

Promotion of cancer stem cell-like formation by administration of anticancer drugs

抗がん剤投与によるがん幹細胞様特性獲得の促進

○Akane Sato^{1,2}, Etsuro Ito^{1,2}

¹Department of Biology, Waseda University ²BioPhenoMA Inc.

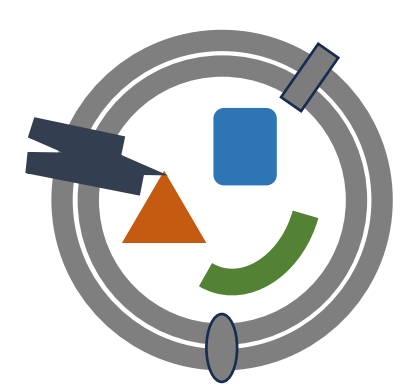
○佐藤 朱音、伊藤悦朗

¹早稲田大学 生物学教室 ²株式会社BioPhenoMA



1. Introduction

Exosome

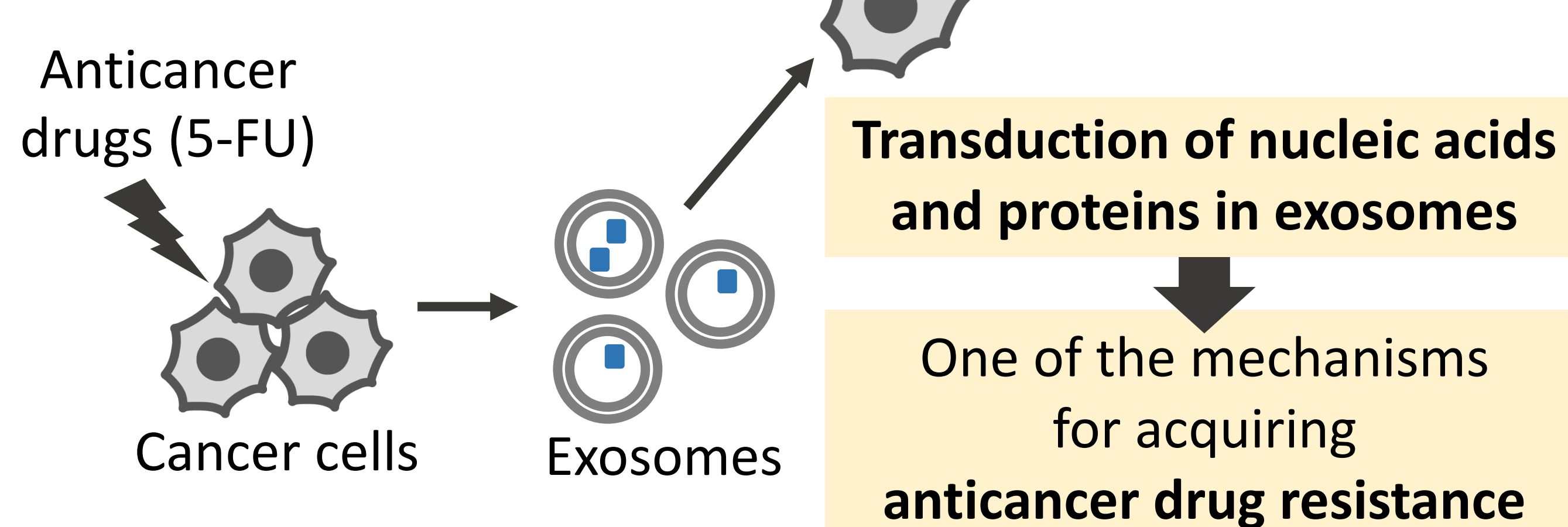


- ◇ Vesicles with lipid bilayers about 100 nm in diameter
 - ◇ They encapsulate lipids, proteins, and nucleic acids
 - ◇ They are transported in the bloodstream to other cells
- An attractive intercellular communication tool in cancer

Exosomes from specimens or media
Exosomal protein → The amount is **very small** → Quantitative studies have not progressed.
→ **Proteins cannot be amplified**

- ◇ We applied our original ultrasensitive protein assay, thio-NAD cycling ELISA.
- ◇ The results have already shown that increased exosomal GRP78 proteins promote tumor progression.

