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Review

The use of monoclonal antibodies for the treatment of atherosclerosis: current status and prospects

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Abstract

Atherosclerosis remains a leading cause of cardiovascular morbidity and mortality worldwide, underlying major conditions such as coronary heart disease and stroke. The pathogenesis of atherosclerosis is tightly linked to chronic inflammation and dysregulated lipid metabolism, processes that are also implicated in other inflammatory diseases like rheumatoid arthritis and psoriasis. Monoclonal antibodies (mAbs) have emerged as a promising therapeutic strategy, offering targeted intervention against key molecular drivers of atherosclerosis. This review summarizes recent advances in the development and clinical application of mAbs targeting both lipid-lowering pathways—such as low-density lipoprotein (LDL) and proprotein convertase subtilisin/kexin type 9 (PCSK9)—and inflammatory mediators, including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-17 (IL-17). Notably, anti-PCSK9 antibodies like alirocumab and evolocumab have demonstrated significant reductions in LDL-C levels and cardiovascular events in large-scale clinical trials. Similarly, antibodies targeting inflammatory cytokines have shown efficacy in reducing vascular inflammation and associated risks. The review also discusses the advantages and limitations of therapeutic mAbs, such as their high specificity, potential for adverse immune responses, and challenges related to tissue penetration and cost. Overall, monoclonal antibody therapy represents a significant advancement in the management of atherosclerosis, with ongoing research aimed at optimizing efficacy, safety, and accessibility. Future directions include the development of novel mAbs and combination therapies to further improve cardiovascular outcomes in patients with atherosclerotic disease.

Keywords: Monoclonal antibodies, Atherosclerosis, Inflammation, PCSK9.

1. Introduction

Atherosclerosis (AS) is a common and severe disease of the arteries that is one of the leading causes of cardiovascular mortality. Atherosclerosis affects millions of people worldwide each year, and its incidence increases with age, reaching 50% in people aged 75 to 79 years [1]. The most common risk factors are hypercholesterolemia (LDL-cholesterol), hypertension, diabetes mellitus, cigarette smoking, age, male gender, and a strong family history (male relative under 55 years and female relative under 65 years). In addition, a sedentary lifestyle, obesity, diets high in saturated and trans fatty acids, and certain genetic mutations contribute to the risk. Since atherosclerosis is a largely asymptomatic condition, it is difficult to accurately determine the incidence. Atherosclerosis is considered the main cause of cardiovascular disease. Atherosclerotic cardiovascular diseases mainly affect the heart and brain: coronary heart disease (CHD) and ischemic stroke. CHD and stroke are the first and fifth causes of death worldwide, respectively [2].

Traditionally, AS is treated with lipid-lowering drugs and surgical interventions such as angioplasty [3]. Statins serve as the cornerstone for reducing low-density lipoprotein cholesterol levels and the risk of major adverse cardiovascular events (MACE) [4]. However, some patients with atherosclerotic cardiovascular disease (ASCVD) require additional drugs to minimize low-density lipoprotein (LDL) levels and MACE risk in addition to statins. In response to the need to discover innovative therapeutic strategies, researchers are increasingly focusing on inflammatory chemokines and adhesion molecules, such as interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), etc. These molecular players attract immune cells, especially cholesterol-laden macrophages, triggering foam cell formation and arterial plaque accumulation [5].

Monoclonal antibodies (mAbs) are highly homogeneous antibodies designed to target only one specific epitope. Numerous novel mAbs focus on inflammation and

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lipid metabolism, which are known as important processes of AS, and the use of mAbs in the treatment of cardiovascular disorders has been demonstrated to significantly enhance the survival of patients. [6].

The analysis of research on antibody-based therapies targeting LDL and pro-inflammatory cytokines is the main focus of this review. Therapeutic antibodies are stable molecules well-suited for targeted therapy, possessing the ability to bind to specific proteins with high specificity and affinity, thereby preventing their pathological effects. Recent advances in antibody technology have enabled the successful clinical application of antibody-based therapeutics, despite several challenges such as incomplete understanding of their mechanisms of action, limited tissue penetration, and reduced immune responses. As of now, the US Food and Drug Administration has approved over 79 antibody-based therapeutics, with more than 570 antibody therapies currently under investigation worldwide. Continued progress in the development of antibody-based therapies targeting atherogenic factors will be crucial for advancing the treatment of chronic inflammatory and cardiovascular diseases [7]. As of now, the US Food and Drug Administration has approved more than 79 antibody-based therapeutics, with over 570 antibody therapies currently under investigation worldwide. The continued development of antibody-based therapies targeting atherogenic factors will be crucial for advancing the treatment of chronic inflammatory and cardiovascular diseases.

