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Role of AMP-activated protein kinase in cancer therapy - Evidence review

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1. ABSTRACT

The analyzed publication is a narrative review on the potential role of AMP-activated protein kinase, or AMPK (an enzyme that senses a reduction in available cellular energy), in tumor biology. The available text is only the abstract: it does not report a new experiment, but summarizes studies suggesting that AMPK activation can reduce growth signals, including mTORC1, and promote adaptive responses to energy deficiency.In paragraph 6.3.1 of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, the citation contributes to the description of a cell that, when energy decreases, slows down proliferation and activates controlled survival mechanisms. Independent studies confirm that AMPK can activate TSC2 and inhibit mTORC1, as well as promote autophagy in cellular models. However, AMPK can also activate mTORC2 under conditions of acute energy stress; the relationship is therefore dependent on the mTOR complex considered and the experimental context. The narrative is well-supported at the molecular level, but does not by itself demonstrate a clinical anti-tumor effect in humans.

ONLINE ARTICLE

ARTICLE INFORMATION

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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 of the publication was whether AMPK could represent a useful target in cancer therapy. The hypothesis discussed is that this protein acts as a sensor of energy status: when ATP (the main molecule that provides immediately usable energy) decreases, AMPK limits energy-consuming processes and promotes processes that regenerate it.The specific reason for its presence in paragraph 6.3.1 is the synthesis of a precise biological step: under conditions of energy deficiency, AMPK can curb signals that support cell growth and proliferation and can contribute to controlled survival responses. The abstract attributes this effect, among other mechanisms, to the phosphorylation of TSC2 (a chemical modification that can change its activity) and the subsequent inhibition of mTOR, a central regulator of cell growth.However, the publication is a narrative review, not a clinical trial or a single experiment. It can therefore summarize biological plausibility and the evidence available at the time, but it cannot prove that AMPK activation prevents or cures cancer in humans.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The available material consists exclusively of the publication's abstract. From this, it appears that the authors conducted a narrative review of the literature on the role of AMPK in cellular metabolism and cancer.The available material does not report a bibliographic search strategy, databases consulted, time frame of the search, inclusion or exclusion criteria for studies, number of selected articles, quality assessment procedure for the evidence, or combined statistical analysis. Participants, sample sizes, dosages, control groups, endpoints, or follow-ups are not reported because the publication does not describe an original trial.

4. RESULTS

The abstract describes AMPK as a regulator of cellular energy balance. In simple terms, when the AMP/ATP ratio increases, signaling lower energy availability, AMPK is activated and reduces energy-expensive cellular activities, such as the synthesis of new proteins and growth. At the same time, it can promote catabolic processes, which are processes that derive energy from the degradation of cellular components.The most relevant passage for the book concerns the AMPK–TSC2–mTORC1 pathway. The abstract reports that AMPK can phosphorylate TSC2, a protein that limits the activity of mTORC1 (a protein complex that promotes protein synthesis and cell growth), thereby reducing proliferative signals. It also reports that, during glucose deprivation, AMPK can activate p53 and promote cell cycle arrest at the G1/S transition, that is, before DNA duplication.The abstract also reports that AMPK can promote autophagy, a process by which the cell recycles internal components, and stabilize p27kip1, a protein that contributes to slowing down the cell cycle. However, it does not provide quantitative values, experimental sample sizes, effect measures, P-values, or details of the individual studies cited. These results are therefore presented as a narrative summary and cannot be evaluated quantitatively from the available material.

5. INTERPRETATION

The primary biological significance is consistent with an energy-saving response: a cell with low energy tends to reduce the construction of new molecules and slow down division. Technically, AMPK can activate TSC2; TSC2 reduces the activation of mTORC1 and, consequently, signals linked to protein synthesis and growth decrease.The pathway documented by the publication subject to the Evidence Review is therefore: energy deficiency AMPK activation increased TSC2 activity and reduction of mTORC1 slowing of cell growth and activation of adaptive responses. Independent experiments have shown that the phosphorylation of TSC2 by AMPK is necessary for part of the response to energy deficiency and that the inhibition of mTORC1 can also occur through Raptor, a component of the mTORC1 complex [1,2].This interpretation does not mean that AMPK is always a cancer brake. Proliferation, autophagy, and survival depend on the cell type, the intensity and duration of the stress, the mutations present, and whether one considers mTORC1 or mTORC2.

