Contribution ID: **19** Type: **poster preferred**

Measures of DNA damage sensitivity correlate bladder cancer cell treatment sensitivity in vitro and outcome in vivo.

Tuesday, 16 October 2012 16:29 (1 minute)

Bladder cancer patients suffer significant rates of treatment failure, including high rates of recurrence and poor outcomes for advanced disease. If mechanisms to improve tumour cell treatment sensitivity could be identified and/or if patient tumour response could be predicted, it should be possible to improve both control and survival rates, i.e. by selecting the most appropriate treatment for those patients with correspondingly sensitive/responsive tumours. Previously, we have shown that induction of radiation-induced DNA damage as measured by alkaline Comet assay (ACA) correlates cell radiosensitivity for a panel of human bladder cancer cell lines in vitro. In the present study we have shown that ACA measures of Cis-platin and mitomycin-C-induced damage also correlate cell chemosensitivity in vitro, with there being predominantly the same rank order for chemosensitivity as for radiosensitivity. Furthermore, ACA studies of radiation-induced damage in different bladder cancer cell DNA substrates (nuclei & nucleoids vs. intact parent cells) suggest that it is a feature retained in the prepared nucleoid bodies that is responsible for the relative damage sensitivity of bladder cancer cells, suggestive of differences in the organisation of the nuclear DNA within resistant/sensitive cell lines. Finally, analysis of tumour samples reveals that lower ACA measures of DNA damage sensitivity correlate with poorer outcomes following treatment; notably this includes the observation of lower measures of induced damage being significantly associated with local recurrence of non-invasive disease and this being a better predictor than the presence of high-risk histology (G3 pT1). In conclusion, this study demonstrates that mechanisms which govern treatment-induced DNA damage are central to bladder cancer cell treatment sensitivity and supports an association between DNA damage resistance and aggressive tumour phenotype in this cancer model.

Primary authors: JONES, G (University of Leicester); BOWMAN, K (University of Leicester); SYMONDS, P (University of Leicester)

Co-authors: COLQUHOUN, A (University Division of Urology, Leicester General Hospital); SHERWOOD, B (University of Leicester); PAYNE, D (University Division of Urology, Leicester General Hospital); SUMMERTON, D (University Division of Urology, Leicester General Hospital); GODDARD, J (University Division of Urology, Leicester General Hospital); MELLON, K (University of Leicester); GRIFFITHS, L (University Division of Urology, Leicester General Hospital); AL MONEEF, M (University of Leicester); KHAN, M (University Division of Urology, Leicester General Hospital); BUTTERWORTH, P (University Division of Urology, Leicester General Hospital); KOCKELBERGH, R (University Division of Urology, Leicester General Hospital); MCKEOWN, S (University of Ulster); SINGH, S (University Division of Urology, Leicester General Hospital); MCKELVEY-MARTIN, V (Univeristy of Ulster); STEWARD, W (University of Leicester)

Presenter: JONES, G (University of Leicester)

Session Classification: Poster Session 1

Track Classification: DNA Damage and Repair