Cancer: Drug resistance



Aim:
To characterize exosomes derived from cells treated with 5-FU

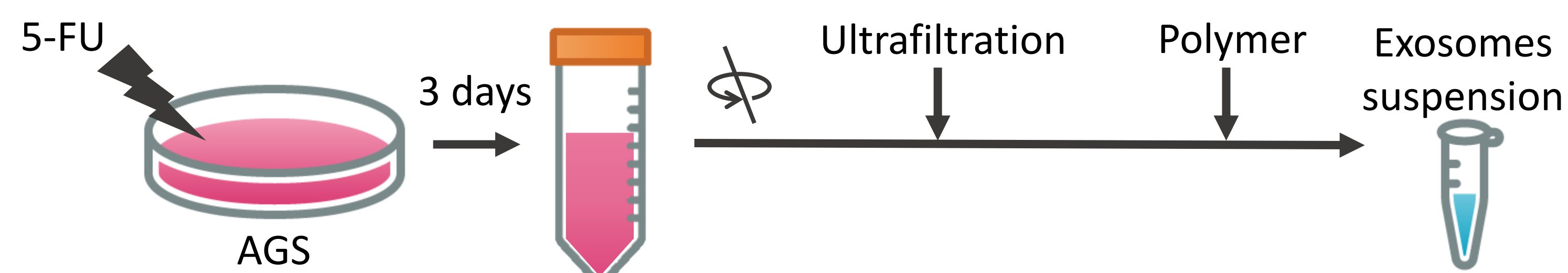
2. Methods

< Cell line > AGS : Cultured human gastric cancer cells

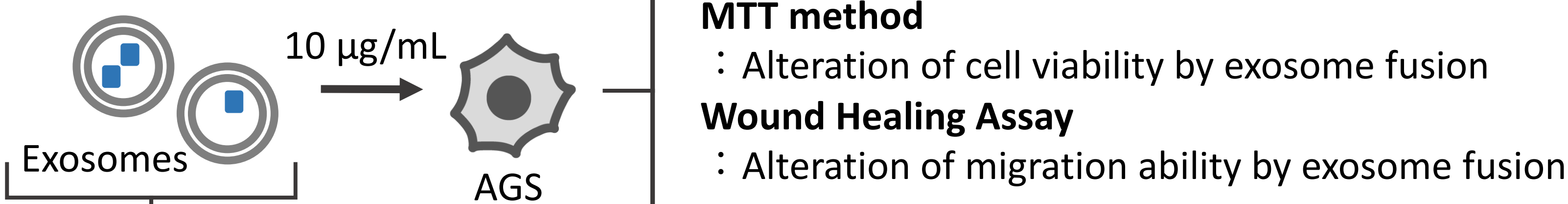
< Anticancer drug > 5-FU : Cont.(PBS), 0 μM(DMF), 10 μM, 30 μM, 50 μM

