Abstract

Ovarian carcinoma is a highly metastatic cancer that is often diagnosed at an advanced stage. As ovarian cancer develops it metastasizes into the peritoneal cavity, where tumors invade the mesothelium. Here tumors encounter a hypoxic microenvironment due to irregular vascularization and stagnant ascites fluid. Microenvironment stress promotes tumors to initiate angiogenesis, the formation of new blood vessels, in order to access oxygen and nutrients from the blood. Further understanding hypoxia-induced angiogenesis is critical for improving patient treatment and identifying novel pharmacological targets. Previous work in our laboratory has identified the Maturin protein as a target of interest in ovarian carcinoma. We hypothesize that Maturin is involved in the hypoxic response of ovarian carcinoma.

Methods

Fig 1: Ovarian Carcinoma Cell Lines (A2780, HEYA8, OVCAR3)

Fig 2: HEYA8 Cell Line Cultured in RPMI Media

Fig 3: A2780, OVCAR3, and HEYA8 cells lines were incubated in a hypoxia chamber for 24 hours. RNA was extracted via a Trizol RNA extraction. Quantitative PCR was performed with the hypoxic RNA compared to RNA extracted from cells cultured in normoxia. Beta actin primers were used as an endogenous positive control. The experiment was repeated three times.

Results

MTURN Expression in Hypoxia

MTURN Knockdown Carboplatin Sensitivity in HEYA8 Cells

Fig 4: Transfected HEYA8 cells were plated in a 96 well plate at 5000 cells/well in 100μl of RPMI media. Cells were incubated 12 hours at 37°C in 5% CO₂ and treated with carboplatin in doses ranging from 1-200μM. After treatment cells were incubated for 48 hours. A MTT Assay was performed and the 590nm absorbance was measured using a plate reader. IC₅₀ of carboplatin concentration was calculated from the concentration response curve.

Conclusions

- MTURN expression is up regulated in response to hypoxia in HEYA8, A2780, and OVCAR3 cell lines
- MTURN knockdown via shRNA reduces HEYA8 proliferation rate in vitro
- MTURN knockdown via shRNA sensitizes HEYA8 cells to carboplatin treatment

Future Studies

- Effect of MTURN knockdown on cell cycle
- Western blot protein expression verification
- Characterization of MTURN expression in mouse tumor models
- Further drug sensitization screening

References & Acknowledgement

3. Supported by U.R.O.P.