Nomenclature/ Terminology

Carcinoid

Clinics: with syndrome

Pathology: tumors with neuroendocrine features

Tumor in one site is not equivalent in another site in the GI tract

They cover the full pathological spectrum from benign ??, (very) low grade and high grade malignancy

Endocrine or neuroendocrine

GI tract with 15 discrete neuroendocrine cell types

Diagnosis

- New TNM classification

- Morphologic , clinically functional, and biological behavior reports
- Immunohistochemically detected peptides do not imply that the patient has clinical symptoms nor does this finding imply that the tumor is functional
- Subtle clinical manifestations may be missed
- No dominant hormone

Selected immunohistochemical markers

- CgA,B,C, Synaptophysin, cell specific markers
- Ki-67
- Neuroendocrine secretory peptide 55 (pancreas)
- Ghrelin (oxyntic mucosa)
- Somatostatin receptors
- CDX2 (ileum, appendix)
- Histidine decarboxylase (pancreas)
- Xenin (duodenum)
- Ck 19 (pancreas)

Endocrine differentiation in gastric cancer

- Stomach epithelial tumors are divided into two major types: Exo-cell type (adenomas and carcinomas) and End-cell type [carcinoid tumors and endocrine cell carcinomas (ECC)].
- Therefore, it has been hypothesized that the origin of stomach cancers is from a progenitor cell specializing towards an Exo-cell lineage
- However, there have been several reports that chromogranin A (CgA), an End-cell differentiation marker, was immunohistochemically found in about 15-70% of human stomach cancers, suggesting the possibility of both Exo-cell and End-cell differentiation in the stomach cancers

Park et al., Int J C1992
Qvigstad et al., Histoch .J 2000
Naritomi et al., Anticancer Res2003
Tatematsu et al., Cancer Sci 2005

CgA-positive Adenocarcinomas

Correlations between clinicopathological findings and the chromogranin A expression in 37 early and 73 advanced stomach cancers [110]

Clinicopathological findings	CgA (+) (n=16)	CgA (-) (n=94)	
Age			
Years (mean ± s.d.)	64.0 ± 10.2	60.9 ± 9.7	
Sex			
Male (n=67)	12	55	18%
Female (n=43)	4	39	9%
Histological classification[a]			
Differentiated (n=56)	7	49	12%
Undifferentiated (n54)	9	45	17%
Depth			
early (n=37)	4	33	11%
advanced (n=73)	12	61	16%
Lymph node metastasis			
Positive (n=63)	10	53	15%
Negative (n=47)	6	41	12%

