

CNS-Specific Antibody Prodrug Activation

Institute of Biologics
Development Center for Biotechnology

Presenter : Jei-Hwa Yu, Ph.D.

Development Center for Biotechnology, DCB



400+ 

RD/BD professionals serving as the innovation hub for early drug development.

36 

Founded in 1984, non-profit RD institution subsidized by the Ministry of Economic Affairs of Taiwan.

1200+ 

The premium drug development entity and connected with 1200+ biotech of TW.

25 

20+ out licensed assets and 5 Spin offs under **out-licensing** and **co-development** model.

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Project Team

Project Team

Unmet Need

Technology

Opportunity

IP/Dev Status

Summary/Contact

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Protein Characterization

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CNS Therapeutic Antibodies Cause Adverse Effect in the Peripheral Blood

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CNS Therapeutic Antibodies

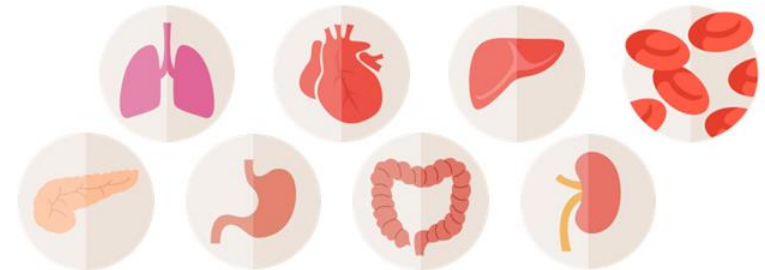
The current CNS disease-related therapeutic antibodies are mainly administered through i.v. or s.c. injection.

Lesion in the CNS



Which Target First?

Antigen Expressed in Non-CNS Tissues



Before reaching the CNS lesions, the antibody interacts with the antigens presented in the peripheral blood or other non-CNS tissues, and causes adverse effects.

Science Overview: Antibody Prodrug

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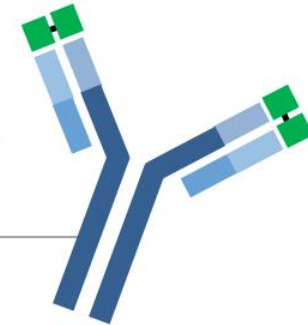
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Antibody Prodrug with CNS-specific Activation Property



- **Reducing Adverse Effects!** Antibody activity is reduced by the protease substrate-containing blocker.
- **CNS-specific Activation!** With the differential expression of the CNS-specific protease, antibody prodrug can be reactivated in the CNS.
- **Various CNS Indications!** Neurodegeneration diseases, oncology, infectious diseases/ inflammation and autoimmune diseases.
- **The first antibody prodrug technology for CNS therapeutics**

