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Chugai's DONQ52, a Multispecific Antibody under Development for Celiac Disease, Non-Clinical Research Results Published in Nature Communications

- Non-clinical research results on DONQ52, a multispecific antibody using Chugai's proprietary antibody engineering technologies, was accepted for publication in a leading multidisciplinary scientific journal
- The potential of DONQ52 to selectively inhibit the immune response to gluten in celiac disease is suggested.
- A Phase I clinical study to investigate DONQ52 in celiac disease is ongoing

TOKYO, December 25, 2023 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that the results of non-clinical research on a multispecific antibody DONQ52 have been published in the Nature Communications. DONQ 52 was discovered by Chugai, and a Phase I clinical study in celiac disease is ongoing. Nature Communications is a leading open access multidisciplinary scientific journal published by the Nature Publishing Group, reporting high-quality research from all areas of life, health, social, physical, chemical and Earth sciences.

" Characterizations of a neutralizing antibody broadly reactive to multiple gluten peptide:HLA-DQ2.5 complexes in the context of celiac disease "
(https://doi.org/10.1038/s41467-023-44083-4)

The following findings were demonstrated in this research, which suggests the potential of DONQ52 to selectively inhibit the immune response to gluten in celiac disease.

- Creation of DONQ52, a novel multispecific anti-gluten peptide:HLA-DQ2.5 (pHLA-DQ2.5) antibody aimed to bind cross-reactively to multiple gluten peptide with different sequence through rabbit immunization and multidimensional antibody engineering.
- *in vitro*, DONQ52 was shown to selectively and broadly recognize more than 25 distinct pathogenic gluten pHLA-DQ2.5, and directly neutralize gluten dependent T-cell activation.
- Structural analysis showed that DONQ52 flexibly recognizes the unique motif of gluten epitopes which are important for the pathogenesis of celiac disease.
- In animal experiments using mice, DONQ52 was shown to demonstrate favorable pharmacokinetics.
- In animal experiments using mice, DONQ52 was shown to block immunity to gluten while not affecting systemic immunity.

"We are very pleased to announce that that the results of basic research on a multispecific antibody DONQ52 discovered by our company have been published in Nature Communications. Although technical hurdles have prevented practical use to date, our non-clinical study shows that specific and broad inhibition of HLA-T cell interactions is a useful therapeutical approach for celiac disease," said Dr. Osamu

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Okuda, Chugai's President and CEO. "We are very much looking forward to the ongoing phase I study of DONQ52 to show a high safety profile and a gluten-specific immunosuppressive effect and that it will become a drug that can contribute to people with celiac disease to which currently no approved therapy exist. Using our world-class antibody engineering technologies, we will work to develop next-generation antibodies that could do things that were impossible with conventional antibodies."

About DONQ52

DONQ52, discovered by Chugai, is a multispecific antibody against complex of HLADQ2.5/gluten peptides and is under development for celiac disease, a hereditary autoimmune disease with no approved therapies. By broadly inhibiting the binding of the complex of HLADQ2.5/gluten peptides to the T-cell receptor, DONQ52 directly neutralizes the activation of T-cells, which are the main cause of celiac disease. Gluten-specific blockade enables long-acting (subcutaneous injection) and high safety profile. DONQ 52 applies Chugai's proprietary antibody engineering technologies including FAST-Ig™ technology[1], a bispecific antibody technology that enhances industrial productivity and achieves greater cross-reactivity to more gluten peptides, and ACT-Fc® technology[2], which is expected to improve pharmacokinetics. A phase I clinical study for celiac disease is ongoing.

Sources

1. Hikaru Koga et al. Efficient production of bispecific antibody by FAST-Ig™ and its application to NXT007 for the treatment of hemophilia A, mAbs, 15:1
2. Atsuhiko Maeda et al. Identification of human IgG1 variant with enhanced FcRn binding and without increased binding to rheumatoid factor autoantibody, mAbs, 9:5, 844-853

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