Single-molecule detection of biomarkers and localized cellular photothermal therapy using nanointerface functionalized optical microfiber

With the support by the National Natural Science Foundation of China, the research team led by Prof. Guan BaiOu (关柏鸥) at the Institute of Photonics Technology, Jinan University, developed ultra-sensitive fiber optic biosensors that are able to detect the breast cancer biomarkers at the single molecule level and to kill the cancer cells through the photothermal effect, which was published in *Science Advances* (2019, 5: eaax4659).

For the early diagnosis of diseases, there is a strong demand for biosensors that can rapidly detect biomarkers at ultralow concentrations or even at the single-molecule level. Compared to other types of biosensors, fiber optic biosensors have distinctive advantages of low cost, small size, flexibility, and being suitable for *in-vivo* applications. However, the relatively low sensitivity at picomolar concentrations strongly hinders their use.

Guan's group has demonstrated the interfacial sensitization technology that can significantly enhance the sensitivity of fiber-optic biosensors. This technology does not depend on the optical structure and is generally applicable to fiber optic transducers such as long-period fiber gratings, D-shape fibers, and micro/nano fibers. They used the tapered microfiber interferometer, which is simple in structure and easy to manufacture, as transducer. The microfiber surface was functionalized with a plasmonic nanointerface consisting of black phosphorus (BP)-supported Au nanohybrids. The nanointerface strongly enhances the interaction between the microfiber evanescent field and the surrounding medium through the localized-surface plasmon resonances (LSPRs) effect. By designing the gold nanohybrid, the plasmon resonance was adjusted to the optical communication window (1 550 nm band) so that the low-cost components commonly used in the optical communication industry can be used to build the sensing system. The sensor was designed to be specifically sensitive to ErbB2 antibodies, a kind of well-established breast cancer biomarker. The sensor was able to detect the ErbB2 target molecules at concentrations ranging from 10 zM to 100 nM, with a detection limit of 6.72 zM, enabling detection at the single-molecule level.

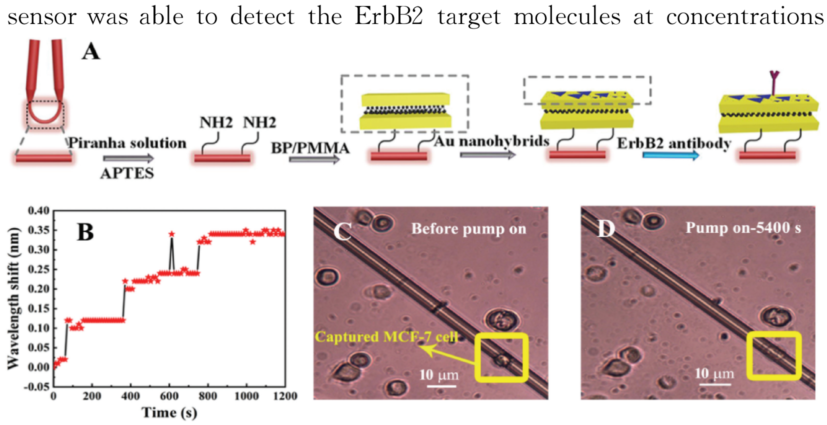

Figure (A) Scheme of the functionalization of the optical microfiber biosensor. (B) Single molecule response of the sensor to ErbB2 (each ErbB2 molecule causes a step change in the sensor output wavelength). (C—D) Optical microscopy images of the microfiber capturing cancer cell and killing it through photothermal effect.

The nanointerface functionalized microfiber can capture the breast cancer cells at an ultralow concentration. The BP-supported Au nanointerface absorbed the 980 nm pump light through the evanescent field to generate heat and heat-treat the cancer cells. When the heat accumulated to a certain extent, the cancel cells were disrupted. This work opens up a possible approach for the integration of cellular diagnosis and treatment.