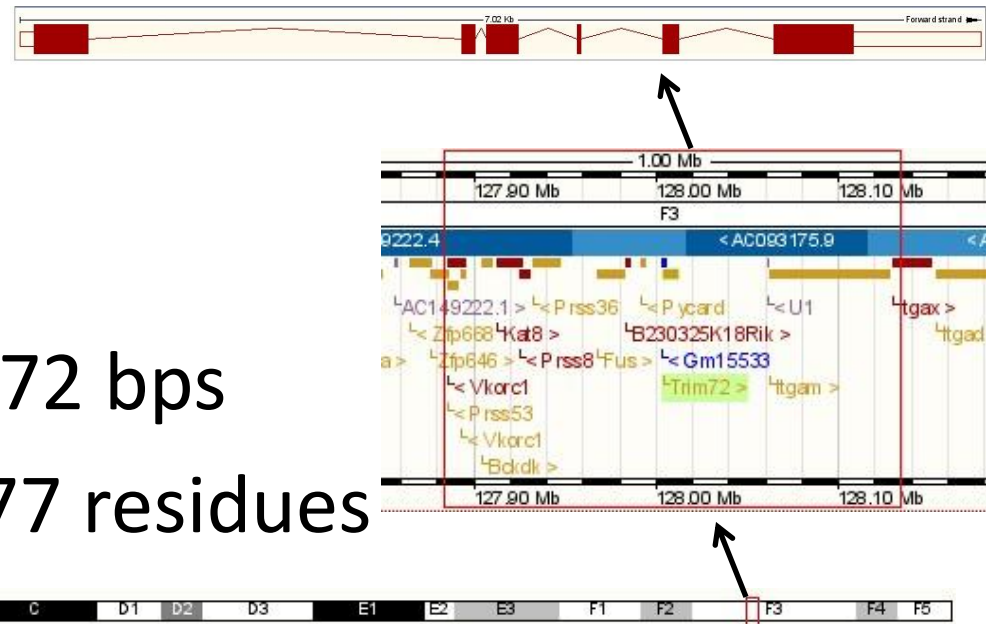


TRIM72: Structure, Evolution & Function

Presenter 吴鸿昆
Team members 张勇 余忠 陈艳敏

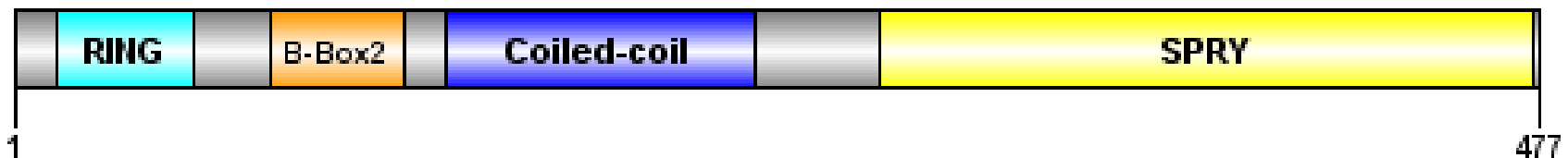
What is TRIM72?

- 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**



Primary Structure

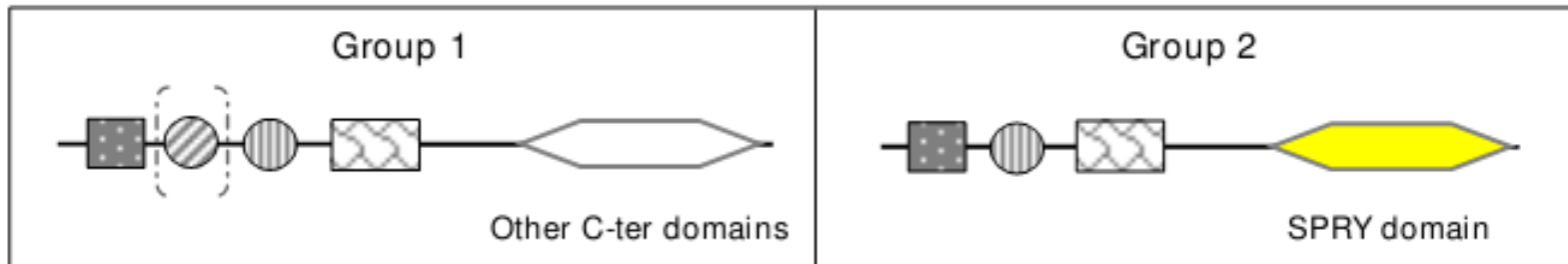
- RING(SM00184): Zinc-finger, E3 ubiquitin ligase activity.
- B-Box2(SM00336): Zinc-finger
- Coiled-coil(**PF05710**)
- SPRY(SM00449)



