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PI3K/PTEN signaling in angiogenesis and tumorigenesis

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1. ABSTRACT

The analyzed publication is a narrative review dedicated to the PI3K/PTEN pathway in cancer and the formation of new blood vessels. Its objective is to describe how PI3K, a protein that transmits signals within the cell, can activate AKT, a kinase that helps regulate metabolism, cell growth, and survival. It is not an experimental study on insulin and does not present a sample of participants or a clinical intervention.In paragraph 4.3 of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, the publication contributes to the passage stating that PI3K prepares the conditions at the cell membrane that allow for the activation of AKT. Independent studies in adipocytes and fibroblasts confirm that PI3K is a relevant step in AKT activation and the insulin response associated with glucose transport. However, research in humans with obesity and type 2 diabetes shows that a reduction in PI3K activity does not necessarily imply a parallel reduction in AKT activation. The narrative is therefore well-supported as a cellular mechanism, but requires caution when transferred directly to all human tissues and metabolic conditions.

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 scientific question addressed by the publication is how the pathway formed by PI3K and PTEN contributes to tumor growth and angiogenesis, i.e., the formation of new blood vessels. The general hypothesis is that PI3K transmits signals that promote cell growth, survival, and proliferation, while PTEN acts as a brake on the same molecular network.Regarding paragraph 4.3 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, the relevant point is not the entire discussion on cancer. It is the segment stating that PI3K activates AKT. In simple terms, PI3K modifies lipids present on the cell membrane and creates an environment that recruits AKT to that site, making its activation possible. The analyzed publication can therefore support the general biological link PI3K AKT. It cannot, on its own, prove that this sequence occurs in the same way in every human tissue or that it determines all the metabolic effects attributed to insulin.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The publication is a review of scientific literature, not a clinical trial or an original experiment conducted on a new cohort of people, animals, or cells. The available abstract indicates that the authors examined studies on the roles of PI3K, PTEN, AKT, and other downstream targets in tumorigenesis and angiogenesis.The full text is not available in the provided material. Consequently, the bibliographic search strategy, the databases consulted, the inclusion and exclusion criteria, the number of selected publications, and any method for assessing the quality of the studies are not reported in the available material. There is also no mention of sample size, a control group, dosages, clinical endpoints, statistical analyses, or follow-up, as the work is presented as a narrative review.

4. RESULTS

According to the abstract, PI3K and PTEN participate in cellular functions such as metabolism, proliferation, cell cycle progression, and survival. PI3K can be activated by growth factors and signals that promote angiogenesis, including vascular endothelial growth factor, known as VEGF. The abstract also reports that amplifications or mutations of PI3K and loss of PTEN are frequent in various human solid tumors.The relevant finding for the book section is the statement that PI3K signaling regulates tumor growth and angiogenesis by activating AKT and other targets. In other words, PI3K is not described as a simple marker: it is positioned upstream of AKT in the signal transduction chain. The abstract does not report numerical values, quantitative results, effect sizes, P-values, or statistical analyses. It is therefore not possible to determine from the available material the quantitative strength of the individual associations discussed in the review.

5. INTERPRETATION

The relevant biological message is that PI3K can act as a connecting link between a signal received by the cell and AKT, a protein that, once activated, modifies many cellular responses. The technical version of this step is that PI3K produces membrane phosphoinositides, lipids that promote the recruitment and activation of AKT through its PH domain, a protein region capable of binding these lipids.This is the segment of the chain documented by the publication that is the subject of the Evidence Review: PI3K AKT. The reference is consistent with the "relay race" metaphor used in the book, provided it is considered a simplification. PI3K does not literally transfer a substance to AKT: it modifies the molecular context of the membrane and allows for the activation of multiple proteins, including AKT. Since the study analyzed is a review focused primarily on angiogenesis and tumors, its use in the context of insulin signaling is mechanistic and does not, by itself, constitute a direct demonstration of the effects of insulin in human metabolic tissues.

