"First International workshop on Sexual Dimorphism In Cancer" | March 22-26-2021

Understanding the gender dichotomy in the antitumor response of 3- Bromopyruvate on a thymoma mouse model

Achyut Bora[1,2], Prof. S.M. Singh[1]
[1]School of Biotechnology, Banaras Hindu University, Varanasi, India
[2] CSIR- Indian Institute of Chemical Biology, Kolkata, India
Email ID- achyutbora.ab@gmail.com

BACKGROUND

3-Bromopyruvate (3-BP) is a promising powerful superior anticancer agent. It can inhibit multiple metabolic enzymes that crucial for the survival of neoplastic cells. It includes hexokinase II (HK2) glyceraldehyde 3-phosphate dehydrogenase GAPDH, succinate dehydrogenase (SDH), pyruvate dehydrogenase (PDH), phosphoglycerate kinase (PGK), and Lactate Dehydrogenase (LDH). Despite, 3-BP displays cytotoxicity against a wide variety of tumors, there is no report that is available regarding the existence of gender dimorphism in differential susceptibility to the antitumor action of 3-BP. Therefore, the present investigation was undertaken to study the gender dichotomy in the antitumor response of 3-bromopyruvate on a thymoma mouse model.

❑ Gender Dimorphism in Cancer

❖Females display higher capability of mounting type-2 versus type-1 immune responses, whereas males seem to prefer type-1 immune responses.

❖Hormones play a dual role in cancer by both promoting and inhibiting the tumor growth.

❖Immune and Endocrine system are the modulator for gender dimorphism in cancer.

OBJECTIVES

❖Investigate the gender dichotomy on tumor progression and survival of tumor-bearing mice upon in-vivo administration of 3-BP.

❖Understanding the gender dimorphism in myelopoiesis differentiation and apoptotic and necrotic mode of death in Bone marrow cells (BMC) on the antitumor response of 3-BP in a thymoma mouse model

METHODOLOGY

Transplanted Dalton's lymphoma (DL) ascetic form *in-vivo* (5×10^5 cells)

Strain: BALB/c (H-2^d) Mice
Age/Weight: 25-30 g./8-12 weeks

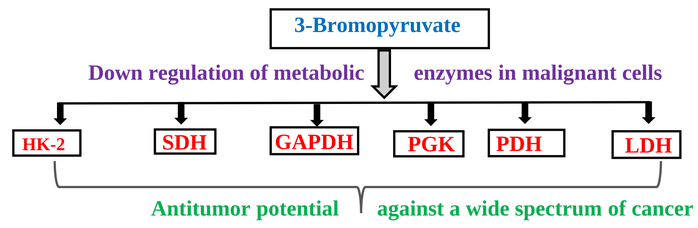
GROUP 1
Control Male (CM)
Injecting with PBS(0.5ml) (Without any chemical treatment)

GROUP 2
Male Treated (MT)
Received a single intraperitoneal injection of a 3-BP solution (4mg/kg/mice body weight, with PBS) alternatively for 2 weeks

GROUP 3
Control Female (CF)
Without any chemical treatment (PBS alone).

GROUP 4
Female Treated (FT)
Received a single intraperitoneal injection of a 3-BP solution (4mg/kg/mice body weight, with PBS) alternatively for 2 weeks

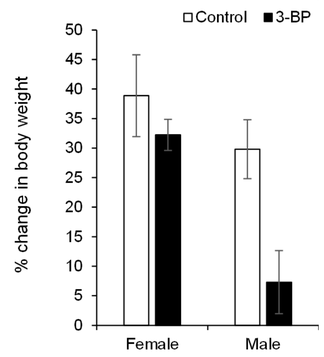
❑ 3-Bromopyruvate (3-BP) is a promising powerful superior anticancer agent



1.Breast 2. Prostate 3. Pancreas,4. Cervix 5.Renal, 6.Ovarian, 7.Colorectal, 8. Hepatic, 9.Melanoma, 10. Mesothelioma, 11. Lung 12. Myeloma 13. Leukemia And 14.Lymphoma

RESULTS

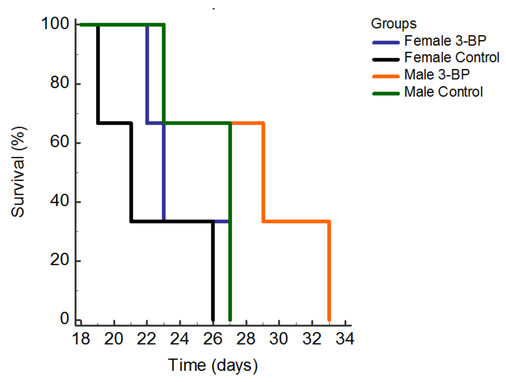
❑Gender-dependent tumor growth inhibition of following *in-vivo* administration of 3-Bromopyruvate (3-BP)



Change in body weight (%)= $\frac{W_f - W_i \times 100}{W_i}$ Where, W_f = weight of mice on day 14th of tumor transplantation and W_i = weight of mice on day 2nd of tumor transplantation

RESULTS

❑Overall survival of mice



➢ The life span of male DL-bearing mice following 3-BP administration was significantly prolonged compared with the female tumor-bearing mice.

