Rapid Plasma Molecular-Targeted Drug Monitoring with Boron-Doped Diamond Electrode

Genki Ogata¹

Takuro Saiki², Yasuo Saijo², Yasuaki Einaga¹, and Hiroshi Hibino^{3,4}

¹ Department of Chemistry, Keio University, 3-14-1 Hiyoshi, Yokohama 223-8522, Japan

² Department of Medical Oncology, Niigata University Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori Chuo-ku, Niigata 951-8510, Japan

⁴ AMED-CREST, AMED, Osaka 565-0871, Japan

ogatag@keio.jp

Compared to conventional cytotoxic anti-cancer drugs, molecular-targeted medications exhibit reduced toxicity. These drugs are administered to patients at fixed doses, without the need for adjustments based on biomedical indices such as body surface area. However, this therapeutic strategy gives rise to significant variability in plasma concentration among individuals, often resulting in notable adverse events that require dosage reduction. Recent clinical investigations have aimed to quantify the relationship between drug concentration and clinical efficacy or toxicity. To enable personalized administration of molecular-targeted drugs, it is essential to directly determine plasma concentrations at the clinical site. In recent years, advancements in medical engineering have led to the development of various portable or wearable biosensors capable of rapid on-site monitoring. Nevertheless, the widespread adoption of these devices has been hindered by inadequate evaluation of accuracy using clinical samples, sensor-to-sensor variability, and the necessity for complex and expensive fabrication processes. To overcome these challenges, we propose a straightforward approach utilizing untreated boron-doped diamond (BDD), an electrochemical material known for its sustainability. As a proof-of-concept, we have chosen pazopanib, a molecular-targeting anticancer drug recommended for monitoring. By utilizing a BDD plate chip with a size of approximately 1 cm2, our sensing system accurately detected pazopanib concentrations in rat plasma samples within the clinically relevant range. Moreover, the chip's response remained stable throughout 60 consecutive measurements, demonstrating excellent repeatability. When we analyzed plasma samples collected from orally administered healthy rats and cancer patients using our system, the measured concentrations closely corresponded to those obtained through liquid chromatography with mass spectrometry. Furthermore, we assessed the reproducibility of the BDD chips. Finally, we developed a portable system comprising a palm-sized sensor housing a chip to facilitate practical implementation. This setup successfully determined drug concentrations from approximately 40 µL of whole blood obtained from dosed rats within a short turnaround time of around 10 minutes. This "reusable" sensor-based approach can expedite point-of-care drug monitoring, advance personalized medicine, and potentially reduce medical expenses.

³ Division of Glocal Pharmacology, Department of Pharmacology, Graduate School of Medicine, Osaka University, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan