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(54) **Title**: CODON-OPTIMIZED RECOMBINANT PHAGE AND METHODS OF USING SAME

(57) **Abstract**: Composition and methods for the detection of one or more target microbe(s) are provided. Compositions of the disclosure include at least one recombinant phage capable of infecting a target microbe, said phage comprising at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker. Compositions of the disclosure may further include an aqueous solution that enhances the ability to detect marker expression upon phage infection of the target microbe. In some embodiments the target microbe include is *Listeria.*

CODON-OPTIMIZED RECOMBINANT PHAGE AND METHODS OF USING SAME

RELATED APPLICATIONS

[0001] This application claims priority to, and the benefit of U.S. Provisional Application No. 61/991,132 filed on May 9, 2014, U.S. Provisional Application No. 62/044,082 filed on August 29, 2014, U.S. Provisional Application No. 62/053,481 filed on September 22, 2014, and U.S. Provisional Application No. 62/086,445 filed December 2, 2014, the contents of each of which are incorporated herein by reference in their entireties.

FIELD OF THE DISCLOSURE

[0002] This disclosure generally relates to the detection of microbes through the use of codon-optimized recombinant phage.

INCORPORATION OF SEQUENCE LISTING

[0003] The contents of the text file named "SAM6-017 SEQ Listing_ST25.txt", which was created on May 7, 2015 and is 155 KB in size, are hereby incorporated by reference in their entirety.

BACKGROUND

[0004] Bacterial contamination and infection is a significant problem to public health and in many other areas. Bacterial food borne diseases pose a significant threat to human health, estimated to cause as many as about 76 million illnesses, 325,000 hospitalizations, and 5,000 deaths in the US annually.

[0005] For example, in 1996, juice that was contaminated with *Escherichia coli* was released into the public by a juice maker and resulted in one death and 66 illnesses. The company paid a $1.5 million fine, and the recall alone cost the company $6.5 million. In 2006, an *E. coli* O157:H7 outbreak from contaminated spinach originating from California resulted in 205 illnesses and 3 deaths. In 2011 a listeriosis outbreak from cantaloupes from Colorado in July, August and September resulted in 30 deaths. That is the second deadliest recorded U.S. outbreak in terms of the number of deaths since the Centers for Disease Control and Prevention began tracking outbreaks in the 1970s. Another recall of cantaloupes in 2012 suggests that the food

supply is still not safe and highlights the general and pervasive need for additional methods and reagents for testing the food supply to identify contamination.

[0006] Another example is bovine mastitis, an infection caused by bacterial cells that results in the inflammation of the bovine breast, reduction in milk yield and a decrease in milk quality. This condition is caused by the bacteria *Staphylococcus aureus* and *Staphylococcus agalactiae*. This reduction in milk yields and quality in the western world alone have been suggested to cause annual financial losses of $3.7 billion.

[0007] Another example is bovine tuberculosis (*Mycobacterium bovis*), a bacteria that causes financial loses worldwide. In 2005, for example, 12 of a herd of 55 cattle in a small Michigan farm tested positive for bovine tuberculosis. The farm was forced to destroy the entire herd of cattle, along with an entire herd of hogs. Tuberculosis testing in cattle requires the animal to be held for 2 days, and tests are false positive 5 percent of the time. Often entire herds have to be quarantined or destroyed. The annual worldwide financial losses have been estimated at $3 billion.

[0008] Tuberculosis is a leading cause of death worldwide. One third of the world's population is infected with Mycobacterium tuberculosis, the bacterium that causes tuberculosis. Every day 25,000 people are infected and 5,000 people die from the disease. Furthermore, due primarily to poor diagnosis, multidrug resistant strains of M. tuberculosis are emerging and the reemergence of tuberculosis as a worldwide epidemic has become a real threat. The worldwide annual market for tuberculosis diagnostics has been estimated at $1.8 billion.

[0009] MRSA is a drug-resistant version of the common *Staphylococcus aureus* bacteria and is contagious, due to the nature of the MRSA bacterium. The bacteria are highly contagious and spread by touch. Approximately 86% of all infections occur within hospitals, and these infections carry a 20% mortality rate. This bacterium costs an average of $21,000 over the standard costs to treat, and kills approximately 19,000 people in the US annually.

[0010] *Listeria monocytogenes* is an intracellular pathogen that can cause invasive disease in humans and animals. Approximately 99% of human listeriosis infections appear to be food borne. While *L. monocytogenes* has been isolated from a variety of raw and ready-to-eat foods, most human listeriosis infections appear to be caused by consumption of RTE foods that permit postcontamination growth of this pathogen. Listeriosis is estimated to be responsible for about

500 deaths per year in the United States, accounting for 28% of annual deaths attributable to known food-borne patho- gens, second only to deaths due to Salmonella infections.

[0011] Methods and systems exist for detecting microbial contamination. Such methods and systems suffer from a number of drawbacks, including the need in most cases to remove a potentially contaminated sample from the environment where it is collected and transferring it to a laboratory environment, where the sample is placed in a culture environment for enrichment and growth over a long period of time, ranging from many hours to days. Additionally, because these labs are frequently offsite there is often a delay in the shipping of a sample to a laboratory. Once enriched, samples are typically analyzed using expensive equipment, traditional culturing methods, PCR and other methods. Thus, current processes often comprise a large time lag between sampling and a result, during which time the sampled conditions may have changed and the results of the assay cannot be utilized to diagnose an infection in a patient or to act on contamination in a lot of manufactured food, for example. Accordingly, new composition, methods, and kits for detecting microbial contamination are needed. Compositions and methods of the present disclosure address these needs.

SUMMARY

[0012] Compositions and methods of the disclosure address the long-felt need in the art for compositions and methods of immediate detection of bacterial infection by a non-technical or layperson at the site of potential contamination.

[0013] Compositions and methods of the disclosure may be used to detect a target microbe within minutes of contacting a recombinant phage of the disclosure to a target microbe. This important feature of the compositions and methods of the disclosure enables the user to not only identify sources of contamination on-site, but also, to contain the target microbe before it can spread. This advantage stands in sharp contrast to existing methods of detecting microbial infections, in which a sample of a potentially contaminated item must be sent to a laboratory to be analyzed using time-intensive and expensive techniques that require specialized scientific training to perform.

[0014] Compositions and methods of the disclosure may be used by a non-technical or layperson. Compositions and kits of the disclosure include at least one recombinant phage, an aqueous solution to contain the recombinant phage and facilitate infection of the target microbe,

a substrate for the marker, and an aqueous solution to contain the substrate for the marker. In a preferred embodiment, each component of the kits of the disclosure are provided in the kit in separate containers. To initiate contact between a recombinant phage and target microbe of the disclosure, the user need only combine the contents of the kit with the target microbe, either directly onto a surface or item of interest or by taking a sample of the surface or item and mixing the test sample in a container with the compositions of the kit. When a recombinant phage of the disclosure contacts the target microbe, a signal is produced that may be detected by visual inspection alone. For example, when the codon-optimized marker of the recombinant phage is luciferase, upon contact with the target microbe in the presence of a marker substrate (e.g. luciferin), visible light will be emitted from the resultant mixture. Enhancement of the signal may be accomplished by decreasing the intensity of light sources in proximity to the resultant mixture.

[0015] Compositions and methods of the disclosure may be used to detect a target microbe at the site of potential contamination. For example, compositions and methods of the disclosure may be used to detect a target microbe in food or an environment containing food and/or other agricultural products at any point along a food supply chain ranging including a location of harvesting or import; a processing or distribution facility; a storage facility; a transportation vehicle; a market, restaurant or point of sale to a consumer; or any point in between. Moreover, compositions and methods of the disclosure may be used to detect bacterial infection in the context of medical treatment, including a field hospital, emergency medical tent, refuge center, clinic, physician office, hospital or any other location at which subjects are at risk of contracting an infection. Government regulatory agencies may also use the compositions and methods of the disclosure to test for contamination of imported products, bodies of water (and in particular, supplies of drinking water), public facilities, and security checkpoints (in the interest of identifying biological hazards and/or weapons).

[0016] Compositions of the disclosure include at least one recombinant phage capable of infecting a target microbe, wherein the recombinant phage contains a codon-optimized marker that, upon contact with the target microbe, produces a detectable signal. Preferred embodiments of the recombinant phages of the disclosure contain a nucleic acid sequence encoding a codon-optimized luciferase enzyme. Codon optimization of the sequence encoding a marker provides the recombinant phage with increased sensitivity and specificity to the target microbe. For

example, when used to detect bacterial contamination in a food sample, distinguishing between those bacteria in the sample that mediate infection (and subsequent illness in animals or humans) from those bacteria that do not cause infection is a significant challenge. Codon optimization of the sequence encoding a the marker of the recombinant phage is a feature that enables the recombinant phage described herein to specifically identify target microbes among bacterial populations that are not harmful.

[0017] Compositions and methods of the disclosure include at least one recombinant phage containing a sequence that encodes a codon-optimized marker to detect microbes. Compositions and methods of the disclosure may also include an optimized aqueous formulation for the detection of microbes in unfavorable conditions or environments. Exemplary unfavorable conditions include, but are not limited to, those conditions or environments in which traces of sanitizing solutions are present that, without the inclusion of the optimized aqueous formulation, may otherwise impede the activity of the recombinant phage of the disclosure.

[0018] Compositions of the disclosure include at least one recombinant phage capable of infecting a target microbe, the phage containing at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker. In certain embodiments, a composition includes at least two, three, four, five, or six recombinant phages capable of infecting a target microbe, wherein each of the phage includes at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker. Compositions of the disclosure may include greater than six recombinant phages capable of infecting a target microbe, wherein each of the phage includes at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker.

[0019] Compositions and methods of the disclosure may be used to contact and/or detect a target microbe located on any surface or material. For example, the target microbe may be located in a liquid, solid or gel. The target microbe may be located on any material, including, but not limited to, glass, metal, brick, concrete, slab, tile, stone, or rug. By way of non-limiting example, the target microbe may be located in or on an agriculture product as well as in or on any surface or portion of an environment in proximity to an agricultural product (e.g. on a floor, sink, or wall). Recombinant phages of the disclosure contain a ribosome binding site. When a composition includes more than one recombinant phage, the ribosome binding site of each phage may be distinct or identical to the ribosome binding sites in the other phages of the composition. In

certain embodiments, the ribosome binding site of each phage is SEQ ID NO: 54. In a related embodiment, the ribosome binding site is 70% identical to SEQ ID NO: 54.

[0020] Recombinant phages of the disclosure contain a codon-optimized marker. In certain embodiments, the codon-optimized marker is luciferase. In a related embodiment, the codon-optimized marker is SEQ ID NO: 36 (also referred to as COP2). Alternatively, the codon-optimized marker is SEQ ID NO: 37 (also referred to as COP3). In another embodiment, the codon-optimized marker further includes an affinity tag. The affinity tag may be a HIS tag.

[0021] In certain embodiments, compositions of the disclosure contain at least one recombinant phage of the composition selected from the group consisting of LP143, A511, LP101, LP124, LP99, LP48, LP125, P100, and LP40. Exemplary compositions of the disclosure include at least one recombinant phage of the composition, wherein the recombinant phage is A511, LP40 or LP124.Alternatively, compositions of the disclosure include A511, LP40 and LP124. In another embodiment, the at least one recombinant phage is A511. In another embodiment, the at least one recombinant phage is LP40. In another embodiment, the at least one recombinant phage is LP124.

[0022] Target microbes of the disclosure include, but are not limited to, *coliform bacteria*, *Escherichia*, *Shigella*, *Listeria*, *Clostridium*, *Vibrio*, *Enterobacteriacae*, *Cronobacter*, *Mycobacterium*, *Staphylococcus*, *Bacillus*, *Campylobacter*, *Pseudomonas*, *Streptococcus*, *Acinetobacter*, *Klebsiella*, *Campylobacter*, and *Yersinia*.

[0023] A target microbe of the disclosure may belong to the genus *Listeria*. Exemplary species of *Listeria* include, but are not limited to, *Listeria* selected from the group consisting of *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, *Listeria ivanovii*, *Listeria grayi*, *Listeria marthii*, *Listeria rocourti*, *Listeria welshimeri*, *Listeria floridensis*, *Listeria aquatic*, *Listeria cornellensis*, *Listeria riparia*, *Listeria weihenstephanensis*, *Listeria flieschmannii*, and *Listeria grandensis*.

[0024] In another embodiment of the disclosure, the target microbe is *Listeria monocytogenes*.

[0025] Compositions of the disclosure include at least one recombinant phage and an aqueous solution, wherein the aqueous solution includes: a) at least one nutrient; b) at least one selective agent suitable to inhibit growth of at least one non-target microbe in an environmental sample or

an agricultural sample; c) at least one vitamin; d) at least one divalent metal; and e) at least one buffering agent capable of maintaining the composition at pH 7.0-7.5. Compositions of the disclosure include at least one recombinant phage and an aqueous solution, wherein the aqueous solution includes: a) at least one nutrient; b) at least one selective agent suitable to inhibit growth of at least one non-target microbe in an environmental sample or an agricultural sample; c) at least one vitamin; d) at least one divalent metal ion; and e) at least one buffering agent capable of maintaining the composition at pH 7.0-7.5. In certain embodiments of the aqueous solution, the at least one nutrient is a culture medium, alcohol, sugar, sugar derivatives, or a combination thereof.

[0026] In certain embodiments of the aqueous solution, the at least one nutrient is Brain Heart Infusion medium, Tryptic Soy Broth, glucose, glycerol, pyruvate, or a combination thereof.

[0027] In certain embodiments of the aqueous solution, the at least one selective agent suitable to inhibit growth of a non-target microbe is LiCl, acriflavine, nalidixic acid, cycloheximide, or a combination thereof.

[0028] In certain embodiments of the aqueous solution, the at least one vitamin comprises yeast extract.

[0029] In certain embodiments of the aqueous solution, the at least one divalent metal or divalent metal ion is $CaCl_2$, MgSO4, or a combination thereof.

[0030] In certain embodiments of the aqueous solution, the at least one buffering agent includes HEPES buffer.

[0031] In a preferred embodiment, the aqueous solution includes Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, and HEPES. For example, the aqueous solution consists of Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, and HEPES (and may be referred to herein as NIB12).

[0032] In another preferred embodiment, the aqueous solution includes Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, HEPES, Tween-80, lecithin, and potassium phosphate. For example, the aqueous solution consists of Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, HEPES, Tween-80, lecithin, and potassium phosphate (and may be referred to herein as NIB14).

[0033] Compositions of the disclosure may include at least one agent to prevent the decomposition of a marker. For example, compositions of the disclosure may include at least one recombinant phage capable of infecting a target microbe, an aqueous solution, and at least one agent to prevent the decomposition of a marker.

[0034] Exemplary compounds prevent decomposition of the marker until after the recombinant phage contacts a target microbe and the marker produces a detectable signal. Exemplary compounds may prevent decomposition of the marker during manufacture, during storage in a kit, during combination with one or more components of a kit, during contact and/or reaction with a substrate in the presence of a target microbe, and/or during production of a signal indicating the presence of a target microbe. For example, following combination of the marker with one or more components of a kit, including a recombinant phage, an aqueous solution, and/or a marker substrate, the compound prevents decomposition of the marker for an hour, 5 hours, 5 to 10 hours, greater than 10 hours or any duration in between. In certain embodiments, the compound prevents decomposition of the marker for less than 5 hours, for between 5 and 10 hours, or for greater than 10 hours.

[0035] In a related embodiment, the compound to prevent the decomposition of a marker substrate prevents decomposition of luciferin.

[0036] In another embodiment, the at least one agent to prevent decomposition of the marker substrate, including those embodiments in which the marker substrate is luciferin, is selected from the group consisting of non-ionic detergents, oxygen scavengers and emulsifiers.

[0037] In another embodiment, the at least one agent to prevent decomposition of the marker substrate, including those embodiments in which the marker substrate is luciferin, is selected from the group consisting of: sodium metabisulfite, sodium thiosulfate, Tween-80, HEPES and lecithin.

[0038] In another embodiment, the composition further includes at least one agent suitable to neutralize a sanitizer present in an environmental sample. Exemplary agents suitable to neutralize a sanitizer include, but are not limited to, sodium metabisulfite, sodium thiosulfate, Tween-80, HEPES and lecithin.

[0039] Compositions of the disclosure may include a substrate for the codon-optimized marker. In certain embodiments, the codon-optimized marker is luciferase. When the codon-optimized marker is luciferase, the substrate includes luciferin.

[0040] Compositions of the disclosure may include a buffer to facilitate a light reaction. For example, compositions of the disclosure include at least one recombinant phage containing a sequence encoding a codon-optimized marker, wherein the marker is a codon-optimized luciferase, the composition includes luciferin as a substrate for the marker, and the composition includes a buffer to facilitate a light reaction.

[0041] The disclosure provides a kit, wherein the kit includes a composition that includes at least one recombinant phage capable of infecting a target microbe, the at least one recombinant phage containing at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker. The composition may include at least one recombinant phage of the disclosure and an aqueous solution of the disclosure. The composition may include at least one recombinant phage of the disclosure, an aqueous solution of the disclosure, and a marker substrate. The composition may include at least one recombinant phage of the disclosure, an aqueous solution of the disclosure, a marker substrate, and a buffer composition to facilitate a light reaction. In certain embodiments of a kit of the disclosure, each of the at least one recombinant phage of the disclosure, an aqueous solution of the disclosure, a marker substrate, and a buffer composition to facilitate a light reaction are stored in separate containers. Kits of the disclosure may optionally include an instrument for obtaining a sample of microbes for testing and/or a sterile container for combining one or more of the compositions of the kit with the target microbe.

[0042] In a preferred embodiment, a kit includes: a first container including at least one recombinant phage capable of infecting a target microbe, said phage containing at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker; a second container including an aqueous solution composition containing Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, HEPES, Tween-80, lecithin, and potassium phosphate; a third container containing a marker substrate; and a fourth container containing a buffer to optimize light detection. In certain embodiments of this kit, the kit further includes a swab and/or a sterile container for mixing the contents of the kit with a target microbe.

This kit may further include a container for facilitating detection of light.

[0043] The disclosure provides methods of determining the presence or absence of a target microbe in an environmental sample, an agricultural sample or both, including: a) contacting an environmental sample, an agricultural sample, or both with a composition of the disclosure to form a test sample; and b) detecting the presence or absence of light thereby determining the presence or absence of a target microbe in an environmental sample and/or an agricultural sample.

[0044] In certain embodiments of the methods of the disclosure, the environmental sample may include a fixed feature of an environment that is not removed from its context within the environment but, rather, is tested in situ. For example, in the environment of a building, the floor may be an environmental sample when the compositions, kits, and methods described herein are applied to a portion of the floor without isolating or removing any portion of the floor for testing. Alternatively, the environmental sample may include a portable feature of an environment that may be removed from its context for testing. For example, in the environment of a building, an individual floor file may be isolated or removed from the surrounding tiles for application of the compositions, kits, and methods of the disclosure. Non-limiting examples of environmental samples include a surface, a container, or a machine or part thereof. Exemplary environments and/or environmental samples also include a processing plant, a storage facility, a health care facility, an educational institution, a loading dock, a cargo hold, a vehicle, an airport, and a customs facility.

[0045] In certain embodiments, the environmental sample is from a health care facility.

[0046] Exemplary the health care facilities include a clinic, an emergency medical services location, a hospice, a hospital ship, a hospital train, a hospital, a military medical installation, a doctor's office, a long term care facility, respite care facility, and a quarantine station.

[0047] Environmental samples of the disclosure may include or be obtained from a food production facility. Exemplary food production facilities include, but are not limited to, a farm, a boat, a food distribution facility, a food processing plant, a food retail location, a home, or a restaurant.

[0048] In certain embodiments of the methods of the disclosure, the agricultural sample includes stock feed or food supply. Agricultural samples may be intended for use by animals (including

research subjects and those animals raised for butchering or entering the food supply) as well as humans. The term food supply includes plant and animal matter, including but not limited to,

[0049] a dairy product, a fruit product, a grain product, a sweet, a vegetable product, a meat product, or any combination thereof. Agricultural and food products may either solid, liquid, or a mixture thereof.

[0050] Exemplary dairy products include food products derived from milk, butter, yogurt, cheese, ice cream, queso fresco, or any combination thereof

[0051] Exemplary fruit products include apples, oranges, bananas, berries, lemons, or any combination thereof.

[0052] Exemplary grain products includes wheat, rice, oats, barley, bread, pasta, or any combination thereof.

[0053] Exemplary sweet products include candy, soft drinks, cake, pie, or any combination thereof.

[0054] Exemplary vegetable products include spinach, carrots, onions, peppers, avocado, broccoli, or any combination thereof. The vegetable product may include

guacamole.

[0055] Exemplary meat products include any portion of a chicken, fish, turkey, pork, beef, or any combination thereof.

[0056] Meat products may include whole muscle meat, ground meats, or any combination thereof.

[0057] It should be appreciated that all combinations of the foregoing concepts and additional concepts discussed in greater detail below (provided such concepts are not mutually inconsistent) are contemplated as being part of the inventive subject matter disclosed herein. In particular, all combinations of claimed subject matter appearing at the end of this disclosure are contemplated as being part of the inventive subject matter disclosed herein. It should also be appreciated that terminology explicitly employed herein that also may appear in any disclosure incorporated by reference should be accorded a meaning most consistent with the particular concepts disclosed herein.

[0058] Other systems, processes, and features will become apparent to those skilled in the art upon examination of the following drawings and detailed description. It is intended that all such additional systems, processes, and features be included within this description, be within the scope of the present disclosure, and be protected by the accompanying claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0059] **Figure 1** is a map of the insertion site in the A511:COP2 engineered phage.

[0060] **Figure 2** is a map of the insertion site in the LP124::COP2 engineered phage.

[0061] **Figure 3** is a map of the insertion site in the LP40::COP2 engineered phage.

[0062] **Figure 4** is a graph comparing the relative detectable light (Relative Light Units, RLU) from healthy and sick cells infected with a mixture of A511, LP40 and LP124 engineered phage comprising either nanoluc luciferase or codon optimized COP2 luciferase.

[0063] **Figure 5** is a graph comparing relative performance in healthy and sick cells of a mixture of A511, LP40 and LP124 engineered phage comprising either the nanoluc luciferase or codon optimized COP2 luciferase.

[0064] **Figure 6** is a graph comparing the relative detectable light from sick cells infected with A511 engineered phage comprising either nanoluc luciferase or codon optimized COP2 luciferase.

[0065] **Figure 7** is a graph comparing relative performance in sick cells of a A511 engineered phage comprising either the nanoluc luciferase or codon optimized COP2 luciferase.

[0066] **Figure 8** is a series of graphs that depict the mean light signal detected in Relative Light Units (RLU) per colony forming units (CFU) in samples of various *Listeria* species infected with recombinant codon-optimized phage version 2 (COP2; v.1.0.2; top panel) or with recombinant optimized phage version 3 (COP3 v.1.0.3; bottom panel). The *Listeria* species used in these experiments are considered "weak signal producers" that do not typically produce strong signal following infection with recombinant luciferase-encoding phages.

[0067] **Figure 9** is a graph that depicts a comparison of the amounts of mean light signal detected (shown as a percentage) in *Listeria* samples that were infected with either recombinant codon-optimized phage version 2 (COP2; v.1.0.2) or with recombinant optimized phage version 3 (COP3 v.1.0.3). The y-axis depicts the mean relative signal increase in percentage, and the x-axis depicts the *Listeria* strain that utilized.

[0068] **Figure 10** is a graph that depicts optimal phage concentration using codon-optimized, luciferase encoding, recombinant phage. The y-axis depicts RLU, and the x-axis depicts phage concentration in PFU/mL.

[0069] **Figure 11** is a graph that demonstrating the effect of the addition of various LiCl concentrations to the 1X TSB buffer in RLU output following infection of bacteria with luciferase encoding phage and normalized to RLU output obtained from 1x BHI buffer. A 3 hour and a 6 hour time point were assayed. The % values are shown on the y-axis.

[0070] **Figure 12** is a graph that summarizes the findings with respect to enzyme activity and infection rate of bacteria exposed to luciferase encoding phage while in the presence of various iterations of the infection buffer formulations and normalized to RLU output obtained from 1x BHI buffer. The % values are shown on the y-axis.

[0071] **Figures 13A and 13B** are a pair of graphs depicting the effect of the addition of HEPES buffer to the Formulation-1 infection buffer. Bacterial cells were exposed, in either Formulation-1 without HEPES or Formulation-1 with HEPES, to luciferase encoding phage, followed by assessment of RLU values normalized to RLU output obtained from 1x BHI buffer. The % values are shown on the y-axis.

[0072] **Figure 14** is a graph that demonstrates the effects of the addition of Tween-80, or Tween-80 and lecithin, or the addition of neither of these components to the Listeria growth broth in the presence of increasing concentrations of quaternary ammonium salts. Bacterial cells were exposed to luciferase encoding phage in the following buffers, Listeria growth broth, Listeria growth broth with Tween-80, or to Listeria growth broth with the addition of both Tween-80 and lecithin. The RLU values are shown on the y-axis.

[0073] **Figure 15** is a graph that summarizes the findings with respect to enzyme activity and infection rate of bacteria exposed to luciferase encoding phage while in the presence of various iterations of the infection buffer formulations and normalized to RLU output obtained from 1x BHI buffer. The % values are shown on the y-axis.

[0074] **Figure 16** is a graph that depicts the results of a lower limit of detection assay in which Formulation-2 (NIB-12) is used as the infection buffer either alone or with the addition of Tween-80. The bacteria were exposed in the presence of either of these infection buffers to luciferase encoding phage, followed by detection of RLU. RLU values are shown on the y-axis.

[0075] **Figures 17A-17D** are a series of graphs and a table that depict the effects of the NIB-14 infection buffer or a base buffer, Letheen, in the presence of various concentrations of the F29 sanitizing solution containing quaternary ammonium compounds. Bacteria were exposed to the different concentrations of the F29 solution for 30 minutes preceding the luciferase encoding phage infection step. The enzyme was also exposed to different concentrations of the F29 solution during the enzymatic activity test. RLU values were then collected. Figure 17A depicts the effects of using either buffer in the presence of various concentrations of F29 on phage infection activity. Figure 17B depicts the effects of using either buffer in the presence of various concentrations of F29 on enzymatic activity. Figure 17C depicts the effects of using either buffer during exposure of the NanoGlo luciferin to various concentrations of the F29 solution. Figure 17D depicts a table with a summary of the results obtained from this series of experiments. When graphs are depicted, the y-axis represents percentage activity compared to no addition of F29.

