### 1-11-5. Medical and Healthcare Applications of Photochemistry

#### Overview

Photodynamic therapy and photoimmunotherapy, which are less invasive treatments for cancer, have been studied and developed by various basic studies and clinical trials in the past two decades. Photodynamic antimicrobial chemotherapy has also attracted attention due to the COVID-19 pandemic. Photoresponsive drug delivery system and photo-uncaging compounds are expected as important photochemical techniques for medical and healthcare fields. Optogenetics and its application for genome editing have great potentials for medical and biological applications.

#### Current Status and Frontiers

This field is closely related to biology, clinical medicine, and the development of medical devices. For an overview of the history up to the mid-2000s, including the current situation, please refer to Section "1-13-5. Medical and Healthcare Applications of Photochemistry" in the Photochemistry Div Report described in Japanese. Recently, various materials have been developed to treat various diseases including cancer. In this section, the several examples are briefly introduced.

**1. Photodynamic therapy (PDT)**

PDT is a cancer treatment that combines photosensitizers and light irradiation (Fig. 1). Talaporfin sodium is one of the photosensitizers that has been put into practical use. Additionally, 5-aminolevulinic acid is converted into fluorescent protoporphyrin IX within cells and accumulates in cancer cells, making it useful for photodynamic diagnosis of cancer. These applications are expanding to various types of cancer. In addition, diverse photosensitizers aimed at achieving high activity and multifunctionality have been developed. For example, photosensitizers have been developed that can damage biomolecules via electron transfer mechanisms even in hypoxic cancer tissues.[1] These photosensitizers can also cause damage via conventional mechanisms involving reactive oxygen species (ROS), which require oxygen. Furthermore, activatable photosensitizers that only exhibit photoactivity within cancer cells have been developed to suppress side effects in normal tissues.[2]

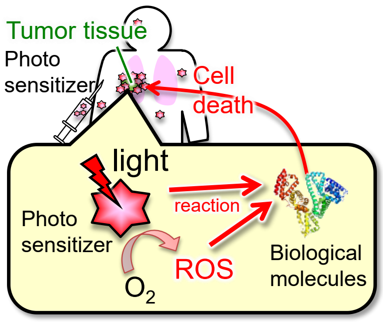

**Figure 1.** Overview of PDT.

**2. Photoimmunotherapy (PIT)**

Cancer treatment using a photosensitizer-antibody conjugate has been commercialized in Japan in 2021 (see Section "1-11-6. Near-Infrared

Photoimmunotherapy").

**3. Photodynamic antimicrobial chemotherapy (PACT)**

Phenothiazine dyes, such as methylene blue, have been used as photosensitizers of PACT, which is one category of PDT. Specifically, PACT is an advantageous method to treat drug-resistant bacteria. Fig. 2 shows the image of PACT to treat a periodontal disease. It is considered that singlet oxygen generation is an important mechanism of PACT. Recently, the electron transfer-mediated oxidation of biomolecules by phenothiazine dyes and the contribution of radical chain reaction have been reported.[3]

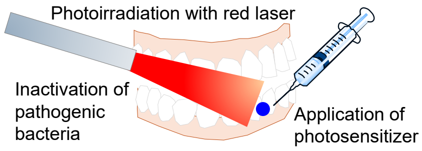


**Figure 2.** Overview of PACT.

**4. Photoresponsive drug delivery system**

Photoresponsive drug carriers capable of releasing encapsulated therapeutic drugs have been developed. These carriers can treat diseases by irradiating the affected area with light (Kataoka et al.).

**5. Photo-uncaging compounds**

Photo-uncaging compounds have been studied that suppress the activity of therapeutic drugs using photolabile protecting groups and then restore their activity through photolysis at the site of disease (Furuta et al., Ohtsuki et al.).

**6. Optogenetics and application for genome editing**

Optogenetics involves expressing photoresponsive proteins in cells through gene transfer and controlling the function of the cells through photoirradiation.[4] It has been reported that the CRISPER-Cas9 system can be introduced with photoresponsive proteins and used for genome editing controlled by photoirradiation.[5] These techniques are expected to be applied to elucidating cell functions and molecular pathology.

## References

1. K. Hirakawa, D. Ouyang, Y. Ibuki, et al., *Chem. Res. Toxicol.*, **31**, 371–379 (2018).
2. H. Horiuchi, et al., *J. Photochem. Photobiol. A*, **403**, 112846–112855 (2020).
3. K. Hirakawa, M. Mori, *ACS Omega*, **6**, 8630–8636 (2021).
4. H. Kandori, *Biophys. Rev.*, **12**, 355–361 (2020).
5. Y. Nihongaki, T. Otabe, M. Sato, *Anal. Chem.*, **90**, 429–439 (2018).

## Future Perspectives and Directions

Development of photosensitizers for cancer phototherapy with minimal side effects and high therapeutic efficacy, and extension of the application range. Practical application to the treatment of a wide range of infectious diseases. Application of photochemical techniques to disease treatment and regenerative medicine.

(Authors: Kazutaka Hirakawa, Hiroaki Horiuchi)