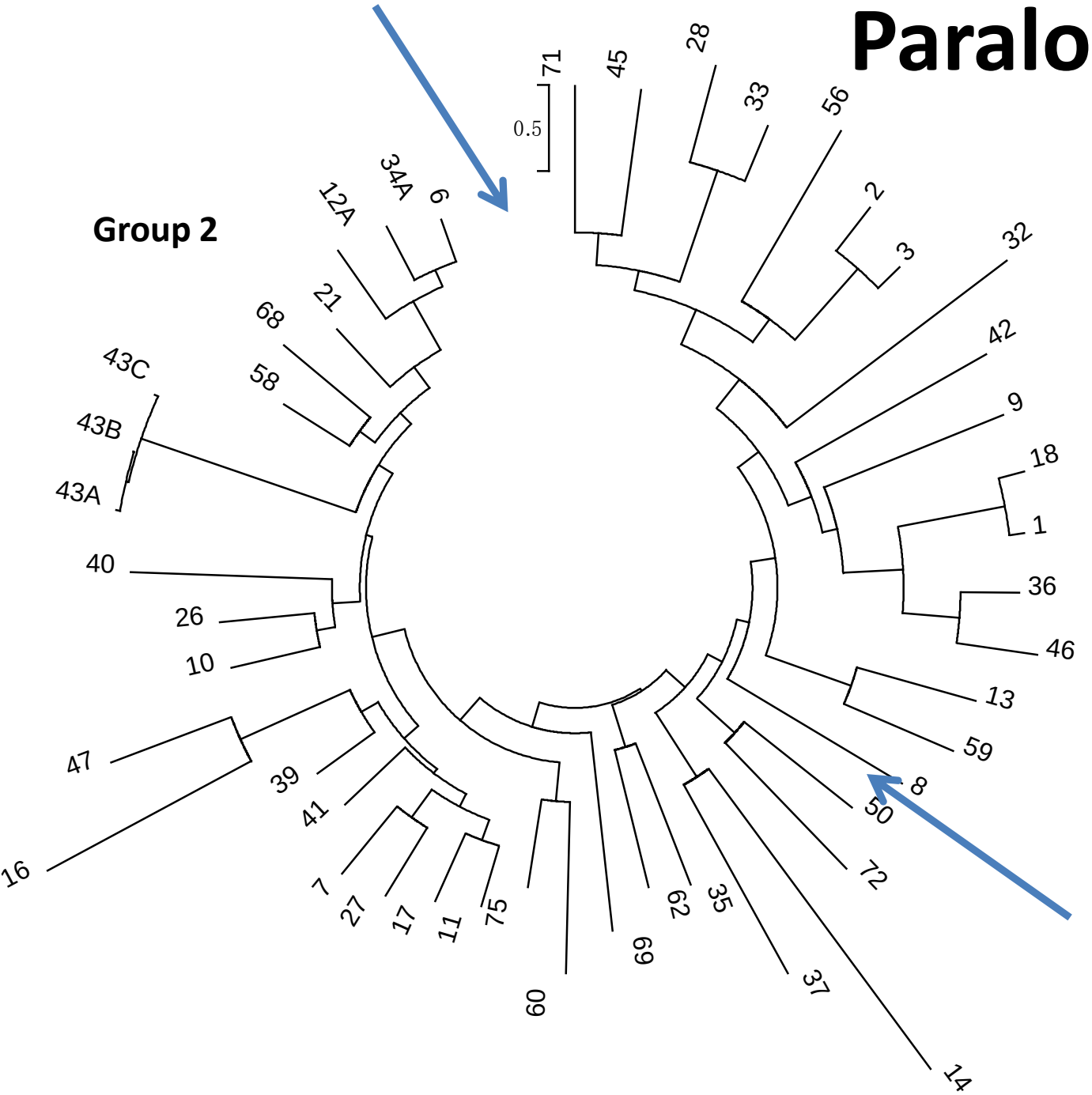


Marco Sardiello et al, BMC Evolutionary Biology.

