BLACKSTONE THERAPEUTICS

CASE STUDY

BST Cannabinoid Analogs and their Impact on A549 Lung Cancer

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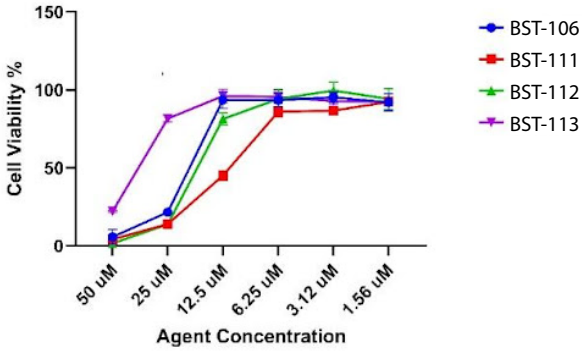
Lung cancer accounts for 12.3% of all new cases with an estimated 130,180 deaths in 2022; it is the 3rd most common cancer in the US with a 22.9% five-year survival rate[1]. Current on-the-market antineoplastics have undesired side effects that patient care: paclitaxel is known for bone marrow suppression and neuropathy in formulations. Our group exploited modified derivatives of rare cannabinoids, exemplified by BST-104 and BST-106 in A549 *in-vitro* studies[3]. These compounds show selectivity to disrupt cancer cells, compared to various other antineoplastic compounds on the market, leading to cell death while allowing healthy cells to proliferate.

Several BST compounds were sent for *in-vitro* testing on non-small cell lung cancer (NSCLC) cell line A549. This cell line is the most common cell line used for drug discovery to learn about properties of tested compounds against lung cancer. The compounds were tested against known antineoplastics that are used in the treatment of lung cancer such as gemcitabine, paclitaxel, and 5-FU (5-fluorouracil). Below in Figure 1, is the comparison of the BST compounds across a varying concentration and their ability to reduce cell viability. BST-106, BST-111, BST-112, and BST-113 have a relatively moderate IC50 value but considering the side effects the known antineoplastics cause and their secondary issues that arise, the ratio of risk:reward is taken into account.

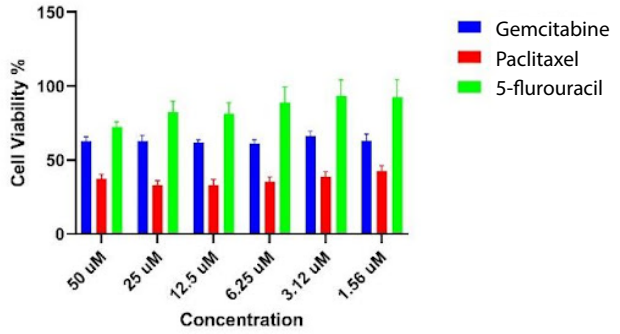


Cell Line	Compound	ICU (μM)
A549	BST-106	20.06
A549	BST-111	14.12
A549	BST-112	18.30
A549	BST-113	38.26

Figure 1: Comparison of effects of BST analogs on A549

Above in figure 1 respectively BST-106 has a 20.06 μM, BST-111 has a 14.12 μM,

BST-112 has a 18.30 µM, and BST-113 has a 38.26 µM IC50 value. Through drug discovery anything at 10 µM or below is considered a hit, with further SAR studies and modifications these compounds IC50 values can increase greatly, increasing their efficacy.



Cell Line	Compound	IC50
A549	5-FU	1.02 µM
A549	Gemcitabine	6.6 nM (lit.)
A549	Pacliltaxel	1.35 nM (lit.)

Figure 2: Comparison of effects on the market antineoplastics

Above in figure 2 shows the cell viability of the antineoplastics that are currently on the market. The antineoplastics were tested at varying concentrations. These compounds are some of the primary treatments used in NSCLC treatment, with paclitaxel being the strongest competitor. Current antineoplastics which are used to treat pancreatic cancer have terrible IC50: cisplatin4 has 18.48 µM IC50 value on MIA-PaCa2 cell line as well as oxaliplatin4 with a 63.2 µM IC50 value.

Below in figure 3 is the comparison of the BST compounds and antineoplastics. At greater concentrations the BST compounds specifically show better efficacy. At these concentrations the known side effects of the known antineoplastics would be detrimental. As well gemcitabine and 5-FU treated cancers can become resistant.

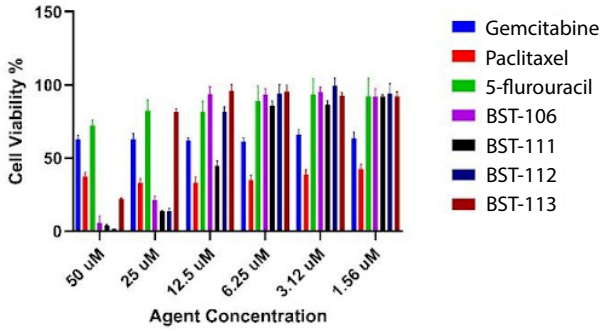


Figure 3: Comparison of effects of antineoplastics and BST analogs

Continuous studies are currently being conducted in *in-vivo* xenograft studies to determine efficacy in live models. As well as increased SAR studies to increase efficacy and lower IC50 values.

References

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4. Yang, W.; Soares, J.; Greninger, P.; Edelman, E. J.; Lightfoot, H.; Forbes, S.; Bindal, N.; Beare, D.; Smith, J. A.; Thompson, I. R.; Ramaswamy, S.; Futreal, P. A.; Haber, D. A.; Stratton, M. R.; Benes, C.; McDermott, U.; Garnett, M. J. Genomics of Drug Sensitivity in Cancer (GDSC): A Resource for Therapeutic Biomarker Discovery in Cancer Cells. *Nucleic Acids Res.* **2013**, 41 (Database issue), D955-61. https://doi.org/10.1093/nar/gks1111.