Background

• Irreversible electroporation (IRE) causes irreversible permeabilization of the cell membrane via short high-voltage electric pulses.
• IRE offers a promising treatment modality for local ablation of pancreatic ductal adenocarcinoma (PDAC).
• We aim to assess preclinical effects IRE on different types of cells in vitro and macrophage infiltration in vivo.

Methods

IRE-treated Cells: KRAS* PDAC cells, murine RAW264.7 macrophages, and murine bone marrow derived macrophages (BMDM) were used in following assays.

Assays: MTS assay assessed cell proliferation following IRE. Transwell migration assessed if IRE treated KRAS* cells affected macrophage migration (Fig. 1).

Immunofluorescence (IF) staining: IF staining assessed the density of CD169+ macrophages on KRAS* tumor tissues from non-treated and IRE treated mice.

Liver metastasis model: PH252 cells (a variant of KRAS* PDAC cells) were inoculated into the spleen of mice to develop a liver metastasis model of PDAC. Tumor growth was monitored by T2 weighted MRI.

Statistics: Significance was determined by one-way ANOVA with $p \leq 0.05$ considered statistically significant.

Results

• KRAS cells were more sensitive to IRE than macrophages (BMDM and RAW264.7).
• IRE treated KRAS* tumor cells promoted macrophage migration. This was confirmed in in vivo experiment, which showed increased tumor infiltration of CD169+ macrophages 24h after IRE.
• PH252 PDAC tumors injected into the spleen metastasized to the liver.

Conclusion

• IRE decreased cell proliferation of tumor cells and influenced macrophage migration. Because of IRE’s effects on macrophages, further studies on the impact of IRE on presentation of tumor associated antigens are warranted.

Future Directions

• Test IRE effects at other voltages and with other cell types.
• Refine tumor model by injecting fewer cells or injecting directly to pancreas.
• Characterize the effects of local IRE treatment on liver metastasis.

References


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