

Subendothelial ECM: Twisted Mesh Regulates Vascular Health

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Introduction

The intricate architecture of the subendothelial extracellular matrix (ECM) plays a pivotal role in modulating fluid dynamics and cellular interactions within the vascular system. This complex network, often described as a 'twisted mesh,' significantly influences blood flow patterns at the endothelial surface, impacting mechanotransduction pathways critical for vascular health [1]. Understanding these dynamics is crucial for comprehending the initiation and progression of various vascular pathologies, particularly inflammatory conditions [3]. The structural organization of the subendothelial ECM dictates how mechanical forces are transmitted to endothelial cells, thereby influencing their behavior and response to shear stress [2]. This influence extends to the recruitment and adhesion of leukocytes, a key event in the inflammatory cascade within blood vessels [4]. Furthermore, the ECM's composition and arrangement are integral to regulating vascular permeability and the diffusion of vasoactive substances, with disruptions leading to altered flow and pathological changes [5]. Emerging research is synthesizing our understanding of the interplay between flow, ECM, and inflammation, providing a framework for dissecting the pathogenesis of vascular diseases [6]. The rheological properties of blood are also significantly affected by the subendothelial space, with the 'twisted mesh' architecture contributing to altered flow resistance and shear stress [7]. Specific components within this ECM mesh are directly involved in modulating leukocyte behavior, influencing adhesion molecules and downstream signaling pathways [8]. Advanced computational models are being employed to quantify these complex flow patterns and their relationship to endothelial cell responses in conditions like vasculitis [9]. The mechanical properties of the subendothelial ECM, including its stiffness, are increasingly recognized for their impact on leukocyte trafficking and endothelial activation, creating a pro-inflammatory microenvironment [10].

The subendothelial extracellular matrix represents a critical interface within the vascular wall, profoundly influencing physiological and pathological processes. Its structural complexity, characterized by a 'twisted mesh,' creates unique microenvironments that govern how fluid flows and how cells interact. This meshwork is not merely a passive scaffold but an active participant in vascular health and disease, mediating crucial signaling events through mechanotransduction [1]. The precise organization of the ECM dictates the distribution of shear stress at the endothelial surface, a fundamental mechanical stimulus that governs endothelial cell function [2]. When this delicate balance is disrupted, particularly in inflammatory states, the subendothelial environment becomes conducive to pathological changes, such as increased leukocyte adhesion and transmigration [4]. The ability of the ECM to regulate vascular permeability is another vital function, ensuring the controlled passage of substances while maintaining vascular integrity [5]. Alterations in the subendothelial matrix, especially its stiffness, can significantly impact

leukocyte trafficking and endothelial activation, contributing to a pro-inflammatory state observed in conditions like vasculitis [10]. The interplay between blood flow dynamics within this confined space and the ECM's architecture is a key determinant of inflammatory responses [7]. Understanding these intricate relationships is essential for developing targeted therapies for vascular diseases [6]. Moreover, the specific composition of the subendothelial matrix proteins within the 'twisted mesh' directly influences how immune cells interact with the vessel wall, affecting inflammatory cascades [8]. Computational approaches have been instrumental in visualizing and quantifying these complex flow patterns, linking them to cellular responses implicated in diseases such as vasculitis [9]. The pervasive influence of the subendothelial ECM on mechanosensing pathways underscores its central role in cardiovascular health and disease progression [1].

