

### Differentiated tissue



+O<sub>2</sub>      -O<sub>2</sub>

Glucose

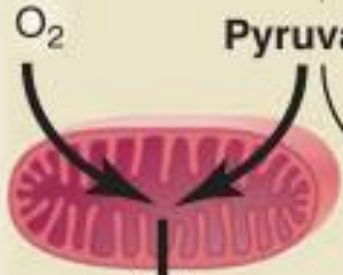
Pyruvate

Lactate

Glucose

Pyruvate

Lactate



CO<sub>2</sub>

**Oxidative phosphorylation**

-36 mol ATP/  
mol glucose

**Anaerobic glycolysis**

2 mol ATP/  
mol glucose

### Proliferative tissue



or



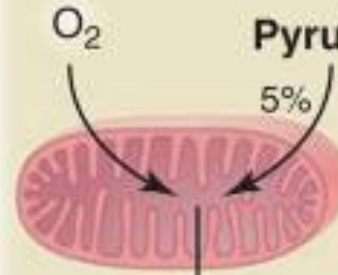
+/-O<sub>2</sub>

Glucose

Pyruvate

5%      85%

Lactate

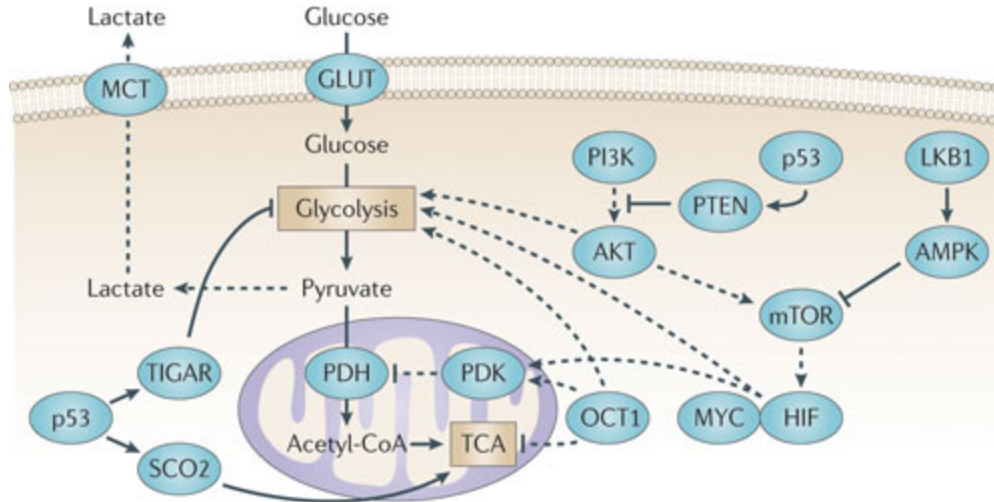


CO<sub>2</sub>

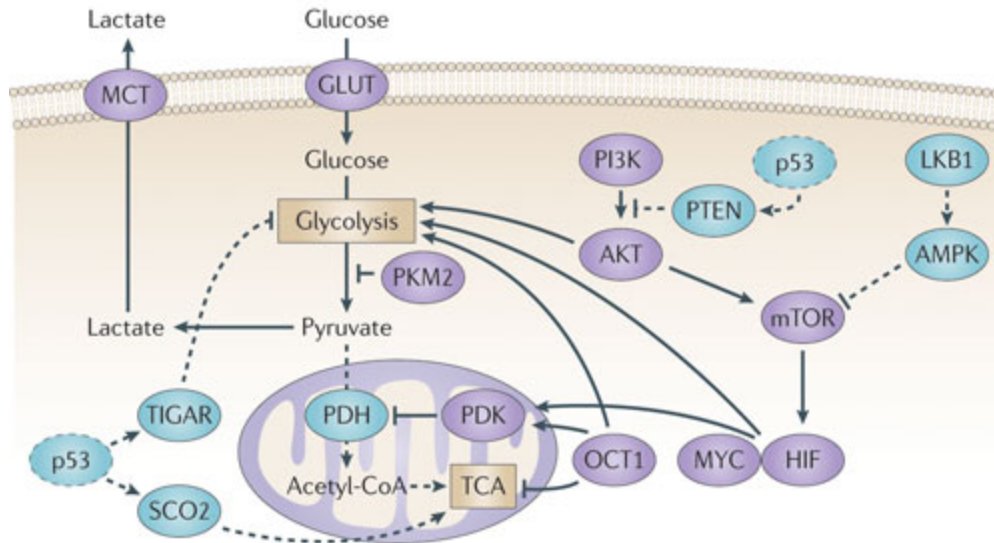
