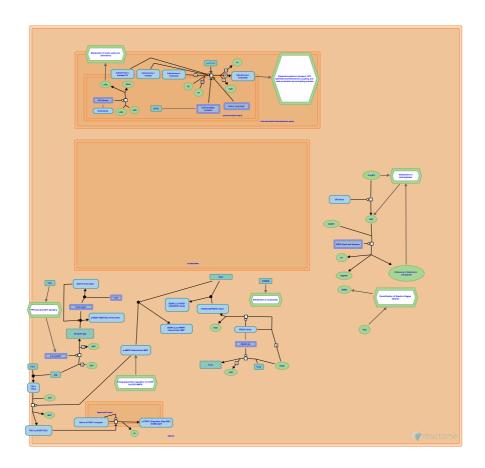


## **TP53 Regulates Metabolic Genes**



European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of <a href="Maintenantoring">Creative Commons Attribution 4.0 International (CC BY 4.0)</a>
<a href="License">License</a>. For more information see our <a href="License">License</a>.

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the <a href="Reactome-Textbook">Reactome-Textbook</a>.

18/05/2024

#### Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

#### Literature references

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142.
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467.
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655.
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph data-base: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968.

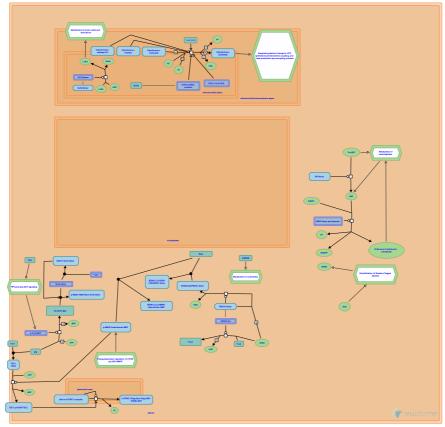
Reactome database release: 88

This document contains 1 pathway and 14 reactions (see Table of Contents)

#### TP53 Regulates Metabolic Genes **ブ**

Stable identifier: R-DME-5628897

**Inferred from:** TP53 Regulates Metabolic Genes (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

#### **GPI dimer isomerizes Fru(6)P to G6P 对**

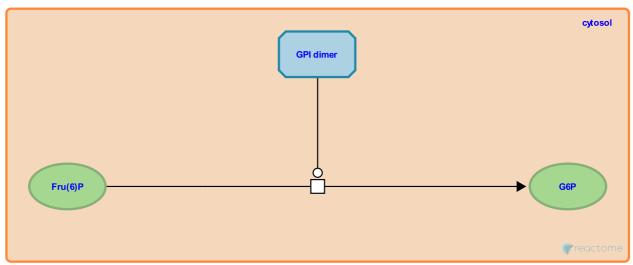
**Location:** TP53 Regulates Metabolic Genes

Stable identifier: R-DME-70475

**Type:** transition

**Compartments:** cytosol

**Inferred from:** GPI dimer isomerizes Fru(6)P to G6P (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

**Followed by:** alpha-D-glucose 6-phosphate + NADP+ => D-glucono-1,5-lactone 6-phosphate + NADPH + H+

# alpha-D-glucose 6-phosphate + NADP+ => D-glucono-1,5-lactone 6-phosphate + NADPH + H+ ↗

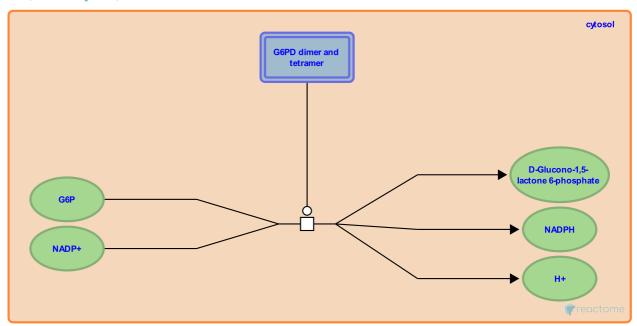
Location: TP53 Regulates Metabolic Genes

**Stable identifier:** R-DME-70377

Type: transition

**Compartments:** cytosol

**Inferred from:** alpha-D-glucose 6-phosphate + NADP+ => D-glucono-1,5-lactone 6-phosphate + NADPH + H+ (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: GPI dimer isomerizes Fru(6)P to G6P

#### 

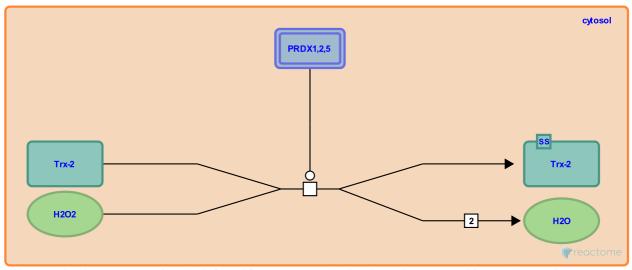
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-3341343

**Type:** transition

**Compartments:** cytosol

**Inferred from:** PRDX1,2,5 catalyze TXN reduced + H2O2 => TXN oxidized + 2H2O (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Followed by: PRDX1 overoxidizes

