**INTRODUCTION**

Endometrioid Ovarian cancer (EnOC) is an uncommon subtype of epithelial ovarian cancer, accounting for approximately 10% of cases. It usually presents at an earlier stage and thus has a better prognosis than high grade serous cancer but remains a significant cause of morbidity and mortality in women in Europe.

Hox genes are members of the homeobox superfamily and best known for their role in embryonic development but their important function in oncogenesis is an exciting and rapidly developing field. There are 39 Hox genes in humans and they have been shown to be dysregulated in many hematological and solid organ cancers, but this work is the first study dedicated to the investigation of the role of Hox genes in EnOC.

**EXPRESSION OF HOX GENES IN EnOC CELL LINES**

High expression of Hox B genes and low expression of Hox D genes was observed in two EnOC cell lines in the CCEL: TOV 112D and CVI 362 (1).

**DYSREGULATION OF HOX GENE EXPRESSION IN EnOC**

Based upon the public database, a sample of 48 FFPE tissues (41 EnOC and 7 normal ovarian/fallopian tube controls) were obtained under NHS REC approval and HOX gene RNA expression determined using NanoString technology. The results are presented below and is concordant with cell line data showing high expression of Hox B genes and low expression of Hox D genes.

**TARGETING HOX GENES IN EnOC CELL LINE TOV 112D**

Our lab has produced a commercially available inhibitor of Hox proteins across all four classes (A to D) and paralogues 1-11, known as HRX9. It was assessed as an inhibitor of HOX protein binding to its co-factor PBX. CXR9 is a control peptide with a single amino acid substitution that renders it inactive. HRX9 and CXR9 were tested on the EnOC cell line TOV 112D using the MTS assay and HRX9 was shown to be cytotoxic with an IC50 of 37 μM.

**SYNERGY BETWEEN HRX9 AND CISPLATIN**

Although HRX9 is cytotoxic in its own right, we investigated whether it could be combined with other commonly used SACT drugs to increase killing power. Platinum drugs are the backbone of chemotherapy used in ovarian cancer, and highly effective, but also highly toxic and poorly tolerated by patients. In addition, the biggest clinical challenge faced in advanced ovarian cancer is the development of Platinum resistance, at which point the disease is incurable and patient life expectancy is less than one year.

Synergy between Cisplatin and HRX9 was assessed using the MTS assay and a Bliss analysis in TOV 112D cells. There was synergy between the two drugs at HRX9 concentrations 20 and 35μM and Cisplatin concentration 10μM.

**REFERENCES**


**DISCUSSION**

In conclusion, Hox genes have been shown to be widely dysregulated in EnOC with a high expression of Hox B class genes particularly Hox B3 and a low expression of Hox D class genes particularly Hox D10. This is true at both a cell line level and also in FFPE tissue. This can be therapeutically targeted using the HRX protein inhibitor HRX9 which shows significant cytotoxicity on its own and synergy when used in combination with Platinum chemotherapy.

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