**Aerobic glycolysis (Warburg effect)**

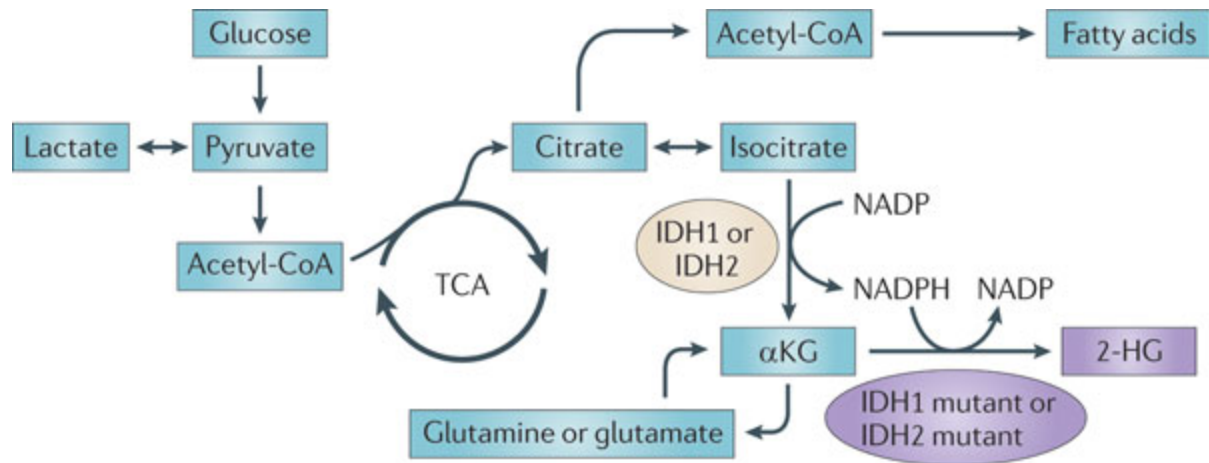
-4 mol ATP/mol glucose

**a Quiescent normal cell**

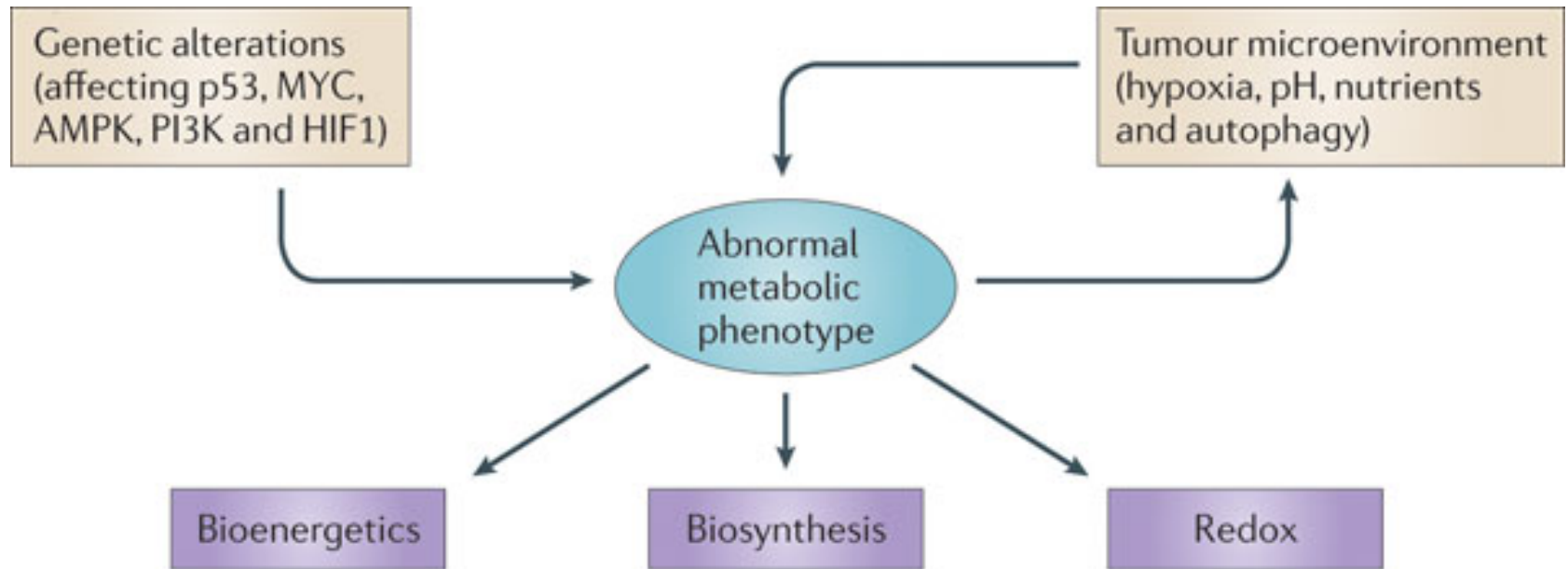


**b Proliferating tumour cell**

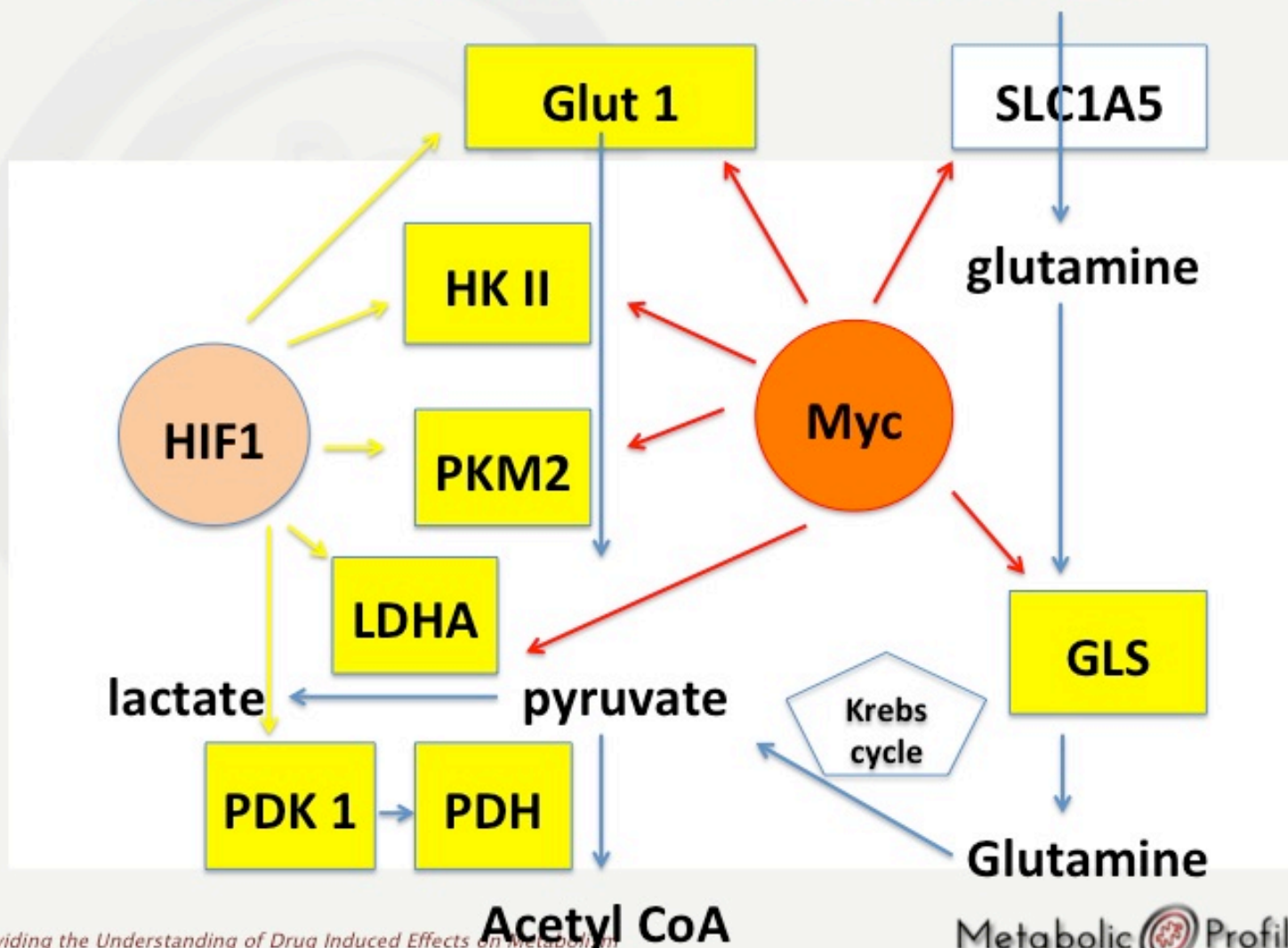




