



水稻中依赖于ATP的解旋酶OsHRQ1蛋白 结构和功能探究

Structure and Function of ATP-dependent Helicase **OsHRQ1** Protein in Rice

G05_06

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Prediction model

Structure and function analysis


Homologous proteins

Functional analysis

Interacting proteins

Functional analysis

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	Homologous proteins Functional analysis
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BACKGROUND

Why focus on **OsHRQ1** ?

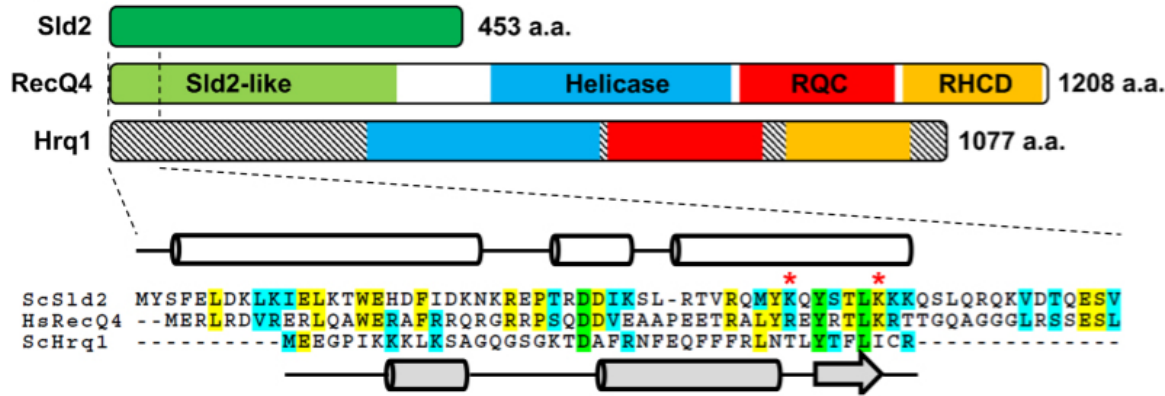
■ OsHRQ1作为RecQ家族的直系同源蛋白

RecQ4: 生物体内遗传物质稳定性的重要维持者

-- 功能: DNA双链解旋、DNA重组、DNA复制、DNA修复...

-- 疾病: 与三种遗传性综合征 (Othmund-Thomson, Baller-Gerold, RAPADILINO)

-- 机制: 尚不清楚



Cody M Rogers. et al. *Nucleic Acids Res.* 2017

■ HRQ1在拟南芥中行使DNA链间交联修复 (Interstrand cross-link repair) 有关功能

-- 范可尼贫血症 (The Fanconi anemia pathway) 信号通路

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● Background

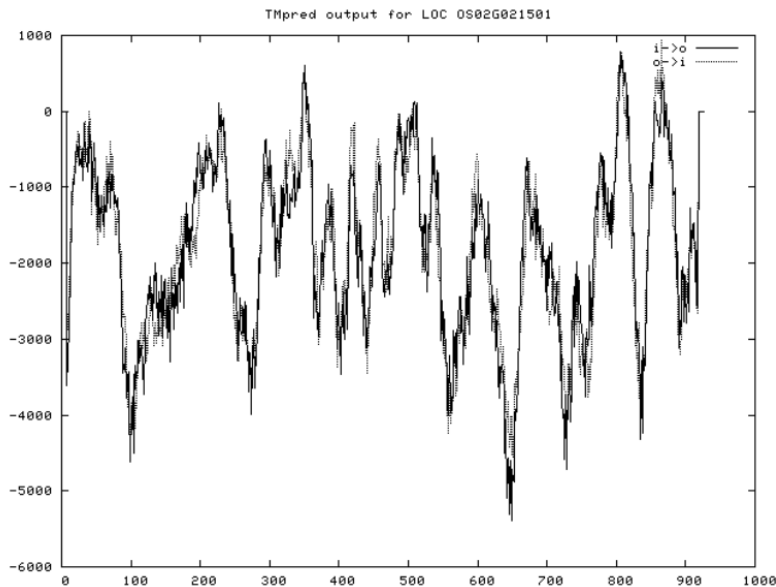
Prediction model
Structure and function analysis

