An overview of selenoproteins and analysis of the selenoprotein W

Group 3

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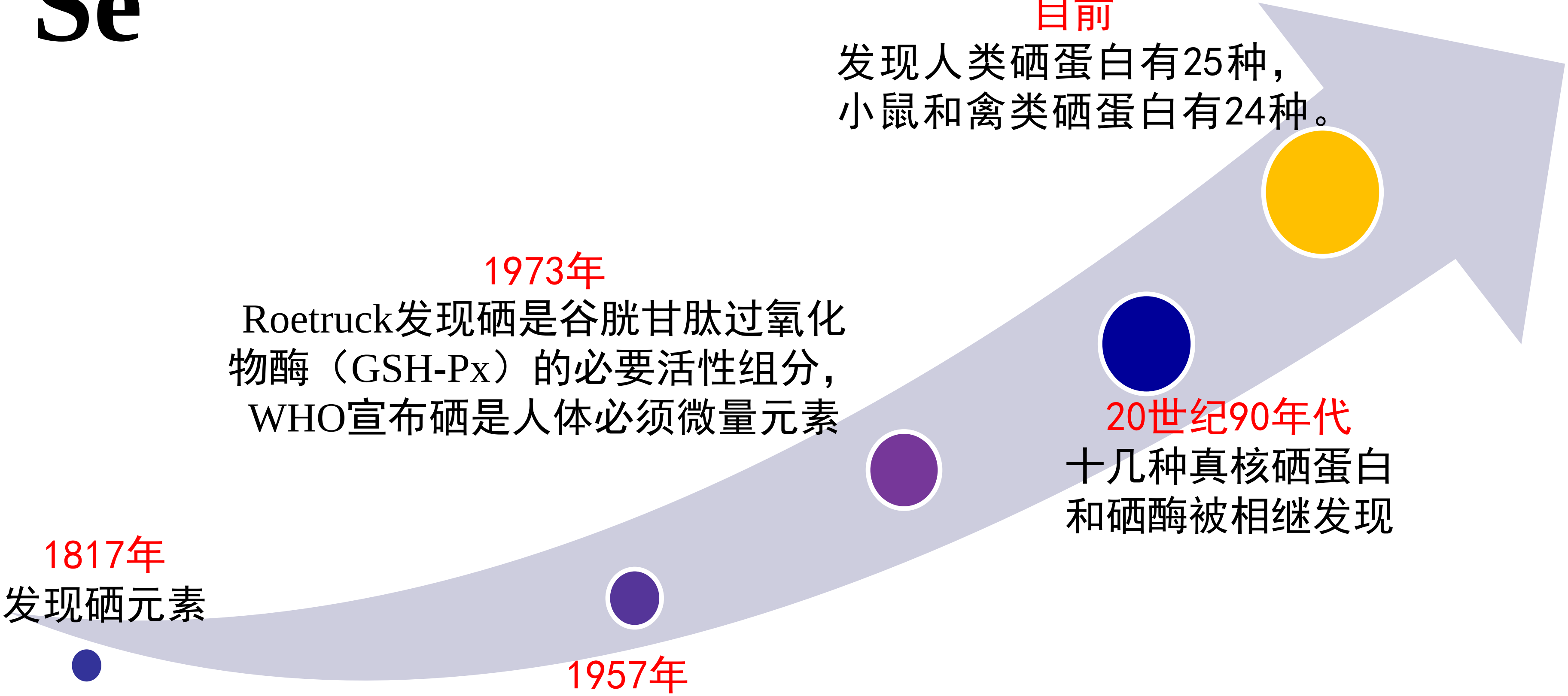
Outline

- Background
- Bioinformatics analysis
- Acknowledgement

Background

Se



1817年
发现硒元素

1957年
Schwarz和Foltz首次证明
硒是动物必须微量元素

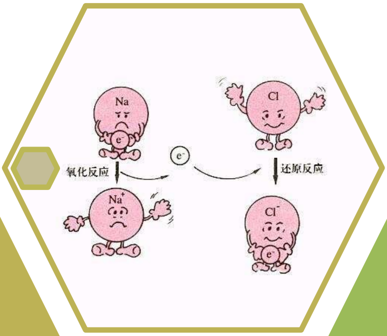
1973年
Roetruck发现硒是谷胱甘肽过氧化物酶（GSH-Px）的必要活性组分，WHO宣布硒是人体必须微量元素