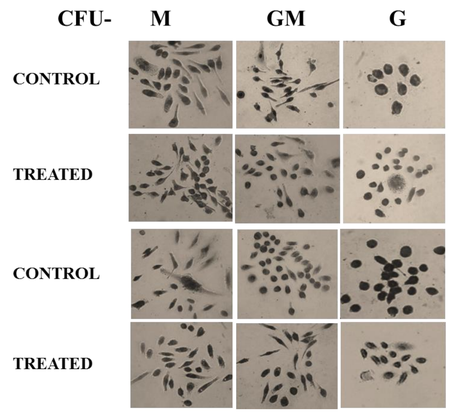
❑Sexual Dimorphism on the effect of in-vivo administration of 3-BP to male and female tumor-bearing mice on the survival of Dalton's lymphoma cells.

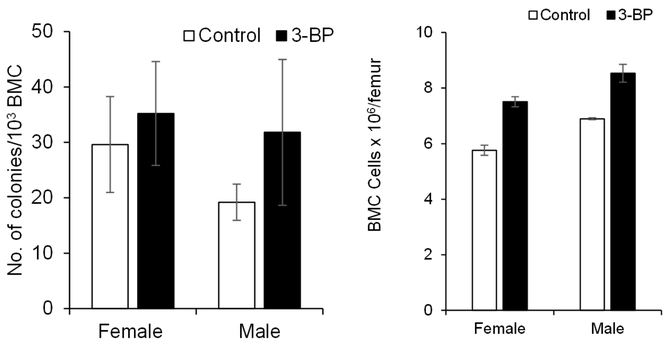
ACKNOWLEDGEMENT

I take this opportunity to sincerely acknowledge to all the members of **Tumor Immunology Lab, School of Biotechnology, Banaras Hindu University, Varanasi** for their guidance and constant supervision.

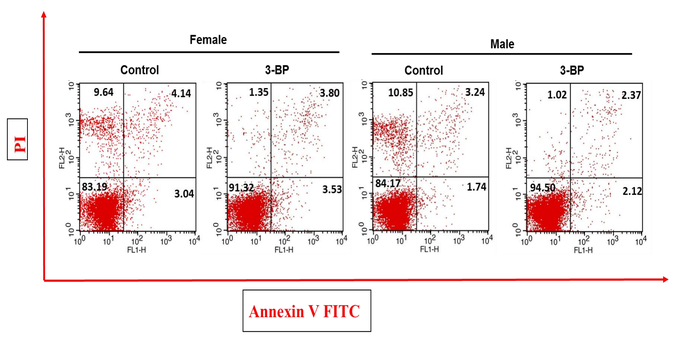
RESULTS

❑Effect of gender on the colony-forming ability of BMC in male and female tumor-bearing hosts

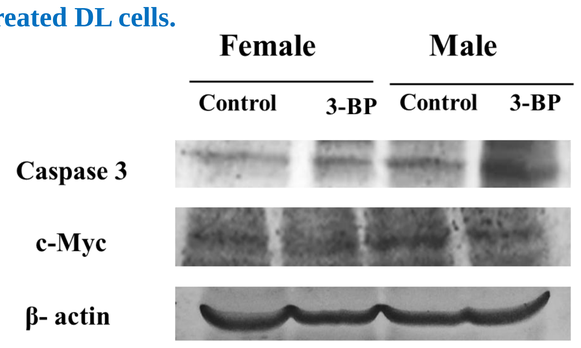




❑Gender dimorphism of 3-BP response on the induction of apoptosis and necrosis in Bone Marrow Cells (BMC).



❑Expression of Caspase 3 and c-Myc proteins in 3-BP treated DL cells.



CONCLUSION

❖ 3-BP administration to male and female tumor-bearing hosts resulted in gender-dependent differential tumor growth retardation. Such gender dichotomy on the antitumor response of 3-BP was associated with a differential impact on cell viability, tumor cell volume, the life span of mice, and expression of cell survival regulatory proteins: c-Myc and Caspase-3. 3-BP administration also showed gender-dependent differential in myelopoiesis differentiation and mode of death of bone marrow cells..

❖ The antitumor effect of 3-BP was found to be better in the male tumor-bearing hosts in comparison to female tumor-bearing hosts.

❖ Hence has a clinical significance in determining its potential therapeutic effect in a gender-specific on cancer.

❑ Reference

➢ Yadav S, Kujur PK, Pandey SK, Goel Y, Maurya BN, Verma A, Kumar A, Singh RP, Singh SM. Antitumor action of 3-bromopyruvate implicates reorganized tumor growth regulatory components of tumor milieu, cell cycle arrest and induction of mitochondria-dependent tumor cell death. Toxicol Appl Pharmacol. 2018 Jan 10.1016/j.taap.2017.12.004. Epub 2017 PubMed PMID:29221953.