

엑소솜 기반 치료용 단백질 전달 기술: EXPLOR의 원리와 적용



최 철 희

KAIST/Cellex Life Sciences, Incorporated

Efficient and rapid cellular delivery of therapeutic proteins via EXPLOR technology

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- 01 Introduction
- 02 POC Study for EXPLOR Technology
- 03 Application of EXPLOR Technology

Key Components of Precision Medicine

"one-size-fits-all" approach

- Stratification → Personalization
- Targeted Therapy

Slides 3

Key Components of Precision Medicine

- Stratification → Personalization
- Targeted Therapy
 1. Specific Targets
 2. Customized Delivery

Slides 4

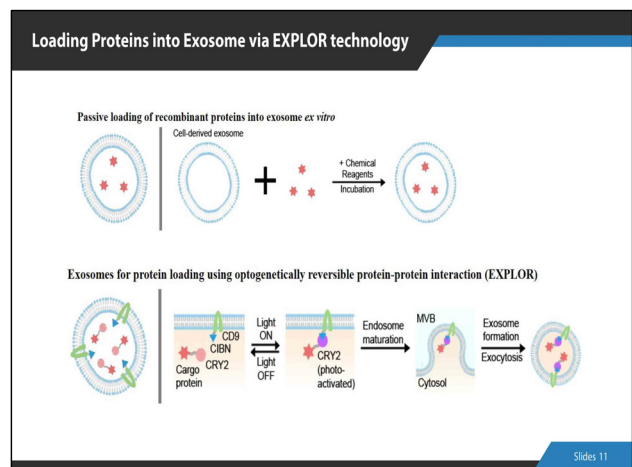
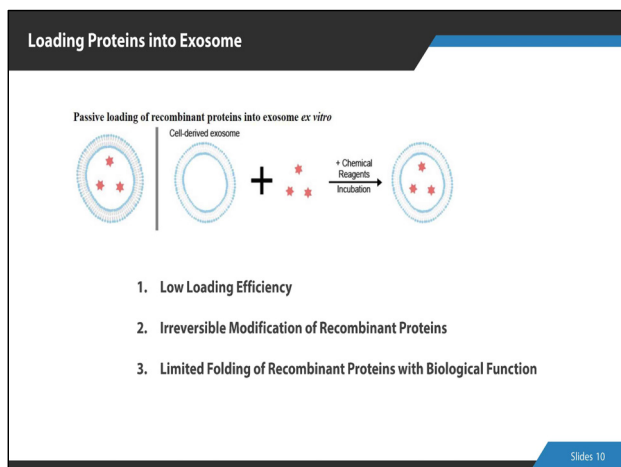
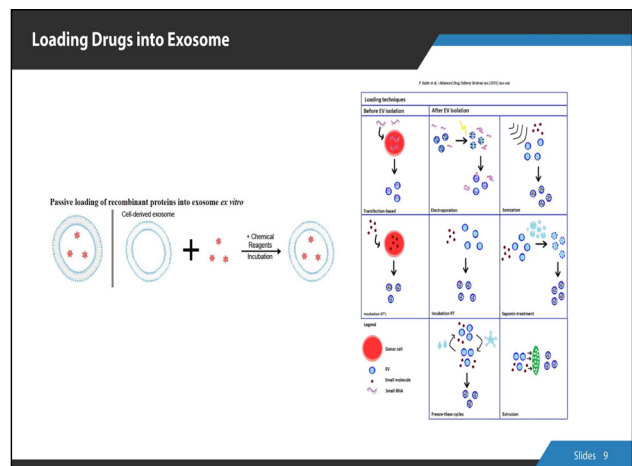
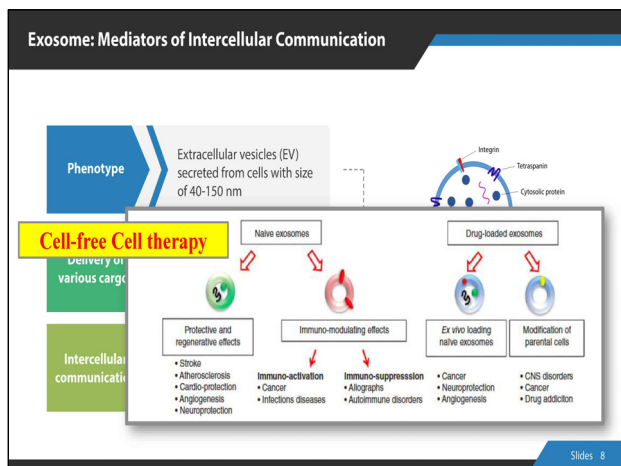
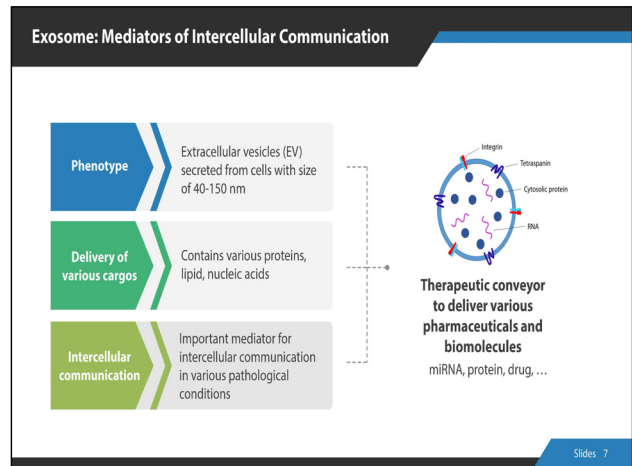
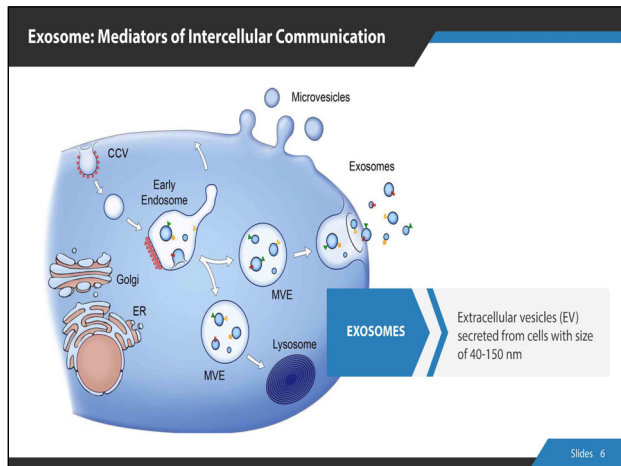
Chemical Drugs vs Protein Drugs

