Received: 30.09.2025 Revised: 26.01.2026 Accepted: 26.02.2026 Published: 07.04.2026

BIOLOGICAL SYSTEMS: Theory and Innovation

ISSN 2706-8382
e-ISSN 2706-8390

Journal homepage: https://bioscience.com.ua/en
Vol. 17, No. 1, 2026, 67-77

UDC 577.27:576.36

DOI: 10.31548/biologiya/1.2026.67

Macrophage signalling pathways and their regulation by cellular microenvironment factors

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Abstract. Macrophages are key cells of innate immunity that play an important role in regulating the inflammatory response, tissue repair processes, and the development of various pathological conditions, in particular, cancer and chronic inflammatory diseases. The functional activity of macrophages is largely determined by microenvironment signals, including cytokines, hormones, growth factors, and pathogen-associated molecular structures. The purpose of the study was to summarise contemporary scientific data on the molecular mechanisms of regulation of functional activity of macrophages under the influence of microenvironment factors and analyse the interaction of signalling pathways that determine their polarisation and functional plasticity. The paper analysed the results of contemporary studies on the regulation of macrophage signalling cascades involving Th1- and Th2-type cytokines, glucocorticoids, transforming growth factor β (TGF-β), and signalling pathways activated by pathogen-associated molecular structures. Activation of receptor complexes, in particular TLR4, has been shown to trigger complex signalling cascades associated with activation of the transcription factor NF-κB and MyD88-dependent signal transmission mechanisms. It was found that the interaction of various signalling molecules can lead to both synergistic and antagonistic effects affecting the expression of genes associated with the inflammatory response, cell adhesion, and lipid metabolism. The generalised data obtained confirmed the concept of a continuum of functional states of macrophages, according to which these cells are able to change their phenotype depending on the conditions of the microenvironment. These results highlighted the importance of investigating the mechanisms of interaction between different microenvironment signals to understand the regulation of macrophage functions. The practical significance of the study lies in the systematisation of recent ideas about the mechanisms of macrophage regulation, which can be used for further research on the molecular basis of the immune response, and for the development of new approaches to the treatment of inflammatory, autoimmune and oncological diseases

Keywords: immune response; TGF-β; cytokines; tumour; growth factors

INTRODUCTION

The cytokine environment of the tumour microenvironment and the nature of the inflammatory infiltrate of tumours often show signs of a chronic inflammatory process that combines the characteristics of both Th1- and Th2-mediated immune responses. Such a mixed immune profile plays an important role in regulating the functional activity of innate immune cells, in

Suggested Citation:

Andriushchenko, A. (2026). Macrophage signalling pathways and their regulation by cellular microenvironment factors. *Biological Systems: Theory and Innovation*, 17(1), 67-77. doi: 10.31548/biologiya/1.2026.67.

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particular macrophages, which are key components of the tumour microenvironment. Research by X. Chen (2022) showed that macrophages can acquire various functional phenotypes under the influence of cytokines, growth factors, and other signalling molecules present in the tissue environment. This phenotypic plasticity determines their involvement in the development of inflammatory responses, tissue remodelling processes, and tumour progression. One of the important signalling factors involved in the development of the tumour microenvironment is transforming growth factor β (TGF-β), which can modulate the functional activity of various cells of the immune system. In particular, it has been shown that TGF-β can significantly affect macrophage differentiation and polarisation, contributing to the development of phenotypes associated with anti-inflammatory activity and tissue remodelling. In turn, X. Bai *et al*. (2025) described the role of inflammatory signalling cascades in regulating cellular response. In addition, macrophage activation can occur under the influence of tissue damage signals that trigger specific molecular mechanisms of cell polarisation during sterile inflammation (Koncz *et al*., 2023). According to C. Chen *et al*. (2023), epigenetic regulatory mechanisms that are activated by microenvironment signalling molecules can control the expression of genes associated with macrophage polarisation, thereby determining their functional state in the processes of inflammation and tissue regeneration. Recently, the role of cytokine receptor-related signalling pathways in the development of specific macrophage phenotypes has attracted particular attention. Increased expression of receptors for individual cytokines can significantly alter the functional properties of these cells. In the context of the tumour microenvironment, it is important to increase the expression of the IL-17BR receptor, which, according to current research, may have prognostic significance in some types of malignancies, in particular in breast cancer. X. Gao *et al*. (2023) showed that activation of appropriate signalling pathways can alter immune responses in tumour tissue and affect the interaction between tumour cells and immune system cells. Given that macrophages can express various receptors for cytokines and growth factors, it can be assumed that the increased expression of IL-17BR observed in breast tumour tissues may be associated with stimulation of macrophages by signalling molecules of the tumour microenvironment, in particular TGF-β. The study by J. Song *et al*. (2024) showed that signalling pathways activated by this factor can alter the transcription programmes of cells and promote the development of functional phenotypes similar to tumour-associated macrophages. Such cells are characterised by the ability to support chronic inflammation, stimulate angiogenesis, and modulate the immune response in the tumour microenvironment.

