

Acetal-Linkage Releasable PEGs

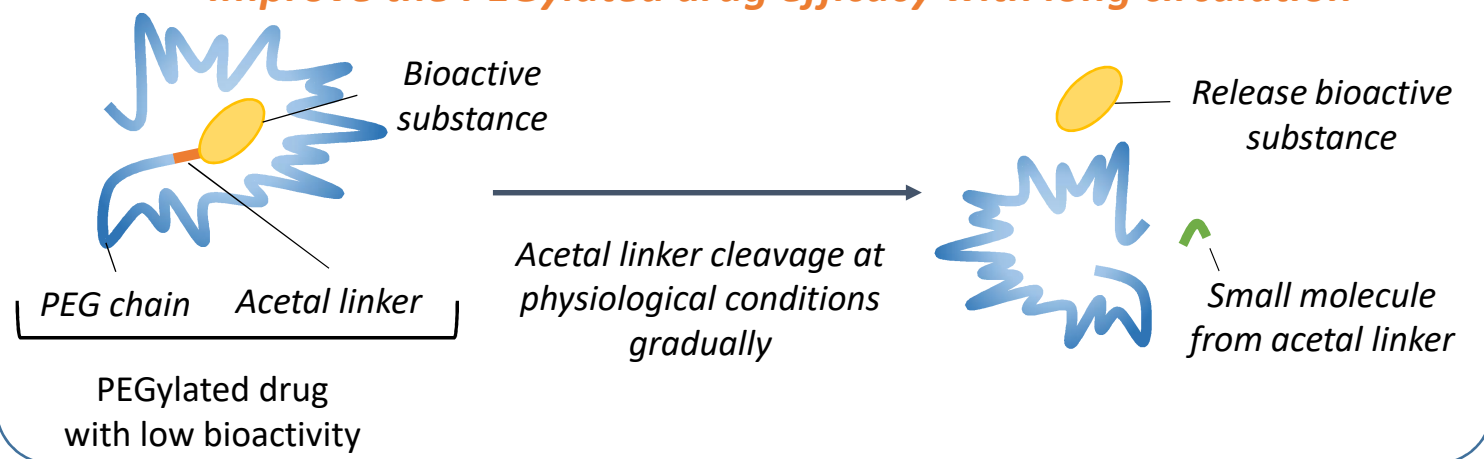
for improving efficacy of PEGylated drugs

NOF has developed releasable PEG derivatives that have cleavable acetal linkers in physiological environment (pH7.4). The PEGylated drug by releasable PEGs release native drug through hydrolysis and 1,4-elimination. The release rate of bioactive substance can be controlled with linker structures.

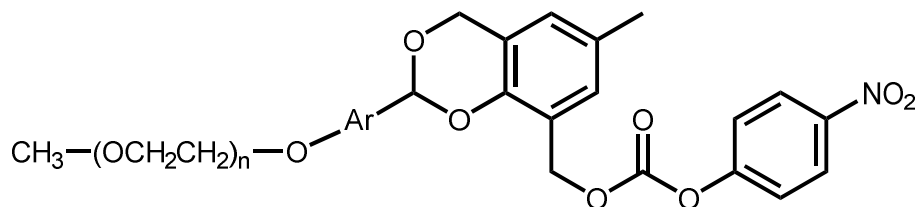
Concept

✓ Control the release speed with linker structures

✓ Improve the PEGylated drug efficacy with long circulation



Acetal-linkage releasable PEG series



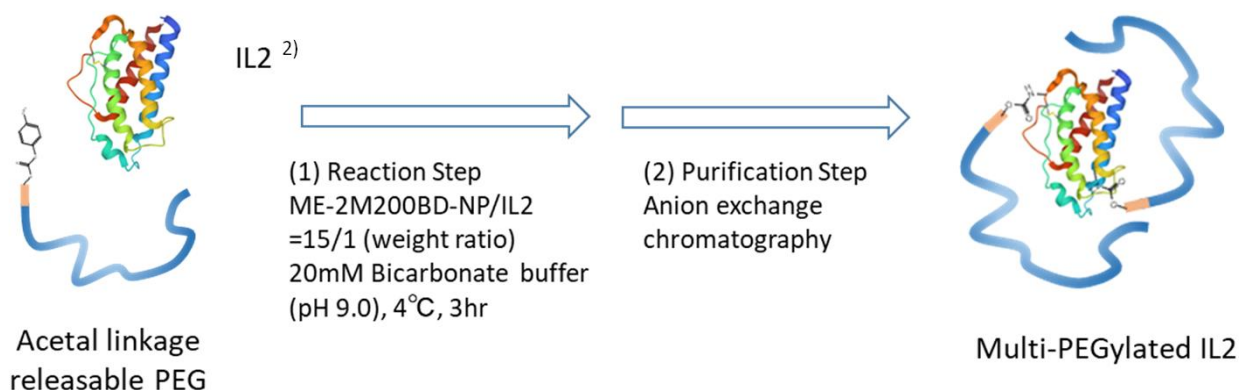
Product name	Aromatic structure (Ar)	<i>In vitro</i> half-life (pH7.4) ¹⁾	Molecular weight
SUNBRIGHT® ME-2M200BD-NP		2.7 d	20,000
SUNBRIGHT® ME-6E200BD-NP		4.1 d	
SUNBRIGHT® ME-3C200BD-NP		7.5 d	
SUNBRIGHT® ME-4E200BD-NP		13.1 d	

1) Insulin was conjugated as model substance. *In vitro* half-life was obtained by curve fitting of the hydrolysis rate.

