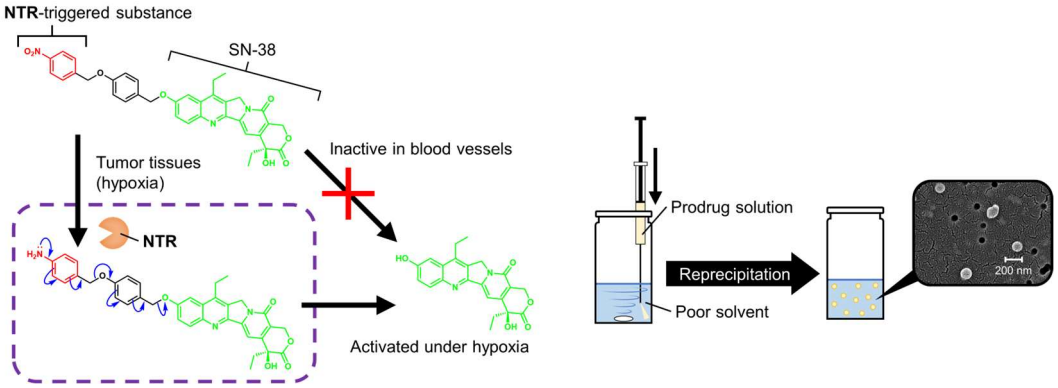
Development of hypoxia-activated anticancer prodrug nanoparticles

([1]*Institute of Multidisciplinary Research for Advanced Materials (IMRAM), Tohoku University*) ○Nagaki Sugeno,[1] Riido Kagaya,[1] Yoshitaka Koseki,[1] Hitoshi Kasai[1]
Keywords: Drug Delivery System; Nanoparticles; Prodrug; Hypoxia

To reduce the side effects of cancer treatment, drug delivery system (DDS) which is a strategy for delivering drugs selectively to cancer has been proposed. Our group reported that carrier-free prodrug nanoparticles can be fabricated by reprecipitation method, and these nanoparticles have the potential to accumulate selectively into tumor tissues due to the enhanced permeability and retention (EPR) effect.[1] However, because most prodrugs is easily activated by factors that are abundant in the body, these nanoparticles may cause non-selective drug release in blood vessels or normal cells.[2]

Given this background, we aimed to develop the prodrug nanoparticles that are activated only in tumor-specific environments. It is known that hypoxia is a common feature of solid tumors and causes overexpression of reduction enzymes such as nitroreductase (NTR). In this study, we designed NTR-triggered prodrug of SN-38, an anticancer drug and fabricated the nanoparticles by reprecipitation method. Furthermore, we evaluated the drug release kinetics using chemical reduction and cytostatic activity *in vitro*. The results supported that the prodrug is activated through reduction of nitro group.



1) H. Kasai, T. Murakami, *et al*., *Angew. Chem. Int. Ed.* **2012**, *51*, 10315–10318. 2) Y. Koseki, Y. Ikuta, *et al*., *Bull. Chem. Soc. Jpn*. **2019**, *92*, 1305–1313.