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Review

Artificial Intelligence-Based Target for Personalized Interventions of Atherosclerosis from Gut Microbiota Signature

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Abstract: Atherosclerosis remains a major driver for cardiovascular disease (CVD), despite advancements in traditional risk factor management therapies. Recent evidence emphasizes the crucial role of the gut microbiome in the progression of atherosclerosis and plaque rupture, highlighting a promising therapeutic avenue. This review focuses on the intertwined relationship between the gut microbiome, its metabolites, and atherosclerosis and CVD, also highlighting the potential therapeutic role of probiotics and prebiotics. Given the diverse and unique gut microbiota signatures among individuals, a one-size-fits-all therapeutic approach is unlikely to be effective. Personalized treatment strategies are therefore necessary. Here, we discussed how Artificial Intelligence (AI) can be leveraged to analyze individual gut microbiome profiles from microbiome sequencing, predict treatment response, and optimize therapeutic strategies based on individual patients, which would significantly improve outcomes of the treatment for atherosclerosis patients.

Keywords: atherosclerosis; probiotics; gut microbiome; cardiovascular disease; artificial intelligence (AI); machine learning (ML); deep learning (DL)

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1. Introduction

Atherosclerosis, a leading cause of cardiovascular disease (CVD), remains a compelling global health issue, contributing to substantial morbidity and mortality across the globe [1,2]. Atherosclerosis is characterized by the build-up of plaques within the arterial walls, comprising lipids, complex sugars, and other blood components. This degenerative chronic vascular disease is a precursor to numerous cardiovascular conditions, such as coronary artery disease, stroke, and peripheral artery disease [3]. The progression of atherosclerosis involves a complex interplay of factors, including lipid metabolism disorders [4], inflammation [5], oxidative stress [6], and endothelial [7] and smooth muscle cell dysfunction [8]. Traditional risk factors, such as diabetes, hypertension, obesity, and smoking, further exacerbate this condition [9]. In addition, there are genetic variants that are reported to predispose to early onset atherosclerosis in the absence of the traditional risk factors [10–12].

Recent scientific advancements have revealed a significant relationship between the gut microbiota and CVD, particularly in relation to atherosclerosis [13,14]. The gut microbiota, a diverse ecosystem comprising approximately 10^{14} microorganisms, predominantly from the phyla Bacteroidetes and Firmicutes, plays a crucial role in regulating homeostasis in human gut and impact overall health [15]. Disruptions of microbial balance, known

as gut dysbiosis, have been implicated in the development of various diseases, including atherosclerotic CVD [16,17] and atherosclerotic plaque stability [18–20]. Studies have shown that gut microbiota and their metabolites are intricately involved in influencing major risk factors of atherosclerosis [21,22], highlighting the critical relationship between diet, gut health, and atherosclerosis outcomes [23].

In light of these findings, in this mini-review, we consider (1) the role of the gut microbiome in atherosclerosis development and progression; (2) the discussion on the most used AI/ML approaches and their application for coronary artery disease (CAD) risk prediction; and (3) AI and ML approaches in atherosclerosis and CAD risk prediction based on gut microbiome signatures, as we also predict treatment responses and optimize therapeutic strategies. Finally, we provide an outlook (refer to Figure 1 and Table S1 in the Supplementary Materials) for putting it all together by using AI/ML approaches to predict atherosclerosis risk predictions and its future potential in offering personalized therapy.

