

We claim:

1. An amplification-free method for identifying a virus in a cell culture, comprising:
lysing eukaryotic cells in a sample of the cell culture;
removing cellular debris from the sample;
concentrating the sample via diafiltration to produce a retentate;
treating the retentate with a nuclease, thereby degrading eukaryotic nucleic acids,
wherein the nuclease comprises one or more endonucleases and one or more RNases;
extracting viral nucleic acids from the nuclease-treated retentate;
preparing a library of the extracted viral nucleic acids for sequencing;
sequencing the extracted viral nucleic acids from the prepared library without amplifying
the extracted viral nucleic acids; and
identifying the virus in the sample.
2. The method of claim 1, wherein the eukaryotic cells are Chinese Hamster Ovary cells.
3. The method of claim 1 or 2, wherein the eukaryotic cells secrete a protein drug product.
4. The method of claim 3, wherein the protein drug product is selected from the group consisting of an antibody or antigen binding fragment of an antibody, a fusion protein, and a recombinant protein.
5. The method of claim 3, further comprising the step of treating the protein drug product to remove the identified virus.
6. The method of any one of claims 1-5, wherein the cells are lysed using a freeze-thaw technique.
7. The method of any one of claims 1-6, wherein the step of removing cellular debris comprises centrifuging the lysed sample to produce a supernatant and filtering the supernatant to remove cellular debris from the sample.

8. The method of any one of claim 1 -7, wherein the virus is an RNA virus.
9. The method of any one of claims 1-7, wherein the virus is selected from the group consisting of Minute virus of mice (MVM), K virus, Mouse Encephalomyelitis virus, and Mouse Adenovirus, MAV1, P12, EMC, lactate dehydrogenase virus (LDV), Polyoma virus, mouse hepatitis virus (MHV) Sendai virus, lymphocytic choriomeningitis virus (LCM), Reo-virus type , Kilham rat virus, and Toolan 's H-1 virus.
10. An amplification-free method for detecting viral nucleic acids in a cell culture, comprising:
lysing eukaryotic cells in a sample of the cell culture to produce cellular debris;
separating the cellular debris to produce a supernatant;
concentrating the supernatant via diafiltration to produce a retentate;
treating the retentate with a nuclease, thereby degrading eukaryotic nucleic acids,
wherein the nuclease comprises one or more endonucleases and one or more RNases;
extracting viral nucleic acids from the nuclease treated retentate;
preparing a library of the extracted viral nucleic acids for sequencing;
sequencing the extracted viral nucleic acids from the prepared library to identify the virus
without amplifying the extracted viral nucleic acids in the sample, and
obtaining viral nucleic acid reads and cellular nucleic acid reads from the sequencing ,
wherein the viral nucleic acid reads are greater than the cellular nucleic acid reads; and
identifying the virus in the sample.
11. The method of claim 10, wherein the viral nucleic acid reads are at least 51% of the total reads obtained from the sequencing.
12. The method of claim 10, wherein the viral nucleic acid reads are between 50 to 99% of the total reads obtained from the sequencing.
13. The method of claim 10, wherein the viral nucleic acid reads are at least 80% of the total reads obtained from the sequencing.

14. The method of claim 10, wherein the viral nucleic acid reads are at least 85% of the total reads obtained from the sequencing.
15. The method of claim 9, wherein the viral nucleic acid reads are at least 90% of the total reads obtained from the sequencing.
16. The method of any one of claims 9-15, wherein the virus is an RNA virus.
17. The method of any one of claim 1-16, wherein the sequencing of the extracted viral nucleic acids from the prepared library is completed within 8 hours of sample preparation.
18. The method of any one of claim 1-17, wherein the sequencing is real-time nanopore sequencing.
19. The method of claim 1, wherein the nuclease is selected from the group consisting of Benzonase®, OmniCleave™, RiboShredder™, and combinations thereof,
wherein Benzonase® is a genetically engineered endonuclease from *Serratia marcescens* produced in *Escherichia coli* strain W3110, OmniCleave™ is an endonuclease derived from *Serratia marcescens* that degrades single- and double-stranded DNA and RNA to di-, tri-, and tetranucleotides, and RiboShredder™ is a mixture of non-mammalian RNases.
20. The method of claim 1, wherein the nuclease is selected from the group consisting of OmniCleave™ and RiboShredder™, and combinations thereof,
wherein OmniCleave™ is an endonuclease derived from *Serratia marcescens* that degrades single- and double-stranded DNA and RNA to di-, tri-, and tetranucleotides, and RiboShredder™ is a mixture of non-mammalian RNases.
21. The method of claim 1, wherein the nuclease comprises OmniCleave™,
wherein OmniCleave™ is an endonuclease derived from *Serratia marcescens* that degrades single- and double-stranded DNA and RNA to di-, tri-, and tetranucleotides.

22. The method of claim 1, wherein the library of the viral nucleic acids is prepared with a library preparation kit.
23. The method of claim 1, wherein the library of the viral nucleic acids is prepared within 15 minutes.
24. An amplification-free method for identifying a virus in a cell culture, comprising:
lysing eukaryotic cells in a sample of the cell culture;
removing cellular debris from the sample;
concentrating the sample via diafiltration to produce a retentate;
treating the retentate with a nuclease, thereby degrading eukaryotic nucleic acids,
wherein the nuclease is selected from the group consisting of Benzonase®, OmniCleave™, RiboShredder™, and combinations thereof,
wherein Benzonase® is a genetically engineered endonuclease from *Serratia marcescens* produced in *Escherichia coli* strain W3110, OmniCleave™ is an endonuclease derived from *Serratia marcescens* that degrades single- and double-stranded DNA and RNA to di-, tri-, and tetranucleotides, and RiboShredder™ is a mixture of non-mammalian RNases;
extracting viral nucleic acids from the nuclease-treated retentate;
preparing a library of the extracted viral nucleic acids for sequencing, wherein the library of the viral nucleic acids is prepared with a library preparation kit; and
sequencing the extracted viral nucleic acids from the library without amplifying the extracted viral nucleic acids; and
identifying the virus in the sample.
25. An amplification-free method for detecting viral nucleic acids in a cell culture, comprising:
lysing cells in a sample of the cell culture to produce cellular debris;
separating the cellular debris to produce a supernatant;
concentrating the supernatant via diafiltration to produce a retentate;

treating the retentate with a nuclease, thereby degrading eukaryotic nucleic acids, wherein the nuclease is selected from the group consisting of Benzonase®, OmniCleave™, RiboShredder™, and combinations thereof,

wherein Benzonase® is a genetically engineered endonuclease from *Serratia marcescens* produced in *Escherichia coli* strain W3110, OmniCleave™ is an endonuclease derived from *Serratia marcescens* that degrades single- and double-stranded DNA and RNA to di-, tri-, and tetranucleotides, and RiboShredder™ is a mixture of non-mammalian RNases;

extracting viral nucleic acids from the nuclease-treated retentate;

preparing a library of the extracted viral nucleic acids for sequencing, wherein the library of the viral nucleic acids is prepared with a library preparation kit;

sequencing the extracted viral nucleic acids from the library without amplifying the extracted viral nucleic acids;

obtaining viral nucleic acid reads and cellular nucleic acid reads from the sequencing, wherein the viral nucleic acid reads are greater than the cellular nucleic acid reads; and

identifying the virus in the sample.