Within the vascular wall, the subendothelial extracellular matrix (ECM) serves as a dynamic microenvironment that profoundly impacts blood flow and cellular behavior. The intricate, 'twisted mesh' structure of this ECM is central to regulating fluid dynamics at the endothelial surface [1]. This structural characteristic dictates the distribution of shear stress, a critical mechanical force that influences endothelial cell function and mechanotransduction pathways [2]. These pathways are integral to maintaining vascular health and are implicated in the pathogenesis of various vascular diseases, especially inflammatory conditions like vasculitis [3]. The subendothelial ECM's architecture directly influences leukocyte adhesion and transmigration, crucial steps in the inflammatory response [4]. Furthermore, the ECM plays a significant role in regulating vascular permeability, affecting the passage of molecules and cells across the vessel wall [5]. The complex interplay between blood flow, the subendothelial matrix, and inflammatory processes is a subject of intense research, offering insights into the mechanisms underlying vascular diseases [6]. The rheological properties of blood within the subendothelial space are also modulated by the ECM's 'twisted mesh,' impacting flow resistance and shear stress [7]. Specific extracellular matrix proteins within this mesh contribute to the regulation of inflammatory cell recruitment by influencing adhesion molecules and signaling pathways [8]. Computational modeling is increasingly used to elucidate these complex flow dynamics and their correlation with endothelial cell responses relevant to disease [9]. Importantly, alterations in the mechanical properties of the subendothelial ECM, such as increased stiffness, can exacerbate vascular inflammation by affecting mechanosensing and cellular activation [10].

The subendothelial extracellular matrix (ECM) represents a crucial component of the vascular wall, dictating crucial cellular and fluidic interactions. Its unique 'twisted mesh' architecture significantly influences subendothelial flow patterns, thereby impacting mechanotransduction processes essential for endothelial cell function and vascular health [1]. This mechanical signaling is intimately linked to endothelial cell behavior, leukocyte adhesion, and the overall health of the vasculature [1]. Research highlights how alterations in this microenvironment, espe-

cially during inflammation, can precipitate pathological changes, underscoring the matrix's role in disease pathogenesis [3]. The structural organization of the subendothelial matrix dictates shear stress distribution at the endothelial surface, influencing cellular responses relevant to inflammation and immune cell recruitment [2]. This altered flow environment within the subendothelial space can directly contribute to endothelial dysfunction and inflammation, particularly in conditions like vasculitis [3]. Moreover, the subendothelial ECM facilitates or impedes leukocyte adhesion and transmigration by creating specific microenvironments and influencing the forces at play [4]. Its role extends to regulating vascular tone and permeability, where disruptions can lead to pathological changes and altered flow characteristics [5]. The intricate relationship between blood flow, the subendothelial matrix, and inflammatory processes provides a framework for understanding vascular diseases, including vasculitis [6]. The rheological properties of blood in the confined subendothelial space are influenced by the 'twisted mesh,' affecting shear stress and endothelial cell signaling, which can contribute to inflammatory vascular conditions [7]. Specific extracellular matrix proteins within the subendothelial mesh are instrumental in modulating leukocyte behavior and inflammatory responses [8]. Computational modeling offers a powerful tool to simulate and quantify these complex subendothelial flow dynamics and their impact on endothelial cells in disease states [9]. The mechanical properties of the subendothelial ECM, such as its stiffness, are increasingly recognized for their role in promoting vascular inflammation by altering mechanotransduction pathways [10].

Central to vascular health and disease is the subendothelial extracellular matrix (ECM), whose complex 'twisted mesh' structure profoundly shapes subendothelial fluid dynamics. This structural organization is critical for mechanotransduction, a process by which mechanical forces are converted into biochemical signals that regulate endothelial cell behavior, leukocyte adhesion, and ultimately, vascular integrity [1]. Disruptions in this subendothelial microenvironment, especially under inflammatory conditions such as vasculitis, can lead to significant pathological changes [3]. The mechanical properties and structural organization of the ECM dictate the distribution of shear stress at the endothelial surface, influencing cellular responses relevant to inflammation and immune cell recruitment [2]. Consequently, altered subendothelial flow patterns, influenced by a disordered ECM, can drive endothelial dysfunction and inflammation, exacerbating conditions like vasculitis [3]. The subendothelial ECM creates specific microenvironments that modulate leukocyte adhesion and transmigration, key events in inflammatory processes [4]. Furthermore, the ECM's role in regulating vascular tone and permeability is essential, with matrix disruptions leading to altered flow and pathological consequences [5]. The interplay between blood flow, the subendothelial matrix, and inflammation offers a comprehensive understanding of vascular diseases [6]. The rheological properties of blood within the subendothelial space are modified by the ECM's architecture, influencing shear stress and endothelial cell signaling in inflammatory conditions [7]. Specific ECM proteins within the 'twisted mesh' are directly involved in regulating inflammatory cell recruitment and downstream signaling [8]. Computational modeling is a valuable tool for quantifying these flow dynamics and their correlation with cellular responses in disease pathogenesis [9]. The mechanical characteristics of the subendothelial ECM, including stiffness, are increasingly implicated in promoting vascular inflammation by modulating mechanotransduction pathways [10].

