A Novel Assay to Predict Cancer Resistance to Cisplatin
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Introduction

• Cisplatin is widely used as chemotherapy drug that induces DNA damage and ultimately triggers apoptosis. However, therapeutic resistance and tumor relapse remains a significant clinical problem.
• Recently, our laboratory developed an assay (Fig. 1) called primer anchored DNA damage detection assay (PADDA) that screens genomic areas for DNA damage¹. PADDA has been shown to detect a dose-dependent increase in DNA damage caused by genotoxic agent (Fig. 2).
• We hypothesized that PADDA will discriminate the ability of cancer cells to repair damage induced by cisplatin, and therefore predict cancer resistance to cisplatin.

Aim

To define the levels of DNA damage induced at p53 nucleotides by cisplatin treatment and to measure the ability of cancer cells to repair damage induced by cisplatin.

Materials & Methods

PADDA was used on a high-throughput setting to quantify DNA damage in human oral cancer cells (SCC-1) exposed to different doses of cisplatin. Cell viability was determined by 3-[(4,5-dimethylthiazol-2-yl)2,5 diphenyl tetrazolium bromide (MTT) assay. Data was analyzed by Student’s t-test.

Results

Figure 5. DNA damage measured by q-PADDA in SCC-1 cells after exposure to cisplatin. SCC-1 cells were treated with 0 µM, 0.1 µM, 50 µM concentrations of cisplatin and allowed to repair damage for 0, 3, 9, 18, 24 & 24 hour time intervals. Data shown as Mean ± S.E.M. * p<0.01.

Conclusion & Societal Impact

• PADDA was able to quantify DNA damage and repair after cisplatin treatment. This information will allow us to determine if resistance to cisplatin is due to effective damage removal or to damage tolerance. This data would facilitate the development of strategies targeting the mechanism of drug resistance.
• This observation has significant clinical importance as it can be used to predict treatment response and direct treatment selection in cancer patients.

Future Directions

• This assay has potential to elucidate the differential efficacy of cisplatin as a chemotherapy drug and act as a preliminary screening method to determine differential cisplatin resistance.
• This project can be extended to determine the genotoxicity and resistance of cisplatin in other head and neck cancer cell lines.
• PADDA can be used to determine if patients will respond or become resistant to not only platinum-based chemotherapy treatments, but also to other treatments that induce DNA damage.

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References