3-Bromopyruvate (3BP) a fast acting, promising, powerful, specific, and effective "small molecule" anti-cancer agent taken from labside to bedside: introduction to a special issue.


Abstract

Although the "Warburg effect", i.e., elevated glucose metabolism to lactic acid (glycolysis) even in the presence of oxygen, has been recognized as the most common biochemical phenotype of cancer for over 80 years, its biochemical and genetic basis remained unknown for over 50 years. Work focused on elucidating the underlying mechanism(s) of the "Warburg effect" commenced in the author's laboratory in 1969. By 1985 among the novel findings made two related most directly to the basis of the "Warburg effect", the first that the mitochondrial content of tumors exhibiting this phenotype is markedly decreased relative to the tissue of origin, and the second that such mitochondria have markedly elevated amounts of the enzyme hexokinase-2 (HK2) bound to their outer membrane. HK2 is the first of a number of enzymes in cancer cells involved in metabolizing the sugar glucose to lactic acid. At its mitochondrial location HK2 binds at/near the protein VDAC (voltage dependent anion channel), escapes inhibition by its product glucose-6-phosphate, and gains access to mitochondrial produced ATP. As shown by others, it also helps immortalize cancer cells, i.e., prevents cell death. Based on these studies, the author's laboratory commenced experiments to elucidate the gene basis for the overexpression of HK2 in cancer. These studies led to both the discovery of a unique HK2 promoter region markedly activated by both hypoxic conditions and moderately activated by several metabolites (e.g., glucose), Also discovered was the promoter's regulation by epigenetic events (i.e., methylation, demethylation). Finally, the author's laboratory turned to the most important objective. Could they selectively and completely destroy cancerous tumors in animals? This led to the discovery in an experiment conceived, designed, and conducted by Young Ko that the small molecule 3-bromopyruvate (3BP), the subject of this mini-review series, is an incredibly powerful and swift acting anticancer agent. Significantly, in subsequent experiments with rodents (19 animals with advanced cancer) Ko led a project in which 3BP was shown in a short treatment period to eradicate all (100%). Ko's and co-author's findings once published attracted global attention leading world-wide to many other studies and publications related to 3BP and its potent anti-cancer effect. This Issue of the Journal of Bioenergetics and Biomembranes (JOBB 44-1) captures only a sampling of research conducted to date on 3BP as an anticancer agent, and includes also a Case
Report on the first human patient known to the author to be treated with specially formulated 3BP. Suffice it to say in this bottom line, "3BP, a small molecule, results in a remarkable therapeutic effect when it comes to treating cancers exhibiting a "Warburg effect". This includes most cancer types.

PMID:

22382780