

PDK (Pyruvate Dehydrogenase Kinase)

PDK is a mitochondrial kinase that regulates cellular energy metabolism by inhibiting the pyruvate dehydrogenase complex (PDC), thus controlling the flow of pyruvate into the tricarboxylic acid (TCA) cycle.

General Information

- **Full name:** Pyruvate Dehydrogenase Kinase
- **Location:** Mitochondrial matrix
- **Function:** Phosphorylates and inhibits the **pyruvate dehydrogenase complex (PDC)**, preventing conversion of pyruvate to acetyl-CoA.
- **Isoforms:** PDK1, PDK2, PDK3, PDK4 (tissue-specific roles)

Role in Metabolism

- Regulates the switch between:
 - **Oxidative metabolism** (via PDC and the TCA cycle)
 - **Anaerobic glycolysis** (producing lactate)
- Active PDK inhibits PDC → ↓ acetyl-CoA → ↓ TCA cycle activity
- Important in hypoxia, fasting, high-fat diets, and cancer metabolism

PDK in Glioblastoma and the Brain

- In glioblastoma (GBM), PDK supports:
 - Aerobic glycolysis (Warburg effect)
 - Immune evasion
 - Rapid tumor growth
- **PDK1 is activated downstream of SYK in microglia**, contributing to:
 - **STAT3 activation**
 - **Pro-tumor microglial plasticity**
 - **Immune suppression within the tumor microenvironment**

Clinical Relevance

- **Diseases:**
 - Cancer (especially GBM)
 - Diabetes and insulin resistance
 - Mitochondrial diseases
 - Neurodegenerative disorders
- **Inhibitors:**
 - **Dichloroacetate (DCA):**
 - Restores oxidative metabolism

- Investigated in cancer and metabolic diseases
- Newer selective inhibitors under development for PDK1 and PDK3

PDK in TREM1-SYK Signaling (GBM Microglia)

1. TREM1 →
2. DAP12 →
3. SYK →
4. **PDK1** →
5. STAT3 →
6. Expression of pro-inflammatory and tumor-supportive genes in microglia

From:

<https://neurosurgerywiki.com/wiki/> - **Neurosurgery Wiki**

Permanent link:

<https://neurosurgerywiki.com/wiki/doku.php?id=pdk>

Last update: **2025/04/30 21:23**

