Letter to the Editor

The human G protein beta3 subunit GNB3 825T polymorphism
Meirhaeghe et al. recently showed that the T allele of a C vs T exchange at position 825 of the gene encoding for the beta3 subunit of heterotrimeric G proteins (GNB3) is associated with enhanced coronary constriction after intracoronary administration of methylergonovine[1]. The 825T allele has also been shown to be associated with an enhanced response after activation of G protein coupled receptors[2–4]. Since most vascular receptors belong to this family of heptahelical receptors, the underlying hypothesis appears conclusive, and thus, nicely confirms our own results in connection with an enhanced coronary vasoconstrictor response after alpha-adrenoceptor activation in carriers of the 825T allele at GNB3[5].

First, we would like to congratulate the authors on their interesting and thorough study. Methylergonovine itself, however, is no selective agonist at a certain receptor. It has been shown to non-selectively activate different vascular receptors, finally resulting in coronary constriction[6]. To further unravel the action by which the GNB3 825T allele increases the coronary vasomotor response, more selective agonists or antagonists are necessary. Following currently published literature, it appears likely that the 825T allele preferably enhances pathways in which pertussis toxin (PTX) sensitive G proteins are involved[2–5]. Consequently we have shown that the coronary vasoconstrictor response after activation of alpha2-adrenoceptors but not after activation of alpha1-adrenoceptors is enhanced in the presence of an 825T allele at GNB3 and may then result in substantial myocardial ischaemia[5]. Since methylergonovine, as the authors correctly state, is also capable of activating vascular alpha-adrenoceptors[6], this mechanism could have substantially contributed to the reported findings of Meirhaeghe et al. and should have been discussed.

C. K. NABER
D. BAUMGART
R. ERBEL
Centre for Internal Medicine,
Essen University, Essen, Germany

References