[0076] **Figures 18A and 18B** are a series of graphs that depict the effects of incubating Letheen or NIB-14 over time with the sanitizing solution, Clorox, prior to the downstream effects on the luciferase encoding phage infection assay. Assay time points for this study included 5, 10, 15, 30, 60 and 120 minutes. Three concentrations of Clorox were assessed over this time, including 500ppm, 1000ppm, and 5000ppm.

[0077] **Figure 19** is a graph that depicts the results of a series of experiments in which stressed cells (*i.e.* cells that were dried for 18 hours on a stainless steel table before further processing) were incubated with various NIB infection buffers, NIB-10, NIB-12 or NIB-14. As a control for the experiments, 1X BHI was used. The stressed cells were exposed in each of these buffers to luciferase encoding phage, and subsequently followed by assessing the RLU for each condition. The enzyme activity was also assessed in the presence of each buffer iteration.

[0078] **Figures 20A-20B** are a series of graphs that depict lower limit of detection assays (also referred to herein as "LLOD") utilizing *L. monocytogenes*, incubated in various foods. LLOD assays were performed with *L. monocytogenes* incubated in 100% (full fat) ice cream and 100% (full fat) milk (Figure 20A) or NIB-14 (as a reference), or in Demi-Fraser broth incubated at 30C in with raw ground beef, deli turkey, guacamole and queso fresco (Figure 20B) for 16 hours. For *L. monocytogenes* in the presence of raw ground beef, deli turkey, guacamole or queso fresco,

the sample was incubated in an equal volume of NIB-14 infection buffer and luciferase encoding phage used for the infection of the microbes in the sample.

[0079] **Figures 21A-21D** are a series of graphs that depict the time course of *L. monocytogenes* detection in various food samples. *L. monocytogenes* was added to the food samples for defined amounts of time, followed by infection with a recombinant, luciferase encoding phage and subsequent detection of the luciferin signal. The food samples used in the assays included turkey (Figure 21A), queso fresco (Figure 21B), guacamole (Figure 21C) and beef (Figure 21D). RLU values are on the y axis.

[0080] **Figure 22A-M** is a series of graphs that depict the time course of *L. innocua* and . *monocytogenes* detection in various food samples. *L. innocua* or *L. monocytogenes* was added to the food samples for defined amounts of time, followed by infection with a recombinant, luciferase encoding phage and subsequent detection of the luciferin signal. The food samples used in the assays included potato salad (Figure 22A, 22B, 22H, and 22I), smoked salmon (Figure 22C, 22D, 22J and 22K), ground turkey (Figure 22E, 22F, 22L and 22M) and sour cream (Figure 22G). RLU values are on the y axis.

[0081] **Figure 23A-B** is a series of graphs that depict the time course of *L. innocua* and *monocytogenes* detection in either pepperoni or spinach.

[0082] **Figure 24A-C** is a series of graphs that depict the time course of detection of *L. seeligeri*, *L. innocua*, and *L. monocytogenes* in turkey, queso, and in guacamole.

[0083] **Figure 25A-D** is a series of graphs that depict the detection of *L.* monocytogenes in various food types when the assay is performed utilizing various dilution of food matrix to incubation buffer.

[0084] **Figure 26** is a sequence alignment of the CPS open reading frame of LP143, A511, LP101, LP124, LP99, LP48, LP125, P100 and LP40 phage.

[0085] **Figure 27** is an amino acid alignment of LP143, A511, LP101, LP124, LP99, LP48, LP125, P100 and LP40 phage.

[0086] **Figure 28** is a sequence alignment of recombinant LP143, A511, LP101, LP124, LP99, LP48, LP125, P100 and LP40 phage engineered with firefly luciferase.

[0087] **Figure 29** is a sequence alignment of recombinant LP143, A511, LP101, LP124, LP99, LP48, LP125, P100 and LP40 phage with nanoluc luciferase.

DETAILED DESCRIPTION

[0088] Compositions, methods, and kits are presented herein for the detection of target microbes through the use of codon-optimized recombinant phage. This disclosure provides recombinant phage with sequence encoding a codon optimized marker, aqueous solutions that enable robust signal detection following contact with the target microbes in a sample. The compositions and methods of the disclosure provide broad detection coverage of a microbe genus, species or a combination of species.

[0089] The composition and buffer components necessary for robust signal detection following infection by codon optimized phage is dependent on the sampled area. For example, at least one recombinant phage is provided in combination with an aqueous solution, that, together, provide optimal for the detection of microbes in an agricultural facility. A particular challenge of detection of microbes in an agricultural facility is the potential for the presence of trace sanitation solutions that may interfere with signal detection. Another embodiment relates to the use of recombinant phage for the detection of microbes in agricultural products themselves, such as, for example, food stuffs intended for human or animal consumption. Detection of microbes in an agricultural sample presents unique challenges in that components of the agricultural sample may contain substances that interfere with signal detection. The aqueous solutions presented herein are formulated to minimize such interference.

[0090] The methods and compositions presented herein are optimized in order to allow the propagation of microbes from a test sample, infection of the microbes with a recombinant phage that encodes a detectable marker, and the quantification of the amounts of the microbes from the sample by way of detection of the recombinant phage marker.

Methods of Making Recombinant Phage

[0091] Any method known in the art can be used to make genetically modified phage from starting phage. For example, U.S. Patent No. 5,824,468 discloses methods of making genetically modified phage. Alternative methods are disclosed in co-pending Application No. 13/627,060, filed September 26, 2012, which is hereby incorporated herein by reference.

[0092] Phage infective engineering (PIE) is used herein to make recombinant phage. PIE methodology is disclosed in U.S. Patent Application No. 14/226,889, which is hereby incorporated herein in its entirety by reference. This method is sometimes referred to herein as phage infective engineering (PIE). This method allows insertion of a heterologous nucleic acid sequence into any desired location of a phage genome. The PIE method utilizes a phage targeting vector (PTV) that is transformed into a phage host cell. The PTV comprises a heterologous nucleic acid sequence (such as an open reading frame encoding a marker) for insertion into a phage genome. The heterologous nucleic acid sequence is flanked by upstream and downstream homology regions, which are located adjacent to the desired insertion site. In some embodiments the homology regions in the vector are directly adjacent in a starting phage genome. Such embodiments allow insertion of the heterologous nucleic acid sequence into the phage genome without a loss of endogenous phage sequence. In some embodiments the homology regions in the vector flank a region of the starting phage genome that is not included in the vector. Such embodiments allow insertion of the heterologous nucleic acid sequence into the phage genome while deleting a region of the starting phage genome at the site of insertion. Such embodiments allow, for example, the replacement of an endogenous phage sequence with a replacement sequence. In some embodiments the starting sequence that is deleted and the replacement sequence display sequence homology, such as homology of at least 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or higher.

[0093] The upstream homology region, downstream homology region, and heterologous nucleic acid sequence are combined in a vector to make a PTV. One example of a suitable vector is pMK4; however, skilled artisans are aware of many suitable vectors that may be used for this purpose. The plasmid may be isolated in any suitable host, such as E. coli. Upon verification, the plasmid is then transformed into a phage host cell. One example of such a cell useful for many Listeria phage is the *L. monocytogenes* strain EGD-e.

[0094] Once the PTV is successfully transformed into the phage host, the initial recombination was performed by incubating the transformed phage host cell with starting phage.

[0095] To assess whether recombination has occurred, the infection is assayed using any suitable method to identify recombinant phage that comprise the heterologous nucleic acid sequence. PCR is one method that may be used. Alternatively, if the heterologous nucleic acid sequence comprises an open reading frame the presence of transcripts encoded by that open reading frame,

the presence of the encoded gene product, or functional readouts of the encoded gene product may be screened for in cultures of cells infected with the resultant phage to identify recombinant phage.

Codon Optimized Phage

[0096] The disclosure provides recombinant phage comprising a heterologous nucleic acid sequence encoding a codon optimized marker. The phage can be LP40, LP48, LP99, LP101, LP124, LP125, LP143, A511, or P100. The marker can be any detectable marker. In one embodiment the marker is luciferase.

[0097] The design of codon optimized phages should take into account a variety of factors, including the frequency of codon usage in a host organism, nearest neighbor frequencies, RNA stability, the potential for secondary structure formation, the route of synthesis and the intended future DNA manipulations of that gene.

[0098] The degeneracy of the genetic code permits the same amino acid sequence to be encoded and translated in many different ways. For example, leucine, serine and arginine are each encoded by six different codons, while valine, proline, threonine, alanine and glycine are each encoded by four different codons.

[0099] However, the frequency of use of such synonymous codons varies from genome to genome among kingdoms and phyla. For example, synonymous codon-choice patterns among mammals are very similar, while evolutionarily distant organisms such as yeast (*S. cerevisiae*), bacteria (such as *E. coli*) and insects (such as *D. melanogaster*) reveal a clearly different pattern of genomic codon use frequencies. In reference to phage codon optimization, codon selection may vary with the species, strain or ribotype of the host to be infected by a particular phage. Additionally, codon usage may vary with the environment in which the host exists, depending on factors such as temperature, pH, pressure, and other external parameters. Further, codon usage may vary with the state of growth in which the host exists, *e.g.* depending on rapid division vs. non-division, or within a healthy or an injured cellular state.

[00100] These differences in codon-choice patterns appear to contribute to the overall expression levels of individual genes by modulating translation initiation rates, as well as peptide elongation rates. Experimental evidence supports this argument; the rate of polypeptide

synthesis depends on the character of the codons being translated, as well as the initial kinetics for transfer RNA ("tRNA") ternary complex formation.

[00101] The preferred codon usage frequencies for a recombinant phage should reflect the codon usages of genes derived from the genome of the intended host organism.

[00102] In some embodiments, a gene can be optimized by replacing codons of the origin species with known preferred codons from a host organism encoding the same amino acid. In some embodiments, a host organism is *Listeria*. In some embodiments, software can be utilized which applies an algorithm to a genetic sequence which will codon optimize the sequence for a specific host organism. In some embodiments, software from DNA 2.0^{TM} can be used to codon optimize a genetic sequence for a specific host organism. Example algorithms for codon optimization *in silico* have been described (*see* Villalobos et al. BMC Bioinformatics. *Gene Designer: a synthetic biology tool for constructing artificial DNA segments. PLoS ONE. 2011 6:e19912.*; US8,635,029; US8,401,708; US8,126,653; US8,005,620; US7,805,252; US7,561,973; US7,561,72.)

[00103] In some embodiments, codon optimization allows for increased expression of phage encoded proteins in a host organism. In some embodiments, the host organism is a bacterium. In some embodiments, codon optimization allows for increased expression of reporter proteins or polypeptides encoded by a recombinant phage in a host organism. In some embodiments, codon optimization of recombinant phage allows for increased expression of a luciferase reported by *Listeria*.

[00104] In some embodiments, *Listeria* phages used for recombination may be selected from A511, LP124, and LP40. In some embodiments, recombinant phages comprise the entirety of the original phage genome. In some embodiments, recombinant phages comprise deletions to the original phage genome and addition of heterologous nucleic acid sequences. In some embodiments, recombinant phages comprise added stop codons. In some embodiments, recombinant phages comprise added ribosome binding sites. In some embodiments, recombinant phages comprise a codon optimized reporter gene. In some embodiments, a reporter gene is a sequence encoding luciferase. In some embodiments, the luciferase reporter gene is a codon optimized NanoLuc sequence optimized for expression in Listeria. In some embodiments, a recombinant phage is an A511 phage comprising added stop codons, an added ribosome binding site, and an added codon optimized NanoLuc sequence. In some embodiments, a recombinant

phage is a LP124 phage comprising added stop codons, an added ribosome binding site, and an added codon optimized NanoLuc sequence. In some embodiments, a recombinant phage is a LP40 phage comprising added stop codons, an added ribosome binding site and added codon optimized NanoLuc sequence.

Optimized Assay Aqueous Solution for Microbial Detection

[00105] The disclosure provides formulations of an aqueous solution which effectively enable bacteria isolated from a test site to be productively infected by recombinant phage. Furthermore, the aqueous solution is capable of preserving the enzymatic activity used in the phage based detection system. A major difficulty encountered in the detection of bacteria using phage based recombinant markers is the potential interactions between sanitation reagents found in the sample and the test reagent compounds that are used to quantify bacterial presence or absence. This problem is augmented given the propensity of facilities to use amounts of disinfectants in excess of the recommended guidelines presented by the Federal Drug Administration (FDA), United States Department of Agriculture (USDA), and Centers for Disease Control (CDC). Overuse of these sanitization agents may lead to obfuscation of true positive or true negative results due to (i) decreasing enzymatic activity required for the phage-based detection system, (ii) lowering the ability of phage to infect bacteria collected from the test site, or (iii) disrupting the bacterial cells to a degree that they are not detectable.

[00106] Collection and processing of a an environmental sample from a test site follows a stepwise process that includes: (a) collection of the sample by way of swabbing the surface with a sponge, followed by immediate placement of the sponge into an isolated container; (b) processing the sample begins with the addition of an aqueous solution (infection buffer), and the addition of a marker encoding phage to the sample collecting sponge; (c) incubation of the solution impregnated sponge at an appropriate temperature range; (d) isolation of the liquid from the sponge by way of centrifugation; and (e) detection of a signal in the liquid with an instrument (*e.g.* luciferase presence with a luminometer). The solution added to the sponge is a buffer that contains reagents that minimize the interaction with components of commonly used sanitization solutions that have been found to reduce signal detection ability (*e.g.* by either reducing phage infection or by reducing enzymatic activity, or by affecting the luciferin substrate). The purposes of the buffer include recovery of the isolated stressed and injured bacteria in order to optimize

phage infection and to optimize downstream signal detection. The marker used for signal detection can be any detectable marker. Preferred detection signal systems include luciferase based assays.

[00107] Ideal formulations of the disclosure would allow for high amounts of signal following phage infection, high amount of signal stability, and the ability to effectively neutralize various components found in sterilization solutions without the loss of either signal or stability. The formulations presented herein make use of additives that serve as neutralizers to overcome these challenges. Commonly found sanitation chemicals that may have the ability to interfere with environmental sample test results include chlorine, quaternary ammonium salts, organic acids and peracids, iodophors, and detergents. Formulations presented herein contain remedies to overcome these agents including, for example, sodium metabisulfite, sodium thiosulfate, lecithin, Tween-80, HEPES and buffering salts.

[00108] Bacterial cells collected from the environment present many additional challenges to the downstream processing required for adequate signal detection. Many of these challenges relate to the health of the cells upon collection. The collected cells may be starved, osmotically stressed, and have underlying oxidative stress. Formulations have been developed, and described herein, to overcome these challenges encountered following the collection of the cells. For example, detailed herein, and specifically in the Examples section, are formulations to overcome osmotic stress (*e.g.* via addition of glycerol), cell starvation (*e.g.* via addition of nutrients including carbon, nitrogen source, sugars and vitamins), and oxidative stress (*e.g.* via the addition of vitamins including those contained in yeast extract). Interaction with non-target biologicals also poses a challenge in the downstream signal detection methods. Formulations presented herein have been optimized to overcome non-target biological interactions via the addition of either nalidixic acid and/or lithium salts.

[00109] The Examples detail various formulations that work well at preserving signal and signal stability (*See* Examples 6-12). A base aqueous solution of the disclosure is Formulation-1 (Table 1). A variation of the base aqueous solution Formulation-1, Forumulation-1A, makes use of additives (*i.e.* 0.08% $MgSO_4$, and 0.1% pyruvate) that further aid in preservation of signal intensity and phage infection (Table 2).

Table 1: Base Infection Buffer Formulation (Formulation 1)

Components	Group	Function
1x Tryptic Soy Broth	Media (nutrients)	Support recovery and growth of stressed cells (provide hydrolyzed amino acids, sugars, minerals)
0.25% LiCl	Selective agents	Prevent or limit growth of competing biologicals
0.002% nalidixic acid	Selective agents	Prevent or limit growth of competing biologicals
0.5% yeast extract	Vitamins (B complex)	Prevent oxidative stress
0.25% glucose	Carbon Source	Nutrient

Table 2: Base Infection Formulation (Formulation 1-A)

Components	Group	Function
1x Tryptic Soy Broth	Media (nutrients)	Support recovery and growth of stressed cells (provide hydrolyzed amino acids, sugars, minerals)
0.25% LiCl	Selective agents	Prevent or limit growth of competing biologicals
0.002% nalidixic acid	Selective agents	Prevent or limit growth of competing biologicals
0.5% yeast extract	Vitamins (B complex)	Prevent oxidative stress
0.25% glucose	Carbon Source	Nutrient
0.08% $MgSO_4$	Ions	Increases infection ability
0.1% sodium pyruvate	Carbon Source	Nutrient

[00110] A preferred embodiment of the aqueous solutions of the disclosure is Formulation-2 (also referred to herein as "NIB-12") (Table 3). As detailed in the Example section, the addition of 20mM HEPES increases enzyme activity and stability, and increases the buffering capacity against pH extremes (*See* Example 7).

[00111] Another preferred embodiment of the aqueous solutions of the disclosure is formulation NIB-14 (Table 4). NIB-14 contains lecithin, Tween-80 and potassium phosphate added to the base components of NIB-12. NIB-14 allows for greater phage infection ability and increased enzymatic activity compared with a base medium (BHI), and also allows for greater

neutralization of remnant sanitizer chemicals in comparison to other aqueous solutions tested (*See* Examples 8 and 11).

Table 3: Infection Formulation 2 (NIB-12)

Components	Group	Function
1x Tryptic Soy Broth	Media (nutrients)	Support recovery and growth of stressed cells (provide hydrolyzed amino acids, sugars, minerals)
0.25% LiCl	Selective agents	Prevent or limit growth of competing biologicals
0.002% nalidixic acid	Selective agents	Prevent or limit growth of competing biologicals
0.5% yeast extract	Vitamins (B complex)	Prevent oxidative stress
0.25% glucose	Carbon Source	Nutrient
0.08% $MgSO_4$	Ions	Increases infection ability
0.1% sodium pyruvate	Carbon Source	Nutrient
20 mM HEPES, pH 7.5	Buffering agents	Neutralize environmental pH extremes

Table 4: Infection Formulation NIB-14

Components	Group	Function
1x Tryptic Soy Broth	Media (nutrients)	Support recovery and growth of stressed cells (provide hydrolyzed amino acids, sugars, minerals)
0.25% LiCl	Selective agents	Prevent or limit growth of competing biologicals
0.002% nalidixic acid	Selective agents	Prevent or limit growth of competing biologicals
0.5% yeast extract	Vitamins (B complex)	Prevent oxidative stress
0.25% glucose	Carbon Source	Nutrient
0.08% $MgSO_4$	Ions	Increases phage infection ability
0.1% sodium pyruvate	Carbon Source	Nutrient
20 mM HEPES, pH 7.5	Buffering agents	Neutralize environmental pH extremes
Tween-80 1.5%	Neutralizer of sanitizers, Non-ionic detergent	Neutralize biguanides (chlorhexidine), bis-phenols (hexachlorophene), phenolic compounds, cresols, formalin, to some extent quaternary ammonium compounds, organic acids, parabens, alcohols
Lecithin 0.22%	Nutrient and Neutralizer	Nutrient and Neutralizer
0.02% Potassium Phosphate, pH7.4	Buffering agents	Neutralize environmental pH extremes

[00112] Table 5 lists the groups and category of the reagents that are included in the aqueous solutions disclosed herein, and the affect that each of these components has on *Listeria* detection.

Table 5: Reagents in Aqueous Solution and Influence on *Listeria* Detection

Group	Category	Components tested	Function	Effect on *Listeria* Detection
Nutrients				
	Carbohydrates	Glucose		positive
		Glycerol	Energy source for	neutral

			stressed cells	
		Mannose		
		Fructose		
		Sucrose		neutral
	Meat and plant extracts	Beef extract	Nutrient source	
		Pancreatic digest of casein	Nitrogen source	
		Papaic digest of soybean meal	Nutrient source	
		Proteose peptone	Nitrogen source	
		Sodium succinate	Energy source	
	Carbon sources	Sodium acetate		
		Acetoin		
		Sodium pyruvate		positive
		Alpha-ketoglutarate		negative
		Sodium malonate		negative
		Sodium citrate		negative
		Ferric ammonium citrate		neutral
	Minerals	Ferric citrate	Iron source, growth enhancer	neutral
		Ferric sulfate		neutral
		Sodium glutamate		
	Nitrogen sources	Ammonium nitrate		
		Ammonium sulfate		
		Urea		
	Amino acids	Sodium glutamate	Energy source for stressed cells	neutral
		Branched-chain amino acids (leucine, isoleucine, valine)	Conversion of cells in stationary phase into growing phase	neutral

		Proline		
		Cysteine		
		Methionine		
	Media	Brain Heart Infusion	Support recovery and growth of stressed cells by providing variety of nutrients(provide hydrolyzed amino acids, sugars, minerals)	positive
		Tryptic Soy Broth		positive
		Buffered Peptone Water		positive
		LPT-6F (BioMerieux)		negative
		Moxalactam	Prevent or limit growth of competing biologicals	neutral
Selective agents	*Antibiotics*	Nalidixic acid		positive
		Polymyxin B		
		Ceftazidime		positive
		Acriflavin		negative
		Carbenicillin		
		Erythromycin		
		Mitomycin C		
		Penicillin G		
		Streptomycin		
		Tetracycline		positive
		Nitrofurantoin		
	Growth inhibitors	Lithium chloride	Prevent or limit growth of competing	optimized for positive

			biologicals	
	Yeast growth inhibitor	Cycloheximide	Antifungal agent	neutral
Vitamins	*B complex*	Yeast extract	Prevent oxidative stress	positive
		Biotin		
		Riboflavin		
		Nicotinamide		
		Calcium panthotenate		
		Cyanocobalamine		
		Pyridoxine		
		Thiamine		neutral
		Lipoic acid		
Divalent metals		Magnesium sulphate	Support enzymatic functions of cells, support phage activity	positive
		Magnesium chloride		
		Ferrous sulphate		negative
		Calcium chloride		neutral
		Zinc sulfate		
Buffering agents	*pH buffers*	Sodium monobasic / sodium dibasic phosphates, pH 7.2	Neutralize environmental pH extremes	
		HEPES, pH 7.4		positive
		MOPS, pH 7.2		positive
Neutralizer of sanitizers	*Oxygen scavenger*	Sodium metabisulfite	Scavenge peroxides, neutralize glutaraldehyde, formaldehyde	positive
		Catalase	Neutralize peroxides	
		Sodium pyruvate	Scavenges peroxides	positive

	Halogens neutralizer	Sodium thiosulfate	Neutralize halogens (iodine, chlorine, sodium hypochlorite, chlorine dioxide, also peroxides, peroxyacids)	negative
	Mercury neutralizer	Sodium thioglycollate		negative
	Non-ionic detergent/ surfactant	Polysorbate 80	Neutralize biguanides (chlorhexidine), bis-phenols (hexachlorophene), phenolic compounds, cresols, formalin, to some extent quaternary ammonium compounds, organic acids, parabens, alcohols	positive
		Polysorbate 20		negative
		Triton X-100		negative
	Emulsifier	Soy based lecithin	Neutralize quaternary ammonium compounds, parabens	positive
		Soy based hydroxylated lecithin		negative
		Phosphocholine chloride		negative
		O-octophosphorylcholine		negative

Detection of microbes in Agricultural Products

[00113] The detection of microbes in agricultural products is essential to maintain food safety. The disclosure provides methods and compositions to rapidly detect microbes in or on

agricultural products with high sensitivity and within a timeframe that is relevant to enabling reaction within a work shirt (less than 8-10 hours). Compositions and methods of the disclosure are particularly beneficial in comparison to currently used methods of microbial detection in that the present invention, (i) has minimal sample preparation, (ii) is capable of detecting microbes in undiluted or minimally diluted matrix of certain foods resulting in less operator and cross-contamination risk, smaller volumes (less cost) and less waste, (iii) has high sensitivity and specificity, and (iv) has a total time to result of less than 8-10 hours.

[00114] Compositions and methods of the disclosure, as described in the Examples section (*see* Examples 13-14), incorporate the use of marker encoding phage, infection buffer/media, and a quantification of the amounts of phage marker present following phage infection of a sample in order to identify microbial presence in food samples. Preferred embodiments of the compositions and methods of the disclosure enable the detection of microbes in various food sources, including fatty foods, such as for example, whole milk, ice cream, queso fresco, and guacamole; salty foods, such as for example, deli turkey; and other foods, such as for example, beef. Preferred, although not limiting, microbial target species for the current invention include species of *Listeria*.

[00115] Unlike all other methods of microbial detection available today, the compositions and methods of the disclosure are capable of detecting target microbes in an undiluted food matrix. These properties contribute to the minimal sample preparation steps and associated rapid processing associated with the use of the present methods and compositions. Unlike other microbial detection methods, the use of the recombinant phage containing the codon-optimized marker sequence in the compositions and methods of the disclosure enables the rapid detection of extremely low numbers of microbes (*e.g. Listeria monocytogenes* in various foods, *see* Example 13), and the detection of microbes in lower limit of detection assays (also referred to herein as "LLOD") of down to 1 CFU in certain foods (*see* Example 14). For example, in LLOD assays from whole milk samples, *Listeria monocytogenes* was detected in quantities as low as 50 cells in 50mL of sample utilizing the recombinant phage based microbe detection system within a two hour period. (*See* Example 8). The detection of *S. enterica* was also assessed in various kinds of foods and was found to have a sensitivity of 1 CFU as well. Both LLOD and time course to detection assays revealed that using the compositions and methods of the disclosure enables the rapid detection of *S. enterica* with no enrichment (*See* Examples 13 and 14).

Recombinant Phage

[00116] The phage LP40, LP48, LP99, LP101, LP124, LP125, LP143, and A511 were selected for engineering. The examples describe making recombinant versions of the phage LP40, LP48, LP99, LP101, LP124, LP125, LP143, A511, and P100, comprising a heterologous nucleic acid sequence encoding a marker. As demonstrated in the examples, those phage are useful, for example, to detect target bacteria, as further disclosed throughout this application.

[00117] Accordingly, this disclosure provides recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker. In some embodiments the recombinant phage comprises a genome comprising a region of at least 1 kb that comprises substantial homology to a region of at least 1 kb of the genome of at least one phage selected from LP40, LP48, LP99, LP101, LP124, LP125, LP143, A511, and P100. In some embodiments the region of homology comprises at least 2 kb, at least 3 kb, at least 4 kb, at least 5 kb, at least 6 kb, at least 7 kb, at least 8 kb, at least 9 kb, at least 10 kb, or more. In some embodiments the region of homology is the entire genome of the recombinant *Listeria* phage. In some embodiments the substantial homology is nucleotide sequence identity of at least 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% across the region of homology.