Mechanism of Action

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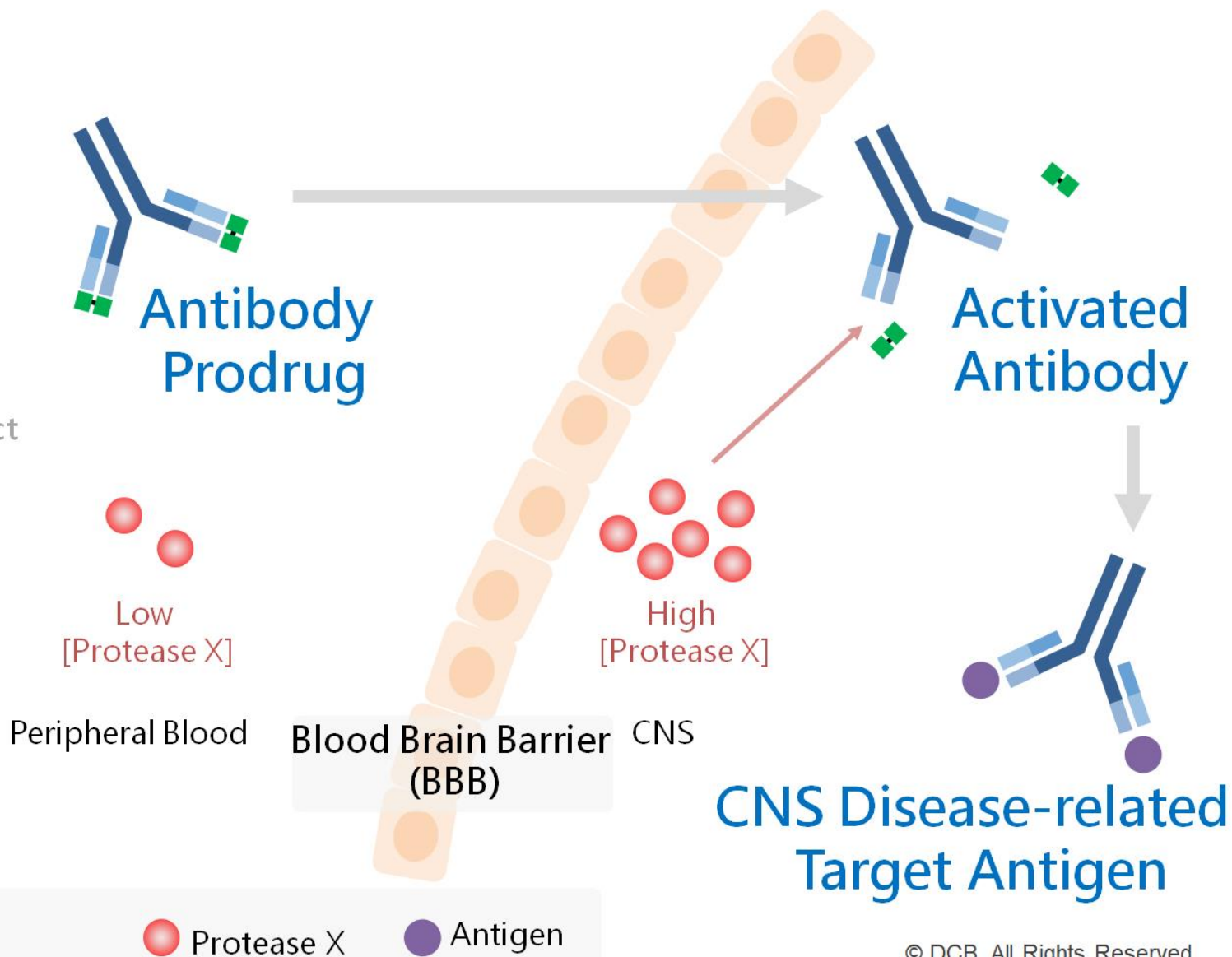
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Protease X Concentration in the Peripheral Blood Does Not Cleave the Prodrug



