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The Role of Extra- and Intracellular pH in the Regulation of Tumor Process

V. A. Kobliakov*

Bloch Russian Cancer Research Centre, Ministry of Health of the Russian Federation, Moscow, 115478 Russia

**e-mail: kobliakov@rambler.ru*

The review presents and discusses data on the role of changes in intra- and extracellular pH caused by aerobic glycolysis in tumor tissue. The main factor in the regulation of glycolysis is the transcription factor HIF α . Compared to normal tissue, the intercellular space in the tumor is acidified and the pH inside the tumor cells increases. Changes in pH are due to the fact that the final product of glucose conversion is not pyruvate, but lactate. Lactate is transported through the cell membrane and acidifies the intercellular space. HIF α also causes the transcription of a number of proton pumps and matrix proteases, which are activated in the acidic environment of the intercellular space. The intercellular matrix is destroyed and allows the tumor cells to be invaded. An increase in intracellular pH stimulates the accelerated passage of the G₂ phase of the cell cycle. The molecular mechanisms of this process are discussed. It is concluded that the main factors of the tumor process, invasion, accelerated proliferation, genome instability are due to aerobic glycolysis (the Warburg effect).

Keywords: glycolysis, HIF α , invasion, malignancy, proteinase, proliferation