#### PRDX1 overoxidizes

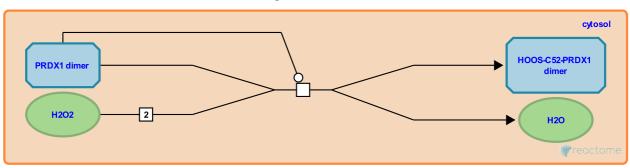
**Location:** TP53 Regulates Metabolic Genes

Stable identifier: R-DME-5631885

**Type:** transition

**Compartments:** cytosol

Inferred from: PRDX1 overoxidizes (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

**Preceded by:** PRDX1,2,5 catalyze TXN reduced + H2O2 => TXN oxidized + 2H2O

Followed by: SESN1,2,3 bind overoxidized PRDX1

#### SESN1,2,3 bind overoxidized PRDX1 **对**

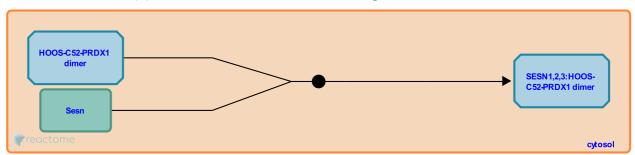
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-5631903

Type: binding

**Compartments:** cytosol

**Inferred from:** SESN1,2,3 bind overoxidized PRDX1 (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

**Preceded by:** PRDX1 overoxidizes

#### p-AMPK phosphorylates TSC1:TSC2 **对**

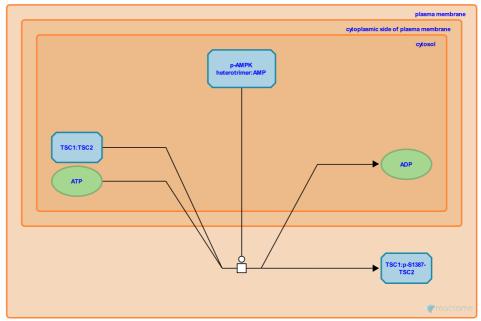
**Location:** TP53 Regulates Metabolic Genes

Stable identifier: R-DME-380927

**Type:** transition

Compartments: plasma membrane, cytosol

Inferred from: p-AMPK phosphorylates TSC1:TSC2 (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

**Preceded by:** Formation of TSC1:TSC2 complex

#### RHEB in mTORC1:RHEB:GTP hydrolyses GTP >

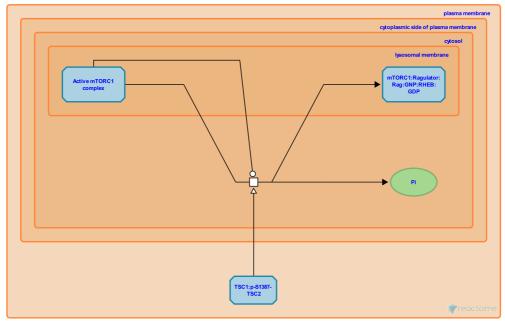
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-380979

**Type:** transition

Compartments: cytosol, lysosomal membrane

Inferred from: RHEB in mTORC1:RHEB:GTP hydrolyses GTP (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

#### SESN1,2,3 bind AMPK **↗**

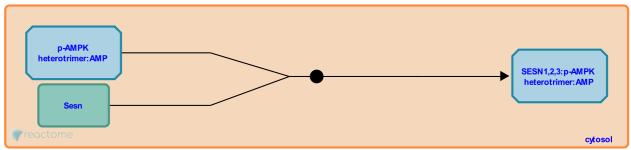
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-5631941

**Type:** binding

**Compartments:** cytosol

Inferred from: SESN1,2,3 bind AMPK (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

#### Formation of TSC1:TSC2 complex **↗**

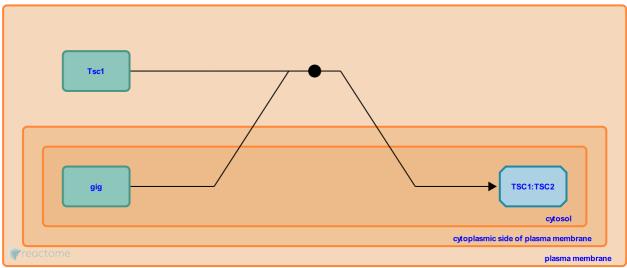
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-165179

**Type:** binding

Compartments: plasma membrane, cytosol

**Inferred from:** Formation of TSC1:TSC2 complex (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Followed by: p-AMPK phosphorylates TSC1:TSC2

#### **AKT phosphorylates TSC2, inhibiting it ↗**

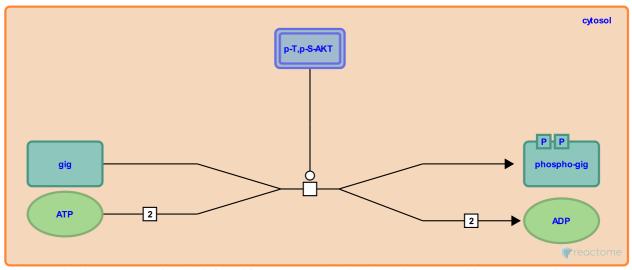
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-198609