< Sample > AGS, Exosomes from AGS treated 5-FU

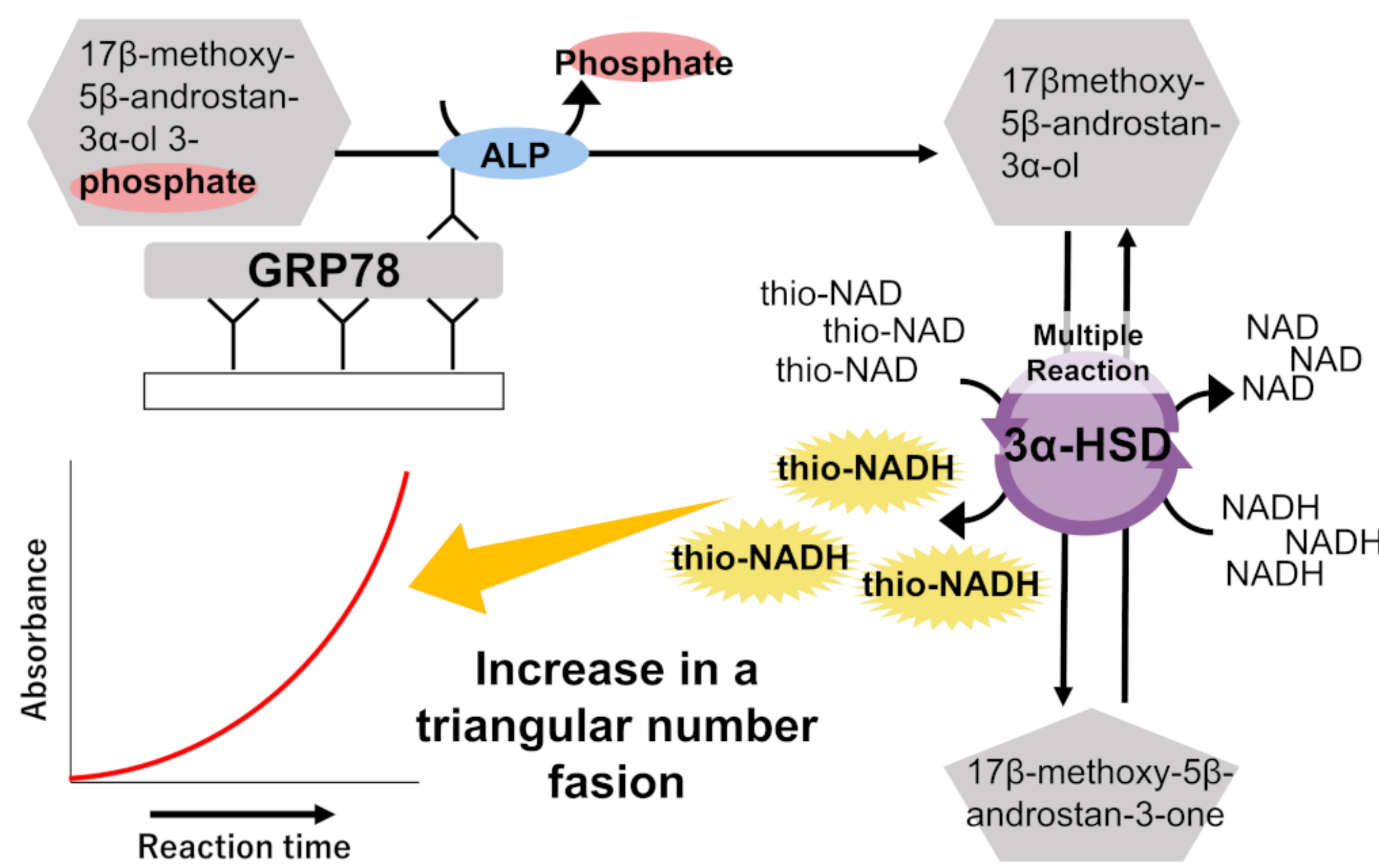
DMF: N,N-dimethylformamide



< Methods >