20世纪90年代
十几种真核硒蛋白
和硒酶被相继发现

目前
发现人类硒蛋白有25种，
小鼠和禽类硒蛋白有24种。

Background

Biological function of Selenium



抗氧化

功能

抗癌

提高免

疫力

清除自

由基

Background

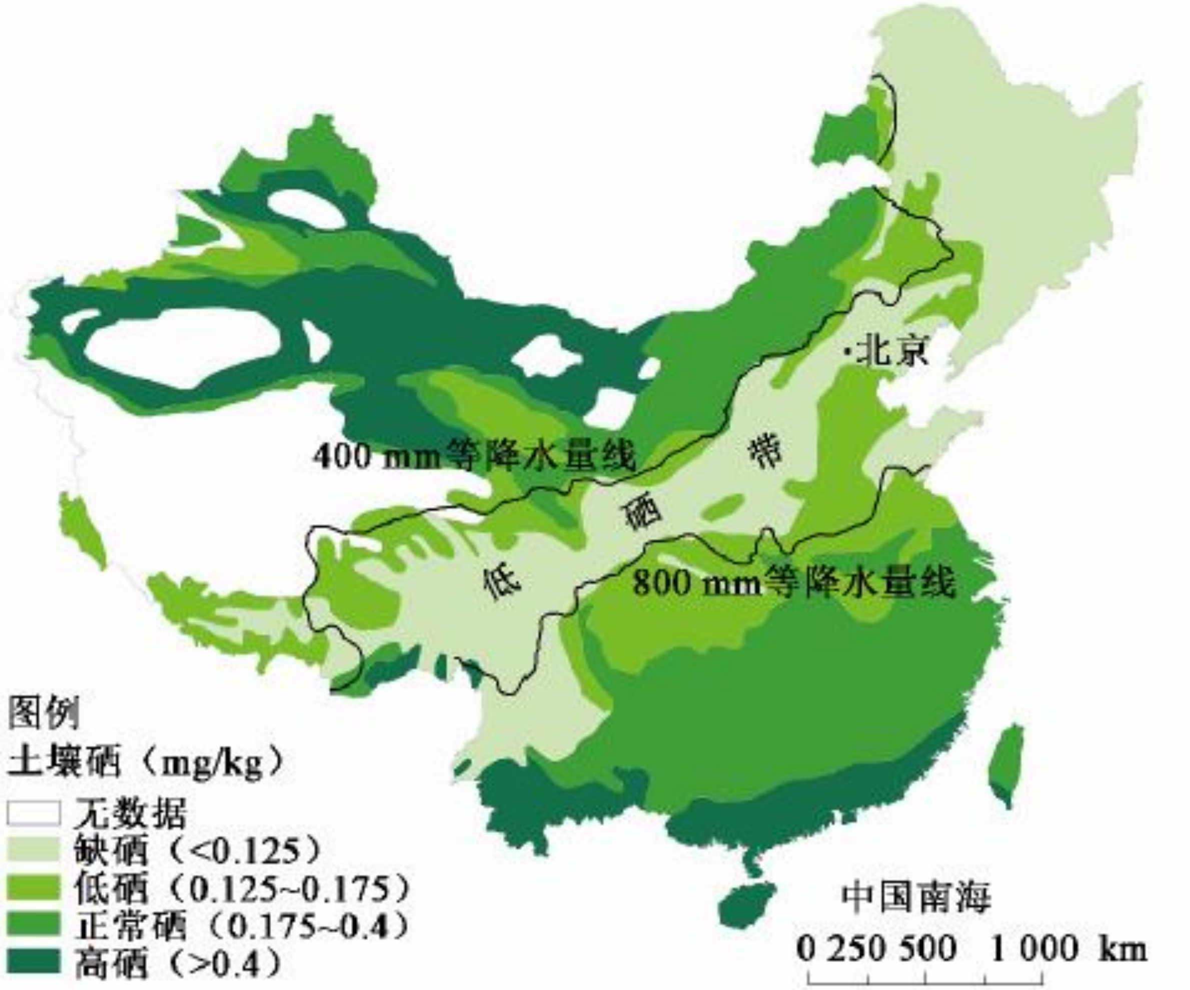


Figure Distribution pattern of soil selenium concentration in China

我国有72%地区缺硒，其中29%的地区严重缺硒。

Background

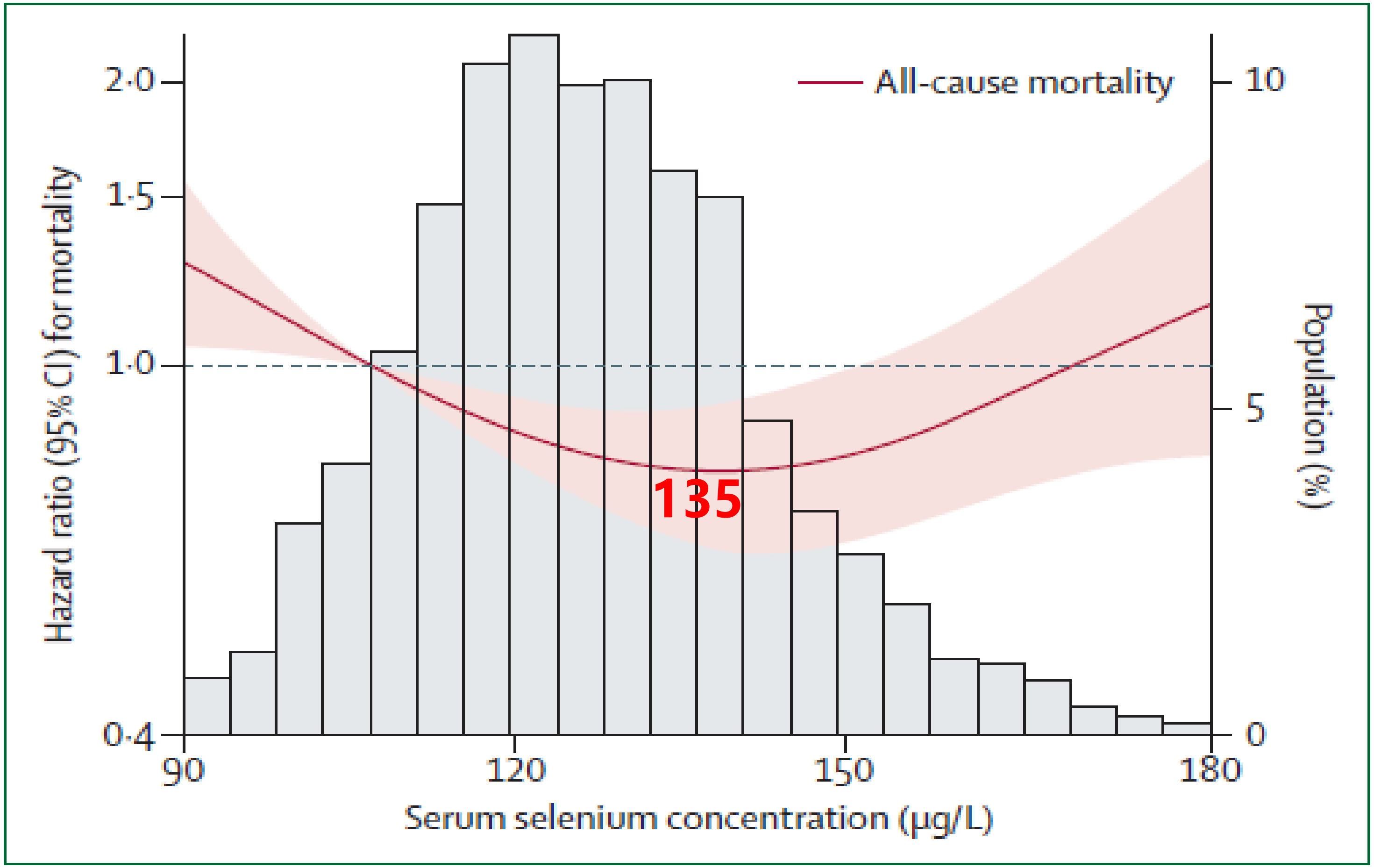


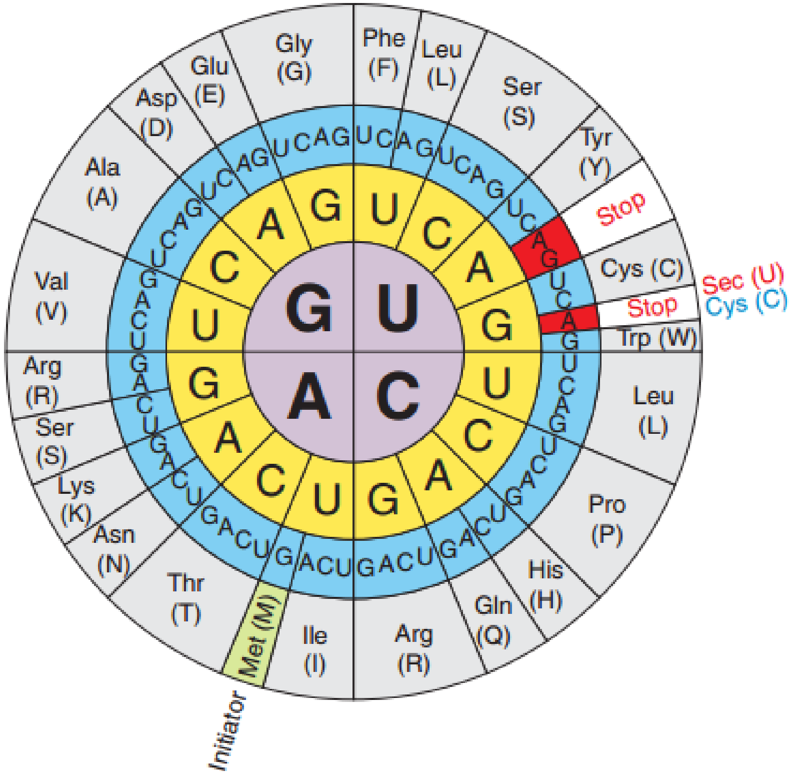
Figure Serum selenium levels and the risk of cardiovascular disease

Margaret P Rayman. 2012, The Lancet.

Background

Selenoprotein

- 硒蛋白（selenoprotein）是指一类含有硒代半胱氨酸（Sec）的蛋白质，承载着硒元素几乎所有的生物学功能。



- 在硒蛋白基因的 3′-非编码区(UTR)存在硒代半胱氨酸插入序列(SECIS)，指导编码区内的 UGA 解码为 Sec。

Background

表 真核生物体内硒蛋白及主要生理功能

硒蛋白	缩写	功能
硒蛋白15	Sep15	蛋白质折叠
甲状腺素脱碘酶1-3	Dio1-3	调控甲状腺激素活化
谷胱甘肽过氧化物酶1-4，6	GPx1-6	氢过氧化物/脂质过氧化物的清除
硒蛋白H	SelH	保护基因组免受氧化损伤
硒蛋白I	SelI	未知
硒蛋白J	SelJ	未知
硒蛋白K	SelK	参与炎症反应
硒蛋白M	SelM	Ca^{2+}稳态
硒蛋白N	SelN	调控肌肉发育
硒蛋白O	SelO	未知
硒蛋白P	SelP	参与硒的转运
硒蛋白S	SelS	参与炎症反应
硒磷酸盐合成酶2	SPS2	硒蛋白的合成
硒蛋白T	SelT	Ca^{2+}稳态；神经内分泌
硫氧还原蛋白还原酶1-3	TrxR1-3	二硫键的还原
硒蛋白U	SelU	未知
硒蛋白V	SelV	未知
硒蛋白W	SelW	未知
蛋氨酸-S-硫氧化物还原酶	SelMrsA	蛋氨酸还原
蛋氨酸-R-硫氧化物还原酶	SelMrsB	蛋氨酸还原

