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Ultra-high concentrations of gaseous nitric oxide show rapid cytotoxic capabilities against colon, breast, pancreatic and other cancer cells in vitro

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Introduction

- High concentrations of Nitric Oxide (NO) are known to have anti-tumor effects, including cancer cell cytotoxicity through DNA damage induction, leading to apoptotic cell death.
- To examine the cytotoxic effect of gaseous NO (gNO) on various cancer types, we exposed 6 cancer cell lines to gNO at ultra-high concentrations, of 10,000-100,000 ppm for up to 10 minutes.
- Cell viability was measured 24 hours after exposure by (figure 1):
  - XTT-based cell proliferation method
  - Colony-forming assay (Clonogenic assay) – measures the ability of a single cell to grow into a colony

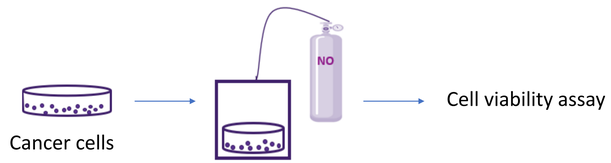
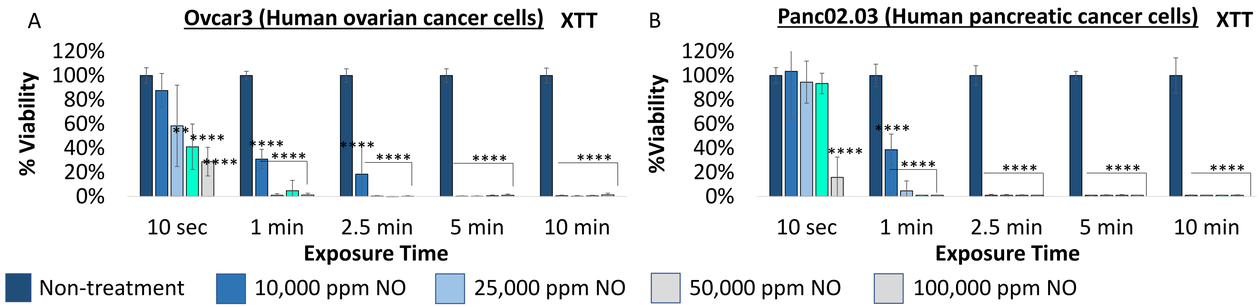


Figure 1. Assay scheme

Results – Short exposure of ultra high concentration gNO limits cell viability in human pancreatic and ovarian cancer cell lines

- Human ovarian (figure 2A) and pancreatic (figure 2B) cancer cell lines were exposed to gaseous nitric oxide at 10,000 ppm - 100,000 ppm NO for 10 seconds to 10 minutes. Cell viability was assessed by XTT assay. Less than 10% of both cell lines are viable after 1 minute of exposure to 25,000 ppm NO.



One-way anova and Dunnet multiple comparison test, compared to non treatment, * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

Figure 2. Human ovarian and pancreatic cancer cell viability after exposure to gNO

Results – Short exposure of ultra high concentration gNO limits cell viability in murine lung, melanoma, colon and breast cancer cell lines

- Mouse lung (figure 3A), melanoma (figure 3B), colon (figure 3C&D) and breast (figure 3E&F) cancer cell lines were exposed to gaseous nitric oxide at 10,000 ppm to 100,000 ppm NO for up to 2.5 minutes. Cell viability was assessed using two assays: XTT and clonogenic assay.
- Similar cell viabilities were achieved with both assays for each cell line. Less than 10% of the cell are viable after 1 minute of exposure to 25,000 ppm NO found in with all cell lines.

