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The human insulin receptor and its relationship with the tyrosine kinase oncogene family - Evidence review

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ONLINE ARTICLE

ARTICLE INFORMATION

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1. ABSTRACT

The analyzed study reconstructed the sequence of the human insulin receptor precursor starting from a complementary DNA clone. It described a protein of 1,370 amino acids, with an alpha subunit facing the outside of the cell and a beta subunit that spans the membrane. This organization makes it biologically plausible that the insulin signal can be received on the cell surface and transmitted inside.In paragraph 4.1 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, the publication contributes primarily to supporting the description of the receptor as a transmembrane structure composed of an external and an internal part. The available abstract alone does not directly demonstrate the shape change induced by insulin nor autophosphorylation. However, independent studies on purified receptors, cell models, and artificially reconstituted complete human receptors confirm that insulin binding is followed by structural changes and promotes the activation of the intracellular component. No directly conflicting evidence has emerged, but the evidence remains primarily biochemical and structural, not clinical.

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 what the primary structure, i.e., the amino acid sequence, of the human insulin receptor was, and whether this protein showed similarities to other proteins capable of transmitting growth signals. The implicit hypothesis was that knowing the receptor's sequence would allow for an understanding of its organization: a portion exposed outside the cell, a region that crosses the membrane, and an internal portion potentially involved in signal transmission.The research is relevant to section 4.1 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi because it documents the structural basis of the popular science image of a protein that connects the outside and the inside of the cell. The study can demonstrate the predicted sequence of the precursor and the presence of segments compatible with the receptor subunits. However, based solely on the available abstract, it cannot directly demonstrate in detail the binding of insulin, the conformational change of the receptor, or the subsequent autophosphorylation.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

Only the abstract of the publication is available. The authors report having deduced the entire 1,370-amino acid sequence of the human insulin receptor precursor from a single complementary DNA clone, which is a DNA copy obtained from messenger RNA. This strategy allows for the reconstruction of the protein sequence encoded by the gene.The available material indicates that the authors analyzed the sequence to identify an initial signal peptide, an alpha subunit, a cleavage site for a maturation enzyme, and a beta subunit containing a transmembrane sequence. Comparisons of sequence similarity with the human epidermal growth factor receptor and proteins of the src family are also reported. The number of biological samples, the origin of the tissues, the selection criteria, the detailed experimental techniques, the controls, the statistical analyses, and the significance values are not reported in the available material.

4. RESULTS

The main result was the prediction of a protein precursor 1,370 amino acids long. In simple terms, the sequence indicated that the receptor was not a uniform protein: it possessed a part intended to be exposed to the outside of the cell and a part intended to communicate with its interior.More precisely, the precursor began with a 27-amino acid signal sequence, which is a short segment that directs the protein toward the cellular pathway that will carry it to the membrane. This was followed by the alpha subunit, a cleavage site for protein maturation, and the beta subunit. The latter contained a 23-amino acid transmembrane sequence, compatible with crossing the lipid bilayer of the cell membrane.The authors also reported sequence similarities with the epidermal growth factor receptor and members of the src family of oncogenes. This means that the insulin receptor shared characteristics with proteins known to have tyrosine kinase activity, i.e., capable of transferring phosphate groups onto tyrosine residues. The abstract does not report functional experiments measuring autophosphorylation after the addition of insulin, nor quantitative data on signal intensity, binding affinity, or changes in the receptor's shape.

5. INTERPRETATION

For a cell, having a transmembrane receptor means being able to transform a message present in the blood into an internal response. The structure described in the study makes the distinction narrated in the book consistent between an external component, which can recognize insulin, and an internal component, which can participate in signal transmission.The segment actually documented by the publication subject to the Evidence Review is therefore primarily this: the insulin receptor is produced as a precursor and includes an alpha subunit, a beta subunit, and a transmembrane region. The similarity to tyrosine kinase proteins reinforces the hypothesis that the intracellular portion has a signaling function. However, stating that insulin binds to the external part, changes the shape of the entire receptor, and activates autophosphorylation requires further functional evidence, which is not reported in the abstract of the analyzed study.

6. INDEPENDENT CONFIRMING EVIDENCE

Initial independent confirmation concerns the passage stating that insulin binding produces a structural change in the receptor. Schenker and Kohanski studied a purified murine insulin receptor in vitro. After insulin binding, the rate of dimer formation between beta subunits increased, as detected by a cross-linking technique—a method of chemically connecting components in close proximity. The result is consistent with a change in the relative arrangement of the beta subunits and the initiation of autophosphorylation. This is direct mechanistic confirmation of the conformational change, but it is not a human experiment, nor does it measure a clinical effect [1].Lee and colleagues examined the insulin receptor using fluorescence spectroscopy, a technique that signals changes in the protein's physical environment. Insulin binding increased the receptor's fluorescence parameters, and the timing of the conformational change was found to be similar to that of autophosphorylation. The authors interpreted these data as an indication that the hormone-induced structural modification increases the rate of autophosphorylation, without necessarily increasing the affinity for ATP, the molecule that provides energy for the reaction. The model was experimental and not clinical, but it consistently links binding, shape change, and activation of the intracellular portion [2].More recent structural evidence was obtained by Gutmann and colleagues using complete human insulin receptors inserted into lipid nanodiscs, which are small artificial membrane discs. Using single-particle electron microscopy, the addition of insulin converted the external part of the receptor from an inverted U-shape to a T-shape. This rearrangement brought the transmembrane regions closer together and promoted the autophosphorylation of the intracellular tyrosine kinase domains. The work does not demonstrate a clinical benefit, but it represents a particularly relevant confirmation of the sequence described in the book: external binding, structural modification, and signal transmission to the interior [3].

7. CONFLICTING EVIDENCE

No directly conflicting evidence of sufficient relevance has been identified; this does not prove the absence of contrary results. The main interpretive limitation is different: various experimental studies may describe different aspects of the same process because they use purified receptors, cells, or artificial membranes. Furthermore, the change in shape observed in these models does not in itself equate to a demonstration of the entire metabolic response in a human organism.The narrative of the paragraph therefore remains structurally and mechanistically consistent. However, a distinction must be maintained between what is shown directly—that is, the architecture of the receptor and its reorganization following insulin binding—and what requires further biological steps, namely the final effects on tissue metabolism and personal health.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the review from independent confirmations and indicates the level at which each piece of evidence supports the narrative of the paragraph.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Molecular sequencing study	Human insulin receptor complementary DNA clone	Identified 1,370-amino acid precursor, alpha subunit, beta subunit, and transmembrane segment	direct confirmation	moderate
[1]	In vitro biochemical study	Purified insulin receptor of murine origin	Insulin increased cross-linking between beta subunits, consistent with a conformational change	direct confirmation	moderate
[2]	Cellular biophysical study	Insulin receptor studied with fluorescence in a murine experimental model	Insulin binding induced conformational changes with timing similar to autophosphorylation	indirect confirmation	moderate
[3]	Structural and biochemical study	Full-length human insulin receptor in lipid nanodiscs	Insulin converted the external structure from U to T and promoted intracellular autophosphorylation	direct confirmation	high

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed has provided an important molecular basis for understanding the human insulin receptor as a protein formed by external, transmembrane, and intracellular components. This is the step in the book's narrative that is directly supported by the available material.

Independent research confirms that insulin induces a reorganization of the receptor and that this reorganization promotes autophosphorylation, the initial step of signal transduction. The narrative is therefore well-supported at a mechanistic level. However, it does not, on its own, allow for the deduction of the complete metabolic response of all tissues or individual clinical consequences.

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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