EDITORIAL

# Age-Related Changes of Caveolin-1 Expression. A New Role for Caveolins?

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In biological terms, caveola are a specialized type of small invaginations (50-100 nanometers) in the plasma membrane of several vertebrate cells that participate in the regulation of a considerable quantity of cellular functions. At cardiovascular level, they are present in almost all cardiac cells including smooth muscle cells, endothelial cells, myocyte, fibroblasts and macrophages. (1)

Caveola were discovered between 1953 and 1955 by Palade and Yamada, who demonstrated the presence of gallbladders that were not related to clathrin in endothelial cells and epithelial cells of the gallbladder. (1) Since then, these cellular structures were studied in order to know their normal functioning and, more recently, in which way their alterations are involved in different pathologies. The organization and function of caveola are given by coat proteins, called caveolins, and adaptation proteins, called cavins. Caveolin, with its three isoforms (caveolin-1, caveolin-2, and caveolin-3), form the backbone and are highly integrated in their function. Caveolin-1 and 2 are present in most of the cardiovascular system cells, while caveolin-3 is present in the smooth muscle, striated and cardiac cells. (1) On the other hand, cavins act as regulators of caveolin functioning.

Functionally, caveola participate in cellular signalling and in the regulation of vesicular transport kinetics, fulfilling in this way numerous activities. (2) Signalling function is produced thanks to the high concentration of receptors and intracellular molecules in the place of invagination, which allow an efficient signal transduction. Among other functions, caveola are inhibitors of the activity of the endothelial enzyme nitric oxide synthase (eNOS) while interacting and form a complex eNOS/caveolin-1 that decreases the formation of nitric oxide (NO). (3) In this way, caveolin-1 is an important regulator of NOS functioning. Alterations of these proteins, in different pathologies, produce modifications in NO metabolism, as it is the case of diabetes, in which the overexpression of caveolin-1 generates a negative regulation of the eNOS activity. (4) In the same way it was demonstrated that aging is associated with an increase in the expression of caveolin-1 in human fibroblasts and the reduction of these caveolins in senescent fibroblasts is able to reverse its phenotype to a level of activity similar to the one of young cells. (5)

In situations of hypovolemia, the activation of NO system during the haemorrhage is an important compensatory mechanism. In this sense, in this current issue of the Argentine Journal of Cardiology, Arreche et al. (6) considered an interesting hypothesis while studying in which way this system of adaptation could be altered with the advancing age and they try to explain these changes with the modifications in caveolin functioning. The authors demonstrate that there is a lower expression of eNOS in the group of adult animals compared with young ones. This was not correlated with the enzyme activity, as it was expressed by the authors, eNOS activity was similar both in adult and young animals. This last piece of information is opposed to the idea of aging associated with an eNOS negative regulation while increasing the expression of caveolin-1. (6) This controversy makes Arreche et al. results more interesting, while arranging the caveolin association/dissociation phenomenon with the eNOS, as although having lower expression of protein, the activity is not modified, probably as a dissociation of the eNOS with caveolin. However, in their study, the authors did not measure the expression and the activity of caveolin-1, which would have helped to answer, at least partially, this question. Surely, this question would be answered in future works.

On the other hand, a state of hypovolemia affects not only to myocyte, but also the vascular component. In this sense, caveola are important regulators of the vascular tone, due to their capacity of modulating eNOS activity. (7) Therefore, it would be interesting to evaluate the eNOS answer, at vascular endothelial level, during acute haemorrhage and also considering aging.

It is clear that there are many questions concerning this interesting topic, particularly in which way could some pathologic states that are often associated with aging as diabetes or hypertension in the adaptive response of NO, associated with hypovolemia and in relation with caveola activity affect. This is important as there is a growing interest about the role of caveola and its structural protein, caveolin-1, in the normal and pathological functioning of the cardiovascular system.

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