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Correction to "Systemic Activation of the Transient Receptor Potential Vanilloid Subtype 4 Channel Causes Endothelial Failure and Circulatory Collapse: Part 2"

In the above article [Willette RN, Bao W, Nerurkar S, Yue TL, Doe CP, Stankus G, Turner GH, Ju H, Thomas H, Fishman CE, Sulpizio A, Behm, DJ, Hoffman, S, Lin Z, Lozinskaya I, Casillas LN, Lin M, Trout RE, Votta BJ, Thorneloe K, Lashinger ES, Figueroa DJ, Marquis R, and Xu X (2008) *J Pharmacol Exp Ther* **326:**443–452], the authors reported an activation of TRPV1 channels (IC_{50} = 50 nM) by the TRPV4 channel activator GSK1016790A in the embedded table of Fig. 1. This was assessed by GSK1016790A-evoked Ca^{2+} influx into TRPV1-transduced HEK cells. Upon further detailed evaluation of the effect of GSK1016790A on TRPV1, the authors were unable to validate this earlier finding and determined that the Ca^{2+} influx observed in previous experiments was due to an endogenous response in human embryonic kidney (HEK) cells in response to GSK1016790A stimulation that is not TRPV1-mediated.

In Supplemental Fig. 2, a new figure shown below (also added online), GSK1016790A evokes a similar Ca^{2+} influx in untransduced (HEK), null-transduced (+Null), and TRPV1-transduced (+TRPV1) HEK cells. The response in TRPV4-transduced cells is much larger, and GSK1016790A demonstrates a greater potency. The authors ruled out the endogenous response in untransduced and null-transduced HEK cells as being TRPV1-mediated in that capsaicin was unable to elicit a response in either group. At the same time, they confirmed the functional expression of TRPV1 in the TRPV1-transduced HEKs, because capsaicin elicited a robust Ca^{2+} influx in the TRPV1-transduced cells. These data indicate that GSK1016790A is not an activator of TRPV1 channels. The *Results* and *Discussion* sections have been changed to reflect these data, including the removal of the TRPV1 potency from the embedded table in Fig. 1.

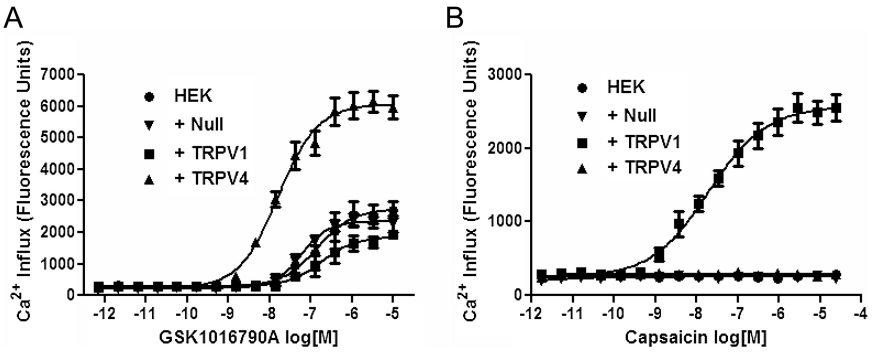
The companion article [Thorneloe et al., *J Pharmacol Exp Ther* **326:**432–442] has been revised to reflect these findings. The third sentence of the *Results* section in the corrected version is as follows: "GSK1016790A was inactive against TRPV1 channels (see accompanying article, Willette et al., 2008), which, based on sequence homology, is the TRP superfamily member closest to TRPV4."

In addition, a number of minor changes have been made to the article as detailed below.

On page 443, in the abbreviation list, the abbreviation "4α-DPP" has been changed to "4α-PDD," and that change has also been made in the text as follows: p. 444, second paragraph, first sentence, and p. 446, first paragraph, last sentence.

On pp. 446 and 447, several figure citations have been changed:

- The two penultimate sentences in the second paragraph now read: "The $TRPV4^{+/-}$ heterozygotic strain exhibited reduced sensitivity to the blood pressure effects of GSK1016790A (Fig. 2C)—the depressor dose was 0.3 mg/kg, and the lethal dose was 1.0 mg/kg (n = 3). TRPV4 gene deletion ($TRPV4^{-/-}$) abolished the hemodynamic effects of GSK1016790A (Fig. 2D)."



Supplemental Fig. 2.

- In the last sentence of the second paragraph, the citation of Fig. 2C has been deleted.
- In the last sentence of the third paragraph (second line of right column), the citation of Fig. 5 has been deleted.
- The last sentence of the second full paragraph in the right column now reads: "However, circulatory collapse induced by GSK1016790A (n = 3) was unaltered in the eNOS$^{-/-}$ strain (Fig. 4B)."
- On the last line of the page and continuing to page 447, the sentence now reads: "At 15 min after GSK1016790A (0.3 mg/kg/15 min), the lung wet weight to body weight ratio was increased approximately 2.5-fold compared with vehicle [0.2 ml of DMSO (1%), 29% β-cyclodextrin] (Fig. 5F)."

On p. 447, in the right column, the third sentence of the first full paragraph now reads: "In the lung, robust TRPV4 staining was observed in epithelium lining secondary and tertiary segments of the airway and in bronchial epithelium and pulmonary artery endothelium (Fig. 6, A and C)."

On p. 449, in the first sentence of the second paragraph of the *Discussion*, the reference citation has been deleted because it does not appear in the reference list.

Finally, on p. 451, the fourth sentence in the second paragraph now reads: "The actions of GSK1016790A in the aorta were absent in vessels obtained from TRPV4 null mouse and abolished by the nonselective TRP channel blocker, ruthenium red."

The online version of this article has been corrected in departure from the print version.

The authors regret these errors and apologize for any confusion or inconvenience they may have caused.