

## CLAIMS

### WHAT IS CLAIMED IS:

1. ~~A microfluidic cartridge for detecting a target nucleic acid comprising:
  - a) ~~an amplification chamber fluidically connected to a valve;~~
  - b) ~~a detection chamber fluidically connected to the valve, wherein the valve is connected to a sample metering channel;~~
  - c) ~~a detection reagent chamber fluidically connected to the detection chamber via a resistance channel, the detection reagent chamber comprising a programmable nuclease, a guide nucleic acid, and a labeled detector nucleic acid, wherein the labeled detector nucleic acid is capable of being cleaved upon binding of the guide nucleic acid to a segment of a target nucleic acid.~~~~
2. ~~The microfluidic cartridge of claim 1, wherein the sample metering channel controls volumes of liquids dispensed in a channel or chamber.~~
3. ~~The microfluidic cartridge of claim 2, wherein the sample metering channel is fluidically connected to the detection chamber.~~
4. ~~The resistance channel of any one of claims 1-3, wherein the resistance channel has a serpentine path, an angular path, or a circuitous path.~~
5. ~~The microfluidic cartridge of any one of claims 1-4, wherein the valve is a rotary valve, pneumatic valve, a hydraulic valve, an elastomeric valve.~~
6. ~~The microfluidic cartridge of any one of claims 1-5, wherein the resistance channel is fluidically connected with the valve.~~
7. ~~The microfluidic cartridge of any one of claims 1-6, wherein the valve comprises casing, comprising a "substrate" or an "over-mold."~~
8. ~~The microfluidic cartridge of any one of claims 1-7, wherein the valve is actuated by a solenoid.~~
9. ~~The microfluidic cartridge of any one of claims 1-8, wherein the valve is controlled manually, magnetically, electrically, thermally, by a bistable circuit, with a piezoelectric material, electrochemically, with phase change, rheologically, pneumatically, with a check valve, with capillarity, or any combination thereof.~~
10. ~~The microfluidic cartridge of any one of claims 5-9, wherein the rotary valve fluidically connects at least 3, at least 4, or at least 5 chambers.~~
11. ~~The microfluidic cartridge of any one of claims 1-10, further comprising an amplification reagent chamber fluidically connected to the amplification chamber.~~

12. The microfluidic cartridge of claim 11, further comprising a sample chamber fluidically connected to the amplification reagent chamber.
13. The microfluidic cartridge of claim 12, further comprising a sample inlet connected to the sample chamber.
14. The microfluidic cartridge of claim 13, wherein the sample inlet is sealable.
15. The microfluidic cartridge of claim 14, wherein the sample inlet forms a seal around the sample.
16. The microfluidic cartridge of any one of claims 12-15, wherein the sample chamber comprises a lysis buffer.
17. The microfluidic cartridge of any one of claims 12-16, further comprising a lysis buffer storage chamber fluidically connected to the sample chamber.
18. The microfluidic cartridge of claim 17, wherein the lysis buffer storage chamber comprises a lysis buffer.
19. The microfluidic cartridge of any one of claims 16-18, wherein the lysis buffer is a dual lysis/amplification buffer.
20. The microfluidic cartridge of any one of claims 17-19, wherein the lysis buffer storage chamber is fluidically connected to the sample chamber through a second valve.
21. The microfluidic cartridge of any one of claims 12-20, wherein the sample chamber is fluidically connected to the amplification chamber through the amplification reagent chamber.
22. The microfluidic cartridge any one of claims 12-20, wherein the sample chamber is fluidically connected to the amplification reagent chamber through the amplification chamber.
23. The microfluidic cartridge of any one of claims 11-22, wherein the microfluidic cartridge is configured to direct fluid bidirectionally between the amplification reagent chamber and amplification chamber.
24. The microfluidic cartridge of any one of claims 1-23, wherein the detection reagent chamber is fluidically connected to the amplification chamber.
25. The microfluidic cartridge of any one of claims 1-24, wherein the amplification chamber is fluidically connected to the detection chamber through the detection reagent chamber.
26. The microfluidic cartridge of any one of claims 1-25, further comprising a reagent port above the detection chamber configured to deliver fluid from the detection reagent chamber to the detection chamber.