Orthology analysis



Paralogy analysis



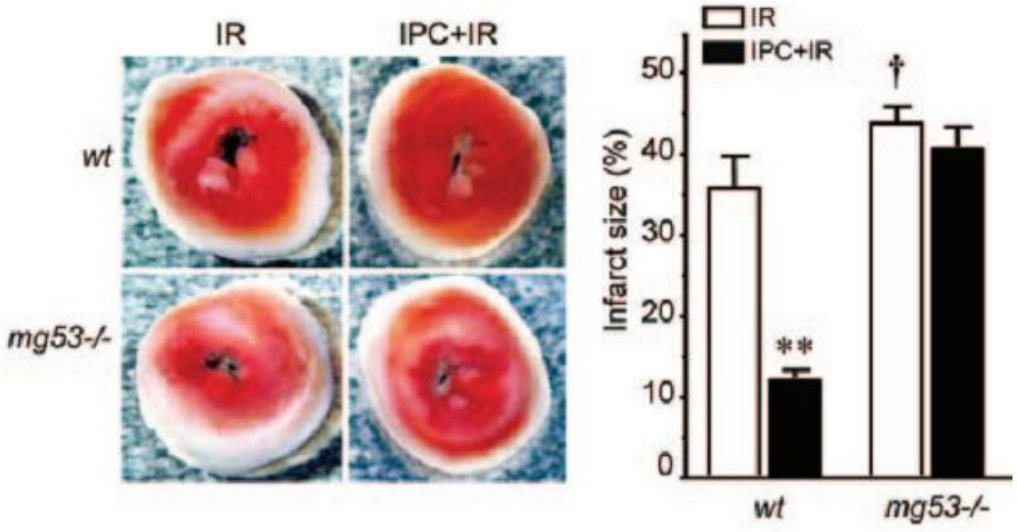
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Function 1

American Heart Association®

MG53 Constitutes a Primary Determinant of Cardiac Ischemic Preconditioning

Chun-Mei Cao, Yan Zhang, Noah Weisleder, Christopher Ferrante, Xianhua Wang, Fengxiang Lv, Yi Zhang, Ruisheng Song, Moonsun Hwang, Li Jin, Jiaojiao Guo, Wei Peng, Geng Li, Miyuki Nishi, Hiroshi Takeshima, Jianjie Ma and Rui-Ping Xiao



- MG53 as a primary component of the cardiac IPC response

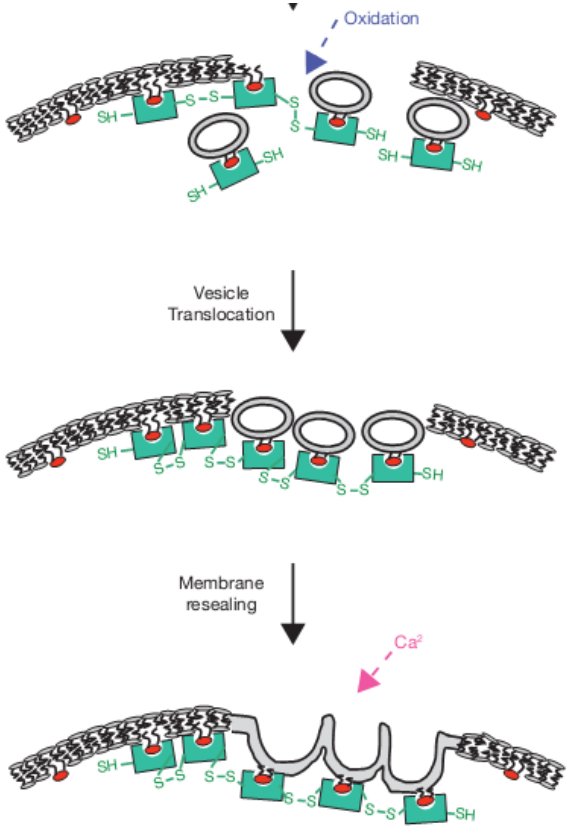
Function 2

nature cell biology

MG53 nucleates assembly of cell membrane repair machinery

Chuanxi Cai[1], Haruko Masumiya[2], Noah Weisleder[1], Noriyuki Matsuda[3], Miyuki Nishi[2,4], Moonsun Hwang[1], Jae-Kyun Ko[1], Peihui Lin[1], Angela Thornton[1], Xiaoli Zhao[1], Zui Pan[1], Shinji Komazaki[5], Marco Brotto[1], Hiroshi Takeshima[2,4,6] and Jianjie Ma[1,6]

- Mice null for MG53 show progressive myopathy and reduced exercise capability, associated with defective membrane-repair capacity.