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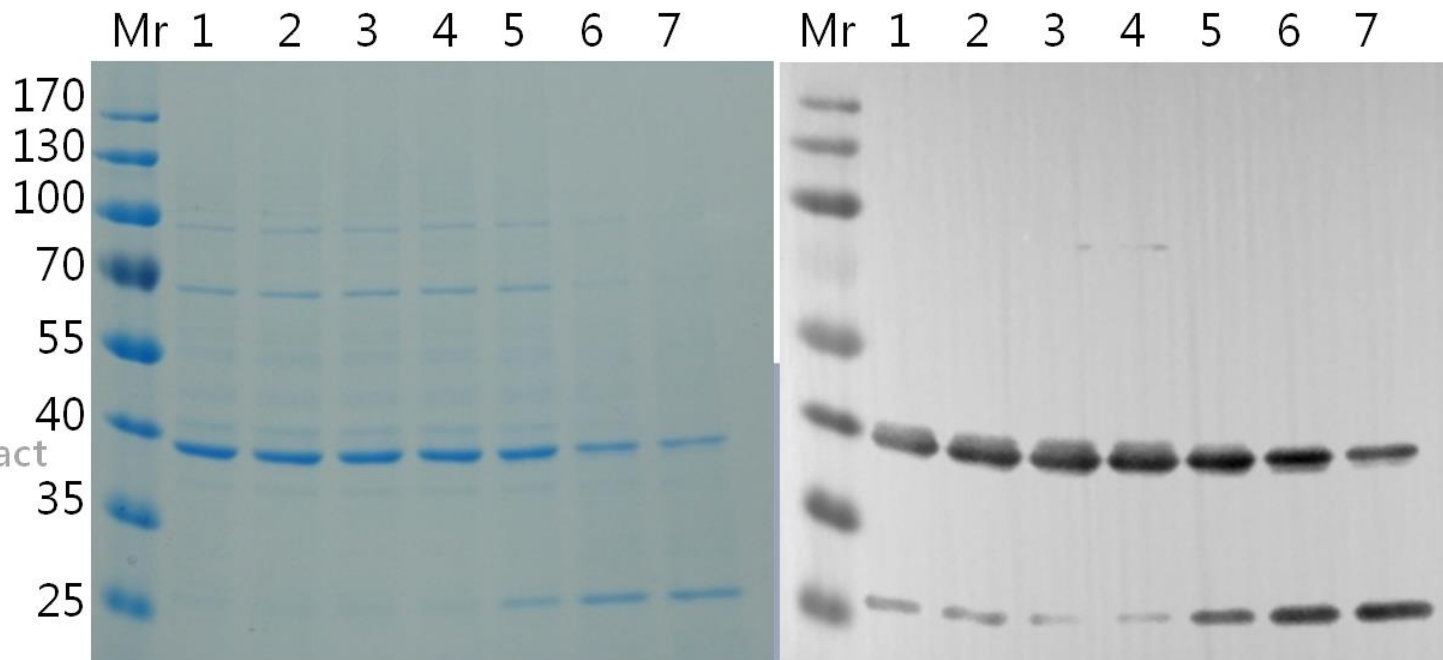