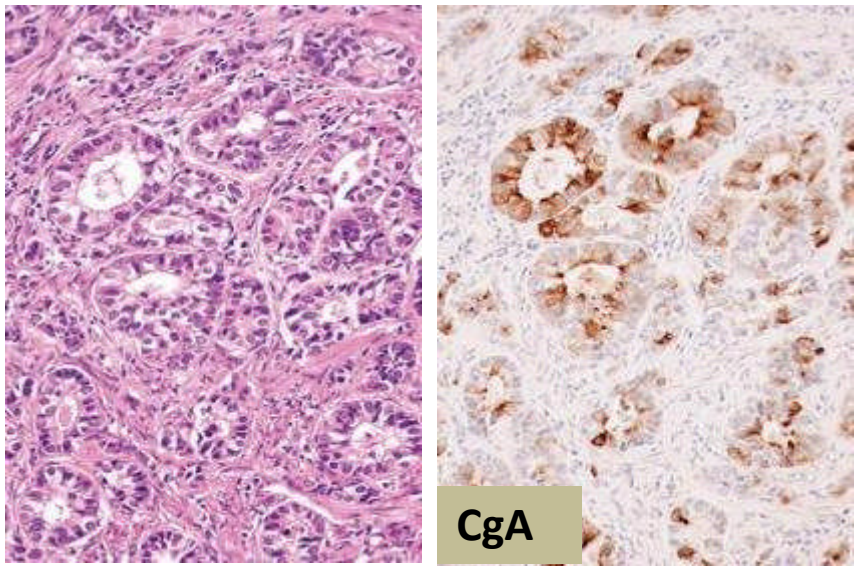
15%

> 10% of CgA Positive Tumor Cells

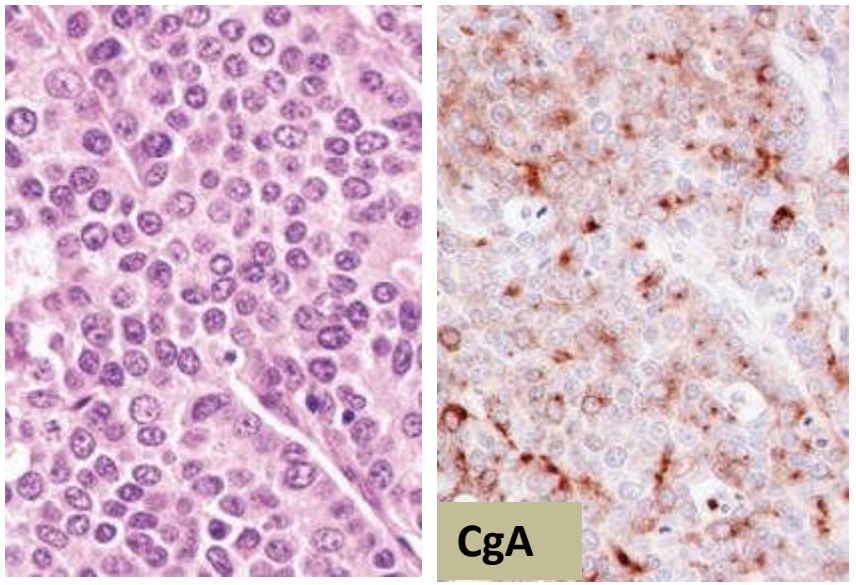
Takenaka et al Hist Histopathol 2007

Endocrine Differentiation

- **Adenocarcinoma with Neuroendocrine Differentiation (ACNED)**
- **Large Cell Neuroendocrine Carcinoma (LCNEC)**



