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摘要 以作者所在课题组近年来的研究工作为基础, 就芯片实验室平台建设及相应的以系统生物学为最终目标的功能化研究作一说明, 对在分子和细胞层面, 甚至是单分子、单细胞水平上实现以规模集成为特征的临床诊断和药物筛选的努力予以特别的关注。

关键词 芯片实验室 系统生物学 功能化 临床诊断 药物筛选

分类号

Laboratory on a Microfluidic Chip

Abstract

The recent achievements of microfluidic chip and its applications, based on the works mainly carried out in the authors' lab are reviewed. The chip fabrication capabilities have been extended into design and fabricate chips with higher degree of complexity in different materials, such as quartz, glass, polymethyl methacrylate (PMMA), and polydimethyl siloxane (PDMS). A set of methods for surface modification of micro-channels on such materials have been developed, which results in better reproducibility and higher efficiency in protein and peptide analysis. The use of novel materials for chip fabrication is also under investigation. A series of microfluidic workstations with integrated chip manipulation as well as laser induced fluorescence (LIF), ultraviolet (UV), electrochemical and chemiluminescence detection modules have been developed to attain the abilities of complex microfluidic control and data acquisition schemes. A single cell/single molecule imagining system was built up for dynamic analysis of molecular or cellular events too. Based on the work mentioned above, different functional units, such as membrane, monolithic, isotachophoresis (ITP) etc were set up and integrated. Glycoform separation of turkey ovalbumin in a lectin monolithic column and an electrophoresis channel was performed on an integrated microchip. And a novel technique has been developed that allows for the coupling of ITP and non-gel sieving electrophoresis for protein analysis in a single microchip and resulting in ~50 fold increase of the sensitivity in comparison with the use of gel electrophoresis only. A single molecule detection (SMD) based technique was developed for simultaneously measuring both bulk flow and near-wall flow velocity in the microchannels. And more recently, an SMD based technology was developed for observing molecular interactions at single molecule level. An ultra-rapid microchip electrophoresis method was established for simultaneous determination intracellular reactive oxygen species (ROS) and reduced glutathione (GSH) related to apoptosis and oxidative stress. In an effort to develop a novel microfluidic based drug screening platform, systematic studies on the interaction between granulocyte colony-stimulating factor (G-CSF) and sulfated oligosaccharides were carried out at both molecular and cellular levels. Doxorubicin induced apoptosis of human hepatocellular carcinoma (HepG2) was studied using the integrated microfluidic device with concentration generator. In the application phase, severe acute respiratory syndrome (SARS) diagnosis based on reverse transcription-polymerase chain reaction (RT-PCR) and microfluidic chip electrophoresis (MCE) with 18 cases, methylation analysis of the P16 gene in 159 samples of patients and references for cancer diagnosis and polymorphism analysis of angiotenigen gene in 226 patients and references with essential hypertension are described. Forty-three up to date references are cited.

Key words lab-on-a-chip systems biology integrated functionalities clinical diagnosis drug screening

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