Parallel assessment of cell viability in cardiac and cancer cells following treatment with sunitinib

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Various cardiopathological effects have been observed following chemotherapy treatment in cancer patients, due to anti-cancer drug-induced cardiotoxicity (CTX). A retrospective study of cancer survivors reported a 50% and 10% incidence of hypertension and heart failure respectively following treatment with the tyrosine kinase inhibitor sunitinib, licensed to treat pancreatic neuroendocrine tumours. The cellular mechanisms underlying CTX are not known. Here, for the first time, we compare the potency of sunitinib in both cardiac cells (primary cardiac fibroblasts (CFs)) and cancer cells (a pancreatic adenocarcinoma cell line (PANC-1)).

Adult rat CFs were isolated by bulk collagenase digestion, maintained in culture and used between passages 1–2. PANC-1 cells, from previously-frozen stocks, were used between passages 41–49. Cells were treated with sunitinib (0–10 µM in CFs; 0–100 µM in PANC-1) for 24 hour prior to epifluorescent imaging for phenotypic assessment. Cell viability was examined by alamar blue assays following 24 hour sunitinib treatment (0–100 µM).

Overall, results indicated increased sensitivity of CFs to sunitinib compared with PANC-1 cells. Phenotypic changes indicative of cell death, including appearance of intracellular vacuoles, were evident in CFs following 1 µM sunitinib treatment whereas similar effects were not induced until 10 µM treatment in PANC-1 cells. Alamar blue assays demonstrated a dramatic increase in CF death compared to PANC-1 death following treatment with 10 µM sunitinib (11.6±0.02 vs 56.5±1.5 (% viability) CF vs PANC-1, n=3). A lower IC_{50} value for sunitinib was required to exert the same effects on CF (IC_{50}5.2 µM) vs PANC-1 (IC_{50}13.5 µM) cell viability.

These results suggest sunitinib can cause lethal effects in cardiac cells at lower doses than those required to induce pancreatic cancer cell death. Future work will aim to identify cellular mechanisms responsible for these toxic effects. Parallel studies in cardiac and cancer cells will be beneficial in distinguishing how focused anti-cancer drug delivery could be improved to avoid CTX.

Keywords: cardiac cells; sunitinib; cancer cells

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