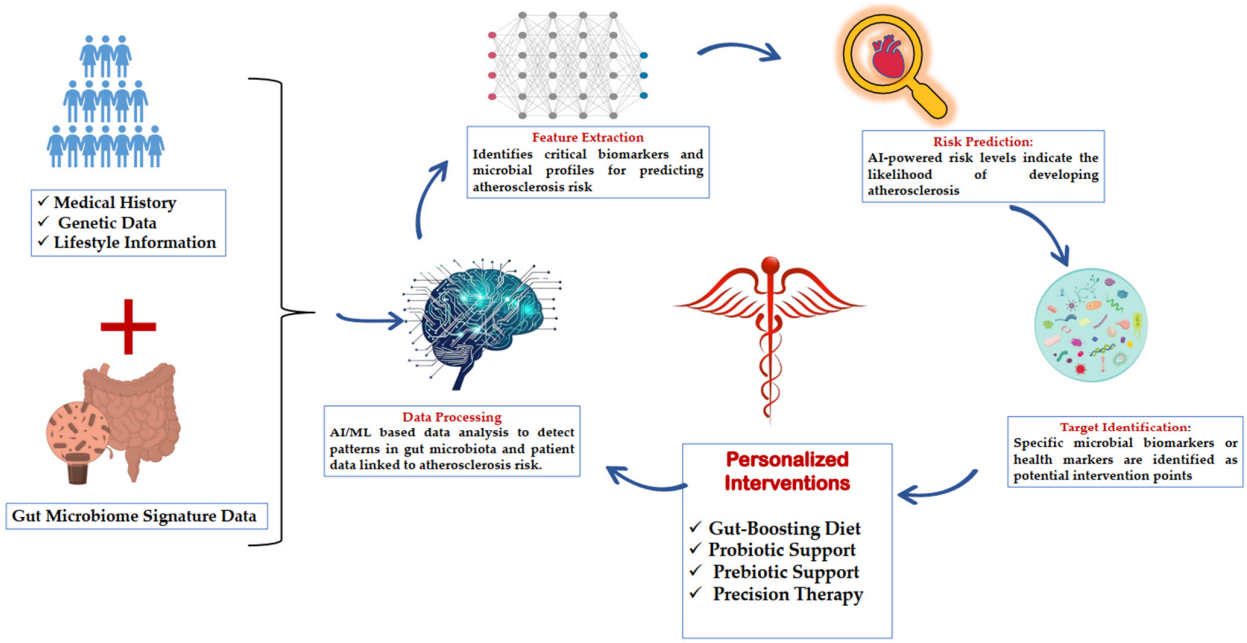

Figure 1. This diagram illustrates an AI-driven pipeline for personalized atherosclerosis interventions by utilizing individual patient data and gut microbiome signatures for tailored treatment strategies.

2. Methodology

This review investigates the role of AI and machine learning (ML) in analyzing gut microbiome data for predicting CVD, particularly atherosclerosis. We conducted an extensive literature search across major scientific databases, including PubMed, Web of Science, Scopus, and Google Scholar. The search used keywords such as "AI and gut microbiome," "machine learning and atherosclerosis," "gut microbiome and CVD prediction," "AI/ML in cardiovascular health," and "microbial signatures in atherosclerosis." Our initial search yielded a large pool of studies, which we carefully screened to ensure relevance to AI/ML applications in gut microbiome analysis related to CVD and atherosclerosis risk. After a thorough filtering process, we selected a total of 45 studies for inclusion in this review. Forty studies primarily addressed AI/ML-based gut microbiome analysis for disease prediction, while 7 studies focused specifically on predicting atherosclerosis or broader CVD outcomes. Inclusion criteria centered on studies that directly applied AI or ML techniques to gut microbiome data specifically for atherosclerosis risk prediction. Selected studies encompassed a variety of AI/ML methods aimed at identifying microbial signatures associated

with atherosclerosis, developing predictive models, and integrating microbiome data into personalized treatment frameworks.

3. The Role of the Gut Microbiome in Atherosclerosis Development and Progression

Gut dysbiosis refers to an imbalance in the microbial communities within the gut, often associated with alterations in microbial composition or the disruption of the mucosal barrier. This imbalance can be triggered by various factors, including high-fat diets, certain diseases, and the overuse of antibiotics. Such changes in gut microbiota composition results in compromised gut permeability, allowing bacterial DNA, metabolites, and endotoxins to enter the bloodstream and other organs [24,25]. Under normal conditions, the gut maintains a strong barrier system such as single-layered intestinal epithelial cells, linked by tight junction proteins, two mucus layers that protect against harmful substances entering circulation [26–28]. The adult gut microbiome is primarily composed of five phyla: *Bacteroidetes*, *Firmicutes*, *Actinobacteria*, *Proteobacteria*, and *Verrucomicrobia*. Among these, *Bacteroidetes* and *Firmicutes* together constitute over 90% of the bacterial species in the gut of healthy individuals [15]. As the dominant genera, *Bacteroidetes* and *Firmicutes* are generally resistant to acute disruptions. However, alterations in their populations are often linked to various pathological conditions in the human body [29].