Interest in studying the effect of TGF-β on macrophages is also related to historical understanding of the sensitivity of these cells to this factor. For a long time, it was believed that mature macrophages are practically unable to respond to TGF-β. K. Zhang & C. Jagannath (2025) showed that monocytes can express a significant number of receptors for this cytokine and respond to its stimulation by reducing inflammatory activity. Simultaneously, the expression of the corresponding receptors decreases during differentiation into macrophages, which leads to a decrease in the sensitivity of cells to TGF-β. However, recent studies show that the response of macrophages to TGF-β can largely depend on the conditions of their differentiation and the composition of the cellular microenvironment. For example, it has been shown that a combination of different signalling stimuli can alter the expression of receptors and the activity of the corresponding signalling pathways. The study by J. Zhang *et al*. (2025) demonstrated that post-transcriptional regulatory mechanisms, in particular m6A-type RNA modifications, can influence the expression of genes associated with macrophage polarisation and promote the development of alternatively activated cell phenotypes. In addition, under physiological conditions, the processes of differentiation and functional activation of macrophages can be influenced by hormonal factors, in particular glucocorticoids. The natural glucocorticoid cortisol is constantly present in the mammalian circulation, which can modulate immune responses. A synthetic analogue of cortisol is dexamethasone, which is widely used in experimental studies to model the effect of glucocorticoids on immune system cells. C. Chen *et al*. (2025) found that glucocorticoids can affect signalling pathways that control the functional state of macrophages, in particular, by

altering cellular protein localisation and regulating intercellular communication. Thus, current data have shown that the development of a functional macrophage phenotype is determined by the complex interaction of signalling molecules of the tumour microenvironment, epigenetic mechanisms, and metabolic processes. Understanding these mechanisms is important for explaining the role of macrophages in the development of the tumour process and may contribute to the development of new approaches to cancer therapy. The purpose of the study was to systematise and critically analyse current ideas about the molecular mechanisms of regulation of functional activity of macrophages in the context of the influence of microenvironment factors, and to elucidate the role of interaction of signalling pathways in the processes of their polarisation and functional plasticity.

MATERIALS AND METHODS

The study was of a review and analytical nature and aimed at systematising current scientific data on the molecular mechanisms of regulation of macrophage signalling pathways under the influence of cellular microenvironment factors. The object of the study was macrophage signalling pathways activated by cytokines, growth factors, hormones, and pathogen-associated molecular structures. The study focused on the molecular mechanisms regulating macrophage polarisation, their functional plasticity, and the interactions among key signalling cascades that determine the development of distinct functional phenotypes of these cells in inflammatory and tumourigenic processes. The search for scientific sources was carried out in the international bibliographic databases PubMed, Scopus, Web of Science, and Google Scholar. The following keywords were used to identify relevant publications: macrophage polarisation, macrophage signalling pathways, tumour microenvironment, cytokine signalling, NF-κB signalling, and TGF-β signalling. The analysis mainly included publications published in 2020-2025 that contain experimental or review data on the mechanisms of macrophage activation. The selection criteria were scientific originality of the results, indexing of the publication in international scientometric databases, and compliance with the research topic.