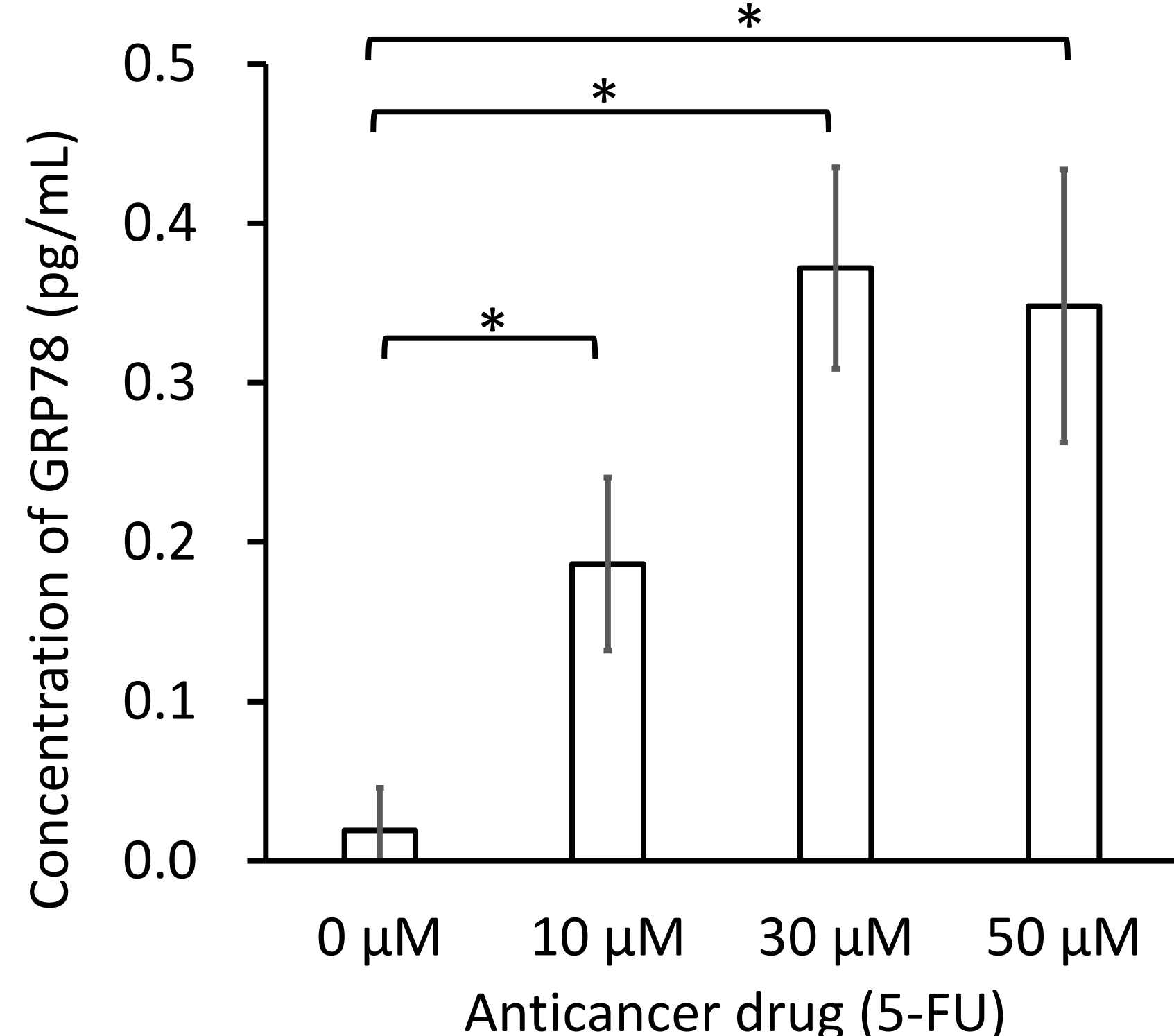
Ultrasensitive ELISA method : Determination of concentration of exosomal GRP78



