A new electrochemical platform based on P450 2C8 for drug discovery

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Cytochrome P450 2C8 is responsible for 10% of drug metabolism in human liver. Among its substrates are the anticancer drug paclitaxel and the antimalarial amodiaquine. In order to meet the need of a reliable and fast drug screening assay for P450, this project aims at the construction of a P450 2C8 electrode.

The CYP2C8 gene was cloned and expressed in *E.coli* leading to 490 nmoles/l of pure protein as determined spectrophotometrically with CO binding. An apparent K_m of 26.2 ± 4.7 μM was measured for the paclitaxel product (HPLC). The recombinant enzyme was then immobilized on glassy carbon (GC) electrodes modified either with the polyelectrolyte PDDA or gold nanoparticles. Cyclic voltammograms of P450 2C8 showed a reversible redox couple centered around –305 mV with both immobilization approaches. Electrochemically driven catalysis of the immobilized protein was also performed by chronoamperometry using paclitaxel as substrate. An apparent K_m of 50 μM was measured, in good agreement with data obtained in solution.

This is the first successful immobilization of an active P450 2C8 on GC electrodes, an important step towards the development of a P450-based drug discovery array.