● **Homologous proteins**
Functional analysis

Interacting proteins
Functional analysis

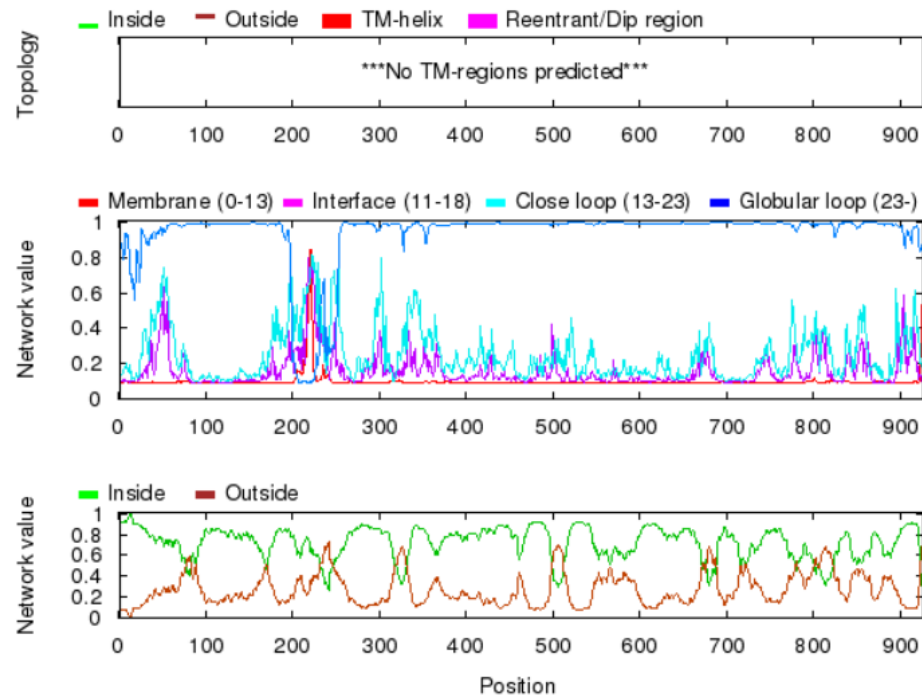
Prediction model

核定位序列 (Nuclear localization sequence, NLS) 预测



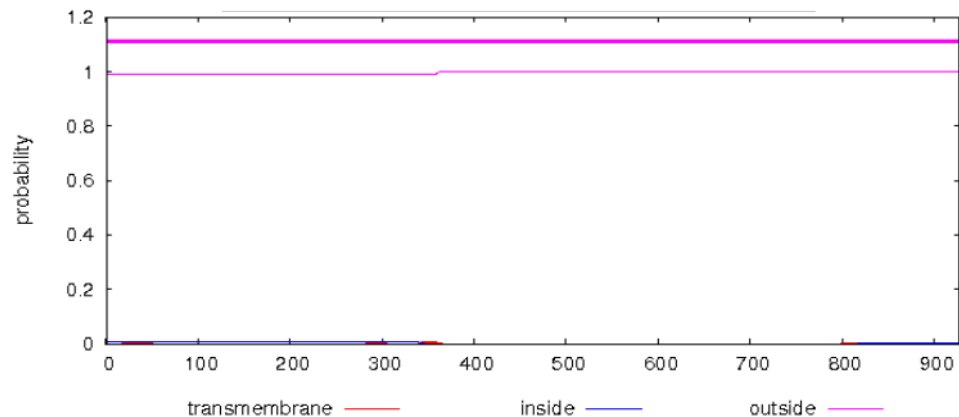
TMpred prediction

跨膜结构域得分 < 1000



OCTOPUS topology

无跨膜结构域

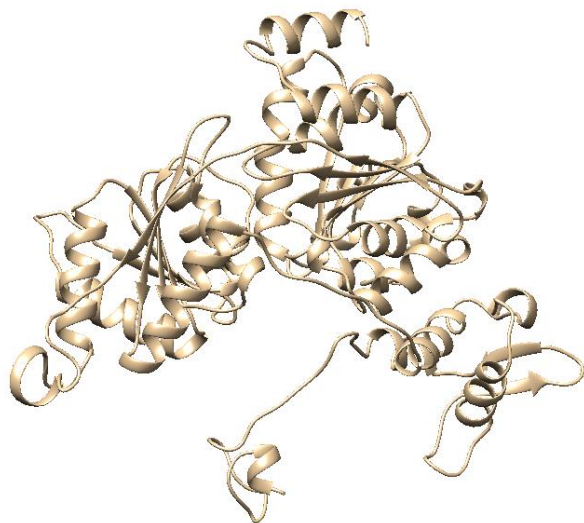


TMHMM prediction

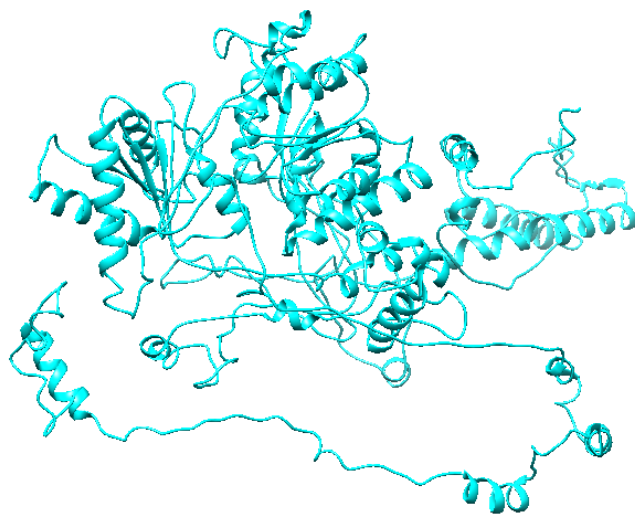
无跨膜结构域

Prediction model

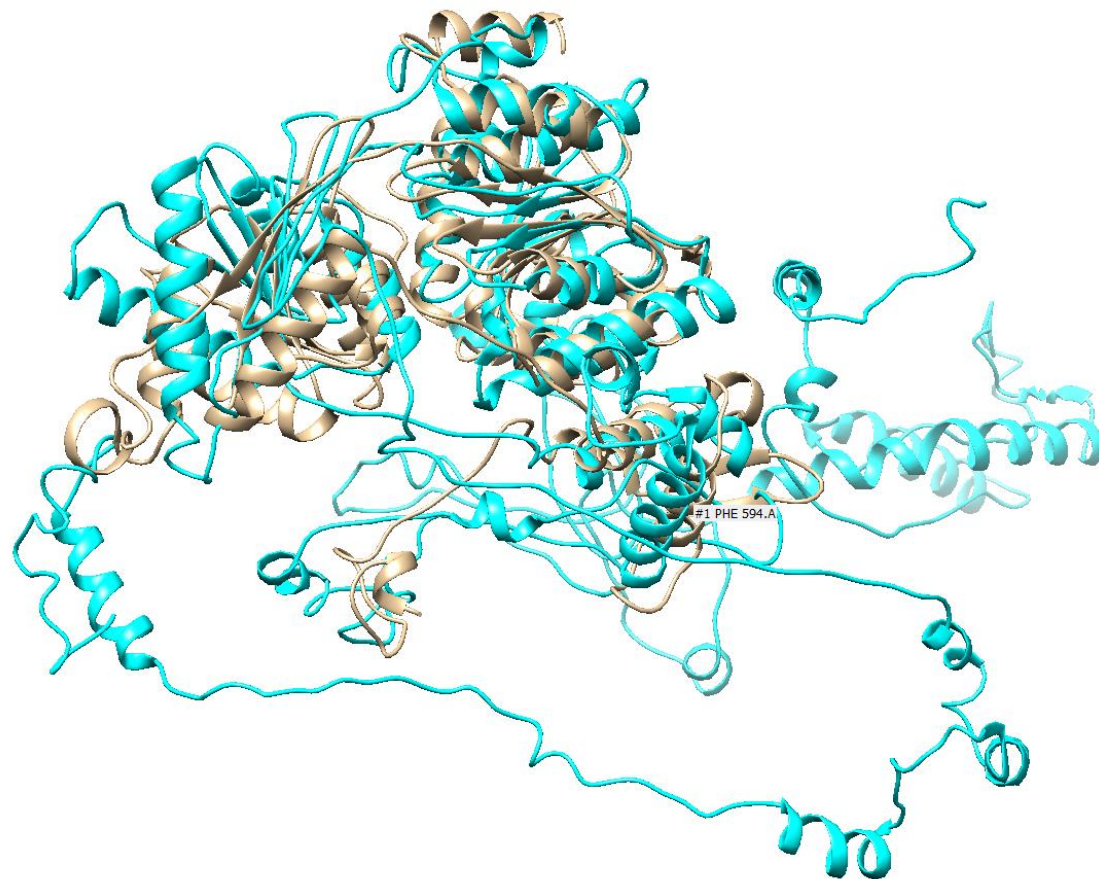
结构预测



Phyre2
172-664 AA



I-TASSER



两种预测模型的结果Magic拟合

Prediction model

结构预测



模板（黄色）： 与ssDNA结合的
耻垢分枝杆菌解旋酶LHR的结构
模板PDB ID: 5v9x

红框： 模板的无规则卷曲序列 (loop)
与DNA单链相结合

蓝色： I-TASSER预测模型

Prediction model

GO 功能预测

分子功能

结合ATP

解旋酶活性

结合DNA

生物过程

rRNA代谢通路

非编码RNA加工

核糖体合成通路

DNA修复

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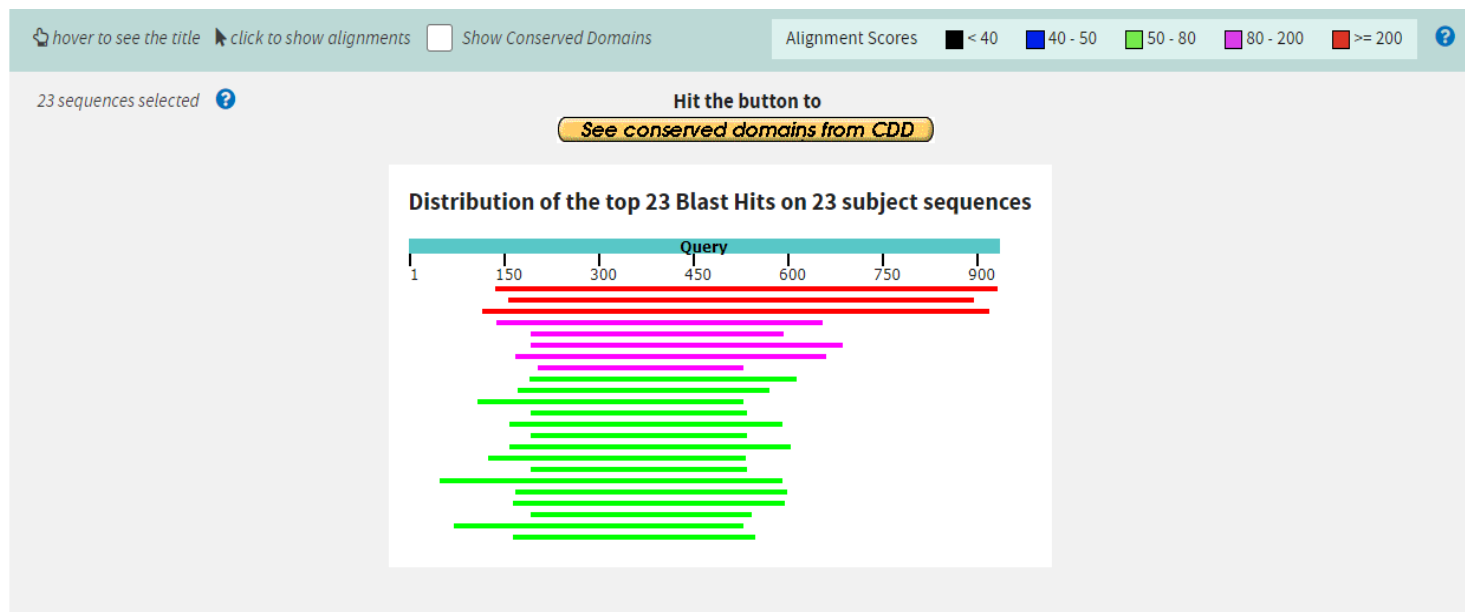
Functional analysis

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Homologous proteins

使用BLAST

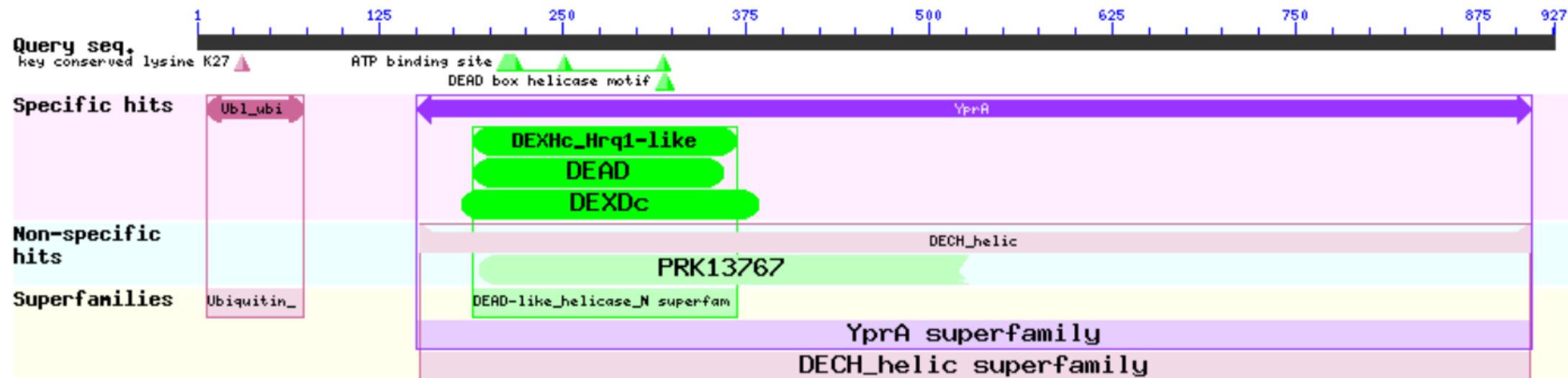


