First Place - Basic Science: Garrett Steers, MD

Introduction - Vitamin C epigenetically regulates cancer-related genes via its induction of the ten-elevation translocation (TET) methylcytosine dioxygenase enzymes, “epigenetic erasers” that demethylate DNA. DNA methyltransferase (DNMT) reverses this process, increasing DNA methylation and decreasing gene expression. Dual oxidase (DUOX) enzymes, producers of hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}), may be silenced in pancreatic cancer (PDAC), with prior studies demonstrating increased expression following pharmacologic ascorbate (P-AscH\textsuperscript{+}, intravenous high-dose vitamin C) treatment. We hypothesize that inhibiting DNMT may act synergistically with P-AscH\textsuperscript{+} to increase DUOX expression, increase H\textsubscript{2}O\textsubscript{2} production, and increase toxicity in PDAC.

Methods – Multiple human PDAC cell lines were treated with 0.5-2 µM of the DNMT inhibitor 5-azacytidine for 5 days +/- 1-2 mM of P-AscH\textsuperscript{+} for 1 h. DUOX1 expression was determined by qPCR and Western blotting. DCFH-DA +/- catalase measured intracellular oxidation, while clonogenic survival measured cytotoxicity.

Results - PDAC cells demonstrated dose-dependent increases in DUOX1 expression on qPCR and Western blot when treated with 5-azacytidine. P-AscH\textsuperscript{+} + 5-azacytidine significantly increased DUOX1 expression in PDAC cells compared to either treatment alone. P-AscH\textsuperscript{+} + 5-azacytidine also induced higher levels of intracellular H\textsubscript{2}O\textsubscript{2} than either treatment alone, while the addition of catalase reversed these effects. PDAC cells treated with P-AscH\textsuperscript{+} + 5-azacytidine demonstrated decreased clonogenic survival compared to either treatment alone (Figure 1).

Conclusions - P-AscH\textsuperscript{+} induces epigenetic changes in PDAC, resulting in increased DUOX1 expression. Combination treatment with 5-azacytidine further increases DUOX1 expression, increasing H\textsubscript{2}O\textsubscript{2} production and decreasing clonogenic survival. These findings suggest a potential epigenetic mechanism to treat PDAC.

![Graph showing clonogenic survival](image-url)