Recent findings highlight a clear connection between gut microbiota and the development and rupture of atherosclerotic plaques [30]. Experimental studies have shown that atherosclerosis is linked to gut microbiota dysbiosis, often characterized by an increased Firmicutes-to-Bacteroidetes (F/B) ratio [17,31–33].

Particularly, specific bacterial strains have emerged as potential indicators or contributors to atherosclerosis. *Escherichia coli* and *Acidaminococcus* have been found in higher concentrations in patients with subclinical carotid atherosclerosis and CAD [34,35].

Notably, *Acidaminococcus*, associated with several inflammatory diseases and a proinflammatory diet, suggests its role as a marker of inflammation in atherosclerosis [36]. Conversely, beneficial bacteria such as *Faecalibacterium prausnitzii*, known for its anti-inflammatory properties, are more abundant in individuals without subclinical atherosclerosis, emphasizing the protective role of certain gut microbes [17,37].

It is worth noting that several promising animal studies have investigated the diverse role of the gut microbiome and its metabolites in atherosclerosis disease progression, though a detailed discussion of these studies is beyond the scope of this mini-review. Furthermore, lipid lowering and therapeutic probiotic supplementation, gut microbiota modulation [38–43], and fecal transplantation have shown promise in managing atherosclerosis and CVD [32,44–46].

4. AI and ML in Gut Microbiome Analysis: Applications in Disease and Cardiovascular Health Risk Prediction

4.1. AI and ML for Multi-Dimensional Gut Microbiome Data Analysis and Disease Prediction

To investigate the correlation between the gut microbiota and human diseases, advanced sequencing techniques such as amplicon-based and whole genome shotgun sequencing are used to characterize microbial communities and their functions. Large-scale projects like the Metagenomics of the Human Intestinal Tract [15,47], the Human Microbiome Project [48], and the Environmental Determinants of Diabetes in the Young study have significantly expanded our knowledge of the gut microbiome's impact on human health. These initiatives have produced extensive genomic data, including resources like the Integrated Gene Catalog and the Unified Human Gastrointestinal Genome and Protein catalogs [49–51].

With advancements in high-throughput technologies, there has been a shift towards longitudinal multi-omics profiling, integrating data from metabolomics, proteomics, genomics, and transcriptomics by using a highly efficient computational system [52–56]. This comprehensive approach offers a more detailed understanding of how the gut microbiota interacts with the host, influenced by factors such as genetics, age, diet, medications, geography, and physical activity [57].

Given the intricacy and volume of multi-omics data, advanced computational techniques are essential to efficiently analyze and process this information to identify significant patterns for disease prediction. AI and ML have emerged as powerful tools for analyzing and integrating multi-omics data, enabling the discovery of hidden patterns and the development of predictive models for phenotypes [58–61]. These models can help identify potential biomarkers associated with human diseases, providing new insights into various disease mechanisms and guiding therapeutic strategies including CVD [62–64].

ML techniques enhance our ability to manage, analyze, and interpret large, multidimensional datasets, including omics data by offering robust tools for data storage, management, classification, pattern recognition, and optimization. These ML methods are invaluable for exploring the complex nature of the human microbiome signature, discovering novel genes and metabolic markers, examining signaling pathways, assessing microbial activity and functional dysbiosis, analyzing bacterial populations, conducting correlation studies, assigning metagenomic taxonomy and function, and performing resistome analysis that has made significant advancements in CVD research [65].

