Journal of Clinical & Experimental Pathology

Kumar et al. J Clin Exp Pathol 2021, 11:S12

Short Communication Open Access

Macrophage Subtypes, Phenotypes, Inflammatory Molecules, Cytokines, and Atherosclerotic Lesions: Atherosclerosis, Metabolic Diseases and Pathogenesis, the Therapeutic Challenges

Rajiv Kumar[1*] **and Mitrabasu Chhillar**[2]

[1]*Department of Chemistry, NIET, National Institute of Medical Science, Delhi, India*

[2]*Department of CBRN Defence, Institute of Nuclear Medicine and Allied Sciences (INMAS), Naval Dockyard, Mumbai, India*

[*]**Corresponding author:** Rajiv Kumar, Department of Chemistry, NIET, National Institute of Medical Science, Delhi, India, E-mail: chemistry_rajiv@hotmail.com

Received date: June 21, 2021; **Accepted date:** July 05, 2021; **Published date:** July 12, 2021

Abstract

Macrophages, the phagocytes are considered the main cause for atherosclerosis, and any change or alteration in their dynamics is identified as the foremost cause for the development of atherosclerotic plaque microenvironment. These biophysical changes stimulus the defenselessness or steadiness of progressive atherosclerotic lesions and promote the route of plaque progression.

Keywords: Macrophages; Inflammation; Progression; Lipids

Description

Macrophages, the phagocytes are considered the main cause for atherosclerosis, and any change or alteration in their dynamics is identified as the foremost cause for the development of atherosclerotic plaque microenvironment. These biophysical changes stimulus the defenselessness or steadiness of progressive atherosclerotic lesions and promote the route of plaque progression. Thereafter, the macrophages are arranged in classes or categories such as subtypes are classically activated M1 and alternatively activated M2 macrophages. More investigations are going on and their participation in vascularization on plaque progression [1]. Macrophage phenotypes influenced endothelial cell activities and enfolded themselves to form bridge nearby vessels. These macrophages subtype displayed pro-inflammatory or anti-inflammatory characteristics and fixed differentiation in the atherosclerotic plaques. The interpretation of the pieces of machinery of macrophage phenotypes, signaling pathways, and mechanical forces of cell machinery can escort in the development of novel therapeutic strategies to treat mycobacterial pathogenesis, atherosclerosis, and metabolic diseases [2]. Inflammation initiated by macrophages changed or alter the macrophage phenotypes and their operational styles in atherosclerotic plaque progression, as a result, several consequences were initiated such as arterial thrombosis, which led to myocardial infarction and other clinical events. In the atherosclerotic plaque microenvironment, the activities of dynamic alterations in macrophage numbers and macrophage differentiation materialized [3]. Macrophages are considered key features of them, which transpired in atherosclerotic lesions, governed the inflammatory milieu and plaque stability [4]. These macrophages can secrete several inflammatory molecules, cytokines, and growth factors. A proper investigation of macrophage phenotypes can provide a scientific look regarding their functioning styles and associated routes. Such findings will defiantly boost the chances of applied for discovering the pharmacological treatment of atherosclerosis and expose hurdle persisted in pathophysiological consequences.

The build-ups of lipids in the vascular wall are referred to as a major root cause that is responsible for the local inflammation, further initiates the expansion and progression of atherosclerosis, macrophages, and identified as the main contributor [5]. The cytokines sculpt are other constituents of the microenvironment for governing the reactivity phenomenon of macrophages and the dynamic plasticity. The proper exploration of mechanisms of biological routes and functional consequences generated by one of the macrophages (M2) lead towards a proper investigation and further categorized into M2a, M2b, M2c, and M2d subtypes, and besides this, the plaque-specific macrophage phenotypes have different varieties i.e. Mox, Mhem, and M4, that will play a specific role in lesion expansion and plaque steadiness in Figure 1 [6]. The elucidation and examinations of the plasticity and modulation of the macrophage phenotype are always considered by the researchers as the main objective. These findings were found suitable for defying the routes of atherosclerosis, metabolic diseases, pathogenesis, and also the newly originated chronic inflammation during the pathogenesis of metabolic diseases as per their beliefs and thoughtfulness.

