Decoding Inherited Bone Marrow Failure Syndromes: Bridging the Gap between Genetic Analysis and Clinical Diagnosis

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Inherited bone marrow failure syndrome (IBMFS) comprises a wide variety of disorders, and new syndromes and genes are continually being identified. Four representative syndromes of particular clinical importance are Fanconi anemia (FA), Diamond-Blackfan anemia (DBA), dyskeratosis congenita (DC), and Shwachman-Diamond syndrome (SDS). Each of these disorders has different clinical manifestations and comorbidities, but they share a common aspect as a cancer predisposition syndrome. Accurate diagnosis is critical not only for the treatment and management of bone marrow failure, but also for lifelong health management. Disease screening tests such as chromosome fragility testing for Fanconi anemia, telomere length measurement for dyskeratosis congenita, and erythrocyte adenosine deaminase for DBA are still important in clinical practice, but SDS lacks a useful screening test. Currently, the diagnosis of IBMFS is mainly based on genetic diagnosis using next-generation sequencing, but genetic analysis using short-read sequencing is sometimes troublesome for *SBDS*, the main causative gene of SDS, due to the presence of its pseudogene. To address these challenges, we performed proteomic analyses on clinical specimens from IBMFS patients and developed several rapid diagnostic methods for IBMFS, including SDS. Our results demonstrate the utility of this approach for accurate and timely diagnosis and improve the management and monitoring of IBMFS patients.