Contemporary studies on the regulation of macrophage functional activity and polarisation were used to establish the theoretical foundation of the research. As part of the study, the approaches proposed by T. Gauthier *et al*. (2023) and A.S.M. Moin *et al*. (2021) were applied to analyse the mechanisms of macrophage activation through M1/M2 polarisation and their functional diversity was evaluated depending on the microenvironment. Special attention was paid to the plasticity of macrophages and their ability to adapt the functional phenotype in response to cellular environmental conditions. The analysis also considered the concept that macrophages can form different phenotypes by responding to signals coming from the microenvironment. The interpretation of the obtained data was carried out based on the concept of functional diversity of macrophages and the integration of signalling pathways that ensured the adaptation of cells to changes in the tissue environment. The study of macrophages of atherosclerotic plaque and their effect on lipid metabolism and inflammatory processes was carried out based on the studies by J.O. Abaricia *et al*. (2020) and E.M. O'Brien & K.L. Spiller (2022). Systematisation of macrophage activation mechanisms under the influence of growth factors and cytokines was carried out in accordance with the approach by Y.H. Lin *et al*. (2020). A significant aspect was the processes of cellular interaction and regulation of the immune response of macrophages. The paper used the method of systematic analysis of literature, which provided for the selection, classification, and critical evaluation of scientific publications. To identify general patterns in the regulation of macrophage signalling pathways, the method of comparative analysis was used, enabling a comparison of the results of various experimental studies. In addition, the method of synthesis of scientific data was applied, which corresponded to the approaches of meta-analytical generalisation of findings and allowed integrating information from various scientific sources.

RESULTS AND DISCUSSION

Identification of the conditions necessary to preserve the ability of macrophages to respond to TGF-β allowed investigating the effect of this growth factor on gene expression in macrophages. An increase in the expression of a number of

transcription-regulating factors involved in the regulation of the immune response and cell adhesion was observed. In addition, genes that are responsible for lipid metabolism can be classified into a separate group. The identified genes are characteristic of macrophages involved in chronic inflammatory processes, such as, for example, atherosclerosis. The correspondence of the resulting macrophage phenotype to macrophages found in atherosclerotic plaque can be traced primarily by the expression of genes involved in lipoprotein metabolism. Thus, J.O. Abaricia *et al*. (2020), E.M. O'Brien & K.L. Spiller (2022) and H. Lin *et al*. (2025) showed that atherosclerotic plaque macrophages express apolipoprotein E (APOE), lectin-like receptor for oxLDL-1 (LOX or OLR1), apolipoprotein C-II (APOC2), sortilin-like receptor L (SORL1 or LR11), LRPAP1, and ABC transporter ABCG1. All of these genes are involved in the regulation of blood cholesterol and are somehow associated with the pathogenesis of atherosclerosis (Boutilier & Elsawa, 2021).

However, macrophages of atherosclerotic plaque, which have a phenotype characteristic of the chronic inflammatory process, are similar in many respects to tumour-associated macrophages. The most striking example of this correspondence is the increased expression of enzymes involved in the synthesis of leukotriene B4. Thus, oesophageal tumour samples showed increased expression of ALOX5AP and LTA4 hydrolase, enzymes necessary for the synthesis of leukotriene B4, whose role in tumour progression and metastasis has been shown to be extremely important, in particular for renal cell carcinoma (Peng *et al*., 2020). Although the phenotype of macrophages obtained in culture when stimulated with IL-4, dexamethasone, and TGF-β reflects only some of the properties of tumour-associated macrophages, it can be argued that the resulting model reflects some of the properties necessary for these cells to participate in tumour pathogenesis. To approach the physiological situation, it is necessary to include in the model other cytokines produced by the tumour, signals received by macrophages as a result of intercellular contacts, and physical factors such as hypoxia. The complexity of the experimental system indicates the feasibility of using mathematical and analytical approaches to more effectively solve the corresponding problems. The analysed data confirmed that macrophages in the human body cannot be divided into only two categories – classically and alternatively activated (Eming *et al*., 2021). The system of mononuclear phagocytes can be visualised as a continuum of functional states, that is, polarisation: at one of the poles of which there are macrophages that actively restore tissue after suppressing the inflammatory response, and at the other – macrophages that actively stimulate inflammation (Fig. 1).