6. INDEPENDENT SUPPORTING EVIDENCE

The most direct confirmation of the central narrative branch comes from cellular experiments by Inoki and colleagues. In cells subjected to energy deprivation, AMPK phosphorylated and activated TSC2. TSC2 phosphorylation was necessary to downregulate protein translation and to control cell size during energy deficiency. Cells lacking TSC2, or possessing a version of TSC2 that cannot be phosphorylated by AMPK, responded less effectively to stress. This study directly confirms the AMPK TSC2 reduction of mTOR signaling segment linked to cell growth and survival; the limitation is that it derives from experimental cellular models, not from cancer patients [1].Gwinn and colleagues reinforced the same narrative by showing a second molecular brake. In mouse embryonic cells lacking TSC2 and p53, AMPK phosphorylated Raptor, an essential component of mTORC1. This modification was required for the inhibition of mTORC1 and for the cell cycle arrest induced by energy stress. The result is important because it indicates that the reduction in growth does not depend exclusively on TSC2: AMPK can also limit mTORC1 by acting directly on the complex. It is an independent mechanistic confirmation of the concept of multi-level growth control, but it remains cellular evidence [2].The link with controlled survival mechanisms is supported by Kim and colleagues. In glucose-deprived cell cultures, AMPK activated ULK1 (a protein that initiates autophagy) through phosphorylation; simultaneously, elevated mTORC1 activity hindered this interaction. Simply put, when energy is scarce, the cell can reduce growth programs and activate internal recycling. This confirms the step related to autophagy, but it does not prove that it is necessarily beneficial: in cancer, autophagy can have different effects depending on the context [3].

7. CONFLICTING EVIDENCE

An important clarification is that mTOR is not a single target. Kazyken and colleagues observed that AMPK, while reducing mTORC1 signaling, can directly activate mTORC2 during acute energy stress. In mouse embryonic fibroblasts, cultured cells, and mouse liver, this activation increased signaling toward AKT and reduced apoptosis, or programmed cell death. Therefore, the effect of AMPK was not a simple generalized inhibition of all mTOR complexes [4].This evidence does not refute the AMPK–TSC2–mTORC1 pathway described in the book, but it limits an overly broad formulation suggesting that AMPK always inhibits mTOR or always reduces cell survival. Under acute stress conditions, mTORC1 inhibition can coexist with mTORC2 activation and increased survival. No directly conflicting evidence sufficiently relevant to the phosphorylation of TSC2 by AMPK has been identified; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the study subject to the review from the independent publications used to verify the individual steps of the narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Narrative review	Literature on AMPK, cellular metabolism, and cancer	Synthesizes that AMPK can inhibit mTOR via TSC2 and promote adaptive responses to energy stress	biologically consistent evidence	preliminary
[1]	Cellular and molecular	Cell lines with normal, absent, or mutated TSC2	AMPK phosphorylates TSC2; this modification contributes to the control of translation, size, and survival during energy deficiency	direct confirmation	moderate
[2]	Cellular and molecular	Mouse embryonic fibroblasts and cell cultures	AMPK phosphorylates Raptor, inhibits mTORC1, and promotes cell cycle arrest during energy stress	indirect confirmation	moderate
[3]	Cellular and molecular	Cell cultures subjected to glucose deprivation	AMPK activates ULK1 and increases autophagy; elevated mTORC1 hinders the process	indirect confirmation	moderate
[4]	Cellular, molecular, and animal	Mouse embryonic fibroblasts, cultured cells, hepatocytes, and mouse liver	AMPK activates mTORC2 and AKT, reducing apoptosis during acute energy stress	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The publication analyzed contributes relevantly to the book's section because it synthesizes the role of AMPK as an energy sensor capable of reducing cell growth signals. The AMPK–TSC2–mTORC1 segment is well-supported at a mechanistic level by independent studies. The link between AMPK, the slowing of proliferation, and autophagy is also moderately supported in cellular models. It remains necessary to distinguish mTORC1 from mTORC2 and not automatically transfer these experimental observations to proven therapeutic effects in humans.

Aggiornato al 25/11/2026. 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.

11. RIFERIMENTI BIBLIOGRAFICI

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