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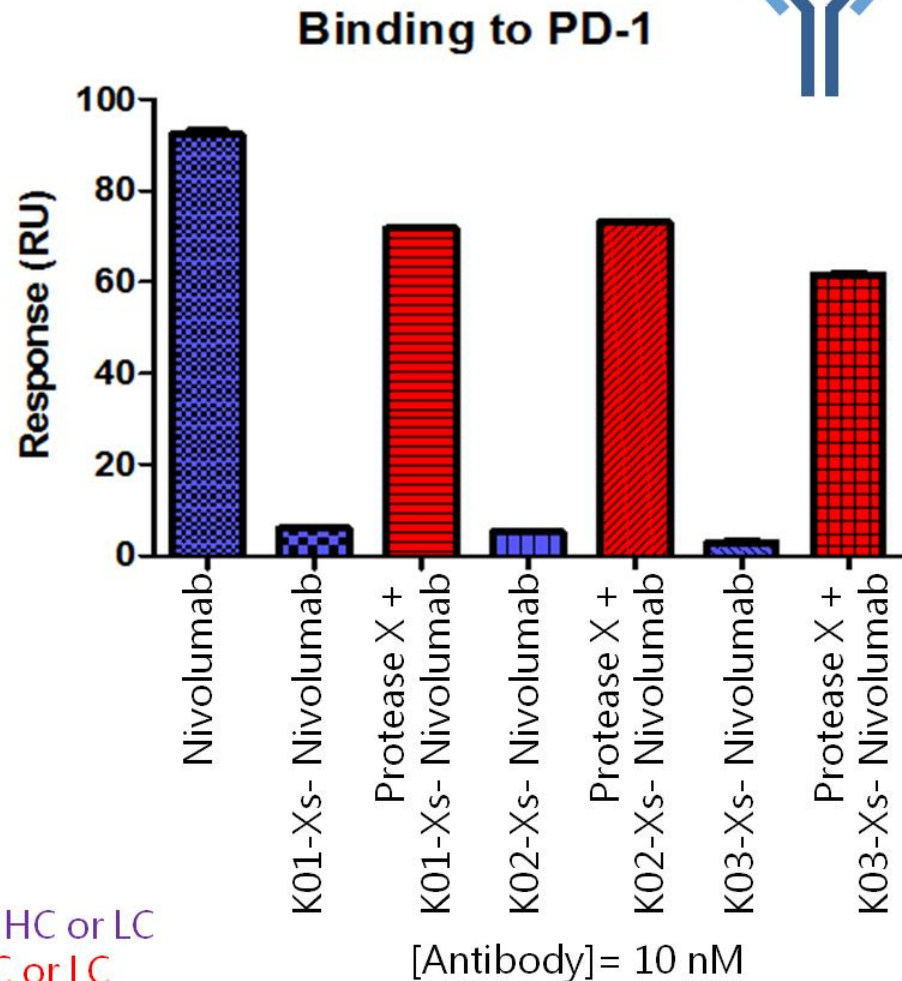
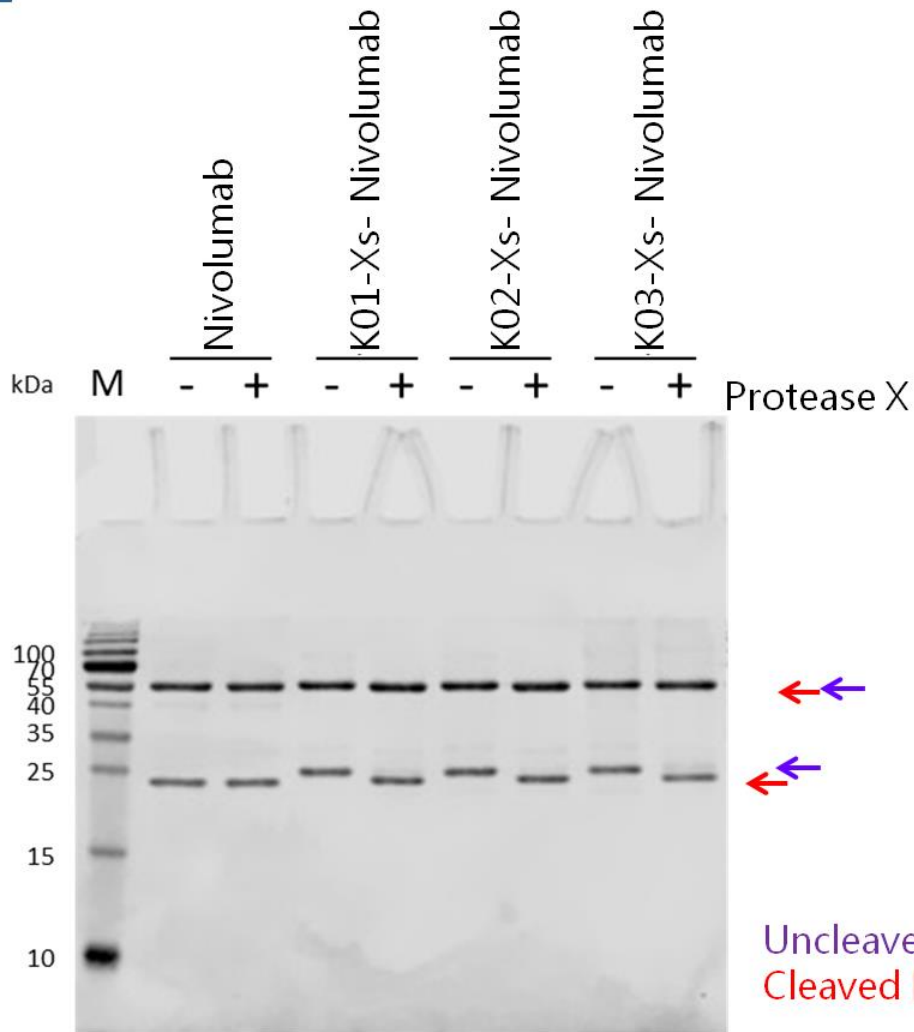