[00118] This disclosure provides the amino acid sequences of the cps gene of the phage LP40 (SEQ ID NO: 6), LP48 (SEQ ID NO: 8), LP99 (SEQ ID NO: 10), LP101 (SEQ ID NO: 12), LP124 (SEQ ID NO: 14), LP125 (SEQ ID NO: 16), LP143 (SEQ ID NO: 18), A511 (SEQ ID NO: 20), and P100 (SEQ ID NO: 22). Accordingly, in some embodiments this disclosure provides recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker, wherein the recombinant *Listeria* phage comprises a nucleic acid sequence that encodes a protein selected from SEQ ID NOS: 6, 8, 10, 12, 14, 16, 18, 20, and 22, and muteins thereof.

[00119] This disclosure also provides the nucleotide sequences of the open reading frames of the cps gene of the phage LP40 (SEQ ID NO: 5), LP48 (SEQ ID NO: 7), LP99 (SEQ ID NO: 9), LP101 (SEQ ID NO: 11), LP124 (SEQ ID NO: 13), LP125 (SEQ ID NO: 15), LP143 (SEQ ID NO: 17), A511 (SEQ ID NO: 19), and P100 (SEQ ID NO: 21). Accordingly, in some embodiments this disclosure provides recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker, wherein the recombinant *Listeria* phage comprises a

nucleic acid sequence selected from SEQ ID NOS: 5, 7, 9, 11, 13, 15, 17, 19, and 21, and nucleic acid sequences comprising substantial homology thereto.

[00120] In some embodiments the recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker comprises a screenable marker. In some embodiments the marker is a luciferase. In some embodiments the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to SEQ ID NO: 2. In some embodiments the luciferase is encoded by a nucleic acid sequence comprising SEQ ID NO: 1 or a nucleic acid sequence comprising substantial homology to SEQ ID NO: 1 capable of encoding a luciferase that is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99 identical to SEQ ID NO: 2. In some embodiments the recombinant *Listeria* phage is selected from LP48::ffluc, LP99::ffluc, LP101::ffluc, LP124::ffluc, LP125::ffluc, LP143::ffluc, A511::ffluc, P100::ffluc, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, P100::COP2, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, and P100::COP3. In some embodiments the recombinant *Listeria* phage is selected from phage comprising genomes comprising substantial homology to at least one phage selected from LP48::ffluc, LP99::ffluc, LP101::ffluc, LP124::ffluc, LP125::ffluc, LP143::ffluc, A511::ffluc, P100::ffluc, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, LP48::COP2, P100::COP2, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, LP48::COP3, and P100::COP3.

[00121] In some embodiments the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to SEQ ID NO: 4. In some embodiments the luciferase is encoded by a nucleic acid sequence comprising SEQ ID NO: 3 or a nucleic acid sequence comprising substantial homology to SEQ ID NO: 3 capable of encoding a luciferase that is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99 identical to SEQ ID NO: 4. In some embodiments the recombinant *Listeria* phage is selected from LP040::nluc, LP124::nluc, LP125::nluc, A511::nluc, P100::nluc, LP040::COP2, LP124:: COP2, LP125:: COP2, A511::

COP2, P100:: COP2, LP040::COP3, LP124:: COP3, LP125:: COP3, A511:: COP3, P100:: COP3. In some embodiments the recombinant *Listeria* phage is selected from phage comprising genomes comprising substantial homology to at least one phage selected from LP040::nluc, LP124::nluc, LP125::nluc, A511::nluc, P100::nluc, LP040::COP2, LP124:: COP2, LP125:: COP2, A511:: COP2, P100:: COP2, LP040::COP3, LP124:: COP3, LP125:: COP3, A511:: COP3, P100:: COP3.

[00122] In some embodiments the heterologous nucleic acid sequence encoding a marker is operatively linked in the recombinant phage genome to at least one regulatory element that is also heterologous to the phage genome. In some embodiments expression of the heterologous nucleic acid sequence encoding a marker in target bacteria is controlled exclusively by regulatory elements that are heterologous to the phage genome.

[00123] In some embodiments the heterologous nucleic acid sequence encoding a marker is operatively linked in the recombinant phage genome to at least one regulatory element that is endogenous to the phage genome. In other words, the heterologous nucleic acid sequence encoding a marker is operatively linked to the endogenous regulatory element by virtue of the location in the starting phage genome where the heterologous nucleic acid sequence encoding a marker is placed. In some embodiments expression of the heterologous nucleic acid sequence encoding a marker in target bacteria is controlled exclusively by regulatory elements that are endogenous to the phage genome. In some embodiments expression of the heterologous nucleic acid sequence encoding a marker in target bacteria is controlled in part by regulatory elements that are endogenous to the phage genome and in part by regulatory elements that are heterologous to the phage genome.

[00124] In some embodiments the recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker comprises more than one heterologous nucleic acid sequence encoding a marker. In some embodiments the recombinant phage comprises multiple copies of the same nucleic acid sequence encoding a marker (*i.e.*, copy encodes the same marker). In some embodiments the recombinant phage comprises copies of more than one type of nucleic acid sequence encoding a marker (*i.e.*, at least two copies encode different markers). In some embodiments the more than one copy are positioned at adjacent locations in the recombinant phage genome. In other embodiments at least one (up to all) of the more than one copy are located at non-adjacent locations in the recombinant phage genome.

[00125] In some embodiments the length of the heterologous nucleic acid sequence is at least 100 bases, at least 200 based, at least 300 bases, at least 400 bases, at least 500 bases, at least 600 bases, at least 700 bases, at least 800 bases, at least 900 bases, at least 1.0 kilobase (kb), at least 1.1 kb, at least 1.2 kb, at least 1.3 kb, at least 1.4 kb, at least 1.5 kb, at least 1.6 kb, at least 1.7 kb, at least 1.8 kb, at least 1.9 kb, at least 2.0 kb, at least 2.1 kb, at least 2.2 kb, at least 2.3 kb, at least 2.4 kb, at least 2.5 kb, at least 2.6 kb, at least 2.7 kb, at least 2.8 kb, at least 2.9 kb, at least 3.0 kb, at least 3.1 kb, at least 3.2 kb, at least 3.3 kb, at least 3.4 kb, at least 3.5 kb, at least 3.6 kb, at least 3.7 kb, at least 3.8 kb, at least 3.9 kb, at least 4.0 kb, at least 4.5 kb, at least 5.0 kb, at least 5.5 kb, at least 5.5 kb, at least 6.0 kb, at least 6.5 kb, at least 7.0 kb, at least 7.5 kb, at least 8.0 kb, at least 8.5 kb, at least 9.0 kb, at least 9.5 kb, at least 10 kb, or more. In some embodiments the length of the heterologous nucleic acid sequence is 500 bases or less, 1,0 kb or less, 1.5 kb or less, 2.0 kb or less, 2.5 kb or less, 3.0 kb or less, 3.5 kb or less, 4.0 kb or less, 4.5 kb or less, 5.0 kb or less, 5.5 kb or less, 6.0 kb or less, 6.5 kb or less, 7.0 kb or less, 7.5 kb or less, 8.0 kb or less, 8.5 kb or less, 9.0 kb or less, 9.5 kb or less, or 10.0 kb or less. In some such embodiments the heterologous nucleic acid sequence comprises a length that is less than the maximum length of heterologous nucleic acid sequence that can be packaged into a phage particle encoded by the phage genome and comprising the phage genome.

[00126] In some embodiments the length of the heterologous nucleic acid sequence is from 100 to 500 bases, from 200 to 1,000 bases, from 500 to 1,000 bases, from 500 to 1,500 bases, from 1 kb to 2 kb, from 1.5 kb to 2.5 kb, from 2.0 kb to 3.0 kb, from 2.5 kb to 3.5 kb, from 3.0 kb to 4.0 kb, from 3.5 kb to 4.5 kb, from 4.0 kb to 5.0 kb, from 4.5 kb to 5.5 kb, from 5.0 kb to 6.0 kb, from 5.5 kb to 6.5 kb, from 6.0 kb to 7.0 kb, from 6.5 kb to 7.5 kb, from 7.0 kb to 8.0 kb, from 7.5 kb to 8.5 kb, from 8.0 kb to 9.0 kb, from 8.5 kb to 9.5 kb, or from 9.0 kb to 10.0 kb.

[00127] In some embodiments the ratio of the length of the heterologous nucleic acid sequence to the total length of the genome of the recombinant phage is at least 0.05, at least 0.10, at least 0.15, at least 0.20, or at least 0.25. In some embodiments the ratio of the length of the genome of the recombinant phage to the length of the genome of the corresponding starting phage is at least 1.05, at least 1.10, at least 1.15, at least 1.20, or at least 1.25.

[00128] In some embodiments the heterologous nucleic acid sequence is inserted into the starting phage genome with no loss of endogenous starting phage genome sequence. In some embodiments the inserted heterologous nucleic acid sequence replaces endogenous starting

phage genome sequence. In some such embodiments the heterologous nucleic acid sequence replaces an amount of endogenous genomic sequence that is less than the length of the heterologous nucleic acid sequence. Thus, in such embodiments the length of the recombinant phage genome is longer than the length of the starting phage genome. In some such embodiments the heterologous nucleic acid sequence replaces an amount of endogenous genomic sequence that is greater than the length of the heterologous nucleic acid sequence. Thus, in such embodiments the length of the recombinant phage genome is shorter than the length of the starting phage genome. In some such embodiments the heterologous nucleic acid sequence replaces an amount of endogenous genomic sequence that is equal to the length of the heterologous nucleic acid sequence.

[00129] In some embodiments the protein or polypeptide encoded by a heterologous open reading frame is modified to reduce cleavage by proteases present in phage host cells. For example, computational algorithms can be used to identify known protease cleavage sites and the sequence of the open reading frame may be modified using conservative substitutions to remove these sites. Alternatively, directed mutagenesis is used to evolve the open reading frame sequence to encode a product that has an increased resistance to at least one protease present in a phage host cell or in the culture of a phage host cell.

[00130] This disclosure also provides isolated nucleic acids obtainable from a recombinant phage of this disclosure. In some embodiments the isolated nucleic acid is an isolated genome of a recombinant phage of this disclosure. In some embodiments the isolated nucleic acid comprises a fragment of less than the total genome of recombinant phage of this disclosure, the fragment comprising at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% of the genome of the recombinant phage. In some embodiments the isolated nucleic acid comprises a fragment of less than the total genome of recombinant phage of this disclosure, the fragment comprising at least 20 bp, at least 50 bp, at least 100bp, at least 500 bp, at least 1 kb, at least 2 kb, at least 3 kb, at least 4 kb, or at least 5 kb of the phage genome. In some embodiments the isolated nucleic acid comprises a fragment that is homologous to a fragment disclosed in this paragraph.

Phage Target Bacteria

[00131] The recombinant phage of this disclosure may be used to detect the presence of bacteria. Detection of target bacteria is based on the ability of the recombinant phage to bind to target bacteria, transfer of the phage genome into the target bacteria, and express the heterologous nucleic acid sequence encoding a marker by the bacteria. Accordingly, the specificity of a method of detecting target bacteria using recombinant phage comprising a heterologous nucleic acid sequence encoding a marker is based on the range of bacterial types that support expression of the marker following exposure to the phage. Sometimes the range of bacterial types that support expression of the marker following exposure to the phage is referred to herein as the "host range" of the phage. The set of bacterial types that make up the host range of the phage is sometimes referred to herein as "target bacteria" for the phage.

[00132] This disclosure provides novel methods of assessing phage host range and thus of defining target bacteria for a phage. In certain embodiments the methods comprise exposing a candidate type of bacteria to a phage in a liquid culture. The ability of the phage to cause clearing of the culture, which reflects infection and lysis of bacteria in the culture by the phage, is an indication that the bacteria in the culture are target bacteria of the phage. As demonstrated in the examples this method is surprisingly more accurate in assessing the true phage host range for a phage than prior art plate-based plaque assays. In some embodiments herein, the "host range" of a phage or the "target bacteria" of a phage are defined based on a set of bacteria that a phage can clear in a liquid culture-based assay.

[00133] While the liquid culture method is an improvement over prior methods and is very useful for many purposes, it does embody all aspects of methods of using a recombinant phage to detect target bacteria. Such methods rely on the ability of the recombinant phage to bind to target bacteria, transfer of the phage genome into the target bacteria, and expression of the heterologous nucleic acid sequence encoding a marker by the bacteria. Accordingly, even if a phage is unable to lyse a liquid culture of a particular bacterial cell type the phage may nonetheless be able to bind to the bacteria type, transfer the phage genome into the target bacteria, and thus cause expression of a heterologous nucleic acid sequence encoding a marker by the bacteria. Indeed, as demonstrated by the examples, assays that detect the presence of the marker in a type of bacteria following exposure to a recombinant phage are in some embodiments more sensitive even than liquid based host range assays. Accordingly, in some embodiments herein, the "host range" of a phage or the "target bacteria" of a phage are defined

by a process that comprises 1) providing a recombinant phage comprising a heterologous nucleic acid sequence encoding a marker; 2) exposing a sample to the phage; and 3) assaying for the presence of the marker in the exposed sample. This type of assay is sometimes referred to herein generally as a "marker host range assay." In some embodiments assaying for the presence of the marker in the exposed sample is by a method comprising detection of an mRNA. In some embodiments assaying for the presence of the marker in the exposed sample is by a method comprising direct detection of marker protein, such as using an antibody. In some embodiments assaying for the presence of the marker in the exposed sample is by a method comprising functional detection of marker protein. For example, if the marker protein is a luciferase the exposed sample may be exposed to luciferin and production of light may be assayed. This method may be adapted to any type of marker disclosed herein and skilled artisans are aware that many variations on the detection method of the marker may be used.

[00134] Certain variables may modify the host range of phage under certain conditions. Conditions that sustain constant bacterial growth and therefore maximal bacteriophage infectivity are seldom found in environments where methods of detecting bacteria are useful. Oligotrophic environments and competition among microorganisms force bacteria to be able to adapt quickly to rough and changing situations. A particular lifestyle composed of continuous cycles of growth and starvation is commonly referred to as feast and famine. Bacteria have developed many different mechanisms to survive in nutrient-depleted and harsh environments, varying from producing a more resistant vegetative cell to complex developmental programs. As a consequence of prolonged starvation, certain bacterial species enter a dynamic non-proliferative state in which continuous cycles of growth and death occur until 'better times' come, a.k.a. restoration of favorable growth conditions and with them the favorable infective condition.

[00135] The infectivity of bacteriophages is determined in part not only by the specificity of their encoded tail fiber recognition proteins, but also by the environmental conditions that are present. That includes but is not limited to the metabolic state of the bacterium the bacteriophage is capable of recognizing. Furthermore, it includes the chemical and physical composition of the environment that the bacteriophage and the bacterium experience when the phage contacts a bacterium. Environmental factors of the solution such as but not limited to pH,

osmolarity, temperature, rheological properties and others all may impact the ability of a bacteriophage to infect a bacterium.

[00136] To account for these variables, the step of exposing a sample of bacteria to a phage in the liquid clearing host-range assay and the marker host range assay may be conducted under defined conditions. The defined conditions may comprise at least one of: a defined time duration, a defined temperature, and the presence of at least one of a) at least one compound selected from carbohydrates and related compounds, b) at least compound selected from nitrogen containing compounds, c) at least compound selected from nucleic acids and related compounds, d) at least compound selected from lipid, e) at least one inorganic compound, and f) at least one organic compound.

[00137] In some embodiments the carbohydrates and related compounds are selected from sugars such as glucose, mannose, and maltose. In some embodiments the carbohydrates and related compounds are selected from carboxy sugars that are degraded by the pentose phosphate pathway, which may but need not generate more moles of NADPH per mole consumed as compared to glucose. In some embodiments the carbohydrates and related compounds are selected from compounds feeding into central metabolism, such as but not limited to a ketoglutarate, D-malic acid, or pyruvic acid. In some embodiments the carbohydrates and related compounds are selected from glycerol and other carbohydrate (or other) osmoprotectants that may but need not provide osmotic support to cells that exist in a potentially weakened or damaged state in the environment. In some embodiments glycerol functions as a volume excluder that increases the efficiency of phage infection. In some embodiments the carbohydrates and related compounds are selected from sugar alcohols, such as aminoethanol.

[00138] In some embodiments the nitrogen containing compounds are selected from ammonium, other amino acid building blocks, and free amino acids. The free amino acid may be any genome encoded standard amino acid or any non-standard amino acid. In some embodiments the amino acid is selected from glutamic acid and glutamine. In some embodiments the amino acid is selected from branched chain amino acids. In some embodiments the nitrogen containing compounds are selected from degradation products of branched amino acids such as propionic acid.

[00139] In some embodiments the nucleic acids and related compounds are selected from nucleotides, nucleosides, deoxynucleotides, and deoxynucleosides. In some embodiments the

nucleic acids and related compounds are selected from metabolites of the nucleotide generation pathways such as inosine.

[00140] In some embodiments the lipid compounds are selected from fatty acids and related compounds. Tween 20, 40, and 80 are converted to fatty acids upon ester hydrolysis and can also be used. In some embodiments the lipid compounds are selected from lecithin and related compounds.

[00141] In some embodiments the inorganic compounds are selected from salts, such as for example thiosulfate.

[00142] In some embodiments the organic compounds are selected from aliphatics, aromatics, heterocyclics, and non-biogenic polymers.

[00143] In some embodiments the at least one compound is selected from:

Compound	**CAS #**
1,2-Propanediol	57-55-6
2-Aminoethanol	141-43-5
Glucuronamide	3789-97-7
Tyramine	60-19-5
b-Phenylethylamine	156-28-5
L-Aspartic Acid	3792-50-5
L-Proline	147-85-3
D-Alanine	338-69-2
D-Serine	312-84-5
L-Glutamic Acid	6106-04-3
L-Asparagine	70-47-3
D-Aspartic Acid	1783-96-6
L-Glutamine	56-85-9
Gly-Asp	
D-Threonine	632-20-2
Gly-Glu	7412-78-4
L-Serine	56-45-1
L-Threonine	72-19-5
L-Alanine	56-41-7
Ala-Gly	687-69-4
Gly-Pro	704-15-4
L-Arabinose	87-72-9
N-Acetyl-D-Glucosamine	7512-17-6
D-Galactose	59-23-4
D-Trehalose	99-20-7
D-Mannose	3458-28-4

Dulcitol	608-66-2
D-Sorbitol	50-70-4
Glycerol	56-81-5
L-Fucose	2438-80-4
D,L-a-Glycerol Phosphate	3325-00-6
D-Xylose	58-86-6
D-Mannitol	69-65-8
D-Glucose-6-Phosphate	3671-99-6
D-Ribose	50-69-1
L-Rhamnose	3615-41-6
D-Fructose	57-48-7
a-D-Glucose	50-99-7
Maltose	69-79-4
D-Melibiose	585-99-9
Thymidine	50-89-5
a-Methyl-D-Galactoside	3396-99-4
a-D-Lactose	63-42-3
Lactulose	4618-18-2
Sucrose	57-50-1
Uridine	58-96-8
D-Glucose-1-Phosphate	56401-20-8
D-Fructose-6-Phosphate	26177-86-637250-85-4
b-Methyl-D-Glucoside	709-50-2
Adonitol	488-81-3
Maltotriose	1109-28-0
2'-Deoxyadenosine	16373-93-6
Adenosine	58-61-7
m-Inositol	87-89-8
D-Cellobiose	528-50-7
Inosine	58-63-9
N-Acetyl-D-Mannosamine	7772-94-3
D-Psicose	551-68-8
L-Lyxose	1949-78-6
D-Saccharic Acid	576-42-1
Succinic Acid	6106-21-4
D-Glucuronic Acid	14984-34-0
D-Gluconic Acid	527-07-1
D,L-Lactic Acid	312-85-6
Formic Acid	141-53-7
D-Galactonic Acid-g-Lactone	2782-07-2
D,L-Malic Acid	6915-15-7

Acetic Acid	127-09-3
D-Glucosaminic Acid	3646-68-2
a-Ketoglutaric Acid	22202-68-2
a-Ketobutyric Acid	2013-26-5
m-Tartaric Acid	147-73-9
a-Hydroxyglutaric Acid-g-Lactone	21461-84-7
a-Hydroxybutyric Acid	19054-57-0
Citric Acid	6132-04-3
Fumaric Acid	17013-01-3
Bromosuccinic Acid	923-06-8
Propionic Acid	137-40-6
Mucic Acid	526-99-8
Glycolic Acid	79-14-1
Glyoxylic Acid	563-96-2
Tricarballylic Acid	99-14-9
Acetoacetic Acid	3483-11-2
Mono-Methylsuccinate	3878-55-5
D-Malic Acid	636-61-3
L-Malic Acid	138-09-0
p-Hydroxyphenyl Acetic Acid	156-38-7
m-Hydroxyphenyl Acetic Acid	621-37-4
Pyruvic Acid	113-24-6
L-Galactonic Acid-g-Lactone	1668-08-2
D-Galacturonic Acid	91510-62-2
Methylpyruvate	600-22-6
Tween 20	9005-64-5
Tween 40	9005-66-7
Tween 80	9005-65-6

[00144] Another approach to modify the host range detected in a host range assay is to pretreat bacteria before exposing the bacterial samples to the phage. This allows for a decoupling of steps designed to modify the state of a bacterial cell (and possibly its susceptibility to phage infection) from conditions used for the infection itself. For example the metabolic rate may be increased during a pre-incubation step, which in turn may increase at least one of the replicative, transcriptive, and translative functions that influence clearing or production of a marker following infection of a bacterial cell by a phage. Furthermore, it is possible that such an incubation period also changes the surface receptor expression, or changes the composition of

the cell wall of the bacterium, which may also modify whether a phage can productively infect the bacteria.

[00145] Accordingly, in some embodiments samples of bacteria are incubated in metabolic stimulation conditions before exposure to the phage for the phage host range assay. In some embodiments exposure of the cells to metabolic stimulation conditions stimulates cell division in the cells. In some embodiments exposure of the cells to metabolic stimulation conditions does not stimulate cell division in the cells. In some embodiments, exposure of the cells to metabolic stimulation conditions stimulates at least one of the replicative, transcriptive, and translative functions that influence clearing or production of a marker following infection of a bacterial cell by a phage.

[00146] As used herein, "metabolic stimulation conditions" are conditions that promote development of a microorganism metabolic state in which the microorganism is permissive to infection and maintenance of a phage life cycle and/or infection followed by expression of a marker gene produce encoded by a heterologous nucleic acid sequence in the genome of the phage. In some embodiments the microorganism prior to exposure to the metabolic stimulation conditions is not permissive to infection and maintenance of a phage life cycle. In other embodiments the microorganism prior to exposure to the metabolic stimulation conditions is in a metabolic state that reduces its susceptibility to infection and maintenance of a phage life cycle compared to a comparable microorganism grown under log phase conditions. In such embodiments exposure of the microorganism to the metabolic stimulation conditions increases the susceptibility of the microorganism to infection and maintenance of a phage life cycle. In some embodiments metabolic stimulation conditions comprise at least one of a permissive temperature, pH, Po_2, and nutrient combination. In some embodiments the target microbe undergoes at least one cell division under metabolic stimulation conditions. In some embodiments the target microbe does not undergo at least one cell division under metabolic stimulation conditions.

[00147] In some embodiments the sample is exposed to metabolic stimulation conditions before the sample is contacted with a phage. In some such embodiments the sample is then removed from metabolic stimulation conditions prior to contacting with a phage while in other embodiments the sample is maintained under metabolic stimulation conditions when contacted by a phage. In some embodiments the sample is exposed to a first set of metabolic stimulation

conditions for a first period of time and then transferred to a second set of metabolic stimulation conditions. In some embodiments the recombinant phage is exposed to the sample while the sample is maintained under the second set of metabolic stimulation conditions. In some embodiments the sample is exposed to metabolic stimulation conditions for from 5 minutes to 24 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 5 minutes to 6 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 10 minutes to 6 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 20 minutes to 6 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 30 minutes to 6 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 1 to 6 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 2 to 6 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 2 to 12 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 3 to 12 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 6 to 12 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for from 12 to 24 hours before the sample is contacted by a phage. In some embodiments the sample is exposed to metabolic stimulation conditions for at least 10 minutes, at least 20 minutes, at least 30 minutes, at least 40 minutes, at least 50 minutes, at least 1 hour, at least 1.5 hours, or at least 2 hours.

[00148] By conducting a host range analysis under at least one embodiment of conditions described in this section it is possible to define conditions that provide a useful level of sensitivity and/or selectivity for a method of detecting target bacteria. In some embodiments the conditions used for the host range analysis are also used for methods of detecting target bacteria using the phage when those phage are used to detect target bacteria in other contexts (i.e., when testing environmental samples).

Methods of Detecting Target Bacteria

[00149] The recombinant phage are useful to detect target microbes. This disclosure provides exemplary recombinant phage and methods of making further recombinant phage. This disclosure also defines the target bacteria of certain disclosed recombinant phage and provides methods of identifying the target bacteria of any phage, including any recombinant phage. Accordingly, this disclosure enables methods of detecting target microbes using recombinant phage. By, among other things, enabling a detailed characterization of the target bacteria of the recombinant phage this disclosure in certain embodiments provides useful methods not available in the prior art.

[00150] The methods are broadly applicable and in view of the teachings of this disclosure skilled artisans will understand how to apply the methods to detect any type of archaea and/or bacteria. In some embodiments the archaea is a Euryarcheota. In some embodiments the archaea is a Crenarcheota. In some embodiments the bacteria is a member of a phyla selected from Actinobacteria, Aquificae, Armatimonadetes, Bacteroidetes, Caldiserica, Chlamydiae, Chloroflexi, Chrysiogenetes, Cyanobacteria, Deferribacteres, Deinococcus-Thermus, Dictyoglomi, Elusimicrobia, Fibrobacteres, Firmicutes, Fusobacteria, Gemmatimonadetes, Nitrospirae, Planctomycetes, Proteobacteria, Spirochaetes, Synergistets, Tenericutes, Thermodesulfobacteria, Thermotogae. In some embodiments the bacteria is at least one Firmicutes selected from Bacillus, Listeria, Staphylococcus. In some embodiments the bacteria is at least one Proteobacteria selected from Acidobacillus, Aeromonas, Burkholderia, Neisseria, Shewanella, Citrobacter, Enterobacter, Erwinia, Escherichia, Klebsiella, Kluyvera, Morganella, Shigella, Yersinia, Coxiella, Rickettsia, Legionella, Avibacterium, Haemophilus, Pasteurella, Acinetobacter, Moraxella, Pseudomonas, Vibrio, Xanthomonas. In some embodiments the bacteria is at least one Tenericutes selected from Mycoplasma, Spiroplasma, and Ureaplasma.