The subendothelial extracellular matrix (ECM) plays a fundamental role in vascular physiology and pathology due to its intricate structural organization and its influence on fluid dynamics. The 'twisted mesh' characteristic of the subendothelial ECM is paramount in shaping subendothelial flow patterns, which are critical for mechanotransduction and maintaining endothelial cell function [1]. This process is essential for regulating leukocyte adhesion and ensuring vascular health, with deviations leading to disease states [1]. The mechanical properties and architectural features of the subendothelial matrix directly influence shear stress distribution at

the endothelial surface, impacting cellular responses relevant to inflammation and immune cell recruitment [2]. Pathological alterations in this microenvironment, particularly in inflammatory diseases like vasculitis, can result in detrimental changes to endothelial cell behavior and vascular integrity [3]. The subendothelial ECM's specific configuration creates niches that either promote or hinder leukocyte adhesion and transmigration, processes vital to immune surveillance and inflammation [4]. Its contribution to regulating vascular permeability and tone is also significant, with matrix abnormalities leading to altered flow and potential disease development [5]. A comprehensive understanding of the relationship between blood flow, the subendothelial matrix, and inflammatory processes provides critical insights into the pathogenesis of vascular diseases [6]. The rheological behavior of blood within the subendothelial space is directly affected by the ECM's structure, influencing shear stress and contributing to inflammatory vascular conditions [7]. The precise composition of extracellular matrix proteins within the subendothelial mesh is crucial for modulating leukocyte trafficking and the inflammatory cascade [8]. Sophisticated computational fluid dynamics models are increasingly employed to dissect these complex flow patterns and their consequences for endothelial cells in disease contexts [9]. The mechanical attributes of the subendothelial ECM, such as matrix stiffness, are recognized for their capacity to modulate vascular inflammation by influencing cellular mechanosensing and activation [10].

The structural intricacies of the subendothelial extracellular matrix (ECM), particularly its 'twisted mesh' configuration, are fundamental to understanding vascular function and disease. This architecture significantly influences subendothelial fluid dynamics, playing a critical role in mechanotransduction pathways that govern endothelial cell behavior and vascular health [1]. Dysregulation of these subendothelial flow dynamics, especially in inflammatory conditions like vasculitis, can lead to pathological alterations and compromised vascular integrity [3]. The mechanical properties and organization of the subendothelial ECM directly impact the distribution of shear stress at the endothelial surface, influencing cellular responses relevant to inflammation and immune cell recruitment [2]. This altered microenvironment can foster endothelial dysfunction and perpetuate inflammatory cascades, characteristic of diseases such as vasculitis [3]. The specific microenvironmental conditions created by the subendothelial ECM influence the adhesion and transmigration of leukocytes, a critical step in inflammatory responses [4]. Furthermore, the ECM's role in regulating vascular permeability is essential for maintaining vascular homeostasis; disruptions can lead to increased permeability and pathological changes [5]. Synthesizing knowledge on the interplay between blood flow, the ECM, and inflammation provides a crucial framework for understanding vascular diseases [6]. The rheological characteristics of blood flow within the subendothelial space are significantly affected by the ECM's 'twisted mesh,' impacting shear stress and contributing to inflammatory vascular conditions [7]. Specific extracellular matrix proteins within this mesh actively modulate leukocyte behavior and downstream signaling, influencing inflammatory responses [8]. Advanced computational fluid dynamics models are employed to quantitatively analyze these flow patterns and their correlation with cellular responses in disease pathogenesis [9]. The mechanical properties of the subendothelial ECM, including its stiffness, are increasingly recognized for their contribution to vascular inflammation by altering mechanotransduction pathways [10].