# MAJOR ONCOGENES



# GLYCOLYSIS: THE WARBURG EFFECT



Oncogenic stimulus

Nucleus

Cytoplasm



MYC gene



Max

MYC

MYC target genes

↑GLUT1, mGluR1

SHMT

↓Integrins, N-cadherin

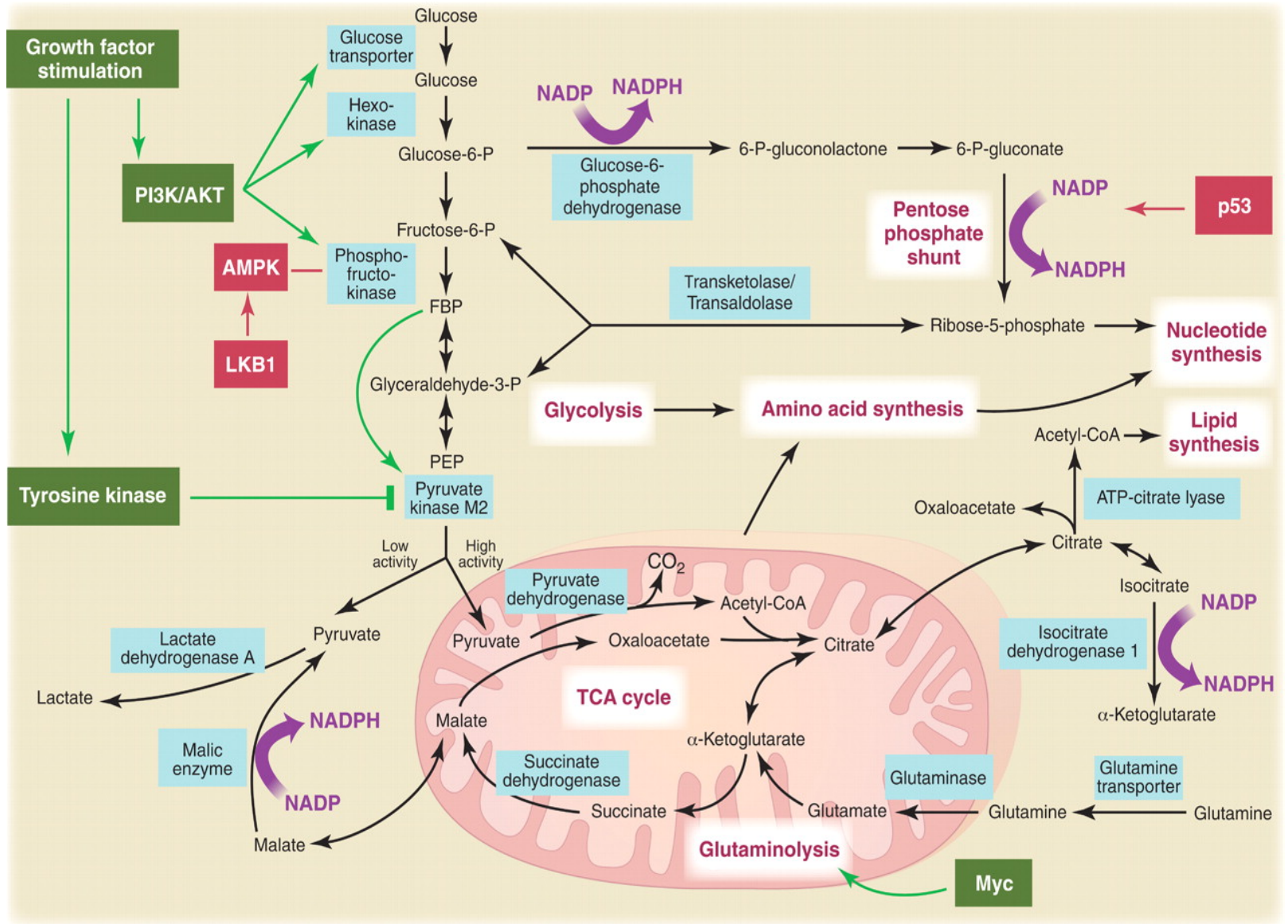
↓p15<sup>INK4B</sup>, p21<sup>CIP1</sup>