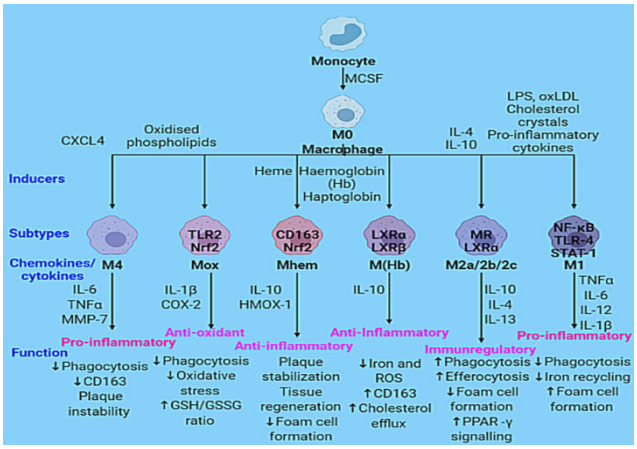

Figure 1: Diagram for illustrating the macrophage subtypes, phenotypes, inflammatory molecules, cytokines, and atherosclerotic lesions. "Acknowledged [biorender.com] for permission to adapt and create the figure".

It was observed that M2 macrophages, extremely heterogeneous which enhanced plasticity to cells, interlinked with the regression of atherosclerosis and secrete the anti-inflammatory factors: IL-10 and TGF-β for stimulating and initiating tissue remodeling, collagen formation, and burying of dead cells via efferocytosis [7]. Further, the aforementioned macrophages participate in the formation of the necrotic core, routes of plaque rupture, and thermogenesis. The physiology of accumulation, metabolism, and chronic inflammatory response is identified as specific causes responsible for the progression of the pathogenesis of diseases such as atherosclerosis, myocardial infarction, and stroke [8]. One of the authors (MB) highlighted the mechanism of atherosclerosis progression, identified few cellular activities of lesions at the time of disease progression, and described macrophage subtypes of atherosclerotic plaques [9].

"Atherosclerosis can be accentuated as an inflammatory insult, initiated in the physiology decades before the disease testified" pointed out by the other author (RK) [10]. But, he also stated that it is not feasible to identify these physiological variations by any detection method in early stages and as of today, no clinical answer or setting existed to continue it. The understanding of the pathogenesis of atherosclerosis can upgrade conceivable strategies intended for its treatment and will enrich the openings by improving target-specific therapies [11]. Different classes of therapies can be offered to heal inflammatory pathways and to inhibit the atherosclerotic route. Metabolic activities and interconnected abnormalities engender new diseases such as hypertension, central obesity, insulin resistance, and atherogenic dyslipidemia, later on, these revealed mechanisms initiate the propagation of the cardiovascular disease and headed it for a fatal condition [12]. The pathogenesis of metabolic activities involves various factors to promote the pathways of inflammation that again propagate cardiovascular diseases [13]. The aforementioned biochemical and biophysical routes initiate oxidative stress and aggravate disease states. Various pharmacological remedies are prescribed to treat atherosclerosis. But, sometimes this therapeutics initiates severe side effects and further worsens it and transformed it into a more complicated stage [14]. Several herbal components were also acclaimed to combat these pathological conditions and aforementioned situations, for example, patients suffering from atherosclerosis also have diabetes. The most important aspects of these investigations are the interpretation of atherosclerotic plaque formation routes and later on, these findings can be exploited to explore the possibilities to search for a better therapeutic option by recommending the aforementioned bioactive compounds as better therapeutics. These natural remedies can intervene and blocked the biological routes by promoting atherosclerosis and other cardiovascular diseases [15].

The inflammatory cytokines were identified as a major component responsible for triggering and perpetuating a dangerous signal response and stimulates atherosclerosis and the same was referred [16]. The investigation of interactions originated between macromolecules and the immune system is a good option to detect various physiological possibilities and search concerning foundations interlinked with the pathophysiology of atherosclerosis and associated with such metabolic activities [17]. Furthermore, the authors suggested and underlined various therapeutic options, which can be specifically applied to target the metabolic irregularities and pathogenesis routes underlined considered in this opinion on macrophage subtypes, phenotypes, inflammatory molecules, cytokines, and atherosclerotic lesions. Therefore, to suggest a piece of better advice for dealing with the therapeutic challenges associated with atherosclerosis, metabolic diseases, and pathogenesis, an urgent need is there to suggest several other scientific bits of intelligence that can be tested.