27. The microfluidic cartridge of any one of claims 1-26, wherein the amplification chamber is fluidically connected to the detection reagent chamber through the detection chamber.
28. The microfluidic cartridge of any one of claims 1-27, wherein the resistance channel is configured to reduce backflow into the detection chamber and the detection reagent chamber.
29. The microfluidic cartridge of any one of claims 2-27, wherein the sample metering channel is configured to direct a predetermined volume of fluid from the detection reagent chamber to the detection chamber.
30. The microfluidic cartridge of any one of claims 1-29, wherein the amplification chamber and detection chamber are thermally isolated.
31. The microfluidic cartridge of any one of claims 1-30, wherein the detection reagent chamber is fluidically connected to the detection chamber.
32. The microfluidic cartridge of any one of claims 1-31, wherein the detection reagent chamber is fluidically connected to the detection chamber via a second resistance channel.
33. The microfluidic cartridge of any one of claims 1-32, wherein the resistance channel or the second resistance channel is a serpentine resistance channel.
34. The microfluidic cartridge of any one of claims 1-33, wherein the resistance channel or the second resistance channel comprises at least two hairpins.
35. The microfluidic cartridge of any one of claims 1-34, wherein the resistance channel or the second resistance channel comprises at least one, at least 2, at least 3, or at least 4 right angles.
36. The microfluidic cartridge of any one of claims 1-35, wherein the amplification chamber comprises a sealable sample inlet.
37. The microfluidic cartridge of claim 36, wherein the sample inlet is configured to form a seal around a swab.
38. The microfluidic cartridge of any one of claims 1-37, wherein microfluidic cartridge is configured to connect to a first pump to pump fluid from the amplification chamber to the detection chamber.
39. The microfluidic cartridge of any one of claims 1-38, wherein microfluidic cartridge is configured to connect to a second pump to pump fluid from the detection reagent chamber to the detection chamber.
40. The microfluidic cartridge of any one of claims 38-39, wherein first pump or the second pump is a pneumatic pump, a peristaltic pump, a hydraulic pump, or a syringe pump.

41. The microfluidic cartridge of any one of claims 1-40, wherein the amplification chamber is fluidically connected to a port configured to receive pneumatic pressure.
42. The microfluidic cartridge of claim 41, wherein the amplification chamber is fluidically connected to the port through a channel.
43. The microfluidic cartridge of any one of claims 11-42, wherein the amplification reagent chamber is connected to a second port configured to receive pneumatic pressure.
44. The microfluidic cartridge of claim 43, wherein the amplification reagent chamber is fluidically connected to the second port through a second channel.
45. The microfluidic cartridge of any one of claims 11-44, wherein the microfluidic cartridge is configured to connect to a third pump to pump fluid from the amplification reagent chamber to the amplification chamber.
46. The microfluidic cartridge of claim 45, wherein the third pump is a pneumatic pump, a peristaltic pump, a hydraulic pump, or a syringe pump.
47. The microfluidic cartridge of any one of claims 1-46, wherein the detection reagent chamber is connected to a port configured to receive pneumatic pressure.
48. The microfluidic cartridge of any one of claims 1-47, wherein the detection reagent chamber is fluidically connected to a third port through a third channel.
49. The microfluidic cartridge of any one of claims 1-48, wherein the microfluidic cartridge is configured to connect to a fourth pump to pump fluid from the detection reagent chamber to the detection chamber.
50. The microfluidic cartridge of claim 49, wherein the fourth pump is a pneumatic pump, a peristaltic pump, a hydraulic pump, or a syringe pump.
51. The microfluidic cartridge of any one of claims 1-50, further comprising a plurality of ports configured to couple to a gas manifold, wherein the plurality of ports is configured to receive pneumatic pressure.
52. The microfluidic cartridge of any one of claims 1-51, wherein any chamber of the microfluidic cartridge is connected to the plurality of ports of claim 50.
53. The microfluidic cartridge of any one of claims 1-52, wherein the valve is opened upon application of current electrical signal.
54. The microfluidic cartridge of any one of claims 1-53, wherein the detection reagent chamber is circular.
55. The microfluidic cartridge of any one of claims 1-53, wherein the detection reagent chamber is elongated.

