A Smart CEST Imaging sensor based on Thermo-sensitive Micelle

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Chemical exchange saturation transfer (CEST) imaging used Diamagnetic CEST (DIACEST) and Paramagnetic CEST (PARACEST) agents are considered as a suitable methods for molecular imaging[1]. To obtain a new MRI sensor that could reflect hyperthermia of the tumor tissue [2], here we develop a novel PARACEST MRI contrast agent which based on the thermally responsive micelle, the sensor presents a temperature correlated change with CEST imaging and obtains us a novel methodology to target the tumor tissues.

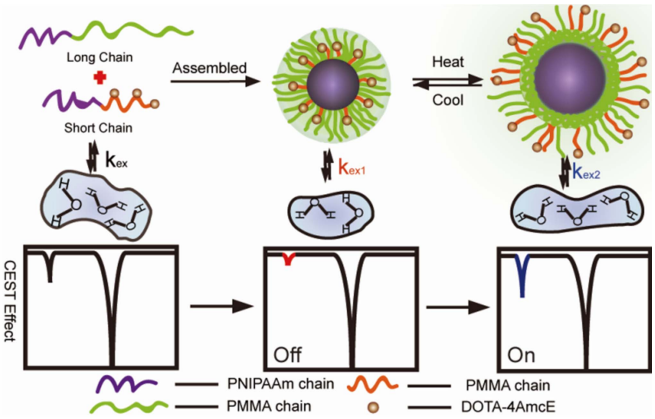

Fig.1 A schematic of CEST spectra change in response to the core-shell structure polymeric micelle

We used a smart copolymer PNIPAAm-b-MMA, which modified with Eu-(DOTAM-Gly-OEt) as a PARACEST contrast agent. The polymer chain PNIPAAm has its low critical solution temperature (LCST), which could stretched as hydrophilic shell under LCST while aggregated as hydrophobic core above LCST. By mixing another length polymer chains under synergistic effect, the amphiphilic chains formed as a mixed micelle with core-shell structure to embed the PARACEST agent as in Fig.1. When the temperature changed around the LCST, the polymeric micelle obtained morphological change, which could concomitant of the proton's environment change. That process could give rise to CEST effect's enhancement as a trigger.

In summary, we have first reported the temperature responsive CEST sensor which could be suitable for body temeprature. The thermo-responsive polymeric micelle was designed as a novel contrast agent due to the PARACEST methods. The modified polymers of Eu-[PNIPAAm-MMA-DO3A] mixed with hydrophilic chain were proved to be detected at lower concentration by CEST. Moreover, we demonstrated that the morphological change of micelle might enhance the CEST imaging intensities, which was modulated by the bound water's external environment and its exchange rate. It indicated that this micelle system could be a good candidate for CEST imaging, and sensitive at human body temperature as well, with respect to normal CEST agent. Based on its smart features, this temperature responsive micelle platform offered great potentials for the human body's tumor detection, and analysis of tissues microenvironment, we envision that the proposed method might broaden the hyperthermia theranostics and nascent stages of tumor detection.

[1]. Ward, K. M., Aletras, A. H., and Balaban, R. S. J.Magn.Reson. 2000, 143: 79-87

[2]. Woods, M., Woessner, D. E., Morrow, J. R. and Sherry, A. D. J Am Chem Soc., 2006, 128: 10155–10162

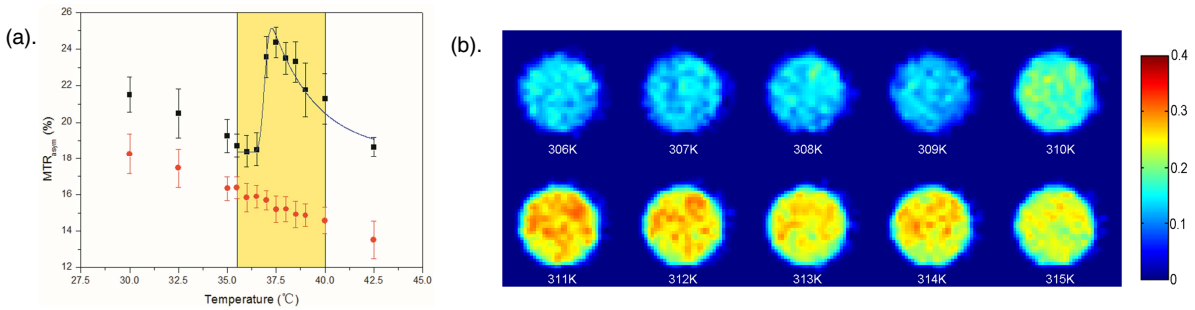

Fig.2 (a). MTR_{asym} fitted as a inflexion curve at the regions of interest with variable temperatures. (b).CEST MRI of variable temperatures.