# Polyphenol-Introduced Polymer/Metal Ion Complex for **Intracellular Antibody Therapeutics**

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### Vision

- Directly targeting intracellular antigens with antibodies opens new treatment possibilities for hard-to-treat cancers.
- Many cancer drivers inside tumor cells remain beyond the reach of current small molecules and antibody drugs.
- Conventional antibodies face poor cellular uptake and become trapped in endosomes, preventing them from reaching their targets.
- Our technology uses innovative DDS nanoparticles—made from polyphenol polymers and metal ions—to deliver antibodies efficiently into cells and release them from endosomes. This breakthrough approach enables precise targeting of intracellular antigens and offers new hope for refractory cancer therapy.

### Marketability

- The global antibody drug market is worth USD 256.28 billion, but almost all products target cell surface antigens. Targeting intracellular antigens could greatly expand treatable cancers and create a new market.
- Triple-negative breast cancer, pancreatic cancer, and small-cell lung cancer cause about 1.13 million new cases worldwide each year. These are cancers with high unmet needs.
- Antibody delivery into cells is still in its early stage worldwide. The main example is a Spanish startup developing preclinical lipidand polymer-based antibody nanoparticles.

#### Innovation

- •This complex DDS nanoparticle can be easily constructed by simply mixing antibodies, polyphenol polymers, and metal ions in water.
- The buffering effect of the complex disrupts the endosomal membrane and delivers the antibody into the cytoplasm.
- Targeting molecules on the surface of the DDS allow selective targeting of cancer cells.

## **Partnering**

#### [ Expected partners ]

Pharmaceuticals · Chemical/Fibers · Medical institute · Biotech/Drug Discovery Service · Venture capitals

#### [ Expectation ]

Active pharmaceutical ingredient (API), Contract manufacturing, Clinical trial execution, Startup support, Joint research and development

### Research Outline

Key Words: #Intracellular Antibody, #Nanotechnology, #Polyphenol

Polyphenol-metal complex DDS nanoparticles boost antibody uptake, promote endosomal escape, and enable effective targeting of refractory cancers.

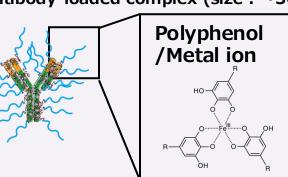
Antibody-loaded nanocomplex-based on polyphenol polymer/metal ion Antibody-loaded complex (size :  $\sim$ 30 nm) 4T1 Cell (Triple-Negative Breast complex DDS





(Fe<sup>3+</sup> or Zr<sup>4+</sup>)

Mixing in Polyphenol aqueous solution



# **Anti-tumor effect**

Cancer) Orthotopic Transplantation Mouse Model

### Non-treatment **◆**Therapeutic intracellular antibody **△Antibody+ nanoDDS** 1,200 Tumor size(mm³) 1,000 800 600 400 200 10 12 14

Reference

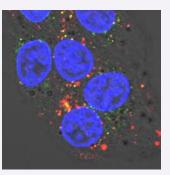
Y. Honda\*, et. al., Journal of Controlled Release, 384, 10, 113929(2025)

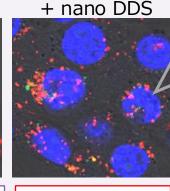
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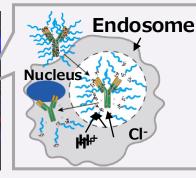
Application Number: PCT/JP2025/3590

### **Endosomal Escape Behavior in Cancer Cells**

Anti-nucleus Antibody (Nucleus/Endosome/Antibody)







At acidic pH, the DDS dissociates, increases osmotic pressure, and disrupts the endosomal membrane.

**Localized on** endosomes or the cell membrane

Recognizing endosomal escape nuclei