[00151] Common bacterial contaminates of food that are detected using the phage and methods disclosed herein include, without limitation, *E. coli* (including without limitation pathogenic *E. coli*, *E. coli* O157:H7, Shiga-toxin producing *E. coli*, *E. coli* O26, *E. coli* 111, *E. coli* O103, *E. coli* O121, *E. coli* O45 and *E. coli* O145), coliform bacteria (which include without limitation, *Citrobacter*, *Enterobacter*, *Hafnia*, *Klebsiella*, *Serratia*), *Shigella*, *Listeria*, *Clostridium* (including *Clostridium botulinum* and *Clostridium perfringens*), *Vibrio* (including *Vibrio cholera* and *Vibrio vulnificus*), *Enterobacteriacae*, *Staphylococcus* (including *Staphylococcus aureus* and *Staphylococcus epidermis*), *Bacillus* (including *Bacillus cereus*),

Campylobacter (including *Campylobacter jejuni*), *Pseudomonas*, *Streptococcus*, *Acinetobacter*, *Klebsiella*, *Campylobacter*, and *Yersinia*.

[00152] The methods comprise providing a sample; exposing the sample to at least a first type of recombinant phage capable of infecting at least a first set of target bacteria, comprising a heterologous nucleic acid sequence encoding at least a first marker and assay for the at least one first marker in the exposed sample. Preferably, the first type of recombinant phage comprises a heterologous nucleic acid sequence; a codon optimized at least first markers. In some embodiments, detection of the first marker in the sample indicates the presence of bacteria of the first set of target bacteria in the sample.

[00153] In certain embodiments the methods comprise providing a sample; exposing the sample to a first type of phage capable of infecting a first set of target bacteria and comprising a heterologous nucleic acid sequence encoding a first marker; exposing the sample to a second type of phage capable of infecting a second set of target bacteria and comprising a heterologous nucleic acid sequence encoding a second marker; and assaying for the presence of the first marker and the second marker in the exposed sample. In some embodiments, detection of the first marker in the sample indicates the presence of bacteria of the first set of target bacteria in the sample. In some embodiments, detection of the second marker in the sample indicates the presence of bacteria of the second set of target bacteria in the sample. In some embodiments the first marker and the second marker are the same, and detection of the marker in the sample indicates the presence of bacteria of at least one of the first set of target bacteria and the second set of target bacteria in the sample.

[00154] In some embodiments, the first set of target bacteria and the second set of target bacteria independently comprise at least two species of a single genus of bacteria. In some embodiments, the first set of target bacteria and the second set of target bacteria independently comprise at least three species of a single genus of bacteria. In some embodiments, the first set of target bacteria and the second set of target bacteria independently comprise at least four species of a single genus of bacteria. In some embodiments, the single genus of bacteria is *Listeria*. In some embodiments, the first set of target bacteria and the second set of target bacteria comprise at least one species of bacteria in common. In some embodiments, the first set of target bacteria and the second set of target bacteria comprise at least two species of bacteria in common. In some embodiments, the first set of target bacteria and the second set of target

bacteria comprise at least three species of bacteria in common. In some embodiments, the first set of target bacteria and the second set of target bacteria comprise at least four species of bacteria in common. In some embodiments, the species of *Listeria* are selected from *Listeria innocua*, *Listeria monocytogenes, Listeria seeligeri, Listeria ivanovii, Listeria marthii, Listeria rocourti* and *Listeria welshimeri*. In some embodiments, the species of *Listeria* are selected from *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, and *Listeria welshimeri*.

[00155] In some embodiments, the target bacteria comprise at least one sig B allelotype of *Listeria innocua* selected from 11, 22, 37, and 56. In some embodiments, the target bacteria comprise at least four allelotypes of *Listeria innocua*. In some embodiments, the at least four allelotypes of *Listeria innocua* are 11, 22, 37, and 56.

[00156] In some embodiments, the target bacteria comprise at least one ribotype of *Listeria monocytogenes* selected from DUP-10142, DUP-1030A, DUP-1030B, DUP-1038B, DUP-1039A, DUP-1039B, DUP-1039C, DUP-1042A, DUP-1042B, DUP-1042C, DUP-1043A, DUP-1044A, DUP-1044B, DUP-1044E, DUP-1045B, DUP-1052A, DUP-1053A, DUP-1062A, and DUP-1062D. In some embodiments, the target bacteria comprise at least nineteen ribotypes of *Listeria monocytogenes*. In some embodiments, the at least nineteen ribotypes of *Listeria monocytogenes* are DUP-10142, DUP-1030A, DUP-1030B, DUP-1038B, DUP-1039A, DUP-1039B, DUP-1039C, DUP-1042A, DUP-1042B, DUP-1042C, DUP-1043A, DUP-1044A, DUP-1044B, DUP-1044E, DUP-1045B, DUP-1052A, DUP-1053A, DUP-1062A, and DUP-1062D.

[00157] In some embodiments, the target bacteria comprise at least one sig B allelotype of *Listeria seeligeri* selected from 3, 20, 24, and 35. In some embodiments, the target bacteria comprise at least four allelotypes of *Listeria seeligeri*. In some embodiments, the at least four allelotypes of *Listeria seeligeri* are 3, 20, 24, and 35.

[00158] In some embodiments, the target bacteria comprise at least one sig B allelotype of *Listeria welshimeri* selected from 15, 27, 32, and 89. In some embodiments, the target bacteria comprise at least four allelotypes of *Listeria welshimeri*. In some embodiments, the at least four allelotypes of *Listeria welshimeri* are 15, 27, 32, and 89.

[00159] In some embodiments, the first set of target bacteria are all members of the same genus. In some embodiments, the second set of target bacteria are all members of the same genus. In some embodiments, all of the target bacteria are *Listeria*. In some embodiments, the target bacteria do not include at least one of *Bacillus cereus, Bacillus megaterium, Bacillus*

subtilis, Enterococcus durans, Enterococcus faceium, Enterococcus hirae, Kocuria varians, Kurthia gibsonii, Kurthia zopfii, Rhodococcus equi, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptococcus equi, Streptococcus galloyticus, Lactobacillus casei, Lactobacillus buchneri, Lactobacillus lactus, Lactobacillus fermentum, Micrococcus lutues, Pseudomonas protogens, Pseudomonas florescens, Aeromonas sp, Serratia liquefaciens, Serratia proteamaculans, Serratia liquefaciens, Bacillaceae bacterium, Serratia proteamaculans, Pseudomonas florescens, Pseudomonas poae, Pseudomonas sp, Pseudomonas fragi, Providencia alcalifaciens, Serratia sp, Serratia grimesii, Hafnia sp., Serratia proteamaculans, Pseudomonas florescens, Chryseobacterium sp., Pseudomonas fragi, and Enterobacteriaceae. In some embodiments, the target bacteria do not include Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Enterococcus durans, Enterococcus faceium, Enterococcus hirae, Kocuria varians, Kurthia gibsonii, Kurthia zopfii, Rhodococcus equi, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptococcus equi, Streptococcus galloyticus, Lactobacillus casei, Lactobacillus buchneri, Lactobacillus lactus, Lactobacillus fermentum, Micrococcus lutues, Pseudomonas protogens, Pseudomonas florescens, Aeromonas sp, Serratia liquefaciens, Serratia proteamaculans, Serratia liquefaciens, Bacillaceae bacterium, Serratia proteamaculans, Pseudomonas florescens, Pseudomonas poae, Pseudomonas sp, Pseudomonas fragi, Providencia alcalifaciens, Serratia sp, Serratia grimesii, Hafnia sp., Serratia proteamaculans, Pseudomonas florescens, Chryseobacterium sp., Pseudomonas fragi, and *Enterobacteriaceae*.

[00160] In some embodiments, the methods further comprise exposing the sample to a third type of phage capable of infecting a third set of target bacteria and comprising a heterologous nucleic acid sequence encoding a third marker. In some embodiments, the methods further comprise exposing the sample to a fourth type of phage capable of infecting a fourth set of target bacteria and comprising a heterologous nucleic acid sequence encoding a fourth marker. In some embodiments, the methods further comprise exposing the sample to a fifth type of phage capable of infecting a fifth set of target bacteria and comprising a heterologous nucleic acid sequence encoding a fifth marker. In some embodiments, the methods further comprise exposing the sample to a sixth type of phage capable of infecting a sixth set of target bacteria and comprising a heterologous nucleic acid sequence encoding a sixth marker. In some embodiments, the methods further comprise exposing the sample to a seventh type of phage

capable of infecting a seventh set of target bacteria and comprising a heterologous nucleic acid sequence encoding a seventh marker. In some embodiments, the methods further comprise exposing the sample to an eighth type of phage capable of infecting an eighth set of target bacteria and comprising a heterologous nucleic acid sequence encoding an eighth marker. In some embodiments, the methods further comprise exposing the sample to a ninth type of phage capable of infecting a ninth set of target bacteria and comprising a heterologous nucleic acid sequence encoding a ninth marker. In some embodiments, the methods further comprise exposing the sample to ten or more types of phage capable of infecting ten or more sets of target bacteria and comprising a heterologous nucleic acid sequences encoding ten or more markers. In some embodiments that utilize three or more types of phage, all of the three or more markers are different. In some embodiments that utilize three or more types of phage, all of the three or more markers are the same. In some embodiments that utilize three or more types of phage, two, three, four, five, six, seven, eight, or nine of the markers are the same.

[00161] In some embodiments, at least one type of phage used in the method is selected from A511, P100, LP40, LP48, LP99, LP101, LP124, LP125, and LP143, and derivatives thereof. In some embodiments, every type of phage used in the method is selected from A511, P100, LP40, LP48, LP99, LP101, LP124, LP125, and LP143, and derivatives thereof.

[00162] In some embodiments, the first marker is a screenable marker. In some embodiments, the first marker is a luciferase. In some embodiments, the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical to SEQ ID NO: 2. In some embodiments, the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical to SEQ ID NO: 4.

[00163] In some embodiments, the phage is selected from LP48::ffluc, LP99::ffluc, LP101::ffluc, LP124::ffluc, LP125::ffluc, LP143::ffluc, A511::ffluc, P100::ffluc, LP48:: COP2, LP99:: COP2, LP101:: COP2, LP124:: COP2, LP125:: COP2, LP143:: COP2, A511:: COP2, P100:: COP2, LP48:: COP3, LP99:: COP3, LP101:: COP3, LP124:: COP3, LP125:: COP3, LP143:: COP3, A511:: COP3, and P100:: COP3. In some embodiments, the phage is selected from LP40::nluc, LP124::nluc, LP125::nluc, A511::nluc, P100::nluc, LP40::COP2,

LP124::COP2, LP125:: COP2, A511:: COP2, P100:: COP2, LP40::COP3, LP124::COP3, LP125:: COP3, A511:: COP3, P100:: COP3.

[00164] In some embodiments, the sample is an environmental sample.

[00165] In some embodiments, the sample is an agricultural sample. In some embodiments the agricultural sample is stock feed or food supply. In some embodiments, the food supply is for human or non-human consumption. In some embodiments, the food supply is a plant or an animal.

[00166] In some embodiments, the agricultural sample in the composition is selected from a dairy product, a fruit product, a grain product, a sweet, a vegetable product, and a meat product. In some embodiments, the dairy product includes foods derived from milk products comprising milk, butter, yogurt, cheese, ice cream and queso fresco. In some embodiments, the fruit product comprises apple, oranges, bananas, berries and lemons. In some embodiments, the grain product comprises wheat, rice, oats, barley, bread and pasta. In some embodiments, the sweet product comprises candy, soft drinks, cake, and pie. In some embodiments, the vegetable product comprises spinach, carrots, onions, peppers, avocado and broccoli. In some embodiments, the vegetable product is guacamole. In some embodiments, the meat product comprises chicken, fish, turkey, pork and beef. In some embodiments, the meat product further comprises deli meats and ground meets, as well as deli turkey and ground beef.

[00167] In some embodiments, the food sample in the composition is selected from a dairy product, a fruit product, a grain product, a sweet, a vegetable product, and a meat product. In some embodiments, the dairy product includes foods derived from milk products comprising milk, butter, yogurt, cheese, ice cream and queso fresco. In some embodiments, the fruit product comprises apple, oranges, bananas, berries and lemons. In some embodiments, the grain product comprises wheat, rice, oats, barley, bread and pasta. In some embodiments, the sweet product comprises candy, soft drinks, cake, and pie. In some embodiments, the vegetable product comprises spinach, carrots, onions, peppers, avocado and broccoli. In some embodiments, the vegetable product is guacamole. In some embodiments, the meat product comprises chicken, fish, turkey, pork and beef. In some embodiments, the meat product further comprises deli meats and ground meets, as well as deli turkey and ground beef.

[00168] In some embodiments, the marker is detected in the sample, indicating the presence of bacteria of the first set of target bacteria in the sample.

[00169] In some embodiments, the target microbe of the method is selected from the group consisting of*coliform bacteria, Escherichia, Shigella, Listeria, Clostridium, Vibrio, Enterobacteriacae, Staphylococcus, Bacillus, Campylobacter, Pseudomonas, Streptococcus, Acinetobacter, Klebsiella, Cronobacter, Mycobacterium, Campylobacter*, and *Yersinia*. In some embodiments, the target microbe is *E. coli*. In some embodiments, the target microbe is *Listeria* selected from the group consisting of *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, *Listeria ivanovii, Listeria grayi, Listeria marthii, Listeria rocourti*, *Listeria welshimeri*, *Listeria floridensis, Listeria aquatic, Listeria fleischmannii, Listeria weihenstephanensis, Listeria cornellensis, Listeria riparia,* and *Listeria grandensis.*

[00170] In some embodiments, the second marker is a screenable marker. In some embodiments, the second marker is a luciferase. In some embodiments, the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical to SEQ ID NO: 2. In some embodiments, the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical to SEQ ID NO: 4.

[00171] In some embodiments, the second type of phage is selected from LP48::ffluc, LP99::ffluc, LP101::ffluc, LP124::ffluc, LP125::ffluc, LP143::ffluc, A511::ffluc, P100::ffluc, LP48::COP2, LP99::COP2, LP101::COP2, LP124::COP2, LP125::COP2, LP143::COP2, A511::COP2, P100::COP2, LP48::COP3, LP99::COP3, LP101::COP3, LP124::COP3, LP125::COP3, LP143::COP3, A511::COP3, P100::COP3. In some embodiments, the second type of phage is selected from LP40::nluc, LP124::nluc, LP125::nluc, A511::nluc, P100::nluc, LP40::COP2, LP124::COP2, LP125::COP2, A511::COP2, P100::COP2, LP40::COP3, LP124::COP3, LP125::COP3, A511::COP3, P100::COP3.

[00172] In some embodiments, the method comprises exposing the sample to the first type of phage and the second type of phage at the same time.

[00173] In some embodiments, the sample is an environmental sample.

[00174] In some embodiments, the first marker is detected in or on the sample, or *in situ*, indicating the presence of bacteria of the first set of target bacteria in or on the sample, or *in situ*. In some embodiments, the second marker is detected in the sample, indicating the presence of

bacteria of the second set of target bacteria in the sample. In some embodiments, the first marker and the second marker are the same, and the marker is detected in or on the sample, or *in situ*, indicating the presence of bacteria of at least one of the first set of target bacteria and the second set of target bacteria in or on the sample, or in the *in situ* location.

[00175] In some embodiments, the sample is exposed to metabolic stimulation conditions before it is exposed to the phage.

[00176] In some embodiments, the methods further comprise incubating the sample under metabolic stimulation conditions for a period of time before exposing the sample to the phage capable of infecting target bacteria.

[00177] In certain embodiments the methods comprise providing a sample; exposing the sample to at least one recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker, the recombinant *Listeria* phage selected from recombinant LP40 and derivatives thereof, recombinant LP48 and derivatives thereof, recombinant LP99 and derivatives thereof, recombinant LP101 and derivatives thereof, recombinant LP124 and derivatives thereof, recombinant LP125 and derivatives thereof, and recombinant LP143 and derivatives thereof; and assaying for the presence of the marker in the exposed sample. In some embodiments, the methods further comprise exposing the sample to at least one recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker, the recombinant *Listeria* phage selected from recombinant A511 and recombinant P100. In some embodiments, detection of the marker in the sample indicates the presence of *Listeria* in the sample.

[00178] In some embodiments, target bacteria of the recombinant Listeria phage comprise at least one species of Listeria selected from *Listeria innocua, Listeria monocytogenes, Listeria seeligeri, Listeria ivanovii, Listeria marthii, Listeria rocourti,* and *Listeria welshimeri*. In some embodiments, detection of the marker in the sample indicates the presence of the at least one species of *Listeria* selected from *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, *Listeria ivanovii*, *Listeria marthii*, *Listeria rocourti*, and *Listeria welshimeri* in the sample.

[00179] In some embodiments, target bacteria of the *Listeria* phage comprise at least one species of *Listeria* selected from *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, and *Listeria welshimeri*. In some embodiments, detection of the marker in the sample indicates

the presence of the at least one species of *Listeria* selected from *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, and *Listeria welshimeri* in the sample.

[00180] In some embodiments, target bacteria of the *Listeria* phage comprise at least one sig B allelotype of *Listeria innocua* selected from 11, 22, 37, and 56, and detection of the marker in the sample indicates the presence of at least one sig B allelotype of *Listeria innocua* selected from 11, 22, 37, and 56. In some embodiments, the at least one *Listeria* phage is capable of infecting *Listeria innocua* sig B allelotypes 11, 22, 37, and 56.

[00181] In some embodiments, target bacteria of the *Listeria* phage comprise at least one ribotype of *Listeria monocytogenes* selected from DUP-10142, DUP-1030A, DUP-1030B, DUP-1038B, DUP-1039A, DUP-1039B, DUP-1039C, DUP-1042A, DUP-1042B, DUP-1042C, DUP-1043A, DUP-1044A, DUP-1044B, DUP-1044E, DUP-1045B, DUP-1052A, DUP-1053A, DUP-1062A, and DUP-1062D; and detection of the marker in the sample indicates the presence of at least one ribotype of *Listeria monocytogenes* selected from DUP-10142, DUP-1030A, DUP-1030B, DUP-1038B, DUP-1039A, DUP-1039B, DUP-1039C, DUP-1042A, DUP-1042B, DUP-1042C, DUP-1043A, DUP-1044A, DUP-1044B, DUP-1044E, DUP-1045B, DUP-1052A, DUP-1053A, DUP-1062A, and DUP-1062D. In some embodiments, target bacteria of the *Listeria* phage comprise *Listeria monocytogenes* ribotypes DUP-10142, DUP-1030A, DUP-1030B, DUP-1038B, DUP-1039A, DUP-1039B, DUP-1039C, DUP-1042A, DUP-1042B, DUP-1042C, DUP-1043A, DUP-1044A, DUP-1044B, DUP-1044E, DUP-1045B, DUP-1052A, DUP-1053A, DUP-1062A, and DUP-1062D.

[00182] In some embodiments, target bacteria of the *Listeria* phage comprise at least one sig B allelotype of *Listeria seeligeri* selected from 3, 20, 24, and 35, and detection of the marker in the sample indicates the presence of at least one sig B allelotype of *Listeria seeligeri* selected from 3, 20, 24, and 35. In some embodiments, target bacteria of the *Listeria* phage comprise *Listeria seeligeri* sig B allelotypes 3, 20, 24, and 35.

[00183] In some embodiments, target bacteria of the *Listeria* phage comprise at least one sig B allelotype of *Listeria welshimeri* selected from 15, 27, 32, and 89, and detection of the marker in the sample indicates the presence of at least one sig B allelotype of *Listeria welshimeri* selected from 15, 27, 32, and 89. In some embodiments, target bacteria of the *Listeria* phage comprise *Listeria welshimeri* sig B allelotypes 15, 27, 32, and 89.

[00184] In some embodiments, the target bacteria comprise at least two species of *Listeria* selected from *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, and *Listeria welshimeri*. In some embodiments, the target bacteria comprise at least three species of *Listeria* selected from *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, and *Listeria welshimeri*. In some embodiments, the target bacteria comprise at least four species of Listeria selected from *Listeria innocua, Listeria monocytogenes, Listeria seeligeri, Listeria ivanovii, Listeria marthii, Listeria rocourti, and Listeria welshimeri*. In some embodiments, the target bacteria do not include at least one of *Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Enterococcus durans, Enterococcus faceium, Enterococcus hirae, Kocuria varians, Kurthia gibsonii, Kurthia zopfii, Rhodococcus equi, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptococcus equi, Streptococcus galloyticus, Lactobacillus casei, Lactobacillus buchneri, Lactobacillus lactus, Lactobacillus fermentum, Micrococcus lutues, Pseudomonas protogens, Pseudomonas florescens, Aeromonas sp, Serratia liquefaciens, Serratia proteamaculans, Serratia liquefaciens, Bacillaceae bacterium, Serratia proteamaculans, Pseudomonas florescens, Pseudomonas poae, Pseudomonas sp, Pseudomonas fragi, Providencia alcalifaciens, Serratia sp, Serratia grimesii, Hafnia sp., Serratia proteamaculans, Pseudomonas florescens, Chryseobacterium sp., Pseudomonas fragi, and Enterobacteriaceae. In some embodiments, the target bacteria do not include Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Enterococcus durans, Enterococcus faceium, Enterococcus hirae, Kocuria varians, Kurthia gibsonii, Kurthia zopfii, Rhodococcus equi, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptococcus equi, Streptococcus galloyticus, Lactobacillus casei, Lactobacillus buchneri, Lactobacillus lactus, Lactobacillus fermentum, Micrococcus lutues, Pseudomonas protogens, Pseudomonas florescens, Aeromonas sp, Serratia liquefaciens, Serratia proteamaculans, Serratia liquefaciens, Bacillaceae bacterium, Serratia proteamaculans, Pseudomonas florescens, Pseudomonas poae, Pseudomonas sp, Pseudomonas fragi, Providencia alcalifaciens, Serratia sp, Serratia grimesii, Hafnia sp., Serratia proteamaculans, Pseudomonas florescens, Chryseobacterium sp., Pseudomonas fragi,* and *Enterobacteriaceae*.

[00185] In some embodiments the sample is exposed to the phage for a period of time before assaying for the presence of a marker in the exposed sample is conducted. In some embodiments the period of time is from 1 minute to 24 hours, from 5 minutes to 12 hours, from 5

minutes to 6 hours, from 5 minutes to 3 hours, from 5 minutes to 2 hours, from 5 minutes to 1 hour, from 5 minutes to 50 minutes, from 5 minutes to 40 minutes, from 5 minutes to 30 minutes, from 5 minutes to 20 minutes, or from 5 minutes to 10 minutes. In some embodiments the period of time is from 1 to 2 hours, from 1 to 4 hours, or from 2 to 4 hours. In some embodiments the period of time is for at least 1 minute, at least 5 minutes, at least 10 minutes, at least 20 minutes, at least 30 minutes, at least 40 minutes, at least 50 minutes, or at least 1 hour.

[00186] In some embodiments any phage and/or parts of phage in the exposed sample are substantially removed before the assaying for the presence of a marker in the exposed sample is conducted.

[00187] In some embodiments of the methods of this disclosure, the methods further comprise comparing a detected level of marker in a test sample to at least one of a positive control and a negative control. The positive and/or negative control may be used to calibrate the assay including for the purpose of defining a positive result and/or a negative result.

Compositions

[00188] The methods of assaying phage host range provided herein allow, in certain embodiments, for the characterization of the host range of phage—and thus definition of target bacteria for phage—at a resolution not previously provided. One use of the methods and of phage characterized by the methods is to identify useful combinations of phage that may be used together in a system to detect target bacteria. In some embodiments such systems provide phage separately and the phage are then mixed before or during an assay. Alternatively, such systems comprise useful mixtures of phage, such as phage provided in a buffer for use in an assay. Compositions comprising useful combinations of phage are also, necessarily, produced during the assay in several embodiments. Accordingly, this disclosure also provides compositions that comprise phage.

[00189] In some embodiments the composition comprises: at least one recombinant Listeria phage comprising a heterologous nucleic acid sequence encoding a marker, the recombinant Listeria phage selected from recombinant A511 and derivatives thereof, recombinant P100 and derivatives thereof, recombinant LP40 and derivatives thereof, recombinant LP44 and derivatives thereof, recombinant LP48 and derivatives thereof, recombinant LP99 and derivatives thereof, recombinant LP101 and derivatives thereof,

recombinant LP124 and derivatives thereof, recombinant LP125 and derivatives thereof, and recombinant LP143 and derivatives thereof and at least one non-phage component selected from Table 5 and/or from at least one of a) at least one compound selected from carbohydrates and related compounds, b) at least compound selected from nitrogen containing compounds, c) at least compound selected from nucleic acids and related compounds, d) at least compound selected from lipid, e) at least one inorganic compound, and f) at least one organic compound. In some embodiments the composition comprises at least one of 1,2-Propanediol, 2-Aminoethanol, Glucuronamide, Tyramine, b-Phenylethylamine, L-Aspartic Acid, L-Proline, D-Alanine, D-Serine, L-Glutamic Acid, L-Asparagine, D-Aspartic Acid, L-Glutamine, Gly-Asp, D-Threonine, Gly-Glu, L-Serine, L-Threonine, L-Alanine, Ala-Gly, Gly-Pro, L-Arabinose, N-Acetyl-D-Glucosamine, D-Galactose, D-Trehalose, D-Mannose, Dulcitol, D-Sorbitol, Glycerol, L-Fucose, D,L-a-Glycerol, Phosphate, D-Xylose, D-Mannitol, D-Glucose-6-Phosphate, D-Ribose, L-Rhamnose, D-Fructose, a-D-Glucose, Maltose, D-Melibiose, Thymidine, a-Methyl-D-Galactoside, a-D-Lactose, Lactulosem Sucrose, Uridine, D-Glucose-1-Phosphate, D-Fructose-6-Phosphate, b-Methyl-D-Glucoside, Adonitol, Maltotriose, 2'-Deoxyadenosine, Adenosine, m-Inositol, D-Cellobiose, Inosine, N-Acetyl-D-Mannosamine, D-Psicose, L-Lyxose, D-Saccharic Acid, Succinic Acid, D-Glucuronic Acid, D-Gluconic Acid, D,L-Lactic Acid, Formic Acid, D-Galactonic Acid-g-Lactone, D,L-Malic Acid, Acetic Acid, D-Glucosaminic Acid, a-Ketoglutaric Acid, a-Ketobutyric Acid, m-Tartaric Acid, a-Hydroxyglutaric Acid-g-Lactone, a-Hydroxybutyric Acid, Citric Acid, Fumaric Acid, Bromosuccinic Acid, Propionic Acid, Mucic Acid, Glycolic Acid, Glyoxylic Acid, Tricarballylic Acid, Acetoacetic Acid, Mono-Methylsuccinate, D-Malic Acid, L-Malic Acid, p-Hydroxyphenyl Acetic Acid, m-Hydroxyphenyl Acetic Acid, Pyruvic Acid, L-Galactonic Acid-g-Lactone, D-Galacturonic Acid, Methylpyruvate, Tween 20, Tween 40, Tween 80.

[00190] In some embodiments the systems or compositions comprise at least two recombinant Listeria phage selected from recombinant LP40 and derivatives thereof, recombinant LP48 and derivatives thereof, recombinant LP99 and derivatives thereof, recombinant LP101 and derivatives thereof, recombinant LP124 and derivatives thereof, recombinant LP125 and derivatives thereof, and recombinant LP143 and derivatives thereof. In some embodiments the systems or compositions comprise at least three, four, five, six, seven, eight, nine, or more recombinant Listeria phage, selected from recombinant LP040 and

derivatives thereof, recombinant LP048 and derivatives thereof, recombinant LP99 and derivatives thereof, recombinant LP101 and derivatives thereof, recombinant LP124 and derivatives thereof, recombinant LP125 and derivatives thereof, and recombinant LP143 and derivatives thereof.

Articles of Manufacture

[00191] In some embodiments the system and or composition comprising at least one recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker is provided in the form of an article of manufacture. Such an article of manufacture is useful, for example, as a means to provide the at least one recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker in combination with other components that can be used together to perform an assay to detect target bacteria. In some embodiments the article of manufacture comprises at least one container comprising the at least one recombinant *Listeria* phage comprising a heterologous nucleic acid sequence encoding a marker.

[00192] In some embodiments the article of manufacture comprises at least one container comprising at least two recombinant *Listeria* phage selected from recombinant LP40 and derivatives thereof, recombinant LP48 and derivatives thereof, recombinant LP99 and derivatives thereof, recombinant LP101 and derivatives thereof, recombinant LP124 and derivatives thereof, recombinant LP125 and derivatives thereof, and recombinant LP143 and derivatives thereof. In some embodiments the systems or compositions comprise at least three, four, five, six, seven, eight, nine, or more recombinant *Listeria* phage, selected from recombinant LP40 and derivatives thereof, recombinant LP48 and derivatives thereof, recombinant LP99 and derivatives thereof, recombinant LP101 and derivatives thereof, recombinant LP124 and derivatives thereof, recombinant LP125 and derivatives thereof, and recombinant LP143 and derivatives thereof. In some embodiments in which the article of manufacture comprises more than one phage all of the phage are provided in separate containers. In other embodiments two or more of the phage are provided in combination in a single container.

[00193] The article of manufacture comprises at least one container comprising at least one recombinant phage selected from A511, P110, LP40, LP48, LP99, LP107, LP124, LP125 and LP143, and derivatives thereof. In some embodiments, the phage comprises a heterologous

nucleic acid sequence encoding a first marker. In some embodiments, the first marker is a screenable marker. In some embodiments, the first marker is a luciferase. In some embodiments, the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical to SEQ ID NO: 2. In some embodiments, the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical to SEQ ID NO: 4. In some embodiments, the luciferase is at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% or at least 99.9% identical to SEQ ID NO: 41. In some embodiments, the first type of phage is selected from LP48::ffluc, LP99::ffluc, LP101::ffluc, LP124::ffluc, LP125::ffluc, LP143::ffluc, A511::ffluc, P100::ffluc, LP48::COP2, LP99::COP2, LP101::COP2, LP124::COP2, LP125::COP2, LP143::COP2, A511::COP2, and P100::COP2, LP48::COP3, LP99::COP3, LP101::COP3, LP124::COP3, LP125::COP3, LP143::COP3, A511::COP3, and P100::COP3 and derivatives of those phage. In some embodiments, the first type of phage is selected from LP40::nluc, LP124::nluc, LP125::nluc, A511::nluc, and P100::nluc. In some embodiments, the first type of phage is selected from A511::COP2, LP124::COP2, LP40::COP2, LP125::COP2, A511::COP3, LP124::COP3, LP40::COP3, and LP125::COP3.

[00194] In some embodiments the article of manufacture further comprises an aqueous solution including one or more reagents from Table 5 and/or at least one non-phage component selected from at least one of a) at least one compound selected from carbohydrates and related compounds, b) at least compound selected from nitrogen containing compounds, c) at least compound selected from nucleic acids and related compounds, d) at least compound selected from lipid, e) at least one inorganic compound, and f) at least one organic compound. In some embodiments, the article of manufacture comprises a container comprising a solution comprising at least one of 1,2-Propanediol, 2-Aminoethanol, Glucuronamide, Tyramine, b-Phenylethylamine, L-Aspartic Acid, L-Proline, D-Alanine, D-Serine, L-Glutamic Acid, L-Asparagine, D-Aspartic Acid, L-Glutamine, Gly-Asp, D-Threonine, Gly-Glu, L-Serine, L-Threonine, L-Alanine, Ala-Gly, Gly-Pro, L-Arabinose, N-Acetyl-D-Glucosamine, D-Galactose, D-Trehalose, D-Mannose, Dulcitol, D-Sorbitol, Glycerol, L-Fucose, D,L-a-Glycerol, Phosphate,

D-Xylose, D-Mannitol, D-Glucose-6-Phosphate, D-Ribose, L-Rhamnose, D-Fructose, a-D-Glucose, Maltose, D-Melibiose, Thymidine, a-Methyl-D-Galactoside, a-D-Lactose, Lactulosem Sucrose, Uridine, D-Glucose-1-Phosphate, D-Fructose-6-Phosphate, b-Methyl-D-Glucoside, Adonitol, Maltotriose, 2'-Deoxyadenosine, Adenosine, m-Inositol, D-Cellobiose, Inosine, N-Acetyl-D-Mannosamine, D-Psicose, L-Lyxose, D-Saccharic Acid, Succinic Acid, D-Glucuronic Acid, D-Gluconic Acid, D,L-Lactic Acid, Formic Acid, D-Galactonic Acid-g-Lactone, D,L-Malic Acid, Acetic Acid, D-Glucosaminic Acid, a-Ketoglutaric Acid, a-Ketobutyric Acid, m-Tartaric Acid, a-Hydroxyglutaric Acid-g-Lactone, a-Hydroxybutyric Acid, Citric Acid, Fumaric Acid, Bromosuccinic Acid, Propionic Acid, Mucic Acid, Glycolic Acid, Glyoxylic Acid, Tricarballylic Acid, Acetoacetic Acid, Mono-Methylsuccinate, D-Malic Acid, L-Malic Acid, p-Hydroxyphenyl Acetic Acid, m-Hydroxyphenyl Acetic Acid, Pyruvic Acid, L-Galactonic Acid-g-Lactone, D-Galacturonic Acid, Methylpyruvate, Tween 20, Tween 40, Tween 80. In some embodiments at least one recombinant *Listeria* phage present in the article of manufacture is present in the aqueous solution comprising at least one non-phage component. In other embodiments the phage and solution are provided separately and may, for example, be combined by a user.

[00195] In another embodiment, the article of manufacture includes a substrate for a light reaction, or other required component for the marker to operate. By way of non-limiting example, the substrate is luciferin.

[00196] In another embodiment, the article of manufacture includes an additional aqueous solution that is optimized for a light reaction, or that provides conditions that are optimal for detection of a marker.

[00197] In some embodiments, the article of manufacture is a kit. The kit may further comprise instructions for performing one or more of the assays described herein.

Definitions

[00198] It is to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting. It must be noted that, as used in the specification and the appended claims, the singular forms “a,” “an” and “the” include plural referents unless the context clearly dictates otherwise.

[00199] The methods and techniques of the present disclosure are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification unless otherwise indicated. See, e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 3d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (2001); Ausubel et al., *Current Protocols in Molecular Biology*, Greene Publishing Associates (1992, and Supplements to 2002); Taylor and Drickamer, *Introduction to Glycobiology*, Oxford Univ. Press (2003); *Worthington Enzyme Manual*, Worthington Biochemical Corp., Freehold, N.J.; *Handbook of Biochemistry: Section A Proteins*, Vol I, CRC Press (1976); *Handbook of Biochemistry: Section A Proteins*, Vol II, CRC Press (1976); *Essentials of Glycobiology*, Cold Spring Harbor Laboratory Press (1999). Many molecular biology and genetic techniques applicable to phage are described in Clokie *et al.*, *Bacteriophages: Methods and Protocols*, Vols. 1 and 2 (*Methods in Molecular Biology*, Vols. 501 and 502), Humana Press, New York, N.Y. (2009), which is hereby incorporated herein by reference.

[00200] This disclosure refers to sequence database entries (e.g., UniProt/SwissProt or GENBANK records) for certain amino acid and nucleic acid sequences that are published on the internet, as well as other information on the internet. The skilled artisan understands that information on the internet, including sequence database entries, is updated from time to time and that, for example, the reference number used to refer to a particular sequence can change. Where reference is made to a public database of sequence information or other information on the internet, it is understood that such changes can occur and particular embodiments of information on the internet can come and go. Because the skilled artisan can find equivalent information by searching on the internet, a reference to an internet web page address or a sequence database entry evidences the availability and public dissemination of the information in question.

[00201] The term "comprising" as used herein is synonymous with "including" or "containing", and is inclusive or open-ended and does not exclude additional, unrecited members, elements or method steps. By "consisting of" is meant including, and limited to, whatever follows the phrase "consisting of" Thus, the phrase "consisting of" indicates that the listed elements are required or mandatory, and that no other elements may be present. By "consisting essentially of" is meant including any elements listed after the phrase, and limited to

other elements that do not interfere with or contribute to the activity or action specified in the disclosure for the listed elements. Thus, the phrase "consisting essentially of" indicates that the listed elements are required or mandatory, but that other elements are optional and may or may not be present depending upon whether or not they materially affect the activity or action of the listed elements.

[00202] As used herein, the term "in vitro" refers to events that occur in an artificial environment, e.g., in a test tube or reaction vessel, in cell culture, in a Petri dish, etc., rather than within an organism (e.g., animal, plant, or microbe).

[00203] As used herein, the term "in vivo" refers to events that occur within an organism (e.g., animal, plant, or microbe). An assay that occurs at least in part in vivo within a microbe may nonetheless occur in vitro if parts of the assay occur outside of the microbe in culture, for example.

[00204] As used herein, the term "isolated" refers to a substance or entity that has been (1) separated from at least some of the components with which it was associated when initially produced (whether in nature or in an experimental setting), and/or (2) produced, prepared, and/or manufactured by the hand of man. Isolated substances and/or entities may be separated from at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, or more of the other components with which they were initially associated. In some embodiments, isolated agents are more than about 80%, about 85%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or more than about 99% pure. As used herein, a substance is "pure" if it is substantially free of other components.

[00205] The term "peptide" as used herein refers to a short polypeptide, e.g., one that typically contains less than about 50 amino acids and more typically less than about 30 amino acids. The term as used herein encompasses analogs and mimetics that mimic structural and thus biological function.

[00206] The term "polypeptide" encompasses both naturally-occurring and non-naturally occurring proteins, and fragments, mutants, derivatives and analogs thereof. A polypeptide may be monomeric or polymeric. Further, a polypeptide may comprise a number of different domains each of which has one or more distinct activities. For the avoidance of doubt, a "polypeptide" may be any length greater two amino acids.

[00207] The term "isolated protein" or "isolated polypeptide" is a protein or polypeptide that by virtue of its origin or source of derivation (1) is not associated with naturally associated components that accompany it in its native state, (2) exists in a purity not found in nature, where purity can be adjudged with respect to the presence of other cellular material (e.g., is free of other proteins from the same species) (3) is expressed by a cell from a different species, or (4) does not occur in nature (e.g., it is a fragment of a polypeptide found in nature or it includes amino acid analogs or derivatives not found in nature or linkages other than standard peptide bonds). Thus, a polypeptide that is chemically synthesized or synthesized in a cellular system different from the cell from which it naturally originates will be "isolated" from its naturally associated components. A polypeptide or protein may also be rendered substantially free of naturally associated components by isolation, using protein purification techniques well known in the art. As thus defined, "isolated" does not necessarily require that the protein, polypeptide, peptide or oligopeptide so described has been physically removed from a cell in which it was synthesized.

[00208] The term "polypeptide fragment" as used herein refers to a polypeptide that has a deletion, e.g., an amino-terminal and/or carboxy-terminal deletion compared to a full-length polypeptide, such as a naturally occurring protein. In an embodiment, the polypeptide fragment is a contiguous sequence in which the amino acid sequence of the fragment is identical to the corresponding positions in the naturally-occurring sequence. Fragments typically are at least 5, 6, 7, 8, 9 or 10 amino acids long, or at least 12, 14, 16 or 18 amino acids long, or at least 20 amino acids long, or at least 25, 30, 35, 40 or 45, amino acids, or at least 50 or 60 amino acids long, or at least 70 amino acids long.

[00209] The term "fusion protein" refers to a polypeptide comprising a polypeptide or fragment coupled to heterologous amino acid sequences. Fusion proteins are useful because they can be constructed to contain two or more desired functional elements that can be from two or more different proteins. A fusion protein comprises at least 10 contiguous amino acids from a polypeptide of interest, or at least 20 or 30 amino acids, or at least 40, 50 or 60 amino acids, or at least 75, 100 or 125 amino acids. The heterologous polypeptide included within the fusion protein is usually at least 6 amino acids in length, or at least 8 amino acids in length, or at least 15, 20, or 25 amino acids in length. Fusions that include larger polypeptides, such as an IgG Fc region, and even entire proteins, such as the green fluorescent protein ("GFP") chromophore-

containing proteins, have particular utility. Fusion proteins can be produced recombinantly by constructing a nucleic acid sequence which encodes the polypeptide or a fragment thereof in frame with a nucleic acid sequence encoding a different protein or peptide and then expressing the fusion protein. Alternatively, a fusion protein can be produced chemically by crosslinking the polypeptide or a fragment thereof to another protein.

[00210] As used herein, a protein has "homology" or is "homologous" to a second protein if the nucleic acid sequence that encodes the protein has a similar sequence to the nucleic acid sequence that encodes the second protein. Alternatively, a protein has homology to a second protein if the two proteins have similar amino acid sequences. (Thus, the term "homologous proteins" is defined to mean that the two proteins have similar amino acid sequences.) As used herein, homology between two regions of amino acid sequence (especially with respect to predicted structural similarities) is interpreted as implying similarity in function.

[00211] When "homologous" is used in reference to proteins or peptides, it is recognized that residue positions that are not identical often differ by conservative amino acid substitutions. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of homology may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well known to those of skill in the art. See, e.g., Pearson, 1994, Methods Mol. Biol. 24:307-31 and 25:365-89.

[00212] The following six groups each contain amino acids that are conservative substitutions for one another: 1) Serine, Threonine; 2) Aspartic Acid, Glutamic Acid; 3) Asparagine, Glutamine; 4) Arginine, Lysine; 5) Isoleucine, Leucine, Methionine, Alanine, Valine, and 6) Phenylalanine, Tyrosine, Tryptophan.

[00213] Sequence homology for polypeptides, which is also referred to as percent sequence identity, is typically measured using sequence analysis software. See, e.g., the Sequence Analysis Software Package of the Genetics Computer Group (GCG), University of Wisconsin Biotechnology Center, 910 University Avenue, Madison, Wis. 53705. Protein analysis software matches similar sequences using a measure of homology assigned to various

substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG contains programs such as "Gap" and "Bestfit" which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organisms or between a wild-type protein and a mutein thereof. See, e.g., GCG Version 6.1.

[00214] An exemplary algorithm when comparing a particular polypeptide sequence to a database containing a large number of sequences from different organisms is the computer program BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990); Gish and States, Nature Genet. 3:266-272 (1993); Madden et al., Meth. Enzymol. 266:131-141 (1996); Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997); Zhang and Madden, Genome Res. 7:649-656 (1997)), especially blastp or tblastn (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)).

[00215] Exemplary parameters for BLASTp are: Expectation value: 10 (default); Filter: seg (default); Cost to open a gap: 11 (default); Cost to extend a gap: 1 (default); Max. alignments: 100 (default); Word size: 11 (default); No. of descriptions: 100 (default); Penalty Matrix: BLOWSUM62. The length of polypeptide sequences compared for homology will generally be at least about 16 amino acid residues, or at least about 20 residues, or at least about 24 residues, or at least about 28 residues, or more than about 35 residues. When searching a database containing sequences from a large number of different organisms, it may be useful to compare amino acid sequences. Database searching using amino acid sequences can be measured by algorithms other than blastp known in the art. For instance, polypeptide sequences can be compared using FASTA, a program in GCG Version 6.1. FASTA provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences. Pearson, Methods Enzymol. 183:63-98 (1990). For example, percent sequence identity between amino acid sequences can be determined using FASTA with its default parameters (a word size of 2 and the PAM250 scoring matrix), as provided in GCG Version 6.1, herein incorporated by reference.

[00216] In some embodiments, polymeric molecules (e.g., a polypeptide sequence or nucleic acid sequence) are considered to be "homologous" to one another if their sequences are at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at

least 98% or at least 99% identical. In some embodiments, polymeric molecules are considered to be "homologous" to one another if their sequences are at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% similar. The term "homologous" necessarily refers to a comparison between at least two sequences (nucleotides sequences or amino acid sequences). In some embodiments, two nucleotide sequences are considered to be homologous if the polypeptides they encode are at least about 50% identical, at least about 60% identical, at least about 70% identical, at least about 80% identical, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical for at least one stretch of at least about 20 amino acids. In some embodiments, homologous nucleotide sequences are characterized by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. Both the identity and the approximate spacing of these amino acids relative to one another must be considered for nucleotide sequences to be considered homologous. In some embodiments of nucleotide sequences less than 60 nucleotides in length, homology is determined by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. In some embodiments, two protein sequences are considered to be homologous if the proteins are at least about 50% identical, at least about 60% identical, at least about 70% identical, at least about 80% identical, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical for at least one stretch of at least about 20 amino acids.

[00217] As used herein, a "modified derivative" refers to polypeptides or fragments thereof that are substantially homologous in primary structural sequence to a reference polypeptide sequence but which include, e.g., in vivo or in vitro chemical and biochemical modifications or which incorporate amino acids that are not found in the reference polypeptide. Such modifications include, for example, acetylation, carboxylation, phosphorylation, glycosylation, ubiquitination, labeling, e.g., with radionuclides, and various enzymatic modifications, as will be readily appreciated by those skilled in the art. A variety of methods for labeling polypeptides and of substituents or labels useful for such purposes are well known in the art, and include radioactive isotopes such as ^{125}I, ^{32}P, ^{35}S, and ^{3}H, ligands that bind to labeled

antiligands (e.g., antibodies), fluorophores, chemiluminescent agents, enzymes, and antiligands that can serve as specific binding pair members for a labeled ligand. The choice of label depends on the sensitivity required, ease of conjugation with the primer, stability requirements, and available instrumentation. Methods for labeling polypeptides are well known in the art. See, e.g., Ausubel et al., Current Protocols in Molecular Biology, Greene Publishing Associates (1992, and Supplements to 2002).

[00218] As used herein, "polypeptide mutant" or "mutein" refers to a polypeptide whose sequence contains an insertion, duplication, deletion, rearrangement or substitution of one or more amino acids compared to the amino acid sequence of a reference protein or polypeptide, such as a native or wild-type protein. A mutein may have one or more amino acid point substitutions, in which a single amino acid at a position has been changed to another amino acid, one or more insertions and/or deletions, in which one or more amino acids are inserted or deleted, respectively, in the sequence of the reference protein, and/or truncations of the amino acid sequence at either or both the amino or carboxy termini. A mutein may have the same or a different biological activity compared to the reference protein.

[00219] In some embodiments, a mutein has, for example, at least 70% overall sequence homology to its counterpart reference polypeptide or protein. In some embodiments, a mutein has at least 75%, at least 80%, at least 85%, or at least 90% overall sequence homology to the wild-type protein or polypeptide. In other embodiments, a mutein exhibits at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% at least 99.5%, at least 99.9% sequence identity, or 98%, or 99%, or 99.5% or 99.9% overall sequence identity.

[00220] As used herein, "recombinant" refers to a biomolecule, e.g., a gene or protein, that (1) is not associated with all or a portion of a polynucleotide in which the gene is found in nature, (2) is operatively linked to a polynucleotide which it is not linked to in nature, or (3) does not occur in nature. Preferably, "recombinant" refers to a biomolecule that does not occur in nature. The term "recombinant" can be used in reference to cloned DNA isolates, chemically synthesized polynucleotide analogs, or polynucleotide analogs that are biologically synthesized by heterologous systems, as well as proteins and/or mRNAs encoded by such nucleic acids. Thus, for example, a protein synthesized by a microorganism is recombinant, for example, if it is synthesized from an mRNA synthesized from a recombinant gene present in the cell. A phage is

"recombinant" if it comprises a recombinant biomolecule. Preferably, a phage is "recombinant" if it comprises a recombinant biomolecule that does not occur in nature. Thus, for example and without limitation, a phage is recombinant if the genome of the phage comprises a recombinant nucleic acid sequence.

[00221] The term "polynucleotide", "nucleic acid molecule", "nucleic acid", or "nucleic acid sequence" refers to a polymeric form of nucleotides of at least 10 bases in length. The term includes DNA molecules (e.g., cDNA or genomic or synthetic DNA) and RNA molecules (e.g., mRNA or synthetic RNA), as well as analogs of DNA or RNA containing non-natural nucleotide analogs, non-native internucleoside bonds, or both. The nucleic acid can be in any topological conformation. For instance, the nucleic acid can be single-stranded, double-stranded, triple-stranded, quadruplexed, partially double-stranded, branched, hairpinned, circular, or in a padlocked conformation. The nucleic acid (also referred to as polynucleotides) may include both sense and antisense strands of RNA, cDNA, genomic DNA, and synthetic forms and mixed polymers of the above. They may be modified chemically or biochemically or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those of skill in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages (e.g., methyl phosphonates, phosphotriesters, phosphoramidates, carbamates, etc.), charged linkages (e.g., phosphorothioates, phosphorodithioates, etc.), pendent moieties (e.g., polypeptides), intercalators (e.g., acridine, psoralen, etc.), chelators, alkylators, and modified linkages (e.g., alpha anomeric nucleic acids, etc.) Also included are synthetic molecules that mimic polynucleotides in their ability to bind to a designated sequence via hydrogen bonding and other chemical interactions. Such molecules are known in the art and include, for example, those in which peptide linkages substitute for phosphate linkages in the backbone of the molecule. Other modifications can include, for example, analogs in which the ribose ring contains a bridging moiety or other structure such as the modifications found in "locked" nucleic acids.

[00222] A "synthetic" RNA, DNA or a mixed polymer is one created outside of a cell, for example one synthesized chemically.

[00223] The term "nucleic acid fragment" as used herein refers to a nucleic acid sequence that has a deletion, e.g., a 5'-terminal or 3'-terminal deletion compared to a full-length reference nucleotide sequence. In an embodiment, the nucleic acid fragment is a contiguous sequence in

which the nucleotide sequence of the fragment is identical to the corresponding positions in the naturally-occurring sequence. In some embodiments, fragments are at least 10, 15, 20, or 25 nucleotides long, or at least 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 nucleotides long. In some embodiments a fragment of a nucleic acid sequence is a fragment of an open reading frame sequence. In some embodiments such a fragment encodes a polypeptide fragment (as defined herein) of the protein encoded by the open reading frame nucleotide sequence.

[00224] As used herein, an endogenous nucleic acid sequence in the genome of an organism (including a phage) (or the encoded protein product of that sequence) is deemed "recombinant" herein if a heterologous sequence is placed adjacent to the endogenous nucleic acid sequence, such that the expression of this endogenous nucleic acid sequence is altered. In this context, a heterologous sequence is a sequence that is not naturally adjacent to the endogenous nucleic acid sequence, whether or not the heterologous sequence is itself endogenous (originating from the same host cell or progeny thereof) or exogenous (originating from a different host cell or progeny thereof). By way of example, a promoter sequence can be substituted (e.g., by homologous recombination) for the native promoter of a gene in the genome of a host cell, such that this gene has an altered expression pattern. This gene would now become "recombinant" because it is separated from at least some of the sequences that naturally flank it.

[00225] A nucleic acid is also considered "recombinant" if it contains any modifications that do not naturally occur to the corresponding nucleic acid in a genome. For instance, an endogenous coding sequence is considered "recombinant" if it contains an insertion, deletion or a point mutation introduced artificially, e.g., by human intervention. A "recombinant nucleic acid" also includes a nucleic acid integrated into a host cell chromosome at a heterologous site and a nucleic acid construct present as an episome. With reference to a phage, a "recombinant phage genome" is a phage genome that contains an insertion, deletion or a point mutation introduced artificially, e.g., by human intervention and does not occur in nature.

[00226] As used herein, the phrase "degenerate variant" of a reference nucleic acid sequence encompasses nucleic acid sequences that can be translated, according to the standard genetic code, to provide an amino acid sequence identical to that translated from the reference nucleic acid sequence. The term "degenerate oligonucleotide" or "degenerate primer" is used to signify an oligonucleotide capable of hybridizing with target nucleic acid sequences that are not

necessarily identical in sequence but that are homologous to one another within one or more particular segments.

