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Exploiting the SARS-CoV-2 Spike Protein Components to Guide Molecular Level Entry of a BAG-1 Inhibitor in the Treatment of Breast and Lung Cancers

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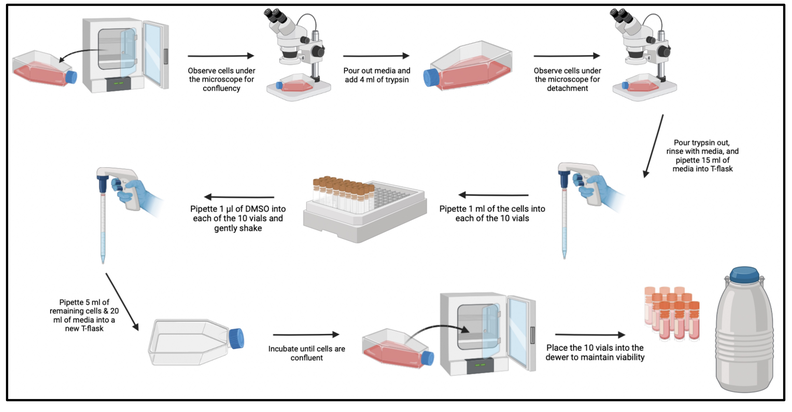
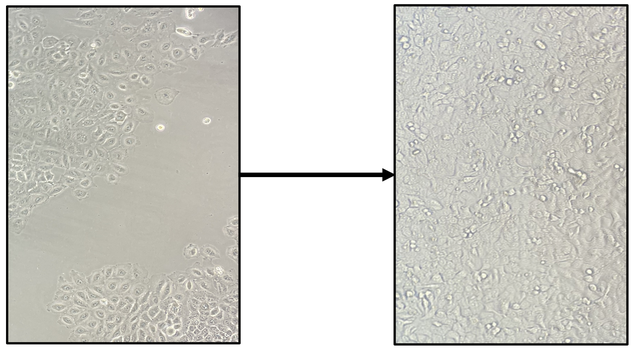
Abstract

Chemoresistance of lung cancer cells is the primary reason as to why limitations occur with cancer treatments. A protein, known as BAG-1, is responsible for many cellular activities including cellular stress response, cell growth, and apoptosis (regulated cell death). When overexpressed, the protein has been linked to the anti-apoptotic behavior of cancer cells. BAG-1 can combine to heat shock proteins (HSPs), a family of helical molecular chaperones that are known to aid in the maturation of proteins, refolding, and degradation. This response plays a crucial role in the study of chemoresistance in cancer patients due to its detrimental nature. Prior, this combination was combated by using a synthesized poly-arginine linked peptide inhibitor alongside cell penetrating peptides (CPPs) through targeted binding domains. However, it has been found that the Spike protein of SARS-CoV-2 uses several small subdomains to efficiently bind to human epithelial cells at the nanomolar level. **This study aims to focus on the binding complex of the BAG-1 and Spike proteins to form an anti-apoptotic inhibitor that can result in a potential specific binding mechanism for drug delivery of lung cancer treatments.**