Rederstorff et al.,2006

Background

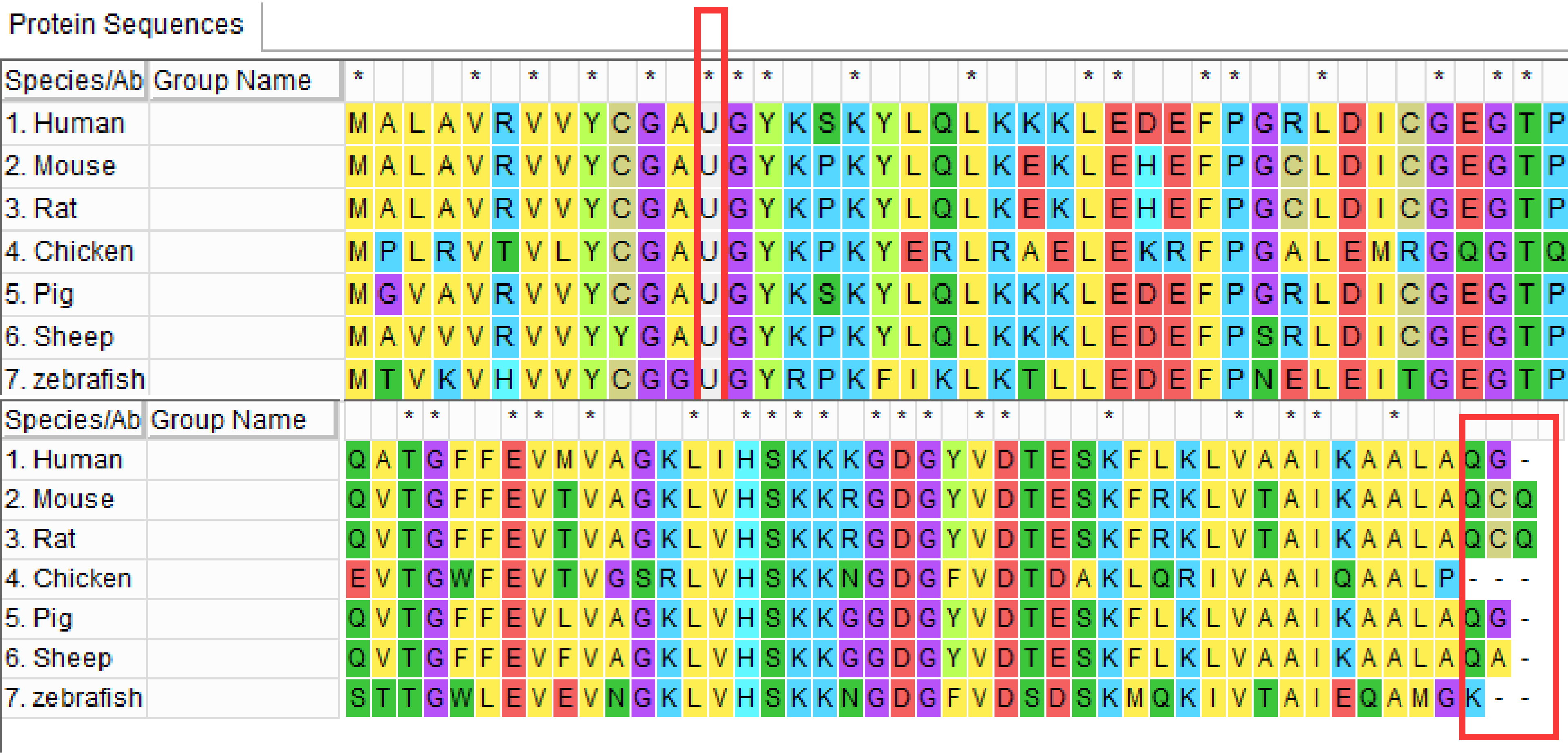
硒蛋白W

- 硒蛋白W是在羊心脏和肌肉细胞中发现一种含硒蛋白质，分子量约为 10 kDa。
- 硒蛋白W主要分布于**骨骼肌和心肌**，缺硒可使肌肉组织中硒蛋白W含量明显下降，并导致白肌病（white muscle disease）。
- 硒蛋白W结合谷胱甘肽（glutathione, GSH）并发挥抗氧化作用，但由于其分子量小，易受外界环境干扰，故其确切的作用机制和功能还有待于进一步的研究。

NCBI查找多物种硒蛋白W的信息

物种	拉丁文名	英文名	RefSeq登陆号	bp	编码区	基因登录号	蛋白质登录号
人	Homo sapiens	Human	NM_003009.3	905	215-478	6415	NP_003000.1
小鼠	Mus musculus	Mouse	NM_009156.2	722	92-358	20364	NP_033182.1
大鼠	Rattus Norvegicus	Rat	NM_013027.3	717	85-351	25545	NP_037159.4
鸡	Gallus gallus	Chicken	NM_001166327.2	860	100-357	100310814	NP_001159799.1
猪	Sus scrofa	pig	NM_213977.1	705	53-316	397032	NP_999142.1
绵羊	Ovis aries	sheep	XM_004023205.3	777	114-377	101119329	XP_004023254.2
斑马鱼	Danio rerio	zebrafish	NM_178287.5	841	136-396	352915	NP_840072.3

