主 論 文 の 要 約

論文題目　Nanowire devices for the analysis of circulating nucleic acid
（循環核酸分析のためのナノワイヤデバイス）

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論 文 内 容 の 要 約

This thesis provides an overview of the development of nanowire devices and demonstrates the possibilities as a nucleic acid analysis platform. The investigations included in this thesis present the overview of nanowire devices for nucleic acid analysis and the concept of how this emergent nanotechnology can be combined across disciplines for addressing different challenges in biomedical applications. This thesis is divided into six chapters.

Chapter 1 provides the general introduction to circulating nucleic acids and their current limitations for implementation in clinical applications, and proposes a concept on why nanowire devices can be utilized to address the challenges of traditional methodologies.

Chapter 2 demonstrates the development of nanowire devices as a nucleic acid isolation platform by exploiting the unique properties of nanowires. Driven by the importance of urinary cell-free DNA (cfDNA) as cancer biomarkers, the effectiveness of cfDNA isolation from body fluids can impact clinical usability, especially for molecular diagnostic. However, cfDNA isolations are currently hampered by the dilution of small fragmented cfDNAs in body fluids. Here the concept of nanowire devices for the isolation of cfDNA was proposed. The studies included in this chapter are focused on the interaction mechanisms between nanowires and nucleic acids using three techniques: (1) isothermal titration calorimetry (ITC) measurement to determine thermodynamic parameters; (2) molecular dynamic (MD) simulations to provide insights into the interaction mechanisms; and (3) Fourier transform infrared (FT-IR) spectrometry to confirm a functional group that interacts with the nanowire surfaces. The

findings in this chapter contribute to the understanding of the interaction mechanisms between nanowires and nucleic acids and provide a basis for the development of nanowire devices as nucleic acid analysis platforms. This chapter demonstrates the unique properties of nanowires assisting the isolation of cfDNA from non-cancer and cancer-related urine samples based on specific chemical interactions, maximizing the effectiveness of the isolation platform that could not be achieved with the conventional methods.

Chapter 3 demonstrates the development of the annealed core-shell nanowire in which nanowires were coated with a metal layer, alumina (Al_2O_3), and annealed at high temperature to enhance the biocompatibility for clinical applications. These nanowires showed good biocompatible performance towards blood plasma samples, which have the potential to be utilized as a platform for RNA-based extraction and detection.

Capture 4 demonstrates the development of nanowire devices integrated with a microheater to detect target cfDNAs using in situ annealed Serinol Nucleic Acid (SNA) probes. This device can denature probes and requires one-step sample loading in the entire workflow, thus avoiding the need for expensive thermocyclers. This work showed the success of DNA detection sensitivity was higher than traditional methods, representing a step forward as an analytical device in nucleic acid detection.

Chapter 5 summarizes the content of this thesis and ends with the outlook on the future development of nanowire devices for the analysis of circulating nucleic acid.

The work in this thesis represents a step forward towards the development of nanotechnology to address the challenges of the traditional methods, providing cutting-edge research as an analytical tool to facilitate the analysis of nucleic acid used in biomedical applications.