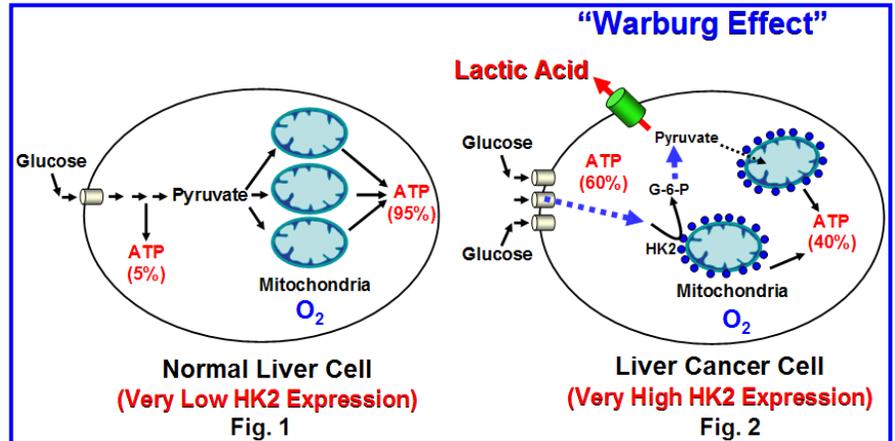


**How Does 3BP (3-bromopyruvate) Work as a Potent Anticancer Agent?**

Patients, scientists and many others are frequently interested in knowing whether 3BP is more effective and less toxic to cancer patients than currently approved chemo-drugs. Certainly, this is the case for experimental animals. In fact, **after several years of study, I have found that 3BP is one of the most effective anti-cancer drugs.** From these same studies I was surprised to see how inefficient currently approved cancer drugs really are. Now, I understand in greater depth the striking and highly selective killing mechanism of 3BP. Specifically, 3BP targets the essential energy production machinery of cancer cells while leaving the same machinery in normal cells preserved. This discovery has been instrumental in propelling a new direction in cancer research focused on selectively targeting the cancer cells' energy production factories. In fact, Dr. Pedersen is the pioneer in this new strategy for targeting cancer cells.

From the brief descriptions numbered below, one will see how 3BP works as an anticancer agent.

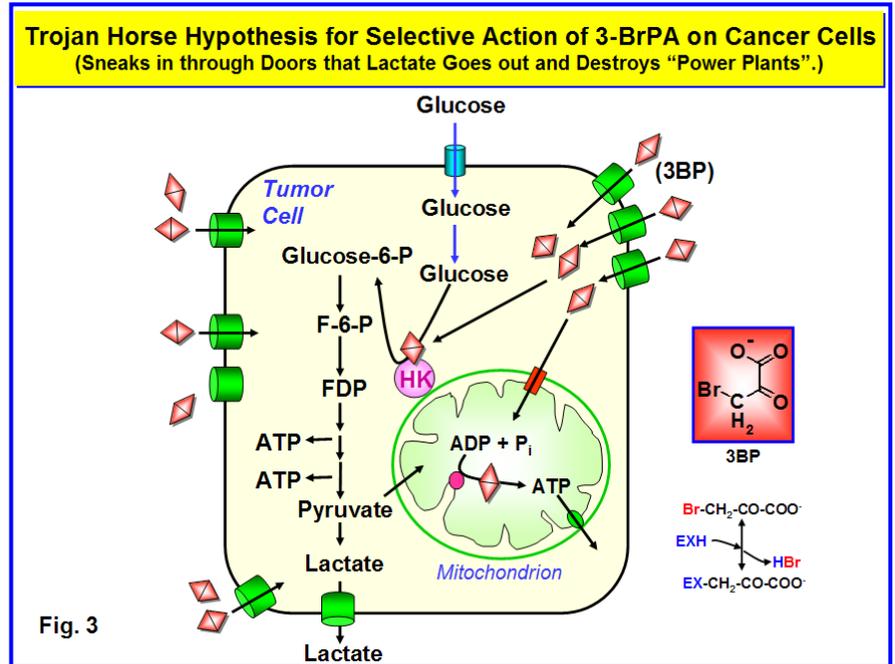
1) There are two energy (ATP) production factories inside the cell, i.e., glycolysis and oxidative phosphorylation by mitochondria. In normal cells (Fig. 1), about 5 % of the total cellular energy (ATP) production is derived from glycolysis and about 95 % from the mitochondria. In cancer cells (Fig. 2), the energy production by glycolysis is significantly increased (up to 60 %). This dramatic increase in glycolysis in cancer cells results in a significant increase in lactic acid production.