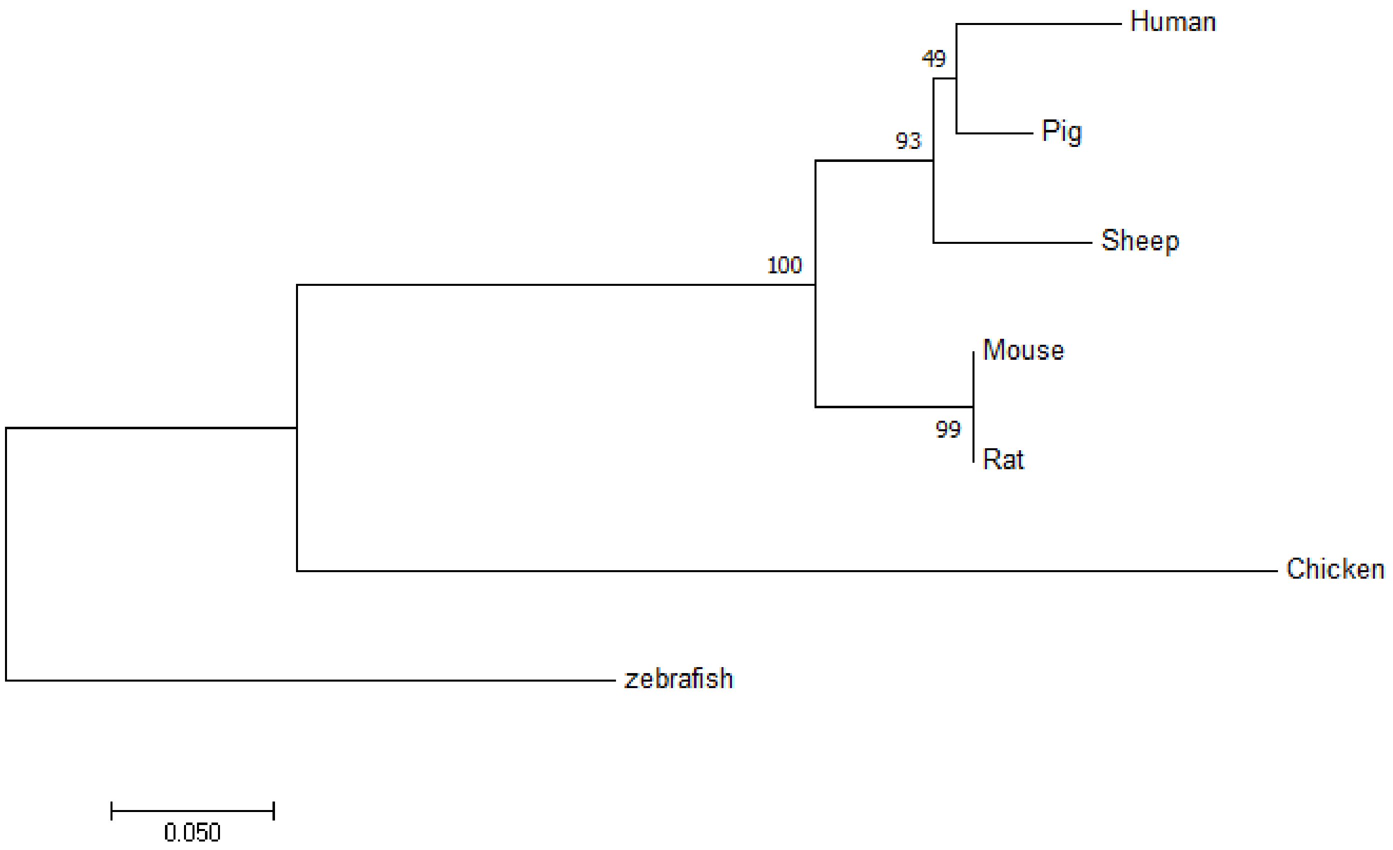
Alignment



Species/Ab	Group Name	*				*		*		*		*	*	*			*				*				*	*			*	*			*				*		*	*	
1. Human		M	A	L	A	V	R	V	V	Y	C	G	A	U	G	Y	K	S	K	Y	L	Q	L	K	K	K	L	E	D	E	F	P	G	R	L	D	I	C	G	E	G	T	P
2. Mouse		M	A	L	A	V	R	V	V	Y	C	G	A	U	G	Y	K	P	K	Y	L	Q	L	K	E	K	L	E	H	E	F	P	G	C	L	D	I	C	G	E	G	T	P
3. Rat		M	A	L	A	V	R	V	V	Y	C	G	A	U	G	Y	K	P	K	Y	L	Q	L	K	E	K	L	E	H	E	F	P	G	C	L	D	I	C	G	E	G	T	P
4. Chicken		M	P	L	R	V	T	V	L	Y	C	G	A	U	G	Y	K	P	K	Y	E	R	L	R	A	E	L	E	K	R	F	P	G	A	L	E	M	R	G	Q	G	T	Q
5. Pig		M	G	V	A	V	R	V	V	Y	C	G	A	U	G	Y	K	S	K	Y	L	Q	L	K	K	K	L	E	D	E	F	P	G	R	L	D	I	C	G	E	G	T	P
6. Sheep		M	A	V	V	V	R	V	V	Y	Y	G	A	U	G	Y	K	P	K	Y	L	Q	L	K	K	K	L	E	D	E	F	P	S	R	L	D	I	C	G	E	G	T	P
7. zebrafish		M	T	V	K	V	H	V	V	Y	C	G	G	U	G	Y	R	P	K	F	I	K	L	K	T	L	L	E	D	E	F	P	N	E	L	E	I	T	G	E	G	T	P

Species/Ab	Group Name			*	*			*	*		*				*		*	*	*	*		*	*	*		*	*				*					*		*	*			*					
1. Human		Q	A	T	G	F	F	E	V	M	V	A	G	K	L	I	H	S	K	K	K	G	D	G	Y	V	D	T	E	S	K	F	L	K	L	V	A	A	I	K	A	A	L	A	Q	G	-
2. Mouse		Q	V	T	G	F	F	E	V	T	V	A	G	K	L	V	H	S	K	K	R	G	D	G	Y	V	D	T	E	S	K	F	R	K	L	V	T	A	I	K	A	A	L	A	Q	C	Q
3. Rat		Q	V	T	G	F	F	E	V	T	V	A	G	K	L	V	H	S	K	K	R	G	D	G	Y	V	D	T	E	S	K	F	R	K	L	V	T	A	I	K	A	A	L	A	Q	C	Q
4. Chicken		E	V	T	G	W	F	E	V	T	V	G	S	R	L	V	H	S	K	K	N	G	D	G	F	V	D	T	D	A	K	L	Q	R	I	V	A	A	I	Q	A	A	L	P	-	-	-
5. Pig		Q	V	T	G	F	F	E	V	L	V	A	G	K	L	V	H	S	K	K	G	G	D	G	Y	V	D	T	E	S	K	F	L	K	L	V	A	A	I	K	A	A	L	A	Q	G	-
6. Sheep		Q	V	T	G	F	F	E	V	F	V	A	G	K	L	V	H	S	K	K	G	G	D	G	Y	V	D	T	E	S	K	F	L	K	L	V	A	A	I	K	A	A	L	A	Q	A	-
7. zebrafish		S	T	T	G	W	L	E	V	E	V	N	G	K	L	V	H	S	K	K	N	G	D	G	F	V	D	S	D	S	K	M	Q	K	I	V	T	A	I	E	Q	A	M	G	K	-	-

Phylogenetic tree



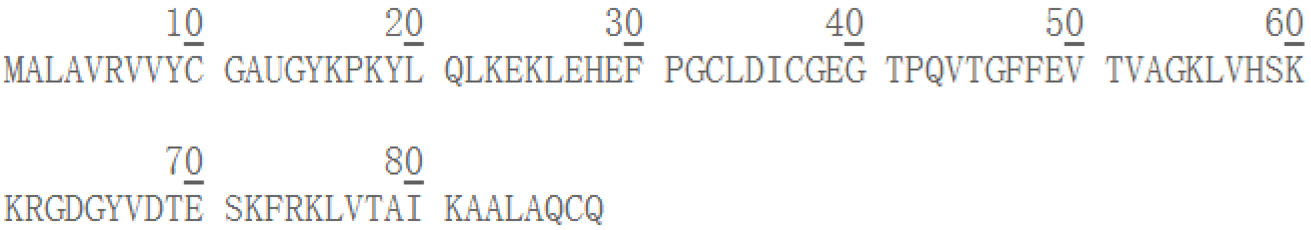
Bioinformatics analysis

ExPASy
Bioinformatics Resource Portal

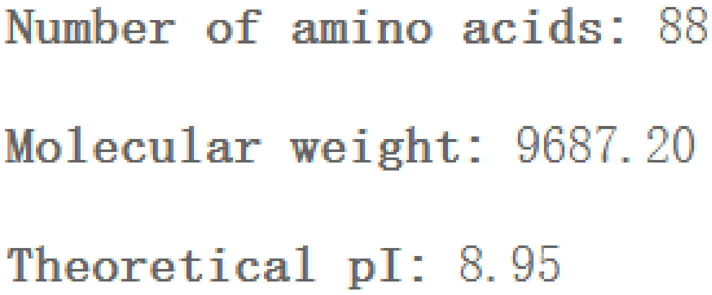
ProtParam　Compute pI/MW

Physical and chemical parameters

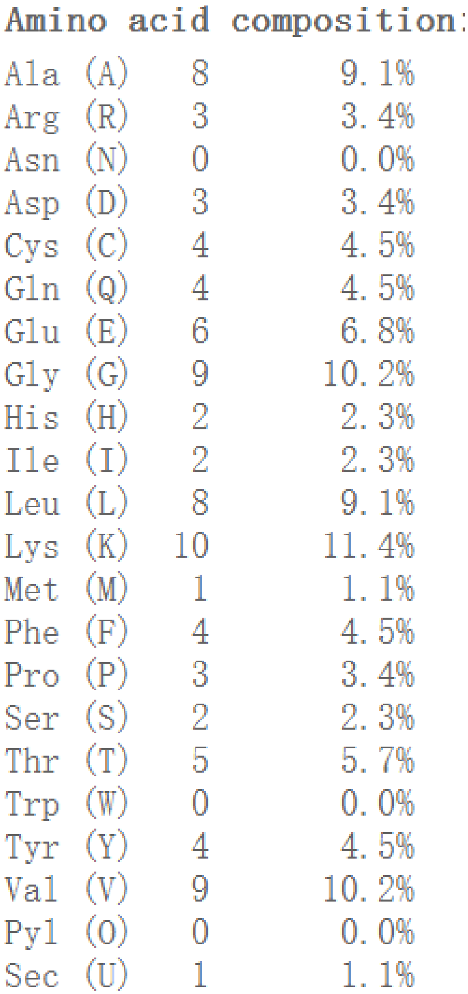
Selenoprotein W of *Mus musculus*



```
        10         20         30         40         50         60
MALAVRVVYC GAUGYKPKYL QLKEKLEHEF PGCLDICGEG TPQVTGFFEV TVAGKLVHSK

        70         80
KRGDGYVDTE SKFRKLVTAI KAALAQCQ
```



```
Number of amino acids: 88

Molecular weight: 9687.20

Theoretical pI: 8.95
```



```
Amino acid composition
Ala (A)   8     9.1%
Arg (R)   3     3.4%
Asn (N)   0     0.0%
Asp (D)   3     3.4%
Cys (C)   4     4.5%
Gln (Q)   4     4.5%
Glu (E)   6     6.8%
Gly (G)   9    10.2%
His (H)   2     2.3%
Ile (I)   2     2.3%
Leu (L)   8     9.1%
Lys (K)  10    11.4%
Met (M)   1     1.1%
Phe (F)   4     4.5%
Pro (P)   3     3.4%
Ser (S)   2     2.3%
Thr (T)   5     5.7%
Trp (W)   0     0.0%
Tyr (Y)   4     4.5%
Val (V)   9    10.2%
Pyl (O)   0     0.0%
Sec (U)   1     1.1%
```