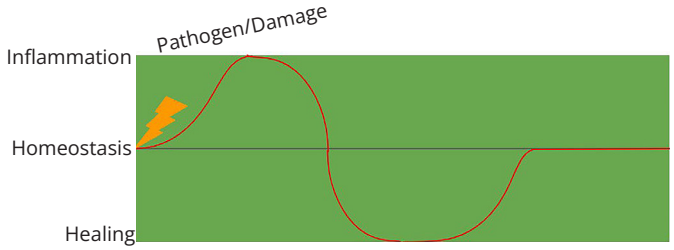

Figure 1. Changes in the macrophage phenotype during the inflammatory response process
Source: compiled by the author

Figure 1 illustrates the transformation of the macrophage phenotype in response to damage or pathogens, showing the transition from a state of homeostasis to inflammatory activation and subsequent tissue healing. A neutral state corresponding to healthy, undamaged tissue can be located between these two poles. The diversity of macrophage phenotypes is explained not only by the different combinations of factors affecting the cell, but also by the sequence of influence of these factors. Macrophages treated with interferons (IFN) a few hours before LPS stimulation were able to produce large amounts of tumour necrosis factor (TNF), in addition, IFN

treatment leads to a change in the response to interleukin-10 (IL-10) (Scott *et al*., 2023; He *et al*., 2024). The ability of macrophages to respond to various stimuli regardless of the phenotype and degree of differentiation led to the creation of the concept of macrophage phenotype plasticity (Zhu *et al*., 2022). According to this concept, macrophages are considered as cells that have the ability to change their state within a continuum of possible states depending on changes that have occurred in their environment. Regardless of the phenotype, macrophages can respond adequately to pathogen-associated molecules (PAMPs), such as LPS or muramyl dipeptide (MDP). In addition, macrophages involved in stimulating the inflammatory response can respond to anti-inflammatory signals and reduce their inflammatory potential (Strizova *et al*., 2023). Cells that have similar adaptation potentials and means to stimulate the strongest inflammatory responses or fibrotic processes pose a potential danger to the body. Over the course of evolution, macrophages have demonstrated the ability to perform their functions smoothly. Their ability to accurately determine the nature and degree of exposure required by the body in each specific situation is the result of complex mechanisms of regulation and adaptation. Macrophages have a receptor system of the highest complexity, which allows them to take an active part in almost any physiological process. Macrophages express receptors for Th1 and Th2 cytokines, hormones, and chemokines, which allows them to integrate innate and acquired immunity. Toll-like receptors and other molecular structure recognition receptors allow macrophages to detect most types of pathogens with high efficiency. A wide range of scavenger receptors, Fc receptors, and complement component receptors make macrophages universal cleaners (Oliver *et al*., 2024). This complexity of the receptor system guarantees the detection of all signals necessary for an effective and timely immune response without exception. However, a highly developed receptor system alone is not enough to form the correct response. The specificity of the macrophage response is determined by complex signal transmission pathways within the cell, which are activated after binding of the ligand to its receptor. For many receptors, there is evidence that the signalling pathway activated by them is not a unidirectional chain of events. Typically, receptor-activated signalling cascades are branched structures that include positive and negative feedback loops that affect the signal chain at different levels (Sim *et al*., 2022).