6. INDEPENDENT SUPPORTING EVIDENCE

Direct confirmation in the insulin context comes from experiments on 3T3-L1 adipocytes, murine cells used as a model for fat cells. Insulin increased the phosphorylation of AKT1/2, which is a chemical modification necessary for its activation. The PI3K inhibitor wortmannin and the experimental reduction of PI3K expression suppressed this phosphorylation. In the same model, the inhibition or reduction of PI3K, PDK1, or AKT1/2 prevented the translocation of

GLUT4, the transporter that brings glucose into the cell, toward the membrane. The study therefore supports the sequence insulin PI3K AKT increased availability of GLUT4 in the membrane, although it remains a cellular experiment and not evidence in humans [1].A second study, also conducted in 3T3-L1 adipocytes, evaluated AKT rendered constitutively active and artificially directed to the membrane. In the absence of insulin, this form of AKT increased glucose uptake and the translocation of GLUT4 to the plasma membrane. The result does not by itself demonstrate every step upstream of AKT, but it confirms the functional role of AKT as a downstream effector of the pathway described in the book [2].More general independent evidence was obtained in fibroblasts stimulated with PDGF, a growth factor other than insulin. In these cells, the activation of AKT and AKT2 was blocked by the PI3K inhibitor wortmannin; furthermore, the in vitro addition of a PI3K lipid product induced AKT activity. This study confirms that the PI3K AKT relationship is not limited to the tumor signaling discussed in the original publication, but is a reproducible principle of growth signal transduction. The limitation is that the model concerns neither insulin nor human metabolic cells [3].Taken together, these independent studies support the central direction of the narrative: PI3K activation promotes AKT activation and, in experimental adipocytes, this pathway participates in the response that increases the presence of GLUT4 in the membrane. The chain is particularly solid at the cellular level; its quantitative translation into different human organs requires specific evidence for each tissue and metabolic condition.

7. CONFLICTING EVIDENCE

An important element of caution comes from a human study that compared skeletal muscle from lean subjects, obese subjects without diabetes, and obese subjects with type 2 diabetes during a hyperinsulinemic-euglycemic clamp, a procedure that keeps glycemia controlled while insulin is administered. In participants with diabetes, the activation of PI3K associated with IRS-1 and IRS-2 was reduced compared to lean subjects, while insulin-induced activation and phosphorylation of AKT1/2 were normal. Glucose transport and utilization were nonetheless reduced in the obese groups, especially in the one with diabetes [4].This result does not negate the PI3K AKT molecular link observed in cellular models. However, it shows that in human muscle with obesity and type 2 diabetes, a measurable decrease in PI3K at the IRS level does not necessarily translate into a proportional decrease in AKT. Compensatory mechanisms, differences between PI3K isoforms, measurement timing, signal localization, or parallel pathways may be involved. This conflicting evidence therefore limits the idea of a linear and identical relationship in every biological context.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the Evidence Review from the independent research used to evaluate the PI3K → AKT pathway in the book's narrative context.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Narrative review	Literature on angiogenesis and tumors	Describes PI3K as a pathway that activates AKT and regulates cellular functions.	biologically consistent evidence	moderate
[1]	Cellular and biochemical	3T3-L1 murine adipocytes and cell-free tests	Inhibition or reduction of PI3K reduced insulin-induced AKT phosphorylation and prevented GLUT4 translocation.	direct confirmation	moderate
[2]	Cellular with genetic manipulation	3T3-L1 murine adipocytes	Constitutively active AKT increased glucose uptake and GLUT4 translocation without insulin.	indirect confirmation	moderate
[3]	Cellular and biochemical	PDGF-stimulated fibroblasts	PI3K inhibition blocked AKT activation; PI3K lipid products induced AKT activity.	indirect confirmation	moderate
[4]	Physiological observational with experimental intervention	Skeletal muscle of lean, obese, and obese adults with type 2 diabetes	In type 2 diabetes, lower PI3K activity associated with IRS coexisted with preserved insulin-stimulated AKT1/2 activation.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The analyzed publication is relevant to the passage in the book that places PI3K upstream of AKT. This relationship is well-supported at the molecular and cellular level by independent evidence, including research in adipocytes that links the PI3K-AKT pathway to the movement of GLUT4 toward the membrane and the increase in glucose uptake.The strength of the confirmation is primarily mechanistic. Research in humans shows that the relationship between PI3K, AKT, and metabolic response can be modulated by disease, the tissue being studied, and compensatory mechanisms. The relay race metaphor remains useful for understanding the general direction of the signal, but it does not describe the full complexity of the insulin network.

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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