56. The microfluidic cartridge of any one of claims 1-53, wherein the detection reagent chamber is hexagonal.
57. The microfluidic cartridge of any one of claims 2-56, wherein a region of the resistance channel is molded to direct flow in a direction perpendicular to the net flow direction.
58. The microfluidic cartridge of any one of claims 2-56, wherein a region of the resistance channel is molded to direct flow in a direction perpendicular to the axis defined by two ends of the resistance channel.
59. The microfluidic cartridge of any one of claims 2-58, wherein a region of the resistance channel is molded to direct flow along the z-axis of the microfluidic cartridge.
60. The microfluidic cartridge of any one of claims 1-59, wherein the valve is fluidically connected to two detection chambers via an amplification mix splitter.
61. The microfluidic cartridge of any one of claims 1-60, wherein the valve is fluidically connected to 3, 4, 5, 6, 7, 8, 9, or 10 detection chambers via an amplification mix splitter.
62. The microfluidic cartridge of any one of claims 1-61, further comprising a second valve fluidically connected to the detection reagent chamber and the detection chamber.
63. The microfluidic cartridge of any one of claims 1-62, wherein the detection chamber is vented with a hydrophobic PTFE vent.
64. The microfluidic cartridge of any one of claims 1-63, wherein the detection chamber comprises an optically transparent surface.
65. The microfluidic cartridge of any one of claims 1-64, wherein the amplification chamber is configured to hold from 10  $\mu$ L to 500  $\mu$ L of fluid.
66. The microfluidic cartridge of any one of claims 11-65, wherein the amplification reagent chamber is configured to hold from 10  $\mu$ L to 500  $\mu$ L of fluid.
67. The microfluidic cartridge of any one of claims 1-66, wherein the microfluidic cartridge is configured to accept from 2  $\mu$ L to 100  $\mu$ L of a sample comprising a nucleic acid.
68. The microfluidic cartridge of any one of claims 1-67, wherein the amplification reagent chamber comprises between 5 and 200  $\mu$ L an amplification buffer.
69. The microfluidic cartridge of any one of claims 1-68, wherein the amplification chamber comprises 45  $\mu$ L amplification buffer.
70. The microfluidic cartridge of any one of claims 1-69, wherein the detection reagent chamber stores from 5 to 200  $\mu$ L of fluid containing the programmable nuclease, the guide nucleic acid, and the labeled detector nucleic acid.
71. The microfluidic cartridge of any one of claims 1-70, comprising 2, 3, 4, 5, 6, 7, or 8 detection chambers.

72. The microfluidic cartridge of claim 71, wherein the 2, 3, 4, 5, 6, 7, or 8 detection chambers are fluidically connected to a single sample chamber.
73. The microfluidic cartridge of any one of claims 1-72, wherein the detection chamber holds up to 100  $\mu$ L, 200  $\mu$ L, 300  $\mu$ L, or 400  $\mu$ L of fluid.
74. The microfluidic cartridge of any one of claims 1-73, wherein the microfluidic cartridge comprises 5-7 layers.
75. The microfluidic cartridge of any one of claims 1-74, wherein the cartridge comprises layers as shown in **FIG. 130B**.
76. The microfluidic cartridge of any one of claims 1-75, further comprising a sample inlet configured to adapt with a slip luer tip.
77. The microfluidic cartridge of claim 76, wherein the slip luer tip is adapted to fit a syringe holding a sample.
78. The microfluidic cartridge of any one of claims 76-77, wherein the sample inlet is capable of being hermetically sealed.
79. The microfluidic cartridge of any one of claims 1-78, further comprising a sliding valve.
80. The microfluidic cartridge of claim 79, wherein the sliding valve connects the amplification reagent chamber to the amplification chamber.
81. The microfluidic cartridge of either of claims 79 or 80, wherein the sliding valve connects the amplification chamber to the detection reagent chamber.
82. The microfluidic cartridge of any one of claims 79-81, wherein the sliding valve connects the amplification reagent chamber to the detection chamber.
83. A manifold configured to accept the microfluidic cartridge of any one of claims 1-82.
84. The manifold of claim 83, comprising a pump configured to pump fluid into the detection chamber, an illumination source configured to illuminate the detection chamber, a detector configured to detect a detectable signal produced by the labeled detector nucleic acid, and a heater configured to heat the amplification chamber.
85. The manifold of claim 84, further comprising a second heater configured to heat the detection chamber.
86. The manifold of any one of claims 84-85, wherein the illumination source is a broad spectrum light source.
87. The manifold of any one of claims 84-86, wherein the illumination source light produces an illumination with a bandwidth of less than 5 nm.
88. The manifold of any one of claims 84-87, wherein the illumination source is a light emitting diode.