BsYprA
(枯草芽孢杆菌)
ScHRQ1
(酿酒酵母)
SpHRQ1
(裂殖酵母)

<input checked="" type="checkbox"/>	RecName: Full=Uncharacterized ATP-dependent helicase YprA [Bacillus subtilis subsp. subtilis str. 168]	504	504	78%	3e-151	36.29%	P50830.1
<input checked="" type="checkbox"/>	RecName: Full=ATP-dependent helicase HRQ1; AltName: Full=Homologous to recQ protein 1 [Saccharomyces cerevisiae S288C]	508	508	83%	1e-148	34.34%	Q05549.1
<input checked="" type="checkbox"/>	RecName: Full=ATP-dependent helicase hrq1; AltName: Full=Homologous to recQ protein 1 [Schizosaccharomyces pombe 972h-]	488	488	78%	1e-141	34.80%	O13983.4
<input checked="" type="checkbox"/>	RecName: Full=Uncharacterized ATP-dependent helicase MJ1574 [Methanocaldococcus jannaschii DSM 2661]	180	180	46%	1e-44	29.89%	Q58969.1
<input checked="" type="checkbox"/>	RecName: Full=Uncharacterized ATP-dependent helicase MTH_1802 [Methanothermobacter thermautotrophicus str. Delta H]	91.4	91.4	42%	3e-17	26.71%	O27830.1

