PRESS RELEASE

Toyama, July 6, 2026

EV-SELEX: A Novel Platform for Rapid G Protein-Coupled Receptor Drug Discovery

Researchers use extracellular vesicles to rapidly identify highly specific DNA aptamers to target G protein-coupled receptors in drug development

G protein-coupled receptors (GPCRs) are important therapeutic targets for numerous diseases. However, developing highly selective drugs for GPCRs remains a challenge. Researchers have now developed a new platform termed extracellular vesicle (EV)-Systematic Evolution of Ligands by Exponential Enrichment, which uses EVs to efficiently isolate potent DNA aptamers. Using this method, they identified an analgesic aptamer that targets μ-opioid receptor to mimic morphine-like activity, demonstrating the platform's potential in accelerating drug discovery for GPCR-related conditions.

G protein-coupled receptors (GPCRs) are the most abundantly expressed proteins in the human body, which regulate diverse physiological processes ranging from pain perception to hormone signaling. Owing to their central roles in health and disease, GPCRs are the targets for a majority of new drugs under development. Despite their importance, discovering drug candidates that bind to GPCRs with high affinity and specificity remains a major challenge, slowing the development of safer therapeutics.

One promising alternative to conventional drugs is the use of DNA aptamers (short, single-stranded DNAs that can fold into unique 3D structures), which are capable of recognizing specific molecular targets. While this holds hope, aptamer development techniques, such as Cell-Systematic Evolution of Ligands by Exponential Enrichment (SELEX), often struggle to produce candidates against complex membrane proteins like GPCRs.

Addressing this challenge, a research team led by Professor Toshihide Tabata from the Faculty of Engineering, University of Toyama, Japan, along with Dr. Mitsushi J. Ikemoto from the Department of Engineering, University of Toyama, and the Institute of Health and Sports Sciences, University of Tsukuba, Japan; Associate Professor Yuji Kamikubo from the Department of Pharmacology, Juntendo University School of Medicine, Japan; and Associate Professor Daisuke Uta from the Faculty of Pharmaceutical Sciences, University of Toyama, have developed a new aptamer selection strategy termed extracellular vesicle (EV)-SELEX. The study was be published in the journal *Communications Biology* on July 7, 2026.

"As neuroscientists, while working on GPCR-mediated synaptic plasticity, we noticed that there are only a limited number of experimental tools to pharmacologically manipulate neuronal GPCRs. This intrigued us to create new and efficient tools for drug development," says Prof. Tabata.

Unlike conventional Cell-SELEX methods, EV-SELEX exploits a natural cellular process in which activated GPCRs are internalized and packaged into EVs. When a ligand binds to a GPCR, the activated receptor along with the ligand, is internalized into the cell through endocytosis. These receptors are packaged into EVs and then released into the extracellular space. The researchers could pick up the receptor-bound ligand by collecting the culture medium around the cells. This minimizes the interference of unrelated membrane proteins and enables efficient selection of DNA aptamers that recognize biologically relevant receptor conformations.

Using this approach, the researchers identified Dapt-μR, a DNA aptamer that can binds to the μ-opioid receptor (MOR) with high specificity. Interestingly, the aptamer did not just recognize the receptor; it also activated it. When tested in cultured cells, the Dapt-μR inhibited cyclic adenosine monophosphate accumulation, a hallmark of MOR activation. The effect was blocked by the MOR antagonist naloxone, which confirmed that the response was specifically mediated through the MOR.

