Glycolysis inhibition for anticancer treatment

The Warburg effect

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AIMS

- Review the peculiarities in the energy metabolism of cancer cells (Warburg effect).
- Review of the different inhibitors of this pathway, and combinations with other therapeutic methods of cancer treatment.

INCREASED AEROBIC GLYCOLYSIS IN CANCER CELLS

•Cancer cell metabolism is characterized by an **increased glycolysis** to generate ATP, and this is due to mitochondrial defects, hypoxia, oncogenic signals and altered metabolic enzymes. Green arrows in figure 1 show how glycolytic pathway is enhanced.

INCREASED GLYCOLYTIC FLUX IN CANCER CELLS

•36 ATPs by glycolysis + OXPHOS.

• 2 ATPs just by glycolysis.

GLYCOLYSIS INHIBITION AS ANTICANCER TREATMENT

• Since maintaining a high level of glycolysis is essential for cancer cells, an inhibition of this pathway may kill the malignant cells. Red arrows in figure 1 show the main drugs that inhibit glycolysis at different levels.

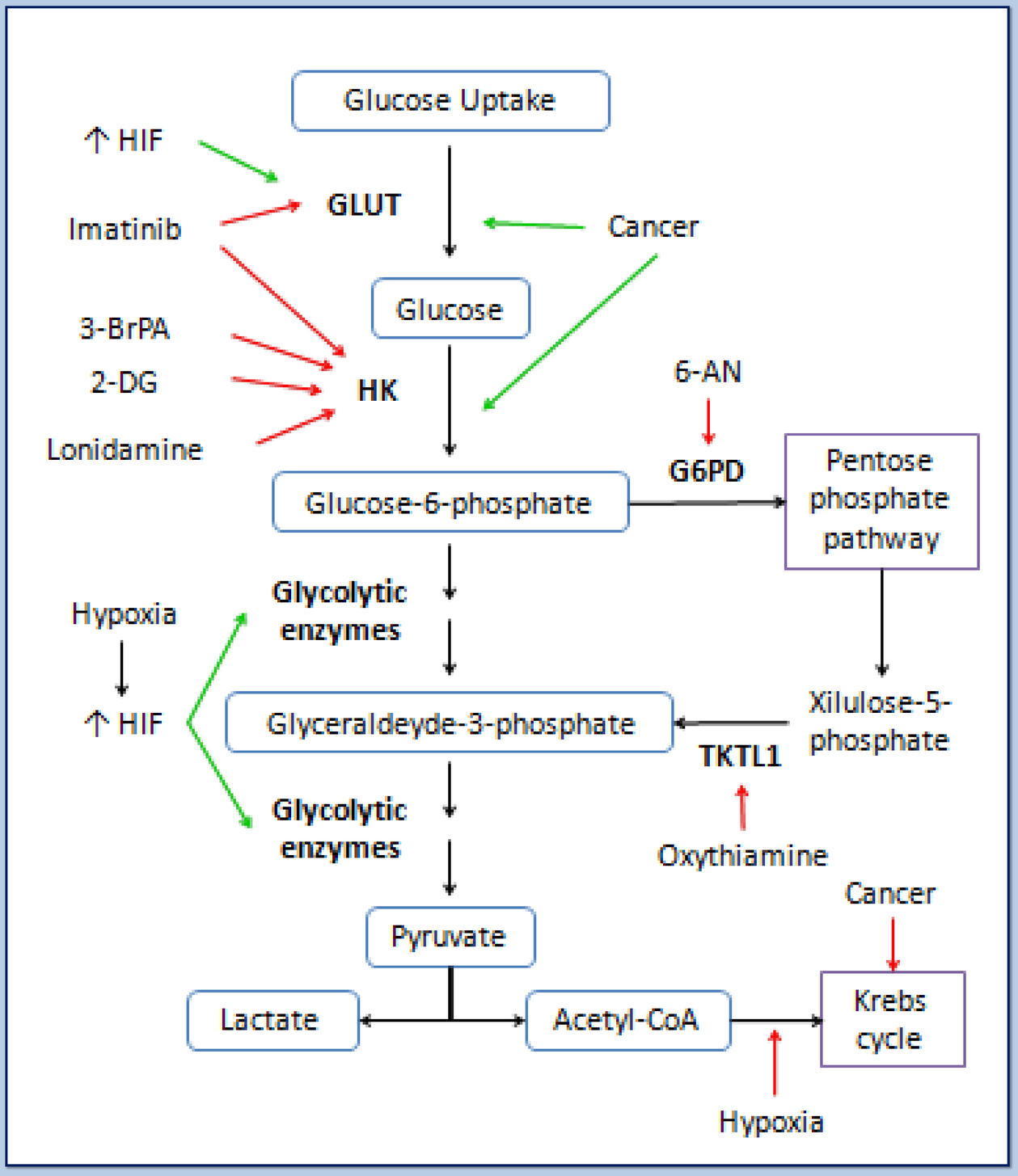

Figure 1. Glycolytic pathway and its metabolic interconnection with the pentose phosphate pathway and the Krebs cycle.

CONCLUSIONS

- There are many causes that can lead to the establishment of the Warburg effect on malignant cells, but the consequence is always a **dependence of the glycolytic pathway to generate ATP**. Therefore, an inhibition of this pathway may end with cancer cells.
- Many drugs can block glycolysis, but without a full effectiveness *in vivo*. Because of it, we can use a combination of these drugs (to exhaust enough the cell) with other types of anticancer therapy (chemotherapy or radiotherapy).