2. Analysis of current studies on the use of monoclonal antibodies in the treatment of atherosclerosis

2.1. Autoantibodies to apolipoprotein B

Prior research has demonstrated that atherosclerotic plaques contain significant levels of autoantibodies that identify different oxidized LDL epitopes [9-12]. Additionally, atheroprotective impacts including a decrease in inflammation in atherosclerotic plaque, have been demonstrated in animal experiments employing IgG antibodies targeted to an epitope of oxidized LDL. MDA-p45, an MDA-modified peptide of apo B-100, raised MDA-p45 IgG concentrations and decreased atherosclerotic plaque formation in apoE-deficient mice. Anti-p45 IgG experiments have repeatedly shown that atherosclerotic plaque growth is inhibited, indicating the potential advantages of using anti-p45 for atherosclerosis treatment [13,14].

Targeting oxLDL (MDA-modified human ApoB-100), MLDL1278a (Orticumab) has anti-inflammatory properties. Orticumab was demonstrated to improve the activity of immune cells, raise insulin sensitivity, and dramatically lower proinflammatory cytokine levels in obese rhesus monkeys in later study [10], [15]. Clinical findings, however, indicated that the degree of arterial disease was negatively correlated with the levels of MDA-modified p45 peptide and p210 autoantibodies; additionally, one study found that an anti-oxLDL antibody did not significantly decrease carotid plaque inflammation in patients who have cardiovascular disease [16]. In a phase II study of 147 patients with atherosclerosis, MLDL1278A given in addition to statin therapy showed no statistically significant differences in lipid and C-reactive protein (CRP) levels compared to controls [17]. A possible explanation for the lack of desired anti-inflammatory effect may be that MLDL1278A targets oxLDL, which is present in inflamed plaques, and in the study conditions, patients on chronic statin therapy had reduced levels of diseased atherosclerotic plaques.

2.2. Anti-PCSK9

LDL-C decreasing is a crucial way to mitigate the illness, and PCSK9 is involved in the molecular process of this reduction. By attaching itself to LDL receptors on the cell surface, circulating plasma LDL is absorbed. The LDL receptor is subsequently reused and expressed on the cell surface, while the absorbed LDL particles are taken to the lysosome and broken down [18]. But when PCSK9 is present, the LDL receptor attaches to PCSK9 to create a PCSK9-LDL receptor-LDL group [19]. Both LDL and LDL receptors are degraded as a consequence of this complex being absorbed into the cell and sent to the lysosome [20]. Higher quantities of LDL cholesterol particles in the plasma, which act as a stimulus for atherosclerosis, occur from the inability to recycle LDL receptors and the decline in the amount of LDL receptors on the cell surface [21].

Serum PCSK9 concentrations may therefore be a helpful predictor of early atherosclerosis, based on a prior study. Pigs with the PCSK9 mutation E670G had higher enzyme activity, thicker intima-media (D374Y), lower hepatic LDL levels, and less atherosclerotic plaque formation [22]. On the other hand, a study that used a PCSK9 loss-of-function mutation revealed that this mutation is linked to the preservation of low levels of cholesterol and, thus, a decrease in the development of atherosclerosis. These findings have made PSCK9 a promising therapeutic target for atherosclerosis, and several studies have been carried out to examine the possibility of functional suppression of PCSK9 by antibody methods. The clinical trials of the antibody as a PCSK9 inhibitor were carried out after monoclonal antibodies that could disrupt the connection between LDL receptor and PCSK9 were discovered to enhance cellular LDL receptor and lower the amount of LDL-C [23].

Alirocumab and evolocumab are the two most popular human monoclonal antibodies that target PCSK9; both have received approval in the US and the EU. More than 27 thousand high-risk individuals who had previous episodes of myocardial infarction, non-hemorrhagic stroke, or symptomatic peripheral artery disease were recruited for a trial to evaluate the clinical impact of evolocumab. While using evolocumab or a placebo, all patients kept taking statins [24]. After 2.2 years of patient follow-up, the frequency of cardiovascular events was calculated by separating both primary and secondary results based on the steady decline in LDL-C levels. The evolocumab group experienced a 59% decrease in LDL-C levels after 48 weeks when compared to the placebo group. Additionally, the evolocumab group experienced a lower rate of the main effects of myocardial infarction, stroke, cardiovascular death, coronary revascularization, and unstable angina (9.8%) compared to the placebo group (11.3%) [25].

