**Direct Electron Transfer Type Oxidoreductases**

**~*what they are, how to use and how to construct*~**

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Current enzymes (oxidoreductases) based metabolite monitoring systems, are categorized into three different principles; 1) the first generation principle which utilizes oxidases as the enzymes and oxygen as the electron acceptor and monitoring liberating hydrogen peroxide, 2) the second generation principle which utilizes oxidases or dehydrogenases as the enzymes and synthetic electron acceptors (mediators) instead of oxygen, and monitoring the formed reduced mediators, 3) the third generation principle which utilizes dehydrogenases capable of transferring electron directly from enzyme cofactor to electrode without the use of oxygen or mediators, designated as the direct electron transfer (DET). All principles will be combined with either electrochemical or optical device to detect generated signals. The third generation principle, employing DET-type enzymes is recognized as the ideal method and ultimate goal of oxidoreductase based biosensing and biodevices. This is because of the following expectations; 1) no mediators or oxygen is required for the sensing, 2) less number of essential reactions for monitoring compared with first and second generation principle, 3) monitoring of substrate by applying a lower potential, consequently reduce the impact of electrochemical ingredients, and 4) simplifying sensor structure and consequently fabrication steps. Among varieties of cofactor binding type oxidoreductases, some dehydrogenases harbor a subunit or a domain specifically functioning to accept electron from the redox cofactor of catalytic site, and transfer electron to the external electron acceptor. Such a subunit or domain acts as a built-in mediator for electron transfer between enzyme and electrode, consequently, makes such enzymes possible to transfer electron directly to electrode, designated as the DET-type enzymes.

In this lecture, the author will summarize the current status of DET-type oxidoreductases by introducing their specific structural and functional features, and how they have been applied to construct bioelectrochemical devices, and the challenges to construct DET-type oxidoreductases from non-DET-type oxidoreductases.