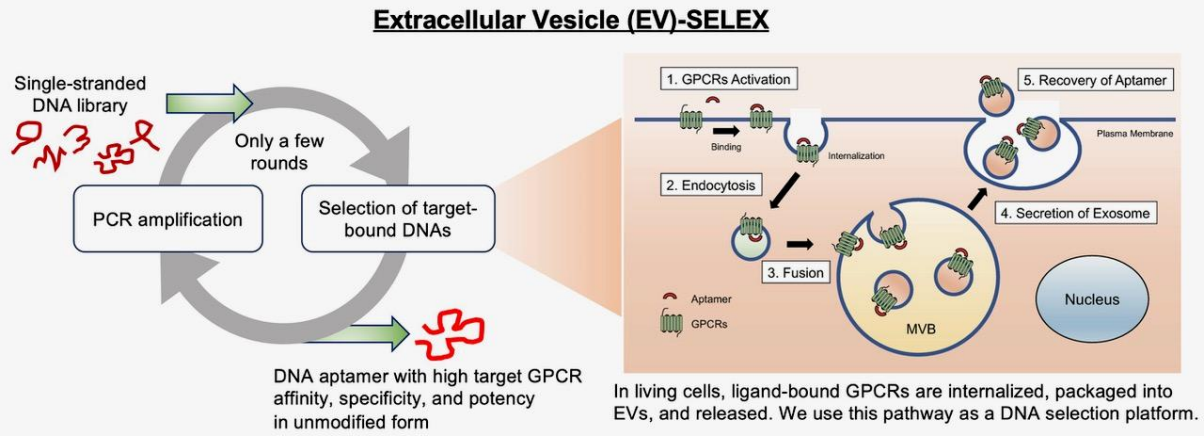
The team further evaluated the biological activity of the aptamer in neuronal and animal models. In neuronal models, Dapt-μR reduced calcium influx, which was consistent with MOR signaling. In mice, Dapt-μR produced analgesic effect following intrathecal administration. These findings denote that the DNA aptamers can function as drug-like molecules capable of triggering a pharmacological response comparable to that of established opioid agonists.

Furthermore, the researchers also compared EV-SELEX with an improved Cell-SELEX protocol and found that the EV-based method enabled the selection of high-affinity, potent aptamers in fewer selection cycles than conventional methods. This improved efficiency suggests that EV-SELEX could markedly reduce the time and effort required to develop therapeutic candidates for GPCRs.

Beyond the development of a promising opioid receptor-targeting aptamer, the study also established EV-SELEX as a versatile platform that could be applied to drug discovery for a wide range of GPCRs involved in neurological disorders, chronic pain, metabolic diseases, cardiovascular conditions, and cancer. In addition to the therapeutic applications, the technology could also generate highly selective molecular tools for studying GPCRs.

“Our new technique, EV-SELEX, can complete drug development in a very short time. It may help pharmaceutical companies efficiently develop therapeutic and/or experimental drugs for the most important drug targets, GPCRs. This technological revolution will greatly promote biomedical science,” concludes Prof. Tabata.

Image



Title: Extracellular vesicle-SELEX for selecting DNA aptamers for target G protein-coupled receptors
Caption: Researchers propose a functional selection method called EV-SELEX that efficiently selects DNA aptamers for GPCRs, paving the way for the development of therapeutic drugs for intractable diseases.
Credit: Prof. Toshihide Tabata from University of Toyama, Japan
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Reference

Title of original paper:	Efficient and Specific Selection of High-Affinity DNA Aptamers Targeting μ-Opioid Receptor via Functional Extracellular Vesicles
Journal:	*Communications Biology*
DOI:	10.1038/s42003-026-10525-0

Additional information for EurekAlert

Latest Article Publication Date:	7 July 2026
Method of Research:	Experimental study
Subject of Research:	Animals
Conflicts of Interest Statement:	The authors declare no competing interests.

About University of Toyama, Japan

University of Toyama is a leading national university located in Toyama Prefecture, Japan, with campuses in Toyama City and Takaoka City. Formed in 2005 through the integration of three former national institutions, the university brings together a broad spectrum of disciplines across its 9 undergraduate schools, 8 graduate schools, and a range of specialized institutes. With more than 9,000 students, including a growing international cohort, the university is dedicated to high-quality education, cutting-edge research, and meaningful social contribution. Guided by the mission to cultivate individuals with creativity, ethical awareness, and a strong sense of purpose, the University of Toyama fosters learning that integrates the humanities, social sciences, natural sciences, and life sciences. The university emphasizes a global standard of education while remaining deeply engaged with the local community.

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About Professor Toshihide Tabata from the University of Toyama, Japan

Dr. Toshihide Tabata is a Professor at the Faculty of Engineering, University of Toyama, Japan. He holds a Masters and PhD in Medicine from Osaka University, Japan. His research interests include neuroscience, neurophysiology, G protein-coupled receptor signaling, synaptic plasticity, and electrophysiology. He has authored more than 75 peer-reviewed publications with over 1,200 citations and has received the Best Poster Award in 2018.

Funding information
This work was supported by Chubu Regional Consortium for Advanced Medicine [A200], the Japan Society for the Promotion of Sciences KAKENHI [15K14985, 23K06170, 19K09323, 18K06461, 22K07319, and 25K10602], First Bank of Toyama [2020-8], University of Toyama Presidential Discretionary Fund [2210620025], and University of Toyama [2210610043].

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