CLAIMS

1. A method of reacting a cell nucleus informational molecule with an analytical biomolecule, comprising contacting a cell nucleus comprising the cell nucleus informational molecule with a nuclear permeability enhancer and reacting the cell nucleus informational molecule with the analytical biomolecule.

2. A method of analyzing a cell nucleus informational molecule comprising:
(a) contacting a cell nucleus comprising a cell nucleus informational molecule with a nuclear permeability enhancer and an analytical biomolecule;
(b) reacting the analytical biomolecule with the cell nucleus informational molecule to provide an analysis complex; and
(c) analyzing the analysis complex, thereby detecting the cell nucleus informational molecule.

3. The method of claim 2, wherein a contiguity preserving element comprises the cell nucleus.

4. The method of any one of claims 1-3 or 30, wherein the cell nucleus informational molecule is DNA, RNA, protein, or a mixture thereof.

5. The method of claim 4, wherein the cell nucleus informational molecule is DNA.

6. The method of any one of claims 1-5, wherein the analytical biomolecule is a transposase or transposome complex, or an antibody, or an oligonucleotide, or a nucleotide, or a reverse transcription primer, or an enzyme.

7. The method of claim 6, wherein the oligonucleotide or nucleotide comprises at least one labeled nucleotide.

8. The method of claim 6, wherein the analytical biomolecule is an enzyme, and the enzyme is an amplification enzyme, a polymerase, a DNA polymerase, an RNA polymerase, a PCR enzyme, a ligase, a Taq DNA polymerase, a Pfu DNA polymerase, an enzyme that mediates in vitro transcription, an integrase, or a nicking enzyme.

9. The method of claim 6, wherein the analytical biomolecule is a transposome complex.

10. The method of claim 9, wherein each transposome complex comprises a transposase and two transposon end compositions comprising transposon end sequences.

11. The method of claim 10, wherein the cell nucleus informational molecule is a 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 analysis complexes.

12. A method of preparing a library of tagged nucleic acid fragments from a cell nuclear target nucleic acid:
(a) providing a contiguity preserving element comprising a single cell nucleus, wherein the single cell nucleus comprises a target nucleic acid;
(b) contacting the contiguity preserving element and single cell nucleus with a nuclear permeability enhancer and an analytical biomolecule; and
(c) reacting the analytical biomolecule with the cell nucleus informational molecule to provide an analysis complex; and
(d) analyzing the analysis complex, thereby detecting the cell nucleus informational molecule.

13. The method of any one of the preceding claims, wherein at least one informational molecule is a protein.

14. The method of any one of claims 1-13, further comprising analyzing a cytoplasmic informational molecule by contacting a cell comprising the cell nucleus with a second

analytical biomolecule, reacting the second analytical biomolecule with the cytoplasmic informational molecule to provide a second analysis complex, and, optionally, analyzing the second analysis complex, thereby detecting the cytoplasmic informational molecule.

15. The method of claim 14, comprising, prior to the contacting, reacting the cytoplasmic informational molecule in the cell comprising the cell nucleus with the second analytical biomolecule in the presence of a nuclear pore blocker and in the absence of a nuclear permeability enhancer, thereby introducing a first tag to the cytoplasmic informational molecule, wherein the reacting with the cell nucleus informational molecule introduces a second tag to the cell nucleus informational molecule.

16. The method of any one of the preceding claims, wherein the analytical biomolecule is a transposome complex, and the method further comprises treating the analysis complex with a polymerase, wherein the polymerase is optionally a strand-displacing polymerase.

17. The method of any one of claims 2-16, wherein analyzing comprises sequencing fragmented and tagged nucleic acids, or amplicons thereof, or copies thereof.

18. The method of any one of the preceding claims, wherein the nuclear permeability enhancer is selected from: compounds that disrupt nuclear pore complex (NPC) hydrophobic interactions, compounds that bind to and/or inhibit nuclear filament proteins, compounds that bind to and/or inhibit clathrin, and nuclear localization signal peptides (NLS).

19. The method of any one of claims 1-17, wherein the nuclear permeability enhancer is a clathrin inhibitor, or is Pitstop-2 (also known as *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, or dynasore, or a synthetic analog thereof.

20. The method of any one of claims 1-17, wherein the nuclear permeability enhancer is a hydrophobicity disrupter, or is an aliphatic alcohol, or is a C_{4-10}-alkyl-diol, or is a cyclic diol,

or is a cycloalkane-diol, or is a vicinal diol, or is *trans*-1,2-cyclohexanediol, n-hexane-1,2-diol, or 1,6-hexane-diol.

21. The method of any one of claims 1-17, wherein the nuclear permeability enhancer is a nuclear localization signal peptide (NLS), or is 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, or an inhibitor of importin β2, or is SV40 Large T-antigen.

22. The method of claim 21, wherein the NLS is covalently linked to the analytical biomolecule.

23. The method of claim 21, wherein the NLS is not covalently linked to the analytical biomolecule.

24. A composition comprising one or more cells and/or one or more cell nuclei, a nuclear permeability enhancer, and an analytical biomolecule.

25. The composition of claim 24, wherein the analytical biomolecule is a transposase or transposome complex, or an antibody, or an oligonucleotide optionally comprising at least one labeled nucleotide, or an optionally labeled nucleotide, or a reverse transcription primer, or an enzyme.

