The proton bomb: acid-base chemistry as an effective treatment paradigm for cancer and neurodegenerative diseases

Historical concepts of the importance of physiological pH at the cellular level have recently gained attention as potential hallmarks of cancer progression and neurodegeneration. Healthy people normally exhibit a physiological pH value of ~7.4, which represents an overall balance between acidic and basic (alkaline) environments within and outside organs and cells. At the cellular level, passage of ions (hydrogen, calcium, etc.) through the cell membrane enables regulation of this balance. This review by Harguindey et al. highlights research that shows cancer and various neurodegenerative diseases to alter the pH of cells in ways which eventually determine their malignancy. Cellular homeostasis is maintained by protein complexes that allow the passage of charged molecules between the cellular compartment and its surrounding environment. Studies show that cells associated with multiple types of cancer and some neurodegenerative diseases, such as Alzheimer's disease, alter this "proton flux" to change intracellular pH, thereby reprogramming cellular processes, including altering levels of proteins responsible for maintaining homeostasis, to promote their disease-specific survival (cancer) or destruction (neurodegeneration). The authors highlight known drugs and hormones that target the "gatekeepers" responsible for these fluctuations and offer promising avenues for potential therapeutic strategies to combat these persistent diseases.