drawn by DOG 2.0

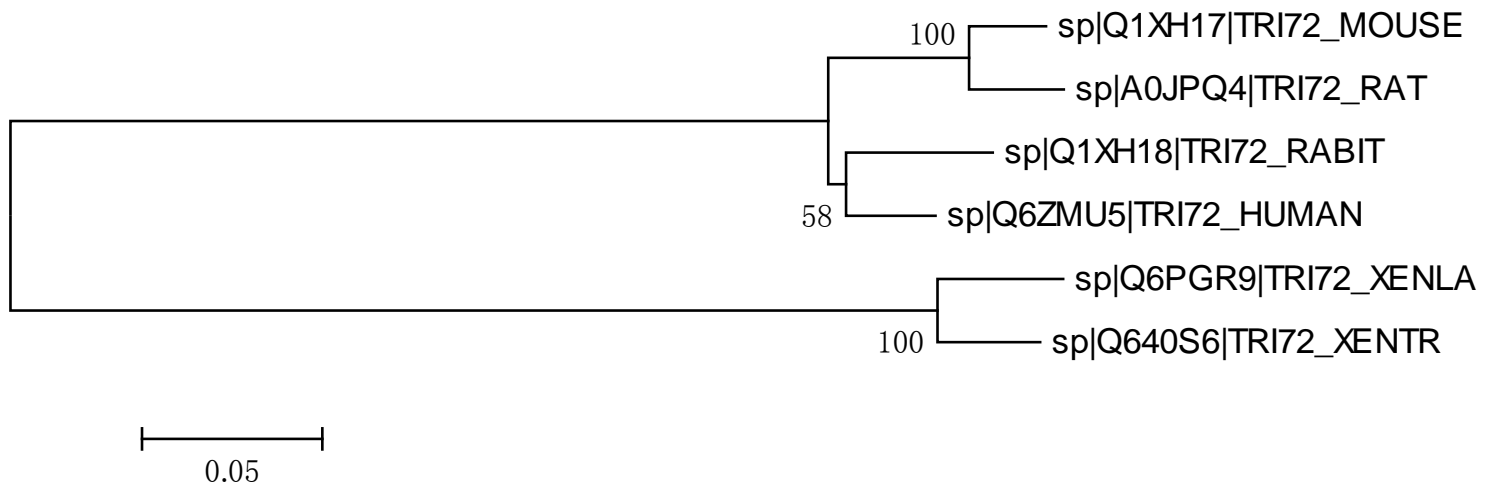
TRIM family (tripartite motif family)

- The TRIM motif includes the following three domains: RING, B-Box, Coiled-coil.
- According to the C-terminus, 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.

