Docket #: S18-375

Monocyte-selective atherosclerosis drug delivery system

Researchers at Stanford have developed a targeted delivery system using carbon nanotubes to specifically deliver cardiovascular drugs to treat atherosclerosis. A feature of atherosclerotic plaque is the accumulation of apoptotic cells. These cells are meant to be cleared out via a phagocytic process known as efferocytosis to prevent the inflammatory consequences associated with the accumulation of apoptotic debris. However, efferocytosis can be turned off by expression of the anti-phagocytic "don't eat me" signal from CD47.
It was recently found that CD47 expression is significantly increased in atherosclerotic cardiovascular disease. Thus, methods that block CD47 signaling could restore efferocytosis and treat atherosclerosis. However, anti-CD47 antibodies have detrimental side effects such as anemia. To overcome this limitation, the inventors have developed a targeted delivery system using single-walled carbon nanotubes (SWNTs) to specifically deliver an inhibitor of the CD47 signaling pathway (downstream of CD47). This method allows the inhibitor to be specifically delivered to the monocytes that perform efferocytosis thereby reactivating them. This technology provides a targeted delivery system to more effectively treat atherosclerosis.

Stage of research
Using mouse models, the inventors showed that pro-efferocytic SWNTs reduced plaque burden in vivo without inducing anemia or compromising safety. Inventors are continuing research on potential utility with other macrophage-specific pathways.

Applications

- Treat or prevent atherosclerosis

Advantages

- New method to treat atherosclerosis by restoring efferocytosis
- Targeted, minimally-invasive, monocyte-selective immunotherapy
- Targeted delivery system:
    - Reduces the required dosage of the drug
    - Minimizes drug-associated side effects
- Compared to stents and surgical treatments, this approach is non-invasive and likely to be as or more efficacious

Publications

- A.M. Flores, N. Hosseini-Nassab, K-U Jarr, J. Ye, X. Zhu, R. Wirka, A.L. Koh, P. Tsantilas, Y. Want, V. Nanda, Y. Kojima, Y. Zeng, M. Lotfi, R. Sinclari, I.L. Weissman, E. Ingelsson, B.R. Smith and N.J. Leeper Pro-efferocytic nanoparticles are specifically taken up by lesional macrophages and prevent atherosclerosis *Nature Nanotechnology* Vol 15 February 2020 154-161.

Patents

- Published Application: WO2020190590
- Published Application: 20220151921

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