CLAIMS:

1. A method for detecting genome-wide re-arrangements in a nucleic acid genome, said method comprising:

(a) contacting a genomic DNA sample obtained from a cell or tissue contacted with a site-specific nuclease with a plurality of transposons comprising a first sequence tag at the 5' end of the transposon, under conditions whereby the plurality of transposons is inserted into the genomic DNA sample and the genomic DNA sample is tagmented into a plurality of nucleic acid fragments each comprising the sequence tag at the 5' ends of a partially double-stranded nucleic acid fragment;

(b) performing a first amplification reaction to amplify the re-arranged tagmented nucleic acid fragments using (i) a first target-specific primer comprising a nucleotide sequence complementary to a region adjacent to a target site, (ii) a second primer comprising a nucleotide sequence identical to a portion of the sequence tag located at the 5' ends of the fragment and (iii) a blocking oligonucleotide comprising a nucleotide sequence complementary to a region on the distal side of the target site relative to the first target-specific primer to produce primary amplification products comprising a nucleotide sequence comprising a re-arranged target sequence;

(c) sequencing the primary amplification products

2. The method of claim 1, wherein the sequence tag comprises a sequence orthogonal to the genome, a unique molecular identifier (UMI), a transposase recognition site, an index sequence or a combination thereof.

3. The method of claim 1, wherein the blocking oligonucleotide comprises an absent or blocked 3' OH, spacers, inverted nucleotides, or other modifications to block extension of the 3' end.

4. The method of claim 1, wherein the blocking nucleotide comprises one or more phosphothorothioate bonds, spacers, or other modifications at the 3' and 5' ends,

to block exonuclease digestion at the 3' and 5' ends, LNA, BNA, PNA, RNA, DNA, modified nucleic acids, or a combination thereof.

5. The method of claim 1, wherein the first and second primers comprise second and third sequence tags.

6. The method of claim 1 further comprising:

prior to (c) performing a second amplification reaction using third and fourth nested primers comprising nucleotide sequences complementary to sequences proximal to the inside ends of the amplified products of (b) and fourth and fifth sequence tags at the 5' ends of the nested primers to produce secondary amplification products comprising a re-arranged target sequence and additional sequence tags.

7. The method of claim 6 further comprising:

performing a third amplification reaction using a fifth and sixth primer comprising nucleotide sequences complementary to the amplified products of the second amplification reaction to produce further enriched tertiary amplification products comprising a re-arranged target sequence.

8. The method of claim 6, wherein the third and/or the fourth primers comprise barcode sequences.

9. The method of claim 7, wherein the fifth and sixth primers comprise a sequencing tag and/or an index sequence.

10. The method of claim 1 further comprising:

prior to (c) performing a second, hemi-nested amplification reaction using the second primer and a third nested primer wherein the third primer comprises a nucleotide sequence complementary to a sequence proximal to target-specific primer end of the amplified products of (b) and optionally a fourth and fifth sequence tags at the

5' ends of the second and/or third primers to produce secondary amplification products comprising a re-arranged target sequence and one or two additional sequence tags.

11. The method of claim 10 further comprising:

performing a third amplification reaction using a fourth and fifth primer comprising nucleotide sequences complementary to the amplified products of the second amplification reaction to produce further enriched tertiary amplification products comprising a re-arranged target sequence.

12. The method of claim 11, wherein the fourth and fifth primers comprise a sequencing tag and/or an index sequence.

13. The method of claim 1 wherein (b) further comprises performing a separate amplification reaction to amplify the re-arranged tagmented nucleic acid fragments using a second target specific primer on the opposite side of the target site.

14. The method of claim 1 further comprising:

prior to (b) contacting the plurality of tagmented nucleic acid fragments with ddNTP or other 3' modified dNTP and a DNA polymerase or terminal deoxynucleotidyl transferase to block all extendable 3' ends.

15. The method of claim 2, wherein the sequence tag comprises uracil.