Generating Cisplatin Resistant HPV-positive HNSCC cell lines

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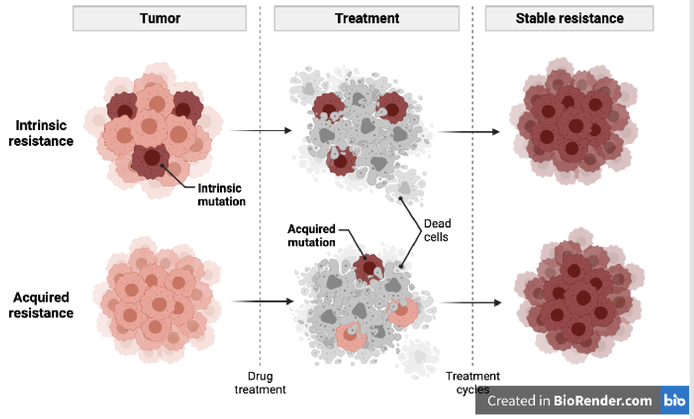
INTRODUCTION

- Acquired or innate resistance to chemotherapy poses a significant challenge in the treatment of head and neck squamous cell carcinoma (HNSCC) resulting in relapse, metastasis and increased mortality.
- Chemotherapy resistance occurs when small populations of cancer cells evade the cytotoxicity of cancer drugs and are able to survive and propagate.



Adapted from "Intrinsic and Acquired Drug Resistance, by BioRender.com (2021). Retrieved from https://app.biorender.com/biorender-templates

- HNSCCs are often treated with a combination of surgery, radiation and chemotherapy, with cisplatin being a standard-of-care chemotherapy drug.
- Human papillomavirus (HPV) is detected in about 25% of all HNSCCs.
  - HPV-associated HNSCCs have distinct molecular mechanisms underlying the cancer progression, when compared to HPV-negative HNSCCs *(Kreimer, 2005)*.
- HPV-positive HNSCC are also known to have significantly better prognosis in response to treatment when compared to HPV-negative HNSCCs *(Fakhry, 2008)*.
  - However, about 15-20% of HPV+ HNSCC patients fail to respond to standard therapy and develop treatment resistance tumours.

RATIONALE

The molecular and genetic basis of cisplatin resistance in HPV-positive HNSCC is not well-defined.

OBJECTIVE

The purpose of this experiment is to generate in-vitro models of cisplatin resistance in five HPV+ HNSCC cell lines for further studies.

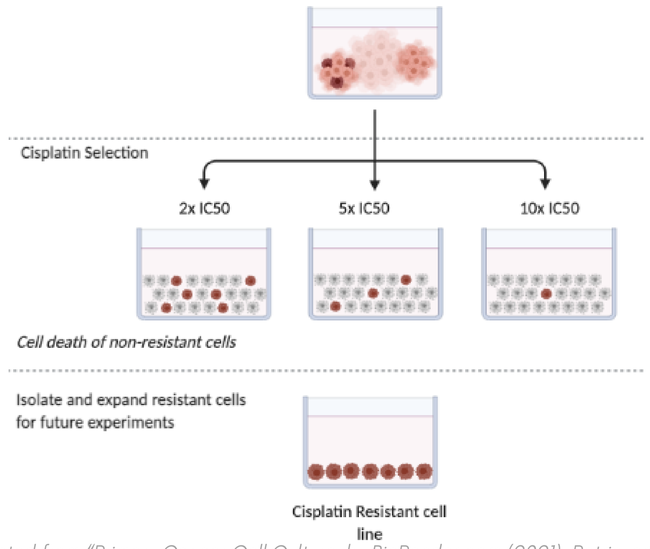
METHODS

DETERMINING THE IC50 VALUES

- The concentration of cisplatin required to kill 50% of cells (IC50) was determined for each of the five HPV+ HNSCC lines.
  - **Cell lines:** UWO23, UWO37, UMSCC47, UPCI:SCC90, 93VU147T

TREATMENT CONDITIONS

- 500,000 of each of the cell lines were plated in three flasks and treated 2x, 5x, and 10x their cisplatin IC50 concentrations respectively.
- The cells were administered cisplatin every 4 days and were frequently observed using a light microscope.



Adapted from "Primary Cancer Cell Culture, by BioRender.com (2021). Retrieved from https://app.biorender.com/biorender-templates

- Once single cell colonies of cisplatin-resistant cells are formed, they will be isolated and expanded.
- Cisplatin resistant cell lines will be used in future experiments.

PRELIMINARY RESULTS

- The IC50 values for each of the cell lines is as follows:
  - **UWO23**: 2.77 µM
  - **UWO37**: 1.90 µM
  - **UMSCC47**: 3.22µM
  - **UPCI:SCC90**: 1.51 µM
  - **93VU147T**: 2.21 µM
- The result indicates UMSCC47 cells are most resistant to cisplatin while UPCI:SCC90 cells are the most sensitive.

DISCUSSION

FUTURE STEPS

- Once the cisplatin resistant cell lines have been generated and expanded, the IC50 values will be calculated again to validate the increased resistance to cisplatin.
- Additionally, the genetic profile of the resistant cells will be explored by sequencing, analysis, and comparison with genome-wide CRISPR knockout screening data.
  - We aim to characterize the genes that may underlie the molecular and genetic basis of cisplatin resistance in HPV+ HNSCC.

CONCLUSION

- The generation of the cisplatin resistant cell lines will allow us to explore the underlying mechanism of cisplatin resistance in HPV+ cell lines.
- Clinically, it will potentially improve the treatment regimen of patients with treatment resistant diseases.

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