【Grant-in-Aid for Scientific Research (S)】

Creation of novel small molecule-based theranostics medical technologies for cancer based on individual visualization of disease characteristics of each patient

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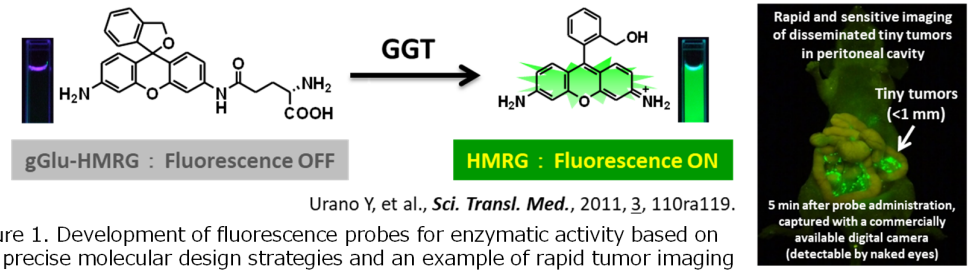
Project Information	Project Number : 24H00050　　Project Period (FY) : 2024-2028 Keywords : Enzymatic acitivity, Cancer, Theranostics, Personalized medicine, Small molecule drugs

Purpose and Background of the Research

●Outline of the Research

In order to solve the problem of leftover cancer cells, which is a major problem in surgical treatment of cancer, the principal investigators have established a method to clearly detect even minute cancers smaller than 1 mm in size. A number of original fluorescence probes were developed that can detect the activity of enzymes such as GGT, whose activity is reported to be increased in cancer cells, and achieved rapid detection of micro metastatic tumors by local application of these probes (Figure 1).



Urano Y, et al., ***Sci. Transl. Med.***, 2011, 3, 110ra119.

Figure 1. Development of fluorescence probes for enzymatic activity based on our precise molecular design strategies and an example of rapid tumor imaging by topical administration to an animal model of peritoneally disseminated cancer

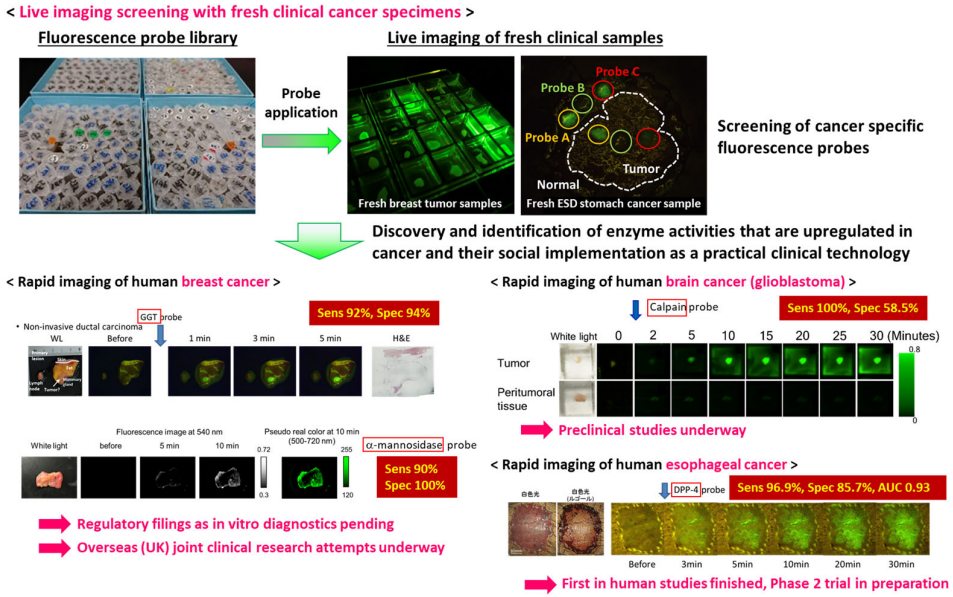


Figure 2. Discovery of cancer-selective imaging probes using a fluorescent probe library, identification of responsible enzymes, and social implementation as a real clinical technology

Furthermore, by constructing a fluorescent probe library and applying it to various human clinical specimens, we screened for fluorescence probes that can selectively detect each cancer type and identified the responsible enzymes. Clinical trials are currently underway for the implementation of some of the fluorescence probes discovered (Fig. 2).

●Research objectives

We aim to establish and expand chemical principles for the development of small molecule theranostic drugs (fluorescent/nuclear medicine diagnostics and prodrug-type/nuclear medicine therapeutics) that are capable of high functionality, to clarify the characteristics of cancer cells in each patient by live imaging, and to select highly effective therapeutic agents and techniques based on this information. Based on this information, we aim to create a completely new and highly effective personalized and precision medical technology to cure diseases with minimal side effects (Figure 3).

Expected Research Achievements

1. Development of novel design principles for nuclear medicine imaging and therapeutic probes capable of intracellular retention by biomarker enzymatic activity, and to build a library of imaging and therapeutic probes.
2. Optimization of novel reactive chemical scaffolds that exhibit cytotoxicity by biomarker enzymatic activity, and comprehensive development of prodrug-type cancer drugs for various types of cancers based on these structures.
3. The functions of above mentioned nuclear medicine imaging and therapeutic probes will be verified to establish theranostics medical technology for deep cancer.
4. The efficacy and side effects of prodrug-type anticancer drugs will be verified using various types of cancer organoids and xenograft to establish highly effective theranostics medical technology.

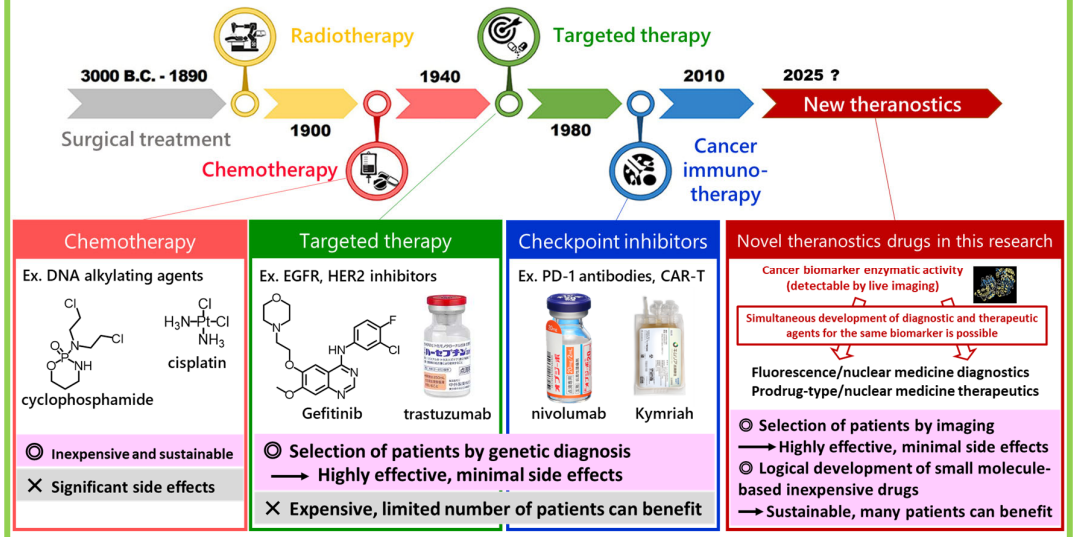


Figure 3. Summary of various cancer treatment technologies, their advantages and problems, and the aim of the theranostic cancer treatment technology to be established in this basic research

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