PRESENCE AND CLINICAL-HISTOLOGICAL CORRELATES OF GHRELIN AND SOMATOSTATIN SYSTEMS COMPONENTS IN GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS AND LUNG CARCINOIDS

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BACKGROUND

Neuroendocrine tumors (NETs) are uncommon neoplasms with increasing incidence and limited therapeutic options. Alterations in somatostatin (SST)/cortistatin (CORT) and ghrelin systems have been associated to development/progression of several cancers.

MATERIALS AND METHODS

Observational retrospective study. Formalin-fixed paraffin-embedded samples were used to determine the mRNA expression of ghrelin and SST/CORT systems components by qPCR, using adjacent non-tumoral and normal tissues control.

RESULTS

Demographic, epidemiological, clinical and pathological characteristics of the cohorts of patients

Table 1: Demographic and clinical characteristics of the two cohorts of patients

	GEP-NETs	Lung-NETs
n (patients)	90	81
Sex (% male)	53,3	50,6
Mean age (years)	54±17	54±15
Incidental diagnosis (%)	37,7	19,2
Functioning tumors (%)	34,4	7,5
Metastasis at diagnosis (%)	46,5	25
Mortality rate (%)	34,1	19,4

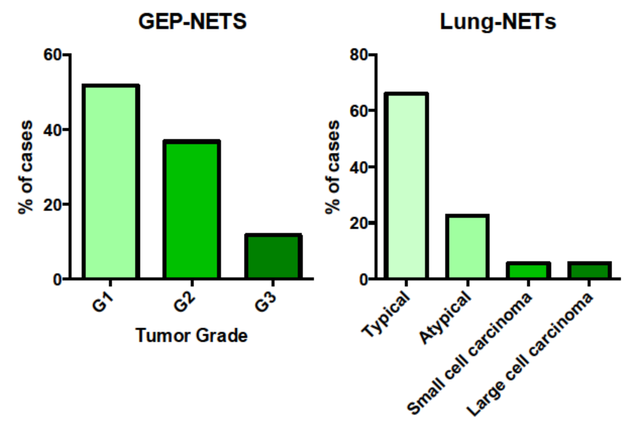

Figure 1: GEP-NETs and Lung-NETs classification. For GEP-NETs the ENETS and WHO classification was used. For Lung NETs the WHO classification was used.

The expression levels of the components of the ghrelin system family are drastically altered in NETs, although the pattern of dysregulation is clearly different between GEP-NETs and lung-NETs