26. The composition of claim 24, wherein the analytical biomolecule is a transposome complex.

27. The composition of claim 24, wherein the analytical biomolecule is an enzyme, where the enzyme is an amplification enzyme, a polymerase, a DNA polymerase, an RNA

polymerase, a PCR enzyme, a Taq DNA polymerase, a Pfu DNA polymerase, an enzyme that mediates in vitro transcription, an integrase, or a nicking enzyme.

28. The composition of any one of claims 24-27, wherein the nuclear permeability enhancer is Pitstop-2, 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, or digitonin.

29. The composition of claim 28, wherein the nuclear permeability enhancer is Pitstop-2, cyclohexanediol, or digitonin.

30. A method of claim 1, comprising:
(a) contacting the cell nucleus comprising the cell nucleus informational molecule with the nuclear permeability enhancer and the analytical biomolecule;
(b) reacting the analytical biomolecule with the cell nucleus informational molecule to provide a modified cell nucleus informational molecule; and
(c) detecting the modified cell nucleus informational molecule.

31. The method of claim 30, wherein the cell nucleus informational molecule is a target nucleic acid, the analytical biomolecule is a transposome complex, and the modified cell nucleus informational molecule is a complex between the transposome complex and the target nucleic acid, wherein the transposome complex does not fragment the target nucleic acid.

32. A method of differentially tagging informational molecules in cells comprising:
selectively delivering a first analytical biomolecule comprising a first tag to a first cellular compartment selected from the group consisting of the cell nucleus, the cytoplasm, and the mitochondria, wherein the first cellular compartment comprises a first informational biomolecule;
reacting the first analytical biomolecule with the first informational molecule to provide a tagged first informational molecule;

selectively delivering a second analytical biomolecule comprising a second tag to a second cellular compartment selected from the group consisting of the cell nucleus, the cytoplasm, and the mitochondria, wherein the second cellular compartment comprises a second informational molecule and is different from the first cellular compartment; and

reacting the second analytical biomolecule with the second informational molecule to provide a tagged second informational molecule, wherein the first and second tags are different.

33. The method of claim 32, wherein the selective delivering of the first analytical biomolecule to the first cellular compartment comprises treating the cell with a permeability enhancer for the first cellular compartment.

34. The method of claim 32 or claim 33, wherein the selective delivering of the first analytical biomolecule to the first cellular compartment comprises treating the cell with a permeability blocker for the second cellular compartment.

35. The method of any one of claims 32-34, wherein the selective delivering of the second analytical biomolecule to the second cellular compartment comprises treating the cell with a permeability enhancer for the second cellular compartment.

36. The method of any one of claims 32-35, wherein the selective delivering of the first analytical biomolecule occurs without substantial delivery of the first analytical biomolecule to the second cellular compartment.

37. The method of any one of claims 32-36, wherein the first cellular compartment is the cytoplasm and the first informational molecule is a cytoplasmic informational molecule, and (a) the second cellular compartment is the cell nucleus and the second informational molecule is a cell nucleus informational molecule or (b) the second cellular compartment is the mitochondria and the second informational molecule is a mitochondrial informational molecule.

38. The method of claim 37, wherein the selective delivering of the first analytical biomolecule to the cytoplasm is done in the presence of a nuclear pore blocker and/or a mitochondrial pore blocker.

39. The method of claim 37, wherein the delivery of the second analytical biomolecule is done in the presence of a nuclear permeability enhancer or a mitochondrial permeability enhancer.

40. The method of any one of claims 37-39, wherein the cytoplasmic informational molecule is RNA.

41. The method of any one of claims 37-39, wherein the cell nucleus informational molecule is DNA or genomic DNA (gDNA).

42. The method of any one of claims 32-36, wherein:

selectively delivering the first analytical biomolecule comprises reacting the first analytical biomolecule with a mitochondrial informational molecule to produce a tagged mitochondrial informational molecule; and

selectively delivering the second analytical biomolecule comprises reacting the second analytical biomolecule with a cell nucleus informational molecule to produce a tagged cell nucleus informational molecule.

43. The method of any one of claims 37-42, wherein the mitochondrial informational molecule is DNA.

44. The method of any one of claims 37-43, wherein the cell nucleus informational molecule is DNA, or is genomic DNA (gDNA).

45. The method of any one of claims 32-44, further comprising lysing the cells to release the tagged informational molecules.

46. The method of any one of claims 12-23 or 32-45, wherein the analytical biomolecule is a transposase or transposome complex, or an antibody, or an oligonucleotide optionally comprising at least one labeled nucleotide, or an optionally labeled nucleotide, or a reverse transcription primer, or an enzyme.

47. The method of claim 45, wherein the analytical biomolecule is an enzyme, wherein the enzyme is an amplification enzyme, a polymerase, a DNA polymerase, an RNA polymerase, a PCR enzyme, a Taq DNA polymerase, a Pfu DNA polymerase, an enzyme that mediates in vitro transcription, an integrase, or a nicking enzyme.

48. The method of any one of claims 32-46, wherein the analytical biomolecule is a transposome complex.

49. The method of any one of claims 32-48, further comprising detecting the tagged informational molecules or their amplicons, wherein the detecting optionally comprises detecting the sequences of the tagged informational molecules or amplicons.

50. The method or composition of any one of the preceding claims, wherein the nuclear permeability enhancer is digitonin.