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**SYNERGISTIC EFFECT OF BIOMIMETIC MACROPHAGE MEMBRANE NANOPARTICLES TO TREAT ATHEROSCLEROSIS**

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Atherosclerosis is a chronic inflammatory disease characterised by an accumulation of plaques inside arterial wall. This process is a leading cause of morbidity and mortality globally. Management of atherosclerosis typically includes surgical interventions and pharmacological interventions. Further, traditional pharmacotherapy for atherosclerosis has a limited efficacy due to systemic distribution and rapid clearance, thereby hindering the availability at the target site of inflammation. While the current medication proves to be effective, the advent of nano-medicine opens an entire field of therapeutic options.

By leveraging the natural capabilities of macrophages, biomimetic nanoparticles (NPs) are engineered to evade the immune system and specifically bind to inflamed tissues. This is achieved by macrophage membrane (MM) coated SHP1i-loaded (MM@Lips-SHP1i) nanoparticles. A dual action mechanism is facilitated by this innovative approach: enhancing the efferocytosis of macrophages and acting as carriers of therapeutic agents. SHP1i is a complex that inhibits the activity of SHP1 enzyme. Further, SHP1i blocks the CD47-SIRPα pathway and promotes efferocytosis of apoptotic cells by macrophages. This results in stabilisation of the atherosclerotic plaque and reduces the occurrence of secondary necrosis, delaying the progression of atherosclerosis. Moreover, in the plaque area, MM@Lips-SHP1i nanoparticles can compete with macrophages to bind to oxidised low-density lipoprotein (oxLDL) and lipopolysaccharides (LPS). This reduces the uptake of new lipids by macrophages, therefore reducing the formation of foam cells and release of pro-inflammatory cytokines.

Furthermore, pro-efferocytic NPs can also deliver therapeutic agents that promote tissue healing, leading to a synergistic effect that combines cell clearance with regenerative medicine. These NPs follow either a passive or active targeting process. Once internalised by macrophages, NPs are broken down by triggers such as pH and enzymes which release the drug exerting the therapeutic effect. They can carry various therapeutic agents such as anti-inflammatory drugs and SHP1 inhibitors in the core. Common core materials include lipids, polymers, inorganic materials, etc..

Lastly, this work focuses on pro-efferocytic NPs, its targeted drug delivery system, efferocytic process, results of the trials conducted, limitations, and its implications on the future of modern medicine