Reply to “Letter to the editor: ‘Is menthol- or icilin-induced vasodilation mediated by the activation of TRPM8?’”

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REPLY: The letter from Dr. Ma (3) highlights the problems that are inevitable in filling in the gaps of our knowledge of the properties of heterologously expressed transient receptor potential (TRP) channels, their expression profiles, and the functional roles in tissues and whole organisms. Not only are multiple TRP isoforms commonly expressed in native cells, but also they often do not fulfill our expectations from studies of exogenously expressed channels in cultured cells (7).

Although TRPA1 has only a very limited sequence homology with TRP melastatin 8 (TRPM8), both channels can be activated by icilin and menthol. It is thus difficult for pharmacological approaches to be conclusive. However, we feel strongly that our combination of methods and the absence of evidence that TRPA1 channels are expressed on vascular myocytes (2) justify our conclusions that TRPM8 channels may, indeed, contribute to vascular tone in the vessels examined in our study with the use of menthol and icilin. The experimental approaches suggested by Ma (3) are all extremely valid. However, nonpharmacological approaches also have their own inherent problems. There are several notable examples within the field of TRP channel study where molecular interventions, such as the deletion of the gene for specific channels, have not had the effects predicted (6, 7). These studies should be done but may not be conclusive in isolation. Thus future and imminent work in the field of vascular TRPM8 and TRPA1 channels should use a combination of all the approaches available, including molecular approaches outlined by Ma (3), but should also have a strong element of functional physiology/pharmacology, using the best ligands available at the time, which are constantly being reviewed (1, 4). Indeed, controversy surrounding the roles of TRPM8 and TRPA1 proteins in cold sensation, and especially conflicting reports on the role of TRPA1 in sensory neurons (5), raises awareness that the answer to the above questions may not be simple.

REFERENCES


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