Patent publication No.: WO2018180914

In vitro evaluation

Preparation of PEGylated IL2 by Acetal linkage releasable PEG



2) Crystal structure of IL2(PDB ID; 1M4C) was cited from RCSB Protein Data Bank.

Cell proliferation assay with Multi-PEGylated IL2

Cell line ; CTLL-2 cells ³⁾

Cell density ; 1.7×10^5 cells/mL

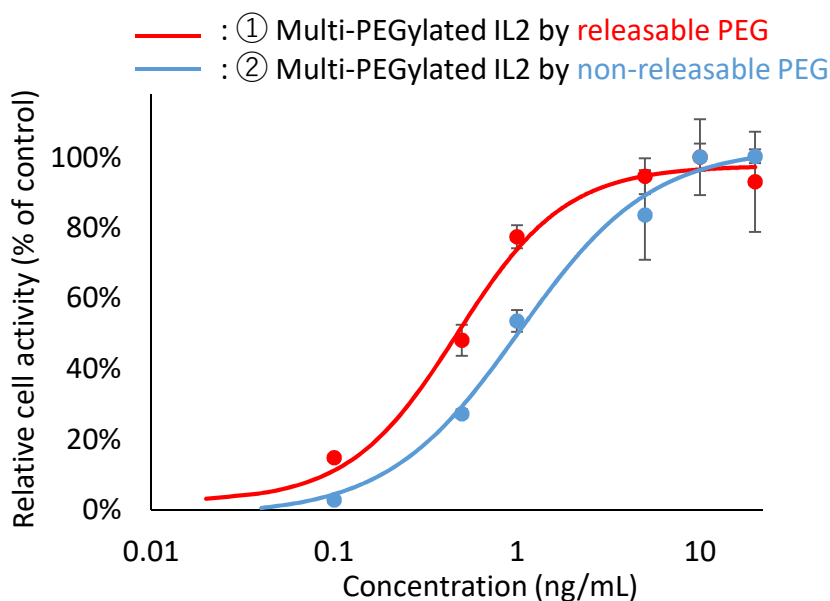
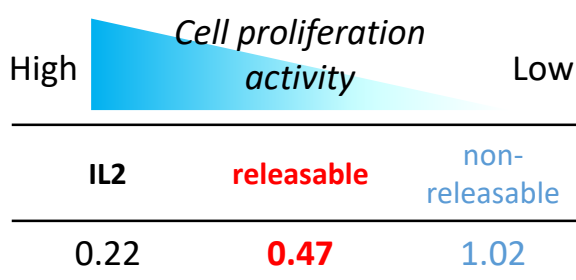
Condition ; 37°C, 5%CO₂, 48hr

Test groups ; Multi-PEGylated IL2 by

① **releasable PEG** (20kDa) 0.1 to 20ng/mL

② **non-releasable PEG** (20kDa) 0.1 to 20ng/mL

EC₅₀ (ng/mL) Value



3) CTLL-2 was provided by the RIKEN BRC through the National BioResource Project of the MEXT, Japan

✓ **PEGylated IL2 by releasable PEG improved the PEGylated IL2 efficacy.**

NOF CORPORATION

Life Science Division
<https://www.dds-drug.com>

Head Office

20-3 Ebisu 4-chome, Shibuya-ku, Tokyo 150-6012 Japan
<http://www.dds-drug.com> E-mail: ddsinfo@nof.co.jp

NOF AMERICA CORPORATION

TEL: +1-866-663-0001 (toll free)
<http://www.nofamerica.com> E-mail: info@nofamerica.com

New York Office

One North Broadway, Suite 912, White Plains, NY 10601, U.S.A.
Tel: +1-914-681-9790 FAX: +1-914-681-9791

San Francisco Office

400 Concar Dr San Mateo, CA 94402, U.S.A.
TEL: +1-650-993-7375 FAX: +1-650-993-7376

Boston Office

One Beacon Street, Boston, MA 02108, U.S.A.
TEL: +1-650-993-7375 FAX: +1-650-993-7376

日油株式会社 ライフサイエンス事業部

〒150-6012 東京都渋谷区恵比寿4-20-3

TEL: +81-3-5424-6741 FAX: +81-3-6837-5348

<http://www.dds-drug.com> E-mail: ddsinfo@nof.co.jp

NOF EUROPE GmbH

Hamburger Allee 2-4, 60486, Frankfurt am Main, Germany

TEL: +49-69-7706-100-0, FAX: +49-69-7706-100-10

<http://www.nofeurope.com> E-mail: info-eu@nofeurope.com

日油(上海)商贸有限公司

上海市长宁区长宁路1027号

兆丰广场34楼3405-3406室 邮编200050

TEL: +86-21-6210-1100 FAX: +86-21-3208-0270

SUNBRIGHT is a registered trademark of NOF CORPORATION in the U.S. and a registered trademark or a trademark in other countries.