# Study of photodynamic therapeutic effect and mechanism of the human pancreatic cancer using Talaporfin

Mizuki IWAI（岩井瑞樹）

[INTRODUCTION] Among various kinds of cancers the pancreatic cancer has currently the lowest survival rate for five years of the patient because of permeation and metastasis at an early stage. Photodynamic therapy (PDT) is expected as most promising technique because of low energy treatment. Though local curative effects of PDT are quite high for superficial cancers, there are few reports for cancer located in deep bodies. In this study PDT was performed on several human pancreatic cancer cell lines using Talaporfin as a photosensory material, and the cytotoxic effect was evaluated under various conditions. Furthermore, by adding an inhibitor for various uptake of Talaporfin, the intracellular shift mechanism was investigated.

[METHOD] The four pancreas cancer cells strain (MiaPaCa-2, AsPC-1, Panc-1, SUIT-2) were used. In the PDT experiment, $2.5\times10^4$cells were seeded on a 96 well-plate, followed by the addition of 100μL/1well of serum-free medium doped with 30mg/mL of Talaporfin. The laser light of 664nm and power density of 2.5~10.0J/cm² was irradiated at 2, 4 and 6 hrs after addition of Talaporfin. Adding 20μL live cell measurement reagent MTS, the cell viability was evaluated by colorimetric analysis of a plate reader. In addition, an endocytosis inhibitor which inhibits the uptake pathway of Talaporfin was added, and comparison with the normal PDT effect was performed.

[RESULTS] The survival rate largely decreased in all cell strain (Fig.1), which supports the effectiveness of PDT on pancreatic cancer cell. In addition, it was suggested that the decrease in cell survival rate depended on the Talaporfin add time and the laser power density. SUIT-2 was the lowest at 16.5% and MiaPaCa-2 was the highest at 34.8%. The PDT results using endocytosis inhibitors (Fig. 2) show inhibitor Dynasore, which inhibits clathrin endocytosis, did not reduce the survival rate in all cell lines. AsPC-1 and MiaPaCa-2 did not reduce survival rate with any inhibitor. Hence, it was suggested that caveolae by the inhibitors Methyl- β-cyclodextrin and Genistein, lipid rough and endocytosis, and clathrin endocytosis by Sucrose and Dynasore are involved in the Talaporfin uptake.

[SUMMARY] The PDT results suggested that Panc-1 was effective for PDT when comparing poorly differentiated Panc-1 and moderately differentiated AsPC-1. In the endocytosis inhibition experiment, AsPC-1 and MiaPaCa-2 decreased the uptake of Talaporfin with all the inhibitors, and the PDT effect could not be confirmed. However, since the PDT effect was confirmed in Panc-1 and SUIT-2, it is necessary to conduct experiments using different pathway inhibitors to confirm the migration pathway of Talaporfin.

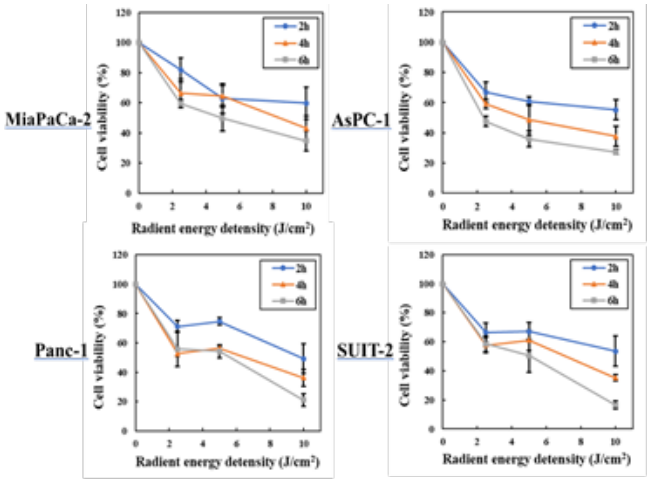


Fig.1 Survival rate change according to the dosage time and the irradiation power, of Talaporfin in various cell strain.

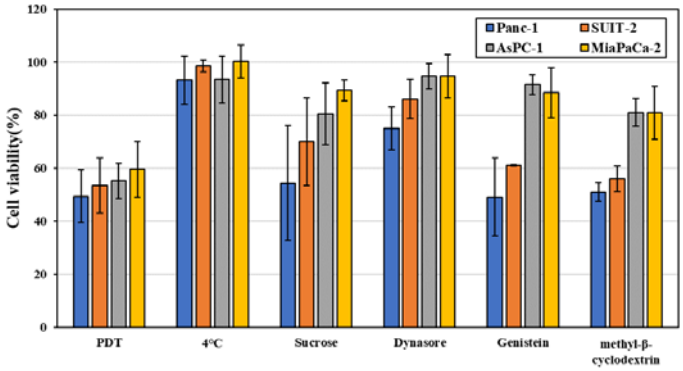


Fig.2 PDT effect of various endocytosis inhibitors.