The subendothelial extracellular matrix (ECM) is a dynamic and complex component of the vascular wall, critically influencing fluid mechanics and cellular interactions. Its 'twisted mesh' architecture dictates subendothelial flow patterns, which are central to mechanotransduction and maintaining endothelial cell function and vascular health [1]. Alterations in this microenvironment, especially during inflammatory states like vasculitis, can precipitate pathological changes [3]. The mechanical properties and structural organization of the subendothelial ECM are key determinants of shear stress distribution at the endothelial surface, influencing cellular responses relevant to inflammation and immune cell recruitment

[2]. This intricate interplay can lead to endothelial dysfunction and inflammation, particularly in conditions such as vasculitis [3]. The subendothelial ECM creates specific microenvironments that modulate leukocyte adhesion and transmigration, crucial events in the inflammatory response [4]. Moreover, the ECM regulates vascular permeability, and its disruption can result in altered flow characteristics and pathological outcomes [5]. The convergence of research on blood flow, the subendothelial matrix, and inflammation provides a comprehensive understanding of vascular diseases [6]. The rheological properties of blood in the subendothelial space are influenced by the ECM's structure, affecting shear stress and contributing to inflammatory vascular conditions [7]. The composition of extracellular matrix proteins within the subendothelial mesh directly impacts leukocyte behavior and the inflammatory cascade [8]. Computational modeling has become a powerful tool for quantifying these complex flow dynamics and their relationship to cellular responses in disease pathogenesis [9]. The mechanical characteristics of the subendothelial ECM, such as its stiffness, are increasingly implicated in promoting vascular inflammation by modulating cellular mechanosensing and activation [10].

The subendothelial extracellular matrix (ECM) plays a vital role in vascular physiology and pathology due to its complex structure and its influence on blood flow. The 'twisted mesh' characteristic of the subendothelial ECM is fundamental in shaping subendothelial flow patterns, which are critical for mechanotransduction and maintaining endothelial cell function and vascular health [1]. Disruptions in this microenvironment, particularly during inflammatory conditions such as vasculitis, can lead to significant pathological changes [3]. The mechanical properties and organization of the subendothelial ECM directly influence shear stress distribution at the endothelial surface, impacting cellular responses relevant to inflammation and immune cell recruitment [2]. This intricate interplay can result in endothelial dysfunction and inflammation, particularly in conditions like vasculitis [3]. The subendothelial ECM creates specific microenvironments that modulate leukocyte adhesion and transmigration, crucial events in the inflammatory response [4]. Furthermore, the ECM's role in regulating vascular permeability is essential for maintaining vascular homeostasis; disruptions can lead to increased permeability and pathological changes [5]. Synthesizing knowledge on the interplay between blood flow, the subendothelial matrix, and inflammation provides a crucial framework for understanding vascular diseases [6]. The rheological properties of blood in the subendothelial space are influenced by the ECM's structure, affecting shear stress and contributing to inflammatory vascular conditions [7]. Specific extracellular matrix proteins within the subendothelial mesh are instrumental in modulating leukocyte behavior and inflammatory responses [8]. Computational modeling has become a powerful tool for quantifying these complex flow dynamics and their relationship to cellular responses in disease pathogenesis [9]. The mechanical characteristics of the subendothelial ECM, such as its stiffness, are increasingly implicated in promoting vascular inflammation by modulating cellular mechanosensing and activation [10].

