TITLE

[0001] COMPOSITIONS AND METHODS FOR MEASURING AND CALIBRATING AMPLIFICATION BIAS IN MULTIPLEXED PCR REACTIONS

CROSS REFERENCE TO RELATED APPLICATIONS

[0002] This application claims the benefit of U.S. Provisional Application No. 61/726,489, filed November 14, 2012 and U.S. Provisional Application No. 61/644,294, filed on May 8, 2012, the entire disclosures of which are hereby incorporated by reference in their entireties for all purposes.

BACKGROUND OF THE INVENTION

Field of the invention

[0003] The present disclosure relates generally to quantitative high-throughput sequencing of adaptive immune receptor encoding DNA (e.g., DNA encoding T cell receptors (TCR) and immunoglobulins (IG) in multiplexed nucleic acid amplification reactions. In particular, the compositions and methods described herein overcome undesirable distortions in the quantification of adaptive immune receptor encoding sequences that can result from biased over-utilization and/or under-utilization of specific oligonucleotide primers in multiplexed DNA amplification.

Description of the Related Art

[0004] The adaptive immune system employs several strategies to generate a repertoire of T- and B-cell antigen receptors, *i.e.*, adaptive immune receptors, with sufficient diversity to recognize the universe of potential pathogens. The ability of T cells to recognize the universe of antigens associated with various cancers or infectious organisms is conferred by its T cell antigen receptor (TCR), which is a heterodimer of an α (alpha) chain from the TCRA locus and a β (beta) chain from the TCRB locus, or a heterodimer of a γ (gamma) chain from the TCRG locus and a δ (delta) chain from the TCRD locus. The proteins which make up these chains are encoded by DNA, which in lymphoid cells employs a unique rearrangement mechanism for generating the tremendous diversity of the TCR. This multi-subunit immune recognition receptor associates with the CD3 complex and binds to peptides presented by either the major histocompatibility complex (MHC) class I or MHC class II proteins on the surface of antigen-presenting cells (APCs). Binding of TCR to the antigenic peptide on the APC is the central event in T cell activation, which occurs at an immunological synapse at the point of contact between the T cell and the APC.