Homologous proteins

保守结构域

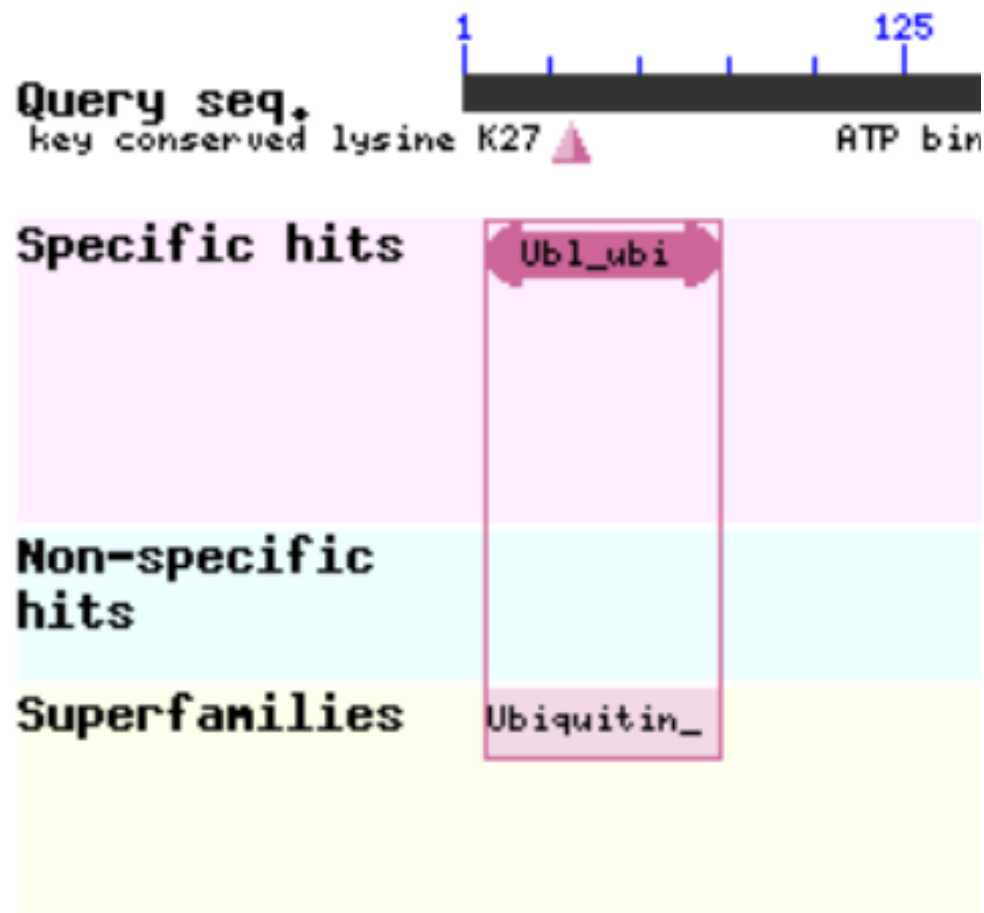


List of domain hits

+	Name	Accession	Description	Interval	E-value
[+]	DECH_helic	TIGR03817	helicase/secretion neighborhood putative DEAH-box helicase; A conserved gene neighborhood ...	152-910	0e+00
[+]	YprA	COG1205	ATP-dependent helicase YprA, contains C-terminal metal-binding DUF1998 domain [Replication, ...	150-911	0e+00
[+]	DEXHc_Hrq1-like	cd17923	DEAH-box helicase domain of Hrq1 and similar proteins; Yeast Hrq1, similar to RecQ4, plays a ...	188-369	5.71e-87
[+]	DEAD	pfam00270	DEAD/DEAH box helicase; Members of this family include the DEAD and DEAH box helicases. ...	189-360	8.50e-31
[+]	DEXDc	smart00487	DEAD-like helicases superfamily;	180-384	4.17e-26
[+]	PRK13767	PRK13767	ATP-dependent helicase; Provisional	192-526	1.26e-19
[+]	Ubl_ubiquitin_like	cd17039	ubiquitin-like (Ubl) domain found in ubiquitin and ubiquitin-like Ubl proteins; Ubiquitin-like ...	7-73	2.52e-03

Homologous proteins

独特的类泛素结构域



■ 类泛素结构域

- 共价修饰目的蛋白
- 介导蛋白质间的相互作用

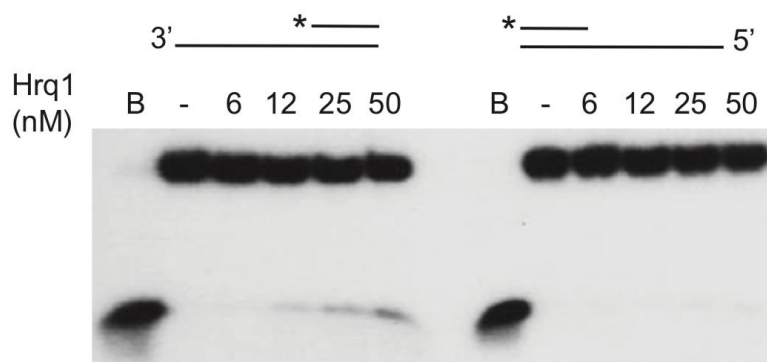
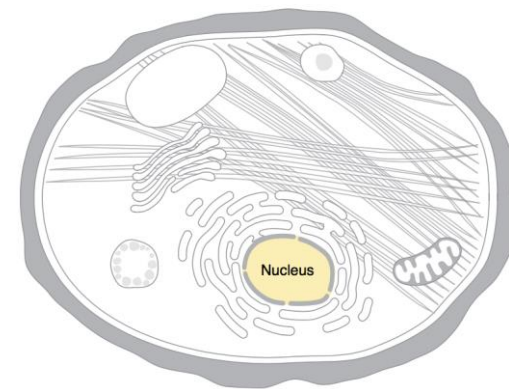
■ K27

