INTRODUCTION
Mesenteric fibrosis (MF) in patients with small intestinal neuroendocrine tumors (SI-NETs) causes significant morbidity and mortality and is poorly understood. MF occurs in up to 50% of SI-NET patients and is caused by a metastatic lesion circumscribed by an extensive fibrotic reaction in the mesentery. There are no biomarkers or radiological criteria to predict complications of SI-NET-associated MF. Due to this lack of knowledge, the UCL/Royal Free London and Erasmus MC Rotterdam, are collaborating to utilise skill sets specific to each centre to then integrate and validate the understanding of MF pathogenesis.

OBJECTIVES
The aim of this study is to identify target genes that will help to determine the pathogenesis of MF in SI-NETs, as well as understanding the crosstalk between tumour cells and cancer-associated fibroblasts during the development of MF. See below:

OUTLINE OF COLLABORATIVE RESEARCH PROGRAMME INTO MESENTERIC FIBROSIS

RESULTS: Models to study interaction between NET cells and fibroblasts

RESULTS: Prevalence of mesenteric metastasis and associated fibrosis, role of sex steroids

RESULTS: transcriptomic analysis of GOT1 and LX2 cell interaction in a paracrine cell culture model

CONCLUSION
• Sexual dimorphism in SI-NET patients was most pronounced in mesenteric disease and the risk of mesenteric metastasis in women increases around menopause. The combination of increased ERα and AR expression in the SI-NET microenvironment suggests a modulating role of sex steroids in the development of the mesenteric metastasis and fibrosis of SI-NETs.
• Unravelling the interactions between SI-NET cells and CAFs and assessment of the effects of different stimuli on fibrogenesis will provide insight into the pathogenesis of MF. This could result in the development of biomarkers for MF and identify therapeutic targets to inhibit cell growth and fibrosis.
• Combining drugs with different modes of action may inhibit release of serotonin and other mediators involved in fibrogenesis more effectively resulting in a significant improvement for patients with SI-NET with MF.

ONGOING EXPERIMENTS

REFERENCES

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