An example of a branched signal transmission pathway is a signalling pathway that is activated by LPS and leads to TNF production. The first control node of this reaction is the stage of recognition of LPS by the receptor complex. To be recognised, LPS must be bound to a lipopolysaccharide-binding protein (LBP). This complex, in turn, binds to TLR4 via the CD14 coreceptor and MD2 adapter protein (Xia *et al*., 2023). The absence of any component of this system leads to a significant decrease in the cell's sensitivity to LPS. Furthermore, this system allows adjusting the cell to a certain level of sensitivity. Thus, the presence of membrane-bound CD14 on the cell surface is required to identify low LPS concentrations, while the presence of soluble CD14 is sufficient to identify high LPS concentrations (Li *et al*., 2020). After recognition by the LPS receptor complex, the adapter protein MyD88 binds to TLR4, which, in turn, leads to activation of IκB kinase (IKK) and phosphorylation of IκB (Palmieri *et al*., 2020). After phosphorylation of IκB, the IκB/NF-κB complex dissociates, and the transcription factor NF-κB is transported to the nucleus, where it activates transcription of NF-κB-dependent genes. However, activated NF-κB not only triggers effector transcription of genes such as TNF, but also includes feedback that suppresses the LPS-activated signalling cascade. Two factors are considered the main regulators of NF-κB activation: A20, which inhibits IKK activation, and IκBα, which forms a stable complex with NF-κB and thus fixes it in the cytoplasm (Liu *et al*., 2022; Volkova *et al*., 2023). Since elevated concentrations of TNF pose a danger to the body, there are additional mechanisms for regulating its production. Thus, AU-rich regions within the untranslated 3'-terminal region of TNF mRNA provide reduced mRNA stability and are involved in suppression of TNF translation (Kashfi *et al*., 2021). In addition, negative regulation of TNF production is also carried out with the involvement of secreted factors such as IL-10 and TNF itself (Fig. 2).

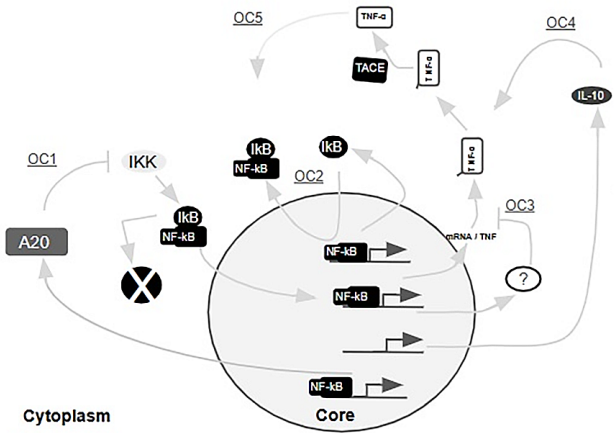

Figure 2. System for regulating TNF production in response to LPS macrophage stimulation
Source: compiled by the author

The LPS-activated signalling pathway branches out at the stage of binding the adapter protein to the receptor complex. Activated TLR4 is able to bind the TRAM/TRIF adapter complex, which triggers a signalling cascade leading to activation of the transcription factor IRF3 and to weaker and later activation of NF-κB (Nakagome & Nagata, 2024). Macrophages recognise LBP-bound LPS by a complex receptor complex that includes CD14, TLR4, and MD2. The TLR4-activated signalling cascade leads to NF-κB activation, which, in turn, enables TNF transcription. Feedback loops (FL) that regulate TNF-α production at the level of the signalling pathway and transcription regulation (FL1 and FL2), at the level of mRNA stability regulation (FL3), and involving secreted TNF-α and IL-10 factors (FL4 and FL5). Although the signal transmission system activated by a single factor remains complex due to the presence of branching signalling pathways and feedbacks, the situation in the body is even more diverse, since the causes of exposure to the cell come from several factors that can cooperate at once. A similar situation is described for IFN, which enhances the macrophage response to LPS (Li *et al.*, 2024). In addition, a similar interaction was shown for the combination of IL-4 and LPS (Muñoz *et al.*, 2020). Thus, cytokines of both Th1 and Th2 types can enhance the antibacterial response of macrophages (Scopelliti *et al.*, 2021). The interaction of multiple cytokines is even more important for anti-inflammatory factors. Cytokines and hormones involved in anti-inflammatory processes often have multifunctional properties and play an important role in the development and maintenance of homeostasis. One of the central roles in maintaining homeostasis belongs to glucocorticoids, which, in addition, are involved in embryonic development and suppression of inflammatory responses (Wu *et al.*, 2021). Similarly, TGF-β is actively involved in embryonic development and regulates fundamental processes such as cell proliferation, differentiation, and migration (Lin *et al.*, 2020). Thus, for effective action in pathological situations, such multifunctional factors must interact with each other to enhance the necessary functions and inactivate each other's potentially dangerous properties. The interaction of anti-inflammatory factors was shown for IL-4 and glucocorticoids in the case of suppression of inflammation, while dexamethasone reduced the level of TNF-α production, and IL-4 suppressed the bactericidal activity of macrophages. At the level of regulation of the expression of individual molecules, dexamethasone significantly enhances the production of CCL18, a CCR3 receptor antagonist (Zhang *et al.*, 2020; Liu *et al.*, 2022). A synergistic effect of IL-4 and dexamethasone was also observed when the expression of the macrophage mannose receptor CD163 (Hirani *et al.*, 2022). In addition to their synergistic effects, dexamethasone and IL-4 are antagonists of macrophage production of various components of the extracellular matrix and enzymes for its rearrangement.

