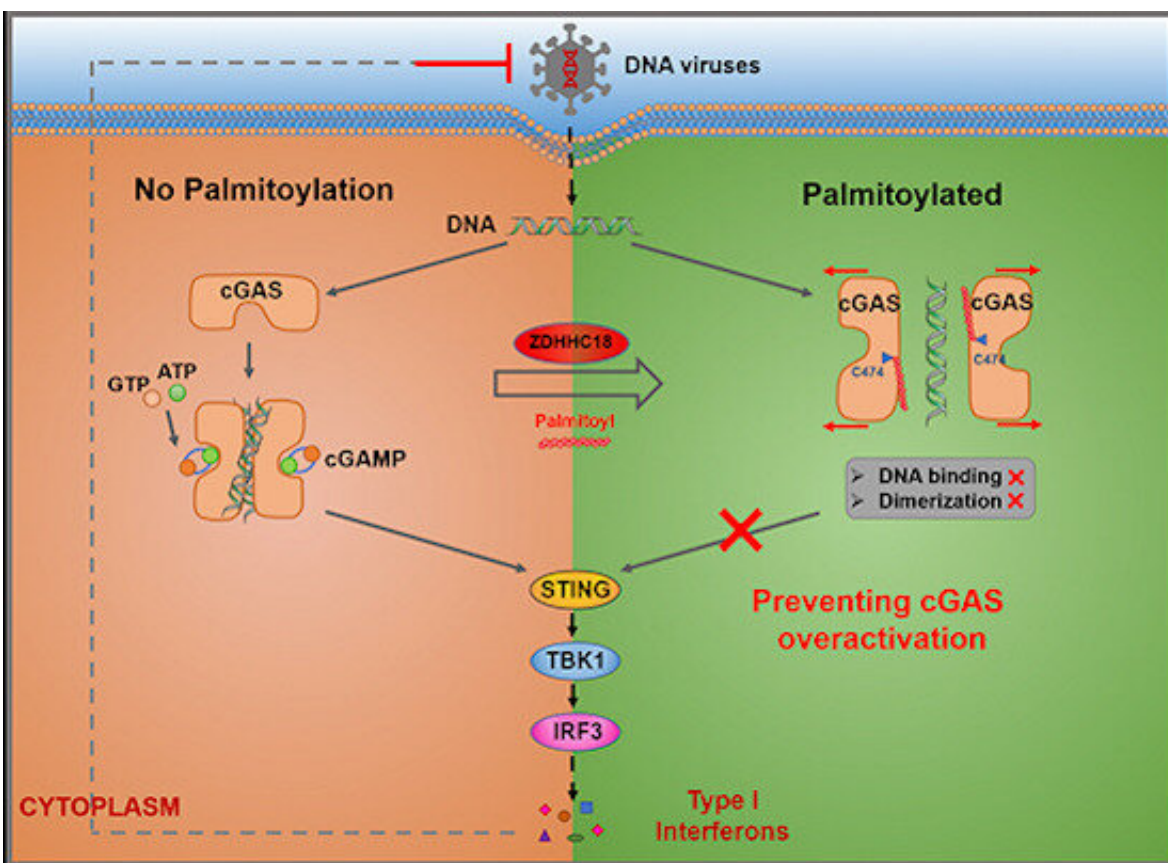


Molecular mechanism of ZDHHC18-mediated palmitoylation of cGAS in innate immunity inhibition

May 12 2022, by Li Yuan



Detection of double-stranded DNA by cGAS triggers innate immune responses. ZDHHC18-mediated palmitoylation of cGAS sheds light on a novel posttranslational modification that leads to the fine-tuning of cGAS-mediated innate immune responses. Credit: *The EMBO Journal* (2022). DOI: 10.15252/emboj.2021109272

Cyclic GMP-AMP synthase (cGAS), a double-stranded DNA (dsDNA) sensing protein, plays an important role in the strong innate immune response induced by pathogen derived nucleic acids.

Previous studies have revealed the essential roles of cGAS in multiple [biological processes](#), including pathogen invasion and autoimmune diseases. cGAS activity must be well regulated to maintain homeostasis, preventing both overinhibition and overactivation.

Recently, a research team led by Prof. Li Guohui from the Dalian Institute of Chemical Physics (DICP) of the Chinese Academy of Sciences (CAS), in collaboration with Prof. Yin Hang's group from Tsinghua University, revealed the molecular mechanism of the ZDHHC18-mediated palmitoylation of cGAS to inhibit innate immunity.

This study was published in *The EMBO Journal* on April 19.

The researchers found that the palmitoyltransferase ZDHHC18 could inhibit the formation of 2:2 cGAS/DNA complex by palmitoylation of the C474 site of cGAS, thereby inhibiting the excessive activation of cGAS and negatively regulating cGAS biological activities.

"We found that palmitoylation of cGAS is a novel inhibitory mechanism of innate immune responses," said Prof Xu. "It provides a potential target for [drug development](#) against [viral infections](#) and autoimmune diseases."

More information: Chengrui Shi et al, ZDHHC18 negatively regulates cGAS-mediated innate immunity through palmitoylation, *The EMBO Journal* (2022). [DOI: 10.15252/emboj.2021109272](https://doi.org/10.15252/emboj.2021109272)

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