Reduced SDS-PAGE

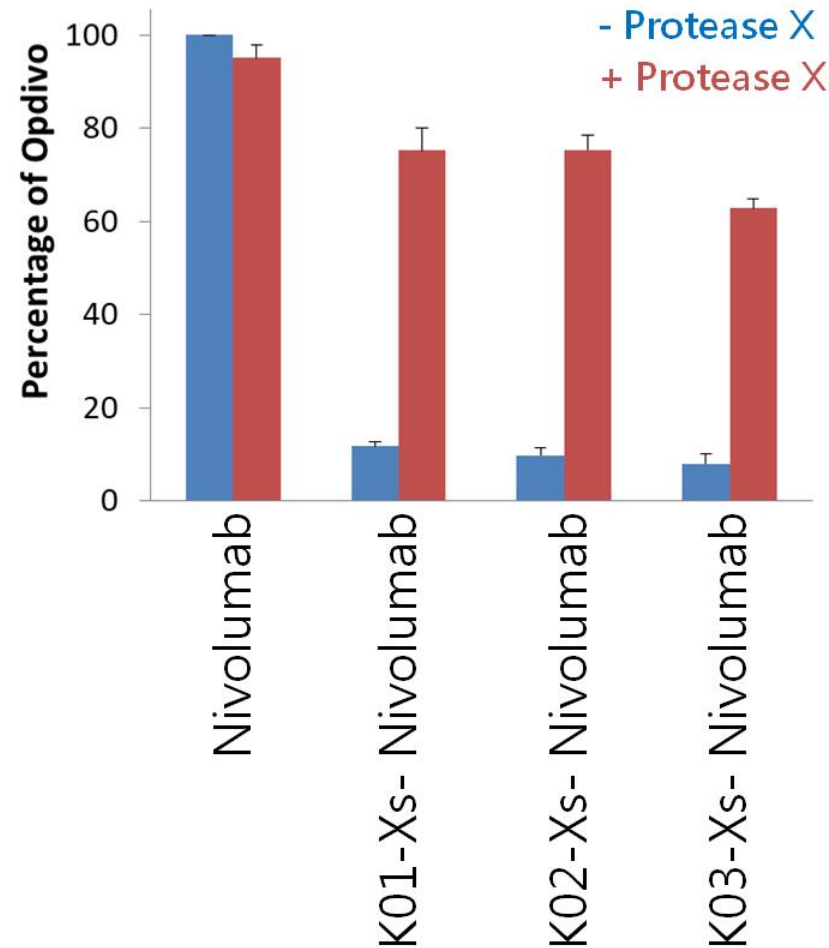
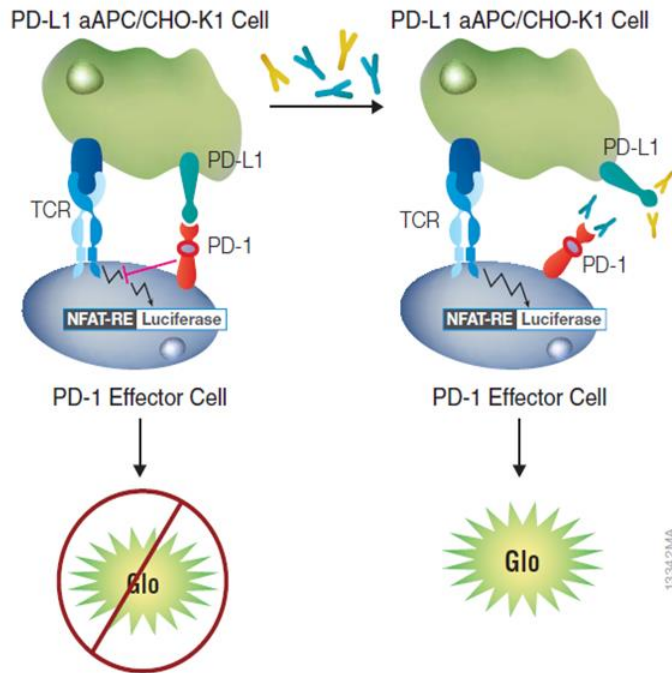
Western Blot

1. Ranibizumab Prodrug, 4 °C
2. Ranibizumab Prodrug, 4 °C + Buffer
3. Ranibizumab Prodrug, 37 °C + Buffer
4. 3 + 0.7 nM Protease X (12.6 µg/L) ◀ Serum Protease X conc.
5. 3 + 114 nM Protease X (2053 µg/L) ◀ CSF Protease X conc.
6. 3 + 1 µM Protease X
7. 3 + 2 µM Protease X

Protease X Digestion Activates Nivolumab Prodrug and Induces Nivolumab and PD-1 Binding