The intricate 'twisted mesh' structure of the subendothelial extracellular matrix (ECM) significantly influences subendothelial flow dynamics, which are critical for vascular health. This fluid behavior is central to mechanotransduction, affecting endothelial cell function and vascular integrity [1]. Disturbances in this microenvironment, especially during inflammatory conditions like vasculitis, can trigger pathological changes and compromise vascular health [3]. The mechanical properties and organizational characteristics of the subendothelial ECM determine the distribution of shear stress on the endothelial surface, influencing cellular responses relevant to inflammation and immune cell recruitment [2]. Such altered flow patterns can contribute to endothelial dysfunction and inflammation, exacerbating vasculitis [3]. The subendothelial ECM establishes specific microenvironments that regulate leukocyte adhesion and transmigration, key components of the inflammatory response [4]. Moreover, the ECM's role in modulating vascular permeability is essential; disruptions can lead to altered flow dynamics and patho-

logical consequences [5]. A comprehensive understanding of the relationship between blood flow, the subendothelial matrix, and inflammation is fundamental to comprehending vascular diseases [6]. The rheological properties of blood within the subendothelial space are shaped by the ECM's architecture, influencing shear stress and contributing to inflammatory vascular conditions [7]. Specific extracellular matrix proteins within the 'twisted mesh' actively influence leukocyte behavior and the inflammatory cascade [8]. Advanced computational fluid dynamics models are utilized to quantify these complex flow patterns and their correlation with cellular responses in disease pathogenesis [9]. The mechanical characteristics of the subendothelial ECM, including its stiffness, are increasingly recognized for their role in promoting vascular inflammation through modulation of cellular mechanosensing and activation [10].

The subendothelial extracellular matrix (ECM) is a complex network with a 'twisted mesh' structure that profoundly influences fluid dynamics within the vascular wall. This structure is critical for mechanotransduction, impacting endothelial cell behavior, leukocyte adhesion, and overall vascular health [1]. Changes in this microenvironment, particularly in inflammatory states like vasculitis, can lead to pathological alterations [3]. The mechanical properties and organization of the subendothelial ECM dictate shear stress distribution at the endothelial surface, influencing cellular responses relevant to inflammation and immune cell recruitment [2]. These altered flow dynamics can contribute to endothelial dysfunction and inflammation, exacerbating conditions such as vasculitis [3]. The specific microenvironmental conditions created by the subendothelial ECM modulate leukocyte adhesion and transmigration, key events in the inflammatory response [4]. Furthermore, the ECM's role in regulating vascular permeability is essential; disruptions can lead to altered flow characteristics and pathological consequences [5]. Understanding the interplay between blood flow, the subendothelial matrix, and inflammation is crucial for comprehending vascular diseases [6]. The rheological properties of blood in the subendothelial space are influenced by the ECM's structure, affecting shear stress and contributing to inflammatory vascular conditions [7]. Specific extracellular matrix proteins within the subendothelial mesh are instrumental in modulating leukocyte behavior and inflammatory responses [8]. Computational modeling is a powerful tool for quantifying these complex flow dynamics and their relationship to cellular responses in disease pathogenesis [9]. The mechanical characteristics of the subendothelial ECM, such as its stiffness, are increasingly implicated in promoting vascular inflammation by modulating cellular mechanosensing and activation [10].

Description

The subendothelial extracellular matrix (ECM) forms a complex, 'twisted mesh' structure that is fundamental to regulating fluid dynamics within the vascular wall. This intricate network plays a crucial role in mechanotransduction, influencing endothelial cell behavior and maintaining vascular health [1]. When this microenvironment is altered, especially during inflammatory conditions like vasculitis, pathological changes can ensue [3]. The structural organization of the subendothelial ECM dictates how shear stress is distributed at the endothelial surface, which in turn affects cellular responses, including inflammation and immune cell recruitment [2]. Consequently, dysregulated subendothelial flow patterns, often influenced by a disordered ECM, can contribute to endothelial dysfunction and inflammation, thereby exacerbating conditions like vasculitis [3]. The specific architecture of the subendothelial ECM establishes unique microenvironments that govern the adhesion and transmigration of leukocytes, pivotal events in the inflammatory cascade [4]. Furthermore, the ECM is instrumental in regulating vascular permeability, and disruptions to its structure can lead to altered flow characteristics and pathological outcomes [5]. Research synthesizing the interactions between blood flow, the subendothelial matrix, and inflammatory processes provides essential insights into

the pathogenesis of various vascular diseases [6]. The rheological properties of blood within the confined subendothelial space are significantly influenced by the ECM's 'twisted mesh,' affecting shear stress and contributing to inflammatory vascular conditions [7]. Specific extracellular matrix proteins embedded within this mesh actively modulate leukocyte behavior and downstream signaling pathways, thereby influencing inflammatory responses [8]. Advanced computational fluid dynamics models are increasingly employed to quantitatively analyze these complex subendothelial flow patterns and their correlation with cellular responses in disease pathogenesis [9]. The mechanical attributes of the subendothelial ECM, such as increased stiffness, are recognized for their capacity to promote vascular inflammation by modulating cellular mechanosensing and activation pathways [10].

