Thus inhibition of p63-related signalling coupled with standard therapies could result in a blockade of tumour progression, even in castrate resistant prostate cancer where only limited therapeutic options are available.

SARS ACADEMIC AND RESEARCH PRIZE: 1159: PHOTOCHEMICAL INTERNALISATION AS A DELIVERY TOOL TO IMPROVE CHEMOTHERAPY FOR ORAL SQUAMOUS CELL CARCINOMA


Background & Aims: Photochemical internalisation (PCI) is based on photodynamic therapy (PDT), and is a light-activated drug delivery technique that increases the bioavailability of therapeutic drugs through photosensitised intracellular release of drugs entrapped within endocytic vesicles. PCI reduces the toxicity in non-target tissues. The aim of this study was to compare the cytotoxicity of PDT and PCI on an oral squamous cell carcinoma cell line (HCPC-1) in vitro.

Method: The HCPC-1 cell line, developed from a hamster buccal pouch carcinoma was used. The ribosome inactivating protein (RIP) toxin, saporin, was used with the photosensitisers, disulfonated tetraphenylporphine (TPPS2a). Blue light was used for PDT and combined with saporin for PCI. Viability was assessed with the MTT assay.

Results: The PCI cytotoxicity was significantly higher than PDT (P < 0.0001) and saporin (P < 0.0001) separately. The ratio to assess synergy A/B, using cell viability, (A=saporin, B=PDT, C=PCI) for HCPC-1 cells was calculated to be 1.04, thus showing a PCI effect.

Conclusion: PCI is able to induce the relocationisation of saporin within cells and therefore enhance cell death in HCPC-1 cells. PCI was also shown to be significantly more cytotoxic than PDT on the HCPC-1 oral cancer cell line.

SARS ACADEMIC AND RESEARCH PRIZE: 1423: A COMPARATIVE STUDY OF THE PROGNOSTIC ROLE OF KI67 AND GEMININ IN BREAST CANCER

Sreekumar Sundara Rajan 1, Andrew Hanby 1, Kieran Horgan 1, Valerie Speirs 2, 1 Leeds Teaching Hospitals NHS Trust, Leeds, UK; 2 Leeds Institute of Molecular Medicine, University of Leeds, Leeds, UK.

Aims: Compared to other markers of cell proliferation, geminin is unique being expressed selectively during the proliferative phase of the cell cycle. We aimed to compare the prognostic significance of geminin with that of Ki67 and other common clinicopathological variables.

Methods: Tissue microarrays containing 291 breast tumours were stained using anti-geminin antibody (NCL-L; 1:12.5) and Ki67 (MIB1; 1:100). Labelling index (LI) was calculated for geminin and the percentage of positive cancer nuclei were determined for Ki67 expression. ROC curve analysis was performed.

Results: Geminin expression was positively correlated with Ki67 expression (r = 0.368, p = 0.001). Survival analysis showed poor BCSS and DFS amongst cases positive for geminin [BCSS-HR 2.85 (1.53, 5.32); DFS-HR 2.63 (1.47, 4.71)] and Ki67 [BCSS-HR 2.62 (1.53, 4.48); DFS-HR 2.28 (1.39, 3.77)]. However, on multivariate analysis, only geminin LI (DFS-HR < 0.001), Hb result (p < 0.008) and tumour size (p < 0.027; No MAD2 expression p = 0.97, 95% CI 0.15-1.51, p = 0.210) were independent predictors.

Conclusions: Geminin expression is a strong and independent predictor of adverse outcome in breast cancer.

SARS ACADEMIC AND RESEARCH PRIZE: 1505: LOW NUCLEAR MAD2 EXPRESSION IS ASSOCIATED WITH LACK OF RESPONSE TO CHEMOTHERAPY AND RADIOThERAPY IN Oestrogen RECEPTOR NEGATIVE BREAST CANCER PATIENTS

Elina Anna O'Reilly 1, Shiva Sharma 1, Michele Harrison 1, Karolina Weiner-Gorzel 1, Garu Kelly 4, Aoife Maugure 3, Janet McCormack 3, Suson Conlon 3, Susan Aberne 3, Caitlin Beggs 3, Richard Bambury 4, Tiffany Dorsey 7, 1 Department of Digital Pathology Core Facility, The Conway Institute, Blackrock, Dublin, Ireland; 2 National Cancer Institute, Bethesda, Maryland, USA; 3 Department of Digital Pathology Core Facility, The Conway Institute, Blackrock, Dublin, Ireland.

Aims: To investigate the clinical importance of MAD2, a key protein in the spindle assembly checkpoint (SAC), which prevents anaphase until successful chromosome segregation occurs. SAC dysfunction results in the induction of cellular senescence, demonstrable by enhanced chemoresistance to paclitaxel (Taxol®). We hypothesize that low MAD2 is predictive of poor response to chemotherapy.

Methods: 81 ER-negative tumours from an established US cohort were assessed for MAD2 expression using immunohistochemistry. Kaplan-Meier graphs and log-rank tests were used to display breast cancer survival. Proportional hazards cox regression was used to estimate hazard ratios and conduct univariate and multivariable analysis.

Results: Patients with high levels of MAD2 display increased breast cancer specific survival (HRHighMAD2: 0.34, 95% CI 0.15-0.76, p = 0.008). Patients with low MAD2 poorly. MAD2 prediction of outcome is limited to those who received chemotherapy (Chemo: HRHighMAD2: 0.31, 95% CI 0.12-0.80, p = 0.015). No chemotherapy: HRHighMAD2: 1.03, 95% CI 0.10-10.6, p = 0.978), or radiotherapy (Radiother: HRHighMAD2: 0.24, 95% CI 0.06-0.85, p = 0.027). No radiother: HRHighMAD2: 0.48, 95% CI 0.15-1.51, p = 0.210). MAD2 expression is predictive in patients who received both chemotherapy and radiotherapy (HRHighMAD2: 0.09, 95% CI 0.02-0.45, p = 0.003).

Conclusion: We believe MAD2 is a predictor of poor outcome after chemotherapy and radiotherapy in TNBC.