# CKIP-1 limits foam cell formation and inhibits atherosclerosis by promoting degradation of Oct-1 by REGγ

With the support by the National Natural Science Foundation of China, the research team directed by Prof. Zhang LingQiang (张令强) at the State Key Laboratory of Proteomics, National Center of Protein Sciences (Beijing), Beijing Institute of Lifeomics, recently reported that CKIP-1 limits foam cell formation and inhibits atherosclerosis by promoting degradation of Oct-1 by REGγ, which was published in *Nature Communications* (2019, 10: 425).

Atherosclerosis-related cardiovascular diseases are the leading cause of mortality worldwide. Macrophages uptake modified lipoproteins and transform into foam cells, triggering an inflammatory response and thereby promoting plaque formation. The regulatory mechanism of this lipoprotein uptake-mediated foam cell formation process remains incompletely understood.

Here they show that casein kinase 2-interacting protein-1 (CKIP-1) is a suppressor of foam cell formation and atherosclerosis. Ckip-1 deficiency in mice leads to increased lipoprotein uptake and foam cell formation, indicating a protective role of CKIP-1 in this process. Ablation of Ckip-1 specifically upregulates the transcription of scavenger receptor LOX-1, but not that of CD36 and SR-A. Mechanistically, CKIP-1 interacts with the proteasome activator REGγ and targets the transcriptional factor Oct-1 for degradation, thereby suppressing the transcription of LOX-1 by Oct-1. Moreover, Ckip-1-deficient mice undergo accelerated atherosclerosis, and bone marrow transplantation reveals that Ckip-1 deficiency in hematopoietic cells is sufficient to increase atherosclerotic plaque formation. Therefore, CKIP-1 plays an essential antiatherosclerotic role through regulation of foam cell formation and cholesterol metabolism.

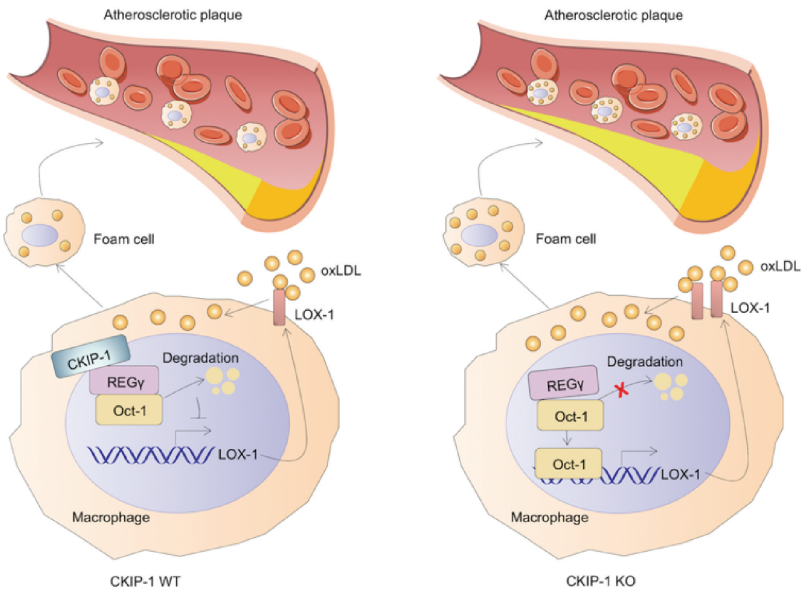


**Figure** A proposed model for the role of CKIP-1 in atherosclerosis.

In summary, they propose a working model that CKIP-1 couples proteasome activator REGγ to target Oct-1 for degradation, thereby suppressing the transcription of LOX-1. CKIP-1 is an intrinsic negative regulator of macrophage lipid uptake, and thus may act as a brake during foam cell formation and atherosclerosis. These data extended the understandings of CKIP-1 as a regulator of inflammatory response as well as atherogenesis progression, suggesting a potential strategy for atherosclerosis treatment based on targeting Oct-1-LOX-1 axis.