LIFE Science Hub
JOURNAL OF SCIENCE
EXPANDING KNOWLEDGE ABOUT NUTRITION AND HEALTH

ORIGINAL RESEARCH
ISSN 2845-7501

Delta5-desaturase mRNA levels increase with simvastatin via SREBP-1 in the early stages, not via PPARalpha, in THP-1 cells - Evidence review

Dott. A. Colonnese[1]

1 Nutritional Biologist, Italy

1. ABSTRACT

The analyzed study evaluated whether simvastatin can increase delta5-desaturase expression in THP-1 cells, a human monocyte cell line, and which genetic regulator is involved. After exposure to 5 micromolar simvastatin, the increase in delta5-desaturase messenger RNA appeared after 12 hours; the increase in its metabolic activity was observed after 24 hours. The authors also detected an early increase in SREBP-1, a protein that activates genes involved in fat synthesis.In the narrative of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, this research contributes to the passage stating that SREBP-1c participates in the initial regulation of delta5-desaturase. Independent studies show that insulin, SREBP-1, and other lipogenic signals can increase FADS1, the gene encoding this enzyme, in experimental monocytes, macrophages, and liver cells. However, the contribution of PPARalpha varies between cell types and species. The evidence therefore primarily supports a cellular mechanism and does not demonstrate that hyperinsulinemia automatically increases arachidonic acid or inflammation in humans.

ONLINE ARTICLE

ARTICLE INFORMATION

Published: November 22, 2026
Updated: November 22, 2026

DOI 10.5281/zenodo.24437054

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 whether simvastatin, in addition to reducing cellular cholesterol synthesis, increased the expression of delta-5 desaturase and whether this effect depended primarily on SREBP-1 or PPAR-alpha. Delta-5 desaturase is an enzyme that introduces a double bond into specific polyunsaturated fatty acids; in the omega-6 pathway, it contributes to the conversion of DGLA (dihomo-gamma-linolenic acid) into arachidonic acid.The publication is relevant to section 5.3.2 because it documents a specific segment of the narrative: in cultured monocytes, a signal that modifies lipid metabolism first increases SREBP-1 and subsequently the messenger RNA of delta-5 desaturase. It does not directly verify the entire insulin SREBP-1c delta-5 desaturase arachidonic acid eicosanoids sequence, nor does it measure inflammatory or clinical outcomes in humans. Furthermore, the experimental signal studied is simvastatin, not insulin.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The authors used THP-1 cells, a human cell line with monocytic characteristics, incubating them with 5 micromolar simvastatin for varying durations. Delta-5 desaturase activity was estimated using the product-to-precursor ratio along the metabolic pathway, following the administration of carbon-14 labeled linoleic acid. The messenger RNA expression of delta-5 desaturase and the regulators SREBP-1 and PPAR-alpha was evaluated over time.To distinguish the potential role of PPAR receptors, the authors employed the PPAR-alpha agonists WY 14643 and fenofibrate, and the PPAR-gamma agonist ciglitazone. They also evaluated the beta-oxidation of linoleic acid, which is the process by which the cell degrades fatty acids to generate energy. The number of replicates, exclusion criteria, details of analytical techniques, statistical methods, significance values, and variability of the results are not reported in the available material.

4. RESULTS

The main result is temporal. In cells treated with simvastatin, the messenger RNA of delta-5-desaturase increased after 12 hours; the enzyme's activity, estimated by the product/precursor ratio, increased after 24 hours compared to controls. In simple terms, the genetic message required to produce the enzyme grew first, and only subsequently did the metabolic transformation attributed to the enzyme itself increase.Simvastatin increased SREBP-1 levels as early as 8 hours. Conversely, after 48 hours, it did not modify either PPARalpha or the beta-oxidation of linoleic acid, a process regulated by PPARalpha. PPARalpha and PPARgamma agonists did not modify the conversion of linoleic acid or the activity of delta-5-desaturase between 8 and 48 hours; however, they did increase the messenger RNA of delta-5-desaturase at 48 hours. Fenofibrate, but not the other agonists indicated, showed a synergistic effect with simvastatin at 48 hours, along with an increase in PPARalpha and beta-oxidation.The abstract does not report absolute values, percentage variations, confidence intervals, or P-values. Therefore, the direction of the observed effects can be described, but not their quantitative magnitude or statistical precision.

5. INTERPRETATION

For the cell, the result suggests that simvastatin may initiate a genetic regulation program that increases the availability of delta-5 desaturase. SREBP-1, or sterol regulatory element-binding protein 1, is a transcription factor: a protein that can increase the reading of specific genes. In this experiment, the increase in SREBP-1 precedes that of the delta-5 desaturase messenger RNA, a sequence consistent with an initial regulatory role.The point supported by the work is therefore SREBP-1 early increase in delta-5 desaturase expression. The authors' interpretation is that SREBP-1 is involved in the early regulation induced by simvastatin, while PPARalpha does not appear to be responsible for the initial phase. This conclusion is reasonable in the THP-1 model, but it does not demonstrate a direct link of SREBP-1c to the FADS1 gene, does not completely separate the SREBP-1 isoforms, and cannot be automatically transferred to primary monocytes, the liver, or the tissues of people

with hyperinsulinemia.