89. The manifold of claim 88, wherein the light-emitting diode produces white light, blue light, or green light.
90. The manifold of any one of claims 84-89, wherein the detectable signal is light.
91. The manifold of any one of claims 84-90, wherein the detector is a camera or a photodiode.
92. The manifold of any one of claims 84-91, wherein the detector has a detection bandwidth of less than 100 nm, less than 75 nm, less than 50 nm, less than 40 nm, less than 30 nm, less than 20 nm, less than 10 nm, or less than 5 nm.
93. The manifold of any one of claims 84-92, further comprising an optical filter configured to be between the detection chamber and the detector.
94. The microfluidic cartridge of any one of claims 1-93, wherein the amplification chamber comprises amplification reagents.
95. The microfluidic cartridge of any one of claims 11-94, wherein the amplification reagent chamber comprises amplification reagents.
96. The microfluidic cartridge of any one of claims 94-95, wherein the amplification reagents comprise a primer, a polymerase, dNTPs, an amplification buffer.
97. The microfluidic cartridge of any one of claims 1-96, wherein the amplification chamber comprises a lysis buffer.
98. The microfluidic cartridge of any one of claims 11-97, wherein the amplification reagent chamber comprises a lysis buffer.
99. The microfluidic cartridge of any one of claims 94-98, wherein the amplification reagents comprise a reverse transcriptase.
100. — The microfluidic cartridge of any one of claims 94-99, wherein the amplification reagents comprise reagents for thermal-cycling amplification.
101. — The microfluidic cartridge of any one of claims 94-99, wherein the amplification reagents comprise reagents for isothermal amplification.
102. — The microfluidic cartridge of any one of claims 94-101, wherein the amplification reagents comprise reagents for transcription-mediated amplification (TMA), helicase dependent amplification (HDA), circular helicase dependent amplification (cHDA), strand displacement amplification (SDA), loop-mediated amplification (LAMP), exponential amplification reaction (EXPAR), rolling circle amplification (RCA), ligase chain reaction (LCR), simple method amplifying RNA targets (SMART), single primer isothermal amplification (SPIA), multiple displacement amplification (MDA), nucleic acid sequence-based amplification (NASBA), hinge-initiated primer-dependent

amplification of nucleic acids (HHP), nicking enzyme amplification reaction (NEAR), or improved multiple displacement amplification (IMDA).

103. ——— The microfluidic cartridge of any one of claims 94-102, wherein the amplification reagents comprise reagents for loop-mediated amplification (LAMP).

104. ——— The microfluidic cartridge of any one of claims 16-103, wherein the lysis buffer and the amplification buffer are a single buffer.

105. ——— The microfluidic cartridge of any one of claims 16-104, wherein the lysis buffer storage chamber comprises a lysis buffer.

106. ——— The microfluidic cartridge of any one of claims 16-105, wherein the lysis buffer has a pH of from pH 4 to pH 5.

107. ——— The microfluidic cartridge of any one of claims 1-106, wherein the microfluidic cartridge further comprises reverse transcription reagents.

108. ——— The microfluidic cartridge of claim 107, wherein the reverse transcription reagents comprise a reverse transcriptase, a primer, and dNTPs.

109. ——— The microfluidic cartridge of any one of claims 1-108, wherein the programmable nuclease comprises an RuvC catalytic domain.

110. ——— The microfluidic cartridge of any one of claims 1-109, wherein the programmable nuclease is a type V CRISPR/Cas effector protein.

111. ——— The microfluidic cartridge of claim 110, wherein the type V CRISPR/Cas effector protein is a Cas12 protein.

112. ——— The microfluidic cartridge of claim 111, wherein the Cas12 protein comprises a Cas12a polypeptide, a Cas12b polypeptide, a Cas12c polypeptide, a Cas12d polypeptide, a Cas12e polypeptide, a C2c4 polypeptide, a C2c8 polypeptide, a C2c5 polypeptide, a C2c10 polypeptide, and a C2c9 polypeptide.