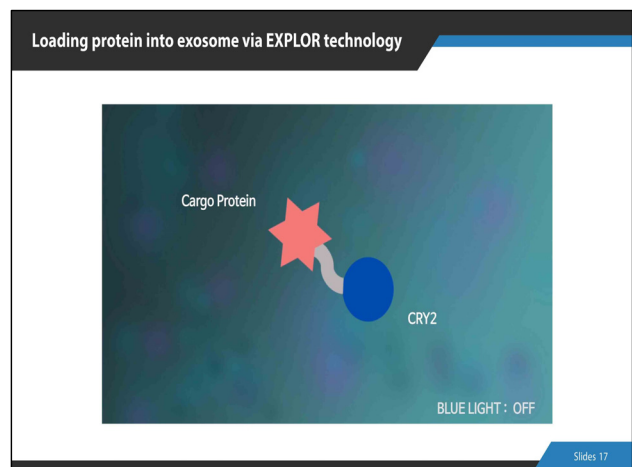
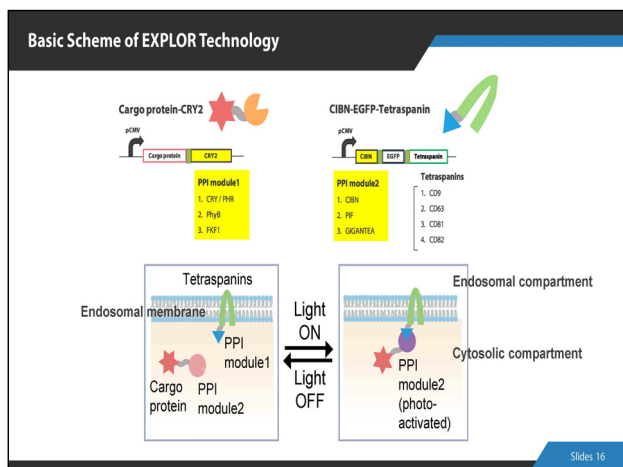
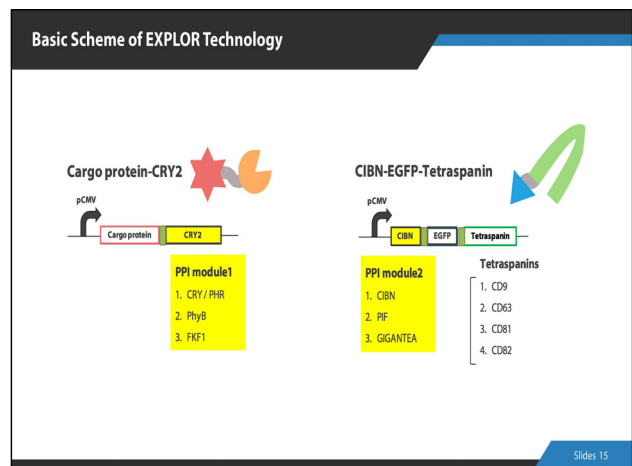
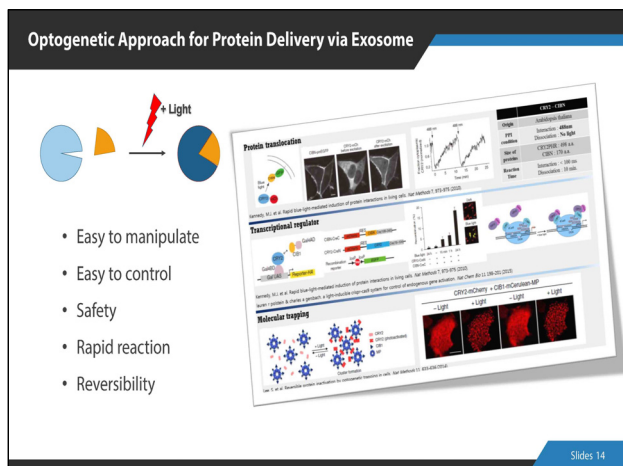
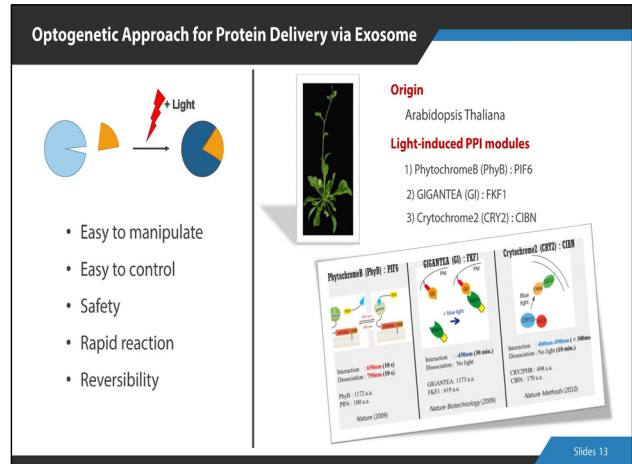
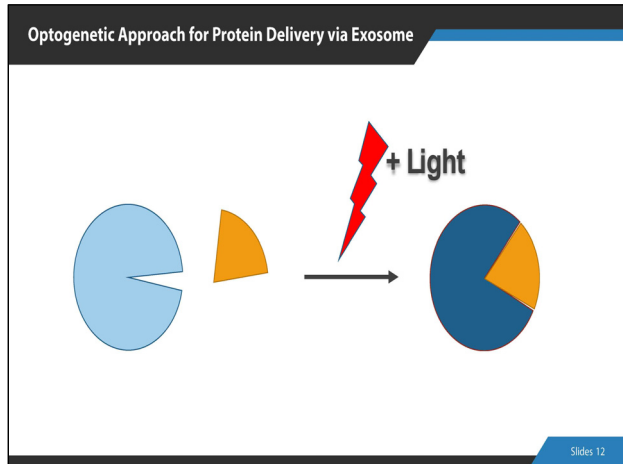
Sensipar® (chemical drug)
Small molecular size
(weight = 393)

