



April 1, 2022  
FunPep Co., Ltd.

**Announcement of the start of joint research with Kumamoto University  
~Toward the Creation of Anti-ANGPTL3 Antibody-Inducing Peptides for Dyslipidemia~**

We are pleased to announce that we have started joint research with Kumamoto University for the creation of antibody-inducing peptides (peptide therapeutic vaccine) against dyslipidemia.

Prof. Yuichi Oike and his research group at the Faculty of Life Sciences, Kumamoto University, are conducting research on the identification of ANGPTL family members and their functions and significance in pathological conditions as well as conducting research on peptide vaccine-based therapies<sup>i</sup>.

In this joint research with Kumamoto University, we will conduct drug discovery research to create drug candidate compounds of antibody-inducing peptides against ANGPTL3<sup>1</sup>, which has garnered attention as a new therapeutic target for dyslipidemia.

Cardiovascular disease, a representative atherosclerotic disease, is a major cause of death, accounting for 32%<sup>ii</sup> of all deaths worldwide in 2019. Prevention of atherosclerotic disease is primarily through the treatment for its risk factor, dyslipidemia. Statins are widely used in the treatment of dyslipidemia to lower LDL cholesterol in the blood, but in cases of familial hypercholesterolemia or in patients at high risk for cardiovascular events who do not respond adequately to statins, statins are used in combination with other drugs, such as PCSK9 inhibitors.

On the other hand, it is also known that atherosclerosis is accelerated by elevated levels of triglycerides in the blood, so ANGPTL3 inhibitors, which lower triglycerides and LDL cholesterol in the blood, are attracting attention. Development of biopharmaceuticals for ANGPTL3 inhibitors is progressing, and in 2021, antibody drugs were approved in the United States and Europe for the treatment of familial hypercholesterolemia. However, the high cost of antibody drugs has raised issues of patient access and financial burden.

The antibody-inducing peptides that we are researching and developing are peptide vaccines that are expected to have therapeutic effects by inducing antibody production in the patient's body. Unlike antibody drugs that are manufactured in biomanufacturing facilities, antibody-inducing peptides can be chemically synthesized to reduce manufacturing costs. Furthermore, after administration, immune cells in the patient's body will continuously produce antibodies for a period of time, so the interval between vaccine administrations is expected to be long.

This feature makes the anti-ANGPTL3 antibody-inducing peptide a drug that is expected to contribute to the treatment of dyslipidemia in the future as a drug that is more economically accessible to patients than expensive antibody drugs through the control of drug costs.

<Terminology>.

1: ANGPTL3 (Angiopoietin-like protein 3)

Angiopoietin-like protein 3 (ANGPTL3) is a hormone-like protein secreted by the liver and involved in lipid metabolism and angiogenesis. ANGPTL3 is known to increase plasma very low-density lipoprotein (VLDL)

levels by inhibiting lipoprotein lipase (LPL) activity. It has also been reported that ANGPTL3 promotes lipolysis by binding directly to adipocytes, thereby increasing blood levels of free fatty acids and glycerol. In addition, it has been reported that humans with ANGPTL3 loss-of-function gene have lower blood LDL-C and triglyceride levels and a significantly lower risk of developing cardiovascular disease compared to those without the mutation. As such, ANGPTL3 inhibitors are actively being developed.

<Reference>.

<sup>i</sup> Fukami H, Morinaga J, Nakagami H, Hayashi H, Okadome Y, Matsunaga E, Kadomatsu T, Horiguchi H, Sato M, Sugizaki T, Kuwabara T, Miyata K, Mukoyama M, Morishita R and Oike Y. Vaccine targeting ANGPTL3 ameliorates dyslipidemia and associated diseases in mouse models of obese dyslipidemia and familial hypercholesterolemia. *Cell Rep. Med.* 2021;2(11):100446

<sup>ii</sup> World Health Organization(WHO) website. Fact Sheets.

[https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))

(Accessed March 2022)