Drs. Pimentel-Santos and Branco reply

To the Editor:

We appreciate the interest[1] in our report[2] in which *ANKH* polymorphisms were not identified as major determinants of susceptibility to ankylosing spondylitis (AS) and do not influence phenotypic characteristics of AS — age at disease onset or results of the Bath AS Disease Activity Index, Bath AS Functional Index, or modified Stoke Ankylosing Spondylitis Spine Score[2].

Occurrence of renal stones was not evaluated in our study of Portuguese patients with AS[2]. There are some data showing an increased prevalence of renal stone formation in patients with AS/spondyloarthritis[3,4]. Moreover it was described that the transmembrane protein *ANKH* is expressed in kidney tissues such as cilia and basal body structures, as well as epithelial cells[5]. Considering the function of *ANKH* as a pyrophosphate transporter and regulator of tissue calcification, a potential role in renal stone formation represents an interesting hypothesis for study. However, no association between *ANKH* and renal stone formation was seen in the study described by Korkmaz and Sayer[1]; it is important to mention that that study was clearly underpowered to elicit evidence for this kind of association.

Despite weak positive associations described by some authors[6,7], there is convincing evidence that the *ANKH* gene has no significant role in AS[2,8]. In addition, no association was identified with this gene and AS susceptibility in large studies using high numbers of nonsynonymous SNP[9] or in genome-wide association studies[10].

There are several concerns regarding the studies focusing on *ANKH* variants: (1) methodological differences (ethnicity, case ascertainment approaches, and *ANKH* marker variants analyzed); and (2) all of them were underpowered to detect genes with small effects consistently. Thus further studies are needed to reach definitive conclusions.

FERNANDO MANUEL PIMENTEL-SANTOS, MD, MSc, CEDOC, Faculdade de Ciências Médicas da Universidade Nova de Lisboa; I Instituto de Biotecnologia e Bioengenharia, Centro de Genómica e Biotecnologia, da Universidade de Trás-os-Montes e Alto Douro, Vila Real; Serviço de Reumatologia, Centro Hospitalar Lisboa Ocidental (CHLO), Hospital de Egas Moniz EPE, Lisbon; JAIME C. BRANCO, MD, PhD, CEDOC, Faculdade de Ciências Médicas da Universidade Nova de Lisboa; Serviço de Reumatologia, CHLO, Hospital de Egas Moniz EPE, Lisbon, Portugal. Address correspondence to Dr. Pimentel-Santos, Faculdade de Ciências Médicas, Universidade Nova de Lisboa - CEDOC, Campo Mártires da Pátria, nº130, Lisbon 1169-056 Portugal; E-mail: pimentel.santos@gmail.com

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