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Editorial

The Trajectory of Recent Developments in Atherosclerosis

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Atherosclerosis is one of the most common causes of cardiovascular disease (CVD), accounting for approximately 7.2 million deaths each year. The American Heart Association stated that the prevalence of atherosclerosis will increase by 18% by 2030 [1]. Atherosclerosis is a chronic inflammatory disease of the great arteries that is the main cause of cardiovascular disease and stroke [2]. Atherosclerosis is an inflammatory disease of the great and important arteries that is the main source of stroke and CVD. It is assumed that atherosclerosis is caused by many factors including environmental and genetic.

Diseases such as stroke and myocardial infarction secondary to atherosclerosis have high mortality worldwide. In humans, clinical complications take several decades to develop. There are various risk factors such as hypertension, hypercholesterolemia, smoking and diabetes mellitus, which play a role in the emergence of atherosclerosis; however, in the pathogenesis of atherosclerosis in general; In addition to existing risk factors, it is believed that there is a vascular and chronic inflammation that starts with the interaction of cells in the arterial wall with each other. In the last 3 decades, the molecular mechanisms leading to the pathogenesis of atherosclerosis have been extensively investigated using genetically modified animals, and it has been noted that drugs such as lipid-lowering statins are very effective ways to prevent and treat atherosclerosis [3].

Atherosclerotic plaques are complex structures made up of vascular cells and immune cells. In maintaining the fluid balance between endothelial barrier integrity, circulation, tissues and vascular homeostasis; vascular endothelial cells play a key role. Studies show an association between endothelial dysfunction, elevated levels of endothelial factors, coronary artery disease, and intensification of atherosclerosis [4,5].

The data obtained in studies on atherosclerosis in human and animal experiments focus on the multifunctional structures of macrophages in the pathogenesis of atherosclerosis. Macrophages are important in intracellular lipid accumulation and formation of foam cells, in the atherosclerotic process [6]. Over time, the foam cells die and necrotic nuclei are formed, consisting of cell debris and cholesterol. In addition, vascular smooth muscle cells (VSMCs) turns from the contractile state to the proliferative state and migrate to the region below the endothelial cells (ECs) to form a "fibrous cap" that prevents rupture of the atherosclerotic lesion. SMC can also differentiate into macrophage-like cells that form foam cells and bone-like cells that store calcium phosphate. Although the lesions may become large enough to impede blood flow, the most clinically significant event is myocardial infarction (MI) resulting from rupture of the lesion or erosion of the endothelium-induced clot formation [7].

In a study by Luo et al., it was thought that CD146, as a new capture signal, could create a new therapeutic for the treatment of atherosclerosis with an effect that captures macrophages in the artery Wall [8]. Moreover, phenotype of macrophages; they are affected by different stimuli that influence their apoptosis, polarization, proliferation and efferocytosis. Recently, the heterogeneity of macrophages involved in atherosclerotic lesions has been examined by methods such as single cell sorting techniques [9]. Due to defective phagocytosis of apoptotic foam

cells, there may be consequences supporting the progression of chronic and unresolved inflammatory diseases such as advanced atherosclerosis [10]. In macrophagic CD146 studies, genetic deletion or targeting with an antibody; As lipid-laden macrophages left atherosclerotic plaques, ApoE-/- mice that received a high-fat diet led to the development of much less complex plaques.

As an alternative pathway, the nitrate-nitrite-NO pathway recycles dietary or endogenous nitrite and inorganic nitrate independently of the NOS system by serial reduction to form bioactive nitrogens, including NO. Signaling with these nitrogen contents is associated with cGMP-dependent or non-cGMP-dependent mechanisms. New approaches to restore NO homeostasis in NOS deficiency and during oxidative stress have potential therapeutic applications in cardiovascular, renal, and metabolic disorders [11].

Urotensin II (U-II) is known as an important vasoactive peptide in humans and various experimental animal models through interaction with the UT receptor. In recent studies, it has been reported that the level of U-II is increased in the plasma of patients with coronary artery disease and atherosclerosis. U-II is particularly expressed in endothelial cells, VSMCs, and inflamed macrophages in human atherosclerotic coronary arteries. Expression of the UT receptor is upregulated with inflammatory stimuli. Activation of the UT receptor; It stimulates proliferation of endothelial cells and VSMCs and monocyte chemotaxis. Therefore, in addition to its primary vasoactive effect, it suggests that U-II and UT receptors play a role in the initiation and/or progression of atherosclerosis [12]. It is also an important player in the inflammatory injury process that causes to the development of inflammatory diseases. Urotensin-II/UTR expression; It stimulates the accumulation of monocytes and macrophages, which promotes expression of adhesion molecules, activation of chemokines, and release of inflammatory cytokines at sites of inflammatory injury. Moreover, U-II is emerging as therapeutic target for associated diseases [13].

