Coronary artery high take-off in rodents and the possible involvement of Smad2


The coronary arteries (CAs) supply the mammalian heart with oxygenated blood. They arise from the right and left aortic valve sinuses at the aortic root. In humans, the occurrence of a CA arising ectopically from the tubular aorta, a condition called high take-off (HTO), is rare (<0.4%) and predisposes to sudden cardiac death. We have shown that HTO is relatively frequent in some laboratory mouse strains, and preliminary studies suggest that the Smad2<sup>rs29725537:C>A</sup> (Smad2<sup>C>A</sup>) allele is associated with HTO in this species. In order to test whether HTO occurs in association with Smad2<sup>C>A</sup> in other rodents, we examined the anatomical origin of the CAs, by means of stereomicroscopy and a corrosion cast technique, in 3,388 specimens belonging to 17 rodent species. In addition, Smad2 DNA sequence from <i>M. musculus</i> was compared by Blastn analyses with that from six of the species examined in which this sequence is known (<i>Mus spretus</i>, <i>Rattus norvegicus</i>, <i>Apodemus sylvaticus</i>, <i>Myodes glareolus</i>, <i>Mesocricetus auratus</i>, <i>Microtus agrestis</i>). HTO occurred in nine out of 17 species studied. The incidence of HTO ranged from 0.4% to 6.5% (low) in three species and from 15.9% to 25% (high) in six species. The Smad2 sequence showed similarities higher than 75% for the whole gene, and higher than 71% for the intron sequence that includes the rs29725537;C>A Single Nucleotide Polymorphism. The Smad2<sup>C>A</sup> allele was identified only in <i>M. spretus</i> and <i>A. sylvaticus</i>, with high incidences of HTO, whereas <i>R. norvegicus</i>, <i>M. glareolus</i>, <i>M. auratus</i> and <i>M. agrestis</i> showed low or null incidences. We conclude that HTO is a common trait in rodents, which does not lead to cardiac pathology probably due to the intramyocardial condition of their CAs, as opposed to the human subepicardial CAs. The Smad2<sup>C>A</sup> allele may be involved in the development of HTO and probably other phenotypes in different rodent species.

Keywords: Coronary arteries, rodents, high take-off, Smad2, anomaly

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