DNA probes relied on charge transport through the π-stack of duplexes

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Single-nucleotide polymorphisms (SNPs) of genes characterize personality of individuals, medicinal importance of which includes risks of various diseases and differences for drug responses (pharmacogenomics). Thus, various enzymeless, chip-based assay systems, so-called DNA-chips, have been proposed for large-scale analysis of SNPs. Among them, electrochemical detection promises to be far superior to existing sensory formats with respect to sensitivity, rapidity, and availability of low-cost portable devices.[1,2]

Our strategy is to use a completely π-conjugated ferrocene-modified nucleoside analogue, of which structure is inspired from our previous studies on molecular recognition chemistry for ferrocene-modified synthetic receptors.[3] We thought that if this nucleoside analogue is connected at 5'-end of a single-stranded oligonucleotide, the modified DNA would behave as a molecular-scale "wire-like" electrochemical probe. When the hybridized duplex with a complementary DNA is attached onto a gold electrode at 3'-end of the probe DNA by means of gold-thiol chemistry, "π-way" will be fully opened from the ferrocene tag of the nucleoside residue to the gold electrodes via the conjugated "acetylene–synthetic base–stacked base pairs" bridges. If a mismatched base pair presents in the duplex, hole transport from the electrodes will be insulated at that position like a blockade of the "π-way" (Fig. 1). This straightforward methodology will meet the criteria in future chip-based genetic analysis for identifying SNPs of individuals.[4,5,6] In this forum, details of this methodology will be presented.

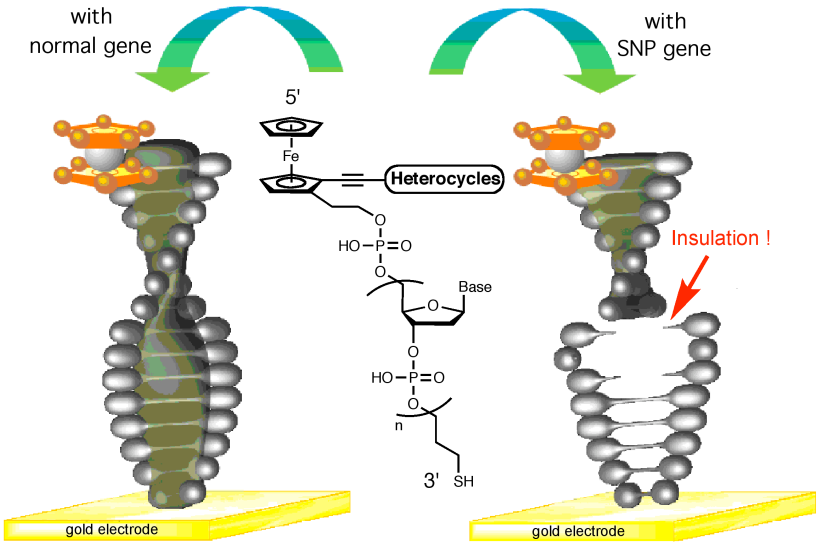

Fig. 1 Chemical structure of electrochemical DNA probes and illustration for discrimination of SNPs

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[2] Barton, J. K. et al. *Nat. Biotechnol.* **2003**, *21*, 1192–1199.
[3] Inouye, M. et al. *Angew. Chem. Int. Ed.* **2001**, *40*, 1746–1748.
[4] Inouye, M. et al. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 11606–11610.
[5] Inouye, M. et al. *e-J. Surf. Sci. Nanotech.* **2005**, *3*, 393–398.
[6] 井上 将彦 他 *化学* **2006**, *61* (No. 3), 12–16.