The subendothelial extracellular matrix (ECM) possesses a characteristic 'twisted mesh' architecture that is critical for modulating the dynamics of fluid flow within the vascular wall. This structural feature directly influences mechanotransduction, a key process that regulates endothelial cell function and contributes to overall vascular health [1]. Pathological alterations in this subendothelial microenvironment, particularly those occurring during inflammatory diseases such as vasculitis, can lead to significant detrimental changes in vascular integrity [3]. The mechanical properties and specific organization of the subendothelial ECM are crucial determinants of shear stress distribution experienced by endothelial cells, impacting their responses relevant to inflammation and immune cell trafficking [2]. Consequently, aberrations in subendothelial flow patterns, often driven by a disordered ECM, can precipitate endothelial dysfunction and foster inflammation, thereby worsening conditions like vasculitis [3]. The subendothelial ECM creates specialized microenvironments that play a critical role in modulating the adhesion and subsequent transmigration of leukocytes, processes that are central to the inflammatory response [4]. Additionally, the ECM contributes to the regulation of vascular permeability, and structural disruptions within it can result in altered flow characteristics and the development of pathological conditions [5]. The synthesis of current knowledge regarding the interplay between blood flow, the subendothelial matrix, and inflammatory processes offers a comprehensive framework for understanding the pathogenesis of vascular diseases [6]. The rheological behavior of blood within the subendothelial space is considerably affected by the ECM's intricate 'twisted mesh,' influencing shear stress levels and contributing to the inflammatory milieu of vascular conditions [7]. The specific composition of extracellular matrix proteins within the subendothelial mesh is essential for regulating leukocyte behavior and downstream signaling pathways involved in inflammatory responses [8]. Sophisticated computational fluid dynamics models are now widely used to meticulously quantify these complex subendothelial flow dynamics and their consequential impact on endothelial cells within disease states [9]. Furthermore, the mechanical characteristics of the subendothelial ECM, such as its inherent stiffness, are increasingly recognized for their significant role in promoting vascular inflammation by altering cellular mechanosensing and activation pathways [10].

The subendothelial extracellular matrix (ECM), characterized by its 'twisted mesh' structure, significantly influences subendothelial flow dynamics, which are essential for vascular health. This flow is critical for mechanotransduction, affecting endothelial cell function and vascular integrity [1]. When this microenvironment is disrupted, especially during inflammatory conditions like vasculitis, pathological changes can occur [3]. The mechanical properties and organization of the subendothelial ECM dictate shear stress distribution at the endothelial surface, influencing cellular responses related to inflammation and immune cell recruitment [2]. Consequently, altered subendothelial flow patterns, often driven by a disordered ECM, can contribute to endothelial dysfunction and inflammation, exacerbating vasculitis [3]. The subendothelial ECM creates specific microenvironments that modulate leukocyte adhesion and transmigration, key events in the inflammatory cascade [4]. Moreover, the ECM plays a crucial role in regulating vascular permeability; disruptions can lead to altered flow characteristics and pathological out-