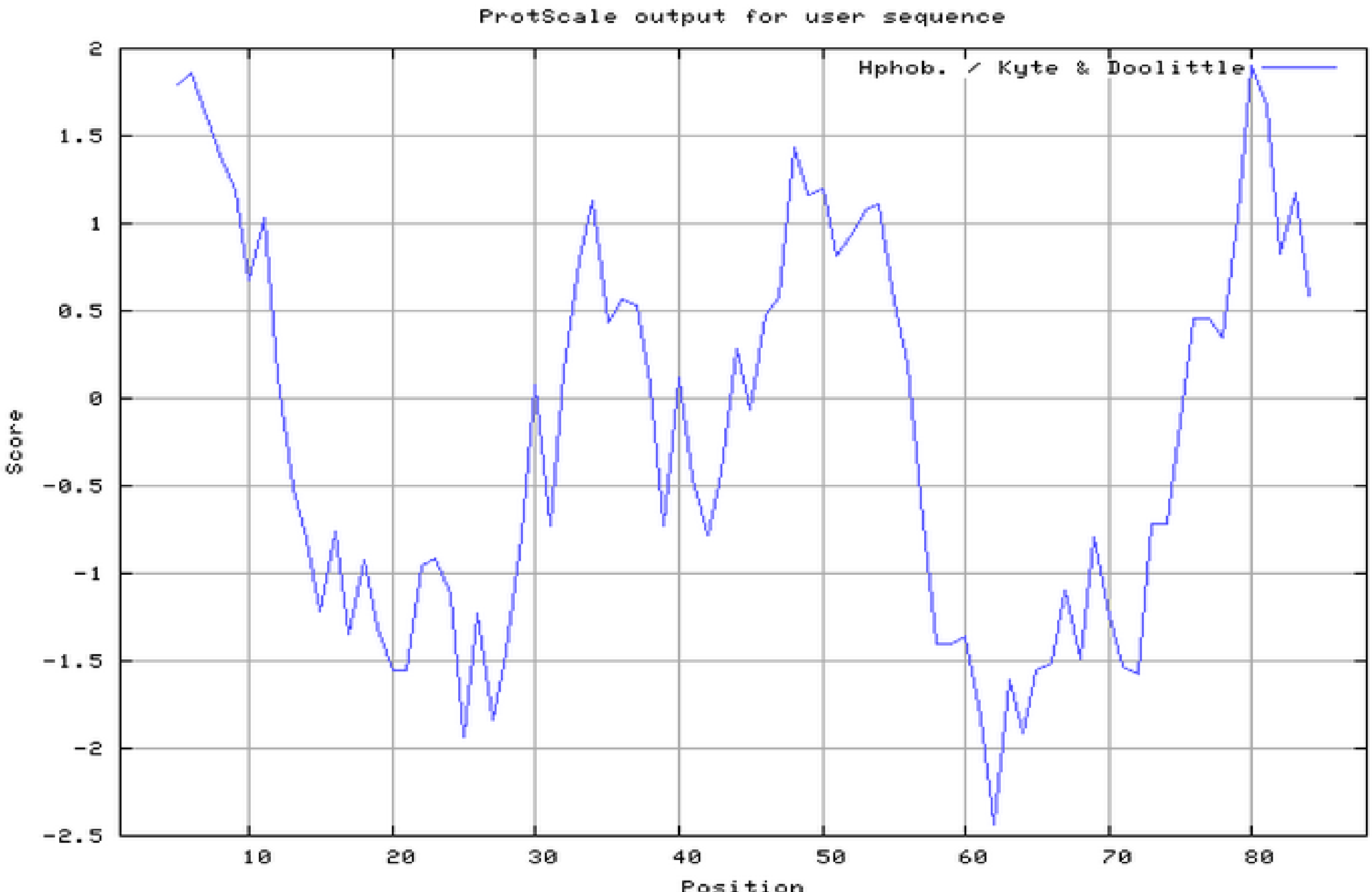
Bioinformatics analysis

ExPASy Bioinformatics Resource Portal

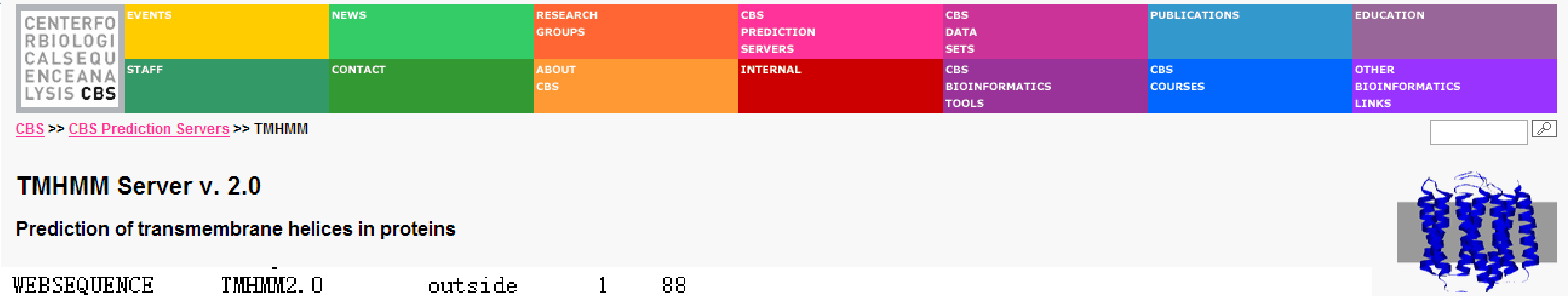
ProtScale

Hydrophilic / Hydrophobic

正值疏水，负值亲水，介于+0.5到-0.5之间的为两性氨基酸。



Bioinformatics analysis

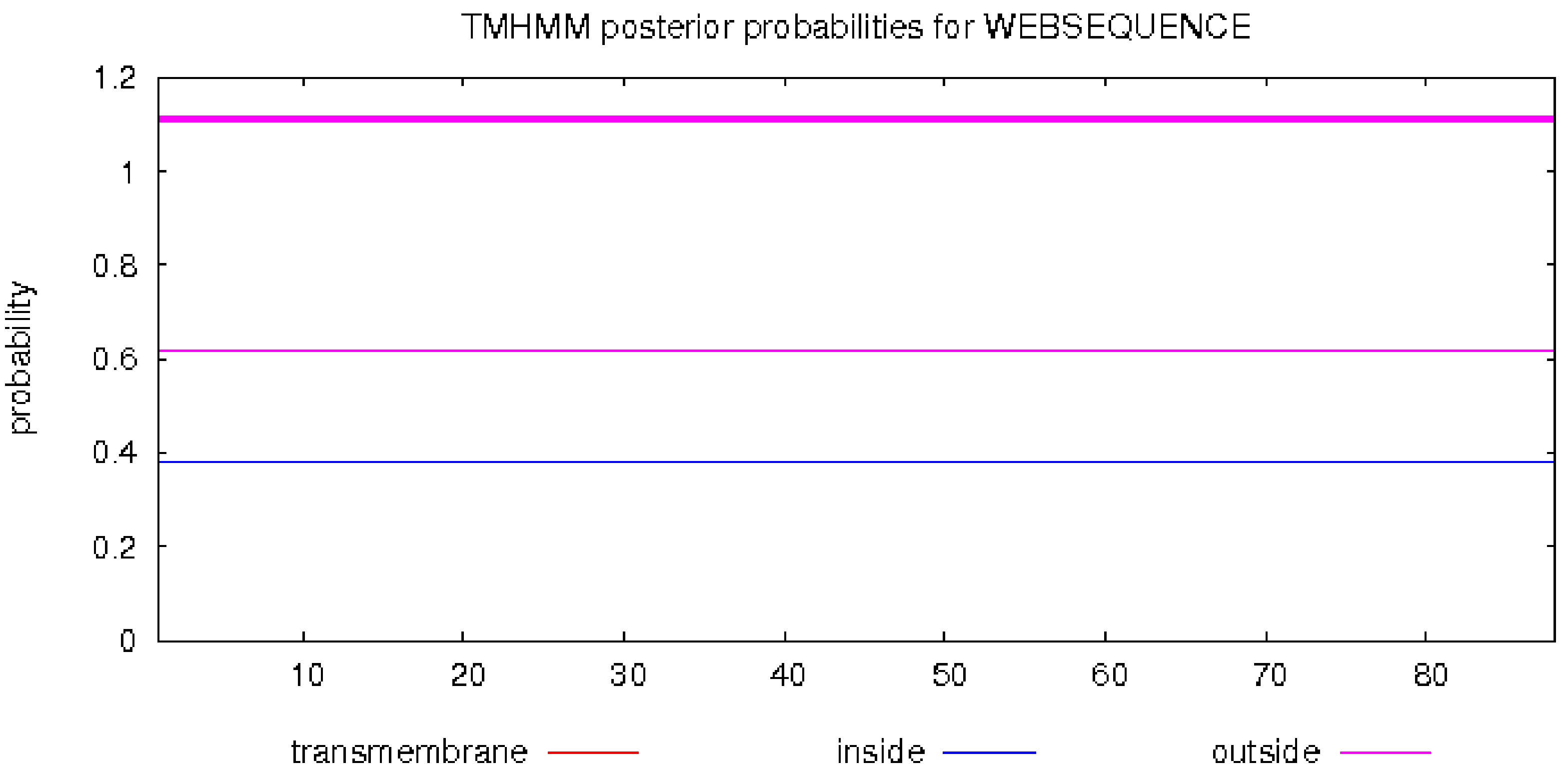


CBS >> CBS Prediction Servers >> TMHMM

TMHMM Server v. 2.0

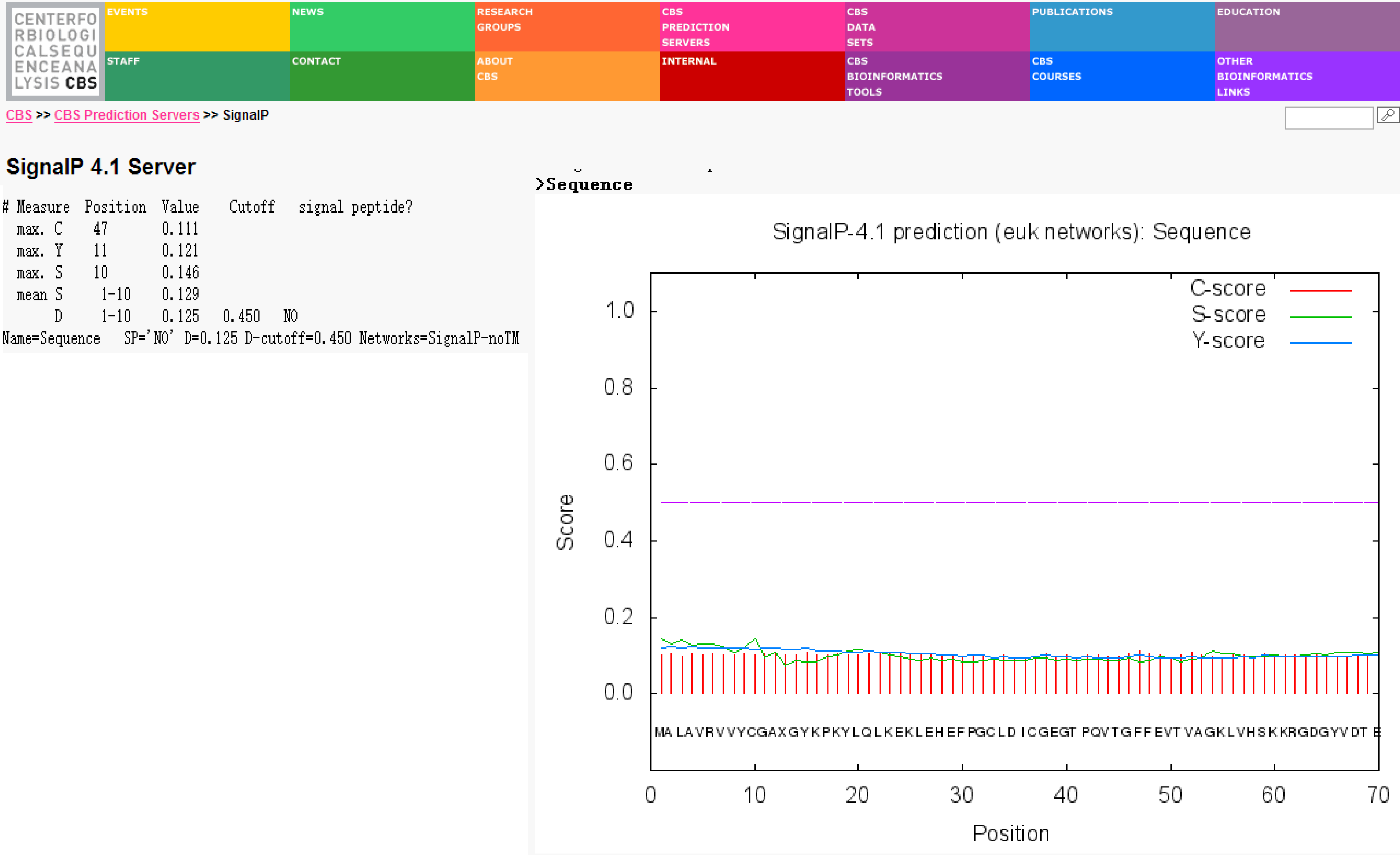
Prediction of transmembrane helices in proteins

```
WEBSEQUENCE      TMHMM2.0         outside       1     88
```



TMHMM posterior probabilities for WEBSEQUENCE

Bioinformatics analysis



SignalP 4.1 Server

```
# Measure  Position  Value    Cutoff   signal peptide?
  max. C    47       0.111
  max. Y    11       0.121
  max. S    10       0.146
  mean S     1-10    0.129
       D     1-10    0.125   0.450    NO
Name=Sequence   SP='NO' D=0.125 D-cutoff=0.450 Networks=SignalP-noTM
```