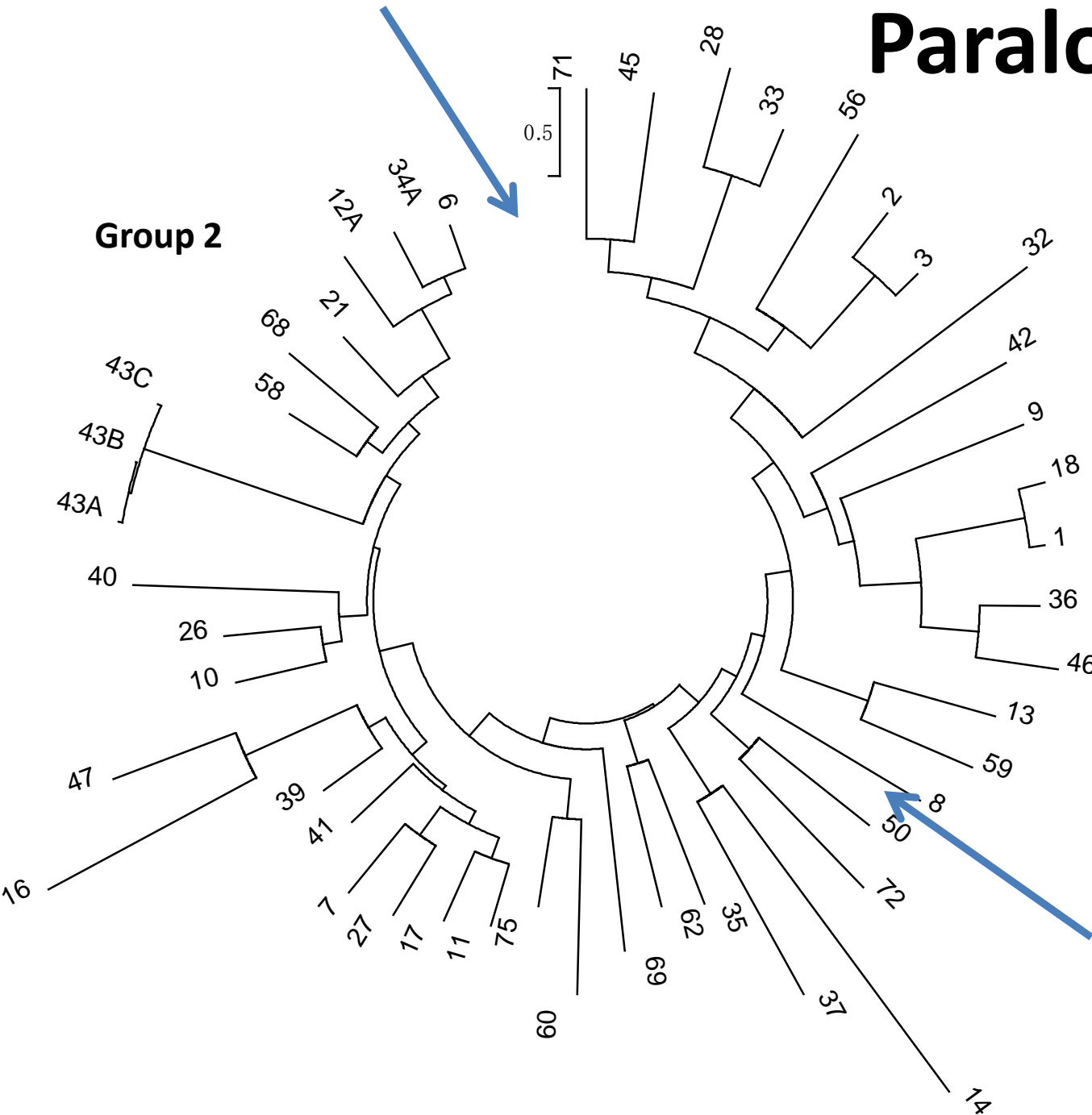


Orthology analysis

Phylogenetic Tree of Different Species by
Maximum Likelihood Method

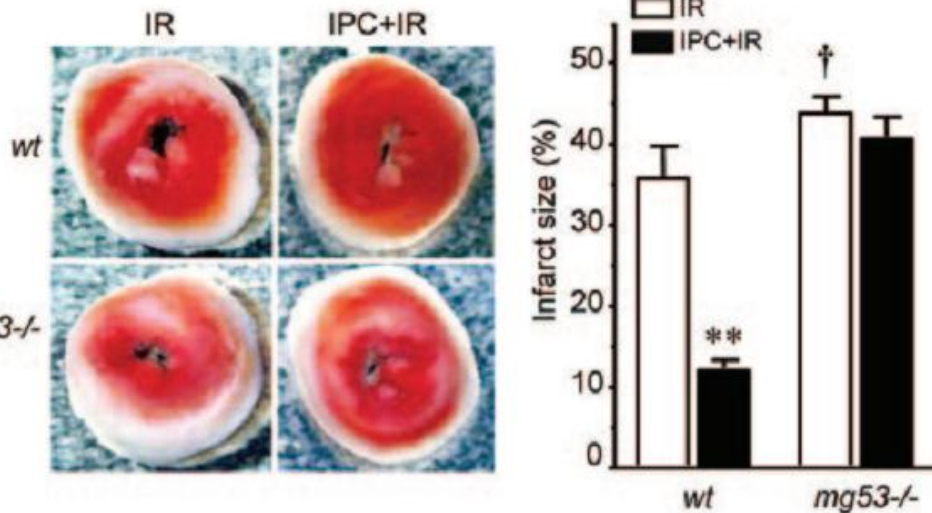


Paralogy analysis



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, Moonsoon Hwang, Li Jin, Jiaojiao Guo, Wei Peng, Geng Li, Miyuki Nishi, Hiroshi Takeshima, Jianjie Ma and Rui-Ping Xiao



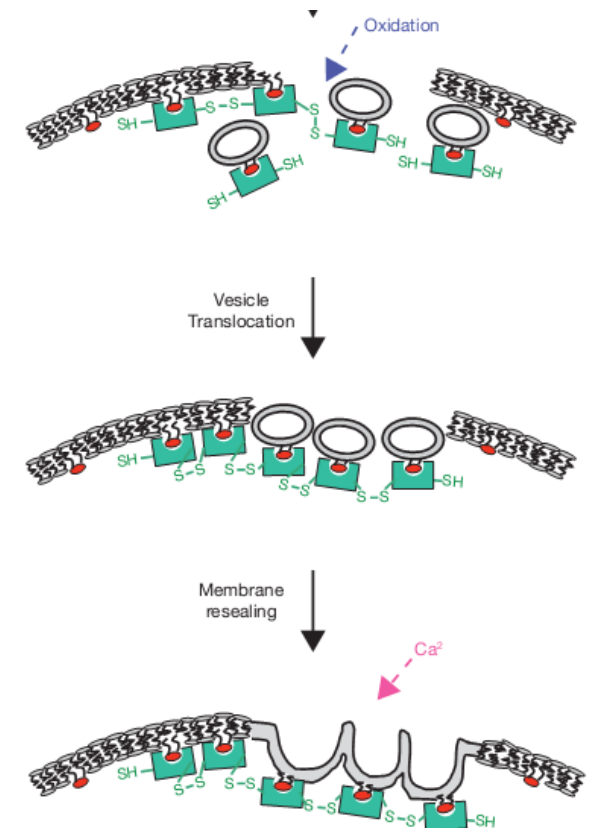
- MG53 as a primary component of the cardiac IPC response

Function 2

MG53 nucleates assembly of cell membrane repair machinery

Chuanxi Cai¹, Haruko Masumiya², Noah Weisleder¹, Noriyuki Matsuda³, Miyuki Nishi^{2,4}, MoonSun Hwang¹, Jae-Kyun Ko¹, Peihui Lin¹, Angela Thornton¹, Xiaoli Zhao¹, Zui Pan¹, Shinji Komazaki⁵, Marco Brotto¹, Hiroshi Takeshima^{2,4,6} and Jianjie Ma^{1,6}