Studies to date have determined that U-II, the most potent vasoconstrictor peptide identified, increases macrophage foam cell formation and VSMCs proliferation, and its levels increase in the plasma of people with hypertension. U-II is important in the formation of atherosclerosis, but its role in atherosclerotic plaque stability is not yet known. In the study of Shiraishi et al., it was defined that increased plasma U-II level increased the production of oxidized low-density lipoprotein and reactive oxygen species. Meanwhile increased CD36; evidence is provided that it stimulates macrophage foam cell formation through expression of scavenger receptor class A and acylCoA: cholesterol acyltransferase-1. Mice deficient in apolipoprotein E are predisposed to develop atherosclerosis. An antagonistic drug against the U-II receptor could be a promising therapeutic strategy against atherosclerosis [14]. Recently, issues regarding the role of the immune response in the development of atherosclerotic lesions have been addressed. There is a particular focus on reducing the risk of cardiovascular disease based on experimental and clinical data supporting the development of immune therapies. The immune inflammatory response in the process of atherosclerosis, modern atherogenesis concepts and potential vaccine targets are also discussed [15].

Consequently; The distribution of U-II and UT within tissue is consistent and their expression can be regulated via autocrine and paracrine mechanisms. U-II has different physiological and pathophysiological activities in the body, such as cell proliferation, vasoconstrictor and vasodilator effects, insulin resistance, neuroendocrine activity, pro-fibrosis, carcinogenic and inflammatory effects, which have only recently been noticed. In fact, U-II is present in the process of inflammatory injury and in the initiation and development of inflammatory diseases. Atherosclerosis is an inflammation-induced disease, and macrophages play a central role in the pathogenesis of atherosclerosis and in the control of all stages of the inflammatory process. Understanding the differentiation of monocytes into pro- or anti-inflammatory macrophages in atherosclerotic lesions and how these cells influence atherosclerotic plaque formation and development has a potential role in managing the atherosclerotic process. U-II expression is increased in atherosclerotic lesions in the coronary artery, carotid artery and aorta. It has been suggested that increased expression of U-II leads to VSMCs proliferation, which accelerates the development of atherosclerotic plaque. It has also been reported that locally released U-II causes coronary vasoconstriction and myocardial ischemia. Recent studies have shown that U-II expression is downregulated in Acute Coronary Syndrome, which is thought to be related to its ability to modulate mechanisms related to plaque stability and instability. These results will demonstrating the behavior of autocrine U-II in the development of the atherosclerotic process by accumulating

macrophage-derived foam cells and continue to elucidate the important role of U-II in the atherosclerotic process. Revealing the histopathological features of arterial grafts associated with atherosclerosis will be useful to shed light on the unknowns to improve late survival after Coronary artery bypass grafting [16]. In addition, factors such as the role of gender as a crucial risk factor in atherosclerosis, modulation of the post-transcriptional atheroma plaque by microRNAs and lncRNAs, and the role of microbiota in atherosclerosis are important to provide a global view of the disease.

Bibliography

1. Benjamin EJ., *et al*. "Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association". *Circulation* 137 (2018): e67-e492.

2. Kong P., *et al*. "Inflammation and atherosclerosis: signaling pathways and therapeutic intervention". *Signal Transduction and Targeted Therapy* 7.1 (2022): 131.

3. Fan J and Watanabe T. "Atherosclerosis: Known and unknown". *Pathology International* 72.3 (2022): 151-160.

4. Shao C., *et al*. "Coronary artery disease: from mechanism to clinical practice". *Advances in Experimental Medicine and Biology* 1177 (2020): 1-36.

5. Jebari-Benslaiman S., *et al*. "Pathophysiology of Atherosclerosis". *International Journal of Molecular Sciences* 23.6 (2022): 3346.

6. Takahashi K., *et al*. "Multifunctional roles of macrophages in the development and progression of atherosclerosis in humans and experimental animals". *Medical Electron Microscopy* 35.4 (2002): 179-203.

7. Björkegren JL M and Lusis AJ. "Atherosclerosis: Recent developments". *Cell* 185.10 (2022): 1630-1645.

8. Luo Y., *et al*. "Macrophagic CD146 promotes foam cell formation and retention during atherosclerosis". *Cell Research* 27.3 (2017): 352-372.

9. Farahi L., *et al*. "Roles of Macrophages in Atherogenesis". *Frontiers in Pharmacology* 12 (2021): 785220.

10. Wang L., *et al*. "Potential Mechanisms and Effects of Efferocytosis in Atherosclerosis". *Frontiers in Endocrinology (Lausanne)* 11 (2020): 585285.

11. Carlström M. "Nitric oxide signalling in kidney regulation and cardiometabolic health". *Nature Reviews Nephrology* 17.9 (2021): 575-590.

12. Loirand G., *et al*. "Urotensin II and atherosclerosis". *Peptides* 29.5 (2008): 778-782.

13. Rex DAB., *et al*. "The network map of urotensin-II mediated signaling pathway in physiological and pathological conditions". *Cell Communication and Signaling* 16 (2022).

14. Shiraishi Y., *et al*. "Chronic urotensin II infusion enhances macrophage foam cell formation and atherosclerosis in apolipoprotein E-knockout mice". *Journal of Hypertension* 26.10 (2008): 1955-1965.

15. Poznyak A V., *et al*. "Vaccination against Atherosclerosis: Is It Real?". *International Journal of Molecular Sciences* 23.5 (2022): 2417.

16. Bahar L and Tuysuz ME. "The relation of left internal mammary artery atherosclerosis with urotensin-II". *Bratislavske Lekarske Listy* 121.7 (2020): 516-521.