Epithelial – Mesenchymal Transition in Pancreatic Cancer

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INTRODUCTION

Pancreatic cancer is one of the leading causes of cancer death, with only a short median survival rate of less than 6 months after diagnosis[1].

The poor prognosis is largely due to therapeutic approaches non-specifically targeting the tumour bulk, often leading to eventual relapse.

To begin to develop more specific, targeted approaches a better understanding of the mechanisms involved in the initiation and progression of pancreatic cancer are required.

There is increasing evidence to suggest that a process known as **Epithelial to Mesenchymal transition (EMT)** maybe responsible for the initiation and metastasis of various cancers.

Originally identified as a crucial physiological process during development, EMT involves epithelial cells undergoing distinct morphological and molecular changes to generate a mesenchymal phenotype. It is this switch from a polarised epithelial cell type to a migratory mesenchymal phenotype that is thought to govern tumour metastasis and subsequent formation of secondary tumours.

With access to resected human pancreatic neoplastic tissue (pre-malignant) we sought to investigate whether there was evidence of EMT.

OBJECTIVES AND METHODS

Use Hematoxylin and eosin (HE) staining and Immunocytochemical staining to:

1.Characterise normal and neoplastic pancreatic tissue for evidence of tissue damage.

2. To identify whether there is evidence of EMT in pancreatic neoplasms and whether this affects hormone expression (Insulin and glucagon) within the islets.

3. Identify potential morphogens involved in EMT during pancreatic cancer.

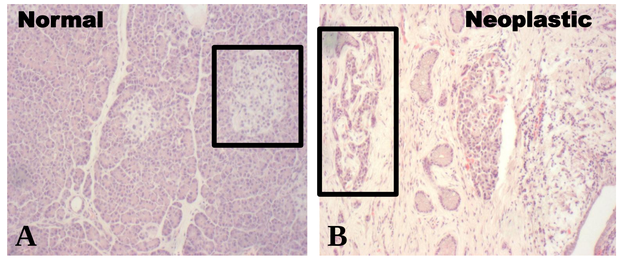

Figure 1: HE staining normal and neoplastic pancreatic tissue.

H and E staining of each normal (A) and Neoplastic (B) indicates differences in tissue morphology. Boxed regions identify islets in each tissue.

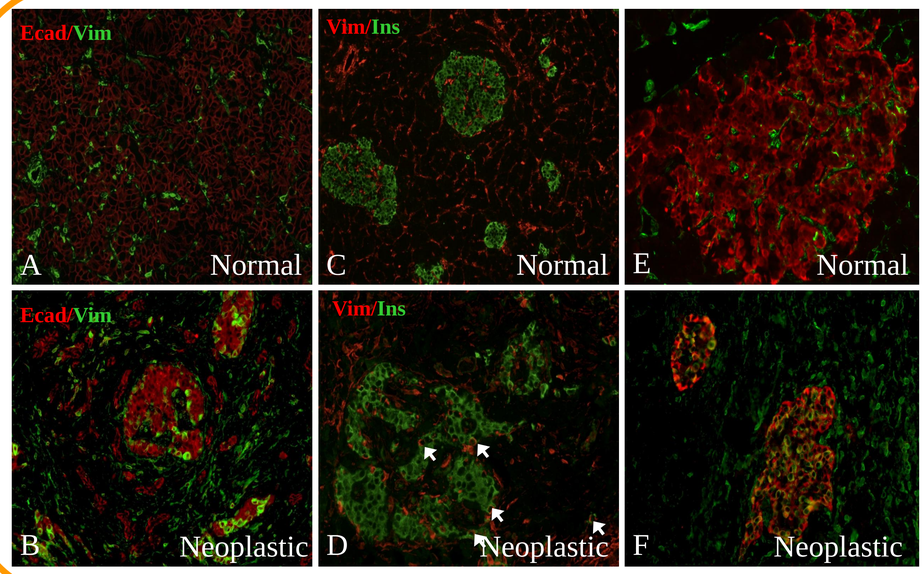

Figure 2: EMT in normal and neoplastic pancreatic tissue.

