PTH-100 DAP3 AND THE DAP3 BINDING CELL DEATH ENHANCER-1 (DELE1) IN HUMAN COLORECTAL CANCER

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Introduction Death association protein-3 (DAP3) was discovered as a responsive protein to interferon-gamma induced cell death and may exert this regulation by interacting with DELE1 (DAP3 Binding Cell Death Enhancer 1) (also known as KIAA0141), a newly discovered mitochondrial stress protein in response to cell stress signals. Whilst DAP3 has been shown to be aberrantly expressed in a limited number of solid tumours, eg. breast cancer and in haematological malignancies (leukaemia), little is known about the relationship between DAP3 and DELE1 in other solid cancers. The present study examined the expression levels of both DAP3 and in DELE1 in colorectal cancers.

Methods A cohort of colorectal tissues from ninety four patients were collected after surgery. Gene transcript levels of both DAP3 and DELE1 were quantitatively assessed by real time polymerase chain reaction. DAP3 and DELE1 proteins in normal colon and tumour tissues were evaluated by immunohistochemistry on tissue arrays. Patients' clinical, pathological and outcome information were collected and evaluated against gene expression levels.

Results Colorectal tumours had significantly higher levels of DAP3 than normal colon tissues ($p < 0.001$) but DELE1 did not show a difference between tumour and normal tissues. Levels of DAP3 and DELE1 had significant association with disease free survival ($p < 0.001$ and $p = 0.043$) and overall survival ($p = 0.006$ and $p = 0.068$ respectively). Levels of both DAP3 and DELE1 were seen to markedly differ between patients who developed recurrence from those who did not. Kaplan Meier models showed a significant difference for both DAP3 and DELE1 in time to recurrence. Neither DAP3 nor DELE1 had differing levels in tumours with or without lymph node involvement. An interesting feature of the expression pattern of both DAP3 and DELE1 was that they significantly correlated in normal colorectal tissues ($r = 0.732$, $p < 0.0001$) but the correlation of expression was not seen in tumour tissues ($p < 0.05$). Collectively, DAP3 ($p = 0.002$) and DELE1 ($p = 0.01$), together with T staging ($p = 0.024$) are independent prognostic indicators for the overall survival of the patients. DAP3 ($p = 0.001$), together with TNM staging ($p = 0.003$), Dukes staging ($p = 0.026$) and Nodal status ($p = 0.024$) are also independent predictors of the disease free survival of patients.

Conclusion Death associated protein DAP3 and its binding protein DELE1 are highly aberrant in colorectal cancers and are prognostic factors for patients' clinical outcomes including overall and disease free survival and indicators for local recurrence.

PTH-101 DO WE NEED A LOWER CUT OFF FOR FAECAL HAEMOGLOBIN IN ANAEMIC PATIENTS?

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Introduction Patients with anaemia may benefit from a lower limit of detection using Faecal Immunochemical Tests (FIT). Herts Valleys CCG instituted the use of FIT for patients presenting with symptoms meeting DG30 and some lower risk NG12 criteria, excluding those with iron deficiency anaemia, mass or rectal bleeding. In our pathway, symptomatic patients with anaemia were considered positive if their FIT result was detectable. We aim to evaluate the benefit of a lower threshold for FIT for the detection of colorectal cancer (CRC) or Significant Bowel Disease (SBD) in our population referred with bowel symptoms and anaemia.

Methods The medical records of all patients undertaking a FIT sample with a minimum of 6 months follow up between June 2019 and July 2020 were reviewed. Recorded outcomes included colorectal cancer, inflammatory bowel disease and high-risk adenomas (defined as polyps of ≥ 1 cm, ≥ 5 polyps or high-grade dysplasia). FIT analysis was performed using a single OC-Sensor analyser (Eiken Chemical Co., Tokyo, Japan). The lower limit of detection $4\mu\text{g/g}$ (LoD) or a fHb cut off of $\geq 10\mu\text{g/g}$, were taken to assess sensitivity, specificity and predictive values in patients with anaemia. Fisher's exact test was used to assess differences between groups. MedCalc® statistical software was used for all calculations.

Results 3460 patients were reviewed. 17% were anaemic, 68% were not anaemic and in 15% the Haemoglobin was unknown. 2% and 5% of anaemic patients were found to have CRC or SBD compared with 1.5% ($p = 0.3$) and 4% ($p = 0.1$) without anaemia. In patients meeting NG12 criteria, 3.7% and 7.6% of anaemic patients compared with 1.9% and 5% without anaemia had CRC ($p = 0.07$) and SBD ($p = 0.09$) respectively. No additional patients with CRC or SBD were identified with a FIT $4-9\mu\text{g/g}$ and anaemia. There was no change in the sensitivity at a threshold of $4-9\mu\text{g/g}$ + anaemia

Abstract PTH-101 Table 1

CRC	FIT threshold ($\mu\text{g/g}$)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
	≥ 4	96 (86–99.5)	49.8 (48–51.5)	2.7 (2.6–2.9)	99.9 (99.5–99.97)
	≥ 4 + Anaemia	94 (83.5–98.8)	74 (72.9–75.8)	5.1 (4.7–5.6)	99.9 (99.7–99.96)
	≥ 10	94 (83.5–98.8)	79 (77.6–80.4)	6.2 (5.6–6.8)	99.9 (99.7–99.96)
SBD	≥ 4	90.2 (83.8–94.7)	50.7 (49–52.4)	6.8 (6.4–7.2)	99.2 (98.7–99.5)
	≥ 4 + Anaemia	87.1 (80.2–92.3)	75.8 (74.3–77.2)	12.5 (11.6–13.5)	99.3 (98.96–99.6)
	≥ 10	87.1 (80.2–92.3)	80.6 (79.2–81.9)	15.1 (13.9–16.4)	99.4 (99.0–99.6)