Loss of DAXX protein expression results in increased radiosensitivity and decreased ischemic sensitivity of BON-1 cells

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INTRODUCTION

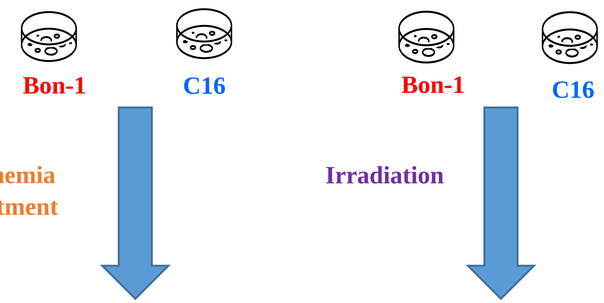
Well-differentiated pancreatic neuroendocrine tumors (PNETs) are a group of aggressive, heterogeneous cancers with highly variable clinical course and increasing incidence rate[1]. Patients often present late with unresectable liver metastases[1,2]. Five-year survival rates for patients with pancreatic neuroendocrine liver metastases (pNLMs) are poor. These pNLMs are often treated with liver-directed therapies including ischemia-based transarterial embolization (TAE), or radioembolization (TARE). Preliminary data has shown poor response to TAE in DAXX-mutated PNETs[3,4]. The purpose of this study was to evaluate the effect of loss of DAXX protein expression on radiosensitivity and ischemia sensitivity of BON1 cells.

AIMS

- **Determine the effect of loss of DAXX protein in Bon-1 cells on radiosensitivity**
- **Assess the effect of loss of DAXX protein in Bon-1 cells on ischemic sensitivity**

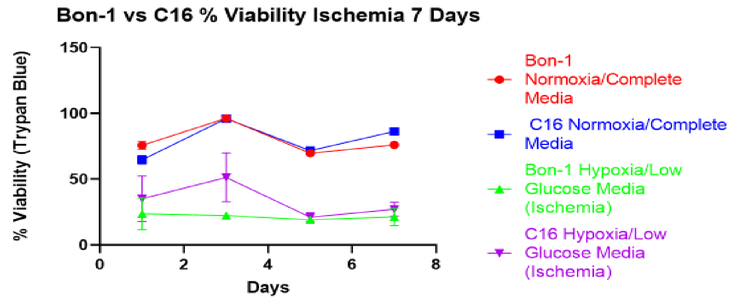
MATERIALS AND METHODS

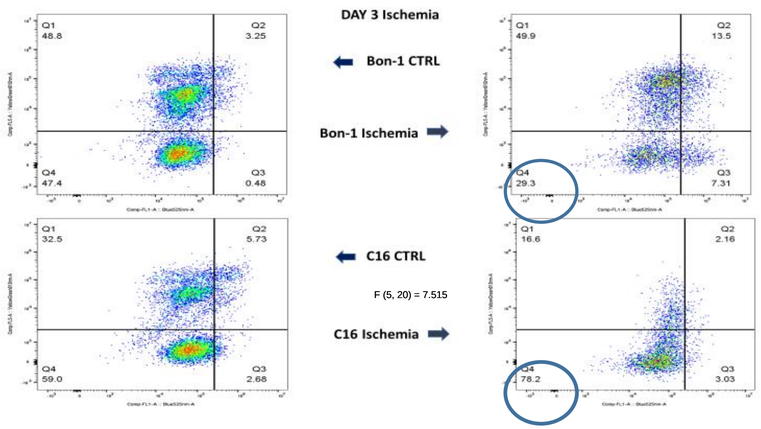
Cell types: BON-1 wild type and CRISPR/Cas9-generated DAXX knockout, C16 cells.



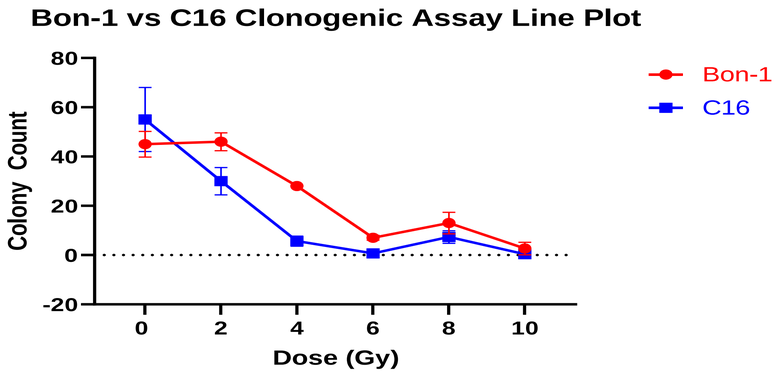
All experiments were performed in triplicate and results analyzed at a 95% confidence interval.

RESULTS

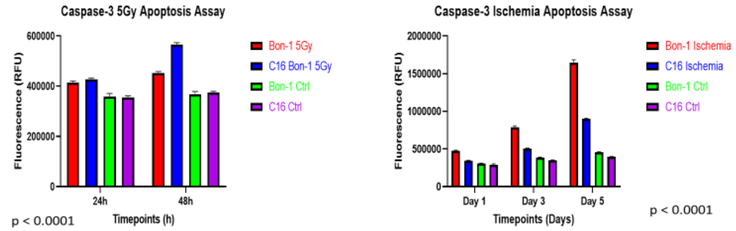




3 days post-ischemia, Bon-1 wildtype had only 29.3% viability compared to C16 with 78.2% viability.



There was a significant difference between Bon-1 wildtype and C16 cells: F(5, 20) = 7.52, p=0.0004.



Left figure: At 48h post-irradiation, C16 showed significantly higher apoptotic activity than Bon-1 at F(3,8) = 278.3, p<0.0001; Right figure: Bon-1 demonstrated significantly increased apoptotic activity compared to C16 cells on all 3 timepoints post-ischemia, F(6, 12) = 620.1, p<0.0001.

CONCLUSIONS

- **Loss of DAXX protein expression resulted in significant transient ischemic resistance, particularly at day 3, in comparison to wildtype BON-1 cells**
- **Significantly increased radiosensitivity in cells with loss of DAXX protein expression as compared with wild type BON-1 cells has been demonstrated.**
- **Additional studies are ongoing, including upstream and downstream analysis of ischemia and radiation stress and correlation with clinical data.**

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