Gastrin drives gastric cancer due to oxyntic atrophy also after Helicobacter pylori eradication

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Dear Editor.

In a recent paper, Take *et al.* reported continued risk of gastric cancer after *Helicobacter pylori* (Hp) eradication when followed endoscopically up to 21.4 years.[1] The higher the degree of atrophy, the higher the yearly risk for gastric cancer.

After 30 years of search we still do not know the mechanism for Hp gastric carcinogenesis. However, Hp infection predisposes to gastric cancer only after having induced some degree of oxyntic atrophy.[2] We therefore proposed that hypergastrinemia secondary to hypoacidity caused Hp induced gastric cancer.[3]

The increased frequency of gastric cancer in patients using proton pump inhibitors (PPIs) after Hp eradication[4] indicates an additive effect of Hp and PPI treatment *via* gastrin.[5] Profound inhibitors of acid secretion should accordingly not be given for the long-term in Hp positive patients and used with caution in previously Hp positive patients.

The proliferative effect of gastrin is concentration dependent without any threshold and maximal effect is reached at a lower concentration than mostly realized.[6,7] The gastrin immunoassays were introduced at a time without knowledge of Hp. Therefore, asymptomatic subjects with Hp infection were included among controls, making present upper normal levels too high.[5] It would have been of interest to know the gastrin values in the patients described by Take *et al.*[1] They also described that gastric cancers of diffuse type seemed to increase with time.[1] This cancer type we have described for more than 20 years to be of Enterochromaffin-like (ECL) cell origin,[8] the target cell of gastrin.

Finally, it should be recalled that we already have an efficient gastrin antagonist, netazepide, without side effects.[9]

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Conflict of interest statement

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References

1. Take S, Mizuno M, Ishiki K, *et al.* Risk of gastric cancer in the second decade of follow-up after Helicobacter pylori eradication. *J Gastroenterol* 2020; 55: 281–288.
2. Uemura N, Okamoto S, Yamamoto S, *et al.* Helicobacter pylori infection and the development of gastric cancer. *N Engl J Med* 2001; 345: 784–789.
3. Waldum HL, Hauso Ø, Sørdal ØF, *et al.* Gastrin may mediate the carcinogenic effect of helicobacter pylori infection of the stomach. *Dig Dis Sci* 2015; 60: 1522–1527.
4. Cheung KS, Chan EW, Wong AYS, *et al.* Long-term proton pump inhibitors and risk of gastric cancer development after treatment for helicobacter pylori: a population-based study. *Gut* 2018; 67: 28–35.
5. Waldum HL and Rehfeld JF. Gastric cancer and gastrin: on the interaction of helicobacter pylori gastritis and acid inhibitory induced hypergastrinemia. *Scand J Gastroenterol* 2019; 54: 1118–1123.

6. Brenna E and Waldum HL. Trophic effect of gastrin on the enterochromaffin like cells of the rat stomach: establishment of a dose response relationship. *Gut* 1992; 33: 1303–1306.

7. Sjöblom SM, Sipponen P, Karonen SL, *et al.* Mucosal argyrophil endocrine cells in pernicious anaemia and upper gastrointestinal carcinoid tumours. *J Clin Pathol* 1989; 42: 371–377.

8. Waldum HL, Aase S, Kvetnoi I, *et al.* Neuroendocrine differentiation in human gastric carcinoma. *Cancer* 1998; 83: 435–444.

9. Fossmark R, Sørdal Ø, Jianu CS, *et al.* Treatment of gastric carcinoids type 1 with the gastrin receptor antagonist netazepide (YF476) results in regression of tumours and normalisation of serum chromogranin A. *Aliment Pharmacol Ther* 2012; 36: 1067–1075.