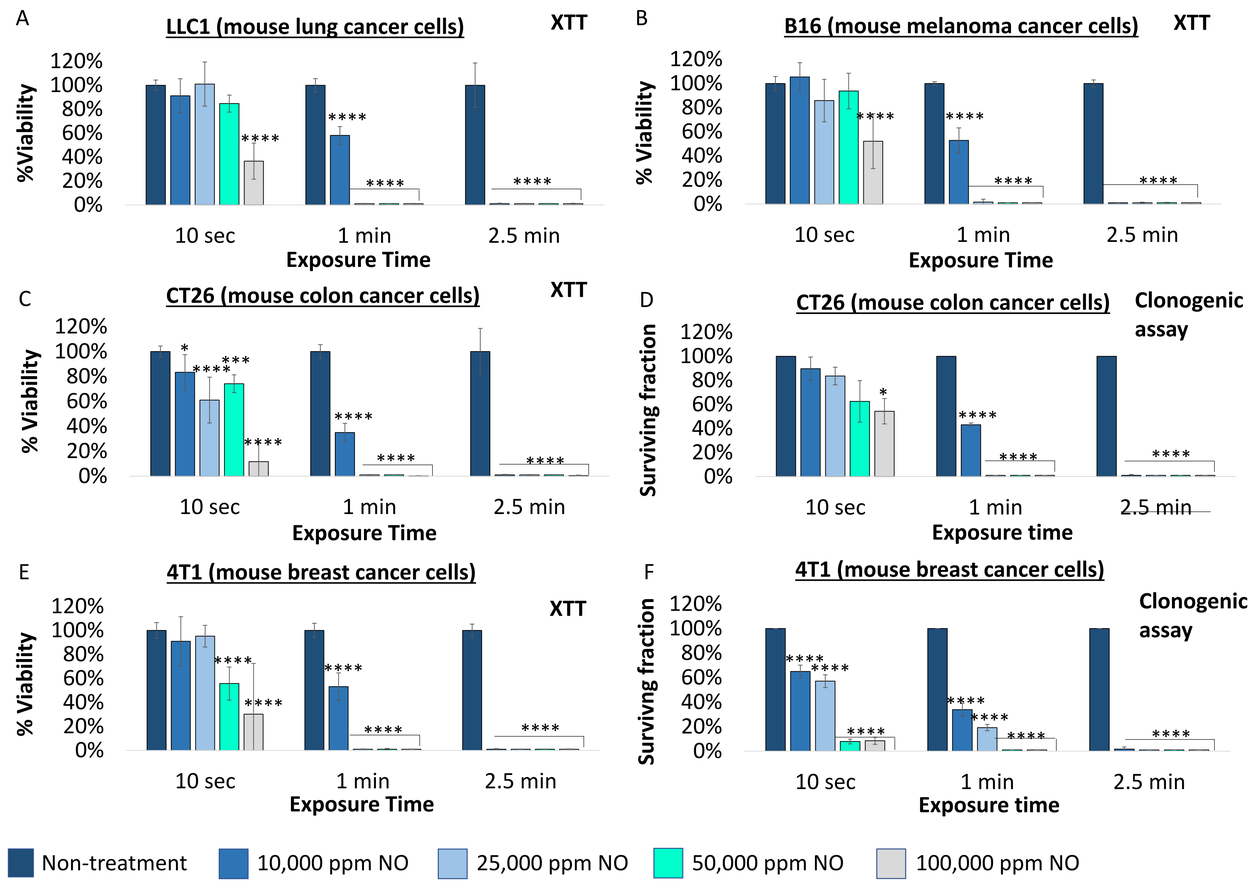


Figure 3. Mouse lung, melanoma, colon and breast cancer cell viability after exposure to gNO

Conclusions

- Exposure of human ovarian and pancreatic cancer cell lines and mouse lung, melanoma, colon and breast cancer cell lines to 10,000 ppm – 100,000 ppm gNO resulted in a dose dependent cytotoxic response.
  - Higher concentrations lead to near instant cell death
  - Lower concentrations require a longer exposure period to elicit cell death
- No viable cells were detected after exposure to 50,000 ppm gaseous NO for 1 minute.
- Together with the known ability of NO to activate and recruit the immune system, these results suggest that gNO may be a potent therapeutic agent for tumor treatment across a range of tumor types.

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