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Classification of gastric carcinomas

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Malignant epithelial tumors of the stomach have traditionally been classified as adenocarcinomas based upon glandular growth pattern and/or mucin positivity. Mucin positivity has been assessed by histochemical methods (PAS and Alcian Blue), both methods being unspecific. However, it is not easy to distinguish between neuroendocrine and exocrine derived malignant tumors as evidenced by the reclassification of gastric tumors occurring in the African rodent Mastomys by Soga from adenocarcinoma to neurondocrine ECL cell carcinomas (GANN Monograph 1969; 8:15-26), and by the similar reclassification of the malignant oxyntic tumors found in mice/rats after long-term dosing with inhibitors of acid secretion by Havu in the middle of the eighties (Digestion 1986; 35 Suppl 1:42-55).

We asked ourselves whether such a misclassification also could occur in man. In our first study (Eur J Gastroenterol Hepatol 1991; 3:245-49) we found that some of the tumor cells in carcinomas of diffuse type according to Lauren showed neuroendocrine differentiation and, interestingly, that virtually all tumor cells were positive for chromogranin A in a cancer of a young women with a 2-years history of flushing after meals (thought to be food allergy, but was histamine flushing). We then went on to collect tumor samples from the operation theater together with blood for serum analyses. In 1998, we published our second study (Cancer 1998; 83:435-44) where we confirmed that a proportion of gastric carcinomas of diffuse type expressed neuroendocrine markers. Later, we used immunohistochemistry with tyramide signal amplification and confirmed that a large portion of gastric carcinomas of diffuse type actually were of neuroendocrine origin (Histochem J 2000; 32:551-56). Interestingly, virtually all carcinomas taken from patients with long-term marked hypergastrinemia (atrophic gastritis with or without pernicious anemia) could be classified as ECL derived (APMIS 2002; 110:132-39). By using chromogranin A immunoelectronmicroscopy we could show that tumor cells contained secretory granules (Appl Immunohistochem Mol Morphol 2010; 18:62-68.)

In recent time we have applied *in situ* hybridization by the use of a new commercially available method (RNAscope) which has improved sensitivity and specificity compared to conventional *in-situ* hybridization (Appl Immunohistochemical Mol Morphol 2013; 21:185-89). We have confirmed neuroendocrine mRNA expression in signet tumor cells, but no expression of mRNA for different mucins. In conclusion, gastric carcinomas of diffuse type are of neuroendocrine and more specifically of ECL cell origin. PAS positivity in these tumor cells is not due to mucin.

Biography

Helge Waldum became M.D. in 1971 at the age of 25 years (University of Oslo, Norway, with a grade reported to the King) and completed two Ph.D.s (University of Tromsø, Norway, 1980 and Université de Paris, France, 1993) and is a specialist in Internal Medicine and Gastroenterology, 1980). He is a Professor at Norwegian University of Science and Technology, Trondheim Norway from 1986 and Head of Department of Gastroenterology and Hepatology, University Hospital of Trondheim, Norway for more than 20 years. He has published more than 350 papers and supervised 18 candidates to Ph.D. Research related to regulation of gastric acid secretion, gastrin and in its target cell, the ECL cell. The role of the ECL cell in physiology, patophysiology and carcinogenesis and the classification of gastric carcinomas have been of particular interest.

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