Enolase, LDH, HK2, PFKM

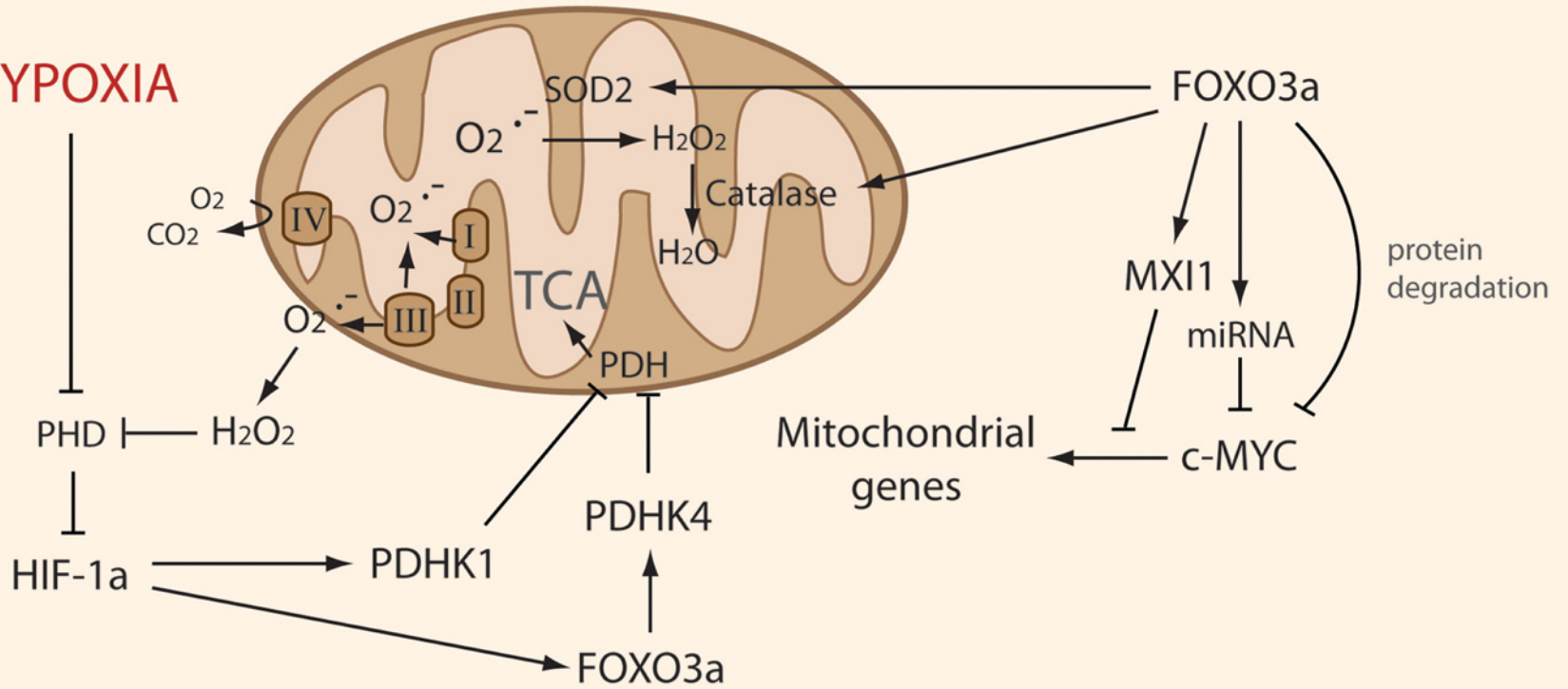
H-ferritin, IRP2

E2F2



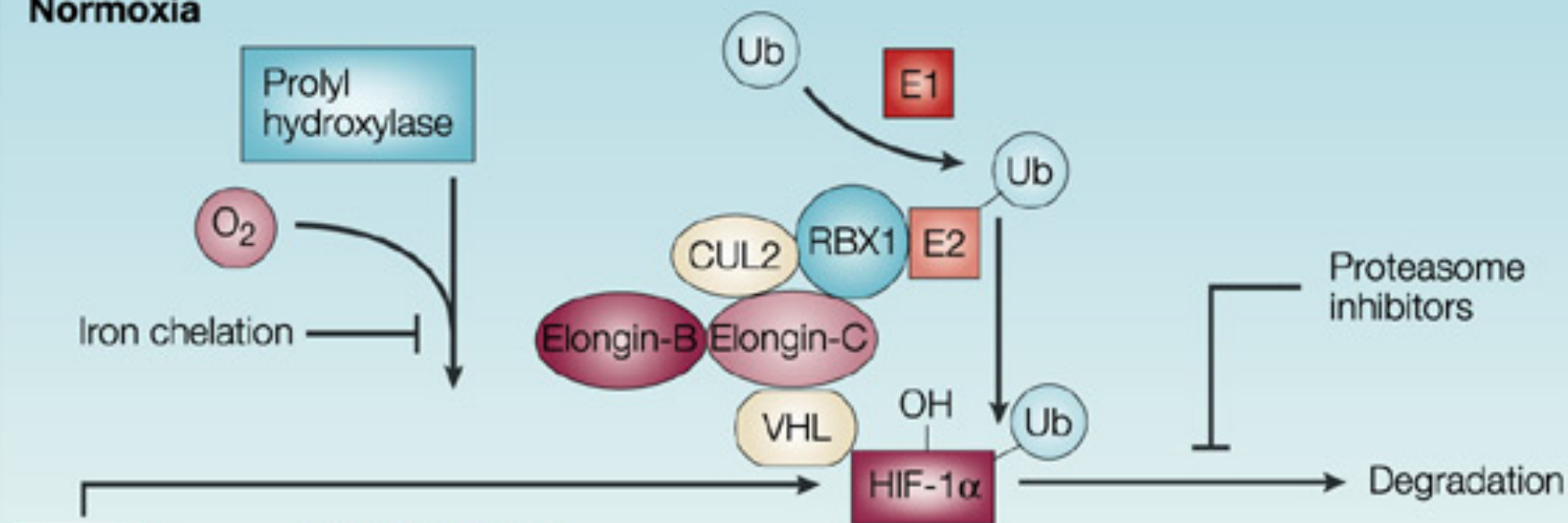


# HYPOXIA





## Normoxia

