Docket #: S22-068

Amphiregulin nanobodies to prevent the development of fibroatheromas

Researchers at Stanford have discovered that nanobodies blocking amphiregulin (AREG) activity have the potential to impede the progression of early-stage atherosclerotic plaque lesions to advanced-stage fibroatheromas.

Coronary artery disease is a chronic inflammatory disease characterized by the build-up of atherosclerotic plaques. In the early stages, the plaques are rich in lipids and can be treated with medication and lifestyle changes. However, as they mature beyond the lipid-rich phase, a subset of activated T-cells within the plaques expresses the pro-fibrotic protein AREG. This protein promotes smooth muscle cell proliferation and fibrosis, leading to advancement of lesions into irreversible advanced-stage plaques, such as fibroatheroma. Fibroatheroma is a major precursor to plaque rupture that could lead to life-threatening acute cardiac syndromes.

To prevent the development of fibroatheromas, Stanford researchers have devised a nanobody-based platform that blocks the attachment of AREG to atherosclerotic plaque lesions, hindering disease progression. The nanobody is a bispecific protein with two immunoglobulin single variable (ISV) domains: one ISV domain binds to AREG and the other domain interferes with vascular smooth muscle cells activity. This nanobody-based platform targeting the root cause of fibroatheroma development could revolutionize treatment strategies for patients with coronary artery disease.

Stage of Development
Proof of concept

Applications

- Atherosclerosis treatment

Advantages

- Specifically targets development of fibroatheromas, which cannot be mitigated with current treatments

Publications

- Chowdhury, R. R., D'Addabbo, J., Huang, X., Veizades, S., Sasagawa, K., Louis, D. M., Cheng, P., Sokol, J., Jensen, A., Tso, A., Shankar, V., Wendel, B. S., Bakerman, I., Liang, G., Koyano, T., Fong, R., Nau, A. N., Ahmad, H., Gopakumar, J., Wirka, R., … Nguyen, P. K. (2022). Human Coronary Plaque T Cells Are Clonal and Cross-React to Virus and Self. *Circulation Research, 130* (10), 1510–1530.

Patents

- Published Application: WO2023172699

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