There are multiple ML algorithms that have been used in various diseases including CVD and atherosclerosis, which are discussed in detail in the following sections. One of the most employed algorithms is Random Forest (RF), a supervised ML method that combines multiple decision trees to boost prediction accuracy [66]. In one study with a Mexican population, RF was utilized to classify individuals into categories such as healthy, prediabetic, or Type 2 diabetes mellitus (T2DM) by analyzing their individual gut microbiota profiles. The model successfully distinguished the gut microbiomes of hyperglycemic individuals with T2DM from those of prediabetic and normoglycemic individuals, identifying specific bacterial species linked to T2DM [67]. In another study using LASSO-based logistic regression, key operational taxonomic units (OTUs) were identified to predict the severity of irritable bowel syndrome (IBS). Random Forest was also applied to classify IBS patients with high sensitivity and specificity [68]. Similarly, ML methods were used to classify fecal samples from individuals with inflammatory bowel disease using shotgun metagenomic data. Various models, including RF, Adaboost, and k-NN + LogitBoost, were trained, with k-NN + LogitBoost showing the best performance after feature selection and cross-validation, demonstrating the power of ML in microbiome-based disease classification [69]. Other ML techniques, such as Naïve Bayes, which assumes class conditional independence, and Gradient Boosting, which identifies nonlinear relationships between features, have been effectively used in microbiome analysis. For example, Gradient Boosting has been employed to integrate host genetics, dietary data, and microbiome profiles, enhancing the accuracy of classification and prediction in complex datasets [70].

Unsupervised ML methods are key exploratory tools used to uncover patterns in data without predefined labels. These techniques help identify underlying data structures and correlation patterns, such as using hierarchical clustering to explore the relationship between microbiota and host-associated disease changes, which aids in disease prediction [71]. For example, in one study, researchers used transcriptomic signatures (RNA-seq) from colonocytes and 16S rRNA data from gut microbiota. They treated colonic epithelial cells with live microbiota from healthy individuals, demonstrating the significant role of the gut microbiota in regulating host gene expression. These findings suggest that ma-

nipulating the microbiome could hold therapeutic potential in the future [72]. A novel method, Adaptive Microbial Signature Profiling for Understanding (aMiSPU), has been introduced to analyze the association between microbiota composition and human health. This data-driven approach utilizes a sum of powered score tests combined with adaptive variable weighting, which integrates microbial abundance with phylogenetic information. This reduces reliance on phylogenetic distance, addressing limitations seen in previous approaches [73]. Additionally, biclustering algorithms, traditionally used in gene expression analysis, are now being applied to detect disease markers, specific genera within the gut microbiome. These methods are particularly effective in identifying overlapping clusters in both microbial and host data, further enhancing their utility in microbiome research and disease diagnostics [74].

Deep learning (DL), a subset of ML, uses artificial neural networks with multiple hidden layers to process large datasets with high abstraction and performance. Unlike traditional ML, DL automatically learns features from raw data, removing the need for manual feature engineering. This makes it a highly advanced and versatile technique for various applications [75].

DL excels in managing vast, high-dimensional data and identifying complex patterns, addressing challenges like missing data and the "curse of dimensionality," where increased input dimensions complicate processing [76]. It can be applied in both supervised and unsupervised settings, making it a powerful tool for complex data analysis [77]. Researchers have recently used advanced ML techniques to enhance the analysis of OTU abundance matrices by integrating spatial data with convolutional neural networks (CNNs). Known for their ability to detect local patterns, CNNs are particularly suited for analyzing spatial microbiome data. In one example, researchers utilized the ResNet-50 model to classify microbiome data from individuals withT2DM, transforming OTU tables into visual representations based on evolutionary relationships. This method significantly outperformed traditional ML approaches in predicting host phenotypes, demonstrating the power of CNNs in microbiome research [78]. In a recent study addressing the growing challenge of antibiotic resistance, researchers developed two deep learning models, DeepARG-SS and DeepARG-LS, to enhance the detection of antibiotic resistance genes (ARGs). These models were designed to analyze both short read sequences and full gene-length sequences. When evaluated across 30 categories of antibiotic resistance, the models demonstrated high precision and recall, significantly outperforming traditional sequence search methods, which often yield high false-negative rates. The DeepARG models, coupled with a newly curated database (DeepARG-DB), expanded the identification of ARGs by leveraging deep learning's capacity to detect a broader range of ARGs without relying on strict cutoffs, offering a more comprehensive and accurate approach to antimicrobial resistance monitoring [79]. A DL framework called Graph-SAGE has been applied to create metagenomic disease graphs, where each sample is represented as a node. The links between nodes are based on a closeness metric, allowing the framework to predict disease states in conditions like inflammatory bowel disease and colorectal cancer. Graph-SAGE outperformed existing ML and DL models in accuracy, and explainable AI was employed to identify specific microbial taxa associated with each condition [80].

