Molecularly Engineered Macrophage-Derived Extracellular Vesicles with Inflammation Tropism and Intrinsic Heme Biosynthesis for Atherosclerosis Treatment

*Guanghao Wu[1], Haiyan Xie[2]**

[1]School of Materials Science and Engineering, Beijing Institute of Technology, Beijing, P.R. China. [2] School of Life Science, Beijing Institute of Technology, Beijing, P.R. China.
E-mail: yswgh110@163.com, hyanxie@bit.edu.cn

Cardiovascular disease is a disorder of the heart and blood vessels, and the leading cause of death in many parts of the world. For the cardiovascular diseases, atherosclerosis is a major contributor to cardiovascular diseases worldwide, and anti-inflammation is a promising strategy for atherosclerosis treatment.[1] Despite the progress made with recent use of nanocarriers, development of effective atherosclerosis targeting and inflammation-alleviation strategy is still challenging.[2] Extracellular vesicles enrich with specific contents (e.g. RNA, DNA, proteins, and small molecules) derived from the parental cells, and thus graft the native biological functions of original cells that may be used for major disease treatments. [3] In this talk, we report the molecularly engineered M2 macrophage-derived extracellular vesicles (M2 EVs) with inflammation-tropism and anti-inflammatory capabilities for atherosclerosis imaging and therapy. These engineered M2 EVs are derived from M2 macrophages and further electroporated with an FDA-approved hexyl 5-aminolevulinate hydrochloride (HAL). After systematic administration, the engineered M2 EVs exhibit excellent inflammation-tropism and anti-inflammation effects *via* the surface-bonded chemokine receptors and released anti-inflammatory cytokines from the anti-inflammatory M2 macrophages. Moreover, the encapsulated HAL can undergo intrinsic biosynthesis and metabolism of heme to generate anti-inflammatory carbon monoxide and bilirubin, which further enhance the anti-inflammation effects and finally alleviate atherosclerosis. Meanwhile, the intermediate protoporphyrin IX (PpIX) of heme biosynthesis pathway permits the fluorescence imaging and tracking of atherosclerosis. These M2 EVs engineered with inherent inflammation tropism and intrinsic biosynthesis of anti-inflammatory molecules can open a new avenue towards the treatment of atherosclerosis.

References

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