ONLINE SUPPLEMENT:

ETHNIC AND GENETIC DETERMINANTS OF CARDIOVASCULAR RESPONSE TO THE SELECTIVE α₂-ADRENOCEPTOR AGONIST DEXMEDETOomidine

Daniel Kurnik, MD,* Mordechai Muszkat, MD, * Gbenga G. Sofowora MD,* Eitan A. Friedman, MD,* William D. Dupont, PhD,† Mika Scheinin, MD, PhD, †† Alastair J. J. Wood, MD,* and C. Michael Stein, MD*

*Departments of Medicine and Pharmacology, Division of Clinical Pharmacology (DK, EAF, MM, GGS, AJJW, CMS), and †Department of Biomedical Statistics (WDD), Vanderbilt University School of Medicine, Nashville, Tennessee; †† Department of Pharmacology, Drug Development and Therapeutics, University of Turku, and Clinical Pharmacology, TYKSLAB, Hospital District of Southwest Finland, Turku, Finland.

Brief title: Dexmedetomidine response, ethnicity, and genes

Word count: 5,722 (total), 249 (abstract); 3 Figures

Address for correspondence: C. Michael Stein, MD, Division of Clinical Pharmacology, 542 RRB, Vanderbilt University School of Medicine, Nashville, TN 37232, Tel: (615) 936-3420, Fax: (615) 936-2746, E-mail: michael.stein@vanderbilt.edu
Genotyping: The *ADRA2C* del322-325 variant was genotyped by DNA fragment analysis as described previously. In short, a fluorescently labeled forward primer (5’-6-FAM-AGACGGACGAGAGCAGCGCA-3’) and a reverse primer (5’-AGGCCTCGCGCAGATGCCGTACA-3’) were used to amplify DNA fragments by polymerase chain reaction. Amplicons were denatured at 95°C for 5 min, and fragment analysis performed on an ABI 3730 Genetic Analyzer and its Genotyper V.1.0.1 software. The *GNB3* C825T polymorphism (rs5443) was performed by allelic discrimination with TaqMan 5’-nuclease assays on an ABI 7900 HT real-time PCR system (Applied Biosystems, Foster City, CA) using validated TaqMan probes. Genotypes were generated using a 95% quality value threshold. To ensure quality control, we included samples of known genotype (as determined by sequencing for the *ADRA2C* del322-325 variant and the detection of restriction fragment length polymorphisms for the *GNB3* C825T variant) with each genotyping run. *ADRA2C* genotypes could be determined in all 73 subjects, and *GNB3* genotypes in 72 of 73 (98.6%).
References


(2) Livak KJ. SNP genotyping by the 5'-nuclease reaction. *Methods Mol Biol.* 2003;212:129-147.

Figure Legend

Figure S1 (online supplement): Blood pressure and plasma norepinephrine responses to dexmedetomidine in ADRA2C and GNB3 genotypes. Boxes represent the interquartile range (IQR), the horizontal line the median, and whiskers the range excluding outliers (defined as values beyond the end of the box plus 1.5-fold IQR, and represented by circles). Neither ADRA2C nor GNB3 genotype was associated with responses to dexmedetomidine.