Other ML models, iMic and gMic, were used to enhance microbiome data analysis by addressing issues like data sparsity and limited sample sizes. iMic translates microbial data into images, utilizing cCNNs to significantly improve prediction accuracy compared to traditional methods. By organizing taxa based on their evolutionary relationships, iMic offers greater precision and robustness, especially in static microbiome datasets. gMic, a graph-based model, focuses on the relationships between taxa using cladogram structures, allowing for accurate predictions even without frequency data. Both models employ

explainable AI techniques to identify key microbial taxa linked to health conditions, making them powerful tools for biomarker discovery and advancing microbiome research [81]. DL has also been employed in the identification of antimicrobial peptides (AMPs) from gut microbiota. Researchers integrated various neural network models, including Long Short-Term Memory (LSTM), Attention, and Bidirectional Encoder Representations from Transformers (BERTs), to create a pipeline for detecting potential AMPs. By analyzing thousands of metagenomic samples, they identified numerous AMP candidates, several of which were shown to be effective against antibiotic-resistant bacteria in animal models [82].

Moreover, a new computational tool named Back-Propagation Neural Network Human-Microbe Disease Association (BPNNHMDA) was introduced to predict connections between microorganisms and human diseases. This tool employs a back-propagation neural network with an optimized activation function and starting weights to predict microbe–disease associations. BPNNHMDA has demonstrated superior performance in case studies involving diseases such as inflammatory bowel disease, asthma, and obesity, further highlighting its potential in microbiome-based disease research [82]. In a recent study, researchers applied ML techniques to uncover the connection between gut microbiome features and immunotherapy response in cancer patients. By integrating 16S rRNA gene sequencing data from multiple cancer cohorts, they identified specific bacterial taxa linked to treatment success. Utilizing a multivariate Selbal analysis, the study differentiated bacterial genera associated with responders and non-responders, demonstrating the power of ML in predicting immunotherapy outcomes. In short, all these models demonstrated robust predictive accuracy, even when cross-validated across different sequencing platforms, including shotgun metagenomics. This highlights the potential of AI approaches in identifying microbiome-based biomarkers, offering a promising strategy for enhancing treatment efficacy across a range of health conditions [83].

4.2. AI and ML in Predicting Cardiovascular Health and Atherosclerosis Through Gut Microbiome Signature

The use of AI and ML in metagenomics and multi-omics is advancing the understanding of the gut microbiome's role in CVD, particularly atherosclerosis. By applying ML algorithms like RF and support vector machines (SVMs), large metagenomic datasets can be analyzed to detect microbial signatures linked to disease progression [64,84]. Researchers have applied ML to investigate the role of gut microbiota in CVD. In a recent study, researchers leveraged 16S ribosomal RNA sequencing data from the American Gut Project to explore gut microbiota variations between individuals with CVD and healthy controls. Taxonomic analysis was carried out using the Naive Bayes classifier with the Greengenes database and enhanced by Linear Discriminant Analysis Effect Size to identify significant microbial differences. To further dissect these differences, the study employed a range of machine learning techniques including decision trees, elastic net, neural networks, RF, and SVM and revealed that distinctive microbial profiles were associated with CVD. Specifically, individuals with CVD had higher levels of genera such as *Bacteroides*, *Subdoligranulum*, and *Clostridium*. In contrast, healthy controls exhibited greater abundances of *Faecalibacterium*, *Ruminococcus*, and *Lachnospira* [64]. Another study applied ML and single-cell analysis to investigate the relationship between the gut microbiome and macrophage activity in atherosclerosis and identified key macrophage-related transcriptomic signatures that are significantly associated with the gut microbiota and upregulated in atherosclerotic plaques [84].

