TO THE EDITOR: We write in response to the recent article by GlaxoSmithKline, King of Prussia, Pennsylvania Kevin S. Thorneloe, Mui Cheung, Dennis A. Holt, and Robert N. Willette

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Hence, we would argue that GSK2193874 is quite a selective TRPV4 antagonist, perhaps the most selective reported in the literature to date.

5) To provide a comprehensive list of selective TRPV4 antagonists in Figure 7, the authors should include GSK2263095 (3), and GSK2220691 and GSK2337429A (1), which represent novel and selective TRPV4 antagonists for use in vitro and in vivo studies. GSK2220691 and GSK2337429 were mentioned on p. 943 but were not included in Figure 7.

6) In Section VII. ANTAGONISTS OF TRPV4, the authors state the following without supporting reference: “Given the problems of collateral injury presented even by a selective TRPV4 antagonist when administered for a therapeutic purpose . . .” We feel that this is not a fair statement due to the lack of reference to support it and that administration of a selective TRPV4 antagonist to humans has yet to be reported.

7) On p. 912 and 943, the authors summarize the conflicting studies in the literature that have used TRPV4 KO mice to evaluate an in vivo role for TRPV4 in osmoregulation. On p. 935 they state that “In the case of animals that have been genetically engineered, there is always a question as to whether loss of the ‘knocked-out gene’ has led to compensatory changes . . . that the knockout phenotype ceases to be a reliable indicator of the function of the knocked out gene.” We agree with the authors that interpretation of KO phenotypes must be done with caution. Hence, we performed rigorous osmoregulatory studies with the selective antagonist GSK2198374 in rats, in which no significant osmoregulatory impact was observed with acute or chronic pharmacological TRPV4 inhibition under various osmolar perturbations (1). It is surprising the authors did not reference our osmoregulatory study with GSK2193874, given their acute awareness of issues surrounding KO phenotypes and the conflicting osmoregulatory data reported with TRPV4 KOs.

8) On p. 935, TRPV4 KNOCKOUT MICE, the first sentence states that two independent TRPV4 KOs have been developed. However, the TRPV4 KOs developed by GSK (reported in Ref. 2) have not been considered as a third TRPV4 KO strain currently utilized by researchers.

Therefore, we would like to request the publication of an erratum. In particular to correct the references to, and er-
errors in, chemical structures, as well as to address the selectivity characterization of GSK compounds.

**DISCLOSURES**

All authors are employees and stockholders of GlaxoSmithKline.

**REFERENCES**