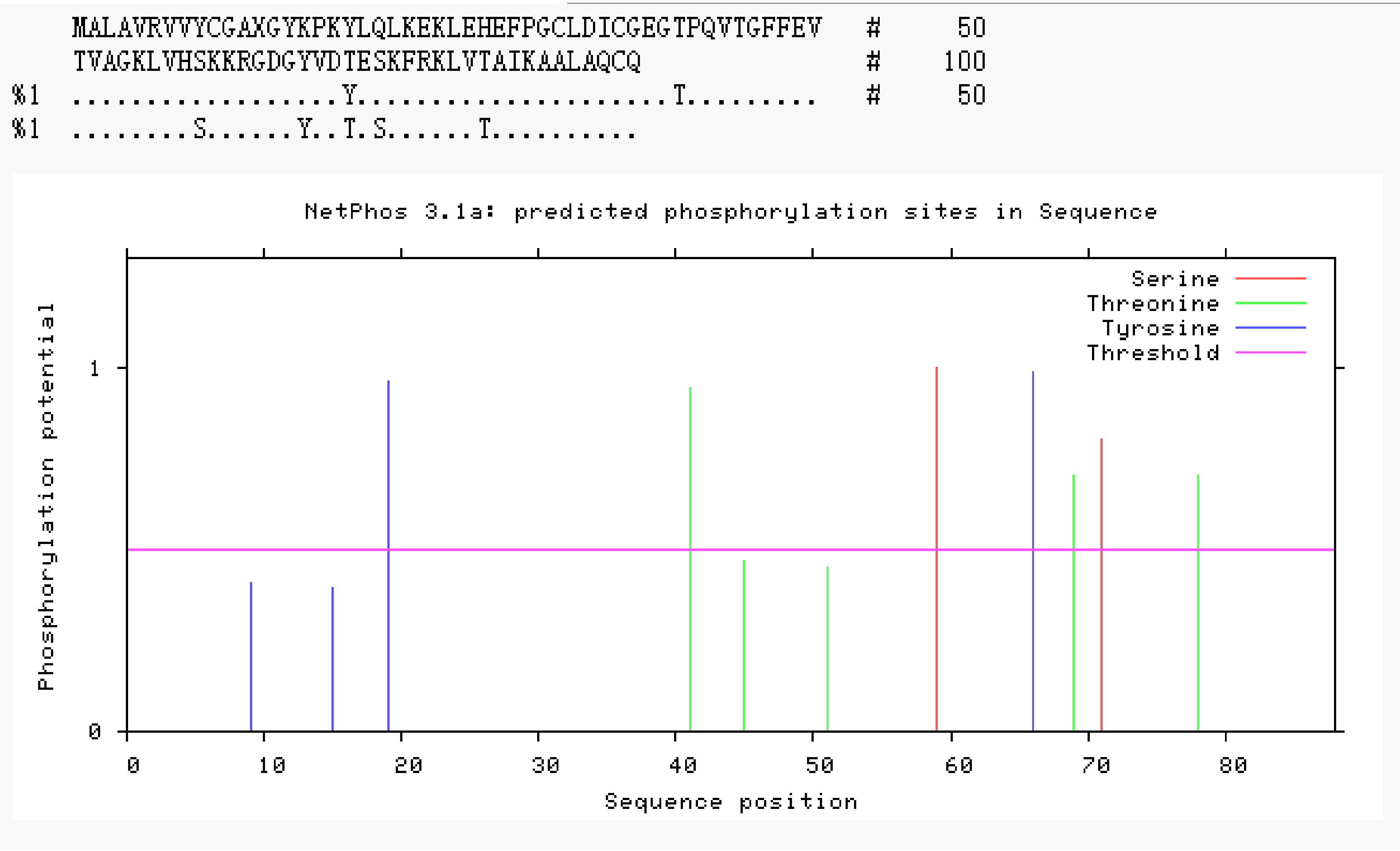
>Sequence

Phosphorylation site

CENTERFORBIOLOGICALSEQUENCEANALYSIS CBS

NetPhos 3.1 Server - prediction results

Technical University of Denmark



```
    MALAVRVVYCGAXGYKPKYLQLKEKLEHEFPGCLDICGEGTPQVTGFFEV   #    50
    TVAGKLVHSKKRGDGYVDTESKFRKLVTAIKAALAQCQ               #   100
%1  ..................Y.....................T.........   #    50
%1  ........S......Y..T.S......T..........
```