113. ——— The microfluidic cartridge of any one of claims 110-112, wherein the Cas12 protein has at least 80%, at least 85%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% sequence identity to any one of SEQ ID NO: 27—SEQ ID NO: 37.

114. ——— The microfluidic cartridge of any one of claims 110-113, wherein the Cas12 protein is selected from SEQ ID NO: 27—SEQ ID NO: 37.

115. ——— The microfluidic cartridge of claim 110, wherein the type V CRISPR/Cas effector protein is a Cas14 protein.

116. ——— The microfluidic cartridge of claim 115, wherein the Cas14 protein comprises a Cas14a polypeptide, a Cas14b polypeptide, a Cas14c polypeptide, a Cas14d polypeptide,

- a-Cas14e polypeptide, a-Cas14f polypeptide, a-Cas14g polypeptide, a-Cas14h polypeptide, a-Cas14i polypeptide, a-Cas14j polypeptide, or a-Cas14k polypeptide.
117. — The microfluidic cartridge of any one of claims 115-116, wherein the Cas14 protein has at least 80%, at least 85%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% sequence identity to any one of SEQ ID NO: 38—SEQ ID NO: 129.
118. — The microfluidic cartridge of any one of claims 115-117, wherein the Cas14 protein is selected from SEQ ID NO: 38—SEQ ID NO: 129.
119. — The microfluidic cartridge of claim 110, wherein the type V CRISPR/Cas effector protein is a Cas $\Phi$  protein.
120. — The microfluidic cartridge of claim 119, wherein the Cas $\Phi$  protein has at least 80%, at least 85%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% sequence identity to any one of SEQ ID NO: 274—SEQ ID NO: 321.
121. — The microfluidic cartridge of any one of claims 119-120, wherein the Cas $\Phi$  protein is selected from SEQ ID NO: 274—SEQ ID NO: 321.
122. — The microfluidic cartridge of any one of claims 1-121, the microfluidic cartridge further providing one or more chambers for in vitro transcribing amplified coronavirus target nucleic acid.
123. — The microfluidic cartridge of claim 122, wherein the in vitro transcribing comprises contacting the amplified coronavirus target nucleic acid to reagents for in vitro transcription.
124. — The microfluidic cartridge of claim 123, wherein the reagents for in vitro transcription comprise an RNA polymerase, NTPs, and a primer.
125. — The microfluidic cartridge of any one of claims 1-124, wherein the programmable nuclease comprises a HEPN cleaving domain.
126. — The microfluidic cartridge of any one of claims 1-125, wherein the programmable nuclease is a type VI CRISPR/Cas effector protein.
127. — The microfluidic cartridge of claim 126, wherein the type VI CRISPR/Cas effector protein is a Cas13 protein.
128. — The microfluidic cartridge of claim 127, wherein the Cas13 protein comprises a Cas13a polypeptide, a Cas13b polypeptide, a Cas13c polypeptide, a Cas13d polypeptide, or a Cas13e polypeptide.
129. — The microfluidic cartridge of any one of claims 127-128, wherein the Cas13 protein has at least 80%, at least 85%, at least 90%, at least 92%, at least 95%, at least

