Available online at www.sciencedirect.com

ScienceDirect

Chronic Diseases and Translational Medicine 2 (2016) 22–26

www.keaipublishing.com/en/journals/cdtm/

www.cdatm.org

Perspective

Changes of junctions of endothelial cells in coronary sclerosis: A review

Li-Zi Zhang*, Sun Lei

Dalian Municipal Women and Children Medical Center, Pathological Department, Dalian Medical University, Dalian, Liaoning 116000, China

Received 4 March 2016

Available online 8 June 2016

Abstract

Atherosclerosis, the major cause of cardiovascular diseases, has been a leading contributor to morbidity and mortality in the United States and it has been on the rise globally. Endothelial cell–cell junctions are critical for vascular integrity and maintenance of vascular function. Endothelial cell junctions dysfunction is the onset step of future coronary events and coronary artery disease.

Keywords: Coronary atherosclerosis; Junctions; Endothelial cells

Atherosclerosis, the major cause of cardiovascular diseases, has been a leading contributor to morbidity and mortality in the United States[1] and it has been on the rise globally. Endothelial cell–cell junctions are critical for vascular integrity and maintenance of vascular function. Endothelial cell junction dysfunction is the onset step of future coronary events and coronary artery disease. After a brief review of the pathophysiology of coronary atherosclerosis, we will discuss the changes of junctions between endothelial cells during coronary sclerosis.

Junctions of coronary artery endothelial cell (ECs)

Vascular endothelial cells are a continuous flat monolayer cells which constitute a dynamic and highly effective cellular barrier between the vessel wall and bloodstream. It regulates fluid and solute balance in addition to movement of molecular/cellular components between the bloodstream and tissues[2] and presents a nonthrombogenic surface for blood flow. As such, the regulation of the endothelial barrier integrity (or permeability) is a central pathophysiologic mechanism of many vascular processes, including wound healing, angiogenesis, and vascular diseases.[3] The endothelial barrier function is predominantly maintained by the interendothelial junction structures

* Corresponding author.
E-mail address: 120091095@qq.com (L.-Z. Zhang).

Peer review under responsibility of Chinese Medical Association.

Production and Hosting by Elsevier on behalf of KeAi

http://dx.doi.org/10.1016/j.cdtm.2016.05.001

including tight junctions, adherence junctions, and gap junctions[4] which is regulated by a complex signaling network.

The formation of coronary sclerosis

Atherosclerosis, the major cause of cardiovascular diseases, has been a leading contributor to morbidity and mortality in the United States and it has been on the rise globally.

Endothelial dysfunction is a predictor of future coronary artery disease (CAD).[5] The changes of endothelium in atherosclerosis include ECs proliferation, atrophy and degeneration. The damaged structure of degenerative EC junctions leads to bareness of subendothelial proliferative fibrous tissue. The barrier functions of vascular endothelium are reduced or lost, leading to extracellular edema and lipid in the blood easily penetrating into the vascular wall. When the functions of vascular enthothelium are damaged and subendothelial collagen tissue is exposed, platelets adhere and aggregate and inflammatory cells and monocytes infiltrate, and then a thrombus is formed.

Changes of tight junction

The tight junction (TJ) is localized at cell–cell contact sites between ECs. It serves as a paracellular barrier to restrict the movement of ions and proteins across tissue boundaries.[6] Dysfunction of the TJ occurs in response to a variety of inflammatory stimuli and also during ischemia, leading to tissue edema and damage. The proteins that form tight junctions include occludin, claudin family members, junctional adhesion molecules 1 to 3, cingulin 7H6, spectrin, and linker proteins, such as the zonula occludens family members (ZO-1/2/3).[7]

Occludin

Occludin, which has four transmembrane domains, forms a rate-limiting transport structure within the intercellular cleft.[8] Occludin contains two extracellular loops forming a junctional seal. The carboxy tail of occludin is linked to the actin cytoskeleton via ZO-1, ZO-2 and ZO-3. ZO-1 plays a central role in the organization and assembly of the transmembrane proteins. ZO-1 protein levels, in contrast to occludin levels, are most likely not regulated by oxidized lipids, vascular endothelial growth fact (VEGF), or shear stress; however, they may be affected by oxidants.[9] The most prominent changes induced by oxidative stress were decreased tyrosine phosphorylation of occludin and increased serine/threonine phosphorylation of ZO-1.

Claudin

Claudins play an essential role in the control of paracellular ions flux and in the maintenance of cell polarity.[10] Claudin has four transmembrane domains but no sequence similarity to occludin. It has not yet been defined as to how these novel proteins interact with occludin or other TJ components. The claudin-5 protein was initially considered to be a TJ component of the claudin protein family.[11]

Junctional adhesion molecules

Junctional adhesion molecules (JAMs), currently are composed of JAM-A, -B, -C,[12] JAM-4, ESAM (EC-selective adhesion molecule), and CAR (coxsackie virus and adenovirus receptor) that localize at cell–cell contacts and are specifically enriched at tight junctions with some being directly implicated in leukocyte transendothelial cell migration.[13]

JAM-A

JAM-1, also known as JAM-A, is a transmembrane protein which is found on endothelial and epithelial cells at cell–cell contacts in particular within tight junctions. JAM-A binds in a homotypic manner to regulate tight junction integrity and permeability.[14] JAM-A may regulate the basic fibroblast growth factor (bFGF) and extracellular signal–regulated kinases (ERK) signaling pathways involved in EC migration, leading to wound repair. JAM-1 has a PDZ domain–binding motif, through which it binds other PDZ domain–containing tight junction proteins, such as zona occuldens protein 1 (ZO-1), partitioning defective-3 homologue (PAR-3), and Afadin 6 (AF-6).[15]

JAM-B

In contrast, JAM-B, also referred to as vascular endothelial-junctional adhesion molecule (VE-JAM) is prominently expressed at intercellular boundaries of the endothelium, particularly in venules. JAM-B is also involved in adhesive processes of lymphocytes.[16]

JAM-C

JAM-C provides a novel molecular target for antagonizing interactions between vascular cells that promote inflammatory vascular pathologies such as in