NEWS RELEASE

February 17th 2022

Epsilon Molecular Engineering, Inc.

EME PUBLISHES NOVEL HUMANIZED SYNTHETIC VHH LIBRARY *"PharmaLogical®* Library" FOR THERAPEUTIC ON ANTIBODIES JORNAL.

Epsilon Molecular Engineering, Inc. (HQ: Saitama, Japan; President & CEO: Naoto Nemoto; "EME") published a research journal paper to Antibodies about humanized VHH synthetic library called" *PharmaLogical*® Library"(*2) on January 30th 2022 (https://www.mdpi.com/2073-4468/11/1/10)which was constructed in collaboration with Mitsui Knowledge Industry Co., Ltd., (HQ: Tokyo, Japan; President & CEO: Kengo Asano; "MKI"). Antibodies is as known as an international, peer-reviewed, open access journal on antibodies. The citation of this research paper is below:

Murakami, T., Kumachi, S., Matsunaga, Y., Sato, M., Wakabayashi-Nakao, K., Masaki, H., Yonehara, R., et al. (2022). Construction of a Humanized Artificial VHH Library Reproducing Structural Features of Camelid VHHs for Therapeutics. Antibodies, 11(1), 10. MDPI AG. Retrieved from http://dx.doi.org/10.3390/antib11010010

VHH (Variable region of camelid heavy chains antibody) is considered as one of the next generations of therapeutic antibodies because of attractive characteristics such as low molecular weight, excellent thermal stability. While existing VHH synthetic libraries have been constructed in the world, they have the issues such as lacking structural characteristics of camelid VHH. To solve the problem, we successfully constructed a synthetic VHH library that remains the structural characteristics of camelid VHHs.

EME constructed an innovative high-throughput screening platform called "The Month." with a combination of our novel humanized VHH synthetic library "*PharmaLogical*® Library" and our core screening technology "cDNA display method(*3)". The Month enables to obtain several VHH clones which have high binding affinity (nM～pM)and high stability from high diversity of library (1013~14) in just a month.

EME has been deploying platform *"The Month"* since April 2021, and we have entered into the joint research and development agreement with many local and international pharmaceutical companies using *"The Month"*. In addition, we have applied this platform to our own researches such as development of pipelines. These researches showed that *"The Month"* enables to obtain hit VHH clones for several targets which were hard to obtain from current existing screening methods, and these humanized VHH hit clones have high affinity and high stability. Therefore, *"The Month"* has been receiving very high evaluations.

For the future direction, EME will approach to the improvement of screening such as *in silico* screening (using AI technology) and construct 2nd generation of "*PharmaLogical*® Library." We believe that this improvement of VHH technology is one of the ways to address the social implement. We have been contributing to patients through new generation VHH drug discovery who are suffering from diseases.

【Features of *PharmaLogical*® Library】

- Design based on crystal structure analysis data of VHH antibodies
  A humanized VHH library was designed based on the structural characteristics resulting from the crystal structure analysis data of the human sequence and VHH that have already been clinically applied to the antibody framework part (FR). The three CDRs (Complementarity Determining Regions) that form the antigen recognition site are designed based on the structural property information obtained from the alpaca-derived VHH, and are known to contribute most to antigen binding. By randomizing the CDR3s, large diversity is demonstrated.
- Design to minimize the frequency on occurrence of amino acids that cause heterogeneity in formulation
  Amino acids that are susceptible to modification and that can cause major structural changes, such as cysteine and proline residues, cause heterogeneity in the formulation process. By designing a CDR that minimizes the frequency of appearance of these amino acids, it can be expected to minimize the problems that arise in the
- Innovative VHH screening method by combining *PharmaLogical®* Library with cDNA display
  The combination of *PharmaLogical®* Library which has a diverse library size of 10^{13-14} (10 trillion to 100 trillion), and a screening system based on the cDNA display technology enables an innovative VHH screening.

＊1 VHH：Variable Domain of Heavy Chain of Heavy Chain Antibody found in camelids. Superior stability and easily molecularly designed than conventional IgG

＊2 *PharmaLogical®* Library：Original Humanized Artificial VHH Library with Structure based Design that contributes to the paratope formation on VHHs

＊3 cDNA display：A Stable and Simple Genotype-Phenotype Coupling Using a Cell-Free Translation System, enabling 10^{13-14} repertories of VHHs to be screened at once

【Epsilon Molecular Engineering】

EME is a biopharmaceutical startup that has been developing innovative modality and drugs based on evolutionary molecular engineering since 2016. Taking advantage of our unique screening technology and molecular design method, we are engaged in research and development of diagnostic agents and reagents for regenerative medicine as well as drug development. With the corporate mission of "creating future biomolecules," we aim to contribute to a wide range of society and people's lives.
Website： https://www.epsilon-mol.co.jp/eng/

【Mitsui Knowledge Industry Co. Ltd. (MKI)】

Under the slogan "Unite Knowledge, Ignite the Future", Mitsui Knowledge Industry Co., Ltd. (MKI) has been creating IT strategies and supporting the digital transformation of its clients as their strategic business partner specializing mainly in information and communication technology.
By utilizing its wealth of "KNOWLEDGE" accumulated through its long experience in technological development and innovation continuing for over half a century, MKI remains consistent in its pursuit to live up to the high expectations of its customers as their most reliable "value creator".
Website: https://www.mki.co.jp/

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