Normal and neoplastic pancreatic tissue co-stained for E-cadherin and vimentin (A and B), Insulin and vimentin (C and D) and Glucagon and vimentin (E and F).

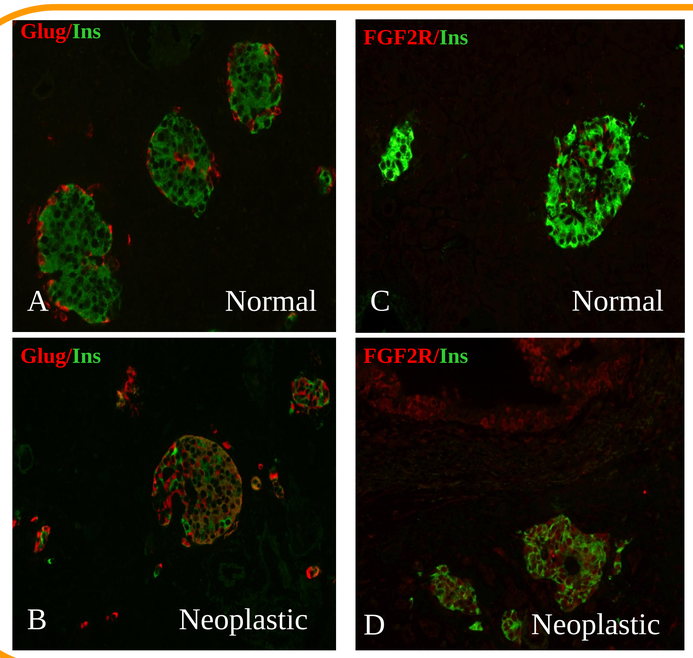

Figure 3: Effects of EMT on hormone expression in normal and neoplastic pancreatic tissue.

Normal and neoplastic pancreatic tissue co-stained for Insulin and glucagon (A and B) and Insulin and FGF2 receptor (C and D)

RESULTS

➢ **RESULTS 1.** Normal tissue exhibits regular islet and tissue morphology, whilst the islets within the neoplastic tissue show areas of damage and fibrosis with clusters of elongated nuclei.

➢ **RESULTS 2.** While absent in normal pancreatic tissue (A), co-expression of E-cadherin (epithelial) and vimentin (mesenchymal) was confirmed in neoplastic tissue (B). Similarly, beta cells (insulin) and alpha cells (glucagon), which in normal pancreatic tissue do not express mesenchymal proteins (C and E), co-express vimentin within the islets of the neoplastic tissue (D and F).

➢ **RESULTS 3.** Normal pancreas tissues shows glucagon and insulin expression is restricted to alpha and beta cells respectively. However, islets within the neoplastic tissue demonstrate co-expression of the two hormones. Furthermore, Immunocytochemical analysis also demonstrated co-expression of FGF2 receptor expression with insulin, which was not evident within islets of normal tissue

CONCLUSION

➢Co-localisation of epithelial (E cadherin) and mesenchymal (vimentin) proteins indicate the occurrence of EMT in pancreatic neoplastic tissue.

➢ Co-expression of vimentin with glucagon and insulin indicates the occurrence of EMT in beta and alpha cells within the islets of the neoplastic tissue.

➢ Morphogens involved in pancreatic cancer and/or EMT cause changes in insulin and glucagon expression as evidenced by the co-expression of these two hormones.

➢Up-regulation of FGF2 receptor and its co-expression with insulin suggests this morphogen may have a role in EMT of beta cells and changes in glucagon/insulin expression in pancreatic cancer.

➢Further understanding of EMT particularly in drug resistance and metastatic potential, could identify new therapeutic targets and increase drug sensitivity.

References: 1.) Gaviraghi, M., P. Tunici, et al. (2011). "Pancreatic cancer spheres are more than just aggregates of stem marker-positive cells." *Bioscience Reports* 31(1): 45-55.