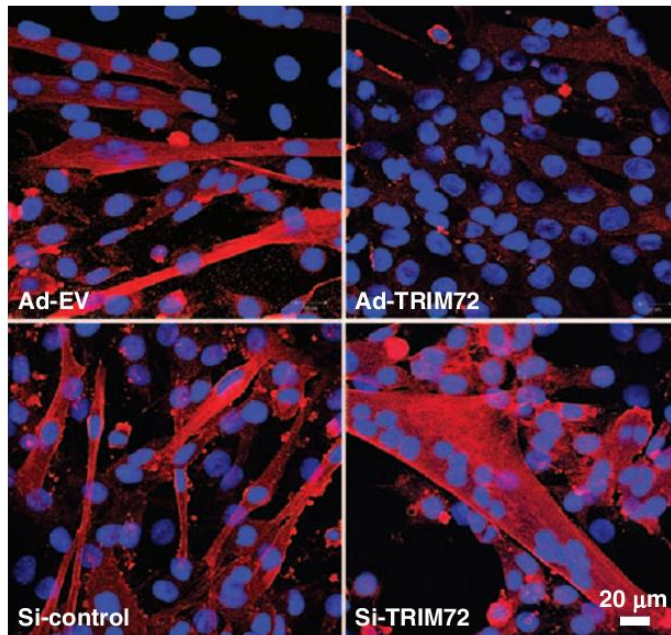
- Mice null for MG53 show progressive myopathy and reduced exercise capability, associated with defective membrane-repair capacity.



Function 3

TRIM72 negatively regulates myogenesis via targeting insulin receptor substrate-1

CS Lee^{1,3}, J-S Yi^{1,3}, S-Y Jung¹, B-W Kim¹, N-R Lee¹, H-J Choo¹, S-Y Jang¹, J Han¹, S-G Chi¹, M Park², J-H Lee² 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 Lv¹, Hong-Kun Wu¹, Jiaojiao Guo¹, Yongxing Cao³, Yanbin Pi³, Xin Zhang³, Li Jin¹, Mao Zhang¹, Peng Jiang¹, Fenghua Liu¹, Shaoshuai Meng¹, Xiuqin Zhang¹, Ping Jiang¹, Chun-Mei Cao¹ & Rui-Ping Xiao^{1,4}

- The important role of MG53 in metabolic syndrome.

Target

- To look for new function of MG53:
- Subcellular Localization
- 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:

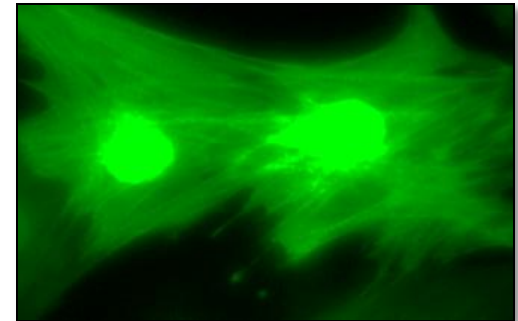


Text Area: Enter multifasta format protein sequence(s) here.

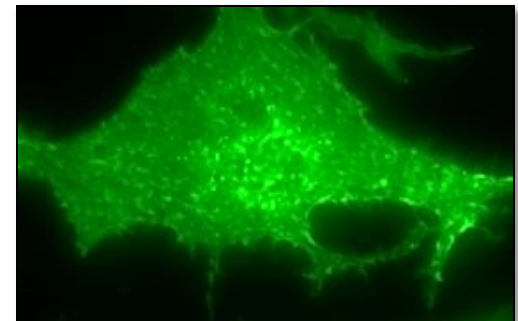
```
MSAAPGLLRQELSCPLCLQLFDAPVTAECGHSFCRACLIRVAGEPAADGTVACPCQAPT  
RPQALSTNLQLSRLVEGLAQVPQGHCCEHLDPLSIYCEQDRTLVCGWCASLGSRHRHLL  
PAAEAQARLKTQLFPQQMQLQEACMRKEKTVAVLEHQLVEVEETVRQFRGAVGEQLGKMR  
MFLAALESSLDREAERVVRGDAGVALRRELSLNSYLEQLRQMEKVEEVADKPQTEFLMK  
FCLVTSRLQKILSESPPPARLDIQLPVISDDFKFQVWKKMFRALMPALEELTFDPSSAHP  
SLVSSSGRRVCECDQKAPPAGEDTRQFDKAVAVVAQQLLSQGEHYWEVEVGDKFRWALG  
VMAADASRRGRHLHAVFSQGLWLLGLRDGKILEAHVEAKEPRALRTPERPARIGLYLSFA  
DGVLAFYDASNPDLVLTPIFSFHERLFGPVYPIFDVVCWHDKGKNAQPLLLVVGPEQEQA
```