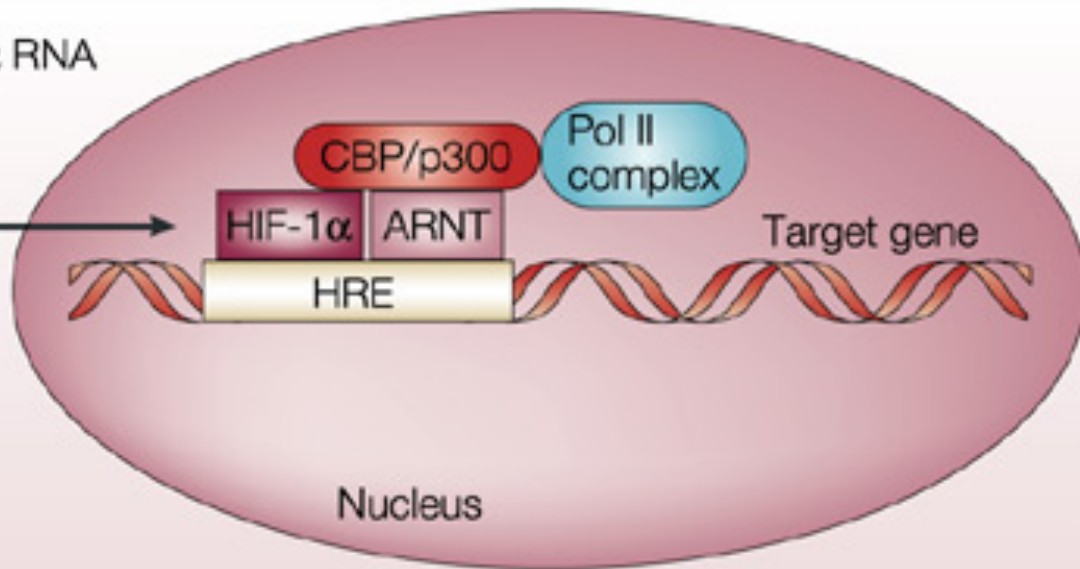


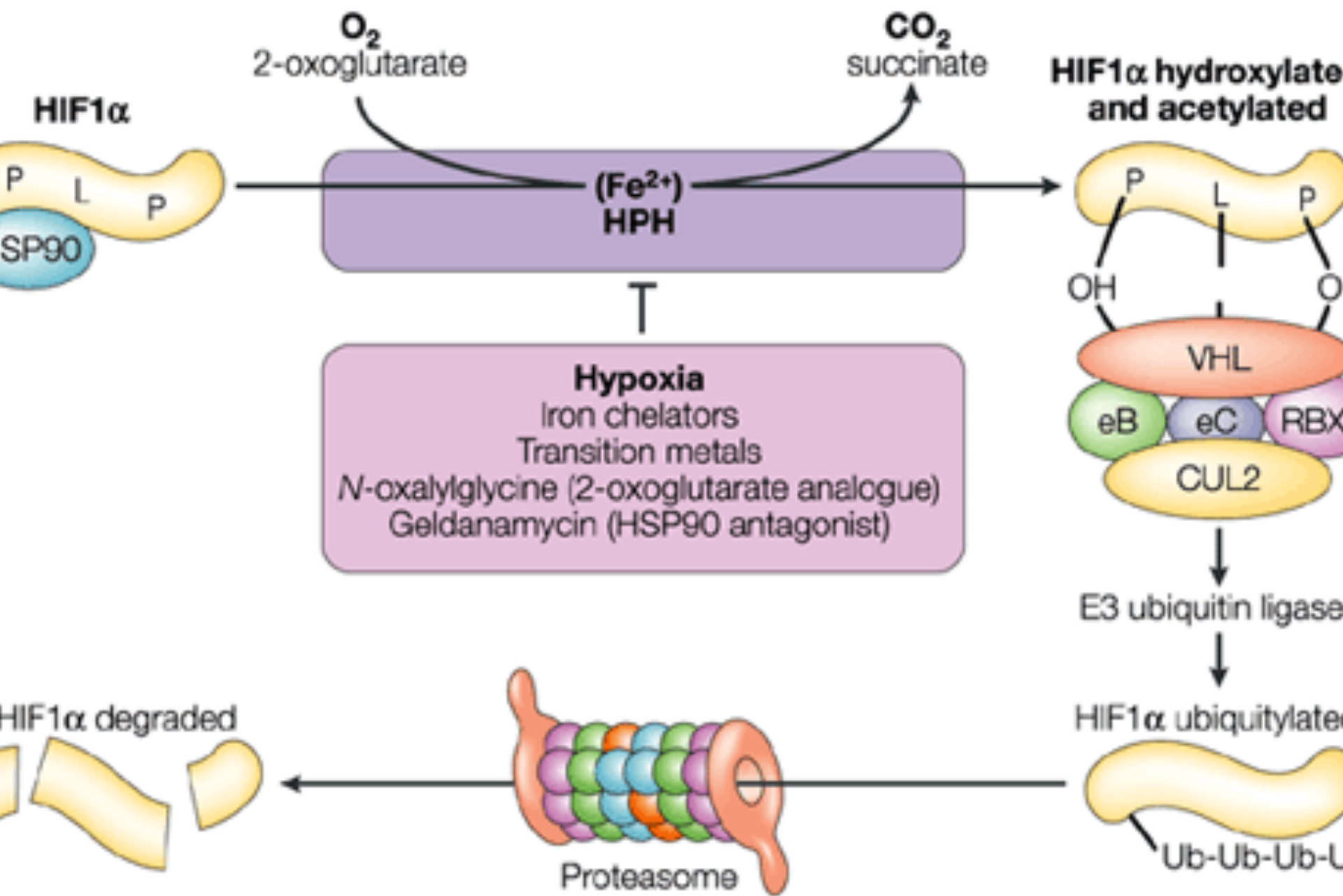
HIF- $\alpha$

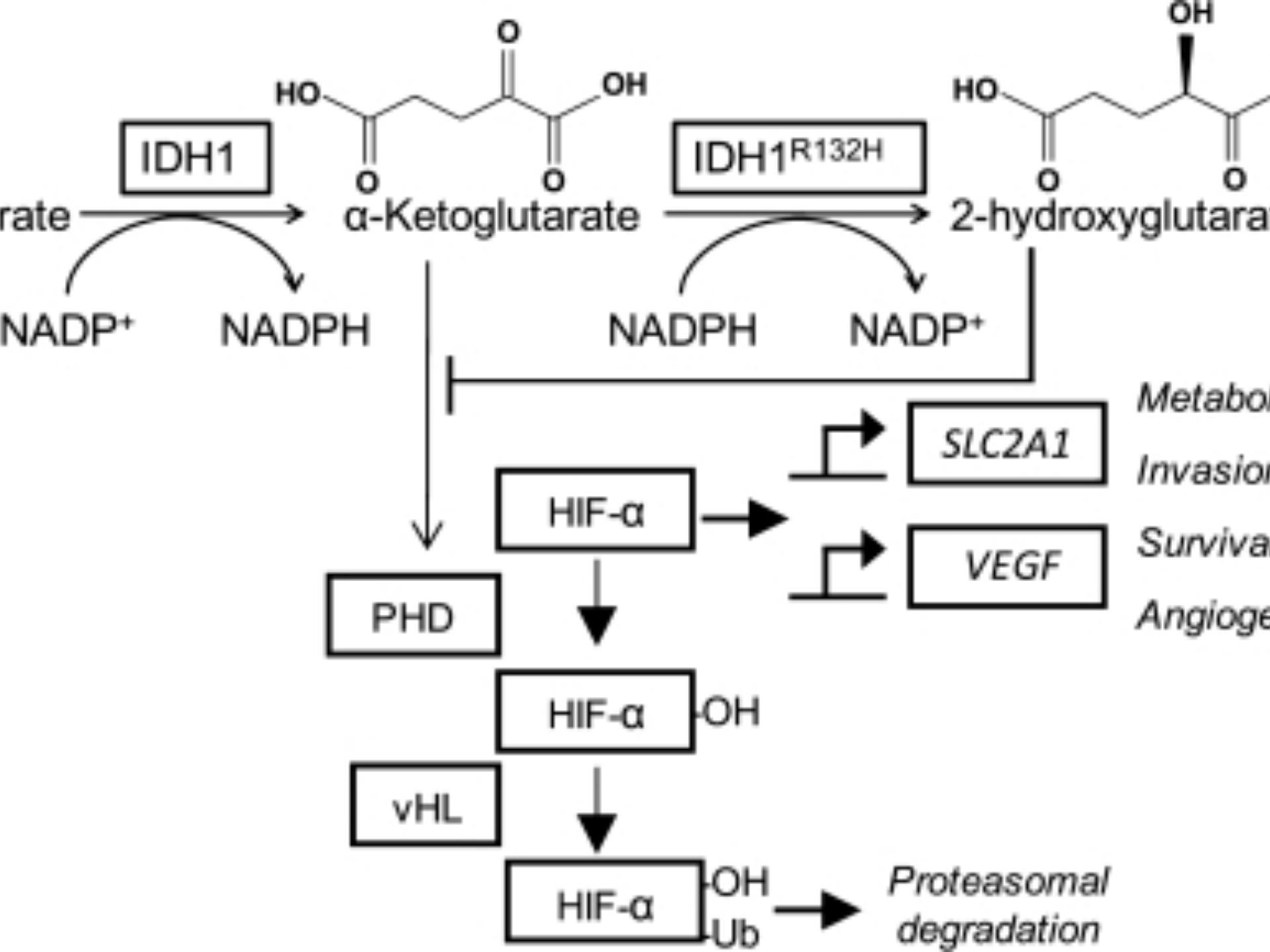


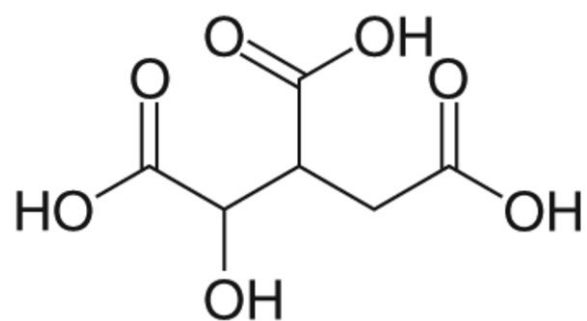