2) Most cancers (> 90 %) exhibit this common metabolic phenotype. This is called the “Warburg Effect”, i.e., significant increase in glycolysis in cancer cells even in the presence of oxygen. The most frequent cancer detection method used clinically, i.e., Positron Emission Tomography (PET) is based on this metabolic phenotype, i.e., the “Warburg effect”.

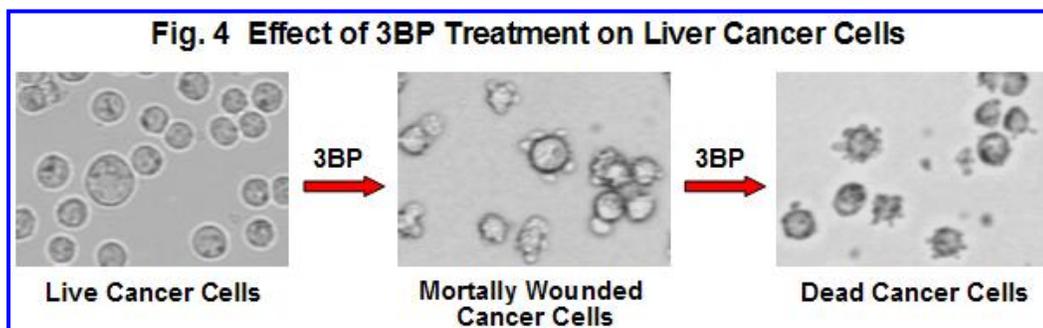
3) Cancer cells that exhibit the “Warburg effect” pump out the produced lactic acid via a transporter (Fig 2; it is depicted as a green cylinder). The number of these transporters (considered as doors or gates) in cancer cells is much greater than in normal cells.

4) 3BP, a lactic acid analog, is a small chemical and mimics the lactic acid chemical structure. It is depicted as a small red diamond in Fig. 3. Therefore, 3BP disguised as lactic acid can “trick” the cancer cells and enter like a Trojan horse (Fig. 3). It has little effect on normal cells as these contain very few lactic acid transporters.



5) Because of 3BP’s highly reactive nature, it destroys the two energy production factories (Fig. 3; one red diamond above the HK means that 3BP is destroying one energy production factory, i.e., glycolysis, and another red diamond inside the mitochondrion means that 3BP is destroying also this energy production factory). Now, the cellular energy (ATP) is depleted very rapidly as 3BP attacks the two factories at the same time causing the cancer cells to rapidly explode (cell membrane rupturing). As an example of this in action, see Fig. 4 (page 2). Here, the healthy cancer

cells are round and iridescent (left picture). However, when they are treated with 3BP (also called 3-BrPA), the cell membranes rupture (middle picture) and then die (see cell debris in the far right picture).



In summary, 3BP should meet the following essential criteria, and **“IT DOES”**:

**A)** It should be cancer cell **specific**; this minimizes cyto-toxicity of normal cells (Fig. 3, page 1)

**B)** It should be highly **effective** in killing cancer cells (Fig. 4); otherwise, slightly damaged or crippled cancer cells will likely develop a new escaping strategy to overcome the anticancer drug attack, e.g., drug resistance and mutations for adaptation.

**C)** It should destroy itself (**suicidal**) after killing cancer cells; otherwise, the anticancer agent will remain after their destruction. This imposes possible risks or danger to normal cells as the original weapon is “on the loose”.

**D)** It should cause cancerous tumors to completely disappear in animals without harming the animals (Fig. 5), i.e., exhibit little or no toxicity, i.e., **be successful *in vivo***.

I hope the above information is helpful to those interested in evaluating how 3BP works. I have dedicated a great portion of my life to this project and will continue to do so **until I see its effectiveness in cancer patients**. Significantly, I have already led earlier projects that have demonstrated in

animals the capacity of this agent to eradicate two of the most vicious types of cancer, liver and lung, while exhibiting little or no apparent toxicity to the animals. In fact, after curing 19 out of 19 rats with advanced cancers, they were shown to live out their normal lives cancer-free and healthy.

Significantly, my invention of 3BP as an anticancer agent is beginning to receive considerable attention, not only in the U.S. but throughout the world.

Thank you very much for your time and attention.

Sincerely,

*Young Hee Ko*

Young Ko, M.S., Ph.D.

