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Biosensing techniques for sensitive immunoassays

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Enzyme labels are still commonly employed to obtain signal amplification in biosensors and bioassays, although in the recent decade many nanomaterial-based ultrasensitive biosensors have been newly developed. One of the main reasons for this is that the enzyme-based biosensors based on enzymatic reactions of horseradish peroxidise (HRP) and alkaline phosphatase (ALP) labels provide high, steady, and reproducible signal amplification. However, the signal amplification by enzymatic reactions is not sufficiently high to achieve ultrasensitive detection of biomolecules that is essential for early and rapid diagnosis of diseases. To circumvent this limitation, enzymatic reactions have been combined with an additional amplification process (i.e., redox cycling) or signal amplification has been increased by using multienzyme labels per detection probe.

Redox cycling, which plays a crucial role in amplifying chemical species in nature, is a process that can repetitively generate or consume signalling species (molecules or electrons) in the presence of reversible redox species. The two reactions (oxidation and reduction) in redox cycling can be obtained either enzymatically, chemically, or electrochemically. Importantly, redox cycling can be readily coupled to enzymatic amplification simply by adding one more chemical (and enzyme) to a solution or by using one more electrode in electrochemical detection.

Electrochemical detection matches well with redox cycling, as it can trigger and take part in redox cycling. In general, electrochemical signals are limited by mass transfer of signalling species to electrodes, and this becomes worse when signalling species in a small volume are consumed in a short period. Redox cycling is effective for regenerating the consumed signalling species, and as a result it provides high steady-state electrochemical signals. One important but often overlooked thing in electrochemical biosensors is that even small instruments can offer very stable voltage/current source and detector, meaning that the effect of electrochemical instruments on biosensor reproducibility can be excluded. Therefore, the combination of redox cycling and electrochemical detection could play an important role in the development of ultrasensitive and reproducible biosensors for point-of-care testing.

In recent years, we have developed new redox cycling schemes combined with enzymatic amplification that allow high signal amplification in a simple format along with low background levels.[1] To minimize unwanted side reactions, a new concept that outer-sphere-reaction-philic species can react slowly with inner-sphere-reaction-philic species was applied. In this presentation, the signal amplification based on (i) electrochemical-chemical (EC) redox cycling using a reducing agent,[2] (ii) electrochemical-chemical-chemical (ECC) redox cycling using a reducing agent and an oxidizing agent,[3] (iii) electrochemical-enzymatic (EN) redox cycling using a redox enzyme,[4,5] and (iv) electrochemical-nanocatalytic (ENc) redox cycling using a nanocatalyst[6] will be introduced. Moreover, our efforts for practically useful biosensors will be presented.

References

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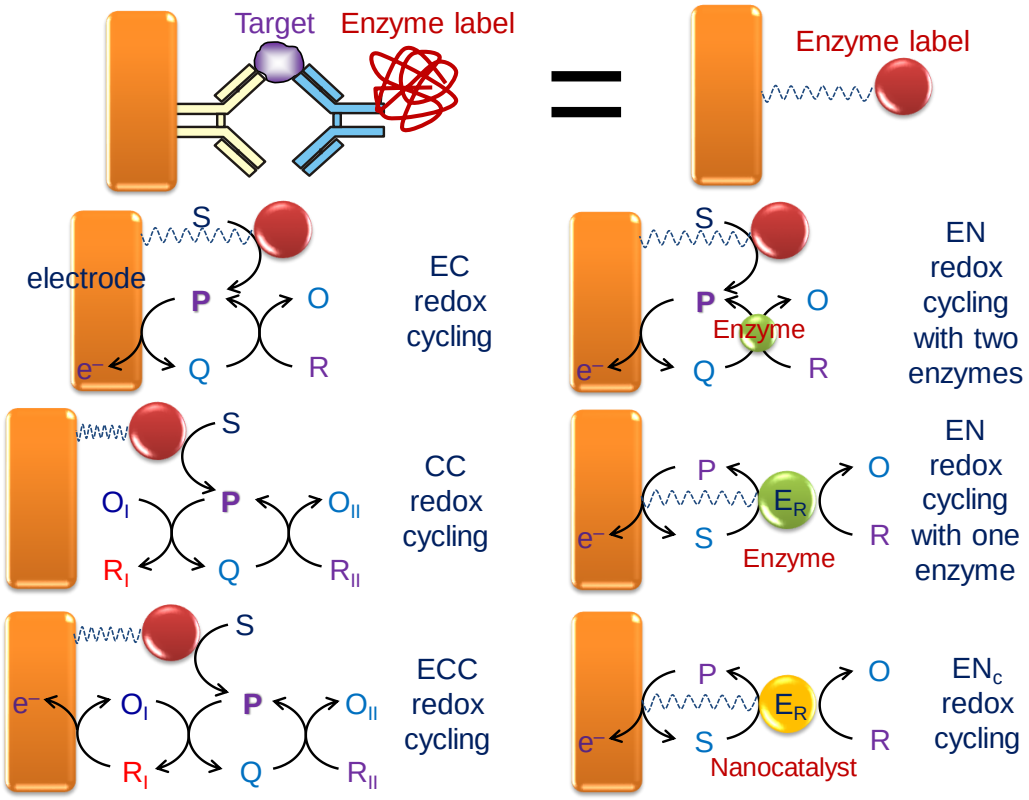

Figure 1. Redox cycling schemes