The analysis confirmed that macrophages are a highly heterogenic population of cells that perform key functions in protecting the body from pathogens, regulating inflammatory processes, repairing tissues, and maintaining tissue homeostasis. Their functional diversity is determined by the microenvironment, which includes cytokines, pathogen-associated signals, and metabolic factors, as emphasised by T. Gauthier *et al*. (2023). Research by M.D. Gans & T. Gavrilova (2020) demonstrated that the involvement of macrophages in the development of chronic inflammation is related to their ability to respond to microenvironment signals and modulate the immune response. According to M. Locati *et al*. (2020), macrophages are characterised by a high level of functional diversity and can form a wide range of phenotypes in response to microenvironment signals. Integration of various signalling pathways ensures that cells adapt to changing tissue environment conditions. A.S.M. Moin *et al*. (2021) described activation using the M1/M2 polarisation model, according to which M1 macrophages are characterised by pronounced pro-inflammatory activity, while M2 macrophages are associated with tissue repair processes and anti-inflammatory regulation. However, the present study showed that this classification does not fully reflect the complexity of the functional states of macrophages in vivo. Research by G.A. Pizzurro & K. Miller-Jensen (2023) demonstrated that macrophage activation is a continuous spectrum of functional states, rather than a set of clearly separated phenotypes. Systemic analysis of macrophage gene expression in various biological contexts has shown the existence of numerous activation programmes that are formed under the influence of microenvironment signals and intracellular regulatory networks. This showed that the functional states of macrophages are determined by complex molecular interactions, and not just by the classical polarisation model. Integrative analysis of macrophage transcriptome profiles in various tissues and inflammatory conditions confirms this concept. In particular, D.E. Sanin *et al*. (2022) identified several conservative transcription programmes that can be grouped into four main functional trajectories: phagocytic, inflammatory, antimicrobial, oxidative stress-related, and tissue remodelling programmes. These trajectories reflect the stages of functional differentiation of macrophages and highlight the role of monocyte-derived macrophages in shaping their functional diversity during inflammation.

An important factor determining the functional state of macrophages is their metabolism. Metabolic reprogramming is necessary to maintain the cellular response to external stimuli and largely determines the functional phenotype of macrophages, as noted by T. Gauthier *et al*. (2023). Classically activated macrophages preferentially use aerobic glycolysis, which provides the synthesis of pro-inflammatory cytokines and antimicrobial factors, while alternatively activated macrophages are characterised by a more active use of oxidative phosphorylation. This study showed that the metabolic regulation of macrophages is much more complex. In turn, Y. Xia *et al*. (2022) demonstrated that transforming growth factor β (TGF-β) can induce a specific functional state of macrophages that does not fully correspond to either the M1 or M2 phenotype. Exposure to TGF-β stimulates glycolysis in macrophages by activating the mTOR-c-MYC signalling pathway and increasing the expression of the glycolytic enzyme PFKL, while inhibiting the production of pro-inflammatory cytokines through SMAD3-dependent transcription regulation. This suggests that metabolic and inflammatory signalling pathways in macrophages can be regulated independently. Impaired metabolic and immune regulation of macrophages also plays an important role in the development of metabolic and inflammatory diseases. Based on the conclusions of A.S.M. Moin *et al*. (2021), patients with obesity and type 2 diabetes exhibit an increase in markers of both M1- and M2-type macrophage activation, which indicates a mixed profile of their activation. Such dysregulation can contribute to the development of chronic inflammation. Therefore, macrophage activation is determined by the complex interaction of transcription programmes, metabolic processes, and microenvironment signals. Therefore, macrophages should be considered as cells with dynamic functional states formed in response to specific tissue and inflammatory signals.