- 97%, or at least 99% sequence identity to any one of SEQ ID NOs: 130—SEQ ID NO: 137.
130. ~~The microfluidic cartridge of any one of claims 127-129, wherein the Cas13 protein is selected from SEQ ID NOs: 130—SEQ ID NO: 137.~~
131. ~~The microfluidic cartridge of any one of claims 1-130, wherein the target nucleic acid is from a virus.~~
132. ~~The microfluidic cartridge of claim 131, wherein the virus comprises a respiratory virus.~~
133. ~~The microfluidic cartridge of claim 132, wherein the respiratory virus is an upper respiratory virus.~~
134. ~~The microfluidic cartridge of claim 131, wherein the virus comprises an influenza virus.~~
135. ~~The microfluidic cartridge of any one of claims 131-133, wherein the virus comprises a coronavirus.~~
136. ~~The microfluidic cartridge of claim 135, wherein the coronavirus target nucleic acid is from SARS-CoV-2.~~
137. ~~The microfluidic cartridge of any one of claims 135-136, wherein the coronavirus target nucleic acid is from an N gene, an E gene, or a combination thereof.~~
138. ~~The microfluidic cartridge of any one of claims 135-137, wherein the coronavirus target nucleic acid has a sequence of any one of SEQ ID NO: 333—SEQ ID NO: 338.~~
139. ~~The microfluidic cartridge of any one of claims 135-138, wherein the guide nucleic acid is a guide RNA.~~
140. ~~The microfluidic cartridge of any one of claims 135-139, wherein the guide nucleic acid has at least 80%, at least 85%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% sequence identity to any one of SEQ ID NO: 323—SEQ ID NO: 328.~~
141. ~~The microfluidic cartridge of any one of claims 135-140, wherein the guide nucleic acid is selected from any one of SEQ ID NO: 323—SEQ ID NO: 328.~~
142. ~~The microfluidic cartridge of any one of claims 1-141, wherein the microfluidic cartridge comprises a control nucleic acid.~~
143. ~~The microfluidic cartridge of claim 142, wherein the control nucleic acid is in the detection chamber.~~
144. ~~The microfluidic cartridge of any one of claims 142-143, wherein the control nucleic acid is RNaseP.~~

- ~~145. — The microfluidic cartridge of any one of claims 142-144, wherein the control nucleic acid has a sequence of SEQ ID NO: 379.~~
- ~~146. — The microfluidic cartridge of any one of claims 142-144, wherein the guide nucleic acid has at least 80%, at least 85%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% sequence identity to any one of SEQ ID NO: 330—SEQ ID NO: 332.~~
- ~~147. — The microfluidic cartridge of any one of claims 142-146, wherein the guide nucleic acid is selected from any one of SEQ ID NO: 330—SEQ ID NO: 332.~~
- ~~148. — The microfluidic cartridge of any one of claims 134-147, wherein the influenza virus comprises an influenza A virus, influenza B virus, or a combination thereof.~~
- ~~149. — The microfluidic cartridge of claim 1-148, wherein the guide nucleic acid targets a plurality of target sequences.~~
- ~~150. — The microfluidic cartridge of claim 1-149, wherein the microfluidic cartridge comprises a plurality of guide sequences tiled against a virus.~~
- ~~151. — The microfluidic cartridge of claim 150, wherein the plurality of target sequences comprises sequences from influenza A virus, influenza B virus, and a third pathogen.~~
- ~~152. — The microfluidic cartridge of any one of claims 1-151, wherein the labeled detector nucleic acid comprises a single stranded reporter comprising a detection moiety~~
- ~~153. — The microfluidic cartridge of claim 152, wherein the detection moiety is a fluorophore, a FRET pair, a fluorophore/quencher pair, or an electrochemical reporter molecule.~~
- ~~154. — The microfluidic cartridge of claim 153, wherein the electrochemical reporter molecule comprises a species shown in **FIG. 149**.~~
- ~~155. — The microfluidic cartridge of any one of claims 1-154, wherein the labeled detector produced a detectable signal upon cleavage of the detector nucleic acid.~~
- ~~156. — The microfluidic cartridge of claim 155, wherein the detectable signal is a colorimetric signal, a fluorescence signal, an amperometric signal, or a potentiometric signal.~~
- ~~157. — A method of detecting a target nucleic acid, the method comprising:~~
- ~~a) providing a sample from a subject;~~
  - ~~b) adding the sample to the microfluidic cartridge of any one of claims 1-156;~~
  - ~~c) correlating the detectable signal of any one of claims 84-156 to the presence or absence of the target nucleic acid; and~~

