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LETTER

To the Editor

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In his letter, Dr. Ueno of Sucampo Pharmaceuticals writes that my review article (1) suggests that lubiprostone is useful to treat diarrhea and is contraindicated in obstipation. This is not true. I made no statement as to the clinical effects of lubiprostone. I raised, however, well-founded doubts about the contention that lubiprostone activates ClC-2. Indeed, the only paper available that supported such a role of lubiprostone at the time of publication of my review showed effects of lubiprostone on currents that displayed a linear I/V relationship (2). These currents are very unlikely to represent ClC-2, which rather mediates inwardly rectifying currents that are slowly activated by hyperpolarization (as published by at least five independent laboratories including my own). Unfortunately, Dr. Ueno, Sucampo, as well as all authors publishing on lubiprostone that I contacted, refused to provide that substance for studying its effect on ClC-2. Therefore, independent tests of lubiprostone on ClC-2 currents have not been possible.

The only knock-out controlled immunohistochemical analysis of ClC-2 available (3,4; and own unpublished results) shows that ClC-2 can be detected in basolateral, but not in apical membranes of intestinal epithelial cells. A basolateral localization of ClC-2 is also compatible with Ussing chamber experiments performed on WT and ClC-2 KO colon (5). As stated in my review, a basolateral localization of ClC-2 suggests that its activation should increase chloride and water reabsorption. Hence, *if* lubiprostone would exert its intestinal effects through an activation of ClC-2, it should worsen rather than alleviate obstipation – an effect which is obviously in contrast to several published reports. In summary, I question the contention that lubiprostone ameliorates obstipation by activating ClC-2.

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