Alirocumab was studied in a multicenter clinical trial involving more than 18,000 patients with acute coronary syndrome (ACS) and conducted for 2.8 years [26]. LDL-C levels were reduced by more than 54% in the Alirocumab group compared to the placebo group, and a reduction in the risk of cardiovascular events, including myocardial infarction, was also noted.

Bococizumab is the other anti-PCSK9 antibody, which presents itself as a humanized mouse antibody. Two large

trials were done in parallel: the PCSK9 Inhibition and Vascular Event Reduction trials. Following 14 weeks, the bevacizumab group's LDL-C concentration was 59% lower than those of the placebo group. The therapy became effective for patients with high risk of cardiovascular events but did not show optimal results for low-risk individuals [27].

2.3. Anti-TNF-α

TNF-α plays a significant role in promoting inflammatory responses in various chronic diseases, including atherosclerosis. It has been observed that macrophages and smooth muscle cells within atherosclerotic plaques produce elevated levels of TNF-α [28]. Crucially, TNF-α was continuously raised in individuals who had had myocardial infarction and were being watched for recurrent MACEs (major adverse cardiovascular events). The proinflammatory cytokine TNF-α has been identified as a powerful therapeutic target for cardiovascular disorders since it has been demonstrated that inflammation plays a crucial role in this condition [29].

The treatment of rheumatoid arthritis has advanced significantly as a result of long-term research on anti-TNF-α therapy, which uses monoclonal antibodies that precisely adhere to and deactivate TNF-α pathological action [30]. Carotid atherosclerotic plaques were discovered in 15% of patients acquiring TNF-α antagonists infliximab and adalimumab in a pilot clinical trial evaluating the effectiveness of anti-TNF-α monoclonal antibodies in psoriatic arthritis, compared to 40% of patients getting traditional DMARDs [31]. Infliximab, an anti-TNF-α antibody, also was used in another clinical trial that showed that patients with rheumatic disorders who took this medicine had a lower risk of cardiovascular disease [32]. Therapy of psoriasis with infliximab considerably decreased cardiovascular risk when compared to other therapies for psoriasis, which have been analyzed during 5 years [33].

Apart from infliximab, other antibodies like golimumab and certolizumab pegol have been developed to target TNF-α. Golimumab is human monoclonal antibody, and certolizumab pegol is a pegylated fragment of an anti-TNF-α antibody [34]. A phase 3 clinical trial revealed that individuals who had moderate to severe psoriasis and received certolizumab pegol were more inclined to demonstrate a decrease in PASI 75 (psoriasis area and severity index >75%) [35]. Golimumab has been approved as single-agent therapy as a drug for inflammatory arthritic diseases including psoriatic arthritis and rheumatoid arthritis; several phase 3 studies have proven its stability and effectiveness, and the effect was not inferior when compared indirectly to other anti-TNF-α therapies [36].

2.4. Anti-IL-1β

Because IL-1 signaling causes the expression of secondary inflammatory cytokines like IL-6, it plays one of the main roles in the launch of inflammation of atherosclerosis and other inflammatory diseases. IL-1α and IL-1β are the two variants of the IL-1 protein; the beta form is considered more significant for the launch of inflammation [37]. The enzyme caspase 1 cleaves the inactive form of IL-1β, pro-IL-1β, to produce the physiologically active form, IL-1β [38]. TNF-α and cholesterol crystals are examples of mediators that enhance the production of IL-1β [39]. While numerous research have been done to investigate its function as a target for therapy in atherosclerosis, IL-1β has not been described as a potential molecular marker for cardiovascular disease due to the contrast to such cytokines as CRP and IL-6, its levels in the blood are difficult to quantify directly [40].

Different rheumatic inflammatory illnesses can be treated with approved mAb canakinumab, a fully human monoclonal antibody against IL-1β. Moreover, some research has demonstrated that canakinumab considerably lowers inflammation without affecting LDL-C, indicating that it could be employed as a medication to inhibit the inflammatory process associated with atherosclerosis development [41].

