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LETTER TO THE EDITOR

Antiepileptic activity of zonisamide on hippocampal CA3 neurons does not depend on carbonic anhydrase inhibition

Dear colleague,

I read with interest your paper on zonisamide and CA II (Thöne et al., 2008). I believe you have attributed some statements to us incorrectly.

We did not report that ''ZNS acts as a highly selective carbonic anhydrase type 2 (CAII) inhibitor.'' In contrast we showed this compound to be a 35-nM inhibitor of CA II and 20 nM of CA VA (the target we were interested for designing antiobesity agents) and reported its X-ray crystallographic structure (which undoubtedly proves its efficient binding to these enzymes, but not its specificity) (De Simone et al., 2005). Furthermore, the full inhibition profile of zonisamide against all mammalian isozymes (CA I XIV) was published by us previously (Supuran, 2008).

Moreover, in contrast to your interpretation, our data showing that some potent CA II inhibitors possessing lipophilic moieties lead indeed to strong anticonvulsants, whereas similar compounds with the same inhibition profile against CA II do not have such properties, strongly suggests that CA II inhibition alone is not enough for designing anticonvulsants (Ilies et al., 2004). Differences in isoforms among the seven present in brain might be involved, or CA inhibition may be unrelated to the mechanism of anticonvulsant action.

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