CLAIMS

1. A method of reacting a cell nuclear target nucleic acid with a transposome complex, wherein the transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences, comprising contacting a cell nucleus comprising the nuclear target nucleic acid with a nuclear permeability enhancer and reacting the transposome complex with the target nucleic acid, wherein the reacting comprises fragmenting the target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form tagged double-stranded nucleic acid fragments, and further wherein the nuclear permeability enhancer increases the permeability of the nuclear envelope without disrupting the nuclear membrane, and wherein the nuclear permeability enhancer is a clathrin inhibitor, *N*-[5-(4-bromobenzylidene)-4-oxo-4,5-dihydro-1,3-thiazol-2-yl]naphthalene-1-sulfonamide, methyl-b-cyclodextrin, phenothiazines, monodansylcadaverine, chloroquine, monensin, hyperosmotic sucrose, dynasore, an aliphatic alcohol, a C_{4-10}-alkyl-diol, a cyclic diol, a cycloalkane-diol, a vicinal diol, *trans*-1,2-cyclohexanediol, n-hexane-1,2-diol, 1,6-hexane-diol, a compound that binds to and/or inhibits nuclear filament proteins, a compound that binds to and/or inhibit clathrin, or a nuclear localization signal peptide (NLS), or a synthetic analog thereof.

2. A method of analyzing a cell nuclear target nucleic acid comprising:
(a) contacting a cell nucleus comprising a cell nuclear target nucleic acid with a nuclear permeability enhancer and a transposome complex, wherein the transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences;
(b) reacting the transposome complex with the target nucleic acid to provide an analysis complex, wherein the reacting comprises fragmenting the target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form tagged double-stranded nucleic acid fragments; and
(c) analyzing the analysis complex, thereby detecting the tagged double-stranded nucleic acid fragments,
and further wherein the nuclear permeability enhancer increases the permeability of the nuclear envelope without disrupting the nuclear membrane and wherein the nuclear permeability enhancer is a clathrin inhibitor, *N*-[5-(4-bromobenzylidene)-4-oxo-4,5-

dihydro-1,3-thiazol-2-yl]naphthalene-1-sulfonamide, methyl-b-cyclodextrin, phenothiazines, monodansylcadaverine, chloroquine, monensin, hyperosmotic sucrose, dynasore, an aliphatic alcohol, a C_{4-10}-alkyl-diol, a cyclic diol, a cycloalkane-diol, a vicinal diol, *trans*-1,2-cyclohexanediol, n-hexane-1,2-diol, 1,6-hexane-diol, a compound that binds to and/or inhibits nuclear filament proteins, a compound that binds to and/or inhibit clathrin, or a NLS, or a synthetic analog thereof;
optionally wherein the cell comprises a contiguity preserving element comprising the cell nucleus.

3. The method of any one of claims 1 or 2, wherein the cell nuclear target nucleic acid is DNA or RNA.

4. The method of claim 3, wherein the cell nuclear target nucleic acid is DNA.

5. A method of preparing a library of tagged nucleic acid fragments from a cell nuclear target nucleic acid, comprising:
(a) providing a contiguity preserving element comprising a single cell nucleus, wherein the single cell nucleus comprises the cell nuclear target nucleic acid;
(b) contacting the contiguity preserving element and single cell nucleus with a nuclear permeability enhancer and a transposome complex comprising a transposase and two transposon end compositions comprising transposon end sequences;
(c) reacting the transposome complex with the cell nuclear target nucleic acid to provide an analysis complex, wherein the reacting comprises fragmenting the target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form tagged double-stranded nucleic acid fragments; and
(d) analyzing the analysis complex, thereby detecting the tagged double-stranded nucleic acid fragments,
wherein the nuclear permeability enhancer increases the permeability of the nuclear envelope without disrupting the nuclear membrane and wherein the nuclear permeability enhancer is a clathrin inhibitor, *N*-[5-(4-bromobenzylidene)-4-oxo-4,5-dihydro-1,3-thiazol-2-yl]naphthalene-1-sulfonamide, methyl-b-cyclodextrin, phenothiazines, monodansylcadaverine, chloroquine, monensin, hyperosmotic sucrose, dynasore, an aliphatic alcohol, a C_{4-10}-alkyl-diol, a cyclic diol, a cycloalkane-diol, a vicinal diol, *trans*-1,2-cyclohexanediol, n-hexane-1,2-diol, 1,6-hexane-diol, a compound that binds to and/or

inhibits nuclear filament proteins, a compound that binds to and/or inhibit clathrin, or a NLS, or a synthetic analog thereof.