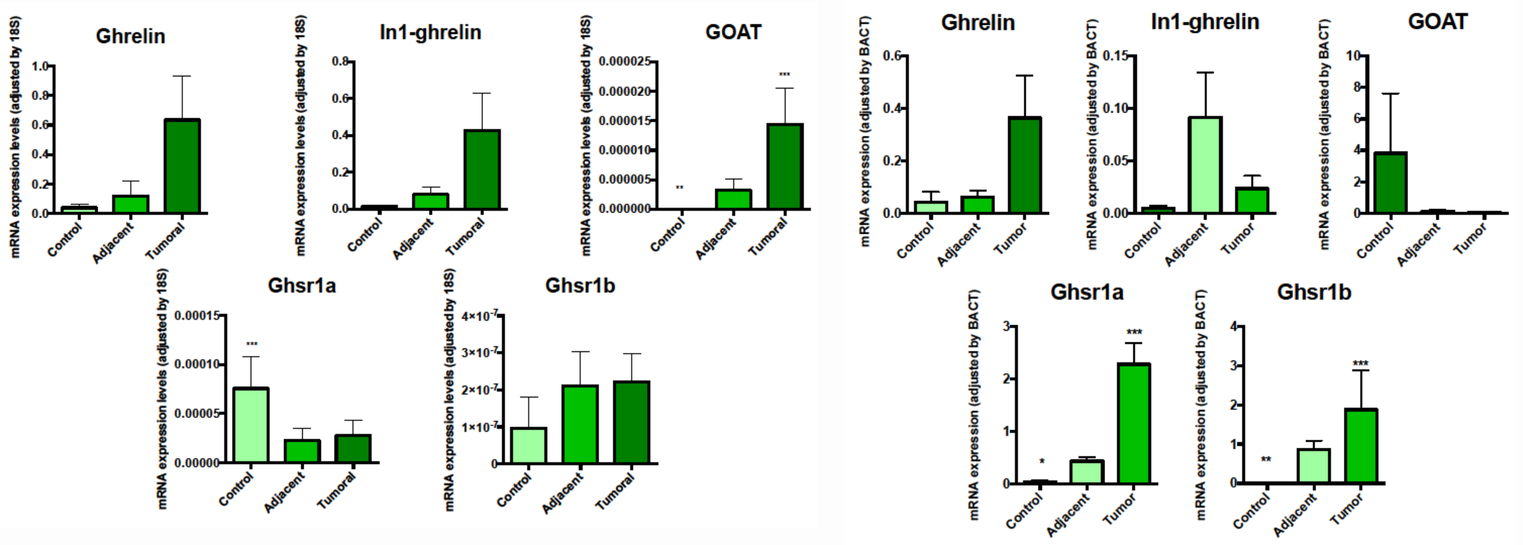

Figure 2: Ghrelin system components expression in GEP-NETs. Ghrelina, In1-ghrelin and GOAT were overexpressed in tumor samples compared with adjacent and control tissue. Data represent the mean±SEM. Asterisks (*, p<0.05; **,p<0.01) indicate significant alterations by one-way Anova.

Figure 3: Ghrelin system components expression in Lung-NETs. The expression of GHSR1a and GHSR1b receptors was increased in tumor tissue. Data represent the mean±SEM. Asterisks (*, p<0.05; **,p<0.01; ***,p<0.001) indicate significant alterations by one-way Anova.

The expression levels of the components of the SST/CORT system family are drastically altered in NETs, showing a relatively similar pattern of dysregulation in GEP-NETs and lung-NETs.

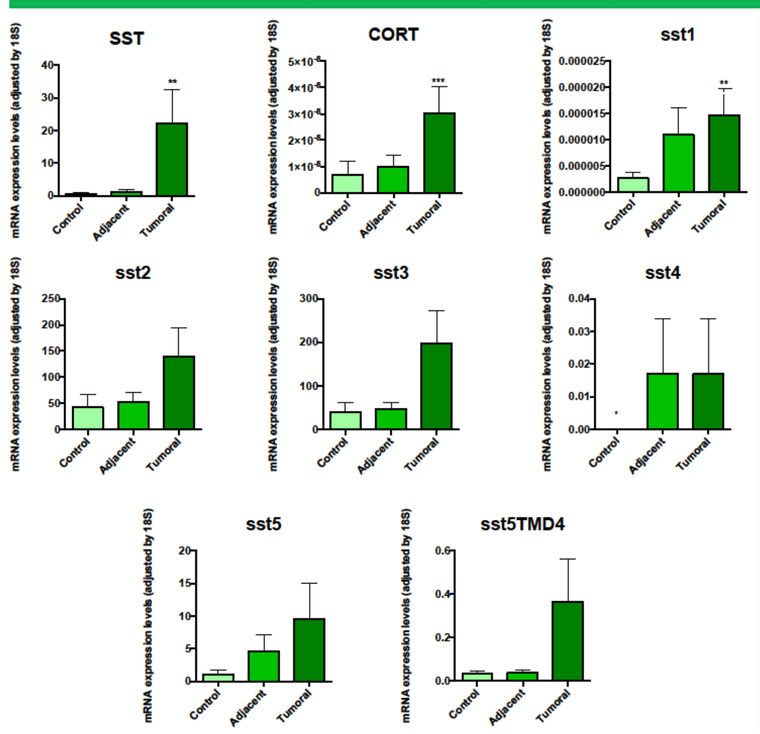

Figure 4: SST/CORT system components expression in GEP-NETs. SST, CORT and some ssts were overexpressed in tumor samples compared to adjacent and control tissue. Data represent the mean±SEM. Asterisks (*, p<0.05; **,p<0.01; ***,p<0.001) indicate significant alterations by one-way Anova.

