# Smooth muscle phenotype in aortic diseases: Are there other histopathological markers besides contractile myofibrils?

To the Editor,

More than 30 years ago, Campbell et al. (1) published their classical paper on phenotypic changes in arterial smooth muscle cell (SMC) populations. This has developed into a highly useful concept explaining arterial wall homeostasis or pathogenesis of many arterial diseases. Vascular SMCs occur between two extreme phenotypes. The synthetic phenotype is responsible for producing most of the vascular extracellular matrix, including collagen, elastin, and glycosaminoglycans, of the ground substance during ontogenesis and growth. Under normal conditions, it gradually differentiates into the contractile phenotype with abundant actin, myosin, and desmin myofibrils, which provide mechanical support even in large elastic arteries. However, under pathological conditions such as atherosclerosis or any other arterial inflammatory disease, mechanical damage, or hypertension (2), cells switch back from the contractile to synthetic phenotype, which often possesses migratory and proliferative capabilities as well. According to our current understanding, this is a hallmark of the progression of atherosclerosis and vascular stenosis (3). The vascular SMC phenotype became a part of the histological classification of atherosclerosis (4) as well as important for assessing the vulnerability of arterial wall, a concept developed and well established in the laboratory of Renu Virmani as recently summarized by Kolodgie et al. (5).

In this issue of the Anatolian Journal of Cardiology, a manuscript entitled "Aortic α-SMA expressions in the aortic disorders and coronary artery disease: an immunohistochemical study," the authors report their findings on the distribution of α-smooth muscle actin in arterial samples taken from patients undergoing surgery for aortic dissection, aortic aneurysm, and coronary artery disease. Similar studies with a valid design are quite rare in the literature for several reasons: first, the number of patients with dissection of thoracic aorta (6) or abdominal aortic aneurysms (7), who are treated with endovascular surgery or hybrid techniques rather than with open surgery, increases. Therefore, collecting representative tissue samples for histological studies from patients undergoing open surgery usually requires a very long time. Second, most aneurysms and dissections of the aorta are accompanied with a partial or complete loss of rotational symmetry of aortic wall. As a consequence, a careful histological sampling is required to avoid sampling bias because assessment of microscopic structure from a small and incomplete part of aortic wall might provide results very different from those present in adjacent site.

From the mechanical point of view, there are other proteins relevant to the mechanical behavior of the aorta besides α-smooth muscle actin. SMCs are supposed to passively maintain the integrity of arterial wall (8) rather than actively contribute to the tension. However, a recent study (9) showed that glycosaminoglycans of the ground substance produced by SMCs are of great mechanical importance, but unfortunately, neglected in many histological studies. Similarly, integrin molecules that connect SMCs to the laminin and type IV collagen of the external lamina and therefore to the whole arterial matrix show different expression patterns in the contractile phenotype ($\alpha1\beta1$, $\alpha7\beta1$, and $\alpha8\beta1$ integrins) than in the synthetic phenotype ($\alpha2\beta1$, $\alpha5\beta1$, and $\alpha v\beta3$ integrins). In the future, we might expect that the mechanical and homeostatic function of vascular SMCs would be better explained when considering molecules binding these cells to the surrounding arterial matrix.

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