Moreover, using the RF algorithm, these genes were identified as critical markers, and their biological significance was further examined through clustering. Single-cell RNA sequencing confirmed macrophage-specific expression, with elevated PLEK levels in unstable plaques, suggesting its potential as a biomarker for disease progression. Key

macrophage-related genes, including PLEK, IRF8, BTK, CCR1, and CD68, were significantly associated with the gut microbiota and upregulated in atherosclerotic plaques, reinforcing PLEK's utility in assessing plaque instability and disease advancement. A predictive nomogram based on these genes demonstrated strong potential for assessing atherosclerosis risk, highlighting the effectiveness of AI and ML in identifying novel biomarkers and advancing our understanding of the gut microbiome's role in CVD [85]. A recent study investigated the relationship between gut microbiota composition and CVD risk in a multi-ethnic cohort using advanced machine learning, specifically XGBoost, and Mendelian Randomization (MR). The researchers predicted the Framingham risk score based on gut microbiota data, identifying protective bacteria such as *Akkermansia muciniphila* and *Ruminococcaceae* UCG-002, particularly against ischemic heart disease, a condition linked to atherosclerosis. A microbial cluster comprising *Christensenellaceae*, *Methanobrevibacter*, and *Ruminococcaceae*, referred to as the CMR cluster, was inversely associated with blood lipid levels and CVD risk, particularly by reducing triglycerides, a key factor in atherosclerosis. The study emphasized the importance of ethnic-specific microbiome profiles, suggesting that personalized interventions tailored to an individual's gut microbiota could be more effective for managing atherosclerosis and overall cardiovascular health [86]. In a similar study, researchers applied bidirectional two-sample Mendelian Randomization to investigate the causal relationships between gut microbiota and blood lipid levels. They analyzed summary statistics from genome-wide association studies for the 211 intestinal fora and blood lipid traits, using advanced Mendelian Randomization techniques. The findings revealed a potential causal link between specific gut microbiota and dyslipidemia. For instance, genera such as *Ruminococcaceae*, *Christensenellaceae*, *Parasutterella*, and *Erysipelotrichaceae* were associated with increased dyslipidemia, whereas *Oscillospira*, *Peptococcus*, and *Desulfovibrionaceae* were linked to lower dyslipidemia levels. After correcting for multiple comparisons, only *Desulfovibrionaceae* showed a significant negative association with ApoB levels. Additionally, the inverse MR analysis did not find significant causal effects of blood lipids on gut microbiota. These findings highlight the intricate relationship between gut microbiota and lipid metabolism, offering insights into potential interventions for managing dyslipidemia and addressing atherosclerosis [87]. Another study examining the association between habitual dairy consumption, gut microbial composition, and cardiometabolic risk factors in aged individuals (40 to 70 years) found a significant link between increased dairy consumption, particularly milk and yogurt, and favorable changes in gut microbial diversity. Higher dairy intake was associated with lower blood triglyceride levels and higher HDL cholesterol, indicating potential cardioprotective effects. ML-based metabolomic profiling identified key metabolites, such as 2-hydroxy-3-methylbutyric acid, 2-hydroxybutyric acid, and L-alanine, which were inversely related to the dairy-microbial profile but positively associated with triglycerides. Triglycerides correlated negatively with bacterial genera like *Ruminococcaceae* and *Haemophilus* and positively with *Cetobacterium* and *Fusobacterium*. HDL cholesterol was inversely associated with Enterobacteriaceae, which was more prevalent in individuals with lower dairy intake [88].

Researchers evaluated the effects of chronic statin therapy on the gut microbiome and serum metabolites in acute coronary syndrome (ACS) patients and healthy controls. It employed 16S rRNA sequencing and serum metabolomics, utilizing ML and PICRUSt2 (Phylogenetic Investigation of Communities by Reconstruction of Unobserved States) for functional predictions, to examine how statin treatment influences microbial composition and related metabolic pathways. Statin therapy notably improved the gut microbiome in ACS patients. Specifically, it reduced harmful bacteria like *Parabacteroides merdae* and boosted beneficial species such as *Bifidobacterium longum* subsp. longum, *Anaerostipes hadrus*, and *Ruminococcus obeum*. These shifts in microbial composition were linked to better

