Abstract

(i). Various cellular biological systems have been engineered to synthesize targeted chemicals for natural product medicines and biofuels catalytically by rewriting genomes. Recent advances in direct evolution of enzymes and gene synthesis lead to the rapid progress in tailoring biocatalysts by protein engineering. Peptides are another of nature’s building blocks with binding specificity, and their robustness and versatility in self-assembly can be exploited to design complex 3D catalytic superstructures. Since catalytic peptides are much smaller than enzymes, the sequences and assembled structures of catalytic peptides are more feasible to be analyzed, optimized, and modeled as compared to enzyme-assembled superstructures. Here we demonstrated to evolve this phage library for the discovery of catalytic viruses that can catalyze general chemical reactions. Since the conventional phage display library is not designed to directly screen viruses on the basis of catalytic turnovers for the targeted reactions, a new approach needs to be developed. The proposed new screening approach combines (i) combinatorial library of catalytic phage viruses that display peptides catalyzing targeted reactions (ii) selection of catalytic viruses via supramolecular gelation of targeted products on phage viruses for the mass-separated panning process. This approach can also be applied to find catalysts for anti-cancer and anti-hypertension drug synthesis via amide condensation reactions.

In Nanotechnology approach, we also investigated new catalysts with shaped nanoparticle. It has been difficult to fabricate nanoparticles less than 20 nm with complex shapes that display a number of atomic edges known to catalyze chemical reactions. We developed a new method to fabricate such Pd nanoparticles by etching specific crystalline faces in oil-water reverse micelles.

Atoms are adsorbed and desorbed at the interface, and we could control this balance crystalline face by face to tether targeted shape and structure of Pd nanoparticles. The resulting Pd nanocages and Pd nanocubes are compared in catalytic activity of Suzuki coupling reactions, and it indicates that the number of exposed atomic edges is critical for the enhanced activity.
A new lab-on-a-chip platform integrating electric cancer cell sensor and cancer cell separation on a micro-fabricated silicon chip is introduced. This sensing platform was designed to distinguish cells in different sizes and shapes by measuring their characteristic impedance signals on polysilicon microelectrodes. Due to the softness of cancer cells as compared to normal cells, cancer cells were observed to swell three times more than normal cells under hyposmotic pressure. By using this sensor chip and protocol, cancer cells can be distinguished from normal cells electronically without biomarkers; as strong hyposmotic stress is applied to cells, only cancer cells increase impedance signals due to the swelling. For example, we have examined six different cancer cell lines from prostate, kidney, ovarian, and breast, and all of these cancer cells were observed to expand their size about 35 – 50% under osmotic pressure and their swellings could be detected sensitively and selectively by the robust impedance measurements of the sensor chip on the order of 5 cells/mL in less than 30 minutes. Aggressive breast cancer cells could be distinguished from less aggressive ones by measuring impedance values of the samples. After cancer cells are detected, cancer cells can be selectively removed from the chip by applying negative dielectrophoresis. Due to the swelling, cancer cells induce distinguished dipole feature as compared to non-swelling normal cells and red blood cells, and this feature allows one to tune the specific AC frequency that only applies the negative-dielectrophoretic force to target cancer cells for the separation. Enrichment of targeted cancer cells in the short time are extremely advantageous for the analysis of circulating tumor cells (CTC), cancer stem cell (CSC), or metastatic cancer cells because they are rare and the subsequent gene analysis of collected cancer cells is beneficial for future personal medicine. The development of such non-invasive screening/separation device for cancer cells with high specificity and selectivity enables more frequent monitoring of the early stage disease development, progress, recovery, and recurrence of cancers.

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