3. Results

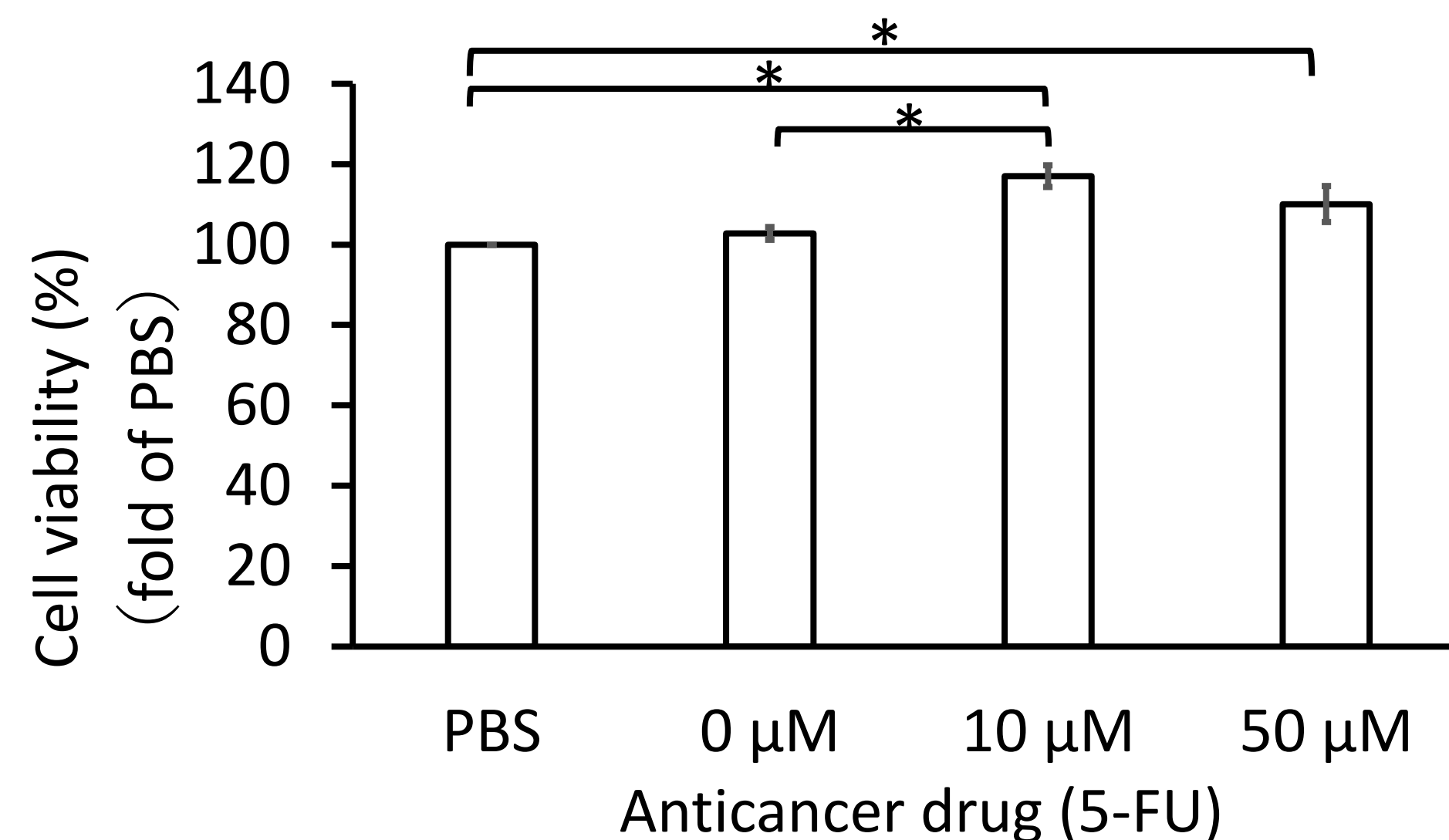
Ultrasensitive ELISA method

- ◇ 5-FU administration was found to release exosomes containing more GRP78.
- ◇ The amount of exosomal GRP78 was also found to increase in response to the concentration of 5-FU administered.