Enbrel® (protein)
Immense molecular size
(weight = 150,000)

1. Highly Specific: Suitable for precision medicine
2. More Complex
3. High Molecular Weight
4. Bio-distribution: Mainly extracellular

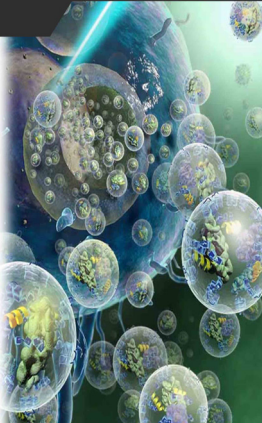
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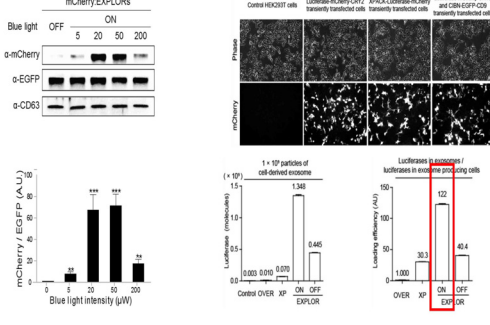


Loading protein into exosome via EXPLOR technology

mCherry EXPLORs

Blue light	OFF	ON	ON	ON	ON
mCherry	+	+	+	+	+
eGFP	-	-	-	-	-
c-CD63	-	-	-	-	-

Control HEK293T cells, Luciferase mCherry CR12 transiently transfected cells, XPACK Luciferase mCherry transiently transfected cells, Luciferase mCherry CR12 with CD63-eGFP CR2 transiently transfected cells

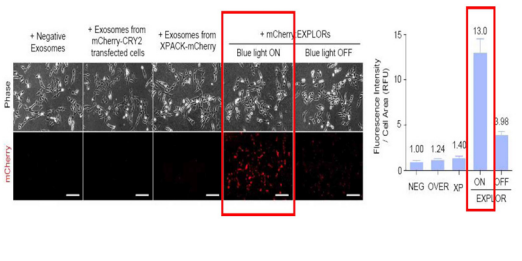


Yim N. et al. (Nature Communications, 2016)

Delivery of Cargo protein via EXPLOR technology

+ Negative Exosomes, + Exosomes from mCherry-CR12 transfected cells, + Exosomes from XPACK-mCherry, + mCherry EXPLORs

Blue light ON, Blue light OFF



Yim N. et al. (Nature Communications, 2016)

Delivery of Functional Protein via EXPLOR technology

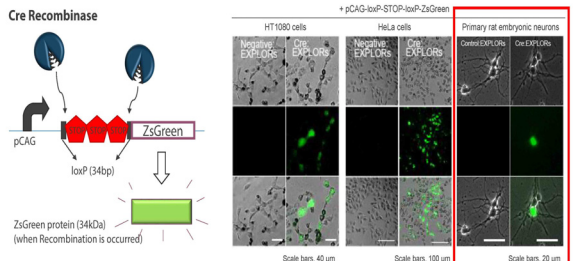
Cre Recombinase

pCAG, loxP (34bp), ZsGreen

ZsGreen protein (34kDa) (when Recombination is occurred)