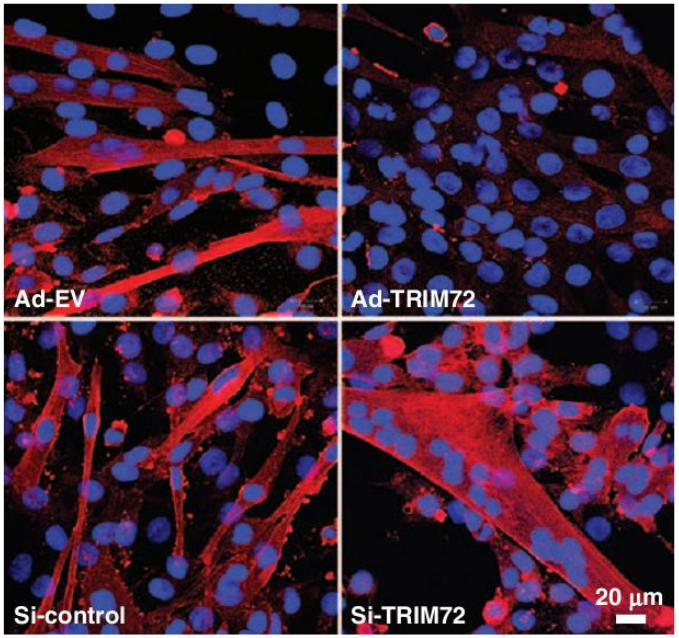
Cell Death and Differentiation (2010) 17, 1254–1265

www.nature.com/cdd

Function 3

TRIM72 negatively regulates myogenesis via targeting insulin receptor substrate-1

CS Lee[1,3], J-S Yi[1,3], S-Y Jung[1], B-W Kim[1], N-R Lee[1], H-J Choo[1], S-Y Jang[1], J Han[1], S-G Chi[1], M Park[2], J-H Lee[2] and Y-G Ko[*,1]



- TRIM72 is a novel antagonist of IRS-1, and is essential as a negative regulator of IGF-induced muscle differentiation

New Function

LETTER

doi:10.1038/nature11834

Central role of E3 ubiquitin ligase MG53 in insulin resistance and metabolic disorders

Ruisheng Song[1,2]*, Wei Peng[1]*, Yan Zhang[1]*, Fengxiang Lv[1], Hong-Kun Wu[1], Jiaojiao Guo[1], Yongxing Cao[3], Yanbin Pi[3], Xin Zhang[3], Li Jin[1], Mao Zhang[1], Peng Jiang[1], Fenghua Liu[1], Shaoshuai Meng[1], Xiuqin Zhang[1], Ping Jiang[1], Chun-Mei Cao[1] & Rui-Ping Xiao[1,4]

- The important role of MG53 in metabolic syndrome.

Target

- To look for new function of MG53:

- Subcellular Localizationodification
- Modification
- Co-expression Protein
- Interaction protein

