**Super-enhanced nano-drug delivery into cancer after near infrared photoimmunotherapy (NIR-PIT)**

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Target-specific drug delivery that treats cancers but leaves normal tissue unharmed, is the ultimate goal of cancer therapy. Nano-sized drugs have virtually limitless synthetic possibilities enabling a variety of payloads to be delivered to the tumor resulting in effective therapy. Tumors have relatively higher concentrations of nano-sized drugs than normal tissue due to the leaky nature of tumor vasculature, a phenomenon known as enhanced permeability and retention (EPR). The EPR effect, while permitting an increase in intratumoral nano-drug concentration, nonetheless has a limited ability to achieve concentrations that take full advantage of the capabilities of nano-sized drugs. Thus, a method for better nano-drug delivery might lead to improved cancer therapy. We have recently developed a new type of highly selective, molecularly-targeted cancer therapy, named near infrared photoimmunotherapy (NIR-PIT), that is based on conjugating a near infrared silica-phthalocyanine dye, IR700, to a monoclonal antibody (MAb) thereby targeting cancer-specific cell-surface molecules [1]. After the administration of the conjugate and the targeted application of light, the intratumoral vascular barrier is significantly disrupted enabling a dramatic (up to 24 fold) increase in nano-drug concentration in NIR-PIT treated cancer tissue compared with non-treated control tumors [2]. In this lecture I will discuss general pharmacokinetic characteristics of nano-sized molecules in the body, especially focusing on drug delivery in cancer tissue and routes of excretion that are important for improving the safety profile. In addition, I will discuss the basis and applications of the NIR-PIT-induced super-enhanced permeability and retention (SUPR) effect that could dramatically improve nano-drug delivery thereby enhancing the therapeutic effects of nano-sized anti-cancer agents.

**References**.

[1] Mitsunaga M. et al. (2011), Cancer Cell-Selective *In Vivo*Near Infrared Photoimmunotherapy Targeting Specific Membrane Molecules.Nature Medicine, 17: 1685–1691.
[2] Sano K. et al. (2013),Super-enhanced permeability and retention effects of nano-particle induced by the photo-immunotherapy. ACS Nano, 7: 717-724.