CONCLUSIONS

The results of the analysis showed that the functional state of macrophages is determined by the complex interaction of signalling pathways that are

activated under the influence of various microenvironment factors. These factors include cytokines, hormones, molecular patterns of pathogens, and other signals that shape specific cellular environment conditions. The complex action of these factors ensures the coordination of cellular responses aimed at maintaining immune homeostasis, regulating inflammatory processes, and adapting cells to environmental changes. Glucocorticoids, TGF-β, and cytokines Th1 and Th2 have been shown to exhibit both synergistic and antagonistic effects in regulating macrophage functional activity. Such interactions determine the level of inflammatory response, tissue repair processes, and the participation of macrophages in the pathogenesis of various diseases, in particular, tumourigenic and inflammatory processes. It was found that the balance between pro-inflammatory and anti-inflammatory signals is an important factor in maintaining the normal functioning of the immune system and preventing the development of pathological changes in tissues. The study confirmed that the development of various macrophage phenotypes is determined not only by a combination of microenvironment factors, but also by the sequence of their effect on the cell. The data obtained support the concept of macrophage plasticity, according to which these cells can change their phenotype within a continuum of functional states depending on changes in the microenvironment. Such plasticity ensures the adaptability of the immune response, but simultaneously can contribute to the development of pathological processes. Further study of the mechanisms of signalling interaction pathways in macrophages is important for understanding the molecular basis of immune regulation and may contribute to the development of new therapeutic approaches for the treatment of inflammatory and oncological diseases. Deepening knowledge about the molecular mechanisms of macrophage polarisation and their functional plasticity is essential for the development of contemporary immunology and biomedicine, and for the creation of new targeted therapy strategies aimed at regulating the activity of these cells in various pathological conditions.

ACKNOWLEDGEMENTS

None.

FUNDING

None.

CONFLICT OF INTEREST

None.

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Сигнальні шляхи макрофагів та їх регуляція факторами клітинного мікрооточення

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Анотація. Макрофаги є ключовими клітинами вродженого імунітету, що відіграють важливу роль у регуляції запальної відповіді, процесах репарації тканин та розвитку різних патологічних станів, зокрема онкологічних і хронічних запальних захворювань. Функціональна активність макрофагів значною мірою визначається сигналами мікрооточення, включаючи цитокіни, гормони, фактори росту та патоген-асоційовані молекулярні структури. Метою роботи було узагальнення сучасних наукових даних щодо молекулярних механізмів регуляції функціональної активності макрофагів під впливом факторів мікрооточення та аналіз взаємодії сигнальних шляхів, що визначають їхню поляризацію і функціональну пластичність. У роботі проаналізовано результати сучасних досліджень, присвячених регуляції сигнальних каскадів макрофагів за участю цитокінів Th1- та Th2-типу, глюкокортикоїдів, трансформувального фактора росту β (TGF-β), а також сигнальних шляхів, активованих патоген-асоційованими молекулярними структурами. Показано, що активація рецепторних комплексів, зокрема TLR4, запускає складні сигнальні каскади, пов'язані з активацією транскрипційного фактора NF-κB та MyD88-залежних механізмів передачі сигналу. Встановлено, що взаємодія різних сигнальних молекул може призводити як до синергічних, так і до антагоністичних ефектів, що впливають на експресію генів, пов'язаних із запальною відповіддю, клітинною адгезією та метаболізмом ліпідів. Отримані узагальнені дані підтвердили концепцію континууму функціональних станів макрофагів, згідно з якою ці клітини здатні змінювати свій фенотип залежно від умов мікрооточення. Ці результати підкреслили важливість вивчення механізмів взаємодії між різними сигналами мікрооточення для розуміння регуляції макрофагальних функцій. Практична цінність роботи полягає у систематизації сучасних уявлень про механізми регуляції макрофагів, що може бути використано для подальших досліджень молекулярних основ імунної відповіді, а також для розробки нових підходів до терапії запальних, аутоімунних та онкологічних захворювань

Ключові слова: імунна відповідь; TGF-β; цитокіни; пухлина; фактори росту