Construction of high efficient biosensors based on isothermal amplification for biomarker analysis

With the support by the National Basic Research Program of China, National Natural Science Foundation of China, and 1000 Young Talent and initiatory financial support from HUST, the research team led by Prof. Xia Fan (**夏帆**) and Prof. Lou Xiaoding (**娄筱叮**) at Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, developed a construction of high efficient biosensors based on isothermal amplification for biomarker analysis, which was published in *Chemical Society Reviews* (2016, 45: 1738—1749).

Developing applicable isothermal amplification strategy with sensitivity, high speed, specificity, accuracy, and automation for biomarkers detection is important for environmental and food security, as well as clinical diagnosis. In recent years, this group has developed three kinds of attractive detection strategies for the detection of oligonucleotides, proteins, and small molecules according to the ratio of the target-to-signal probe that is the N:N amplification ratio, the 1:N amplification ratio, and the 1:N^2 amplification ratio.

Sandwich structure, a traditional DNA structure in biomarker analysis, is limited by sensitivity because a DNA target can only hybridize to a single signal probe. In order to improve the traditional sandwich structure, they designed a supersandwich structure containing multiple signal probes, in which the ratio of target to signal probe is N:N. Such N:N strategy was also constructed in the artificial ion channels and exhibited high ON-OFF ratio.

In the 1:N amplification strategy, the target can be recycled and result in that one target would yield multiple signal outputs. For instance, they reported a noninvasive, direct, and bidirectional colorimetric approach for telomerase analysis in urine samples of bladder cancers based on difunctional gold nanoparticle (GNP) probes with multiple visual signals. In this strategy, one telomerase can produce an ssDNA containing multiple TTAGGG repeats which would then hybridize with different reporter probes from different GNPs. They have demonstrated that the proposed method is sensitive and selective enough to distinguish among bladder cancer patients, inflammation patients, and healthy individuals.

More excitingly, they designed a functional molecular beacon (MB) and developed a one-pot hairpin-mediated quadratic enzymatic amplification (HQEA) for miRNA detection (1:N^2). In this method, not only the target miRNA but also the synthesized DNA caused by miRNA reaction can be simultaneously recycled. Both the target miRNA and the synthesized DNA can release signals of MBs, leading to an ultra-high sensitivity. After being challenged with crude extractions from MCF-7, PC3 cell lines, and even breast cancer tissues, the HQEA method also exhibited great sensitivity and selectivity.

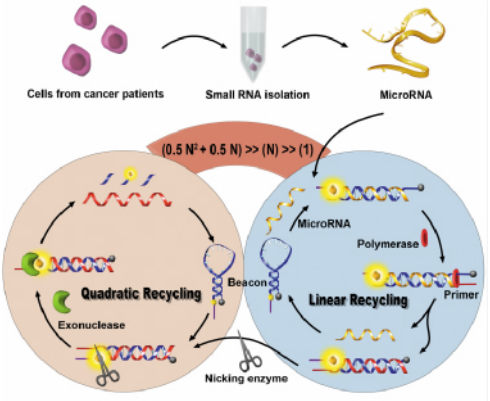

Figure The scheme of the HQEA strategy.