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Accurate and High-Coverage Immune Repertoire Sequencing Reveals Characteristics of Antibody Repertoire Diversification in Young Children with Malaria

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Accurately measuring the immune repertoire sequence composition, diversity, and abundance is important in studying repertoire response in infections, vaccinations, and cancer immunology. Using molecular identifiers (MIDs) to tag mRNA molecules is an effective method in improving the accuracy of immune repertoire sequencing (IR-seq). However, it is still difficult to use IR-seq on small amount of clinical samples to achieve a high coverage of the repertoire diversities. This is especially challenging in studying infections and vaccinations where B cell subpopulations with fewer cells, such as memory B cells or plasmablasts, are often of great interest to study somatic mutation patterns and diversity changes. Here, we describe an approach of IR-seq based on the use of MIDs in combination with a clustering method that can reveal more than 80% of the antibody diversity in a sample and can be applied to as few as 1,000 B cells. We applied this to study the antibody repertoires of young children before and during an acute malaria infection. We discovered unexpectedly high levels of somatic hypermutation (SHM) in infants and revealed characteristics of antibody repertoire development in young children that would have a profound impact on immunization in children.