6. INDEPENDENT SUPPORTING EVIDENCE

A first independent study directly examined the effect of insulin on THP-1 cells. The authors observed that insulin induced the expression of FADS1, FADS2, and SREBP-1c in a dose- and time-dependent manner. FADS1 is the gene for delta-5 desaturase. This result confirms the passage in the book stating that experimental monocytes respond to an anabolic signal by increasing the expression of desaturase genes; however, as this is a cell line, it does not demonstrate the effects of insulin on circulating monocytes in humans [1].In a different model, primary rat liver cells treated with insulin showed an approximately fourfold increase in the nuclear fraction of SREBP-1. In the same system, insulin increased delta-5 desaturase messenger RNA by up to 1.5 times. Furthermore, experimentally increasing the nuclear form of SREBP-1c boosted the delta-5 desaturase transcript by approximately 3.6 times; the addition of insulin did not produce a further increase. This data reinforces the idea that SREBP-1c may mediate part of the insulin signal, but the model is hepatic and animal-based [2].A further study on human macrophages showed that the activation of LXR, a nuclear receptor involved in lipid metabolism, increased the expression of FADS1 and FADS2 and boosted the synthesis of polyunsaturated fatty acids. Inhibiting the maturation of SREBP-1 strongly reduced the expression of the two desaturases. The authors also detected an increase in arachidonic acid in macrophage phospholipids. This is a biologically consistent confirmation of the SREBP-1 desaturase increased cellular availability of arachidonic acid pathway, but the upstream signal was LXR and not insulin [3].

7. CONFLICTING EVIDENCE

The conclusion of the original study concerns the early phase in THP-1 cells and does not state that PPARalpha can never regulate delta-5 desaturase. This distinction is precisely what is important. In mice fed with fenofibrate, a PPARalpha agonist, the hepatic expression of delta-5 and delta-6 desaturase increased; troglitazone, a PPARgamma agonist, did not produce the same effect. The study also showed the activation of desaturases by SREBP-1 in the murine liver [4].This evidence does not invalidate the result of the analyzed work: instead, it indicates that PPARalpha can contribute to the regulation of desaturases in a different context, namely mouse liver, dietary exposure to a fibrate, and observation not limited to the first few hours. The regulation of FADS1 is therefore dependent on the tissue, the stimulating signal, and the observation time. No directly conflicting evidence sufficiently relevant to the early sequence of simvastatin SREBP-1 delta-5 desaturase messenger RNA in THP-1 cells has been identified; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the initial experimental result from independent publications that confirm or define the scope of the book's narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Cellular	THP-1 cells	Simvastatin increased SREBP-1 at 8 hours, delta-5 desaturase mRNA at 12 hours, and enzymatic activity at 24 hours.	direct confirmation	moderate
[1]	Cellular	THP-1 cells	Insulin increased the expression of SREBP-1c, FADS1, and FADS2 in a time- and dose-dependent manner.	direct confirmation	moderate
[2]	Cellular and animal	Primary rat hepatocytes and mouse models	Insulin and nuclear SREBP-1c increased delta-5 desaturase expression.	indirect confirmation	moderate
[3]	Cellular and animal	Human macrophages and ApoE-deficient mice	LXR activation increased FADS1/FADS2 and cellular arachidonic acid through an SREBP-1-dependent mechanism.	biologically consistent evidence	moderate
[4]	Animal	Fegato di topo	SREBP-1 increased desaturases; fenofibrate increased delta-5 and delta-6 desaturase through PPARalpha.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The analyzed study pertinently supports the idea that an early increase in SREBP-1 may accompany and precede the increase in delta-5 desaturase expression in THP-1 monocytes. Independent research makes the mechanism quite well-supported at the cellular level and in animal models. However, extending this chain to persistent hyperinsulinemia, eicosanoid production, and inflammatory outcomes in humans remains preliminary. PPARalpha does not appear decisive in the early phase of the original model, but it may regulate desaturases in other tissues and conditions.

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.

11. RIFERIMENTI BIBLIOGRAFICI

[1] **Insulin induces fatty acid desaturase expression in human monocytes**
Arbo et al., 2011
Scandinavian Journal of Clinical and Laboratory Investigation
DOI: https://doi.org/10.3109/00365513.2011.566350

[2] **Regulation of hepatic fatty acid elongase and desaturase expression in diabetes and obesity**
Wang et al., 2006
Journal of Lipid Research
DOI: https://doi.org/10.1194/jlr.M600177-JLR200

[3] **Liver X Receptor Activation Promotes Polyunsaturated Fatty Acid Synthesis in Macrophages**
Varin et al., 2015
Arteriosclerosis, Thrombosis, and Vascular Biology
DOI: https://doi.org/10.1161/ATVBAHA.115.305539

[4] **Dual regulation of mouse Δ5- and Δ6-desaturase gene expression by SREBP-1 and PPARa**
Matsuzaka et al., 2002
Journal of Lipid Research
DOI: https://doi.org/10.1016/S0022-2275(20)30193-0