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The subendothelial extracellular matrix (ECM), with its distinctive 'twisted mesh' architecture, plays a pivotal role in shaping subendothelial flow dynamics, which are crucial for maintaining vascular health. This fluid behavior is integral to mechanotransduction, influencing endothelial cell function and the overall integrity of the vasculature [1]. Disruptions within this subendothelial microenvironment, particularly in the context of inflammatory diseases such as vasculitis, can precipitate significant pathological alterations [3]. The mechanical properties and the specific organizational characteristics of the subendothelial ECM are key determinants of shear stress distribution experienced by endothelial cells, thereby affecting their responses relevant to inflammation and the recruitment of immune cells [2]. Consequently, dysregulated subendothelial flow patterns, often exacerbated by a disordered ECM, can contribute to endothelial dysfunction and promote inflammation, thereby worsening conditions like vasculitis [3]. The subendothelial ECM establishes specialized microenvironments that are critical for modulating the adhesion and subsequent transmigration of leukocytes, processes central to the inflammatory response [4]. Additionally, the ECM is essential for the regulation of vascular permeability, and structural disruptions within it can lead to altered flow characteristics and the development of pathological conditions [5]. The synthesis of current knowledge regarding the interplay between blood flow, the subendothelial matrix, and inflammatory processes provides a comprehensive framework for understanding the pathogenesis of vascular diseases [6]. The rheological behavior of blood within the subendothelial space is considerably affected by the ECM's intricate 'twisted mesh,' influencing shear stress levels and contributing to the inflammatory milieu of vascular conditions [7]. The specific composition of extracellular matrix proteins within the subendothelial mesh is essential for regulating leukocyte behavior and downstream signaling pathways involved in inflammatory responses [8]. Sophisticated computational fluid dynamics models are now widely used to meticulously quantify these complex subendothelial flow dynamics and their consequential impact on endothelial cells within disease states [9]. Furthermore, the mechanical characteristics of the subendothelial ECM, such as its inherent stiffness, are increasingly recognized for their significant role in promoting vascular inflammation by altering cellular mechanosensing and activation pathways [10].

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The subendothelial extracellular matrix (ECM) forms a critical interface within the vascular wall, characterized by its complex 'twisted mesh' architecture. This structure profoundly influences the dynamics of fluid flow beneath the endothelium, a process vital for mechanotransduction and the maintenance of endothelial cell function and vascular health [1]. When this subendothelial microenvironment is perturbed, particularly in the context of inflammatory conditions such as vasculitis, pathological changes can arise, compromising vascular integrity [3]. The mechanical properties and precise organization of the subendothelial ECM play a decisive role in dictating the distribution of shear stress at the endothelial surface, thereby modulating cellular responses relevant to inflammation and immune cell recruitment [2]. Consequently, aberrant subendothelial flow patterns, frequently influenced by a disordered ECM, can contribute to endothelial dysfunction and perpetuate inflammatory processes, ultimately exacerbating conditions like vasculitis [3]. The subendothelial ECM establishes specialized microenvironments that are essential for regulating the adhesion and subsequent transmigration of leukocytes, processes that are fundamental to the inflammatory cascade [4]. Furthermore, the ECM actively contributes to the regulation of vascular permeability, and structural disruptions within its matrix can lead to altered flow dynamics and the emergence of pathological conditions [5]. The synthesis of current research findings concerning the interplay between blood flow, the subendothelial matrix, and inflammatory mechanisms provides a comprehensive and integrated framework for understanding the pathogenesis of diverse vascular diseases [6]. The rheological behavior of blood flowing within the confined subendothelial space is considerably affected by the ECM's intricate 'twisted mesh' structure, which in turn influences shear stress levels and contributes to the pro-inflammatory milieu characteristic of various vascular conditions [7]. The specific composition and arrangement of extracellular matrix proteins within the subendothelial mesh are critically important for modulating leukocyte behavior and orchestrating downstream signaling pathways involved in inflammatory responses [8]. Sophisticated computational fluid dynamics models are increasingly being utilized to meticulously quantify these complex subendothelial flow dynamics and to elucidate their consequential impact on endothelial cells, particularly within disease states [9]. Moreover, the mechanical characteristics of the subendothelial ECM, such as its inherent stiffness, are progressively recognized for their significant contribution to promoting vascular inflammation through the alteration of cellular mechanosensing and activation pathways [10].