Anti-HIF-1 $\alpha$  RNA

## Hypoxia

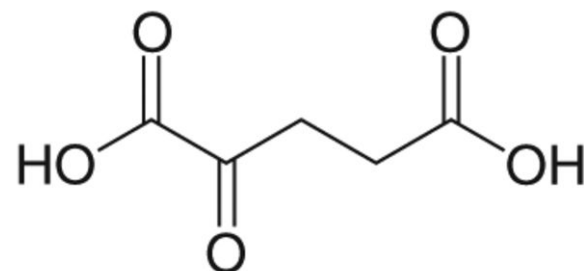
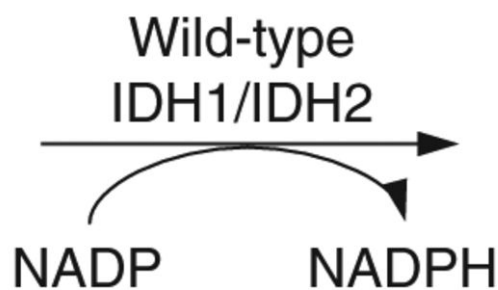




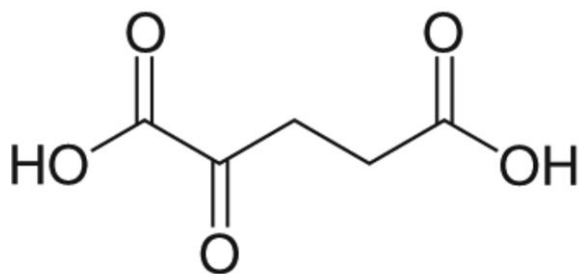




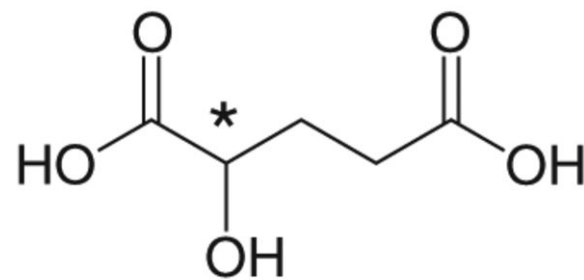
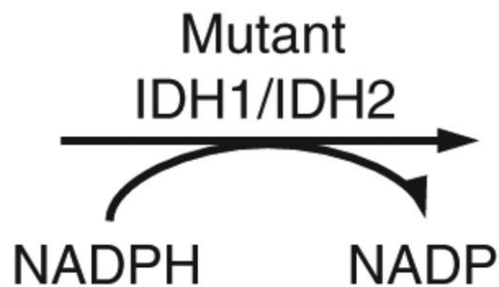
Isocitrate



$\alpha$ -KG + CO<sub>2</sub>



$\alpha$ -KG



D2HG