Subcellular Localization

WoLF PSORT

Protein Subcellular Localization Prediction

about WoLF PSORT WoLF PSORTについて links Example Output

Please select an organism type:
- (•) Animal
- ( ) Plant
- ( ) Fungi

Please select input method:
- (•) From Text Area
- ( ) From File

Input Filename:
选择文件 未选择文件

Text Area: Enter multifasta format protein sequence(s) here.

```
MSAAPGLLRQELSCPLCLQLFDAPVTAECGHSFCRACLIRVAGEPAADGTVACPCCQAPT
RPQALSTNLQLSRLVEGLAQVFQGHCEEHLDPLSIYCEQDRTLVCGVCASLGSHRGHRLL
PAAEAQARLKTQLPQQKMQLQEACMRKEKTVAVLEHQLVEVEETVRQFRGAVGEQLGKMR
MFLAALESSLDREAERVRGDAGVALRRELSSLNSYLEQLRQMEKVLEEVADKPQTEFLMK
FCLVTSRLQKILSESPPPARLDIQLPVISDDFKFQVWKKMFRALMPALEELTFDPSSAHP
SLVVSSSGRRVECSDQKAPPAGEDTRQFDKAVAVVAQQLLSQGEHYWEVEVGDKPRWALG
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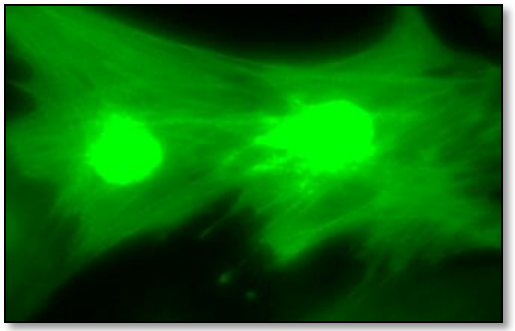
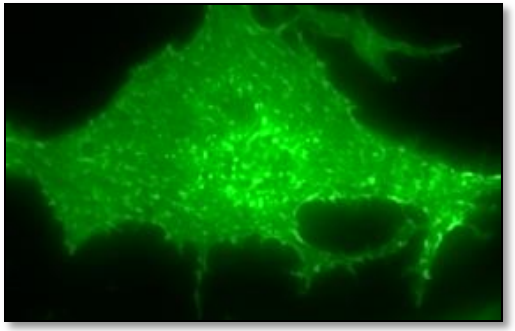
提交 clear

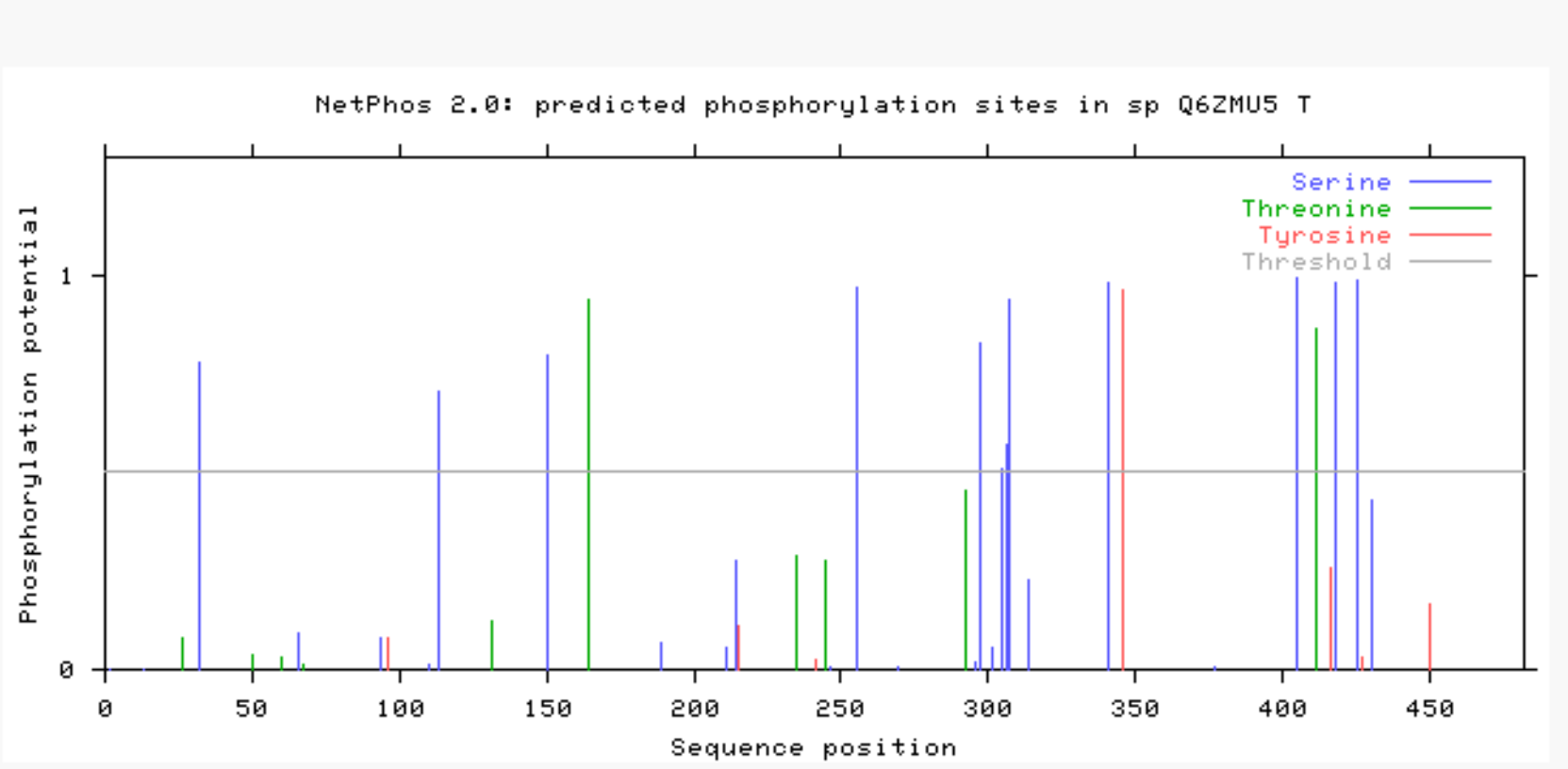




