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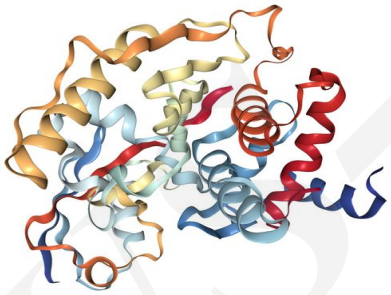
Sortilin-induced lipid accumulation and atherogenesis are suppressed by HNF1b SUMOylation promoted by flavone of *Polygonatum odoratum*

Key words: atherosclerosis; lipid accumulation; HNF1b; PAOA-flavone; SUMOylation

Research Summary

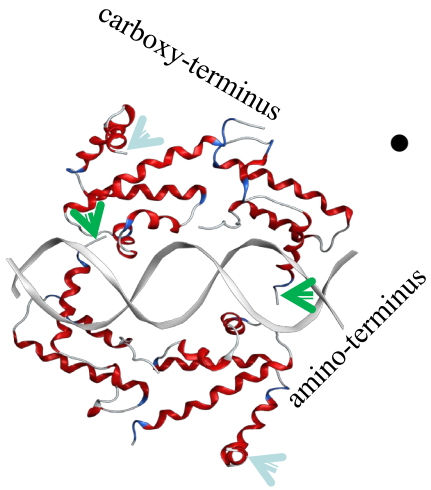
This article mainly focused on sortilin-mediated lipid metabolism and aortic atherosclerosis suppressed by PAOA-flavone-promoted HNF1b SUMOylation and demonstrated as follow:

PAOA-flavone



SUMO1 protein

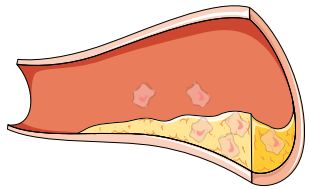
THP-1 macrophage



HNF1b

- **HNF1b transcriptionally suppressed sortilin expression and macrophage lipid accumulation to inhibit aortic lipid deposition and the development of atherosclerosis.**
- **PAOA-flavone facilitated SAE1-catalyzed SUMOylation of the HNF1b protein enhanced anti-atherosclerotic effect.**

LDLR$^{-/-}$ & ApoE$^{-/-}$ mice



atherosclerosis

Innovation points

● **Objective** to investigate the impact of HNF1b on macrophage sortilin-mediated lipid metabolism and aortic atherosclerosis and to further explore the role of PAOA-flavone-promoted SUMOylation in the atheroprotective efficacy of HNF1b

● **Summary of** PAOA-flavone-promoted SAE1-catalyzed SUMOylation of HNF1b to elevate cellular levels of HNF1b protein, then to suppress sortilin expression and sortilin-mediated lipid accumulation in macrophages and to alleviate aortic lipid deposition and atherosclerosis development.

● **Emphasis of** PAOA-flavone-promoted SAE1-catalyzed SUMOylation to enhance the atheroprotective efficacy of HNF1b, relieving foam cell formation and the development of aortic AS lesions.

Innovation points

A series of comprehensive Figures were generated to summarize the effect of PAOA-flavone-promoted the SUMOylation of HNF1b protein on macrophage sortilin-mediated lipid metabolism and aortic atherogenesis.

Figure 1 | HNF1b inhibited sortilin expression and alleviated macrophage cholesterol accumulation *in vitro*.

Figure 2 | HNF1b suppressed sortilin expression and ameliorated aortic atherogenesis *in vivo*.

Figure 3 | PAOA-flavone elevated HNF1b expression and inhibited macrophage sortilin levels and lipid accumulation.

Figure 4 | PAOA-flavone enhanced the SUMO1ylation of HNF1b protein.

Figure 5 | PAOA-flavone facilitated SAE1-catalyzed SUMOylation of the HNF1b protein to repress macrophage sortilin expression and lipid accumulation.

Figure 6 | PAOA-flavone upregulated the expression of SAE1 and HNF1b to resist aortic lipid deposition and atherosclerosis *in vivo*.