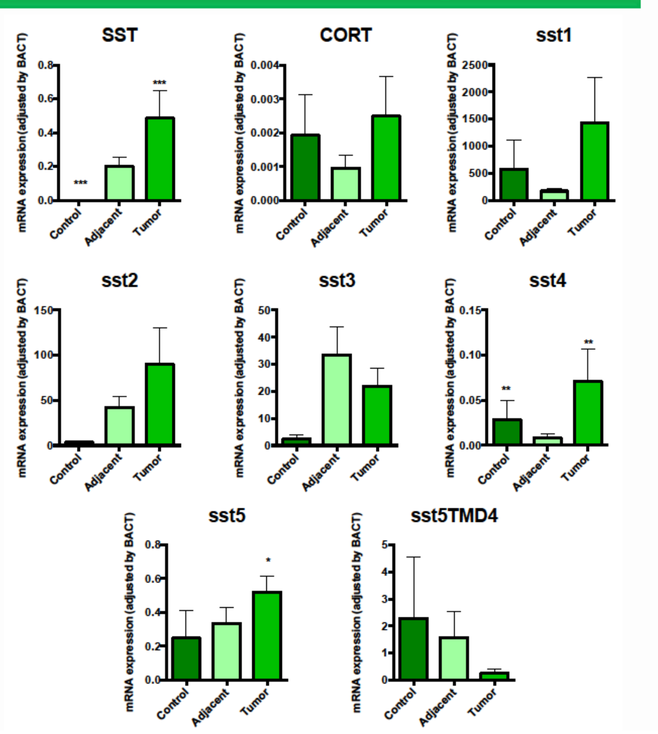

Figure 5: SST/CORT system components expression in Lung-NETs. SST and some receptors were overexpressed in tumor samples compared to adjacent and control tissue. Data represent the mean±SEM. Asterisks (*, p<0.05; **,p<0.01; ***,p<0.001) indicate significant alterations by one-way Anova.

The expression of certain SST/CORT and ghrelin system components was associated to epidemiological parameters in GEP-NETs.

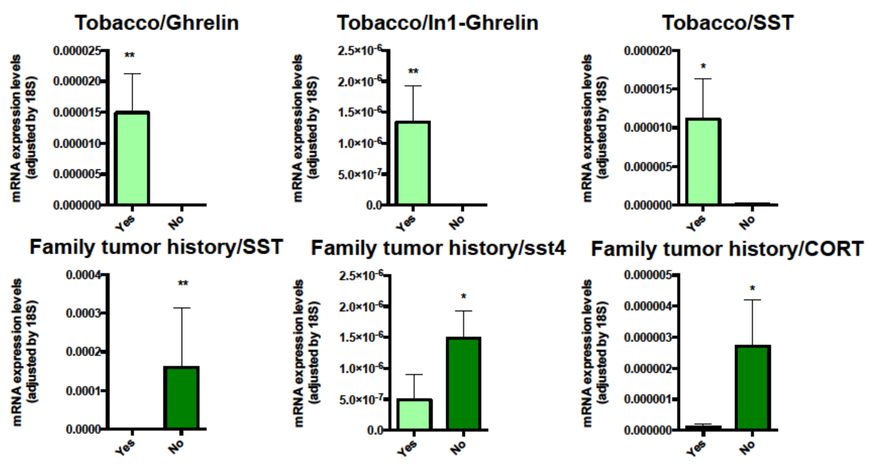

Figure 6: Correlations between epidemiological and molecular parameters in GEP-NETs. Asterisks (*, p<0.05; **,p<0.01) indicate significant associations by U Man-Whitney test.

The expression of certain SST/CORT and ghrelin system components was associated to clinical and histological parameters in GEP-NETs.

