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Regulation of innate immune cell function by mTOR - Review of the evidence

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1. ABSTRACT

The analyzed publication is a scientific review describing mTOR, a regulatory protein capable of integrating nutrient availability, energy, and immune signals, as a coordinator of innate immune cell functions. The available text is only the abstract; therefore, details on the bibliographic research, study selection criteria, and analysis of individual experiments are not included in the available material.In section 5.8 of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, the publication contributes to the narrative that persistent mTOR activation may predispose macrophages to sustain an inflammatory response through metabolic changes and the regulation of cytokine production. Independent studies in murine macrophages, human immune cells, and antigen-presenting cells confirm that mTOR can influence polarization, selective mediator production, and antigen presentation. However, an experiment on human monocytes observed that pharmacological inhibition of mTOR can increase, rather than reduce, certain cytokines induced by a bacterial stimulus. Overall, the chain is biologically consistent and supported primarily by experimental models, but it does not prove that a metabolic condition in humans automatically produces chronic inflammation through this single mechanism.

ONLINE ARTICLE

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MISSION

LIFE Science Hub – Journal of Science was founded with the aim of making scientific knowledge accessible without giving up methodological rigour, quality of sources and authoritativeness of content. The journal promotes the dissemination of knowledge in the health, nutrition, medical and longevity sciences, building a bridge between the world of research and society.

Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

Free from political, industrial and commercial influence, the journal stands as an authoritative and independent editorial space, dedicated to promoting scientific culture, professional development and the growth of health awareness among the public.

2. ANALYZED STUDY

The research question was how mTOR, short for *mechanistic target of rapamycin* (a protein that links nutrient availability to cell growth and activity programs), influences innate immune cells. In simple terms, the authors examined whether this system can help macrophages, monocytes, and other sentinel cells obtain the resources necessary to move, produce alarm signals, and present antigens.The publication is relevant to the paragraph because it identifies mTOR as a metabolic regulator of the macrophage response. Its specific contribution to the narrative is the segment stating that mTOR can reconfigure cellular metabolism and modulate cytokine responses, macrophage polarization, and antigen presentation. However, it is not a study that directly proves that hyperinsulinemia causes chronic inflammation in humans, nor that persistent mTOR activation inevitably produces the same outcome in every tissue.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The publication is a narrative review of the literature, not a single clinical, animal, or cellular experiment. The abstract states that the review focuses on the role of mTOR in controlling the effector responses of innate immune cells, including metabolic regulation, protein translation, cytokine responses, antigen presentation, macrophage polarization, and cell migration.Since the available material contains only the abstract, the number of publications included, the databases consulted, the search period, the inclusion and exclusion criteria, the characteristics of the experimental models analyzed, and a formal method for assessing the quality of evidence are not reported in the available material. Furthermore, quantitative endpoints, statistical analyses, or follow-ups are not reported, as these elements are not typically characteristic of a narrative review described only through an abstract.

4. RESULTS

The central finding reported in the abstract is conceptual: mTOR is described as a regulator that links immune cell activation to its nutritional and energy status. In practice, when an innate cell receives a danger signal, it must not only recognize it: it must also produce energy, proteins, and lipids to support movement, growth, and the secretion of mediators.The authors report that mTOR reconfigures cellular metabolism and regulates protein translation, which is the production of proteins based on genetic instructions. The abstract also indicates a role in the cytokine response, macrophage polarization, antigen presentation, and cell migration. Cytokines are communication proteins that can amplify or limit inflammation, while polarization refers to the functional orientation assumed by the macrophage in response to the context.The abstract does not report sample sizes, concentrations, percentage differences, P-values, hazard ratios, or quantitative measures of effects. It is therefore not possible to attribute to the publication a numerical estimate of the magnitude by which mTOR would increase or decrease specific cytokines. The documented point is that the mTOR network can shape the innate response, not that it always acts in the same direction.

5. INTERPRETATION

For the reader, the biological message is that a macrophage does not produce inflammation simply because it recognizes a danger signal: it must also be metabolically equipped to do so. mTOR can contribute to this preparation by regulating how the cell uses its resources. This function makes it plausible that a persistent alteration of the system could change the way a macrophage responds to stimuli.The progression supported by the publication that is the subject of the Evidence Review is therefore: nutrient availability and intracellular signals mTOR regulation modification of macrophage metabolism and functions variation in the inflammatory response. However, the available text does not demonstrate the entire sequence proposed in the paragraph, from persistent metabolic stimulation to the recruitment of many immune cells into the tissue.Caution is essential because mTOR is not a simple on-off switch. It can form different cellular complexes, act at different stages of the response, and produce effects that depend on the cell type, the stimulus received, and the duration of activation. Therefore, the book's formula is scientifically more robust if interpreted as a possible mechanistic predisposition, rather than an inevitable consequence in humans.