预测共7个磷酸化位点
Ser:2
Thr:3
Tyr:2

Bioinformatics analysis

2NPB

NMR solution structure of mouse SelW

DOI: 10.2210/pdb2npb/pdb

Classification: OXIDOREDUCTASE

Deposited: 2006-10-27 **Released**: 2006-11-14

Deposition author(s): Aachmann, F.L., Fomenko, D.E., Soragni, A., Gladyshe

Organism: Mus musculus

Expression System: Escherichia coli

Mutation(s): 2

Experimental Data Snapshot

Method: SOLUTION NMR

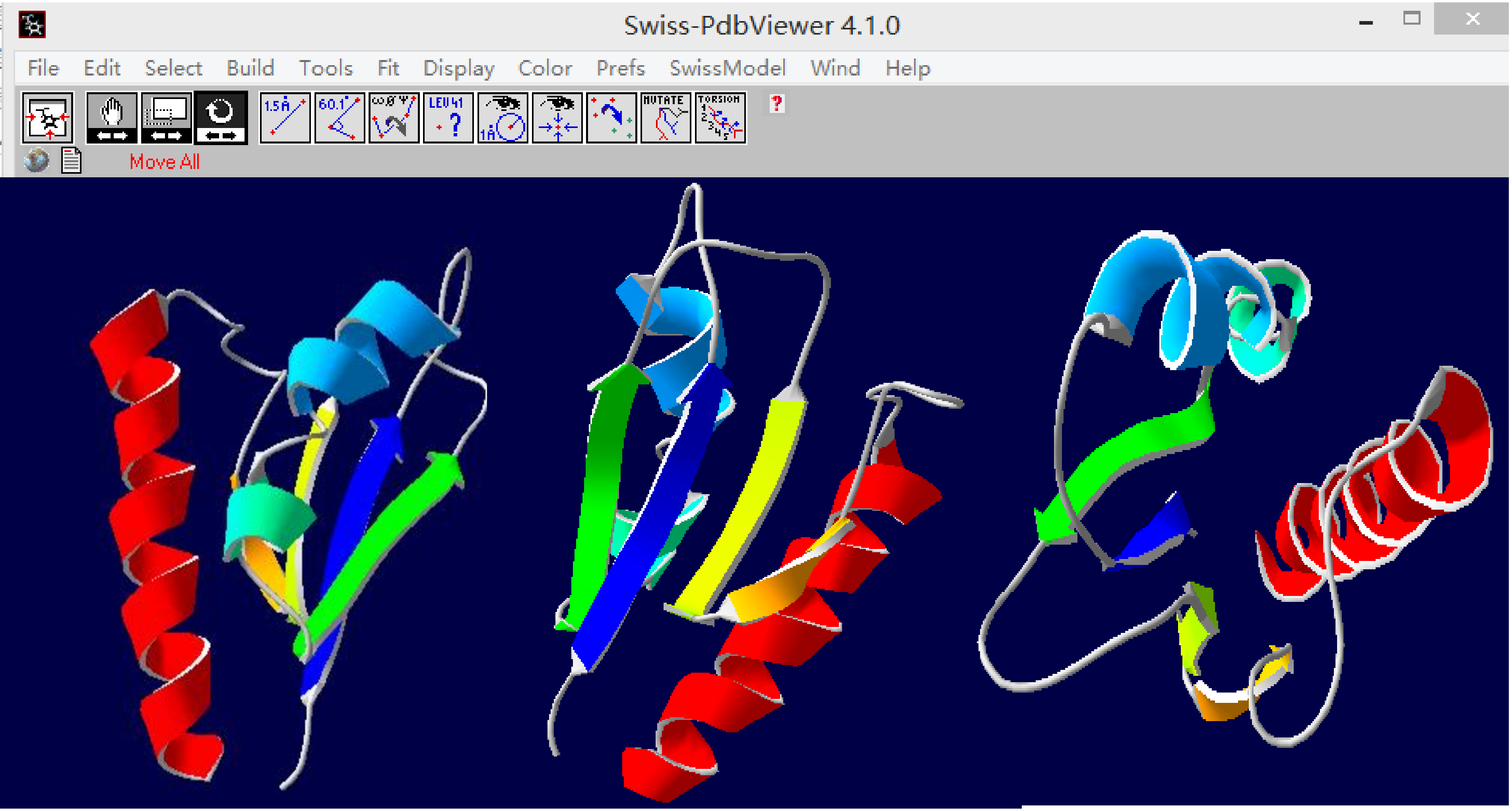
Conformers Calculated: 96

Conformers Submitted: 20

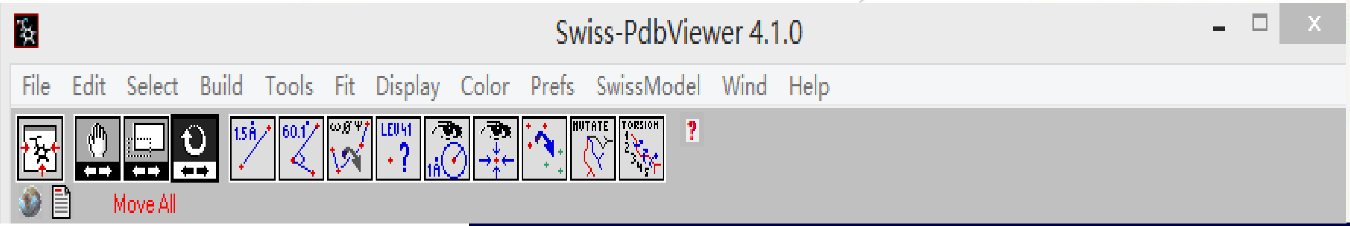
Selection Criteria: Target Function

wwPDB Validation

Bioinformatics analysis



Bioinformatics analysis



Phyre²

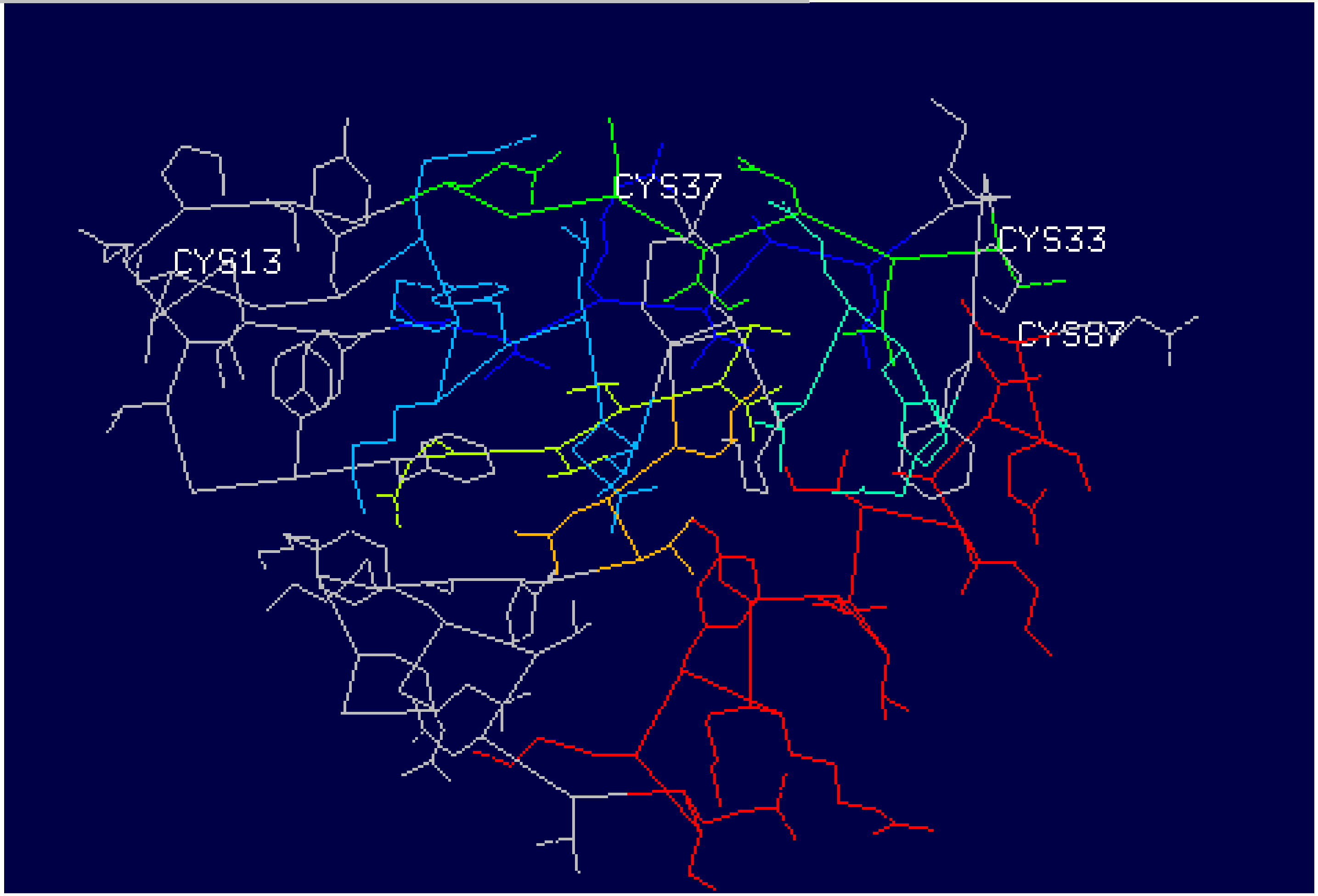
Protein Homology/analogY Recognition Engine V 2.0

Cys:13

33

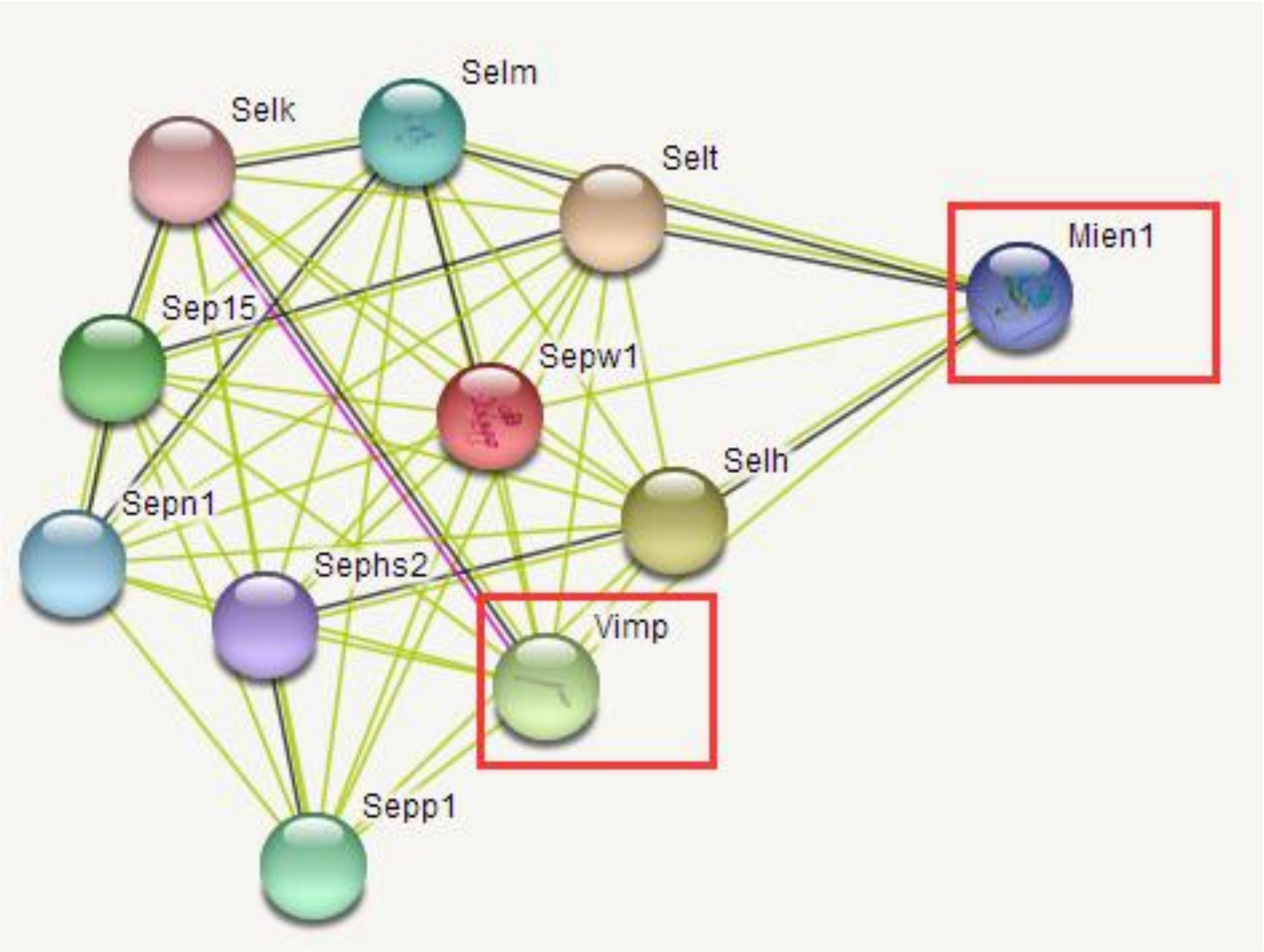
37

87



Protein-protein interaction

- ✓ 谷胱甘肽依赖的抗氧化剂
- ✓ 氧化还原
- ✓ 硒缺乏疾病



Half day on the web, saves you half mouth in the lab!

Acknowledgement

- ✓ **Professor Luo Jingchu**
- ✓ **Group 03 members**
- ✓ **All the classmates**

Thanks for your attention