- d) ~~optionally quantifying the detectable signal, thereby quantifying an amount of the target nucleic acid present in the sample.~~
158. ~~— The use of a microfluidic cartridge according to any one of claims 1-156 in a method of detecting a target nucleic acid.~~
159. ~~— The use of a system according to any one of claims 1-156 in a method of detecting a targeting nucleic acid.~~
160. ~~— The use of a programmable nuclease in a method of detecting a target nucleic acid according to any one of claims 30-63, 66, 150, 153.~~
161. ~~— The use of a composition according to any one of claims 66-87 in a method of detecting a target a nucleic acid.~~
162. ~~— The use of a DNA-activated programmable RNA nuclease in a method of assaying for a target deoxyribonucleic acid from a virus in a sample according to any one of claims 88, 90-106 or 151.~~
163. ~~— The use of a DNA-activated programmable RNA nuclease in a method of assaying for a target ribonucleic acid from a virus in a sample according to any one of claims 88, 90-106, or 152.~~
164. ~~— The use of a programmable nuclease in a method of detecting a target nucleic acid in a sample according to any one claims 108-120, 123-148 or 156.~~
1. A composition comprising a programmable nuclease having at least 80% sequence identity to SEQ ID NO: 37 and a non-naturally occurring guide nucleic acid.
  2. The composition of claim 1, wherein the programmable nuclease has at least 85%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% sequence identity to SEQ ID NO: 37, optionally wherein the programmable nuclease is SEQ ID NO: 37.
  3. The composition of any one of claims 1 or 2, wherein the programmable nuclease comprises three partial RuvC domains, optionally wherein the programmable nuclease comprises a RuvC-I subdomain, a RuvC-II subdomain, and a RuvC-III subdomain.
  4. The composition of any one of claims 1-3, wherein the non-naturally occurring guide nucleic acid comprises a crRNA.
  5. The composition of any one of claims 1-4, wherein the non-naturally occurring guide nucleic acid comprises RNA having at least 10 nucleotides that hybridize to a region in a target nucleic acid adjacent to a protospacer adjacent motif.
  6. The composition of any one of claims 1-5, further comprising a buffer, optionally wherein the buffer comprises a buffering agent, a salt, glycerol, a detergent, or any combination thereof.

7. The composition of claim 6, wherein:
- a) the buffering agent is HEPES;
  - b) the salt is potassium acetate, magnesium acetate, sodium chloride, magnesium chloride, or any combination thereof;
  - c) the buffer comprises glycerol; and/or
  - d) the detergent is Tween, Triton-X, or any combination thereof.
8. The composition of claim 6 or 7, wherein a pH of the buffer is approximately 7.5.
9. The composition of any one of claims 1-8, wherein a pH of the composition is from 7 to 8, optionally wherein a pH of the composition is 7.5.
10. The composition of any one of claims 1-9, wherein the programmable nuclease exhibits catalytic activity at a temperature from 25°C to 45°C.
11. The composition of any one of claims 1-10, wherein the programmable nuclease exhibits catalytic activity after heating the composition to a temperature of greater than 45°C and restoring the temperature to from 25°C to 45°C.
12. The composition of any one of claims 1-11, further comprising a reporter, optionally wherein the reporter comprises a detector nucleic acid and a detection moiety.
13. The composition of claim 12, wherein the detection moiety comprises a fluorescent moiety, a quenching moiety, a fluorescent dye, an infrared dye, an ultraviolet dye, a fluorescence resonance energy transfer (FRET) pair, a polypeptide, a biotin, an avidin, a streptavidin, a polysaccharide, a polymer, or a nanoparticle.
14. The composition of claim 12 or 13, wherein the detector nucleic acid comprises DNA, RNA, or a combination thereof.
15. The composition of any one of claims 1-14, further comprising an amplification reagent, optionally wherein the amplification reagent comprises a primer, a recombinase, a single-stranded DNA binding (SSB) protein, a DNA polymerase, an RNA polymerase, a deoxynucleotide triphosphate, a nucleotide triphosphate, a reverse transcriptase, a helicase, a ligase, or any combination thereof.
16. A method of assay for a segment of a target nucleic acid in a sample, the method comprising:
- a) contacting the sample to:
    - i. a reporter comprising a detector nucleic acid; and
    - ii. the composition of any one of claims 1-15, wherein the non-naturally occurring guide nucleic acid hybridizes to a segment of the target nucleic acid; and

b) assaying for a signal produced by cleavage of the detector nucleic acid.

17. The method of claim 16, wherein the signal is present prior to cleavage of the detector nucleic acid and changes upon cleavage of the detector nucleic acid or wherein the signal is absent prior to cleavage of the detector nucleic acid and is present upon cleavage of the detector nucleic acid.

18. The method of claim 16 or 17, wherein the signal is calorimetric, potentiometric, amperometric, optical, or piezo-electric signal, optionally wherein the optical signal is a fluorescent or colorimetric signal.

19. The method of any one of claims 16-18, further comprising amplifying the target nucleic acid.