[00227] The term "percent sequence identity" or "identical" in the context of nucleic acid sequences refers to the residues in the two sequences which are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over a stretch of at least about nine nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about 32, and even more typically at least about 36 or more nucleotides. There are a number of different algorithms known in the art which can be used to measure nucleotide sequence identity. For instance, polynucleotide sequences can be compared using FASTA, Gap or Bestfit, which are programs in Wisconsin Package Version 10.0, Genetics Computer Group (GCG), Madison, Wis. FASTA provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences. Pearson, Methods Enzymol. 183:63-98 (1990). For instance, percent sequence identity between nucleic acid sequences can be determined using FASTA with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) or using Gap with its default parameters as provided in GCG Version 6.1, herein incorporated by reference. Alternatively, sequences can be compared using the computer program, BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990); Gish and States, Nature Genet. 3:266-272 (1993); Madden et al., Meth. Enzymol. 266:131-141 (1996); Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997); Zhang and Madden, Genome Res. 7:649-656 (1997)), especially blastp or tblastn (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)).

[00228] The term "substantial homology" or "substantial similarity," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% of the nucleotide bases, as measured by any well-known algorithm of sequence identity, such as FASTA, BLAST or Gap, as discussed above.

[00229] Alternatively, substantial homology or similarity exists when a nucleic acid or fragment thereof hybridizes to another nucleic acid, to a strand of another nucleic acid, or to the complementary strand thereof, under stringent hybridization conditions. "Stringent hybridization conditions" and "stringent wash conditions" in the context of nucleic acid hybridization

experiments depend upon a number of different physical parameters. Nucleic acid hybridization will be affected by such conditions as salt concentration, temperature, solvents, the base composition of the hybridizing species, length of the complementary regions, and the number of nucleotide base mismatches between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art. One having ordinary skill in the art knows how to vary these parameters to achieve a particular stringency of hybridization.

[00230] In general, "stringent hybridization" is performed at about 25°C below the thermal melting point (Tm) for the specific DNA hybrid under a particular set of conditions. "Stringent washing" is performed at temperatures about 5°C lower than the Tm for the specific DNA hybrid under a particular set of conditions. The Tm is the temperature at which 50% of the target sequence hybridizes to a perfectly matched probe. See Sambrook et al., Molecular Cloning: A Laboratory Manual, 2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989), page 9.51. For purposes herein, "stringent conditions" are defined for solution phase hybridization as aqueous hybridization (i.e., free of formamide) in 6xSSC (where 20xSSC contains 3.0 M NaC1 and 0.3 M sodium citrate), 1% SDS at 65°C for 8-12 hours, followed by two washes in 0.2xSSC, 0.1% SDS at 65°C for 20 minutes. It will be appreciated by the skilled worker that hybridization at 65°C will occur at different rates depending on a number of factors including the length and percent identity of the sequences which are hybridizing.

[00231] As used herein, an "expression control sequence" refers to polynucleotide sequences that affect the expression of coding sequences to which they are operatively linked. Expression control sequences are sequences that control the transcription, post-transcriptional events and translation of nucleic acid sequences. Expression control sequences include appropriate transcription initiation, termination, promoter and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (e.g., ribosome binding sites); sequences that enhance protein stability; and when desired, sequences that enhance protein secretion. The nature of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include promoter, ribosomal binding site, and transcription termination sequence. The term "control sequences" is intended to encompass, at a minimum, any component whose presence is essential for expression, and can also encompass an

additional component whose presence is advantageous, for example, leader sequences and fusion partner sequences.

[00232] As used herein, "operatively linked" or "operably linked" expression control sequences refers to a linkage in which the expression control sequence is contiguous with the gene of interest to control the gene of interest, as well as expression control sequences that act in trans or at a distance to control the gene of interest.

[00233] As used herein, a "vector" is intended to refer to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid," which generally refers to a circular double stranded DNA loop into which additional DNA segments may be ligated, but also includes linear double-stranded molecules such as those resulting from amplification by the polymerase chain reaction (PCR) or from treatment of a circular plasmid with a restriction enzyme. Other vectors include cosmids, bacterial artificial chromosomes (BAC) and yeast artificial chromosomes (YAC). Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome (discussed in more detail below). Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., vectors having an origin of replication which functions in the host cell). Other vectors can be integrated into the genome of a host cell upon introduction into the host cell, and are thereby replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "recombinant expression vectors" (or simply "expression vectors").

[00234] The term "recombinant host cell" (or simply "recombinant cell" or "host cell"), as used herein, is intended to refer to a cell into which a recombinant nucleic acid such as a recombinant vector has been introduced. In some instances the word "cell" is replaced by a name specifying a type of cell. For example, a "recombinant microorganism" is a recombinant host cell that is a microorganism host cell. It should be understood that such terms are intended to refer not only to the particular subject cell but to the progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term "recombinant host cell," "recombinant cell," and "host cell", as used

herein. A recombinant host cell may be an isolated cell or cell line grown in culture or may be a cell which resides in a living tissue or organism.

[00235] As used herein, "bacteriophage" refers to a virus that infects bacteria. Similarly, "archaeophage" refers to a virus that infects archaea. The term "phage" is used to refer to both types of viruses but in certain instances as indicated by the context may also be used as shorthand to refer to a bacteriophage or archaeophage specifically. Bacteriophage and archaeophage are obligate intracellular parasites that multiply inside bacteria/archaea by making use of some or all of the host biosynthetic machinery (i.e., viruses that infect bacteria). Though different bacteriophages and archaeophages may contain different materials, they all contain nucleic acid and protein, and can under certain circumstances be encapsulated in a lipid membrane. Depending upon the phage, the nucleic acid may be either DNA or RNA but not both and it can exist in various forms.

[00236] As used herein, "heterologous nucleic acid sequence" is any sequence placed at a location in the genome where it does not normally occur. A heterologous nucleic acid sequence may comprise a sequence that does not naturally occur in a particular bacteria/archaea and/or phage or it may comprise only sequences naturally found in the bacteria/archaea and/or phage, but placed at a non-normally occurring location in the genome. In some embodiments the heterologous nucleic acid sequence is not a natural phage sequence; in some embodiments it is a natural phage sequence, albeit from a different phage; while in still other embodiments it is a sequence that occurs naturally in the genome of the starting phage but is then moved to another site where it does not naturally occur, rendering it a heterologous sequence at that new site.

[00237] A "starting phage" or "starting phage genome" is a phage isolated from a natural or human made environment that has not been modified by genetic engineering, or the genome of such a phage.

[00238] A "recombinant phage" or "recombinant phage genome" is a phage that comprises a genome that has been genetically modified by insertion of a heterologous nucleic acid sequence into the phage, or the genome of the phage. Preferably, a "recombinant phage" or "recombinant phage genome" is a phage that does not occur in nature, i.e., does not comprise a genome that occurs in nature. In some embodiments the genome of a starting phage is modified by recombinant DNA technology to introduce a heterologous nucleic acid sequence into the genome at a defined site. In some embodiments the heterologous sequence is introduced with no

corresponding loss of endogenous phage genomic nucleotides. In other words, if bases N1 and N2 are adjacent in the starting phage genome the heterologous sequence is inserted between N1 and N2. Thus, in the resulting recombinant genome the heterologous sequence is flanked by nucleotides N1 and N2. In some cases the heterologous sequence is inserted and endogenous nucleotides are removed or replaced with the exogenous sequence. For example, in some embodiments the exogenous sequence is inserted in place of some or all of the endogenous sequence which is removed. In some embodiments endogenous sequences are removed from a position in the phage genome distant from the site(s) of insertion of exogenous sequences.

[00239] A "phage host cell" is a cell that can be infected by a phage to yield progeny phage particles.

[00240] "Operatively linked" or "operably linked" expression control sequences refers to a linkage in which the expression control sequence is contiguous with coding sequences of interest to control expression of the coding sequences of interest, as well as expression control sequences that act in trans or at a distance to control expression of the coding sequence.

[00241] A "coding sequence" or "open reading frame" is a sequence of nucleotides that encodes a polypeptide or protein. The termini of the coding sequence are a start codon and a stop codon.

[00242] The term "expression control sequence" as used herein refers to polynucleotide sequences which affect the expression of coding sequences to which they are operatively linked. Expression control sequences are sequences which control the transcription, post-transcriptional events and translation of nucleic acid sequences. Expression control sequences include appropriate transcription initiation, termination, promoter and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (e.g., ribosome binding sites); sequences that enhance protein stability; and when desired, sequences that enhance protein secretion. The nature of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include promoter, ribosomal binding site, and transcription termination sequence. The term "control sequences" is intended to include, at a minimum, all components whose presence is essential for expression, and can also include additional components whose presence is advantageous, for example, leader sequences and fusion partner sequences.

[00243] As used herein, a "phage genome" includes naturally occurring phage genomes and derivatives thereof. Generally (though not necessarily), the derivatives possess the ability to propagate in the same hosts as the parent. In some embodiments the only difference between a naturally occurring phage genome and a derivative phage genome is at least one of a deletion and an addition of nucleotides from at least one end of the phage genome if the genome is linear or at least one point in the genome if the genome is circular.

[00244] As used herein, "target microbe" includes bacteria, however, this term may also include other unicellular pathogens that cause infection in animals and/or humans. Preferred target microbes are bacteria.

[00245] As used herein, "target bacteria" are bacteria that can be infected by a phage to yield a detectable output or signal. For example, a detectable output includes cell lysis. Thus, lysis of bacterial cells by a phage indicates that the bacterial cells are "target bacteria" of that phage. Another example of a detectable output is expression of a marker following infection of a bacterial cell by a phage. Suitable markers include RNAs and polypeptides.

[00246] As used herein, a "marker" includes selectable and/or screenable markers. As used herein, a "selectable marker" is a marker that confers upon cells that possess the marker the ability to grow in the presence or absence of an agent that inhibits or stimulates, respectively, growth of similar cells that do not express the marker. Such cells can also be said to have a "selectable phenotype" by virtue of their expression of the selectable marker. For example, the ampicillin resistance gene (AmpR) confers the ability to grow in the presence of ampicillin on cells which possess and express the gene. (See Sutcliffe, J.G., *Proc Natl Acad Sci U S A.* 1978 August; 75(8): 3737–3741.) Other nonlimiting examples include genes that confer resistance to chloramphenicol, kanamycin, and tetracycline. Other markers include URA3, TRP and LEU, which allow growth in the absence of said uracil, tryptophan and leucine, respectively.

[00247] As used herein, a "screenable marker" is a detectable label that that can be used as a basis to identify cells that express the marker. Such cells can also be said to have a "screenable phenotype" by virtue of their expression of the screenable marker. (In general selectable markers may also function as screenable markers in so far as the gene product of the selectable marker may be used as a basis to identify cells that express the marker independently of the function of the gene product to confer selectability on cells that express it.) Any molecule that can be differentially detected and encoded by the recombinant phage can serve as a screenable

marker. A screenable marker can be a nucleic acid molecule or a portion thereof, such as an RNA or a DNA molecule that is single or double stranded. Alternatively, a screenable marker can be a protein or a portion thereof. Suitable protein markers include enzymes that catalyze formation of a detectable reaction product. An example is a chemiluminescent protein such as luciferase or variations, such as luxAB, and β-galactosidase. Another example is the horseradish peroxidase enzyme. Proteins used to generate a luminescent signal fall into two broad categories: those that generate light directly (luciferases and related proteins) and those that are used to generate light indirectly as part of a chemical cascade (horseradish peroxidase). The most common bioluminescent proteins used in biological research are aequorin and luciferase. The former protein is derived from the jellyfish *Aequorea victoria* and can be used to determine calcium concentrations in solution. The luciferase family of proteins has been adapted for a broad range of experimental purposes. Luciferases from firefly and Renilla are the most commonly used in biological research. These proteins have also been genetically separated into two distinct functional domains that will generate light only when the proteins are closely co-localized. A variety of emission spectrum-shifted mutant derivatives of both of these proteins have been generated over the past decade. These have been used for multi-color imaging and co-localization within a living cell. The other groups of proteins used to generate chemiluminescent signal are peroxidases and phosphatases. Peroxidases generate peroxide that oxidizes luminol in a reaction that generates light. The most widely used of these is horseradish peroxidase (HRP), which has been used extensively for detection in western blots and ELISAs. A second group of proteins that have been employed in a similar fashion are alkaline phosphatases, which remove a phosphate from a substrate molecule, destabilizing it and initiating a cascade that results in the emission of light.

[00248] Other suitable screenable markers include fluorescent proteins. Fluorescent proteins include but are not limited to blue/UV fluorescent proteins (for example, TagBFP, Azurite, EBFP2, mKalama1, Sirius, Sapphire, and T-Sapphire), cyan fluorescent proteins (for example, ECFP, Cerulean, SCFP3A, mTurquoise, monomeric Midoriishi-Cyan, TagCFP, and mTFP1), green fluorescent proteins (for example, EGFP, Emerald, Superfolder GFP, Monomeric Azami Green, TagGFP2, mUKG, and mWasabi), yellow fluorescent proteins (for example, EYFP, Citrine, Venus, SYFP2, and TagYFP), orange fluorescent proteins (for example, Monomeric Kusabira-Orange, mKOκ, mKO2, mOrange, and mOrange2), red fluorescent

proteins (for example, mRaspberry, mCherry, mStrawberry, mTangerine, tdTomato, TagRFP, TagRFP-T, mApple, and mRuby), far-red fluorescent proteins (for example, mPlum, HcRed-Tandem, mKate2, mNeptune, and NirFP), near-IR fluorescent proteins (for example, TagRFP657, IFP1.4, and iRFP), long stokes-shift proteins (for example, mKeima Red, LSS-mKate1, and LSS-mKate2), photoactivatible fluorescent proteins (for example, PA-GFP, PAmCherry1, and PATagRFP), photoconvertible fluorescent proteins (for example, Kaede (green), Kaede (red), KikGR1 (green), KikGR1 (red), PS-CFP2, PS-CFP2, mEos2 (green), mEos2 (red), PSmOrange, and PSmOrange), and photoswitchable fluorescent proteins (for example, Dronpa). Several variants and alternatives to the listed examples are also well known to those of skill in the art and may be substituted in appropriate applications.

[00249] Other suitable markers include epitopes. For example, a protein comprising an epitope that can be detected with an antibody or other binding molecule is an example of a screenable marker. An antibody that recognizes the epitope can be directly linked to a signal generating moiety (such as by covalent attachment of a chemiluminescent or fluorescent protein) or it can be detected using at least one additional binding reagent such as a secondary antibody, directly linked to a signal generating moiety, for example. In some embodiments the epitope is not present in the proteins of the phage or the target microorganism so detection of the epitope in a sample indicates that the protein comprising the epitope was produced by the microorganism following infection by the recombinant phage comprising a gene encoding the protein comprising the epitope. In other embodiments the marker may be a purification tag in the context of a protein that is naturally present in the target microorganism or the phage. For example, the tag (e.g., a 6-His tag) can be used to purify the heterologous protein from other bacterial or phage proteins and the purified protein can then be detected, for example using an antibody.

[00250] As used herein, an "environmental sample" is a sample obtained from any setting other than a laboratory cell culture setting. Generally, though not necessarily, an environmental sample is obtained from a setting that comprises at least one of a) a temperature that does not support maximum growth and/or metabolism of bacterial cells, b) a nutrient profile that does not support maximum growth and/or metabolism of bacterial cells, and c) bacterial cells that are not target bacteria for a phage used in an assay. In some embodiments some or all of the bacteria present in an environmental sample are not in a metabolically active state. Without limitation,

environmental samples may be obtained from industrial plants, food processing plants, veterinary sources, food, livestock, medical settings and surfaces, schools, assisted living centers, cruise ships, other confined quarters and homes. The surface may be of any material. By way of non-limiting example, the surface can be metal, glass, wood, brick, concrete, tile, rug and the like. The surface can also be on an agricultural product. The sample can also be found inside of an agricultural produce. The "environmental sample" can be *in situ*, in other words, the assay can be performed at the site itself, rather than removed from the site. Alternatively, the "environmental sample" can be removed for assay from a collection point, as through the use of an absorbent material, such as a cotton swab to physically collect the sample.

[00251] As used herein, "agricultural" refers to cultivated or wild plants, animals, and fungi. The term also refers to stock feed or food supply. "Food supply" encompasses food for either human or non-human animal consumption. Accordingly, an "agricultural sample" refers to a sample from of, within, or on the exterior of a plant, animal and fungi.

Table 32

	Phage						Aqueous Solution	
Embodiments	A511::COP2	LP124::COP2	LP40::COP2	A511::COP3	LP124::COP3	LP40::COP3	Aqueous Solution composition comprising Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, MgSO4, pyruvate, HEPES	Aqueous Solution composition comprising Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, MgSO4, pyruvate, HEPES, Tween-80, lecithin, and potassium phosphate
1	X							
2		X						
3			X					
4				X				
5					X			
6						X		
7	X	X						
8	X		X					
9	X			X				

10	X				X			
11	X					X		
12	X						X	
13	X							X
14		X	X					
15		X		X				
16		X			X			
17		X				X		
18		X					X	
19		X						X
20			X	X				
21			X		X			
22			X			X		
23			X				X	
24			X					X
25				X	X			
26				X		X		
27				X			X	
28				X				X
29					X	X		
30					X		X	
31					X			X
32						X	X	
33						X		X
34	X	X	X					
35	X	X		X				
36	X	X			X			
37	X	X				X		

38	X	X					X	
39	X	X						X
40	X		X	X				
41	X		X		X			
42	X		X			X		
43	X		X				X	
44	X		X					X
45	X			X	X			
46	X			X		X		
47	X			X			X	
48	X			X				X
49	X				X	X		
50	X				X		X	
51	X				X			X
52	X					X	X	
53	X					X		X
54		X	X	X				
55		X	X		X			
56		X	X			X		
57		X	X				X	
58		X	X					X
59		X		X	X			
60		X		X		X		
61		X		X			X	
62		X		X				X
63		X			X	X		
64		X			X		X	
65		X			X			X

66		X				X	X	
67		X				X		X
68			X	X	X			
69			X	X		X		
70			X	X			X	
71			X	X				X
72			X		X	X		
73			X		X		X	
74			X		X			X
75			X			X	X	
76			X			X		X
77				X	X	X		
78				X	X		X	
79				X	X			X
80				X		X	X	
81				X		X		X
82					X	X	X	
83					X	X		X
84	X	X	X	X				
85	X	X	X		X			
86	X	X	X			X		
87	X	X	X				X	
88	X	X	X					X
89	X	X		X	X			
90	X	X		X		X		
91	X	X		X			X	
92	X	X		X				X
93	X	X			X	X		

94	X	X			X		X	
95	X	X			X			X
96	X	X				X	X	
97	X	X				X		X
98	X		X	X	X			
99	X		X	X		X		
100	X		X	X			X	
101	X		X	X				X
102	X		X		X	X		
103	X		X		X		X	
104	X		X		X			X
105	X		X			X	X	
106	X		X			X		X
107	X			X	X	X		
108	X			X	X		X	
109	X			X	X			X
110	X			X		X	X	
111	X			X		X		X
112	X				X	X	X	
113	X				X	X		X
114		X	X	X	X			
115		X	X	X		X		
116		X	X	X			X	
117		X	X	X				X
118		X	X		X	X		
119		X	X		X		X	
120		X	X		X			X
121		X	X			X	X	

122		X	X			X		X
123		X		X	X	X		
124		X		X	X		X	
125		X		X	X			X
126		X		X		X	X	
127		X		X		X		X
128		X			X	X	X	
129		X			X	X		X
130		X			X			X
131			X	X	X	X		
132			X	X	X		X	
133			X	X	X			X
134			X	X		X	X	
135			X	X		X		X
136			X		X	X	X	
137			X		X	X		X
138				X	X	X	X	
139				X	X	X		X
140	X	X	X	X	X			
141	X	X	X	X		X		
142	X	X	X	X			X	
143	X	X	X	X				X
144	X	X	X		X	X		
145	X	X	X		X		X	
146	X	X	X		X			X
147	X	X	X			X	X	
148	X	X	X			X		X
149	X	X		X	X	X		

150	X	X		X	X		X	
151	X	X		X	X			X
152	X	X		X		X	X	
153	X	X		X		X		X
154	X	X		X			X	
155	X	X			X	X	X	
156	X	X			X	X		X
157	X		X	X	X	X		
158	X		X	X	X		X	
159	X		X	X	X			X
160	X		X	X		X	X	
161	X		X	X		X		X
162	X		X	X			X	
163	X		X		X	X	X	
164	X		X		X	X		X
165	X		X		X	X		
166	X			X	X	X	X	
167	X			X	X	X		X
168	X			X	X		X	
169		X	X	X	X	X		
170		X	X	X	X		X	
171		X	X	X	X			X
172		X	X	X		X	X	
173		X	X	X		X		X
174		X	X		X	X	X	
175		X	X		X	X		X
176		X		X	X	X	X	
177		X		X	X	X		X

178			X	X	X	X	X	
179			X	X	X	X		X
180	X	X	X	X	X	X		
181	X	X	X	X	X		X	
182	X	X	X	X	X			X
183	X	X	X		X	X	X	
184	X	X	X		X	X		X
185	X	X		X	X	X	X	
186	X	X		X	X	X		X
187	X		X	X	X	X	X	
188	X		X	X	X	X		X
189		X	X	X	X	X	X	
190		X	X	X	X	X		X

[00252] While the disclosure has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the disclosure. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the disclosure. All such modifications are intended to be within the scope of the claims appended hereto.

EXAMPLES

Example 1: Design of codon optimized phage

[00253] Recombinant phage were designed for increased expression of the luciferase reporter. Phages selected for recombination were A511, LP124, and LP40. The capsid (CPS) nucleotide sequences for A511 (SEQ ID NO: 19), LP124 (SEQ ID NO: 13) and LP40 (SEQ ID NO: 5) are provided herewith. The NanoLuc luciferase reporter was selected for recombination by phage optimization. Phage optimization was performed using DNA 2.0™ software. The software uses an algorithm described Villalobos et al. (see Villalobos et al. BMC Bioinformatics. *Gene Designer: a synthetic biology tool for constructing artificial DNA segments. PLoS ONE. 2011 6:e19912.*) to replace synonymous codons with those preferred by a host organism, in this case listeria.

[00254] The codon optimized Nanoluc (COP2; SEQ ID NO: 36) was inserted into the phage CPS open reading frame following stop codons and a ribosome binding site (SEQ ID NO: 54) using methods as described in Example 19 herein. Primers used in engineering listeria phage include pMAK upf (SEQ ID NO: 55), dbono380 (SEQ ID NO: 56), SO472 (SEQ ID NO: 57), SO473 (SEQ ID NO: 58), SO474 (SEQ ID NO: 59) and dbono 382 (SEQ ID NO: 62) oligos. A sequence map of the insertion site for A511::COP2 recombinant phage (SEQ ID NO: 39) recombinant phage is shown in FIG. 2 indicating the location of insertion of the COP2 reporter, ribosome binding site and the flanking sequence following CPS. A sequence map of the insertion site for LP124::COP2 recombinant phage (SEQ ID NO: 39) is shown in FIG. 2 indicating the location of insertion of the COP2 reporter, ribosome binding site and the flanking sequence following CPS. A sequence map

of the insertion site for LP40::COP2 recombinant phage (SEQ ID NO: 40) is shown in FIG. 3 indicating the location of insertion of the COP2 reporter, ribosome binding site and the flanking sequence following CPS.

[00255] Recombinant phage comprising the native NanoLuc luciferase was compared to recombinant phage comprising the codon optimized COP2 luciferase. Comparisons utilized a mixture of recombinant phage. The COP2 mixture comprising the A511:COP2, LP124::COP2, and LP40::COP2 phages. These experiments were done using a cocktail of A511::COP2, LP124::COP2, and LP40::COP2. The final concentration of each phage is 1.5e7 pfu/ml, the final concentration of the mixture is 4.5e7 pfu/ml. The mixture of NanoLuc phages comprised phages selected from Example 19. Protocols for the comparison assay are as follows.

[00256] On Sponge infections with NanoLuc and COP2 Phage Mixture:

[00257] 3 sponges (3M spongestick w/ Letheen broth) were used for each condition. The stick was removed from each sponge, and the sponges were squeezed to remove Letheen broth. ~100 CFU of *Listeria monocytogenes* CDW 1554 were spiked onto each sponge:

[00258] Healthy cells: 5ml overnight culture (18-24h in 0.5X BHI) diluted 1:4 into 0.5X BHI and incubated at 30°C shaking at 180rpm for 2 hours. 100µl of a $1e^{-6}$ dilution was spiked into each sponge. Healthy cells, in this case, refer to an overnight culture that has reached stationary phase being back-diluted to re-enter log phase.

[00259] Sick cells: 250µl of a CDW 1554 overnight culture diluted to ~1e7 CFU/ml in BHI+1% glucose was spread on a 4"x4" square on a stainless steel table. Cells were allowed to dry overnight (18-24h). Cells were recovered using a cotton swab moistened with Letheen Broth, and placed in a conical tube containing 2ml of Letheen Broth. Cells were allowed to recover for 30 minutes at 30°C. Cells were diluted in 0.5X BHI to the point where 100µl should contain ~100 CFU. 100µl was spiked onto each sponge. The model mimics a factory condition where cells are surviving on a steel surface that may or may not have food contact. Sick cells are less metabolically active and produce less light upon phage infection than their healthy counterparts.

[00260] Conditions:

3 sponges with NanoLuc phage mixture/ no cells

3 sponges with NanoLuc phage mixture/ 100 CFU Healthy CDW 1554
3 sponges with NanoLuc phage mixture/ 100 CFU Sick CDW 1554
3 sponges with COP2 phage mixture/ no cells
3 sponges with COP2 phage mixture/ 100 CFU Healthy CDW 1554
3 sponges with COP2 phage mixture/ 100 CFU Sick CDW 1554

[00261] Infection:

[00262] After cells were spiked onto sponges, phage was mixed as follows:
7ml of phage solution (9e8 pfu/ml), (NanoLuc or COP2), was added to 77ml of NIB-10 infection buffer.
6ml of the appropriate phage mixture was added to each sponge, with a brief massage to mix the solution into the sponge ensuring complete coverage.
Sponges were placed at 30°C for 6 hours.

[00263] Detection:

[00264] Sponges were squeezed to separate the liquid from the sponge. 1000µl of liquid was removed from each sponge and placed in a microcentrifuge tube. Tubes were spun at 16,000g for 1 minute. 300µl was transferred to an Eppendorf microcentrifuge tube. 300µl of Nano-Glo detection reagent was added to each tube.

[00265] Samples were read in a Berthold Sirius-L luminometer using a 20 second kinetic read. RLU values across the last 16 seconds of the read were averaged resulting in the RLU value for each sample.

