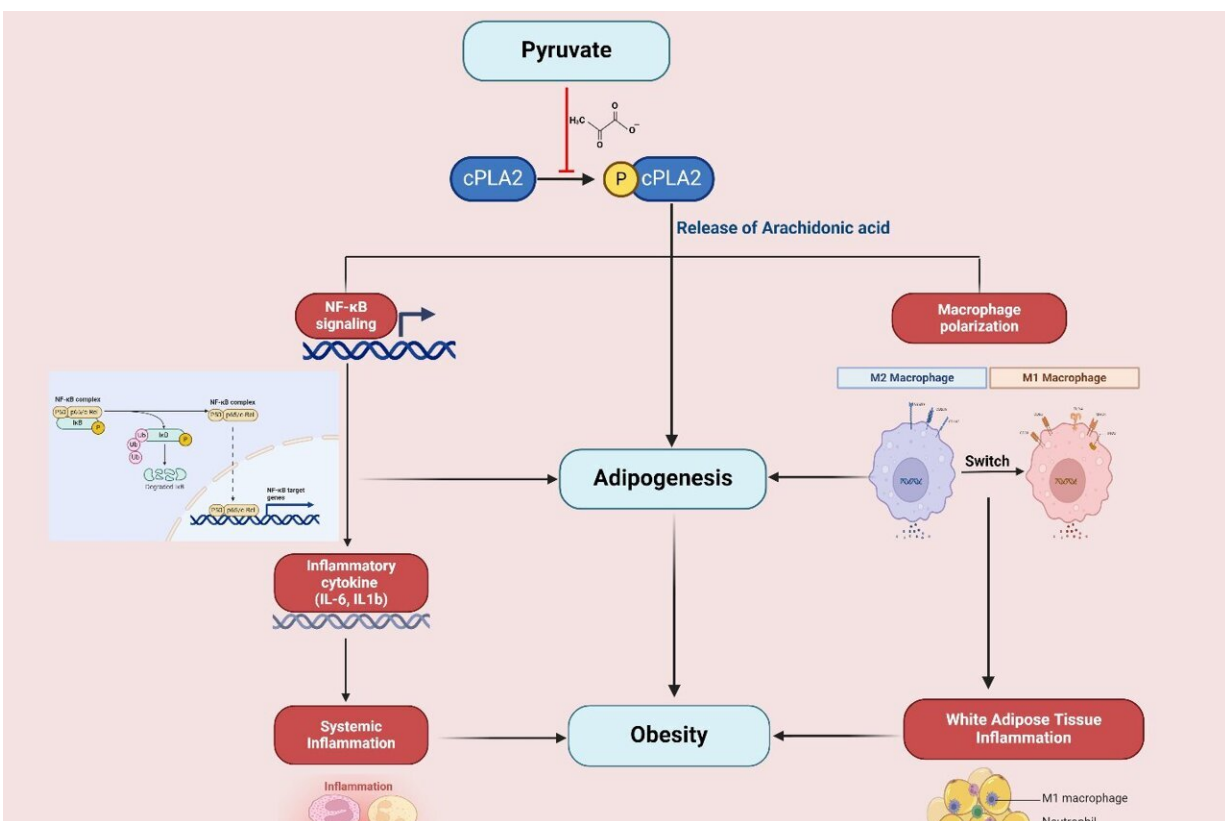


Dietary pyruvate targets cytosolic phospholipase A2 to mitigate inflammation and obesity in mice

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The mechanism of action of pyruvate by targeting cPLA2 and inhibiting cPLA2-mediated downstream signaling. Credit: Sadaf Hasan, Nabil Ghani, Xiangli Zhao, Julia Good, Amanda Huang, Hailey Lynn Wrona, Jody Liu, Chuan-ju Liu

An article in *Protein & Cell* discusses the multifactorial nature of obesity, highlighting its association with chronic low-grade inflammation, or meta-inflammation, which contributes to metabolic disorders. The paper is titled "[Dietary pyruvate targets cytosolic phospholipase A2 to mitigate inflammation and obesity in mice.](#)"

Pyruvate, a glycolytic metabolite, was found to inhibit adipogenic differentiation in vitro and significantly prevent HFD-induced weight gain and inflammation in mice. Through drug affinity responsive target stability, proteomics, and cellular thermal shift assays, cPLA2 was identified as a target of pyruvate.

Mice with global cPLA2 ablation showed diminished protective effects of pyruvate, confirming the importance of the pyruvate/cPLA2 interaction in mitigating obesity and inflammation. The study underscores pyruvate's potential as a therapeutic option for obesity, given its previous clinical use and safety.

Key findings from the study include:

1. Pyruvate was shown to inhibit the differentiation of preadipocytes into adipocytes. In vitro studies demonstrated that pyruvate downregulated key adipogenic transcriptional markers such as PPAR γ and CEBP α , along with adipocyte-related genes like Fabp4. Pyruvate reduced intracellular lipid and triglyceride accumulation, indicating its effectiveness in suppressing adipogenesis across different cell types.
2. In vivo experiments with male C57BL/6 mice indicated that pyruvate administration significantly prevented HFD-induced weight gain and central adiposity. Pyruvate-treated mice exhibited lower body weights and reduced abdominal circumferences compared to untreated HFD-fed [mice](#). This was accompanied by a decrease in [white adipose tissue](#) (WAT)

- inflammation and metabolic dysregulation.
3. The study identified cPLA2 as a novel target of pyruvate using drug affinity responsive target stability, proteomics, and cellular thermal shift assays. cPLA2 plays a critical role in adipocytic differentiation and [chronic inflammation](#). Mice with global ablation of cPLA2 displayed a significant reduction in the protective effects of pyruvate, confirming the interaction between pyruvate and cPLA2 as essential for mitigating inflammation and obesity.
 4. Reduction of Inflammatory Markers: Pyruvate administration resulted in the downregulation of various inflammatory genes, including IL-6, IL-1B, CCL2, and TNF α . The study showed that pyruvate's anti-inflammatory effects were mediated through the inhibition of cPLA2, which in turn reduced the NF- κ B-dependent expression of pro-inflammatory cytokines.

The study establishes pyruvate as a promising therapeutic agent against obesity and its related inflammatory and [metabolic disorders](#). By targeting cPLA2, pyruvate effectively inhibits adipogenesis, reduces WAT inflammation, and prevents HFD-induced weight gain.

These findings highlight the potential of pyruvate as an anti-inflammatory and anti-obesity supplement that could be integrated into regular diets or used as a dietary supplement.

Given its previous clinical use, pyruvate presents a safe and viable alternative for [obesity](#) treatment. The study's insights into the molecular mechanisms of pyruvate provide a basis for further research and development of [pyruvate](#)-based interventions for metabolic diseases.

More information: Sadaf Hasan et al, Dietary pyruvate targets cytosolic phospholipase A2 to mitigate inflammation and obesity in mice, *Protein & Cell* (2024). [DOI: 10.1093/procel/pwae014](https://doi.org/10.1093/procel/pwae014)

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