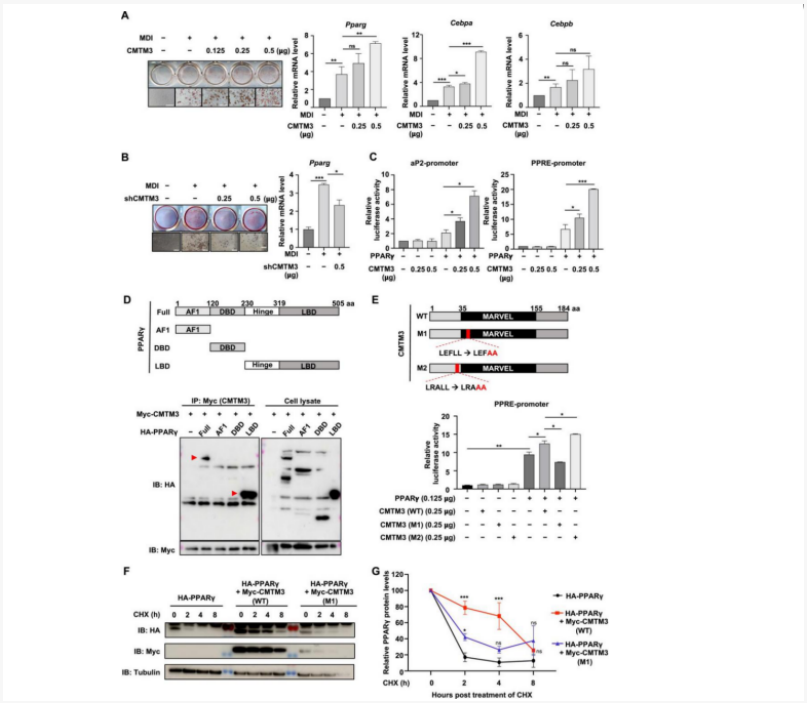
How a tumor suppressor became a key to fat cell development

FAYETTEVILLE, GA, UNITED STATES, August 1, 2025 /EINPresswire.com/ -- A protein once known solely for its cancer-suppressing roles is now making waves in obesity research. Scientists have discovered that CMTM3, a membrane-associated protein, significantly boosts the formation of fat cells by regulating PPARγ, a master gene in adipogenesis.



CMTM3 is a positive regulator during adipocyte differentiation.

Adipogenesis, the process of forming mature fat cells, is central to energy balance and obesity-related diseases. At the heart of this transformation is PPARγ, a nuclear receptor that activates genes essential for fat storage and cell maturation. While many regulators of PPARγ have been identified, the possible role of CMTM3—until now primarily viewed as a tumor suppressor—remained largely unexplored. Recent hints from cancer studies raised the possibility that CMTM3 might interact with PPARγ, but its role in fat biology had never been examined. Due to these gaps, there is a strong need to investigate how CMTM3 functions in adipocyte development and metabolic regulation.

In a collaborative effort, researchers from Chonnam National University, Ewha Woman's University, and Wenzhou Medical University have revealed a surprising function of CMTM3 in fat metabolism. Their study (DOI: 10.1016/j.gendis.2025.101699), published on May 30, 2025, in Genes & Diseases, shows that CMTM3 not only binds directly to PPARγ but also enhances its transcriptional activity and protein stability during fat cell differentiation. This discovery broadens our understanding of CMTM3 and offers a new angle on obesity research.

To uncover the function of CMTM3 in fat cell biology, the researchers conducted a series of cellular and molecular experiments. When CMTM3 was overexpressed in 3T3-L1 preadipocytes,

the cells showed increased lipid accumulation and higher levels of Pparg and Cebpa—key markers of adipogenesis. Conversely, silencing CMTM3 led to diminished fat cell formation and lower expression of these genes.

Digging deeper, the team found that CMTM3 physically interacts with PPARγ, particularly through its MARVEL domain, which contains an LXXLL motif known to mediate protein-protein interactions in nuclear receptor signaling. Mutations in this motif disrupted PPARγ activation and reduced the stability of the PPARγ protein. In contrast, wild-type CMTM3 extended the half-life of PPARγ, effectively boosting its regulatory power. These results demonstrate that CMTM3 not only supports the transcriptional activity of PPARγ but also protects it from degradation, acting as a crucial enhancer during adipocyte differentiation.

“This was an unexpected but exciting finding,” said Dr. Kwang Youl Lee, corresponding author of the study. “CMTM3 has long been considered mainly in the context of cancer, but we now see that it has an equally important role in fat cell biology. By enhancing both the activity and stability of PPARγ, CMTM3 stands out as a key player in adipogenesis. This opens up intriguing possibilities for metabolic disease intervention.”

The discovery of CMTM3’s role in regulating fat cell development opens a new chapter in the search for obesity treatments. By acting upstream of PPARγ, CMTM3 emerges as a promising molecular target for modulating adipogenesis. This could lead to innovative therapies that either boost or inhibit fat cell formation depending on the clinical need—ranging from obesity and metabolic syndrome to lipodystrophy. Furthermore, the findings encourage broader exploration of proteins like CMTM3 that may carry dual functions in both cancer biology and metabolism.

References
DOI
10.1016/j.gendis.2025.101699

Original Source URL
https://doi.org/10.1016/j.gendis.2025.101699

Funding Information
This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (No. 2019R1A5A2027521).

Lucy Wang
BioDesign Research
email us here

we have missed, please do bring it to our attention. Your help is welcome. EIN Presswire, Everyone's Internet News Presswire™, tries to define some of the boundaries that are reasonable in today's world. Please see our Editorial Guidelines for more information.