Protease X Digestion Restores the Function of Nivolumab Prodrug



[Antibody]= 27.85 nM

In Vivo Bevacizumab Prodrug Activation in the Brain

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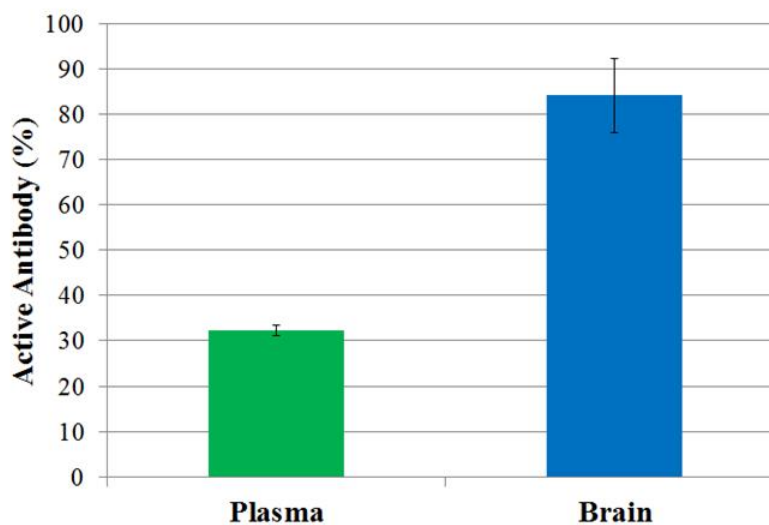
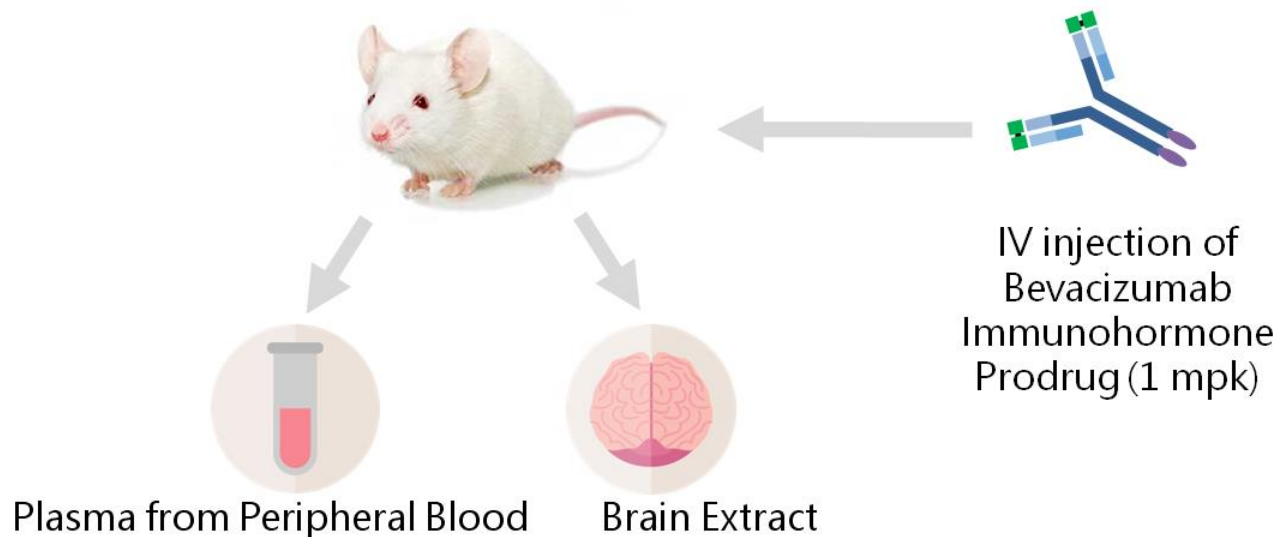
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4 hours post-injection

Possibility, Status, and Strategy

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IP

PCT (2017), US (2016) and TW (2017) Patents Applied

Partnership

- Non-exclusive Licensing
- Co-development
- Other Ways of Partnership

Expect in the Future

- BBB Penetration-Enhanced Antibody Technology

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DCB's CNS Prodrug Platform

- Low antigen binding activity of antibody drug in the peripheral blood
- CNS-specific activation of the antibody prodrug
- This technology has been applied in 4 antibody prodrugs
- The first antibody prodrug technology for CNS therapeutics

BD Contact

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Thank you for your attention



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Development Center for Biotechnology