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(54) Title: SYSTEMS AND METHODS FOR CLONAL REPLICATION AND AMPLIFICATION OF NUCLEIC ACID MOLECULES FOR GENOMIC AND THERAPEUTIC APPLICATIONS

(57) Abstract: The present invention provides for methods, reagents, apparatuses, and systems for the replication or amplification of nucleic acid molecules from biological samples. In one embodiment of the invention, the nucleic molecules are isolated from the sample, and subjected to fragmenting and joining using ligating agents of one or more hairpin structures to each end of the fragmented nucleic molecules to form one or more dumbbell templates. The one or more dumbbell templates are contacted with at least one substantially complementary primer attached to a substrate, and subjected to rolling circle replication or rolling circle amplification. The resulting replicated dumbbell templates or amplified dumbbell templates are used in numerous genomic applications, including whole genome *de novo* sequencing; sequence variant detection, structural variant detection, determining the phase of molecular haplotypes, molecular counting for aneuploidy detection; targeted sequencing of gene panels, whole exome, or chromosomal regions for sequence variant detection, structural variant detection, determining the phase of molecular haplotypes and/or molecular counting for aneuploidy detection; study of nucleic acid - nucleic acid binding interactions, nucleic acid - protein binding interactions, and nucleic acid molecule expression arrays; and testing of the effects of small molecule inhibitors or activators or nucleic acid therapeutics.



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