health outcomes for patients. This multi-omics approach revealed that these microbial changes were connected to disease severity and patient outcomes, largely through their effects on key metabolites like fatty acids and prenol lipids. In summary, statin treatment appears to positively influence the gut microbiome, leading to improved metabolite profiles and reduced metabolic risk in ACS patients [57]. A recent study explored the effects of gut microbiota alterations and metabolic disruptions on atherosclerosis, with a focus on antibiotic treatment. Using male Apolipoprotein E knockout mice, the researchers applied advanced ML techniques, such as Weighted Gene Co-Expression Network Analysis and RF, to examine metabolic changes and found that antibiotic treatment led to disturbances in tryptophan and lipid metabolism, resulting in decreased microbial diversity. Specifically, reductions were noted in bacterial families such as *Ruminococcaceae* and *Lachnospiraceae* from Clostridia and *Porphyromonadaceae* from Bacteroidetes, which correlated with increased atherosclerosis severity. Similar patterns were observed in a human cohort, where lower serum tryptophan levels and diminished gut microbiome diversity were associated with atherosclerotic conditions [88].

5. Conclusions and Future Direction

AI and ML have revolutionized gut microbiome research, providing unprecedented opportunities to predict and potentially prevent CVD, including atherosclerosis. The gut microbiome's pivotal role in metabolic and immune regulation underscores its direct influence on cardiovascular health. The AI-driven analysis of multi-omics data (metagenomics, genomics, transcriptomics, proteomics, metabolomics) has significantly advanced our understanding of gut dysbiosis and its links to disease. ML models and deep learning techniques have identified key microbial biomarkers and predicted disease risks with greater accuracy than traditional methods. In the context of cardiovascular health, AI has unveiled associations between microbial metabolites and CVD risk, enabling the prediction of precise risk profiles and facilitating personalized treatment strategies.

However, while gut microbiome signatures present promising pathways for personalized insights, it is essential to underscore that microbiome-based predictions should not be viewed in isolation due to the complex, multifactorial nature of cardiovascular disease risk. The gut microbiome interacts dynamically with various lifestyle factors, such as diet, medications, smoking, and physical activity, all of which may significantly influence its composition and impact on CVD and atherosclerosis. An overly narrow focus on microbiome signatures alone may therefore carry the risk of superficial or incomplete assessments.

In the context of cardiovascular health, AI has unveiled associations between microbial metabolites and CVD risk, enabling the prediction of precise risk profiles and facilitating personalized treatment strategies. Future research should therefore focus on building integrative models that incorporate a broader range of factors alongside microbiome data to better reflect the intricate nature of CVD pathogenesis and provide more reliable predictions and interventions. Expanding multi-omics integration is also crucial to further unravel the complexities of the gut microbiome's role in atherosclerosis and CVD. Developing advanced models capable of handling diverse high-throughput sequence data and providing explainable insights will be crucial for translating AI predictions into actionable clinical research and practice.

Moreover, AI-driven insights could play an instrumental role in identifying individualized therapies, which take into account the influence of both gut microbiota and lifestyle factors. This approach could enable the design of specific probiotic compositions, dietary recommendations, or other lifestyle modifications based on personalized data, aimed at restoring gut balance and reducing atherosclerosis and CVD risk. These efforts could help restore gut balance, prevent gut dysbiosis, and mitigate atherosclerosis and CVD risk. Ef-

forts should also prioritize refining predictive models for earlier diagnoses and developing personalized treatments that improve cardiovascular outcomes on a global scale. However, gut microbiota composition can be influenced by several factors such as diet, medication, smoking status, physical activity, and so forth. Therefore, it would be highly challenging to make a judgment based on the analysis of the microbiome in terms of atherosclerosis and CVD risk without including the effects of other lifestyle/health-related variables as gut microbiota changes factors in close supervision and research. This invites the utmost need of further research, clinical trials, and definitely machine learning approaches to analyze large datasets that would eventually give us a full picture of how an individual gut microbiota signature can be used as a therapeutic target for personalized treatments in the near future.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/synbio3010002/s1, Table S1: Highlights the application of AI and ML techniques in microbiome analysis for predicting atherosclerosis and CVD risk.

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