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Advancing Therapeutic Drug Monitoring Using Mass Spectrometry with Dried Blood Spot Sampling and Metabolomics

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Precision medicine has gained significant attention in recent years, with therapeutic drug monitoring (TDM) playing an important role in its advancement. Dried blood spot (DBS) sampling has emerged as a promising alternative to conventional venous blood sampling for TDM, yet certain limitation remains. To address these challenges, our group has developed several LC-MS/MS strategies for DBS analysis, including a post-column infused internal standard (PCI-IS) technique to mitigate variations in DBS blood volume.[1] Additionally, we establish a protocol for a comprehensive evaluation of the hematocrit (Hct) effect on DBS.[2] These methods have been successfully applied to quantify direct oral anticoagulant concentrations in DBS samples.[3] Given the growing significance of monoclonal antibodies (mAbs) in therapeutic treatments, we further developed an LC-MS/MS method to quantify mAbs in DBS.[4] Beyond drug quantification, metabolomics has been widely utilized to investigate clinical markers. Recently, we integrated metabolomics with TDM to assess voriconazole-induced hepatotoxicity. A panel combining glycocholate levels with voriconazole trough concentrations (AUROC = 0.827) significantly improved the predictive performance of voriconazole trough concentrations alone (AUROC = 0.555) in identifying hepatotoxicity.[5] This is the first attempt to integrate TDM and targeted metabolomics to enhance the detection of drug-induced toxicity, underscoring the novelty and potential impact of this approach in advancing TDM.