HT1080 cells, HaLa cells, Primary rat embryonic neurons

+ pCAG-loxP-STOP-loxP-ZsGreen



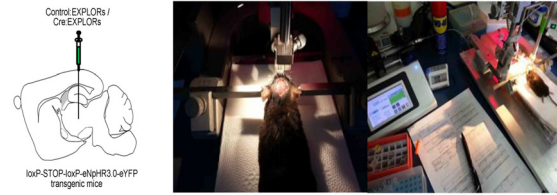
Yim N. et al. (Nature Communications, 2016)

Delivery of Functional Protein via EXPLOR technology

500 µg EXPLORs were injected into the ventrolateral part of brain in each mouse. (-2.8 mm anteroposterior [AP]; -2.2 mediolateral [ML]; 3.8 dorsoventral [DV])

Control EXPLORs / Cre EXPLORs

loxP-STOP-loxP-eYFP transgenic mice



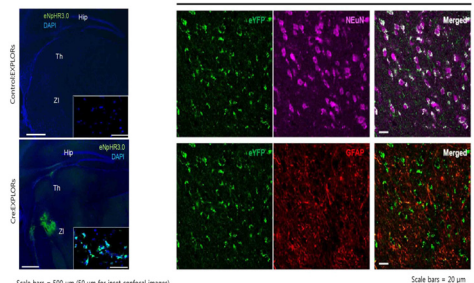
Yim N. et al. (Nature Communications, 2016)

Delivery of Functional Protein via EXPLOR technology

Cre EXPLORs

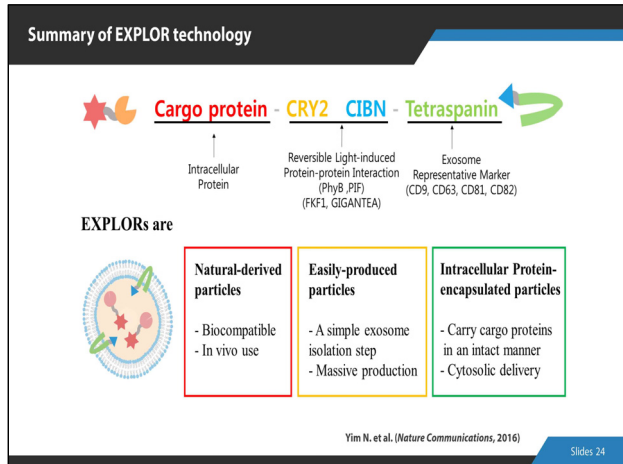
Control EXPLORs, Cre EXPLORs

eYFP, NeuN, Merge, eYFP, GFAP, Merge



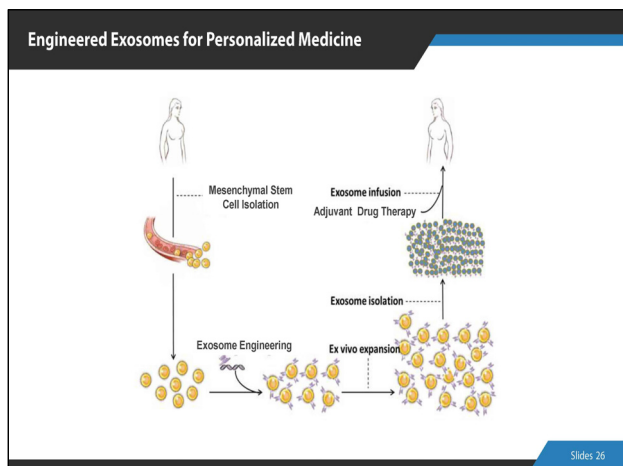
Scale bars = 500 µm (50 µm for inset cortical images)
Hipp: hippocampus, Th: Thalamus, Z: Zona incerta

Yim N. et al. (Nature Communications, 2016)



SUMMARY

- EXPLOR technology can be applied for active loading and delivery of therapeutic proteins (i.e., super repressor IκB, srIκB and GBA) with high efficiency
- Treatment of srIκB-loaded exosomes can block TNF-α-induced nuclear translocation of active NF-κB and subsequent induction of pro-inflammatory gene expression *in vitro* and attenuates LPS-induced septic shock mortality and tissue damage *in vivo*.



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