In the CANTOS study of 17,000 patients with coronary heart disease (CHD), it was found after 48 months from the start of the study that the groups of subjects receiving canakinumab at doses of 50, 150 and 300 mg were characterized by a decrease in the level of CRP by 26%, 37% and 41%, respectively, compared with patients in the control group [42]. Also, for patients taking canakinumab, a decrease in the risk of developing cardiovascular events was noted without changing the composition of lipid components of the patients' serum [43].

2.5. Anti-IL-17

There is ongoing debate over IL-17's mode of action in atherosclerosis. Atherosclerotic plaque development is increased by IL-17A, according to several research [44], [45], whereas some studies demonstrate the contrary [46], [47]. Variations in the surroundings, including the location of plaque and the concentrations of other chemokines and cytokines, might be the cause of the uncertainty around the function of IL-17A. By decreasing endothelial expression of VCAM-1, which is involved in monocyte attraction and atherosclerotic plaque stability, several studies have documented a protective impact of IL-17A. Moreover, low IL-17 levels were linked to the reappearance of significant cardiovascular incidents within a year following therapy associated with cardiovascular diseases in a cohort trial involving more than 1,000 individuals suffering from acute myocardial infarction [48].

Regarding IL-17-targeted medications, secukinumab is the first human monoclonal antibody to be authorized for clinical application. It has had positive results in treating psoriasis and related psoriatic diseases [49] – [51]. Secukinumab had noticeably superior results compared to etanercept, a receptor that targets TNF-α, and adalimumab [52]. Furthermore, only low-risk adverse reactions were linked to long-term secukinumab usage [53]. Ixekizumab, a different monoclonal antibody that targets IL-17A, was just authorized for use in treating plaque psoriasis. In clinical studies, treatment with ixekizumab resulted in complete clearance of psoriatic plaques in up to 37% of patients with plaque psoriasis. Brodalumab interferes with the next signaling cascade by acting on the IL-17 receptor A chain and preventing IL-17 from attaching to its receptor. Brodalumab had an improved impact on psoriatic condition than secukinumab [54].

The data on the above-described monoclonal antibodies for the treatment of atherosclerosis are summarized in Table 1.

3. Advantages and disadvantages of monoclonal antibody therapy for atherosclerosis

3.1. Targeted treatment

Among the advantages of protein therapeutics such as mAbs over conventional small molecule drugs are their high specificity, allowing precise action, and their long half-life, allowing for infrequent administration. In addition, molecular engineering technologies have allowed mAb structure to be fine-tuned for specific therapeutic actions and to minimize immunogenicity, thereby improving the risk-benefit ratio. This is reflected in mAbs having approval rates of approximately 20% compared to 5% for new chemical entities [55]. One of three processes is necessary for mAbs to be clinically effective: (1) Fab domain (antigen binding site) specific binding to the target to improve or restrict a significant physiological impact; (2) Fc domain (constant domain) binding to cell surface receptors leading to immune-related effector activities such as complement-dependent cytotoxicity, antibody-dependent phagocytosis, or antibody-dependent cell-mediated cytotoxicity; and (3) complement accumulation on multimeric immune complexes between the target and the mAb and subsequent stimulation of complement-dependent cytotoxicity [56]. The antibody's functional properties, such as effector function activity, are determined by Fc. In cases when a mAb's effector function is undesirable, mAbs can be designed to alter the Fc region, or isotypes that are not as good at promoting effector functions [57].

3.2. Lower risk of side effects

Monoclonal antibodies generally have a minimal risk of severe adverse drug reactions (ADRs). In 163 randomized controlled trials (RCTs) and 46 extension studies, the frequency of adverse events for nine biologic medicines used alone or as additional therapy in any application (apart from HIV/AIDS) was compared with any other drug or placebo in a meta-analysis of research. However, the incidences of serious side effects, including severe infection complications, lymphoma, and heart failure were not distinctive from the control group (placebo or other therapy) in these studies [58]. This analysis demonstrated that biological agents were linked to a significantly lower incidence of overall ADRs when compared with other therapy or placebo. It should be mentioned that target and non-target adverse effects are not differentiated in this analysis. Target toxicities, which are unique to the mAb utilized and the therapeutic region in which it was employed, are probably responsible for the bulk of adverse drug reactions (ADRs) documented in the trials. Despite the short duration of the trials that comprise this analysis (median 6 months for RCTs and 13 months for open-label extension studies), prior research indicates that MAT's safety characteristics hold steady over time [59].