[00266] As shown in Table 6, the mixture of phages comprising codon optimized luciferase (COP2) shows a 2.6 fold increase in relative light units (RLU) per colony forming units (CFU) over recombinant phage encoding basic NanoLuc when infecting healthy Listeria cells. In a comparison of recombinant phage mixtures infected sick cells (*e.g.* cells that have dried on a counter surface, or been subjected to cleaning agents) the codon optimized COP2 encoding phage mixture shows a 4.1 fold increase in RLU/CFU over regular NanoLuc encoding phage mixtures (*see* FIG. 4). When normalized as an indication of performance, the codon optimized COP2 encoding phage perform at 264% of their NanoLuc encoding counterparts in healthy cells (*see* Table 7 and FIG. 5). In sick cells, the COP2 encoding phage perform at 409% of their NanoLuc encoding counterparts (*see* Table 12 and FIG. 5). This significant enhancement in the output of light from the

recombinant phage encoding codon optimized COP2 improves the detectable limits of Listeria contamination.

Table 6.

	RLU/CFU Healthy	RLU/CFU Sick
NanoLuc	365.50	83.32
COP2	965.87	340.95

Table 7.

	Healthy Cells	Sick Cells
NanoLuc	100%	100%
COP2	264%	409%

[00267] Further experiments were performed using a single A511 phage engineered with COP2 to compare reporter signal in sick cells. As shown in Table 8, the A511 phage comprising codon optimized luciferase (COP2) shows a 3.3 fold increase in relative light units (RLU) per colony forming units (CFU) over recombinant A511 phage encoding basic NanoLuc when infecting sick Listeria cells (*see* FIG. 6). When normalized as an indication of performance, the codon optimized COP2 encoding A511 phage perform at 330% of their NanoLuc encoding counterparts in sick cells (*see* Table 9 and FIG. 7). This significant enhancement in the output of light from the recombinant phage encoding codon optimized COP2 improves the detectable limits of Listeria contamination and use of a single phage type in a detection assay.

Table 8.

	A511::nluc	A511:COP2
RLU/CFU	283.57	935.82

Table 9.

	A511::nluc	A511:COP2
Signal	100.00%	330.01%

Example 2: Design of Codon-optimized Phage V3 (COP3)

[00268] Additional codon optimization was performed with recombinant phage in an effort to further increase the expression levels of the luciferase reporter. Phages selected for optimization were A511, LP124 and LP40. The NanoLuc luciferase reporter was selected for recombination by phage optimization. Coding sequence optimization was performed using DNA 2.0™ software. The software uses an algorithm described Villalobos et al. (see Villalobos et al. BMC Bioinformatics. *Gene Designer: a synthetic biology tool for constructing artificial DNA segments. PLoS ONE. 2011 6:e19912.*) to replace synonymous codons with those preferred by a host organism.

[00269] The purpose of this round of codon optimization was to create a custom codon optimization algorithm specific for *Listeria*. For these experiments, a set of 24 codon-optimized variants were designed and constructed by DNA 2.0 ™. These variants allowed for testing a variety of hypotheses concerning codon usage. The set of the new 24 codon-optimized variants (COP3) were cloned into the A511 vector. These plasmids were transformed into the *Listeria monocytogenes* strain EGD-e, and isolated using phage infective engineering (PIE) methodology described in Example 19 above.

[00270] The 24 variants of the COP3 phages were isolated and purified by ultracentrifugation. The isolated and purified COP3 phages were compared with COP2 and the non-codon optimized NanoLuc phages. The relative signal strength was generated across a subset of *Listeria* strains and normalized to COP2. These data were then traced back to specific changes in the codon usage profile. These data pointed to the improved COP3 phage herein referred to as W40_VIP_MLi178 ("VIP178") (*see* SEQ ID No.: 37) as the most improved variant. This version of NanoLuc was used to create three new engineered phages: A511::VIP178, LP124::VIP178, and LP40::VIP178 (also referred to herein as A511::COP3, LP124::COP3 and LP40::COP3).

[00271] The phages were engineered using the primers described herein. The primers pMAK upf (*see* SEQ ID No.:55) and DBONO380 (*see* SEQ ID No.:56) were used to amplify the upstream homology fragments for each phage. The VIP178 fragment was amplified using the SO670 (*see* SEQ ID No.:64) and SO671 (*see* SEQ ID No.:65).The downstream homology fragments were amplified using the primers S0672 (*see* SEQ ID No.:66) and DBONO382 (*see* SEQ ID No.:60).

[00272] Signal intensity levels of COP2 and COP3 phages were assessed as detailed below in Example 3.

Example 3: Signal Comparison of COP2 and COP3 Phages

[00273] In order to assess any differences in intensity or robustness of signal provided by the COP2 and COP3 phages, a screen was performed in which the signal intensity was determined by using the assay described below.

[00274] For these assays the following materials were used: Validation Plates (342 strains across Listeria species), Omni-Tray with 0.5x BHI agar, Deep-Well 96-well plate (Axygen), Clear flat-bottom 96-well plate (Evergreen),White flat-bottom 96-well plate (Greiner Bio-One), Plate-sealing film (breathable), 15mL conical tubes, Letheen Broth, 0.5x BHI, NIB-14, Nano-Glo, Substrate, Nano-Glo Buffer, 200µL multichannel pipette, 1000µL multichannel pipette, 20µL multichannel pipette, 96-pin replicator tool (frogger).

[00275] The detailed protocol used in these assays is described below.

Protocol

Day 0

[00276] Stamp out validation plates 1 through 3 and greatest misses plate onto 0.5x BHI agar Omni-tray plate using the 96-pin replicator tool.

[00277] Incubate plates at 35°C overnight (18h)

Day 1

[00278] Fill wells of 96-well DeepWell with 1mL of 0.5x BHI

[00279] Inoculate DeepWell with colonies from stamped-out plates

[00280] Incubate plates at 30°C for 24h, shaking

Day 2

[00281] 1. Dilute all phage variants in NIB-14 to 9E7 pfu/mL in a final volume of 20mL

[00282] a. (For lower phage concentration tests, dilute variants to 3E7 pfu/mL and/or 1E7 pfu/mL)

[00283] b. Note: GM plate is not a full plate — use the empty wells to act as negative controls for the assay

[00284] 2. Add 180µL of Letheen Broth to all wells of four (4) clear, flat-bottom 96-well plates

[00285] 3. Label plates from 1E-1 through 1E-4 dilution

[00286] 4. Add 900µL of Letheen Broth to all wells of a 96-well deep-well plate

[00287] a. Label deep-well plate as the 1E-5 dilution

[00288] 5. Repeat previous steps 2 through 5 three additional times, one set for each plate of overnight culture

[00289] a. i.e. Validation Plates 1, 2, 3, and Greatest Misses

[00290] 6. For each culture, transfer 20µL from every well of overnight culture to corresponding well of 1E-1 dilution plate

[00291] 7. Pipette mix 10-15x

[00292] 8. Repeat steps 6 and 7, transferring from 1E-1 plate to 1E-2 plate, then from 1E-2 plate to 1E-3 plate, then from 1E-3 plate to 1E-4 plate.

[00293] 9. Transfer 100µL from every well of 1E-4 dilution plate to corresponding well of 1E-5 dilution plate for a total volume of 1000µL in each well of the deep well plate

[00294] 10. Repeat previous step until there is a 1E-5 cell dilution for each phage variant being tested, plus COP2, for each overnight culture

a. e.g. if testing three variants:

i. Validation plate 1 - four (4) plates at 1E-5 dilution

ii. Validation plate 2 - four (4) plates at 1E-5 dilution

iii. Validation plate 3 - four (4) plates at 1E-5 dilution

iv. GM Plate - four (4) plates at 1E-5 dilution

[00295] 11. Dilute 1E-5 dilution of 1839 from Validation Plate 2 — 50µL into 450µL of Letheen (1:10 total dilution — 1E-6 dilution from overnight culture)

[00296] 12. Plate 100µL of -6 dilution onto BHI plate and incubate overnight at 35°C

[00297] 13. For each strain plate, transfer 100µL of phage/NIB-14 mixture for each phage variant being tested

[00298] 14. Start with COP2

[00299] 15. Stagger each set by ≈20 minutes (or as you see fit) to allow time to read between strain plates

[00300] 16. Recommended: Complete infection for all variants on Plate 1, then all variants of Plate 2, etc.

[00301] 17. Incubate plates at 30°C for 6h

[00302] 18. Mix necessary amount of Nano-glo buffer with substrate (≈5ml / plate)

[00303] 19. Transfer 40µL of from each well of infection plate to corresponding wells of white, flat-bottom plate

[00304] Add 40µL of mixed Nano-Glo reagent

[00305] Detect on Glomax 96

[00306] Steady Glo - 0s delay, 0.5s integration

Analysis:

[00307] COP3 target panel consists of strains producing between 100 RLU/CFU and 1000 RLU/CFU with COP2 assay

[00308] Compare signal of target strains with COP2 phage cocktail to COP3 phage cocktail candidate

[00309] Plate 100µL of 1E-6 dilution for target strains onto BHI plate to calculate RLU/CFU of COP3 target strains for COP2 and COP3

[00310] Data acquired in the comparison of the COP2 and the COP3 phages are shown in Figures 8 and 9. The signal comparison assays demonstrate that there was a broad increase in signal intensity across tested *Listeria* species with the use of the COP3 phage in comparison with the COP2 phage. The data further indicate that there was a six time (6X) mean signal increase across all the tested conditions with the use of COP3 in comparison to COP2. The full listing of *Listeria* strains used in these studies is shown in Table 10.

Table 10: Full Listing of *Listeria* Strains Assessed in COP2 and COP3 Signal Intensity Assay

Plate	NP Strain #	Strain ID	Species	Well
1	1814	FSL C2-010	*Listeria ivanovii*	a1
1	1815	FSL C2-011	*Listeria ivanovii*	a2
1	1816	FSL H6-011	*Listeria seeligeri*	a3
1	1817	FSL H6-169	*Listeria seeligeri*	a4
1	1818	FSL H6 017	*Listeria welshimeri*	a5
1	1819	FSL H6-105	*Listeria welshimeri*	a6
1	1820	FSL C2-008	*Listeria innocua*	a7
1	1821	FSL X1-017	*Listeria innocua*	a8
1	1822	FSL J1-023	*Listeria innocua (hemolytic)*	a9
1	1823	FSL W3-075	*Listeria innocua (hemolytic)*	a10
1	1824	FSL S4-120	*Listeria marthii*	a11
1	1825	FSL S4-965	*Listeria marthii*	a12
1	1826	FSL F6-920	*Listeria rocourtiae*	b1
1	1827	FSL C1-056	*Listeria monocytogenes*	b2
1	1828	FSL J1-177	*Listeria monocytogenes*	b3
1	1829	FSL J1-094	*Listeria monocytogenes*	b4
1	1830	FSL C1-115	*Listeria monocytogenes*	b5
1	1831	FSL J1-169	*Listeria monocytogenes*	b6
1	1832	FSL J1-049	*Listeria monocytogenes*	b7
1	1833	FSL W1-112	*Listeria monocytogenes*	b8
1	1834	FSL J1-110	*Listeria monocytogenes*	b9
1	1835	FSL J1-129	*Listeria monocytogenes*	b10
1	1836	FSL W1-110	*Listeria monocytogenes*	b11
1	1837	FSL J1-107	*Listeria monocytogenes*	b12
1	1838	FSL J1-175	*Listeria monocytogenes*	c1
1	1839	FSL F6-367 (MACK)	*Listeria monocytogenes*	c2
1	1840	FSL J1-208	*Listeria monocytogenes*	c3
1	1869	WSLC 3009	*Listeria ivanovii*	c4
1	1879	FSL N4-221	*Listeria monocytogenes*	c5
1	1878	EGD-e	*Listeria monocytogenes*	c6
1	1880	FSL L3-159	*Listeria monocytogenes*	c7
1	1881	FSL T1-323	*Listeria monocytogenes*	c8
1	1882	FSL H5-725	*Listeria monocytogenes*	c9
1	1883	FSL T1-922	*Listeria monocytogenes*	c10
1	1884	FSL H1-251	*Listeria monocytogenes*	c11
1	1885	FSL L3-501	*Listeria monocytogenes*	c12
1	1886	FSL R2-069	*Listeria monocytogenes*	d1
1	1887	FSL H1-030	*Listeria monocytogenes*	d2

1	1888	FSL L4-019	*Listeria monocytogenes*	d3
1	1889	FSL T1-027	*Listeria monocytogenes*	d4
1	1890	FSL T1-041	*Listeria monocytogenes*	d5
1	1891	FSL R8-5241	*Listeria seeligeri*	d6
1	1892	FSL R8-5247	*Listeria seeligeri*	d7
1	1893	FSL R8-5253	*Listeria seeligeri*	d8
1	1894	FSL R8-5513	*Listeria seeligeri*	d9
1	1895	FSL R8-6629	*Listeria seeligeri*	d10
1	1896	FSL R8-6635	*Listeria seeligeri*	d11
1	1897	FSL R8-6659	*Listeria seeligeri*	d12
1	1898	FSL R8-6665	*Listeria seeligeri*	e1
1	1899	FSL R8-6852	*Listeria seeligeri*	e2
1	1900	FSL R8-5085	*Listeria innocua*	e3
1	1901	FSL R8-5091	*Listeria innocua*	e4
1	1902	FSL R8-5098	*Listeria innocua*	e5
1	1903	FSL R8-5255	*Listeria innocua*	e6
1	1904	FSL R8-5293	*Listeria innocua*	e7
1	1905	FSL R8-5295	*Listeria innocua*	e8
1	1906	FSL R8-5306	*Listeria innocua*	e9
1	1907	FSL R8-5440	*Listeria innocua*	e10
1	1908	FSL R8-5442	*Listeria innocua*	e11
1	1909	FSL R8-5448	*Listeria innocua*	e12
1	1910	FSL R8-7026	*Listeria welshimeri*	f1
1	1911	FSL R8-7641	*Listeria seeligeri*	f2
1	1912	FSL R8-7061	*Listeria innocua*	f3
1	1913	FSL R8-6826	*Listeria seeligeri*	f4
1	1914	FSL R8-7454	*Listeria welshimeri*	f5
1	1915	FSL R8-7548	*Listeria innocua*	f6
1	1916	FSL R8-6667	*Listeria innocua*	f7
1	1917	FSL R8-1903	*Listeria welshimeri*	f8
1	1945	FSL L5-079	*Listeria welshimeri*	f9
1	1946	FSL S10-1450	*Listeria welshimeri*	f10
1	1947	FSL S10-1451	*Listeria welshimeri*	f11
1	1948	FSL S4-081	*Listeria welshimeri*	f12
1	1949	FSL S4-101	*Listeria welshimeri*	g1
1	1950	FSL S10-030	*Listeria seeligeri*	g2
1	1951	FSL S10-320	*Listeria seeligeri*	g3
1	1952	FSL S10-1602	*Listeria seeligeri*	g4
1	1953	FSL L5-075	*Listeria seeligeri*	g5
1	1954	FSL L5-046	*Listeria seeligeri*	g6
1	1955	FSL L5-104	*Listeria seeligeri*	g7
1	1956	FSL R8-7575	*Listeria seeligeri*	g8
1	1957	FSL S4-178	*Listeria seeligeri*	g9

1	1958	FSL S4-135	*Listeria seeligeri*	g10
1	1959	FSL S4-158	*Listeria innocua*	g11
1	1960	FSL S10-784	*Listeria innocua*	g12
1	1961	FSL F6-1168	*Listeria innocua*	h1
1	1962	FSL R8-5961	*Listeria innocua*	h2
1	1963	FSL R8-6922	*Listeria innocua*	h3
1	1964	FSL R8-7352	*Listeria innocua*	h4
1	1965	FSL R8-5598	*Listeria innocua*	h5
1	1966	FSL R8-6733	*Listeria innocua*	h6
1	1967	FSL R8-5942	*Listeria innocua*	h7
1	1968	FSL S10-034	*Listeria seeligeri*	h8
1	1969	FSL S10-1611	*Listeria seeligeri*	h9
1	1970	FSL L5-054	*Listeria seeligeri*	h10
1	1971	FSL L5-085	*Listeria seeligeri*	h11
1	1972	FSL R8-6868	*Listeria seeligeri*	h12
2	1839	FSL F6-367 (MACK)	*Listeria monocytogenes*	a1
2	1840	FSL J1-208	*Listeria monocytogenes*	a2
2	1869	WSLC 3009	*Listeria ivanovii*	a3
2	1973	FSL R8-6545	*Listeria seeligeri*	a4
2	1974	FSL R8-6949	*Listeria seeligeri*	a5
2	1975	FSL S4-167	*Listeria seeligeri*	a6
2	1976	FSL S4-180	*Listeria seeligeri*	a7
2	1977	FSL N1-064	*Listeria welshimeri*	a8
2	1978	FSL R8-8163	*Listeria welshimeri*	a9
2	1979	FSL R8-7524	*Listeria welshimeri*	a10
2	1980	FSL R8-7486	*Listeria welshimeri*	a11
2	1981	FSL R8-6035	*Listeria welshimeri*	a12
2	1982	FSL R8-5807	*Listeria welshimeri*	b1
2	1983	FSL S4-182	*Listeria welshimeri*	b2
2	1984	FSL R2-630	*Listeria welshimeri*	b3
2	1985	FSL F6-1131	*Listeria welshimeri*	b4
2	1986	FSL R8-7041	*Listeria welshimeri*	b5
2	1987	FSL R8-5837	*Listeria welshimeri*	b6
2	1988	FSL R8-6136	*Listeria welshimeri*	b7
2	1989	FSL S4-289	*Listeria welshimeri*	b8
2	1990	FSL H6-027	*Listeria seeligeri*	b9
2	1991	FSL H6-079	*Listeria seeligeri*	b10
2	1992	FSL H6-185	*Listeria seeligeri*	b11
2	1993	FSL R8-6874	*Listeria seeligeri*	b12
2	1994	FSLR8-6880	*Listeria seeligeri*	c1
2	1995	FSL R8-7629	*Listeria seeligeri*	c2
2	1996	FSL S4-544	*Listeria seeligeri*	c3
2	1997	FSL R8-5764	*Listeria innocua*	c4

2	1998	FSL R8-5802	*Listeria innocua*	c5
2	1999	FSL R8-6012	*Listeria innocua*	c6
2	2000	FSL R8-6355	*Listeria innocua*	c7
2	2001	FSL R8-6369	*Listeria innocua*	c8
2	2002	FSL R8-6476	*Listeria innocua*	c9
2	2003	FSL R8-7175	*Listeria innocua*	c10
2	2004	FSL R8-6888	*Listeria innocua*	c11
2	2005	FSL R8-6672	*Listeria innocua*	c12
2	2006	FSL S10-1311	*Listeria innocua*	d1
2	2007	FSL F6-1159	*Listeria innocua*	d2
2	2008	FSL F6-1126	*Listeria innocua*	d3
2	2009	FSL S6-120	*Listeria innocua*	d4
2	2010	FSL R8-5594	*Listeria innocua*	d5
2	2011	FSL R8-7181	*Listeria innocua*	d6
2	2012	FSL R2-632	*Listeria innocua*	d7
2	2013	FSL L3-851	*Listeria innocua*	d8
2	2014	FSL S10-1377	*Listeria innocua*	d9
2	2015	FSL S10-114	*Listeria welshimeri*	d10
2	2016	FSL S10-115	*Listeria welshimeri*	d11
2	2017	FSL S10-117	*Listeria welshimeri*	d12
2	2018	FSL S10-119	*Listeria welshimeri*	e1
2	2019	FSL S10-121	*Listeria welshimeri*	e2
2	2020	FSL R8-0056	*Listeria welshimeri*	e3
2	2021	FSL R8-1198	*Listeria welshimeri*	e4
2	2022	FSL R8-7403	*Listeria welshimeri*	e5
2	2023	FSL R2-631	*Listeria welshimeri*	e6
2	2024	FSL F6-267	*Listeria monocytogenes*	e7
2	2025	FSL F6-406	*Listeria monocytogenes*	e8
2	2026	FSL H5-592	*Listeria monocytogenes*	e9
2	2027	FSL H1-219	*Listeria monocytogenes*	e10
2	2028	FSL H1-121	*Listeria monocytogenes*	e11
2	2029	FSL W3-072	*Listeria monocytogenes*	e12
2	2030	FSL N4-239	*Listeria monocytogenes*	f1
2	2031	FSL N3-293	*Listeria monocytogenes*	f2
2	2032	FSL F3-319	*Listeria monocytogenes*	f3
2	2033	FSL F2-738	*Listeria monocytogenes*	f4
2	2034	FSL N3-881	*Listeria monocytogenes*	f5
2	2035	FSL N4-048	*Listeria monocytogenes*	f6
2	2036	FSL N4-696	*Listeria monocytogenes*	f7
2	2037	FSL N4-242	*Listeria monocytogenes*	f8
2	2038	FSL H4-364	*Listeria monocytogenes*	f9
2	2039	FSL H4-147	*Listeria monocytogenes*	f10
2	2040	FSL H4-946	*Listeria monocytogenes*	f11

2	2041	FSL S4-461	*Listeria monocytogenes*	f12
2	2042	FSL F6-206	*Listeria monocytogenes*	g1
2	2043	FSL F6-224	*Listeria monocytogenes*	g2
2	2044	FSL L3-739	*Listeria monocytogenes*	g3
2	2045	FSL N3-008	*Listeria monocytogenes*	g4
2	2046	FSL N3-022	*Listeria monocytogenes*	g5
2	2047	FSL J1-108	*Listeria monocytogenes*	g6
2	2048	FSL J1-119	*Listeria monocytogenes*	g7
2	2049	FSL C1-122	*Listeria monocytogenes*	g8
2	2050	FSL J1-126	*Listeria monocytogenes*	g9
2	2051	FSL F3-285	*Listeria monocytogenes*	g10
2	2052	FSL R6-288	*Listeria monocytogenes*	g11
2	2053	FSL N1-021	*Listeria monocytogenes*	g12
2	2054	FSL H1-208	*Listeria monocytogenes*	h1
2	2055	FSL N3-034	*Listeria monocytogenes*	h2
2	2056	FSL L5-072	*Listeria monocytogenes*	h3
2	2057	FSL S6-131	*Listeria monocytogenes*	h4
2	2058	FSL N3-278	*Listeria monocytogenes*	h5
2	2059	FSL R2-282	*Listeria monocytogenes*	h6
2	2060	FSL H5-770	*Listeria monocytogenes*	h7
2	2061	FSL F6-207	*Listeria monocytogenes*	h8
2	2062	FSL F6-236	*Listeria monocytogenes*	h9
2	2063	FSL H5-795	*Listeria monocytogenes*	h10
2	2064	FSL N3-246	*Listeria monocytogenes*	h11
2	2065	FSL R2-062	*Listeria monocytogenes*	h12
3	1839	FSL F6-367 (MACK)	*Listeria monocytogenes*	a1
3	1840	FSL J1-208	*Listeria monocytogenes*	a2
3	1869	WSLC 3009	*Listeria ivanovii*	a3
3	2066	FSL R2-437	*Listeria monocytogenes*	a4
3	2067	FSL M1-004	*Listeria monocytogenes*	a5
3	2068	FSL L4-352	*Listeria monocytogenes*	a6
3	2069	FSL F6-605	*Listeria monocytogenes*	a7
3	2070	FSL V1-001	*Listeria monocytogenes*	a8
3	2071	FSL F6-464	*Listeria monocytogenes*	a9
3	2072	FSL R8-2748	*Listeria monocytogenes*	a10
3	2073	FSL R6-908	*Listeria monocytogenes*	a11
3	2074	FSL L3-802	*Listeria monocytogenes*	a12
3	2075	FSL F3-056	*Listeria monocytogenes*	b1
3	2076	FSL J2-020	*Listeria monocytogenes*	b2
3	2077	FSL S4-914	*Listeria monocytogenes*	b3
3	2078	FSL F6-467	*Listeria monocytogenes*	b4
3	2079	FSL F6-655	*Listeria monocytogenes*	b5
3	2080	FSL F6-352	*Listeria monocytogenes*	b6

3	2081	FSL H5-781	*Listeria monocytogenes*	b7
3	2082	FSL K2-147	*Listeria monocytogenes*	b8
3	2083	FSL V1-026	*Listeria monocytogenes*	b9
3	2084	FSL H5-572	*Listeria monocytogenes*	b10
3	2085	FSL K2-065	*Listeria monocytogenes*	b11
3	2086	FSL H4-120	*Listeria monocytogenes*	b12
3	2087	FSL F6-184	*Listeria monocytogenes*	c1
3	2088	FSL F6-191	*Listeria monocytogenes*	c2
3	2089	FSL H1-099	*Listeria monocytogenes*	c3
3	2090	FSL J1-116	*Listeria monocytogenes*	c4
3	2091	FSL R2-192	*Listeria monocytogenes*	c5
3	2092	FSL J1-225	*Listeria monocytogenes*	c6
3	2093	FSL R2-500	*Listeria monocytogenes*	c7
3	2094	FSL R2-501	*Listeria monocytogenes*	c8
3	2095	FSL E1-159	*Listeria monocytogenes*	c9
3	2096	FSL F6-355	*Listeria monocytogenes*	c10
3	2097	FSL F6-382	*Listeria monocytogenes*	c11
3	2098	FSL F3-200	*Listeria monocytogenes*	c12
3	2099	FSL K2-143	*Listeria monocytogenes*	d1
3	2100	FSL N1-176	*Listeria monocytogenes*	d2
3	2101	FSL N1-417	*Listeria monocytogenes*	d3
3	2102	FSL L3-051	*Listeria monocytogenes*	d4
3	2103	FSL T1-107	*Listeria monocytogenes*	d5
3	2104	FSL T1-408	*Listeria monocytogenes*	d6
3	2105	FSL F6-396	*Listeria monocytogenes*	d7
3	2106	FSL H5-806	*Listeria monocytogenes*	d8
3	2107	FSL F6-551	*Listeria monocytogenes*	d9
3	2108	FSL F6-446	*Listeria monocytogenes*	d10
3	2109	FSL F6-315	*Listeria monocytogenes*	d11
3	2110	FSL V1-022	*Listeria monocytogenes*	d12
3	2111	FSL R2-132	*Listeria monocytogenes*	e1
3	2112	FSL R2-273	*Listeria monocytogenes*	e2
3	2113	FSL N3-277	*Listeria monocytogenes*	e3
3	2114	FSL F6-358	*Listeria monocytogenes*	e4
3	2115	FSL F6-194	*Listeria monocytogenes*	e5
3	2116	FSL R2-763	*Listeria monocytogenes*	e6
3	2117	FSL R2-765	*Listeria monocytogenes*	e7
3	2118	FSL R2-764	*Listeria monocytogenes*	e8
3	2119	FSL N1-225	*Listeria monocytogenes*	e9
3	2120	FSL N1-227	*Listeria monocytogenes*	e10
3	2121	FSL N1-048	*Listeria monocytogenes*	e11
3	2122	FSL K2-131	*Listeria monocytogenes*	e12
3	2123	FSL F6-222	*Listeria monocytogenes*	f1

3	2124	FSL F6-249	*Listeria monocytogenes*	f2
3	2125	FSL N3-065	*Listeria monocytogenes*	f3
3	2126	FSL H4-699	*Listeria monocytogenes*	f4
3	2127	FSL L4-241	*Listeria monocytogenes*	f5
3	2128	FSL S4-643	*Listeria monocytogenes*	f6
3	2129	FSL R2-073	*Listeria monocytogenes*	f7
3	2130	FSL F3-224	*Listeria monocytogenes*	f8
3	2131	FSL N4-334	*Listeria monocytogenes*	f9
3	2132	FSL R2-070	*Listeria monocytogenes*	f10
3	2133	FSL F6-421	*Listeria monocytogenes*	f11
3	2134	FSL F6-449	*Listeria monocytogenes*	f12
3	2135	FSL J2-054	*Listeria monocytogenes*	g1
3	2136	FSL S4-024	*Listeria monocytogenes*	g2
3	2137	FSL H1-111	*Listeria monocytogenes*	g3
3	2138	FSL K2-022	*Listeria monocytogenes*	g4
3	2139	FSL S4-066	*Listeria monocytogenes*	g5
3	2140	FSL R2-067	*Listeria monocytogenes*	g6
3	2141	FSL R2-293	*Listeria monocytogenes*	g7
3	2142	FSL F6-323	*Listeria monocytogenes*	g8
3	2143	FSL F6-216	*Listeria monocytogenes*	g9
3	2164	FSL F6-360	*Listeria monocytogenes*	g10
3	2165	FSL F6-313	*Listeria monocytogenes*	g11
3	2166	FSL R2-031	*Listeria monocytogenes*	g12
3	2167	FSL R2-050	*Listeria monocytogenes*	h1
3	2148	FSL T1-313	*Listeria monocytogenes*	h2
3	2149	FSL R8-0875	*Listeria monocytogenes*	h3
3	2150	FSL R2-317	*Listeria monocytogenes*	h4
3	2151	FSL F6-335	*Listeria monocytogenes*	h5
3	2152	FSL R6-653	*Listeria monocytogenes*	h6
3	2153	FSL L3-135	*Listeria monocytogenes*	h7
3	2154	FSL L3-143	*Listeria monocytogenes*	h8
3	2155	FSL L3-167	*Listeria monocytogenes*	h9
3	2156	FSL N3-031	*Listeria monocytogenes*	h10
3	2157	FSL J1-101	*Listeria monocytogenes*	h11
3	2158	FSL F6-154	*Listeria monocytogenes*	h12

Example 4: Effect of Phage Concentration on Signal Intensity

[00311] Assays were performed to determine the effect of phage concentration on the resultant signal intensity following infection with the codon-optimized phage. *See* Figure 10. For these experiments, two-fold serial dilutions of the COP2 phage (v1.0.2)

cocktail were added to the infection buffer. 200 CFU of *Listeria monocytogenes* (NP#1839) were infected at various concentrations of phage. The infected samples were incubated for 6 hours at 30°C. The luciferase signal was detected using the Glomax 96 luminometer. The resultant signal intensities for the various concentrations of phage used was plotted on a graph for comparison of signal. The data from these experiments indicate that the concentration for maximum signal is approximately between $1.5X10^6$ to $1.8X10^6$ pfu/mL. *See* Figure 10. All assays were performed minimally in triplicate.