6. INDEPENDENT SUPPORTING EVIDENCE

Direct confirmation of the segment regarding persistent activation comes from an experimental study on mice with selective deletion of *Tsc1* in myeloid cells. TSC1 is a protein that normally limits the mTORC1 complex; its absence therefore produced constitutive, or continuous, activation of mTORC1. Macrophages obtained from these animals showed an increased response to pro-inflammatory stimuli and a reduced ability to adopt an interleukin-4-induced program, which is associated with tissue repair and regulation. The experiments include bone marrow-derived macrophages and *in vivo* mouse models; they therefore support a causal relationship in the animal model, but do not quantify the human risk of chronic inflammation [1].A second study observed, in peripheral blood mononuclear cells taken from healthy volunteers and stimulated with bacterial lipopolysaccharide, that mTOR was activated within one hour. Treatment with rapamycin, an mTOR inhibitor, reduced the expression and production of interleukin-6 and interleukin-10, without reducing the production of TNF-alpha. This result confirms that mTOR can selectively support the production of certain cytokines during an inflammatory response, but also shows that not all cytokines depend on this pathway in the same way [2].A further step in the narrative concerns the ability of innate cells to communicate with lymphocytes. In murine macrophages and dendritic cells, lipopolysaccharide activated the PI3K-AKT-mTOR pathway, and mTOR was found to be necessary for the formation of lysosomal tubules and for the surface exposure of the major histocompatibility complex class II. This complex allows for the display of antigenic fragments to T lymphocytes. The evidence therefore confirms that mTOR can promote antigen-presenting function, but does not by itself demonstrate lymphocyte activation in the human body [3].

7. CONFLICTING EVIDENCE

A study on primary human monocytes provided a relevant result, yet one that contradicts the idea that mTOR always supports inflammation. Following stimulation with lipopolysaccharide, catalytic inhibition of mTOR increased the production of interleukin-1 beta, interleukin-6, and tissue factor, a protein that promotes coagulation. The authors linked this increase to higher transcriptional activity of NF-kB and changes in the metabolism of NAD+, a molecule essential for many energy reactions [4].This evidence does not deny that mTOR can support certain inflammatory responses in other models. However, it indicates that, in human monocytes exposed to a bacterial stimulus, mTOR can also act as a brake on specific pro-inflammatory genes. The differences may depend on the cell type, the distinction between mTORC1 and mTORC2, the type of inhibitor used, the duration of the stimulus, and the phase of the response. No further directly conflicting evidence of sufficient relevance has been identified; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication that is the subject of the review from the independent research used to evaluate the specific narrative of the paragraph.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Narrative review	Literature on innate immune cells	Describes mTOR as a regulator of metabolism, cytokines, polarization, and antigen presentation	biologically consistent evidence	moderate
[1]	Animal and cellular	Mice with myeloid deletion of Tsc1 and bone marrow-derived macrophages	Constitutive activation of mTORC1 increases pro-inflammatory responses and reduces IL-4-induced polarization	direct confirmation	moderate
[2]	Ex vivo cellular	Mononuclear blood cells from healthy volunteers stimulated with lipopolysaccharide	mTOR inhibition reduces lipopolysaccharide-induced IL-6 and IL-10, without reducing TNF-alpha	direct confirmation	moderate
[3]	Cellular and animal	Murine macrophages and dendritic cells	mTOR is required for lysosomal remodeling and increased surface exposure of MHC-II after stimulation	indirect confirmation	moderate
[4]	Ex vivo cellular	Primary human monocytes stimulated with lipopolysaccharide	mTOR inhibition increases lipopolysaccharide-induced IL-1 beta, IL-6, and tissue factor	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The role of mTOR as a regulator of metabolism and innate immune cell function is well-supported at both biological and experimental levels. The analyzed publication was therefore used consistently to explain why a metabolically reprogrammed macrophage can modify its inflammatory response.The narrative that persistent mTOR activation promotes a pro-inflammatory state is confirmed primarily in murine macrophages and certain cellular systems. However, it cannot be automatically transferred to every immune cell or clinical situation: in human monocytes, mTOR can also limit specific inflammatory responses. The entire proposed chain therefore requires validation in humans, through studies that simultaneously measure metabolic status, mTOR activity, macrophage function, and clinical

outcomes.

Aggiornato al 24/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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