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

Ad-GFP

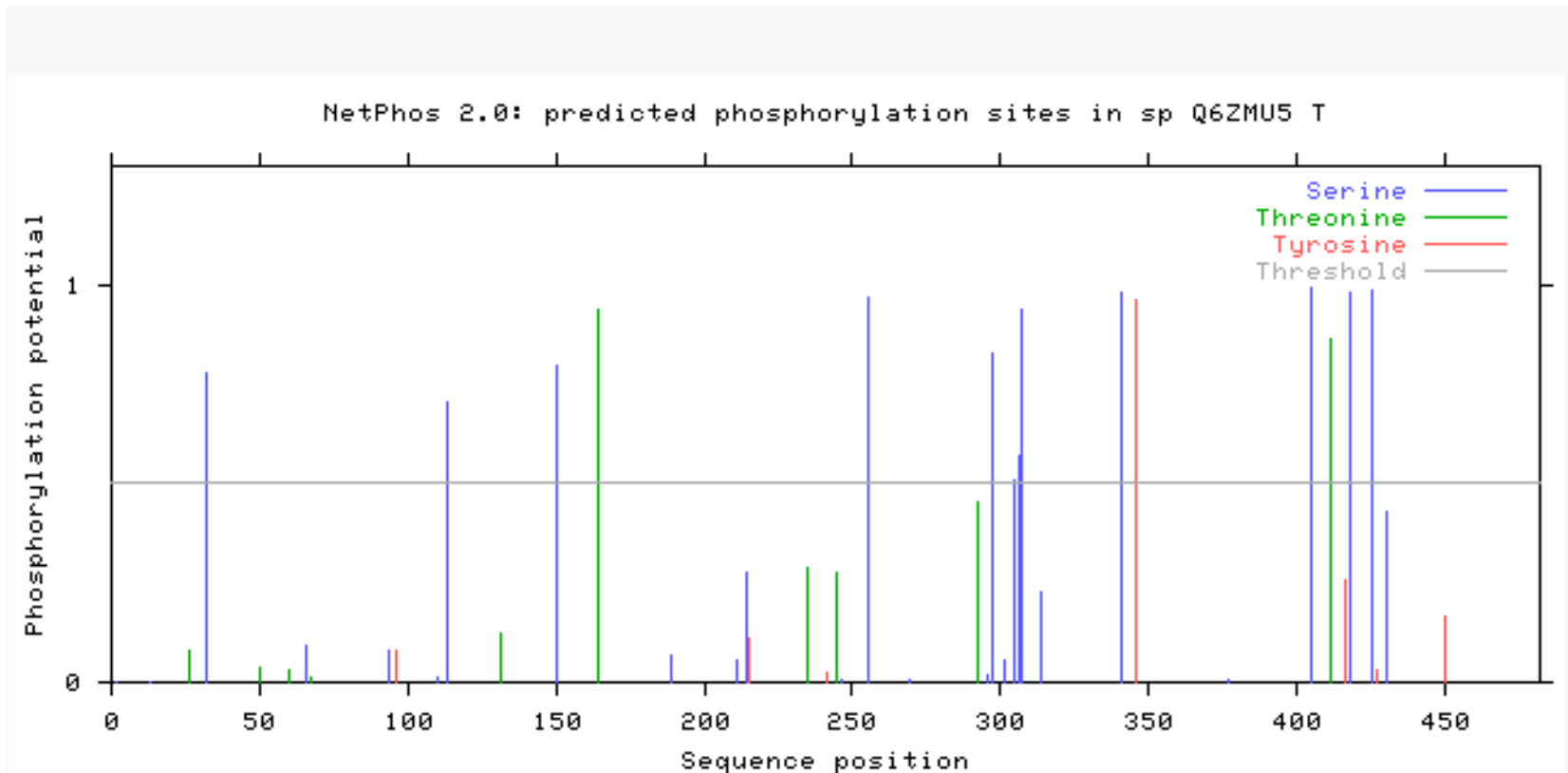


Ad-MG53-GFP



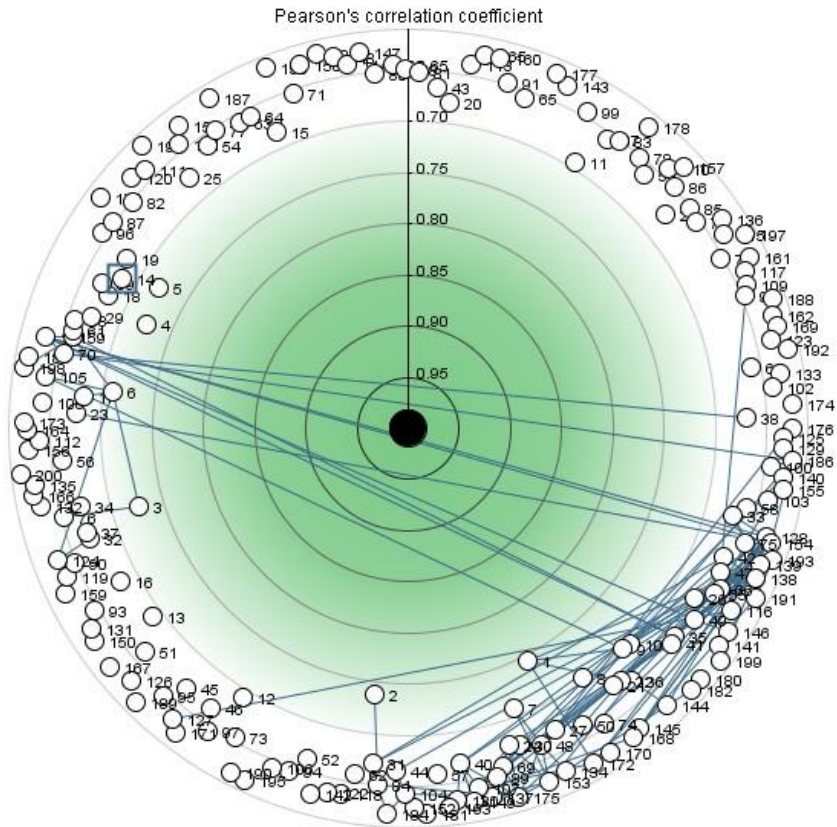
Phosphorlation Site

- Expasy的NetPhos 2.0

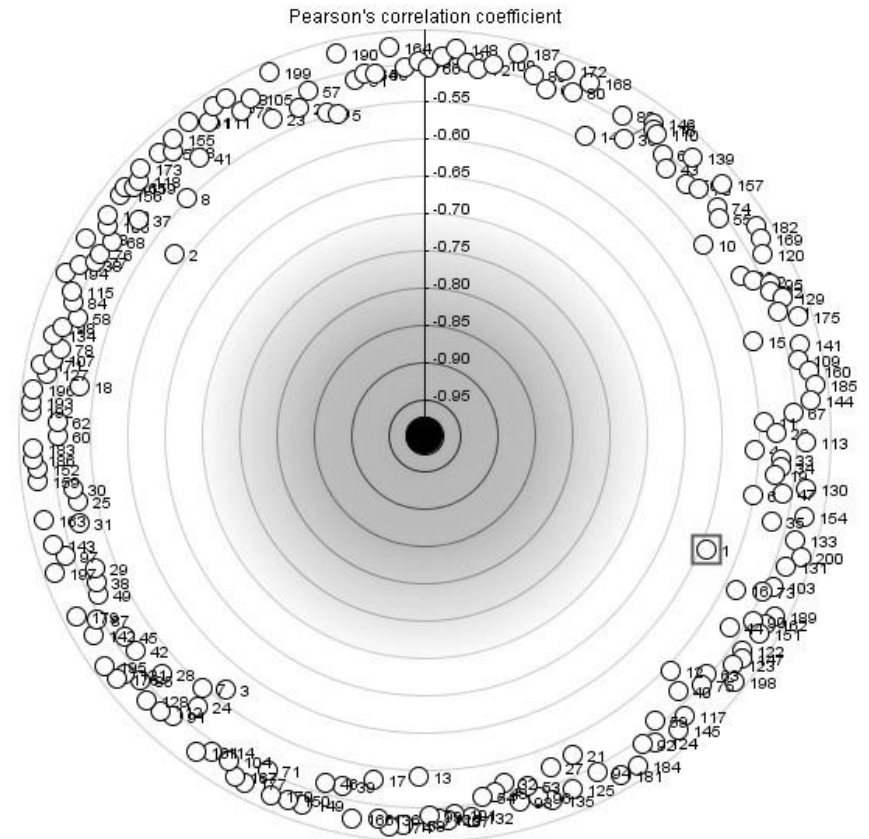


Co-expression Protein

