Reviewer's report

Title: Nitric oxide—an endogenous inhibitor of gastric acid secretion in isolated human gastric glands

Version: 1 Date: 5 March 2004

Reviewer: Koji Takeuchi

Reviewer's report:

General
This paper describes the effect of nitric oxide (NO), both occurred endogenously and given exogenously, on histamine- and cAMP-stimulated gastric acid secretion in the isolated human gastric gland preparations in vitro, using [14C]-aminopyrine. The results seem to be interesting and consistent, yet some additional data should be required to support the author’s conclusion.

---------------------------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Lots of data have so far reported concerning the influence of NO on acid secretion, and the results remained controversial. The present study supports the inhibitory effect of NO on acid secretion at the parietal cells, consistent with the finding by Brown et al. This is the first study using human isolated gastric glands, yet to raise the originality the following points should be addressed.

1. To further support the inhibitory effect of endogenous NO on acid secretion, the amount of NO should be measured in the present isolated gland preparation before and after addition of L-arginine or the NO synthase inhibitors such as L-NAME or L-NNA.

2. The authors discussed the possible involvement of cGMP in the inhibitory action of NO. This point should be verified in the present study. It would not be difficult to confirm the idea whether cGMP plays a mediator role in the negative action of NO in acid secretion. The authors should examine the effect of dbcGMP on histamine- and cAMP-stimulated [14C]-aminopyrine uptake or the effect of methylene blue (guanylate cyclase inhibitor) on the action of NO donors.

3. Isolated gastric gland preparations may include enterochromaffin-like (ECL) cells, the most important endocrine cells for acid secretion. This histamine containing cells are capable of releasing histamine in response to cAMP. Several studies showed the inhibitory action of NO on histamine release from ECL cells. It is possible that NO suppresses cAMP-stimulated acid secretion by inhibition at both parietal cells and ECL cells. The authors should make extensive discussion on this point.

Minor comments

Page 4, line 12: Takeuchi and coworkers

Page 4, line 3-4 from the bottom: the experiments reported in Refs. 13 and 14 were in vivo but not in vitro.

Figure 3: The legend did not well correspond to this figure. The authors should replace (a) and (b) in the legend or the figure.

---------------------------------------------------------------

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

---------------------------------------------------------------

Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: None