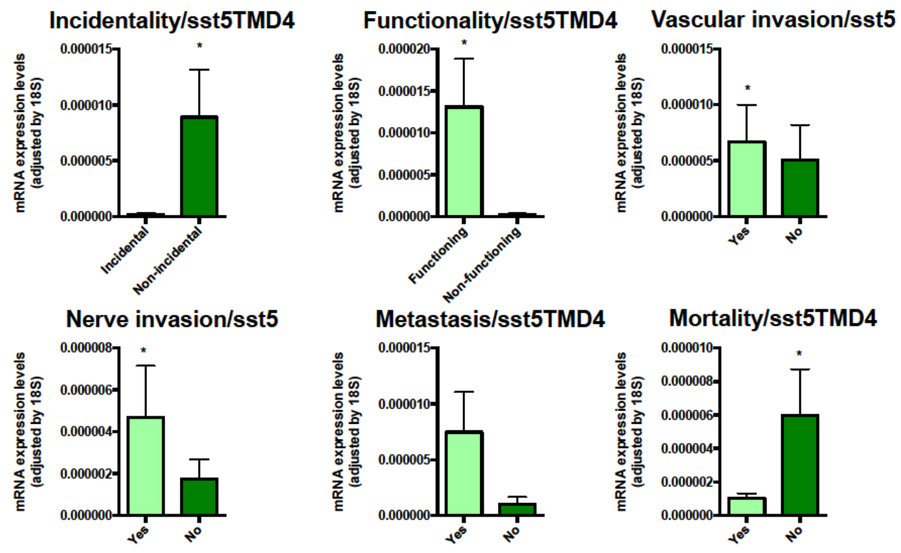

Figure 7: Correlations between clinical, histological and molecular parameters in GEP-NETs. Asterisks (*, p<0.05; **,p<0.01) indicate significant associations by U Man-Whitney test.

The expression of certain SST/CORT and ghrelin system components was associated to epidemiological, clinical and histological parameters in lung-NETs.

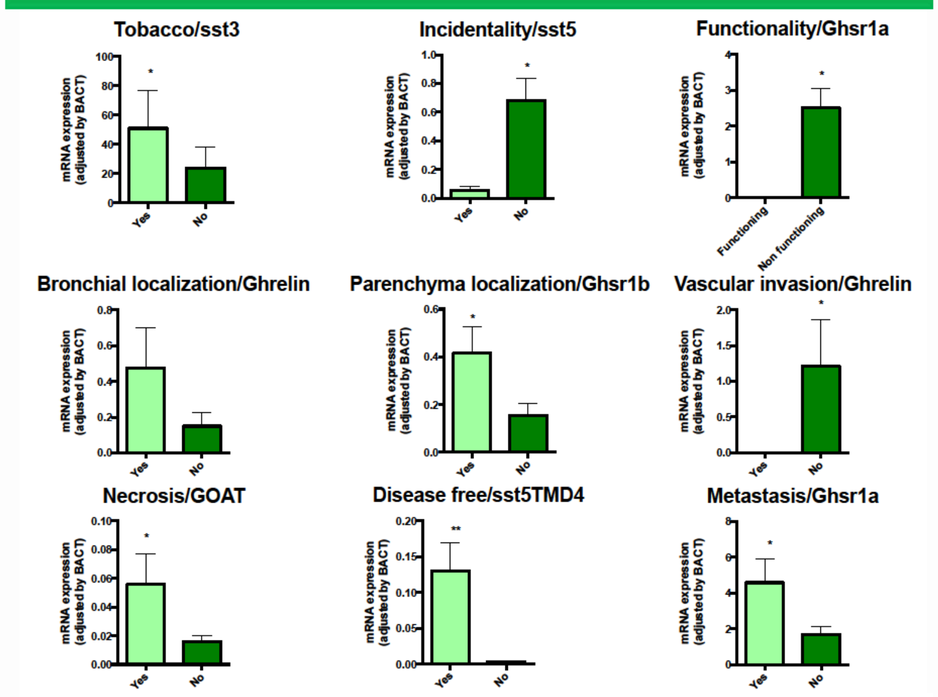

Figure 8: Correlations between epidemiological, clinical, histological and molecular parameters in Lung-NETs. Asterisks (*, p<0.05; **,p<0.01) indicate significant associations by U Man-Whitney test.

CONCLUSIONS: Our results reveal a notably widespread expression of key SST/CORT/ghrelin systems components in GEP-NETs and LC, where they display clinical-histological correlates.

Specific SST/CORT/ghrelin systems components could provide novel, valuable markers for NET patient management.