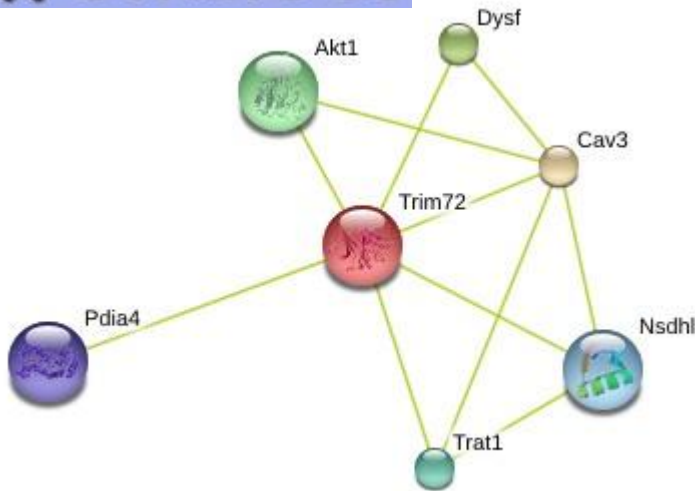
Positive correlation



Negative correlation



Interaction Protein Prediction



Help [?](#) Query: Search

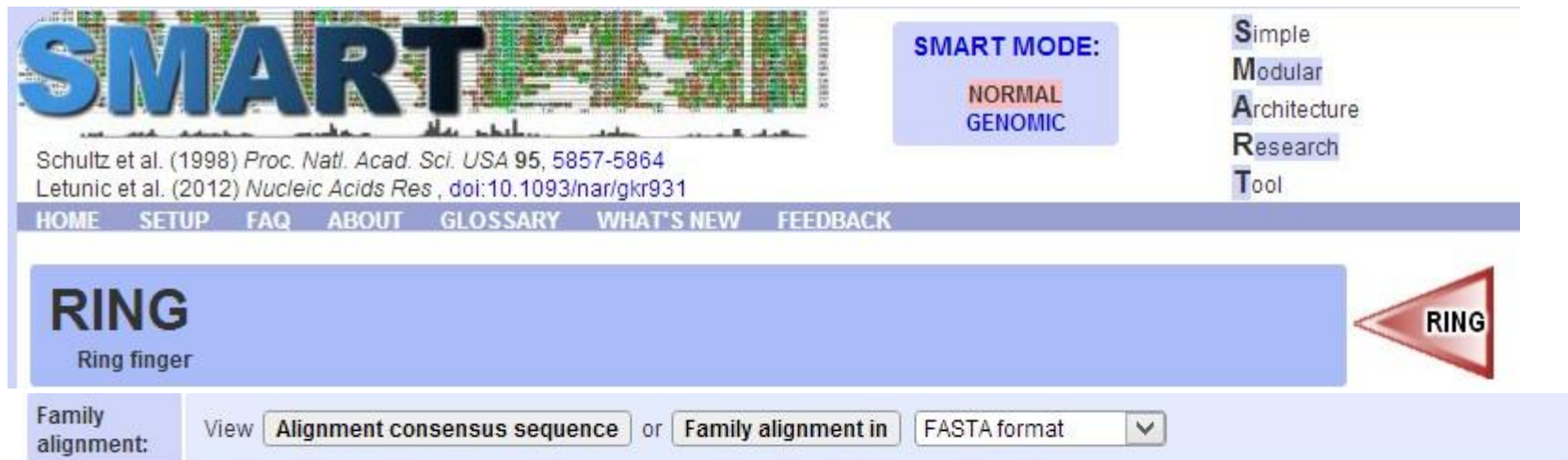
Click on the links below to display the results for each selected service