Tubular LCNEC

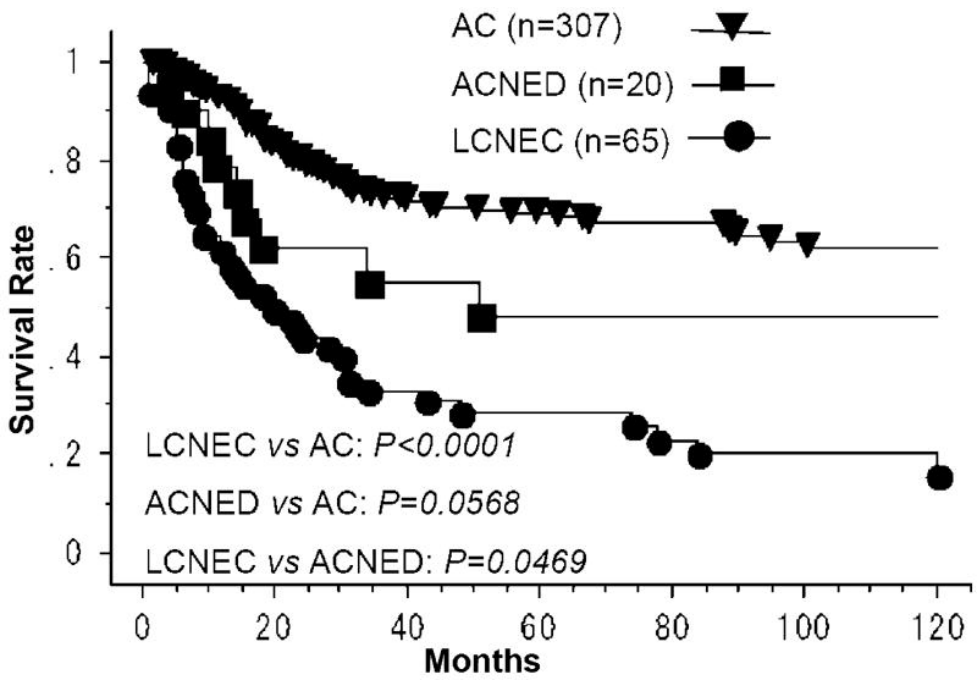


Solid LCNEC

Jiang, Am J Surg Pathol 2006

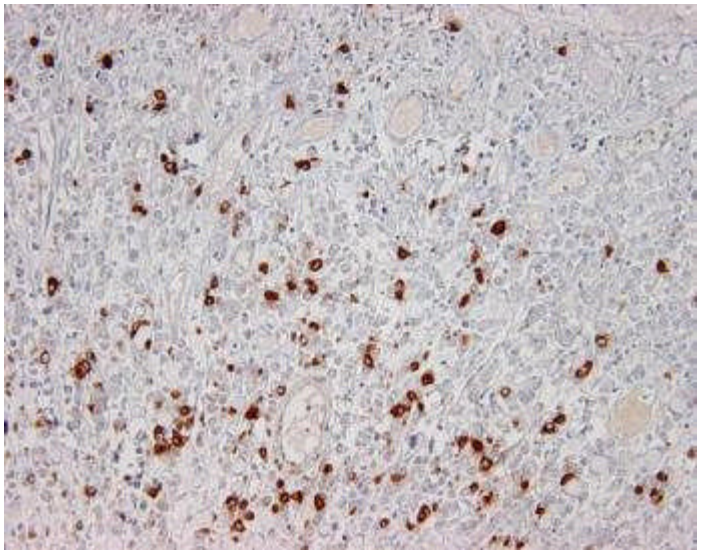
AC
ACNED < 20%
LCNEC > 20%

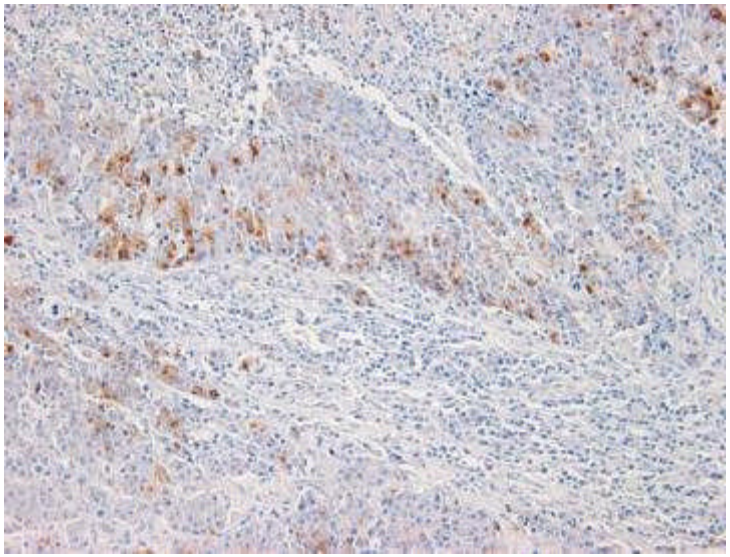
CUT OFF 20% positivity for CgA or Syn



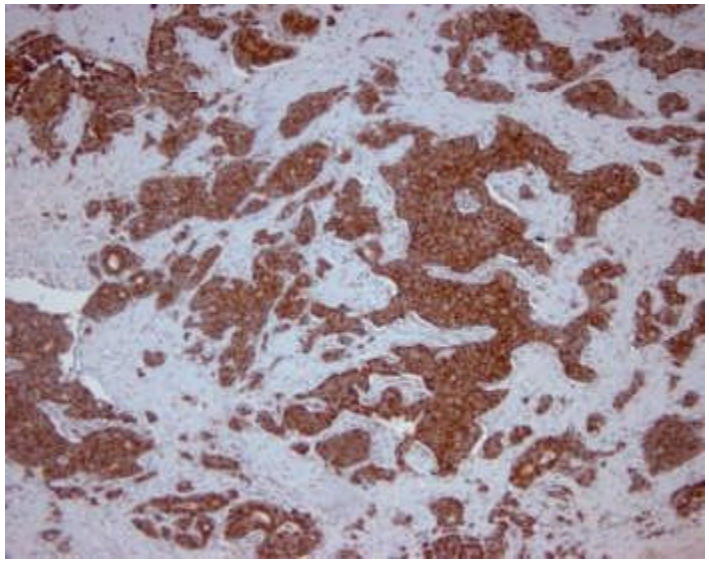
Jiang, Am J Surg Pathol 2006

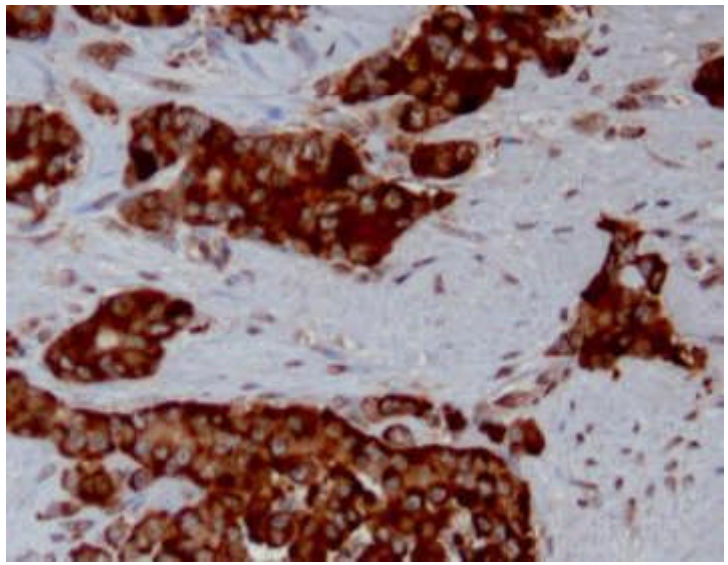
ACNED





LCNEC





Tumori, 94: suppl, 2008

Exocrine-endocrine modulation in Gastric Cancer

V.Canzonieri, L. Memeo°, T.Perin, D.Rossi, R.Cannizzaro