主 論 文 の 要 約

論文題目　Oxide-nanowire microfluidic devices for the analysis of cancer-related nucleic acids
(がん関連核酸分析のための酸化物ナノワイヤーマイクロ流体デバイス)

氏　　名　Marina Binti Musa

論 文 内 容 の 要 約

In this thesis, several oxide nanowire microfluidic devices were utilized for capturing CpG rich DNAs which have been widely known as biomarkers in cancer-related genes. The research includes the capture of unmethylated and methylated DNAs with CpG sites. The selected oxide nanowires are ZnO nanowires, ZnO/ZnO (core/shell) nanowires, ZnO/TiO_2 (core/shell) nanowires, ZnO/Al_2O_3 (core/shell) nanowires and ZnO/SiO_2 (core/shell) nanowires.

Chapter 1 of the thesis gives an overview of the research background which includes the DNA methylation on CpG rich sequence and well-established methods commonly used for the analysis of this target DNA including the bisulfite treatment, restriction enzyme analysis and protein immunoprecipitation. Limitations of the previous methods were discussed, hence a method based on oxide nanowires microfluidic devices was proposed. Owing to the advantages of the different oxide materials; ZnO, TiO_2, Al_2O_3 and SiO_2, the materials were utilized in the fabrication of core/shell nanowires and their potential to capture the target DNAs was investigated.

Chapter 2 describes the optimization of important parameters in the design of ZnO/SiO_2 (core/shell) nanowires which include the length and diameter of nanowires, aspect ratios and spacing between nanowires. Statistical analysis on the studied parameters was performed and their relationship with the capture efficiency of the

ssDNAs was discussed. Considering the small sizes of ssDNAs, there should be sufficient trapping region for high capture efficiency of the ssDNAs. The relationship between the spacing between nanowires and the gyration radius of the ssDNAs to achieve high capture efficiency has been proposed. Hence, the optimal spacing between nanowires sufficient as a trapping region for capturing the ssDNAs as they traverse through the nanowires was reported which enabled high capture efficiency of ssDNAs (86.7%).

In Chapter 3, the performance of different core/shell nanowires; ZnO/ZnO, ZnO/Al_2O_3 and ZnO/SiO_2 for capturing ssDNAs under varying pH was described. The possible interactions between the nanowires and DNAs which include from the phosphate and nucleobase side were proposed. These include the explanation on the influence of surface charge and hard-soft acid-base (HSAB) principle as described in the previous research. Each oxide nanowires microfluidic device showed high capture efficiency near neutral pH and ZnO/Al_2O_3 (core/shell) nanowires were proposed as the best candidate for applications in biological fluids with varying pH.

Chapter 4 describes the result of the discrimination of CpG rich DNAs with different methylation level using ZnO/ZnO (core/shell) nanowires microfluidic device. The proposed method exhibited different affinity towards the unmethylated and highly methylated DNAs which showed its potential to be further extended for the analysis of DNA methylation in clinical analysis. Possible factors which allow the discrimination were discussed including the hydrophobicity and hydrophilicity, and electron donor and acceptor properties of the DNAs and ZnO/ZnO nanowires.

In Chapter 5, the capability of ZnO/ZnO, ZnO/TiO_2, ZnO/Al_2O_3 and ZnO/SiO_2 (core/shell) nanowires to discriminate DNA methylation level and DNA methylation site was discussed. Different trends in capture efficiency were shown by all oxide nanowires as the methylation level varies from 0% CpG methylation, 12.5% CpG methylation, 25% CpG methylation, 50% CpG methylation and 100% CpG methylation. Besides, the capability of the oxide nanowires to discriminate DNAs with different methylation sites had been discussed using the DNAs with 12.5% CpG methylation and 25% CpG methylation.

Last but not least, Chapter 6 concludes the importance of the findings and the future plans to prove the suitability of the proposed method for applications in clinical diagnosis.