- 此类蛋白中较为保守的一个位点
- 涉及介导蛋白质间相互作用的机理

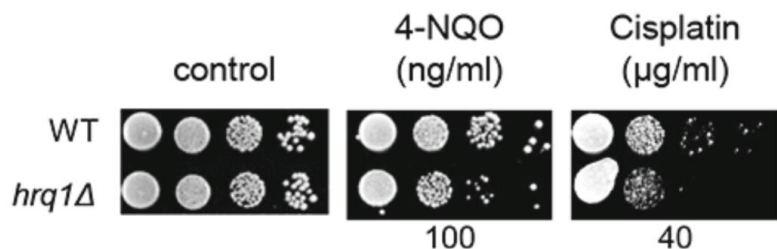
Homologous proteins

ATP-dependent helicase **ScHRQ1**

- 酿酒酵母 *Saccharomyces cerevisiae* (strain ATCC 204508 / S288c)
- 注释信息完善
- 与 OsHRQ1 有 35% 的一致性



Substrate unwound (fmol) 0.02 0.1 0.2



- DNA复制过程中3'-5' 解旋酶活性
- 维持基因组稳定性
 - ✓ 核酸切除修复(nucleotide excision repair, NER)
 - ✓ DNA 链间交联修复
- 影响端粒长度的稳定

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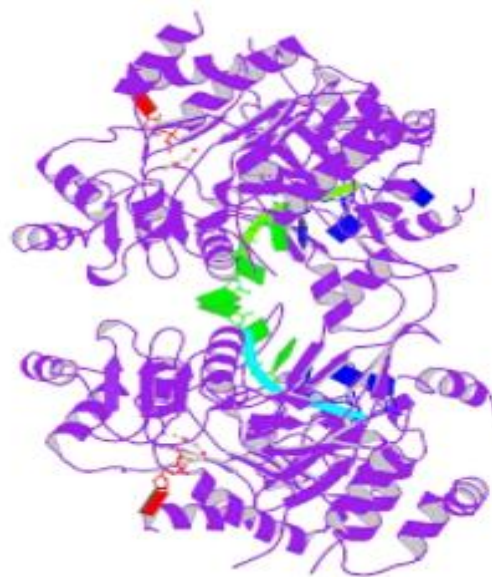
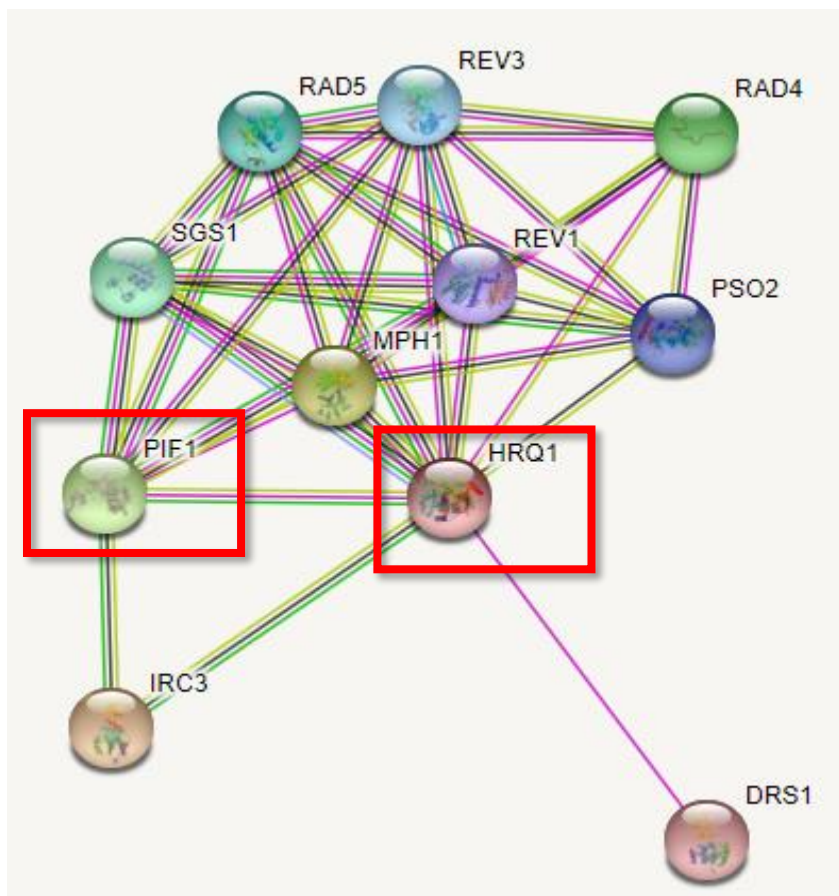
Functional analysis

