Autophagy Inhibition is Associated with chemosensitivity in Neuroblastoma cell line

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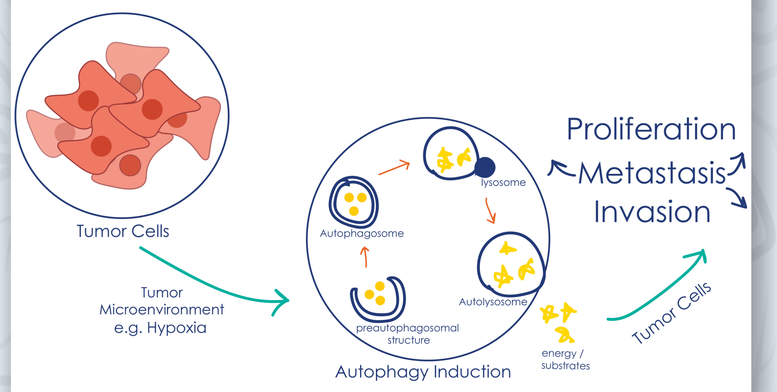
"Does autophagy inhibition increase sensitivity of SK-N-AS neuroblastoma cells to cisplatin?"

ABSTRACT

Neuroblastoma is the most common type of cancer diagnosed in children aged between one and five years old. According to the American Society of Clinical Oncology, children diagnosed with high-risk neuroblastoma have around 50% 5-year survival rate. A common chemotherapy treatment often given to children with high-risk neuroblastoma is Cisplatin (Platinol).[1] Unfortunately, the use of cisplatin is often met with chemoresistance due to the induction of autophagy; a degradation system present inside the cell. This interesting cellular pathway is double-faced sword; it can either suppress tumor progression promote tumorigenesis.[2] There is a current gap in research regarding the use of chemotherapy concurrently with autophagy inhibition in neuroblastoma. It is envisioned that the use of Bafilomycin A-1 will decrease the resistance of SK-N-AS cells and produce cytotoxic effects.

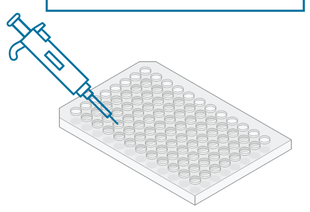
KEY STUDIES

- **Autophagy can either activate cell death and suppress tumor progression or promote cell survival in cancer cells. [2]**
- **Cisplatin treatment increased autophagic activity in human cervical cancer cell lines. [3]**
- **Bafilomycin-A1 successfully increased chemosensitization to Cisplatin in several cancer cell lines *in vitro*. [4]**



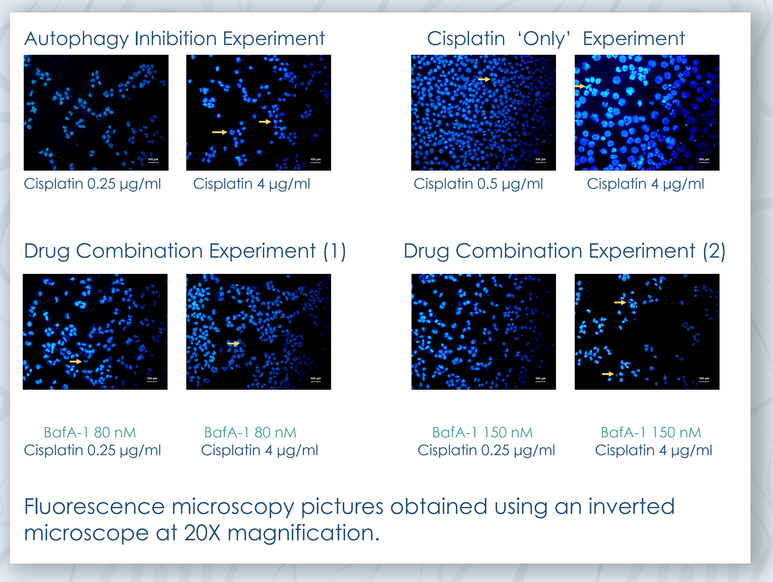
METHODOLOGY

MTT ASSAY



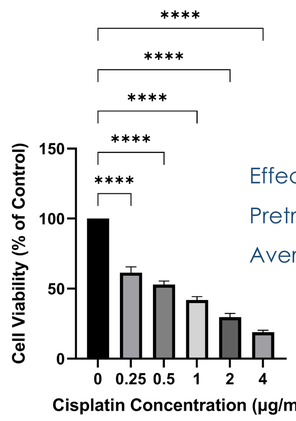
NUCLEIC ACID STAINING

The current research study aims to investigate the use of Bafilomycin A-1, an autophagy inhibitor, with the concurrent use of Cisplatin to observe if it decreases neuroblastoma resistance to Cisplatin. For these purposes, neuroblastoma cell line; SK-N-AS, were either pre-treated with a fixed concentration of Bafilomycin A-1, followed by increasing concentrations of Cisplatin or treated with a combination of both Bafilomycin A-1 as well as Cisplatin. Cell viability was assessed using MTT cytoxicity assay. Untreated and treated Neuroblastoma cells were then fluorescently stained to visualize nuclear DNA.

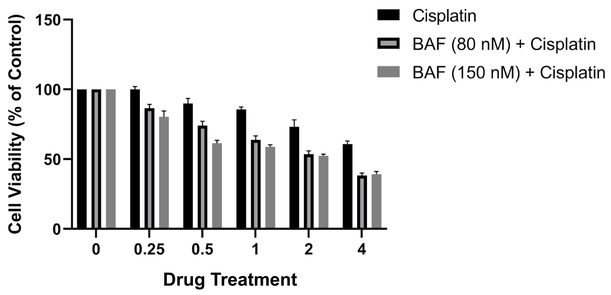


Fluorescence microscopy pictures obtained using an inverted microscope at 20X magnification.

PRELIMINARY RESULTS



Effect of Autophagy Inhibition using Pretreatment with Bafilomycin-A1 on Average Cell Viability of SK-N-AS Cells



Effect of Combination Treatments Vs Cisplatin Alone on Average Cell Viability of SK-N-AS Cells. Combination Treatments were prepared by combining increasing concentrations of Cisplatin (0.25 to 4 ug/ml) with BAF-A1.

CONCLUSION

- Autophagy inhibition using Bafilomycin A-1 increases the sensitivity of SK-N-AS cells to Cisplatin.
- DNA fragmentation at high concentrations of Bafilomycin A-1 and cisplatin indicates cell death.
- Further investigation is needed to confirm preliminary findings as well as identify type of cell death and the underlying effects on gene expression.

REFERENCES

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