**Type:** transition

**Compartments:** cytosol

**Inferred from:** AKT phosphorylates TSC2, inhibiting it (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Followed by: p-S939,T1462-TSC2 binding to 14-3-3 dimer is negatively regulated by DDIT4

#### p-S939,T1462-TSC2 binding to 14-3-3 dimer is negatively regulated by DDIT4 7

Location: TP53 Regulates Metabolic Genes

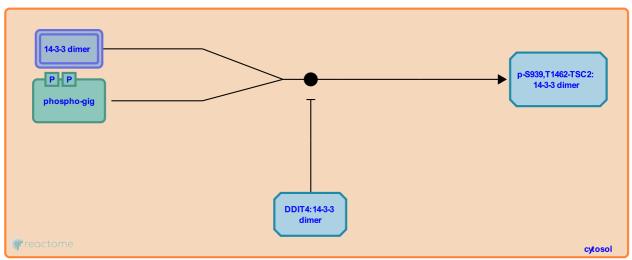
Stable identifier: R-DME-5632732

**Type:** binding

**Compartments:** cytosol

**Inferred from:** p-S939,T1462-TSC2 binding to 14-3-3 dimer is negatively regulated by DDIT4 (Homo sapi-

ens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Preceded by: AKT phosphorylates TSC2, inhibiting it

#### DDIT4 binds 14-3-3 dimer 7

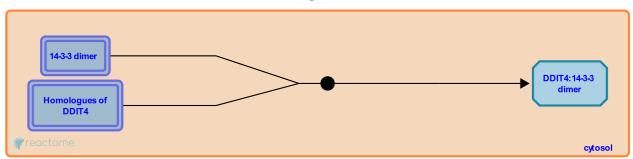
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-5632738

Type: binding

**Compartments:** cytosol

Inferred from: DDIT4 binds 14-3-3 dimer (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

#### Electron transfer from reduced cytochrome c to molecular oxygen 7

**Location:** TP53 Regulates Metabolic Genes

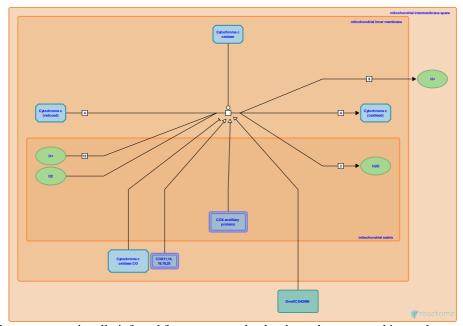
Stable identifier: R-DME-163214

**Type:** transition

Compartments: mitochondrial inner membrane, mitochondrial intermembrane space, mitochondrial

matrix

**Inferred from:** Electron transfer from reduced cytochrome c to molecular oxygen (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

#### 

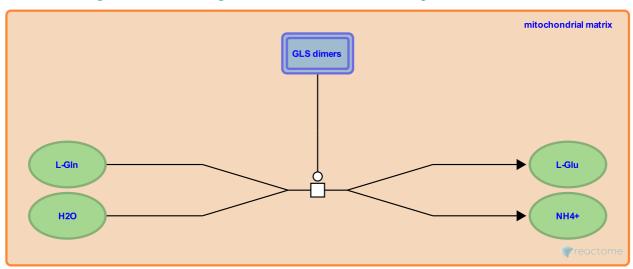
Location: TP53 Regulates Metabolic Genes

Stable identifier: R-DME-70609

**Type:** transition

**Compartments:** mitochondrial matrix

**Inferred from:** glutamine + H2O => glutamate + NH4+ [GLS] (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

### **Table of Contents**

ntro	duction	1
¥ TI	P53 Regulates Metabolic Genes	2
$\rightarrow$	GPI dimer isomerizes Fru(6)P to G6P	3
<b>}</b>	alpha-D-glucose 6-phosphate + NADP+ => D-glucono-1,5-lactone 6-phosphate + NADPH + H+	4
ʹ	PRDX1,2,5 catalyze TXN reduced + H2O2 => TXN oxidized + 2H2O	5
$\rightarrow$	PRDX1 overoxidizes	6
ʹ	SESN1,2,3 bind overoxidized PRDX1	7
$\rightarrow$	p-AMPK phosphorylates TSC1:TSC2	8
$\rightarrow$	RHEB in mTORC1:RHEB:GTP hydrolyses GTP	9
$\rightarrow$	SESN1,2,3 bind AMPK	10
ʹ	Formation of TSC1:TSC2 complex	11
ʹ	AKT phosphorylates TSC2, inhibiting it	12
ʹ	p-S939,T1462-TSC2 binding to 14-3-3 dimer is negatively regulated by DDIT4	13
ʹ	DDIT4 binds 14-3-3 dimer	14
﴾	Electron transfer from reduced cytochrome c to molecular oxygen	15
<b>}</b>	glutamine + H2O => glutamate + NH4+ [GLS]	16
Γable	e of Contents	17