Interacting proteins

Functional analysis

Interacting proteins

ScHRQ1与ScPIF1互作



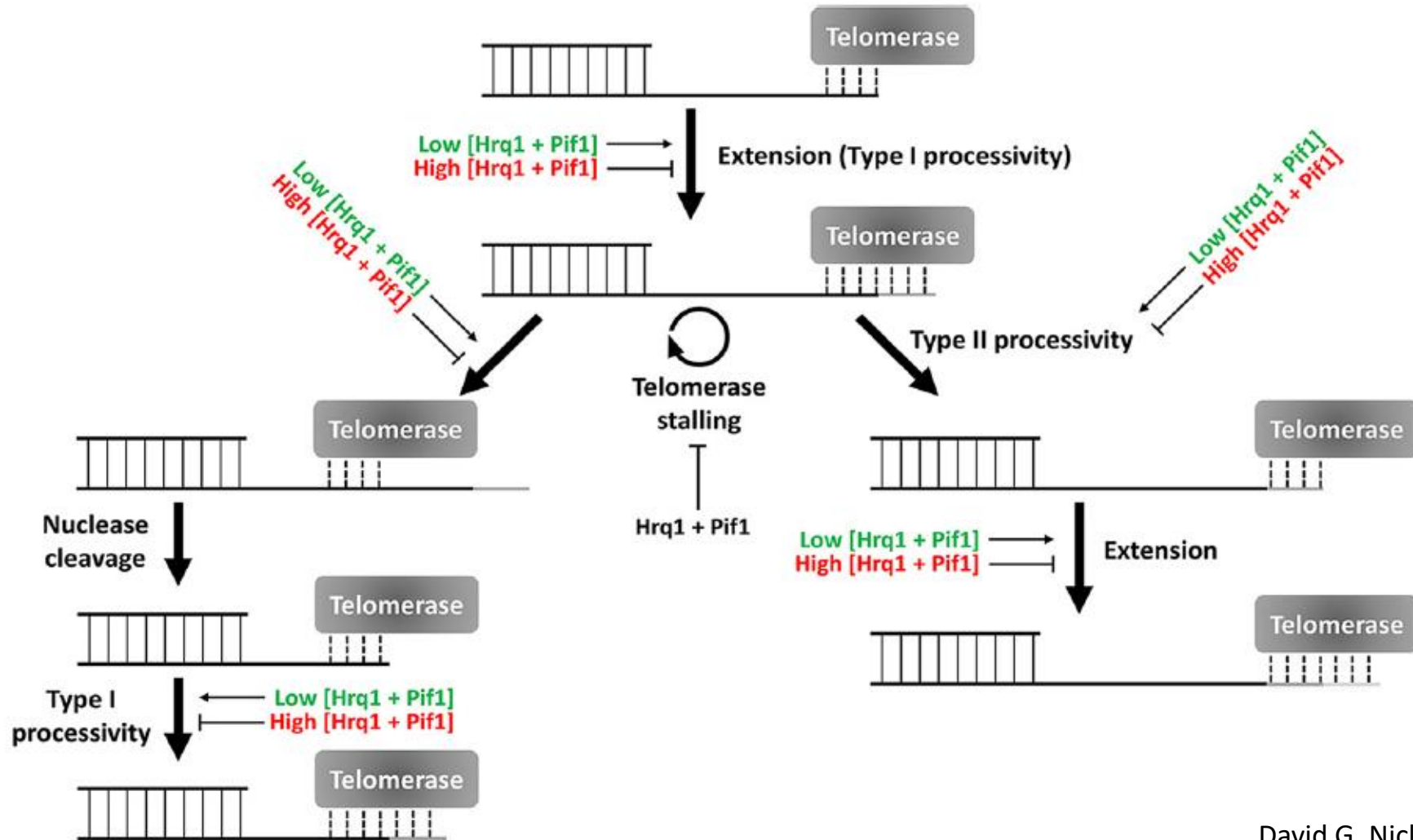
名称	ATP-dependent DNA helicase PIF1
登录号	P07271
长度	859 AA
亚细胞定位	细胞核 & 线粒体
功能	端粒酶抑制剂； 参与DNA修复和重组

ScPIF1 结构
PDB ID: 5O6B

Interacting proteins

ScHRQ1与ScPIF1互作

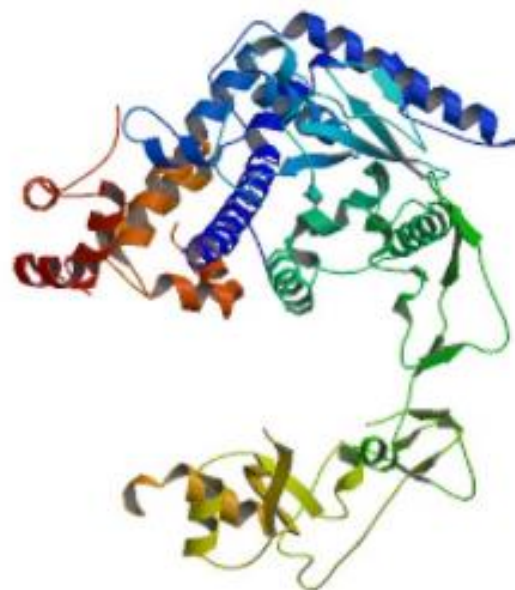
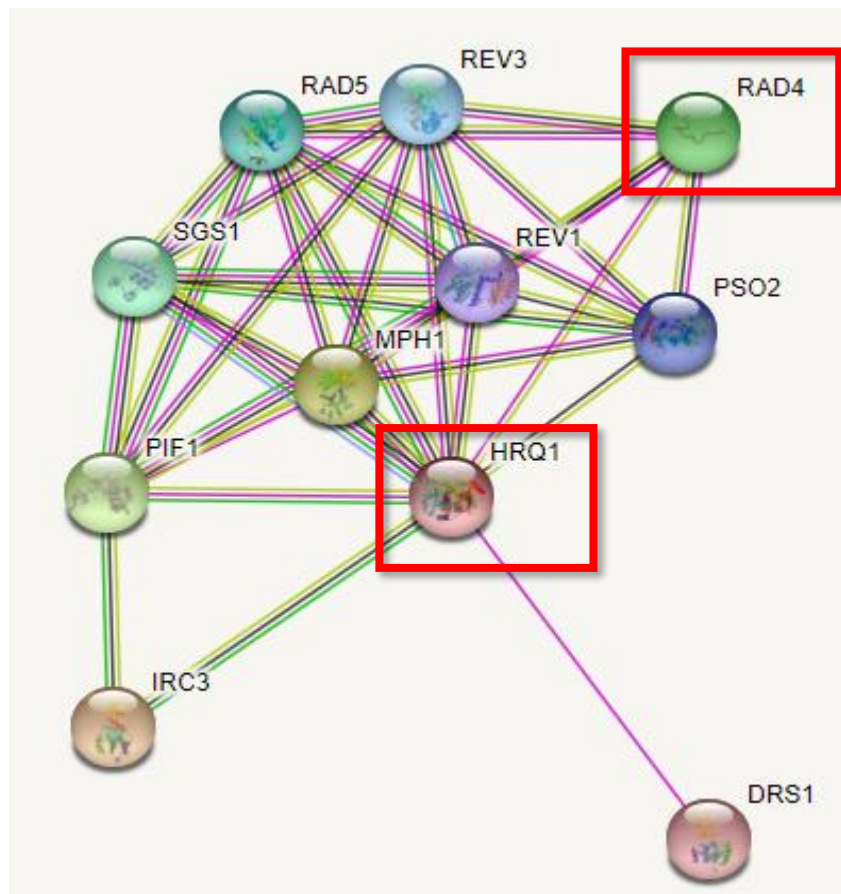
- HRQ1与PIF1的协同作用确保了酿酒酵母细胞内端粒长度的稳态。