6. A method of reacting a cell nuclear target nucleic acid with a transposome complex, wherein the transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences, comprising contacting a cell nucleus comprising the nuclear target nucleic acid with a nuclear permeability enhancer and reacting the transposome complex with the target nucleic acid, wherein the reacting comprises fragmenting the target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form tagged double-stranded nucleic acid fragments, and further wherein the nuclear permeability enhancer increases the permeability of the nuclear envelope without disrupting the nuclear membrane, and wherein prior to the contacting, reacting a cytoplasmic target nucleic acid with a second transposome complex comprising a transposase and two transposon end compositions comprising transposon end sequences in the presence of a nuclear pore blocker and in the absence of a nuclear permeability enhancer, wherein the reacting introduces a first tag to the cytoplasmic target nucleic acid and a second tag to the cell nuclear target nucleic acid.

7. A method of analyzing a cell nuclear target nucleic acid comprising:
(a) contacting a cell nucleus comprising a cell nuclear target nucleic acid with a nuclear permeability enhancer and a transposome complex, wherein the transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences;
(b) reacting the transposome complex with the target nucleic acid to provide an analysis complex, wherein the reacting comprises fragmenting the target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form tagged double-stranded nucleic acid fragments; and
(c) analyzing the analysis complex, thereby detecting the tagged double-stranded nucleic acid fragments,
and further wherein the nuclear permeability enhancer increases the permeability of the nuclear envelope without disrupting the nuclear membrane and wherein prior to the contacting, reacting a cytoplasmic target nucleic acid with a second transposome complex comprising a transposase and two transposon end compositions comprising transposon

end sequences in the presence of a nuclear pore blocker and in the absence of a nuclear permeability enhancer, wherein the reacting introduces a first tag to the cytoplasmic target nucleic acid and a second tag to the cell nuclear target nucleic acid.

8. The method of claim 5, wherein the contiguity preserving element comprises the nuclear membrane, optionally wherein the method further comprises embedding the nucleic acid from a single cell in a polymer matrix, optionally wherein the polymer matrix is agarose, polyacrylamide, or alginate.

9. The method of any one of the preceding claims, further comprising analyzing a cytoplasmic target nucleic acid by contacting the cell with a second transposome complex comprising a transposase and two transposon end compositions comprising transposon end sequences, reacting the second transposome complex with the cytoplasmic target nucleic acid to provide a second analysis complex, wherein the reacting comprises fragmenting the target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form tagged double-stranded nucleic acid fragments, and, optionally, analyzing the second analysis complex, thereby detecting the tagged cytoplasmic double-stranded nucleic acid fragments.

10. The method of any one of the preceding claims, further comprising treating the tagged double-stranded nucleic acid fragments with a polymerase, wherein the polymerase is optionally a strand-displacing polymerase.

11. The method of any one of claims 2-5 or 8-10, wherein analyzing comprises sequencing of the double-stranded nucleic acid fragments, or amplicons thereof, or copies thereof.

12. The method of any one of claims 1-11 or the composition of claim 15, wherein the nuclear permeability enhancer is a NLS, SV40 Large T-antigen (PKKKRKV), the NLS of nucleoplasmin (KR[PAATKKAGQA]KKKK or AVKRPAATKKAGQAKKKLD), K-K/R-X-K/R, EGL-13 (MSRRRKANPTKLSENAKKLAKEVEN), c-Myc (PAAKRVKLD), TUS-protein (KLKIKRPVK), the acidic M9 domain of hnRNP A1,

KIPIK from the yeast transcription repressor Matα2, a PY-NLS sequence, an inhibitor of importin β2, or SV40 Large T-antigen.

13. The method of any one of claims 1-12, wherein the nuclear permeability enhancer is a NLS covalently linked to the transposome complex.

14. The method of claim of any one of claims 1-12, wherein the nuclear permeability enhancer is a NLS not covalently linked to the transposome complex.

15. A composition comprising one or more cells and/or one or more cell nuclei, a nuclear permeability enhancer, and a transposome complex,
a) wherein the nuclear permeability enhancer increases the permeability of the nuclear envelope without disrupting the nuclear membrane and wherein the nuclear permeability enhancer is a clathrin inhibitor, *N*-[5-(4-bromobenzylidene)-4-oxo-4,5-dihydro-1,3-thiazol-2-yl]naphthalene-1-sulfonamide, methyl-b-cyclodextrin, phenothiazines, monodansylcadaverine, chloroquine, monensin, hyperosmotic sucrose, dynasore, an aliphatic alcohol, a C_{4-10}-alkyl-diol, a cyclic diol, a cycloalkane-diol, a vicinal diol, *trans*-1,2-cyclohexanediol, n-hexane-1,2-diol, 1,6-hexane-diol, a compound that binds to and/or inhibits nuclear filament proteins, a compound that binds to and/or inhibit clathrin, or a NLS, or a synthetic analog thereof, and
b) wherein the transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences.