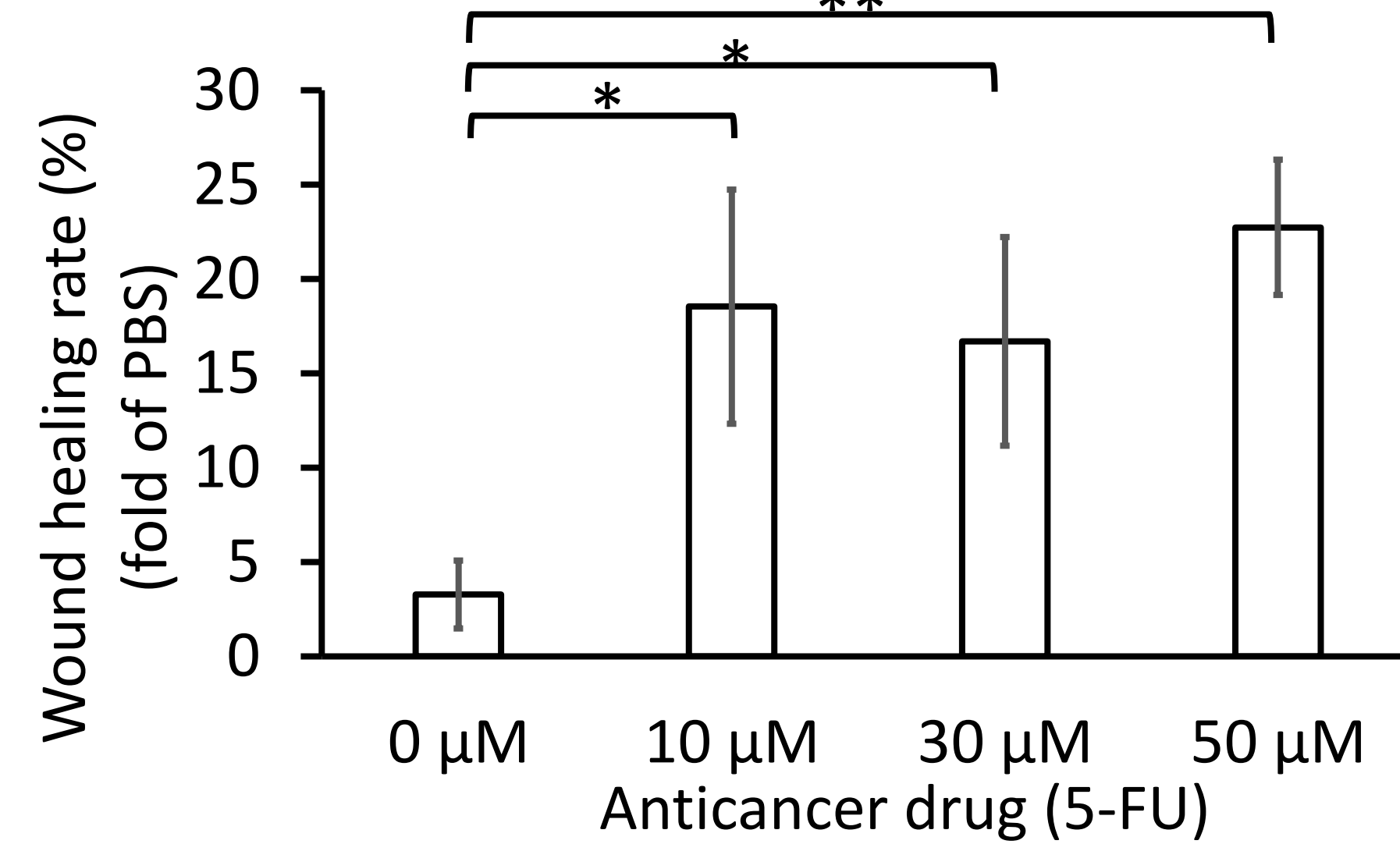
MTT assay

- ◇ Fusion of exosomes secreted by 5-FU treated gastric cancer cells increases cell viability.



Wound healing assay

- ◇ Fusion of exosomes secreted by 5-FU treated gastric cancer cells increases wound healing rate.



→ Exosomes secreted by 5-FU treated gastric cancer cells alter cell characteristics to become cancer stem cell-like (high survival and migration)

→ Together with previous studies, this suggests that exosomal GRP78 may be involved in changes in cell characteristics.

4. Discussion

- ◇ Our findings on exosomal GRP78 were obtained under more clinically relevant anticancer drug administration conditions.
- We would like to study the direct relationship between GRP78 in exosomes and drug resistance.
- ◇ We will test our hypothesis in an experimental system using nude mice.