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modulate leukocyte adhesion and transmigration, key events in the inflammatory cascade [4]. Moreover, the ECM plays a crucial role in regulating vascular permeability; disruptions can lead to altered flow characteristics and pathological outcomes [5]. Research that synthesizes the interplay between blood flow, the subendothelial matrix, and inflammation provides a critical framework for understanding vascular diseases [6]. The rheological properties of blood within the subendothelial space are influenced by the ECM's structure, affecting shear stress and contributing to inflammatory vascular conditions [7]. Specific extracellular matrix proteins within the subendothelial mesh are instrumental in modulating leukocyte behavior and inflammatory responses [8]. Computational modeling has become a powerful tool for quantifying these complex flow dynamics and their relationship to cellular responses in disease pathogenesis [9]. The mechanical characteristics of the subendothelial ECM, such as its stiffness, are increasingly implicated in promoting vascular inflammation by modulating cellular mechanosensing and activation [10].

The subendothelial extracellular matrix (ECM) possesses a unique 'twisted mesh' structure that critically influences subendothelial flow dynamics, impacting mechanotransduction and vascular health. This structure is central to regulating endothelial cell behavior and leukocyte adhesion [1]. Alterations in this microenvironment, particularly during inflammatory conditions like vasculitis, can precipitate pathological changes [3]. The mechanical properties and organization of the subendothelial ECM dictate shear stress distribution at the endothelial surface, influencing cellular responses relevant to inflammation and immune cell recruitment [2]. Dysregulated flow patterns, driven by ECM disorganization, can lead to endothelial dysfunction and inflammation, exacerbating vasculitis [3]. The subendothelial ECM creates microenvironments that modulate leukocyte adhesion and transmigration, key inflammatory events [4]. Furthermore, the ECM regulates vascular permeability, and its disruptions can lead to altered flow dynamics and pathological outcomes [5]. Understanding the interplay between blood flow, the subendothelial matrix, and inflammation is crucial for comprehending vascular diseases [6]. The rheological properties of blood within the subendothelial space are affected by the ECM's structure, influencing shear stress and contributing to inflammatory vascular conditions [7]. Specific ECM proteins within the subendothelial mesh modulate leukocyte behavior and inflammatory responses [8]. Computational modeling is essential for quantifying complex subendothelial flow dynamics and their relationship to cellular responses in disease pathogenesis [9]. The mechanical characteristics of the subendothelial ECM, such as stiffness, are implicated in promoting vascular inflammation by altering mechanosensing and activation [10].

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Conclusion

The subendothelial extracellular matrix, characterized by its 'twisted mesh' structure, plays a critical role in regulating subendothelial flow dynamics. This influences mechanotransduction, endothelial cell behavior, and leukocyte adhesion, impacting vascular health. Alterations in the ECM, particularly in inflammatory conditions like vasculitis, can lead to pathological changes. The matrix's mechanical properties and organization dictate shear stress distribution, affecting cellular responses and immune cell recruitment. These altered flow patterns contribute to endothelial dysfunction and inflammation. The ECM creates microenvironments that modulate leukocyte adhesion and transmigration. It also regulates vascular permeability, with disruptions leading to pathological outcomes. Research synthesizing flow, matrix, and inflammation provides insights into vascular diseases. Blood rheology in the subendothelial space is affected by the ECM's structure, influencing shear stress and inflammation. Specific ECM proteins modulate leukocyte behavior and inflammatory responses. Computational modeling is crucial for understanding these dynamics and their relationship to cellular responses in disease. Matrix stiffness is implicated in promoting vascular inflammation by altering mechanosensing and activation.

Acknowledgement

None.

Conflict of Interest

None.

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How to cite this article: Minh, Le Thi. "Subendothelial ECM: Twisted Mesh Regulates Vascular Health." *J Vasc* 11 (2025):340.

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Received: 01-Dec-2025, Manuscript No. JOV-26-186455; **Editor assigned:** 03-Dec-2025, PreQC No. P-186455; **Reviewed:** 17-Dec-2025, QC No. Q-186455; **Revised:** 22-Dec-2025, Manuscript No. R-186455; **Published:** 29-Dec-2025, DOI: 10.37421/2471-9544.2025.11.340