Interacting proteins

ScHRQ1与ScRAD4互作

- RAD4 在HRQ1上位，HRQ1与RAD4相互作用共同完成DNA损伤修复过程。



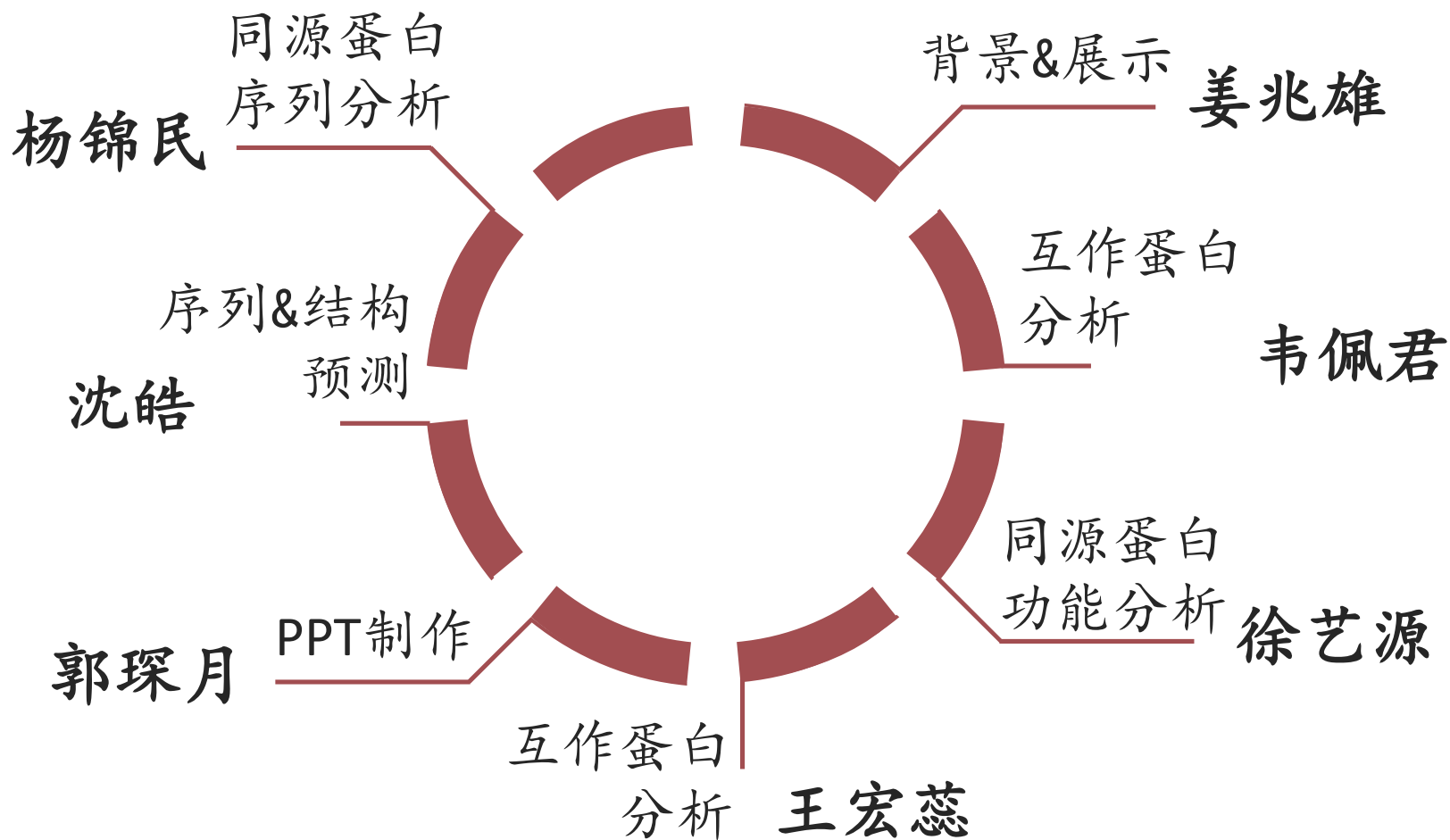
名称	DNA repair protein RAD4
登录号	P14736
长度	754 AA
亚细胞定位	细胞核 & 细胞质
功能	DNA损伤的核苷酸切除修复

ScRAD4-RAD23结构
PDB ID: 2QSF

References

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7. Kwon S.H., Choi D.H., Lee R., Bae S.H. *Saccharomyces cerevisiae* Hrq1 requires a long 3'-tailed DNA substrate for helicase activity. *Biochem. Biophys. Res. Commun.* 427:623-628(2012)
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9. David G. Nickens et al. The *Saccharomyces cerevisiae* Hrq1 and Pif1 DNA helicases synergistically modulate telomerase activity in vitro. *J. Biol. Chem.* 2018
10. Do-Hee Choi et al. Hrq1 Facilitates Nucleotide Excision Repair of DNA Damage Induced by 4-Nitroquinoline-1-Oxide and Cisplatin in *Saccharomyces cerevisiae*. *Journal of Microbiology.* 2014

Group Members





Thanks!

BACKGROUND

范可尼贫血症信号通路

The Fanconi anemia pathway (FA)

- 修复受损的DNA，尤其是链间交联（ICL）。
- DNA ICL被FANCM和相关蛋白直接识别，这些蛋白募集了FA核心复合物。
- FA核心复合物是单泛素化的FANCD2和FANCI。单泛素化的FANCD2 / FANCI成为活性形式，并与一系列DNA修复蛋白相互作用，促进下游修复途径。
- 范可尼贫血是由至少13个FA基因之一的突变引起的，其特征是先天性生长异常、骨髓衰竭和癌症易感性等。

