

Response to Comment on: Kretowski et al. (2007)
Polymorphisms of the Renin-Angiotensin System Genes
Predict Progression of Subclinical Coronary
Atherosclerosis: *Diabetes* 56:863–871

Adam Kretowski^{1,2} and Marian Rewers¹

We totally agree with van Beers and Meuwese (1) that our study strongly supports the association of angiotensinogen (AGT) M235T polymorphism with coronary artery calcification (CAC) progression in subjects with type 1 diabetes. However, we also believe that the additive effect of ACE and/or angiotensin type 1 receptor (ATR1) genes on CAC progression is supported by data included in our study (2).

In the logistic regression analysis among subjects with type 1 diabetes, AGT TT genotype and ATR1 AA+AC genotypes, but not ACE ID genotype, independently predicted CAC progression. When the interaction between AGT TT and ACE ID genotypes had been added to the model, this interaction was found to have a significant

effect on CAC progression ($OR_{AGT\ TT \times ACE\ ID} = 3.6, P = 0.037$), with the suggestive deviance of two studied models ($\chi^2 = 4.094, P = 0.043$). Unfortunately, we were unable to perform a test of the two-way interaction between AGT TT and ATR1 AA/AC or a test of three-way interaction due to complete separation of the data.

However, the additive effect of the AGT-ATR1 genotype combinations on the frequencies of CAC progression is supported by data in Table 4 of our study (2). CAC progression was significantly higher among subjects with the suggested AGT-ATR1 genotype combinations [TT-AA+AC vs. TT-CC: 39.5% (15/38) vs. 0.0% (0/8), $P = 0.039$, Fisher's exact test] among subjects without hypertension/albuminuria and those with albuminuria/hypertension but not treated with ACE/ARB during the follow up.

REFERENCES

1. van Beers EJ, Meuwese MC: Comment on: Kretowski et al. (2007) Polymorphisms of the renin-angiotensin system genes predict progression of subclinical coronary atherosclerosis: *Diabetes* 56:863–871. *Diabetes* 56:e5, 2007. DOI: 10.2337/db07-0400
2. Kretowski A, McFann K, Hokanson JE, Maahs D, Kinney G, Snell-Bergeon JK, Wadwa RP, Eckel RH, Ogden L, Garg S, Li J, Cheng S, Erlich HA, Rewers M: Polymorphisms of the renin-angiotensin system genes predict progression of subclinical coronary atherosclerosis. *Diabetes* 56:863–871, 2007

From the ¹Barbara Davis Center for Childhood Diabetes, University of Colorado at Denver and Health Sciences Center, Aurora, Colorado; and the ²Department of Endocrinology, Diabetology, and Internal Medicine, Medical University of Bialystok, Bialystok, Poland.

Address correspondence to Adam Kretowski, University of Colorado at Denver and Health Sciences Center—Barbara Davis Center for Childhood Diabetes, 1775 N. Ursula St., Mail Stop A140, P.O. Box 6511, Aurora, CO 80045-6511. E-mail: kretowski@uchsc.edu.

Received for publication 23 March 2007 and accepted 24 March 2007.

DOI: 10.2337/db07-0410

© 2007 by the American Diabetes Association.