- The result shows TRIM72 existed both in the nuclear and cytocol, which is matched with our experimental data.

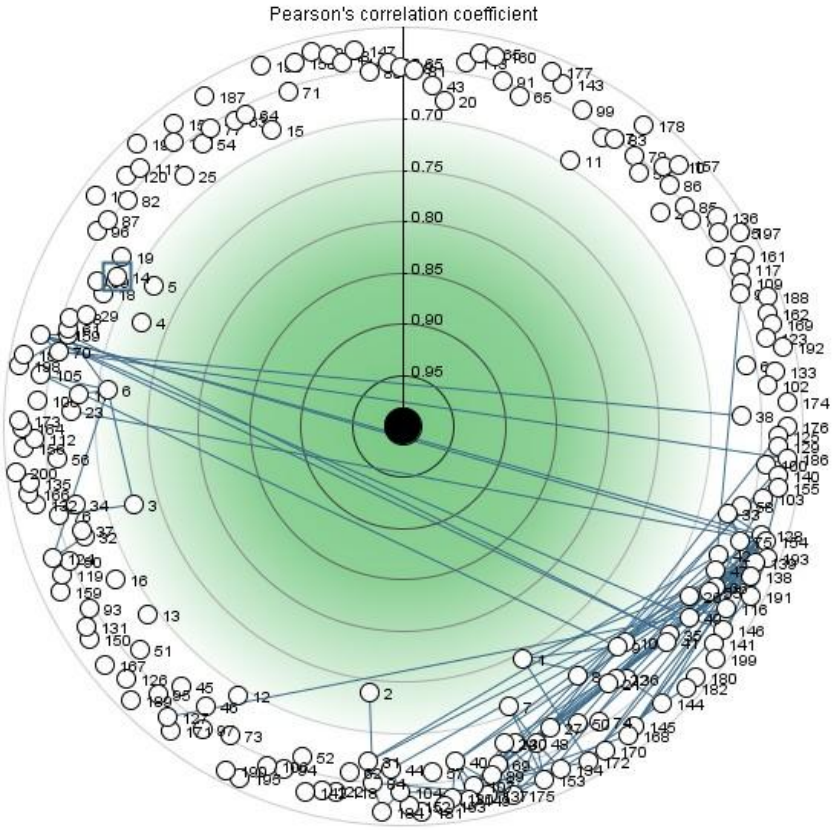
Phosphorlation Site

- **Expasy的NetPhos 2.0**

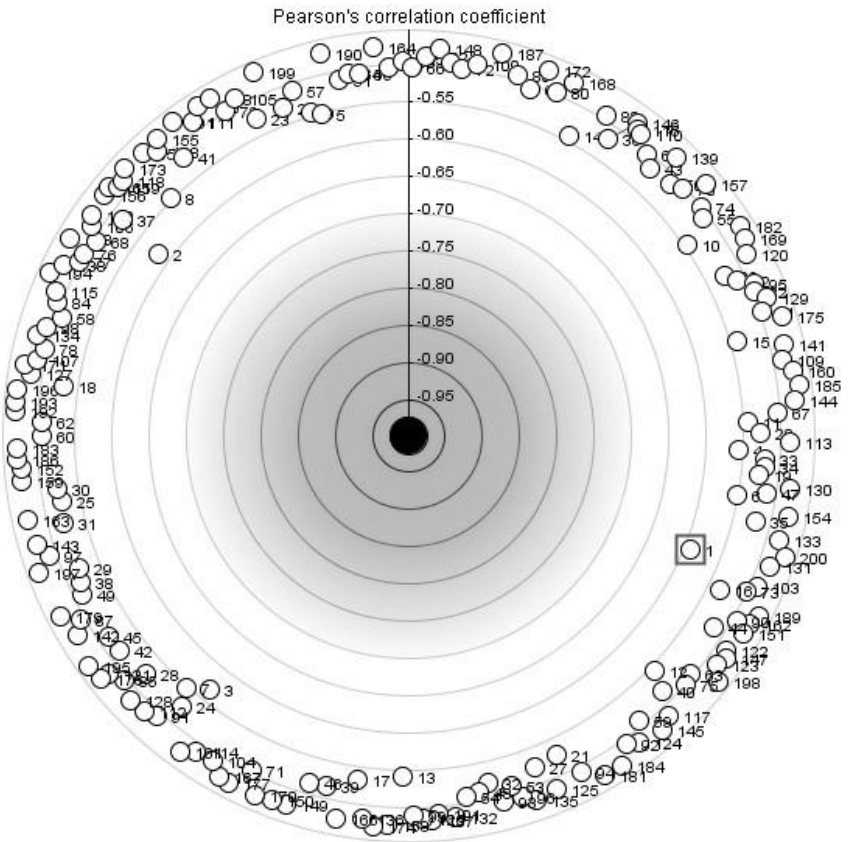


Co-expression Protein

Positive correlation

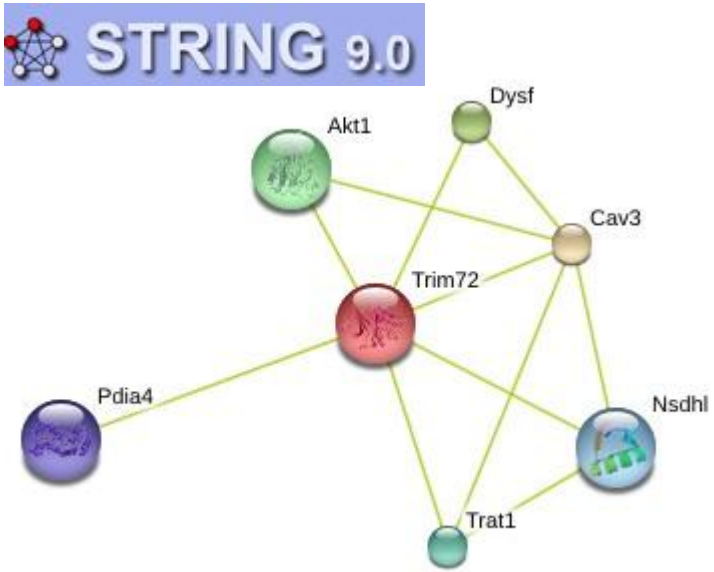


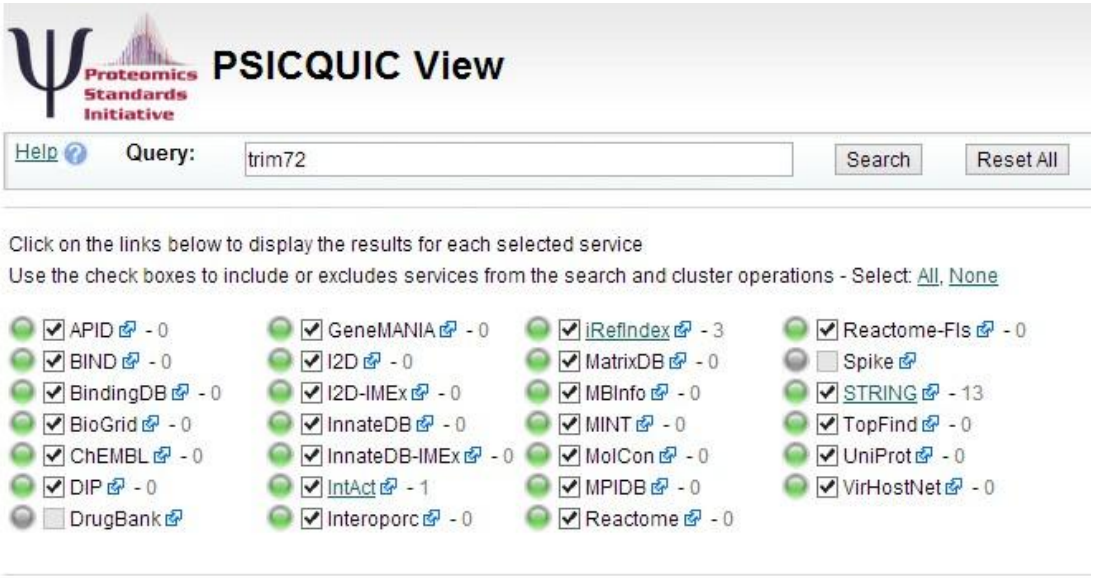
Negative correlation



GENEVESTIGATOR
shaping biological discovery