References

1. Jinnouchi H, Guo L, Sakamoto A, Torii S, Sato Y, et al. (2020) Diversity of macrophage phenotypes and responses in atherosclerosis. Cellu Mole Life Sci 77: 1919-1932.
2. Momtazi-Borojeni AA, Abdollahi E, Nikfar B, Chaichian S, Ekhlasi-Hundrieser M (2019) Curcumin as a potential modulator of M1 and M2 macrophages: new insights in atherosclerosis therapy. Heart Failure Rev 24: 399-409.
3. Saqib U, Sarkar S, Suk K, Mohammad O, Baig MS, et al. (2018) Phytochemicals as modulators of M1-M2 macrophages in inflammation. Oncotarget 9: 17937-17950.
4. Tomiotto-Pellissier F, Bortoleti BT da S, Assolini JP, Gonçalves MD, Carloto ACM, et al. (2018) Macrophage polarization in leishmaniosis: Broadening horizons. Frontiers Immun 9: 2529.
5. Zhang M, Hutter G, Kahn SA, Azad TD, Gholamin S, et al.(2016) Anti-CD47 treatment stimulates phagocytosis of glioblastoma by M1 and M2 polarized macrophages and promotes M1 polarized macrophages in vivo. PloS One 11: e0153550.
6. Cardilon-Reis L, Gruber S, Schreier SM, Drechsler M, Papac-Milicevic N, et al. (2012) Interleukin-13 protects from atherosclerosis and modulates plaque composition by skewing the macrophage phenotype. EMBO Mol Med 4: 1072-1086.
7. Ma Y, Mouton AJ, Lindsey ML (2018) Cardiac macrophage biology in the steady-state heart, the aging heart, and following myocardial infarction. Translat Res 191: 15-28.
8. Tay C, Liu YH, Kanellakis P, Kallies A, Li Y, et al. (2018) Follicular B cells promote atherosclerosis via T cell-mediated differentiation into plasma cells and secreting pathogenic immunoglobulin G. Arterioscler Thromb Vasc Biol 38: 71-84.
9. Kumar R, Chhikara BS, Gulia K, Chhillar M (2021) Cleaning the molecular machinery of cells via proteostasis, proteolysis and endocytosis selectively, effectively, and precisely: intracellular self-defense and cellular perturbations. Mol Omi 17: 11-28.
10. Andreou DE, Andreadou I (2009) Atherosclerosis: An inflammatory disease. Pharmakeftiki 22: 83-96.
11. Van Duijn J, van Elsas M, Benne N, Depuydt M, Wezel A, et al. (2019) CD39 identifies a microenvironment-specific anti-inflammatory CD8+ T-cell population in atherosclerotic lesions. Atheroscl 285: 71-78.
12. Paramel G V, Karadimou G, Eremo AG, Ljungberg LU, Hedin U, et al. (2020) Expression of CARD8 in human atherosclerosis and its regulation of inflammatory proteins in human endothelial cells. Sci Rep 10: 1-11.
13. Kim M, Sahu A, Hwang Y, Kim GB, Nam GH, et al. (2020) Targeted delivery of anti-inflammatory cytokine by nanocarrier reduces atherosclerosis in Apo E−/-mice. Biomater 226: 119550.
14. Kumar R, Gulia K (2021) The convergence of nanotechnology-stem cell, nanotopography-mechanobiology, and biotic-abiotic interfaces: Nanoscale tools for tackling the top killer, arteriosclerosis, strokes, and heart attacks. Nano Sel 2: 655-687.
15. Li J, Lin S, Vanhoutte PM, Woo CW, Xu A (2016) Akkermansia muciniphila protects against atherosclerosis by preventing metabolic endotoxemia-induced inflammation in Apoe-/-Mice. Circul 133: 2434-2446.
16. Grassin-Delyle S, Abrial C, Salvator H, Brollo M, Naline E, et al. (2020) The role of toll-like receptors in the production of cytokines by human lung macrophages. J Innate Immun 12: 63-73.
17. Abdolmaleki F, Gheibi Hayat SM, Bianconi V, Johnston TP, Sahebkar A (2019) Atherosclerosis and immunity: A perspective. Trends Cardiovas Med 29: 363-371.