3.3. Target toxicity

Because mAbs interact directly with the target molecule (protein or receptor) or process within the intended tissue, their toxicity may be linked to their pharmacologic efficacy. For instance, there is a higher chance of mild bleeding when using the platelet aggregation inhibitor abciximab [60]. This side effect is brought on by abciximab's purported pharmacologic action, which inhibits platelet

Table 1. Analysis of current mAbs developments for the treatment of atherosclerosis.

mAb	Target	Basic studies results	Future directions
Orticumab	MDA-modified peptide of apo B-100	Reduction in inflammation was shown in a primate model but was not achieved in a clinical study (phase II).	Potentially, efficacy may be demonstrated in clinical trials in patients with extensive atherosclerotic lesions with elevated oxLDL levels.
Alirocumab Evolocumab	PCSK9	Significant decreasing of LDL-C level and reduction of risk of cardio-vascular events (phase III).	With the approval of these antibodies for use in the treatment of hypolipidemia, it is possible to use their structure as prototypes for the development of improved versions of humanized antibodies.
Bococizumab		Decreasing of LDL-C level in high-risk group, no primary endpoint was achieved in low-risk group (phase III).	Further clinical studies in different patient cohorts are needed.
Infliximab and Adalimumab	TNF-α	Reduction of atherosclerotic lesions in patients with arthritis and psoriasis.	Clinical trials are needed to examine the use of these antibodies to reduce signs of atherosclerosis in patients with CVD.
Infliximab		Reducing the risk of cardiovascular events in patients with arthritis and psoriasis.	
Golimumab and Certolizumab pegol		Reducing the inflammation in patients with arthritis and psoriasis.	
Canakinumab	IL-1β	Reducing the hCRP level in patients with CHD. Decreasing the risk of long-term cardiovascular events.	Since canakinumab does not have a direct effect on dyslipidemia, it is proposed to develop combination therapy using canakinumab as an anti-inflammatory component for the treatment of atherosclerosis.
Secukinumab, Brodalumab and Ixekizumab	IL-17A	Significant decrease of the plague formation for patients with psoriasis.	Clinical trials are needed to examine the use of these antibodies to reduce signs of atherosclerosis in patients with CVD.

aggregation by inhibiting glycoprotein IIb/IIIa. On the other hand, mAbs may interact with the target antigen in tissues different than the designated tissue, which could result in toxicity. For instance, it is believed that the expression of the target antigen, EGFR, in human keratinocytes is connected to the skin toxicity linked to cetuximab, a monoclonal antibody that blocks the epidermal growth factor receptor (EGFR) and is authorized for colorectal and head and neck malignancies [61]. Numerous mAb safety profiles are distinct to their target and therapeutic field and are associated with antigens and targets.

3.4. Non-target toxicity

mAbs can also cause off-target, non-specific toxicity; for instance, hypersensitivity reactions are frequently seen and are believed to be connected to the immunogenicity of mAbs. It is noteworthy that the proportion of human to non-human content sequence is the primary determinant of mAb immunogenicity [62]. mAbs that include a significant amount of non-human sequence are likely to trigger a host immune response because they are perceived as "foreign." Increased elimination and side effects such as infusion or injection site responses could lead to a reduction in mAb effectiveness. The development of fully human mAbs and the production of mAbs from human germline sequences may lessen the danger of immunogenicity, but they are unable to completely eradicate it as immunogenic ability is influenced by elements other than the primary sequence, including the mAb formula, storage-induced mAb accumulation, protein conformation, glycosylation, and impurities resulting from the manufacturing process, container system, and conditions of storage [63].

4. Future prospects

The future of atherosclerosis treatment lies in personalized medicine and new drugs. Current research is focused on promising anti-inflammatory strategies and exploring new treatment options for atherosclerosis [64]. One intriguing direction is use of newly developed monoclonal antibodies. Several key clinical trials are currently underway to study the effects of various drugs. For example, the ZEUS trial is designed to evaluate the effect of ziltivekimab on reducing cardiovascular events in individuals with established atherosclerotic cardiovascular disease, chronic kidney disease, and inflammation [65]. Also, the GOLDILOX-TIMI trial is a phase IIB study evaluating the anti-inflammatory potential of MEDI6570, a monoclonal antibody, and its effect on atherosclerotic and heart failure events in patients with a history of MI [66].