16. A method of differentially tagging target nucleic acids in cells comprising:
selectively delivering a first transposome complex, wherein the transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences, comprising a first tag to a first cellular compartment selected from the cytoplasm or the mitochondria, wherein the first cellular compartment comprises a first target nucleic acid;
reacting the first transposome complex with the first target nucleic acid, wherein the reacting comprises fragmenting the first target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form first tagged double-stranded nucleic acid fragments;

selectively delivering a second transposome complex, wherein the transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences, comprising a second tag to the cell nucleus, wherein the cell nucleus comprises a second target nucleic acid; and

reacting the second transposome complex with the second target nucleic acid, wherein the reacting comprises fragmenting the second target nucleic acid into double-stranded nucleic acid fragments and tagging with transferred strands from the transposon end compositions to form second tagged double-stranded nucleic acid fragments wherein the first and second tags are different, optionally wherein the nuclear permeability enhancer increases the permeability of the nuclear envelope without disrupting the nuclear membrane; and

optionally detecting double-stranded nucleic acid fragments or their amplicons, wherein the detecting optionally comprises detecting the sequences of the double-stranded nucleic acid fragments or amplicons.

17. The method of claim 16, wherein the selective delivering of the first transposome complex to the first cellular compartment comprises treating the cell with a permeability enhancer for the first cellular compartment.

18. The method of claim 16 or claim 17, wherein the selective delivering of the first transposome complex to the first cellular compartment comprises treating the cell with a nuclear pore blocker.

19. The method of any one of claims 16-18, wherein the selective delivering of the second transposome complex to the cell nucleus comprises treating the cell with a nuclear permeability enhancer.

20. The method of any one of claims 16-19, wherein the selective delivering of the first transposome complex occurs without substantial delivery of the first transposome complex to the cell nucleus.

21. The method of any one of claims 16-20, wherein the first cellular compartment is the cytoplasm and the first target nucleic acid is a cytoplasmic target nucleic acid, and the

second cellular compartment is the cell nucleus and the second target nucleic acid is nuclear target nucleic acid.

22. The method of claim 21, wherein the selective delivering of the first transposome complex to the cytoplasm is done in the presence of a nuclear pore blocker.

23. The method of claim 21 or 22, wherein the selective delivering of the second transposome complex is done in the presence of a nuclear permeability enhancer.

24. The method of any one of claims 21-23, wherein the cytoplasmic target nucleic acid is RNA.

25. The method of any one of claims 21-24, wherein the cell nucleus target nucleic is DNA or genomic DNA (gDNA).

26. The method of any one of claims 16-20, wherein:

selectively delivering the first transposome complex comprises reacting the first transposome complex with a mitochondrial target nucleic acid to produce a tagged mitochondrial double-stranded nucleic acid fragment; and

selectively delivering the second transposome complex comprises reacting the second transposome complex with a nuclear target nucleic acid to produce a tagged nuclear double-stranded nucleic acid fragment.

27. The method of claim 26, wherein the mitochondrial target nucleic acid is DNA.

28. The method of claim 26 or 27, wherein the cell nucleus target nucleic acid is DNA or genomic DNA (gDNA).

29. The method of any one of claims 16-28, further comprising lysing the cells to release the tagged double-stranded nucleic acid fragments.

30. The method of any one of claims 16-29, wherein the nuclear permeability enhancer is a clathrin inhibitor, *N*-[5-(4-bromobenzylidene)-4-oxo-4,5-dihydro-1,3-thiazol-2-yl]naphthalene-1-sulfonamide, methyl-b-cyclodextrin, phenothiazines,

monodansylcadaverine, chloroquine, monensin, hyperosmotic sucrose, dynasore, an aliphatic alcohol, a C_{4-10}-alkyl-diol, a cyclic diol, a cycloalkane-diol, a vicinal diol, *trans*-1,2-cyclohexanediol, n-hexane-1,2-diol, 1,6-hexane-diol, a compound that binds to and/or inhibits nuclear filament proteins, a compound that binds to and/or inhibit clathrin, or a NLS, or a synthetic analog thereof.