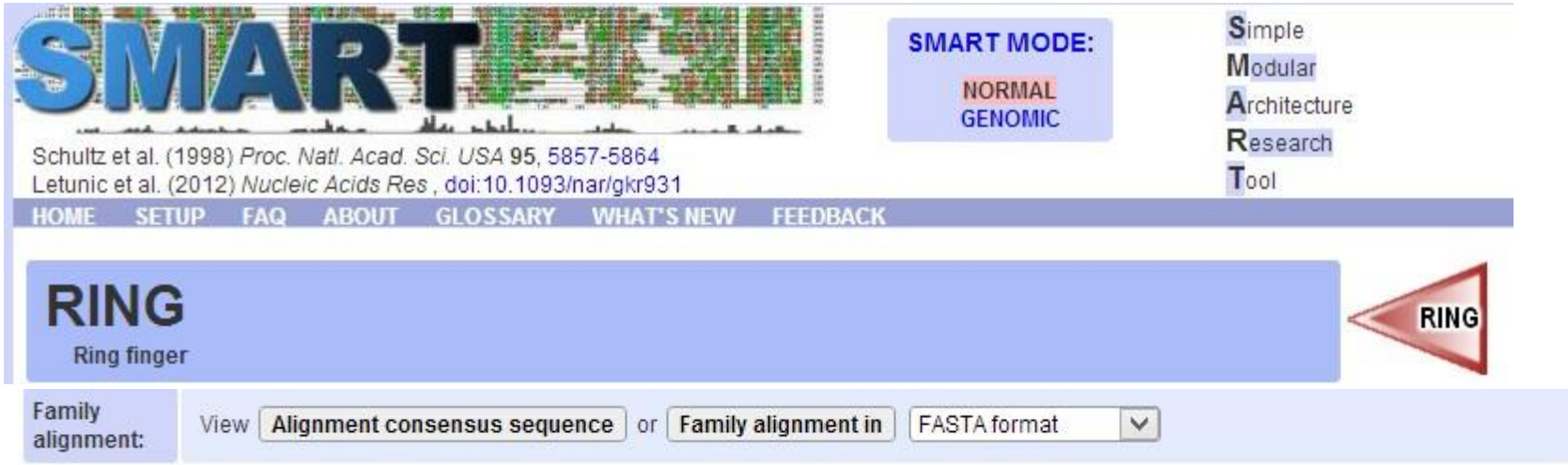
Interaction Protein Prediction

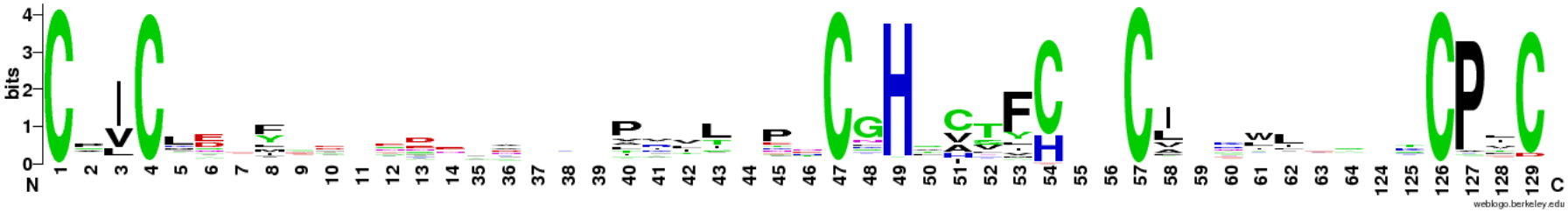




Which domain is responsible for the interaction with IRS1?

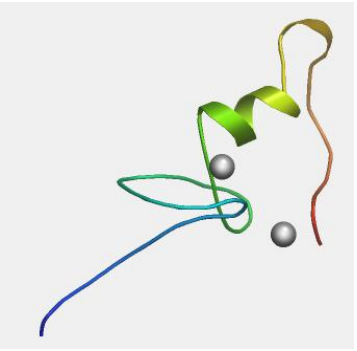
- We have already known that RING domain is necessary for the E3 ligase activity.
- Which amino acid is important?

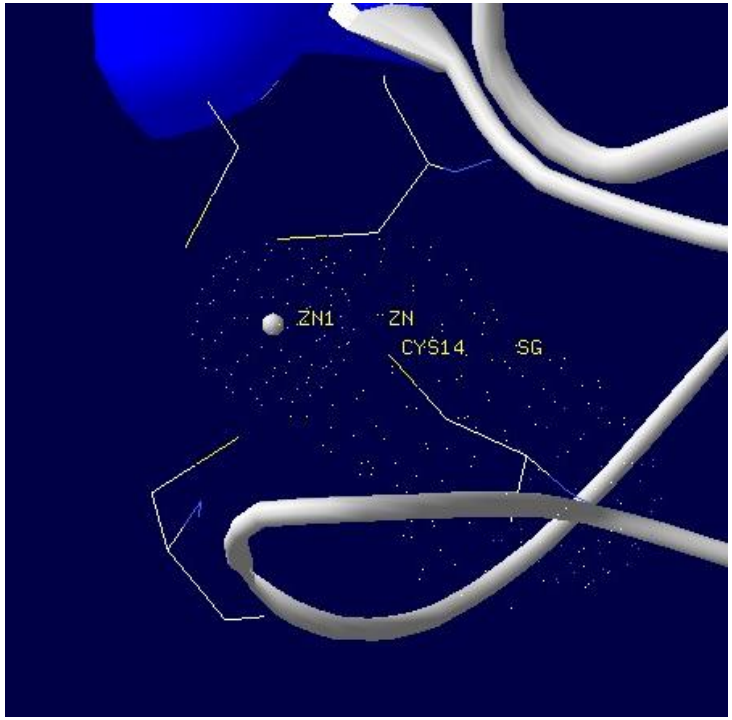


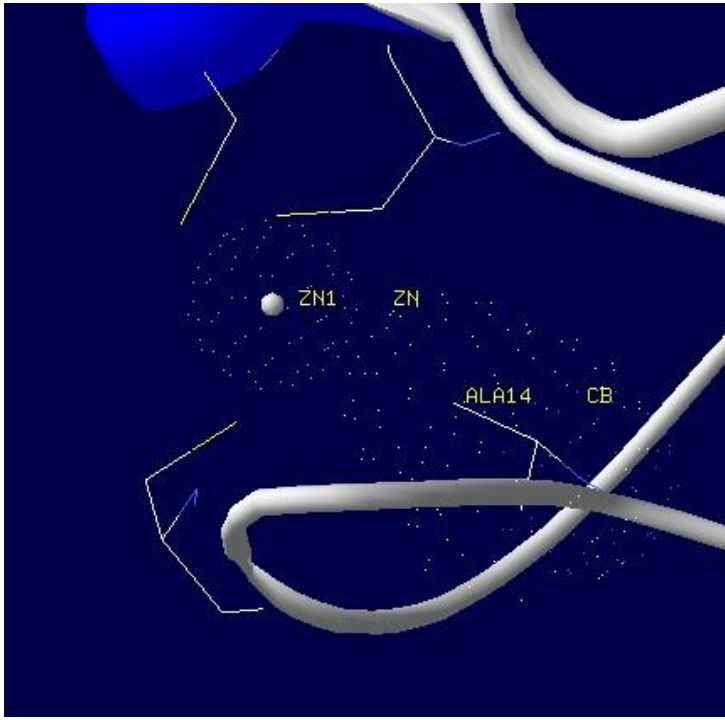


drawn by weblogo

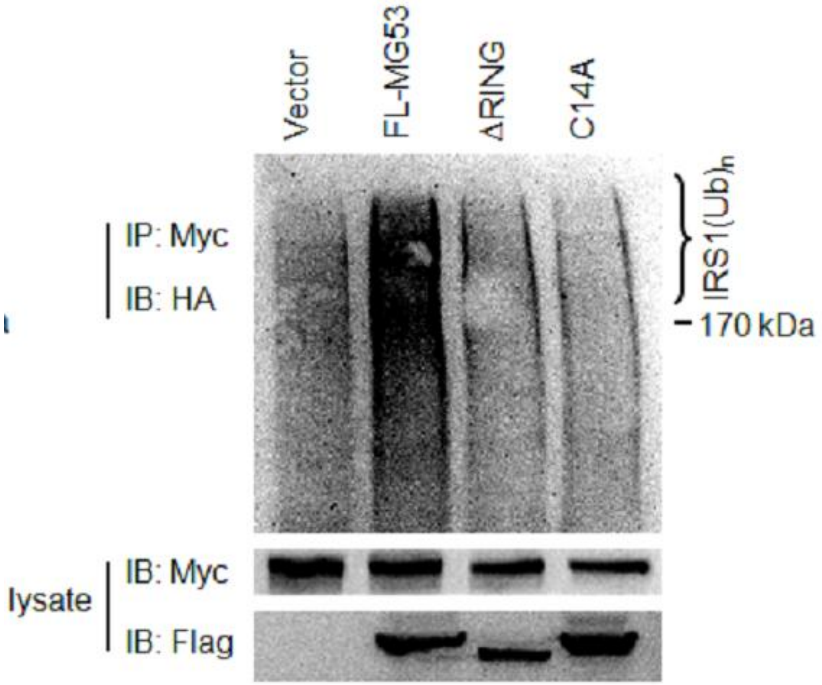
- Cystine is very conservative.
- Zn binding







- In order to delete E3 activity, we can easily mutate the first C to A.
- Thus, we generate mutant C14A.



RuiSheng Song *et al,* Nature(received).

Thanks

- We all recognize that there is somewhat law existing in the nature.
- 我们都承认生命运行有其内在规律可循
- Bioinformatics discover intrinsic principle using mathematics.
- 生物信息学是通过计算的方法发现生命的内在规律
- Bioinformatics is a mighty tool.
- 那么生物信息学一定是强大的工具！