Use the check boxes to include or excludes services from the search and cluster operations - Select: [All](#), [None](#)

- | | | | |
|---|---|---|--|
| <input checked="" type="checkbox"/> APID ? - 0 | <input checked="" type="checkbox"/> GeneMANIA ? - 0 | <input checked="" type="checkbox"/> iRefIndex ? - 3 | <input checked="" type="checkbox"/> Reactome-FIs ? - 0 |
| <input checked="" type="checkbox"/> BIND ? - 0 | <input checked="" type="checkbox"/> I2D ? - 0 | <input checked="" type="checkbox"/> MatrixDB ? - 0 | <input type="checkbox"/> Spike ? |
| <input checked="" type="checkbox"/> BindingDB ? - 0 | <input checked="" type="checkbox"/> I2D-IMEx ? - 0 | <input checked="" type="checkbox"/> MBIInfo ? - 0 | <input checked="" type="checkbox"/> STRING ? - 13 |
| <input checked="" type="checkbox"/> BioGrid ? - 0 | <input checked="" type="checkbox"/> InnateDB ? - 0 | <input checked="" type="checkbox"/> MINT ? - 0 | <input checked="" type="checkbox"/> TopFind ? - 0 |
| <input checked="" type="checkbox"/> ChEMBL ? - 0 | <input checked="" type="checkbox"/> InnateDB-IMEx ? - 0 | <input checked="" type="checkbox"/> MolCon ? - 0 | <input checked="" type="checkbox"/> UniProt ? - 0 |
| <input checked="" type="checkbox"/> DIP ? - 0 | <input checked="" type="checkbox"/> IntAct ? - 1 | <input checked="" type="checkbox"/> MPIDB ? - 0 | <input checked="" type="checkbox"/> VirHostNet ? - 0 |
| <input type="checkbox"/> DrugBank ? | <input checked="" type="checkbox"/> Interporc ? - 0 | <input checked="" type="checkbox"/> Reactome ? - 0 | |

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?



The image shows a screenshot of the SMART database interface. At the top left is the SMART logo with a background of a protein domain alignment. Below the logo are two citations: "Schultz et al. (1998) Proc. Natl. Acad. Sci. USA 95, 5857-5864" and "Letunic et al. (2012) Nucleic Acids Res, doi:10.1093/nar/gkr931". To the right of the logo is a "SMART MODE:" section with "NORMAL GENOMIC" selected. Further right is a vertical menu with options: "Simple", "Modular", "Architecture", "Research", and "Tool". Below the logo and citations is a navigation bar with links: "HOME", "SETUP", "FAQ", "ABOUT", "GLOSSARY", "WHAT'S NEW", and "FEEDBACK". The main content area features a large blue box with the text "RING" and "Ring finger" below it. To the right of this box is a red triangle pointing left with the word "RING" inside. At the bottom left is a "Family alignment:" section with a "View" dropdown menu. The menu is currently set to "Alignment consensus sequence" and is followed by the text "or Family alignment in" and a "FASTA format" dropdown menu.

