British Journal of Pharmacology

DOI:10.1111/j.1476-5381.2010.01139.x
www.brjpharmacol.org

LETTER TO THE EDITOR

Knockout controls and the specificity of cannabinoid CB_2 receptor antibodies

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Received
16 October 2010
Accepted
11 November 2010

Linked Article
To view the reply from Atwood and Mackie visit http://dx.doi.org/10.1111/j.1476-5381.2010.01140.x

In Atwood and Mackie's (2010) excellent review of the status of the cannabinoid CB_2 receptor, evidence for CB_2 receptor expression in the cerebellum obtained with immunohistochemistry is discussed. This includes a discussion of work published by my colleagues and myself (Ashton *et al.*, 2006). In addition to the studies reviewed, Suarez *et al.* (2008; 2009) have also published results for cannabinoid receptor immunolabelling in the rodent brain, including the cerebellum. The second of these studies (Suarez *et al.*, 2009) is notable because it uses cannabinoid receptor knockout mice to test for antibody specificity. These studies are particularly relevant to the issues discussed by Atwood and Mackie, who critically discussed the use of controls in immunohistochemistry, including the use of knockout mice. Suarez *et al.* (2008) reported widespread neuronal CB_2 receptor immunolabelling in the cerebellum, in contrast to our results (Ashton *et al.*, 2006). Suarez *et al.* (2009) then reported widespread neuronal CB_2 receptor immunolabelling in the hippocampus, using the same antibody. In this later paper, knockout controls for both CB_1 and CB_2 receptor antibodies were used. However, close investigation of the published images reveals that the CB_2 receptor antibody gives a very similar – but fainter – staining pattern in the knockout mouse as in the wild-type mouse. In contrast, staining patterns are very different between knockout and wild-type strains for CB_1 receptor immunolabelling. Therefore, these studies illustrate a rule that convincing knockout controls on antibody specificity should show the *redistribution* rather than the *reduction* of immunolabelling. These investigations therefore provide an informative addition to Atwood and Mackie's comprehensive review.

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