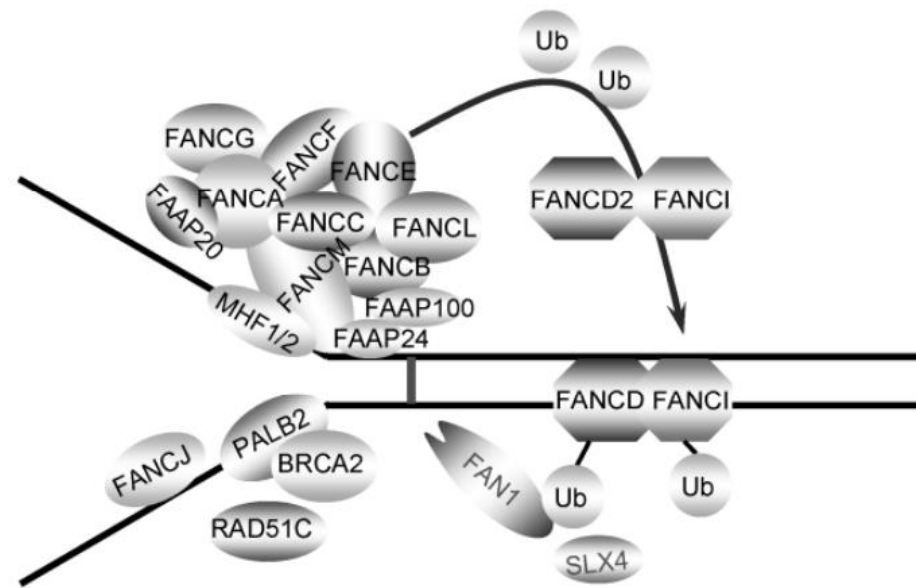
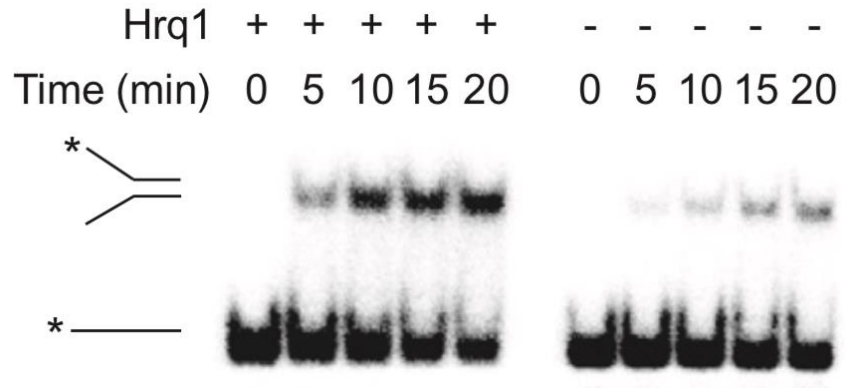


图1 范可尼贫血症信号通路作用模式图

Homologous proteins

ATP-dependent helicase **ScHRQ1**



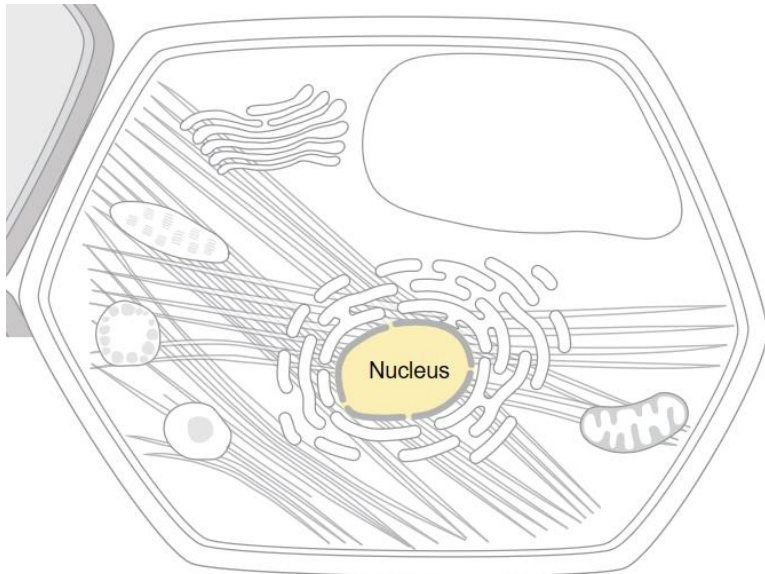
Helicase & DNA strand annealing activities

Affects telomere length by a non-catalytic mechanism.

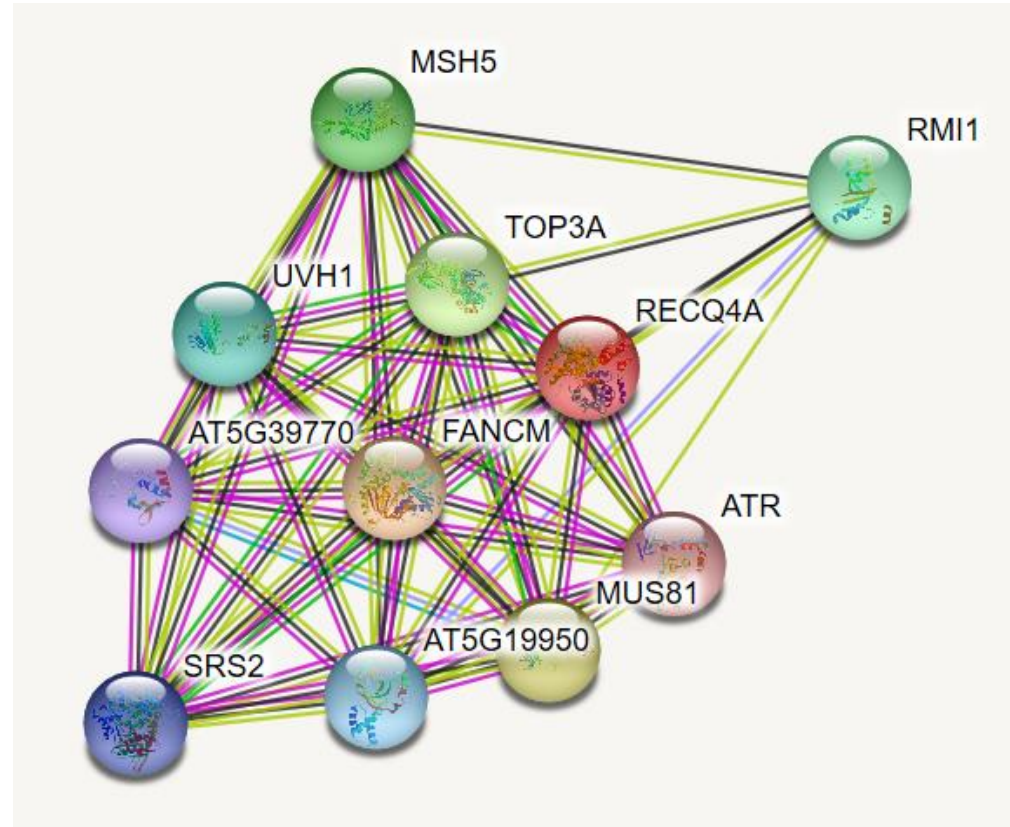
- *HRQ1* suppressed telomere addition (TA) to DSBs, an activity it shares with Pif1
- probably through inhibiting telomerase by competing with it for ssDNA binding
- also important for telomerase-independent telomere maintenance.

Homologous proteins

in *Arabidopsis thaliana*



AtRECQ4A



<https://string-db.org/network/3702.AT1G10930.1>

Homologous proteins in *Arabidopsis thaliana*

AtHRQ1

- 参与DNA的交联修复
- 与范科尼贫血症相关的核酸酶FAN1和复制后修复的ATP酶RAD5A有共同的途径

