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Press Release

C4U Corporation

C4U and Jichi Medical University Enter Into an Agreement on Co-Ownership of a Patent Right

C4U Corporation ("C4U") is pleased to announce that we have recently acquired a co-ownership interest in the patent right over the invention titled "Engineered Proteins" ("the Invention") from Jichi Medical University.

The Invention involves an engineered CRISPR-Cas12 enzyme (engineered AsCas12f) with high genome editing activity, developed by the University of Tokyo, Kyoto Prefectural University of Medicine, Jichi Medical University, and the National Agriculture and Food Research Organization. The Invention basically matured into the patent in September 2024 as Japanese Patent No. 7560818.

The CRISPR-Cas systems are classified into two classes (Class 1 and Class 2) and six types (Types I to VI). The Class 1 system, which cleaves target sequences via a complex of multiple proteins, includes Types I, III, and IV, while the Class 2 system, which cleaves target sequences via a single protein, includes Types II, V, and VI. CRISPR-Cas3, which C4U aims to commercialize, belongs to Class 1, Type I, whereas the widely used CRISPR-Cas9 (Type II) and CRISPR-Cas12 (Type V) belong to Class 2.

Among Type V system, Cas12f (AsCas12f), derived from *Acidibacillus sulfuroxidans* and recently discovered as the smallest CRISPR-Cas enzyme, is less than one-third the size of CRISPR-Cas9. However, it previously faced the challenge of low genome editing activity.

In this invention, AsCas12f variants with higher genome editing efficiency were developed by modifying Cas and the guide RNA based on mutant screening and three-dimensional structural information.

This novel, compact genome editing tool (enAsCas12f) is expected to find applications not only in *in vivo* gene therapy but also in fields such as agriculture and plant science, as high cellular transduction efficiency can be achieved by utilizing viral vectors.

C4U is currently preparing to pursue partnerships across various industrial sectors to facilitate the commercialization of this invention. By leveraging both CRISPR-Cas3 and the engineered AsCas12f, C4U will continue to advance the practical application of genome editing technologies developed in Japan.

About C4U Corporation

C4U is a privately held biotech company originated from the University of Osaka, and focused on the development of safe and efficient gene therapies utilizing its proprietary next generation CRISPR-Cas3 gene editing platform. In comparison to the CRISPR-Cas9 platform, CRISPR-Cas3 presents the distinct benefits of: 1) no off-target by the higher selectivity of deletion site (improved safety); 2) efficient knockouts by the larger deletion of gene sequences; and 3) an entirely independent patent portfolio. C4U has been granted a worldwide exclusive license to CRISPR-Cas3 by the University of Osaka for use in eukaryotic cells thus simplifying sublicensing transactions which is in sharp contrast to the complex and heavily litigated CRISPR-Cas9 patent landscape. C4U promotes the development of novel treatments for various diseases, including hereditary

disorders, through both in-house research and collaborations with other companies, while simultaneously working to expand its CRISPR-Cas3 platform for application across a wide range of industries. <https://www.crispr4u.jp/en/>

Contact Information

Address : Yamadaoka 2-8, Suita, Osaka 565-0871, Japan

E-mail : info@crispr4u.com