HYPOXIA INDUCIBLE FACTOR PATHWAY (PW:0000360)

**Description**

Maintaining adequate levels of oxygen is crucial for the proper functioning of cells and tissues as either excess or deficiency of oxygen can have profound pathological consequences. Oxygen is the terminal electron acceptor of the respiratory chain - the electron transport pathway (ETC) whose resulting electrochemical proton gradient drives the synthesis of ATP. ETC also produces reactive oxygen species (ROS) and it is thought that the switch to glycolysis for ATP production when oxygen levels decrease.

**Pathway Diagram:**

- **normoxic conditions**
  - Hif1a+O2
  - Hif1a-O2
  - Hif target genes
  - hypoxic conditions
  - Hif pathway constitutively active irrespective of oxygen levels

**Entities**

- Protein
- Small Molecule
- Treatment
- Cell Process
- Disease
- Cell Object
- Pathway
- Complex
- Functional Class

**Relationships**

- Binding
- Unknown Reaction
- Regulation
- Expression
- Metabolism
- Gene Synthesis
- Promoter Binding
- Prokaryotic Transcription
- Posttranslational
- Cell Transport
- Direct Regulation
- Chemical Reaction

**Shapes**

- Nuclear receptors
- Kinases
- Phosphatases
- Extracellular protein
- Ligands

**GO TO:**

- Genes
- Altered Pathway
- Additional Elements

**Disease annotations to Pathway Genes**

**ALTERED HYPOXIA INDUCIBLE FACTOR PATHWAY (PW:0001102)**

**Description**

Hypoinducible factor (Hif) pathway is the master regulator of oxygen homeostasis. Under normoxic conditions, the Hif alpha proteins are subject to hydroxylation by prolyl and asparagyl hydroxylases whose own enzymatic activities are oxygen dependent and require iron and 2-oxoglutarate as cofactors. The modified proteins are recognized by von Hippel-Lindau (VHL), the component of E3 ubiquitin ligase complex that targets them for proteasomal degradation (the modified asparagine blocks the interaction).