Subculture



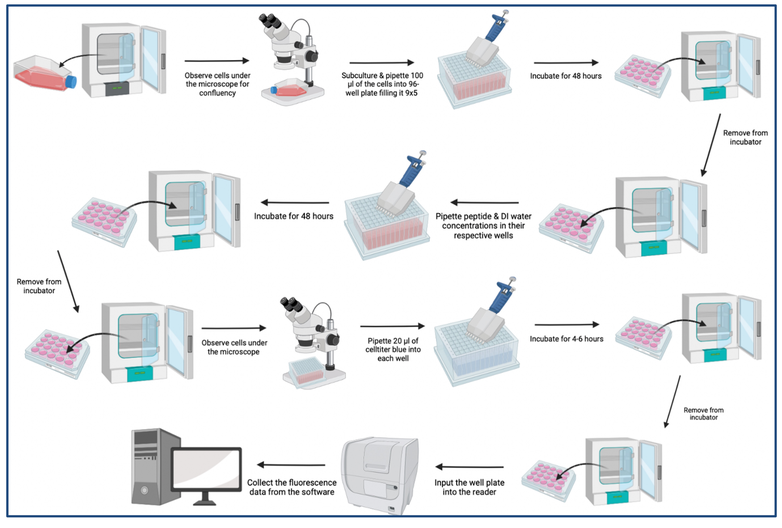
Cell Growth



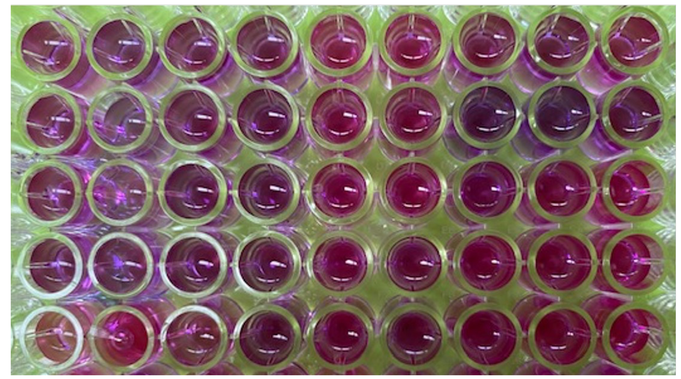
Three days into incubation. Cells are not confluent.

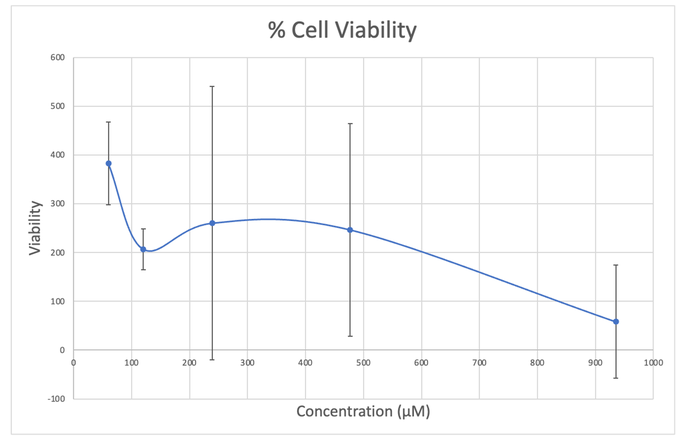
A week after incubation. 100% confluency present.

Peptide Toxicity Study



Cell Viability





Conclusion & Future Direction

- Water does not cause starvation to the cells due to dilution
- 10% ethanol makes a good control for the study
- This delivery method proves to be a viable option in the delivery of cancer therapeutics
- Future Direction: Examine the use of the Spike protein subdomain as peptide penetrators by conducting another toxicity study

References

- Gui, L., Zhang, X. H., Qiao, Z. Y., & Wang, H. (2020). Cell-penetrating peptides and polymers for improved drug delivery. *ChemNanoMat*, *6*(8), 1138–1148. https://doi.org/10.1002/cnma.202000118
- *Liraglutide - generic peptides*. Polypeptide. (2022, March 17). Retrieved June 27, 2022, from https://www.polypeptide.com/news/generic-peptides/liraglutide/
- *Liraglutide*. Uses, Interactions, Mechanism of Action | DrugBank Online. (n.d.). Retrieved June 27, 2022, from https://go.drugbank.com/drugs/DB06655
- Puray-Chavez, M., LaPak, K. M., Schrank, T. P., Elliott, J. L., Bhatt, D. P., Agajanian, M. J., Jasuja, R., Lawson, D. Q., Davis, K., Rothlauf, P. W., Jo, H., Lee, N., Tenneti, K., Eschbach, J. E., Mugisha, C. S., Vuong, H. R., Bailey, A. L., Hayes, D. N., Whelan, S. P. J., … Kutluay, S. B. (2021). Systematic analysis of SARS-COV-2 infection of an ACE2-negative human airway cell. https://doi.org/10.1101/2021.03.01.433431
- *Reference ID: 4144309 - Food and Drug Administration*. (n.d.). Retrieved June 27, 2022, from https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022341s027lbl.pdf
- Schematics made with BioRender. (http://biorender.com)
- Zakaria, N., Satar, N. A., Abu Halim, N. H., Ngalim, S. H., Yusoff, N. M., Lin, J., & Yahaya, B. H. (2017). Targeting lung cancer stem cells: Research and clinical impacts. *Frontiers in Oncology*, *7*. https://doi.org/10.3389/fonc.2017.00080

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