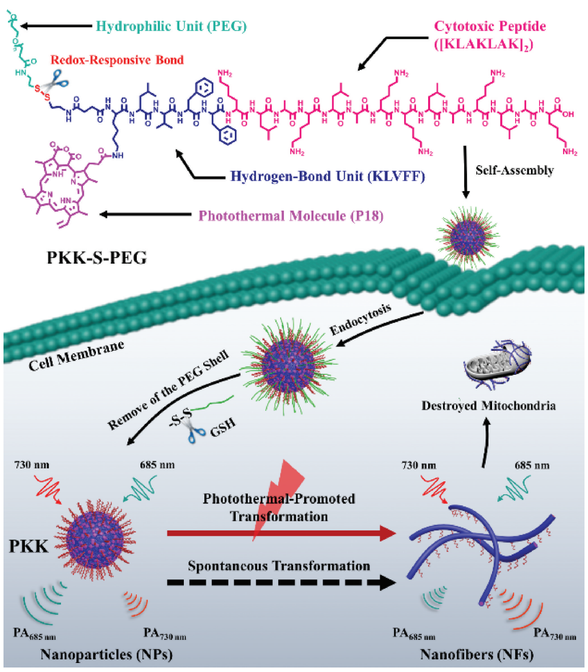
Photothermal-promoted morphology transformation *in vivo* monitored by photoacoustic imaging

With the support by the National Natural Science Foundation of China and the Chinese Academy of Sciences, the research team led by Prof. Chen Hao (陈浩) from Huazhong Agricultural University and Prof. Wang Hao (王浩) from the National Center for Nanoscience developed a new strategy for nanomaterials morphology transformation *in vivo*, which was published in *Nano Letters* (10.1021/acs.nanolett.9b04752).

As a multifunctional platform, peptide-based nanomaterials have attracted much attention in the field of biomedicine. Nanofibers assemblies of peptide have unique size effect and multivalent binding ability, which can enhance the biological function of drug molecules. "*In vivo* self-assembly", as an emerging strategy for constructing nanomaterials *in vivo*, has proved to be a promising biotechnology for disease diagnosis and treatment. The nanofibers were built at the tumor or infected site *in situ*, which has bright prospects in the fields of cancer treatment, bacterial infection treatment, and tumor medical imaging.

In vivo assembly rate control is very important for regulating the biological effects of nanomaterials. Generally, the aggregation process of peptide nanofibers is slow, and the spontaneous formation of nanofiber structures takes a long time. Inspired by the effect of temperature on the formation of amyloid fibers, the researchers devised a photothermal-promoted morphology transformation (PMT) strategy to accelerate the formation of nanofibers *in vivo*. By introducing the temperature control unit Purpurin-18 into the central position of the polypeptide sequence, the *in vivo* nanofiber formation rate was successfully regulated.



Scheme Photothermal-promoted transformation strategy accelerates the formation of fibrous nanodrug to destroy mitochondria in cells, and the re-assembly process is monitored by photoacoustic (PA) imaging.

Purpurin-18 produces photothermal effect under near infrared light, causing temperature rise. The primary nucleation of the fiber is accompanied by the increase of enthalpy and entropy. In the nucleation process, the primary nucleation rate of nanofibers will be greatly accelerated with the increase of temperature. Anti-tumor tests showed, compared with the spontaneous process, the rate of transformation increases by ca. 4 times in the PMT process. Owing to the raise of the assembly rate, the tumor accumulation of drugs is ca. 2-fold faster? than that without photo irradiation, which inhibits the tumor growth effectively. The formation of nanofibers was monitored by new photoacoustic imaging techniques.

Excitingly, the PMT strategy can effectively promote the nanofiber formation of peptide drugs *in vivo*, which helps the accumulation of drug molecules at the tumor site. Through the noninvasively artificial control on assembly dynamics *in vivo*, the PMT strategy provides a new insight for developing the intelligent theranostics.