Ziltivekimab is a novel human antibody directed against the IL-6 ligand. The trial to evaluate reduction of inflammation in patients with advanced chronic kidney disease using antibody-mediated IL-6 inhibition was a randomized, double-blind, phase 2 study of participants (n=264) with moderate to severe chronic kidney disease and high-sensitivity CRP levels of at least 2 mg/L [67]. Subjects were randomly assigned to receive placebo or ziltivekimab (at different doses) subcutaneously every 4 weeks for 24 weeks. The study compared the change in CRP levels after 12 weeks of treatment as the primary outcome. Following 12 weeks, the 7.5 mg group's median levels of CRP decreased by 77%, the 15 mg group's by 88%, and the 30 mg group's by 92%, while the placebo group's levels decreased by 4%. Dose-dependent reductions were also observed for inflammatory markers. The drug was well tolerated and there were no serious adverse events. The results of this study are extremely strong, with significant prognostic potential, and this IL-6 inhibitor can be considered as effective as canakinumab [68].

Tocilizumab and sarilumab are monoclonal antibodies to the IL-6 receptor. Endothelial function has been shown to improve with tocilizumab in patients at high risk of CAD despite elevated LDL-C levels. The ASSAIL-MI (Assessment of Anti-IL-6 Treatment in Myocardial Infarction) study was a double-blind, placebo-controlled, randomized trial in patients with acute MI [69]. Participants were randomized to receive either a single 280 mg infusion of tocilizumab or placebo. The primary endpoint was myocardial salvage index, measured by magnetic resonance imaging 3–7 days after the event. The tocilizumab group had higher myocardial salvage index scores and a significant difference was seen in the CRP area under the curve, with a median of 1.9 mg/L/h (interquartile range [IQR] 0.9 to 4.9) in patients receiving tocilizumab compared with 8.6 mg/L/h (IQR 5.0 to 17.9) in the placebo group ($p < 0.001$). There was a 21% difference between the final infarct size at 6 months in the tocilizumab and placebo groups [70].

5. Discussion

In the AS landscape, inflammation is intricately intertwined with lipid metabolism abnormalities and other risk factors including oxidative stress, endothelial injury, aging and smooth muscle cell migration, collectively accelerating disease progression. Traditionally considered an irreversible condition, AS received a transformative discovery from the GLAGOV study [71]. This study revealed the potential of monoclonal antibody therapy, specifically evolocumab, to modulate plaque volume, outperforming statin monotherapy. Such findings highlight the enormous promise inherent in monoclonal antibody therapy. Antibody treatments have a range of outcomes; some patients report great symptom improvement, while others experience negative side effects including worsening cardiovascular disease [72]. In certain instances, antibodies that target IL-17a and IL-12/23 have additionally behaved as pathogens, and briakinumab was taken off the market because it increased MACE.

Thus, it's critical to maintain surveillance of the negative consequences of novel antibody treatments for cardiovascular disease. In order to overcome the negative effects or apply the proper treatment based on the circumstances and surroundings of each patient, it would be highly beneficial to ascertain the precise mechanism of action of the target molecules [73]. Antibodies that block different molecules, including the ANGPTL family, CD47, and CD31, are being developed and are undergoing clinical trials as well as the antibodies listed in the article [74, 75].

6. Conclusion

Monoclonal antibody therapies have emerged as a promising and innovative approach for the treatment of atherosclerosis, targeting both lipid metabolism and inflammatory pathways central to disease progression. Clinical evidence demonstrates that antibodies against PCSK9 significantly reduce LDL cholesterol levels and cardiovascular events, while those targeting pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-17 show potential

in modulating vascular inflammation and improving outcomes in patients with chronic inflammatory and cardiovascular diseases. Despite these advances, challenges remain, including incomplete understanding of mechanisms of action, limited tissue penetration, high costs, and the risk of adverse immune responses. Continued research and development are essential to optimize the efficacy, safety, and accessibility of monoclonal antibody therapies. As our understanding of the molecular mechanisms underlying atherosclerosis deepens, monoclonal antibodies are poised to play an increasingly important role in personalized medicine and the comprehensive management of atherosclerotic disease.

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