

CLAIMS

1. A method of sequencing a nucleic acid, comprising:
providing a sample comprising a nucleic acid;
contacting the sample with a DNA-binding molecule comprising a DNA dye;
contacting the sample with an insertional enzyme complex to produce tagged nucleic acid fragments, wherein the insertional enzyme complex is inhibited by the DNA-binding molecule; and
sequencing the tagged nucleic acid fragments to produce sequence reads;
wherein the sample comprises primary nucleic acids and secondary nucleic acids, wherein the primary nucleic acids comprise nuclear DNA and wherein the secondary nucleic acids comprise mitochondrial DNA (mtDNA) or extrachromosomal DNA, and wherein the DNA-binding molecule preferentially binds secondary nucleic acids over primary nucleic acids.
2. The method of Claim 1, wherein the sample is a population of cells, a single cell, a population of cell nuclei, or a single cell nucleus.
3. The method of Claim 1 or 2, wherein the DNA dye comprises Hoechst™ dye, SYBR™ Gold, Sytox™ Orange, PicoGreen™, or Qubit™.
4. The method of any of Claims 1-3, wherein the insertional enzyme complex is a transposome comprising a transposase.
5. The method of any of Claims 1-4, wherein sequencing is performed by assay for transposase-accessible chromatin sequencing (ATAC-seq) or by whole genome sequencing.
6. The method of Claim 5, wherein ATAC-seq comprises bulk ATAC-seq or single cell ATAC-seq.
7. The method of any of Claims 1-6, wherein the method inhibits, reduces, or eliminates sequencing reads of secondary nucleic acids.

8. A method of inhibiting, reducing, or eliminating sequencing reads of secondary nucleic acids, comprising:

providing a sample comprising primary nucleic acids and secondary nucleic acids, wherein the primary nucleic acids comprise nuclear DNA and wherein the secondary nucleic acids comprise mitochondrial DNA (mtDNA) or extrachromosomal DNA;

contacting the sample with a DNA-binding molecule, wherein the DNA-binding molecule comprises a DNA dye that preferentially binds secondary nucleic acids; and

performing DNA transposition on open chromatin, wherein the secondary nucleic acids are not transposed or are transposed at lower efficiency than the primary nucleic acids.

9. The method of Claim 8, wherein the sample is a population of cells, a single cell, a population of cell nuclei, or a single cell nucleus.

10. The method of Claim 8 or 9, wherein the DNA dye comprises Hoechst™ dye, SYBR™ Gold, Sytox™ Orange, PicoGreen™, or Qubit™.

11. The method of Claim any of Claims 8-10, wherein the DNA transposition is performed using an assay for transposase-accessible chromatin sequencing (ATAC-seq) or whole genome sequencing from gDNA or from single cells.

12. The method of Claim 11, wherein ATAC-seq comprises bulk ATAC-seq or single cell ATAC-seq.

13. The method of any of Claims 8-12, wherein contacting the sample with the DNA-binding molecule blocks or reduces transposition into the secondary nucleic acids.

14. The method of any of Claims 8-13, further comprising sequencing the nuclear DNA.