SMART

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

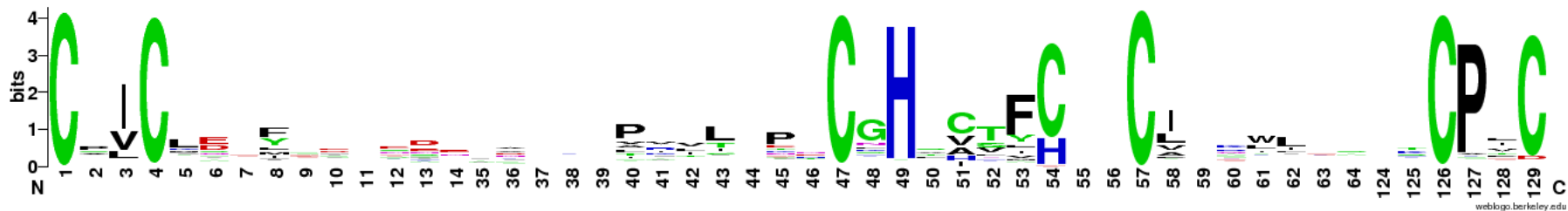
SMART MODE:
NORMAL
GENOMIC

Simple
Modular
Architecture
Research
Tool

HOME SETUP FAQ ABOUT GLOSSARY WHAT'S NEW FEEDBACK

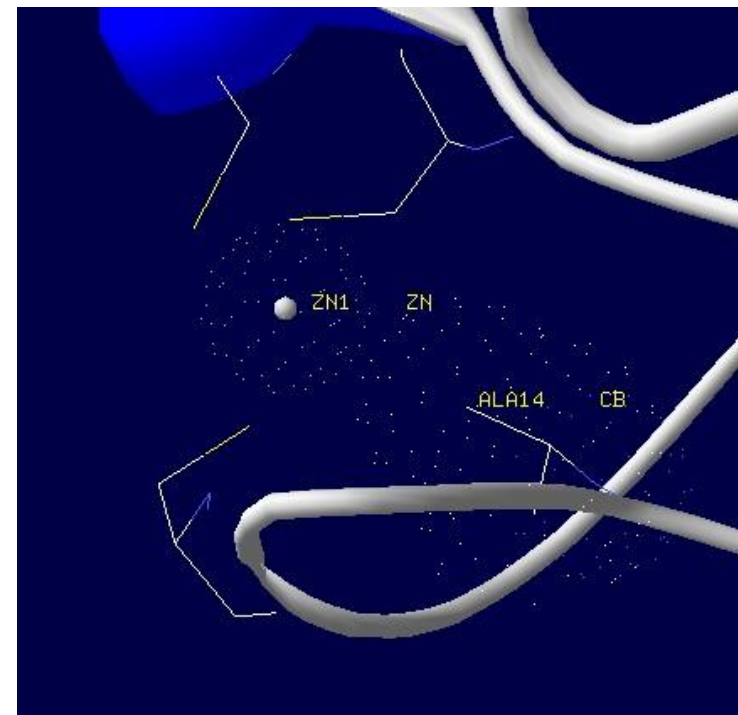
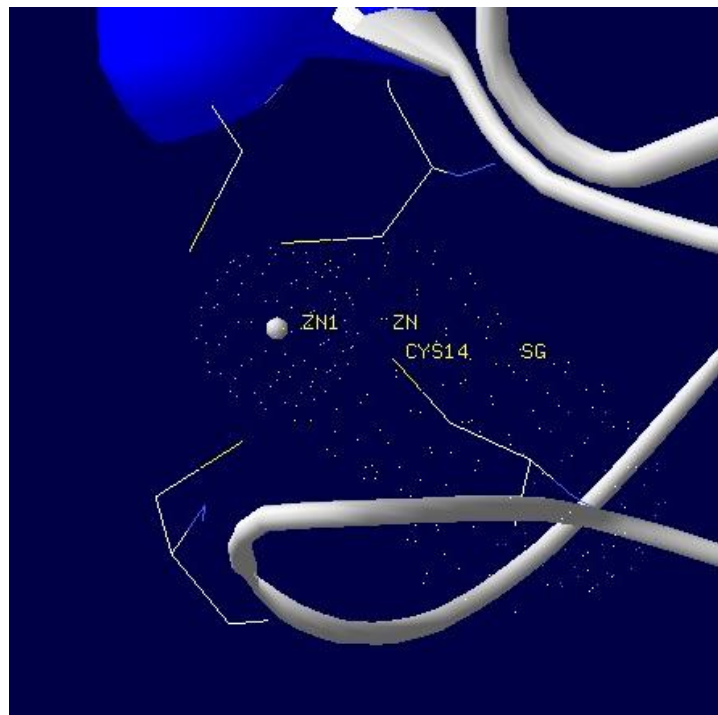
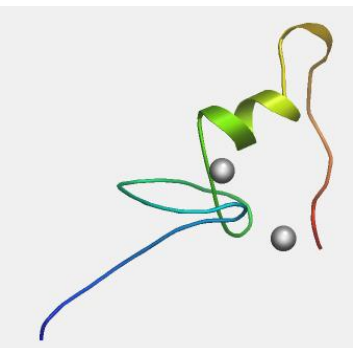
RING
Ring finger

Family alignment: View or

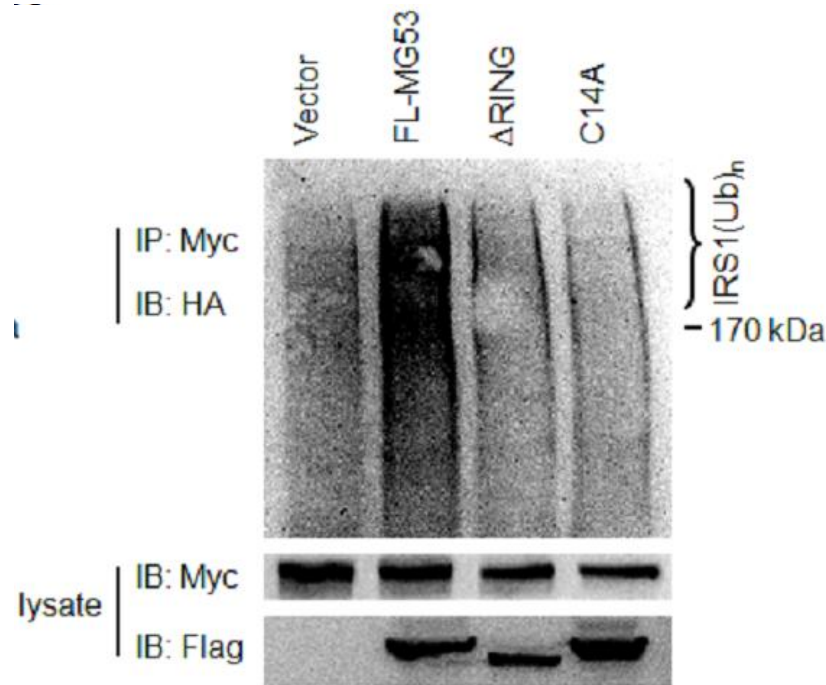


drawn by weblogo

- 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！