

# Comet assay measures of *cis*-platin and mitomycin C-induced DNA crosslink formation predicts bladder cancer cell chemosensitivity *in vitro*.

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## Background:

- Chemotherapy (CT) is used extensively in cancer treatment, but suffers from limited response rates and is frequently associated with significant morbidity and mortality.
- Therefore, where treatment options exist, it is desirable to reserve CT for patients whose tumours will respond.
- To facilitate this, attention is turning to the development of techniques that provide predictive information about tumour chemosensitivity, as a means of enhancing patient selection for CT treatment.

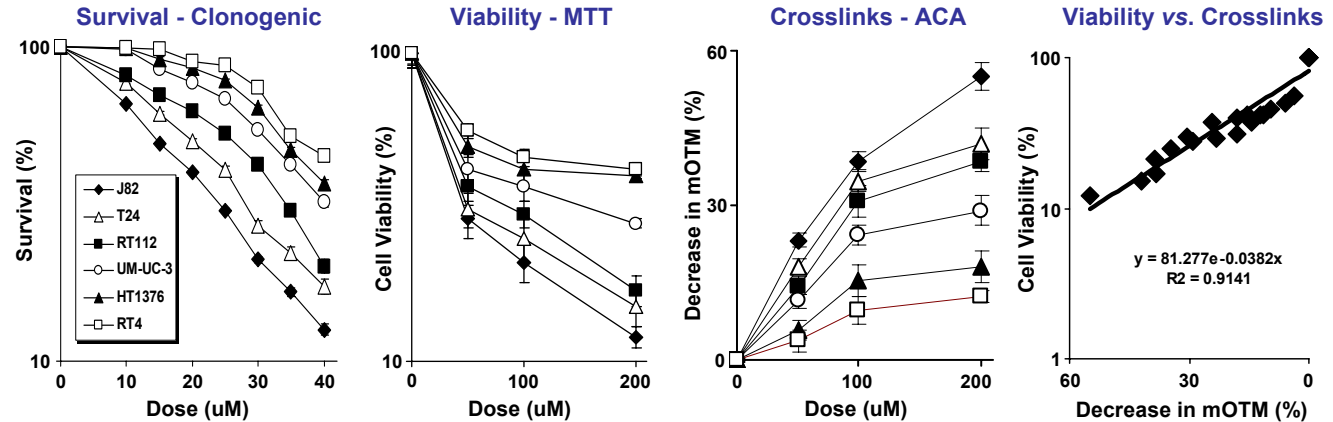
## Methods:

- The alkaline comet assay (ACA) is a technique for assessing DNA damage formation and repair, at the level of individual cells.
- ACA is ideal as a clinical test; it is simple, rapid, inexpensive and requires low cell numbers.
- Recently, we have demonstrated ACA to be predictive of cell radiosensitivity for a panel of human bladder cancer cell lines (AL Moneef *et al. British J. Cancer* (2003) **89**, 2271-2276).
- In the present study, harvested cells were treated in suspension for one hour at 37°C in eppendorf tubes with two commonly used DNA crosslinking chemotherapeutic agents; *cis*-platin (CP) and mitomycin C (MMC).
- Levels of CP and MMC-induced DNA crosslink damage, as assessed using a modified version of ACA, were compared to measures of cell survival (clonogenic) and cell viability (MTT).

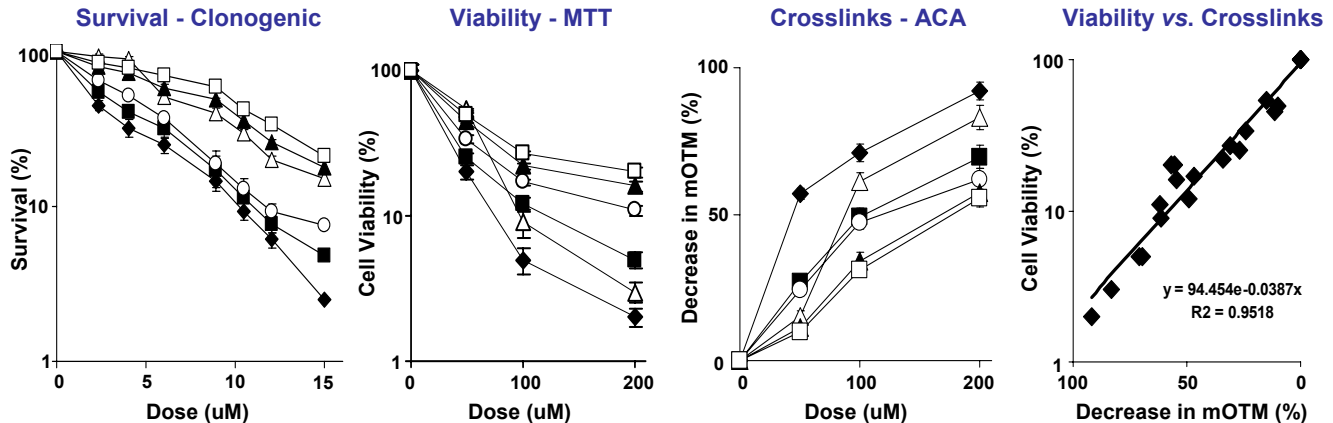
## Results:

- For both agents, clear dose response curves were obtained, with the more chemosensitive cell lines displaying higher levels of crosslink formation.
- In particular, there were high degrees of correlation between measures of cell viability and crosslink formation ( $R^2 > 0.91$ ), including an anomalous differential behaviour noted for T24 cells treated with MMC.
- Interestingly, the most chemosensitive cells tended to be the most radiosensitive and *vice versa*. This suggests that for these cell lines the same factor(s) may be responsible for radiosensitivity and chemosensitivity, both of which are predicted by ACA.

## CP STUDIES



## MMC STUDIES



## Conclusions & Significance:

- These preliminary studies demonstrate that ACA can predict cancer cell chemosensitivity *in vitro*.
- To determine whether this technique can be applied to identify patients with chemosensitive tumours, clinical studies using cells derived from tumour biopsies need to be undertaken.
- If ACA is demonstrated to be predictive of chemosensitivity/outcome *in vivo*, then patients with sensitive tumours could then be considered suitable candidates for treatment with chemotherapy.
- Alternatively, patients with chemo-resistant disease could be offered alternative intervention, for example, surgery.