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Introduction: Pancreatic cancer is recognized as a highly malignant and incurable disease worldwide, with a 5-year overall survival rate of only 8%[1]. Polyphenols, abundantly found in plants, display anticarcinogenic properties[2].
Objectives and Methods: We aimed to compare the effect of a Catechin:Lysine complex (Cat:Lys) on cell proliferation rates, culture growth, cell viability, apoptosis rates, migration and metabolism in two human pancreatic cancer cell lines (PANC-1 and AsPC-1) and in a non-tumorigenic human pancreatic cell line (H6c7).
Results: PANC-1, AsPC-1 and H6c7 cells were exposed to Cat:Lys (0.01-1 mM) for 24h. Cat:Lys induced a concentration-dependent decrease in cell proliferation, culture growth and cell viability in the two cancer cell lines (PANC-1 and AsPC-1). In contrast, in the noncancerous cell line H6C7, a concentration-dependent reduction in proliferation was found but culture growth and viability were only affected by higher concentrations of Cat:Lys (0.1-1 mM). Furthermore, in the cancer cell lines (PANC-1 and AsPC-1), Cat:Lys (0.01-1 mM) caused a concentration-dependent increase in the apoptotic index and a reduction in the migratory capacity, but no significant effect of Cat:Lys on these two parameters was observed in the non-cancer cell line, H6c7. The pro-apoptotic effect of Cat:Lys (0.1 mM) is JAK/STAT signaling pathway-dependent in PANC-1 cells and WNT signaling pathway-dependent in AsPC-1 cells, and the antimigratory effect is JAK/STAT signaling pathway-dependent in AsPC-1 cells. Moreover, Cat:Lys concentration-dependently decreased ^{3}H-deoxy-D--glucose uptake by H6c7 cells, but had no inhibitory effect on ^{3}H-DG uptake by the cancer cell lines. Also, Cat:Lys reduced ^{3}H-lactate uptake by the cancer cell lines (PANC-1 and AsPC-1 cells) but increased ^{3}H-lactate uptake by H6c7 cells. Finally, Cat:Lys decreased lactate production in PANC-1 and AsPC-1, but increased it in H6c7 cells.
Conclusions: Our results show that Cat:Lys has a potent cytotoxic, antiproliferative, antimigratory and pro-apoptotic effect in pancreas cancer cells, and a much more limited effect in non-cancer epithelial pancreas cells.

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2 – Pathways of estrogen metabolism underlying the association between *Schistosoma haematobium* and bladder cancer

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Introduction: Squamous cell carcinoma (SCC) is a malignant, poorly differentiated neuroendocrine neoplasm. SCC is the common form of bladder cancer in rural Africa where *S. haematobium* is prevalent. In contrast, the majority of bladder cancer in developing countries and regions not endemic for urogenital schistosomiasis is transitional cell carcinoma (TCC) that arises from the transitional epithelium lining of the bladder. The parasite eggs trapped in the bladder wall release antigens and other metabolites (presumably evolved to expedite egress to the urine, and hence to the external environment). However, the phenomenon leads to haematuria and to chronic inflammation, in turn increasing risk of SCC of the bladder. In addition to the hormone--like effects of the parasite estradiol-related molecules on the endocrine and immune system of the host, in relation to cancer initiation metabolites of estrogens can be also considered as carcinogenic chemicals.
Methods: For the purpose of this study we used cell lines (CHO and HCV29), animal models, immuno(histo)chemistry and RT-PCR.
Results: We observed hormonal imbalance caused by estrogen-like molecules produced by schistosomes. These molecules are catechol estrogen-3,4-quinones, the major carcinogenic metabolites of estrogens. We also observed down-regulation of estrogen receptor by schistosomes in urothelial cells and bladders of CD-1 mice and estrogen metabolism-associated CYP2D6 and IL6-174G/C polymorphisms in *S. haematobium* infected patients.
Conclusion: Accordingly, the hypothesis that underpins our work is that metabolism of estrogens and production of depurinating estrogen-DNA adducts leads to parasite metabolite-promoted host cell DNA damage, and ultimately urogenital schistosomiasis associated SCC.

3 – Role of the MITOchondrial fission protein Drp1 as a prognosis and predictive biomarker in the treatment of differentiated thyroid cancer (ROMITO-DRP1)

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Introduction: Differentiated thyroid cancer (DTC) is the most common endocrine cancer. Prognosis relies on clinical and histopathological factors and treatment is based on surgery and radioiodine (131I). Despite an overall good prognosis, 10-15% of those will eventually recur, become 131I-refractory and/or evolve to distant metastases. A pattern of dysregulation of the mitochondrial fission protein DRP1 (Dynamin-related protein 1) has been described in different tumour models, where its expression has been implicated in chronic mitochondrial fission, mitochondrial dysfunction,cancer cell invasion and migration,and resistance to targeted therapies.
Objectives: We hypothesize that DRP1 may have a role in the progression of DTCand therefore be a relevant target in delaying or overcoming treatment resistance.
Methods: In the first part of our project, we evaluated the relationship between DRP1 expression(by immunochemistry) and clinico-pathological features in a series of 259 cases follicular cell-derived thyroid carcinomas.
Results and conclusions: DRP1 expression was positive in 90.3% of the cases, and was significantly associated withpapillary and oxyphilichystotypes, non-capsulated tumors,tumor capsule and thyroid capsule invasion,and higher number of 131I treatments.The expression of DRP1 was lower among patients who presented with lymph node metastases and with distant metastases, although not statistically significant. The significant association between DRP1 expression and thyroid capsule invasion, and to a lesser extent, extrathyroidal invasion, may indicate that DRP1 is required for the invasiveness properties of tumor cells in earlier stages of the tumorigenesis. Whether DRP1 may also play a role in lymph node invasion and/or distant metastization remains unclear. If any such association exists in DTC, it seems to fall in the opposite direction.The association between higher mean DRP1 expression and predictors of poor prognosis will be further elucidated by the investigation of the role of DRP1 in TC cell lines with different genetic backgrounds.

4 – The effect of oxidative stress induced by *tert*-butylhydroperoxide (TBH) upon *in vitro* intestinal sugar transport

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