Example 5: Alterations in the 5' UTR Results in Increased Signal Intensity

[00312] Optimization of the 5' UTR was performed by utilizing DNA 2.0 ™. The changes to the 5' UTR included modifications of spacer DNA and/or changes in the nucleotide sequence of the ribosome binding site (RBS). These sequences, including the original UTR sequence, can be found in the informal sequence listing at SEQ ID No.: 90-97. Multiple variants were produced, several of which resulted in greater than a 200% mean signal increase over the COP2 (v1.0.2) phage signal. *See* Table 11. For these assays, optimized UTR variants were linked to a modified NanoLuc construct called COPD12 (*see* SEQ ID No. 53).

Table 11: Codon-optimized 5' UTR Results in Increased Signal Intensity

Variant	Mean Signal Increase over v1.0.2
UTR2	264%
UTR4	289%
UTR7	232%

[00313] The 5' UTR changes that resulted in increased signal intensity were combined with the best-performing COP3 codon-optimized variant (*i.e.* 40_VIP178) to assess whether this combination would result in increased signal in comparison to either the 5'UTR optimization or the COP3 variant alone. The results surprisingly show that the combined variants do not have increased signal in comparison to the COP3 variant that does not contain an altered 5' UTR sequence. *See* Table 12.

Table 12: COP3 Combined with 5'UTR Modification Does Not Result in Greater Signal Intensity

Variant	Mean Signal Increase over v1.0.2
UTR2_178	182%
UTR3_178	185%
UTR7_178	332%
40_VIP178	**468%**
UTR2	243%
UTR3	154%
UTR7	191%

Example 6: Selection of Base Media

[00314] Media were screened for the ability to support high infection rate and high signal intensity following infection with phage encoding a luciferase marker. Bacterial cells were purposefully stressed by way of drying for 18 hours on a stainless steel table, followed by re-suspension in brain-heart infusion medium (BHI) for 30 minutes. The recovered cells were then infected with phage containing a luciferase marker for 6 hours followed by testing of the enzymatic activity using unpurified phage lysate and NanoLuc reagent. All media tested gave similar RLU output.

[00315] BHI and TSB media were further titrated to assess whether there was an increase in RLU at different concentrations of base media. The data indicate that stressed cells recovered best in 1X TSB medium. Additional benefits of the 1X TSB medium include that the TSB does not contain animal byproducts, it contains more nutrients, and there is better consistency of the product among different lots tested.

Example 7: Selection of Media Additives—selective agents, neutralizers, and nutrients

[00316] Select components were added to the media in order to remedy known stressors to cells, and to reduce the possibility for other chemicals interfering with the test results. To this end, lithium chloride was added at defined concentrations to the selected 1X TSB base medium, followed by infecting the cells with a luciferase containing phage, and lastly by assaying the RLU detectable as a function of the percentage of lithium chloride added to the media. Lithium chloride was selected as an additive in order to overcome, prevent or limit growth of competing biologicals. The data from these

experiments indicate that, lithium chloride added at 0.25% resulted in the highest RLU at both 3 hours and 6 hours post-infection. (*See* Figure 11).

[00317] Components selected to overcome cell starvation and oxidative stress, glucose and yeast extract, respectively, were titrated in 1X TSB, followed by infection of the bacteria with luciferase containing phage, and lastly by assaying the RLU detectable as a function of the percentage of either glucose or yeast extract. Based on the RLU levels at the 3 hour and 6 hour assay points, 0.25% glucose and 0.5% yeast extract were selected.

[00318] Antifungal agents were also added to the base medium and tested in order to determine whether there is a decrease in RLU activity, either as a result of loss of enzyme activity or because of reduced infection ability. The anti-fungal agents tested included cycloheximide solution in DMSO. Neither cycloheximide nor DMSO resulted in a decrease in the infection rate or in the enzymatic activity.

[00319] The effect of divalent cations added to Formulation-1 was assessed. $MgSO_4$ or $CaCl_2$ was added to Formulation-1, followed by infection of bacteria with luciferase encoding phage, and assessment of resultant RLU. Addition of $MgSO_4$ to Formulation-1 resulted in a marked increase in the RLU activity in comparison to the addition of $CaCl_2$. The beneficial activity on resultant RLU activity led to the creation of Formulation-1A, which contains 0.08% $MgSO_4$. (*See* Table 2 and Figure 12).

[00320] The addition of alternative carbon sources, through the addition of alpha-ketoglutarate, glutamate, malonate and citrate to Formulation-1 demonstrated that glucose sustained RLU activity more effectively.

[00321] A comparison of enzyme activity and infection ability with various media formulations indicated that a preferred embodiment of the formulation includes the base Formulation-1, with the addition of 0.08% MgSO4 and 0.1% pyruvate (also referred herein as Formulation-1A). (*See* Figure 27).

[00322] HEPES was also titrated into Formulation-1A to investigate whether addition of HEPES resulted in higher RLU activity than without the addition of the buffer. The data indicated that 20mM HEPES was ideal in both the 3 hour and the 6 hour assay time points for high RLU activity. Furthermore, the addition of pyruvate further increased RLU activity. (*See* Figures 13A and 13B). The resultant formulation that incorporates all of

the components of Formulation-1A, with the addition of HEPES, is herein referred to as Formulation-2 or as NIB-12. (*See* Table 3).

Example 8: Formulation NIB-14

[00323] Based on the information gleaned from the effects acquired through the addition of additives to the base TSB formulation (*see* Example 7 above), other components were selectively added to generate another preferred embodiment of the formulation, which is particularly well suited for resisting the negative impact of chemicals found in sanitizing solutions on both enzymatic stability and phage infection. Of particular interest are additives that are geared towards reducing the interference from quaternary ammonium salts found in various sanitizing solutions including among others: "Sani-Step," "Sani-Save," "Boost-FT," "Quorum Clear V," "Whisper V," "Sparkle QF-BH," "F29". Particularly good candidates that have the capability of reducing interference of quaternary ammonium salts are Tween-80 and lecithin.

[00324] The addition of Tween-80, either alone or in combination with lecithin, to the Formulation-2 (NIB-12) medium allowed for protection of the samples from interference by quaternary ammonium salts. (*See* Figure 14). Without the addition of either Tween-80 or of lecithin to Listeria Growth Broth, there was no detectable RLU when the solution contained 7.81ppm of quaternary ammonium salts. However, the resistance to quaternary ammonium salts was also increased by the addition of Tween-80 alone. In this case, there was a sustained, detectable RLU in the presence of up to 62.5ppm quaternary ammonium salts. The amount of resistance to quaternary ammonium salts was further increased through the addition of both lecithin and Tween-80. With the addition of both reagents to Listeria Growth Broth, there was detectable RLU up to 125ppm quaternary ammonium salts. Another preferred embodiment of the media contains 1.5% of Tween-80 and 0.22% of lecithin. This formulation is herein referred to as NIB-14, the full formulation of which is detailed in Table 4.

[00325] The stability of the NIB-14 medium was also tested at temperatures, 4 $^{\circ}$C and 30 $^{\circ}$C, and normalized to that of the standard base medium 0.5X BHI. The data indicate that NIB-14 remains stable at both 4 $^{\circ}$C and 30 $^{\circ}$C.

Example 9: Phage Infection and Enzyme Activity

[00326] A systematic comparison of RLU values as a function of additive component was performed on various media formulations. (*See* Figure 15). The effects of different additives on both enzymatic activity, as well as infection ability, was measured and compared by way of assessing RLU across the different conditions. The data indicate that the highest infection ability was found in Formulation-1 (with Mg and pyruvate) and Formulation-2 supplemented with HEPES. Specifically, addition of Mg, pyruvate and/or 0.25% Tween-80 had a large impact in increasing infection ability.

[00327] While large gains were found in the infection ability with the additions listed above, modest differences were observed with regard to promoting enzymatic activity by way of additives to the formulations.

Example 10: Effects of Media Formulation on Lower Limit of Detection Assays

[00328] The influence of media formulation on the ability to detect small quantities of cells was assessed by performing lower limit of detection assays (also referred to herein as "LLOD"). For these experiments, two variations of Formulation-2 were assessed (*see* Table 3). The two conditions tested included either the standard Formulation-2 (*see* Table 3), or the standard Formulation-2 containing 0.25% of Tween-80. For these experiments, stressed 1554 bacterial cells were collected on sponges and incubated with the appropriate formulation medium. Cells were titrated over a range of values in order to have a graphical output in the LLOD assay ranging from 1 cell to 1000 cells. In the two conditions measured, the standard Formulation-2 (NIB-12) performed better in terms of detection sensitivity when compared with the standard formulation containing 0.25% Tween-80. (*See* Figure 16).

Example 11: Use of NIB-14 in the Presence of Varying Amounts of Sanitizers

[00329] The NIB-14 formulation included the use of neutralizers (*e.g.*Tween-80 and lecithin) meant to play a role in reducing the effects of remnant amounts of sanitizers in a sample. As such, NIB-14 was shown to allow for high amounts of infection and subsequent signal stability. (*See* Example 8). Subsequent assays, meant to ascertain the levels of

protection provided by the NIB-14 formulation towards various kinds remnant sanitizer samples were performed.

[00330] For these assays, the following were taken into account: (i) evaluation of whether the products glow on their own (*i.e.* in the absence of cells, phage and/or enzyme), (ii) evaluation of the effect of sanitizing chemicals on NanoGlo substrate (in the absence of cells, phage and/or enzyme), (iii) evaluation of the role that NIB-14 plays in the neutralization of remnant sanitizing chemicals by comparison of the effects obtained by the addition of NIB-14 versus those of the base bacterial growth medium, Letheen formulated to neutralize quaternary ammonium compounds. These assays incorporated the evaluation of the deleterious effects that the sanitizing compounds have at either (i) the point of phage infection, (ii) enzymatic activity, or (iii) direct effect on the NanoGlo luciferin substrate. To determine the effect of the sanitizing chemicals on phage infection, the 1893 cell-type was used at a density of 900 cells per well BHI basal medium, and further incubated with serially diluted (into either NIB-14 or Letheen buffer) sanitizing chemicals for 30 minutes. Following the 30 minute incubation period, the luciferase marker containing phage was added in BHI medium, and the samples were further allowed to incubate for an additional 3 hours at 30 °C. The enzyme was then detected by the addition of the NanoGlo luciferin substrate and luminescence measurement. In another variant of this assay, meant to ascertain the remnant sanitizer chemical interaction with the enzymatic activity, the sanitizer chemicals were added to the enzyme only in either NIB-14 or in Letheen for 3 hours at 30 °C. Another variant of this assay involved the direct incubation of the sterilization chemical with the NanoGlo luciferin substrate in the absence of either cells, phage or enzyme. In another version of this assay, the sanitizer chemicals were added at various time intervals (*e.g.* 5min to 120min) directly to the NIB-14 or to the Letheen, followed by the addition of cells and phage and incubated for 3 hours at 30 °C.

[00331] Control assays revealed that there were no false positive luminescence signals in the absence of the NanoGlo luciferase substrate.

[00332] The sanitizer solution, F29, which contains quaternary ammonium salts, was diluted to a final concentration of 0.26%, for a total quaternary ammonium salt concentration of approximately 300ppm for use in these assays. The recommended usage amounts of F29 for cleaning purposes is 150ppm of the active ingredient for a 3 minute duration of direct contact on non-food surfaces, and 400-800ppm in entryways. The assays

indicate that both the infection ability and the enzymatic activity are protected by the use of the NIB-14 medium in comparison to the Letheen medium. (*See* Figures 17A-17D). Greater than 20% phage infection rate was retained in exposures of up to 2600ppm of F29, and enzymatic activity of near 100% was maintained in exposures of up to 2600ppm of F29 during incubation with the NIB-14. (*See* Figures 17A and 17B, respectively). The effect of incubating different amounts of the F29 sanitizer with the NanoGlo substrate also indicated that the addition of NIB-14 in the assays had a beneficial protective effect on preserving the NanoGlo substrate, when compared to water. (*See* Figure 17C). A summary of the findings indicates that the addition of NIB-14 is beneficial at the phage infection step, the enzymatic step, and also provides protection of the NanoGlo substrate. (*See* Figure 17D).

[00333] Another sanitizer used to assess the protective ability of NIB-14 was Quorum Clear. The Quorum Clear sanitizer contains quaternary ammonium salts. The recommended usage concentration for Quorum Clear is a 3% solution. Addition of the NIB-14 medium was able to preserve up to 50% phage infection ability and enzyme activity at concentrations of Quorum Clear of up to 2.0% and 3.0%, respectively. NIB-14 was also able to provide protection to the NanoGlo substrate during exposures to Quorum Clear.

[00334] Another commonly used sanitizer component that was tested in the microbial detection system assays was hydrogen peroxide (H_2O_2). As in the previously described assays, the protective ability of NIB-14 was determined in situations where various concentrations of the sanitizing component were added either during the phage infection step, the enzymatic activity step, or to the NanoGlo substrate. The data indicate that NIB-14 provides protection to peroxide presence in comparison to Letheen. (*See* Figure 17A, 17B and 17D). The data do not indicate protection by NIB-14 to the NanoGlo substrate. (*See* Figure 17C). However, there are no deleterious effects to the NanoGlo substrate during exposure to peroxide at concentrations recommended for sanitizing (*i.e.* 500ppm).

[00335] Boost FT was another sanitizer used in the microbial detection system assays to determine the protective effects of NIB-14 in the microbial detection assays. Boost FT contains a combination of quaternary ammonium salts, peroxide (H_2O_2), and EDTA at elevated pH. The recommended concentration of use for Boost FT is 0.7%

concentration of the active ingredient. Addition of the NIB-14 medium was able to preserve up to 50% phage infection ability and enzyme activity at concentrations of Boost FT of up to 0.07% and greater than 0.7%, respectively. However, the increase noted in enzymatic activity may largely be due to oxidization of the NanoGlo substrate. The need for additional neutralization of peroxides was demonstrated.

[00336] The effects of another commonly used sanitizer, Clorox, and the protective benefits of NIB-14 medium on the microbial detection system in these conditions were assayed. The data indicated that at concentrations of greater than 400ppm of hypochlorite there was no infection signals detected. Likewise, enzymatic activity was also negatively affected in media tested, NIB-14 and Letheen. The hypochlorite concentrations that were tested did not negatively impact the NanoGlo substrate. An additional assay performed with the Clorox sanitizer was a time-course assay in which RLU was measured following incubation of Clorox for defined periods of time in either Letheen or in NIB-14, followed by addition of this solution to the microbial detection system assays. The data show that NIB-14 has a strong neutralization capacity in terms of allowing higher RLU activity with progressive time in Clorox. (*See* Figures 18A and 18B).

[00337] Further investigation into the addition of oxygen scavengers into the NIB-14 formulation was assessed. Data acquired from the microbial detection system assays demonstrated that the addition of either 2mM sodium metabisulfite or 0.05% sodium thiosulfate reduced the oxidizing effect of peroxide in the assay. The oxidizing effect of the peroxide found in Boost FT was lowered in the assays with either neutralizer when the effect on substrate signal alone was assessed. The addition of 2mM sodium metabisulfite was especially beneficial in lowering the signal at the highest Boost FT concentrations that were caused by peroxides when enzyme and infection activity were tested.

Example 12: Comparison of Infection Buffers in Stressed Cell Infection Assays

[00338] A direct comparison of infection and enzymatic activity using stressed cells infected with recombinant luciferase encoding phage was performed utilizing NIB buffers. These tests measured the direct performance of NIB-10*, NIB-12, and NIB-14 with regard to enhancing either enzymatic activity or infection rate. The base buffer, 1X BHI, was used as a comparison buffer for these tests. For the stressed cell assays, bacterial cells were

purposefully stressed by way of drying for 18 hours on a stainless steel table followed by downstream processing. The effect of the buffers was assessed either during the infection stage or during the enzymatic processing stage. Subsequently, the RLU activity was recorded for each of the buffer conditions.

[00339] The data indicate that NIB-12 (*see* Table 3) had the greatest beneficial effect during the infection step, as indicated by the highest RLU values among all of the buffers tested. (*See* Figure 9). The second most beneficial buffer in enhancing the infection step was NIB-14. This buffer offers instead higher neutralization power against residual sanitizers. The influence of the buffers was not as pronounced during the enzymatic activity phase; however, of the NIB buffers tested, NIB-12, supported the most enzymatic activity, followed by the similar enzymatic activity rates of both NIB-10 and NIB-14 as determined by RLU output. (*See* Figure 19).

*NIB-10 is composed of: 1X BHI, 0.5% LiCl, 0.002% nalidixic acid, 0.2% yeast extract, 2mM CaCl2, 40 mM HEPES, pH 7.4, 1mM sodium metabisulfite, 0.1% sodium thiosulfate, 0.5% Tween-80, and 0.1% lecithin.

Example 13: Lower Limit of Detection Assays in the Detection of Microbes in Food

[00340] Lower limit of detection assays ("LLOD") were performed with whole milk that had received a defined amount of *Listeria monocytogenes*. For these assays, 25 mL of 100% (full fat) whole milk, 25 mL of NIB-14 infection buffer (*see* Table 4), and $4.5X10^7$ pfu/mL recombinant marker encoding phage were used. The recombinant phage had luciferase as the recombinant marker. The results of the LLOD assays revealed that within 2 hours of the addition of *L. monocytogenes* to the food sample there was detectable signal in the assays, wherein up to 50 cells in a 50 mL sample was detectable. (*See* Figure 20A). These data indicate that up to 50 CFU of *L. monocytogenes* was detectable in the assays.

[00341] LLOD assays for the detection of *L. monocytogenes* were also performed with other foods including raw ground beef, deli turkey, guacamole and queso fresco. (*See* Figure 20B). The data from the LLOD assays with these foods also indicate that the target microbe was detectable at CFUs of between 1 and 10.

Example 14: Time Course Detection Assays for Microbes in Food

[00342] Assays to establish the amount of time before the detection of defined amounts of *L. monocytogenes* is possible were performed with food samples of turkey, guacamole, queso fresco, raw ground beef, potato salad, smoked salmon, and sour cream. For these assays, *L. monocytogenes* was added to the food sample, followed by waiting for a defined amount of time prior to adding the recombinant luciferase encoding phage for at least 2 hours, and subsequent assessment of the luciferin signal in the microbial detection assay. Depending on the kind of food in the assay, different dilutions of food matrix to incubation buffer were performed. The dilutions for the different foods assessed were: guacamole 1:3, ground beef (80/20) 1:3, whole milk 1:1, ice cream 1:1, queso fresco 1:1 and deli turkey 1:3. For example, for the detection of *L. monocytogenes* in deli turkey samples, 25 g of food matrix was spiked with either 2 or 20 CFU and then incubated with 75 mL NIB-14. Following the incubation, a sample of the NIB-14 liquid was incubated with the recombinant phage for 3 hours.

[00343] The results indicated that the detection of *L. monocytogenes* was found after 6 hours at both the 2 and 20 CFU conditions in the deli turkey food samples (Figure 21A), after 4 hours for the 20 CFU condition and 24 hours for the 2 CFU condition in the queso fresco samples (Figure 21B), after 8 hours in the 20 CFU condition for the guacamole samples (Figure 21C), and there was no detectable *L. monocytogenes* found at either the 2 or the 20 CFU conditions for the beef samples (Figure 21D). (*See* Figures 21A-D).

[00344] A comparison between the amounts of time before the detection of *L. monocytogenes* and *L. innocua* is presented in Figure 22A-M. For these experiments a four hour resuscitation/enrichment of the bacteria was performed followed by a three hour incubation with the luciferase encoding phage. The data indicate that the detection of *L. monocytogenes* is possible at lower CFU values when compared to the detection of *L.innocua.* As is indicated by the graphs, both bacteria species are detectable with the assay system. (*See* Figure 22 A-M).

[00345] Another time course to detection was performed using *L. monocytogenes* and *L. innocua* incubated in either pepperoni or spinach. (*See* Figure 23A-B). For these experiments a four hour resuscitation/enrichment of the bacteria was performed followed by a three hour incubation with the luciferase encoding phage. The data indicate there are

differences with regard to the time of incubation before which the bacteria are detected in either the spinach or the pepperoni. However, both bacterial species were detectable with the assay system by 6 hours of incubation.

[00346] A time course to detection assay was also performed using three species of *Listeria*, *L. seeligeri*, *L. innocua*, and *L. monocytogenes* incubated in turkey, queso, and in guacamole. (*See* Figure 24A-C). The data indicate that the detection of the various species of *Listeria* is dependent on food matrix type (*e.g.* shorter time to detection in Turkey) and the *Listeria* species.

[00347] Another time course to detection assay was performed utilizing various dilutions of food matrix (American cheese, spinach, pepperoni and ground chicken) to incubation buffer. (*See* Figure 25A-D). For these assays, *L. monocytogenes* was incubated for defined amounts of time (as illustrated in the graphs in Figure 25A-D) with dilutions of food matrix to the incubation buffer indicated in parentheses within Figure 25. The data indicate that food matrix, as well as the dilution of matrix to incubation buffer, has a role in the time course to detection of the *Listeria* species in these assays.

Example 15: *Listeria* Panel

[00348] A bacterial strain panel comprising a diverse combination of Listeria species and subspecies was selected for characterization of *Listeria* phages. The panel comprises strains that have been isolated from various geographic and environmental niches including food processing plants and food retail locations. Special consideration was given to obtain bacterial strains from food processing environments with sufficient geographic separation to maximize natural variation within the bacterial strain panel.

[00349] The panel as assembled initially contained 272 Listeria isolates and represents the four major species of *Listeria* (*L. monocytogenes, L. innocua, L. welshmeri* and *L. seelingri*) (Table 13). Within each species the panel comprises representative isolates of various subspecies to ensure sufficient depth of coverage to allow for meaningful extrapolation of the data to the subspecies in general. The selection of strains for the bacterial panel were based on the prevalence of particular strains within the food environment and associated with human disease. Environmental screening of retail food stores used allelotyping to identify the most commonly identified Listeria subspecies and identified that certain allelotypes were often highly represented among the population of

species identified. (Williams, S. K. et al., J Food Prot 74, 63–77 (2011); Sauders, B. D. et al., Appl Environ Microbiol 78, 4420–4433 (2012).) Ten (10) *L.* monocytogenes strains from each of the most common ribotypes represented from isolates from food and human disease were selected for the collection. These populations are largely overlapping and have a strong correlation in prevalence and, therefore, represent the strains most useful to identify in food processing plants. When looking at breadth of coverage of *L. monocytogenes* strains based on ribotypes isolated in human disease and food processing plants, the panel as constructed represents ~86% and 91% coverage, respectively. The purpose for selecting 10 strains of each *L. monocytogenes* ribotype was to allow for the identification of natural variation within a group to ensure a reasonably complete coverage of the *L. monocytogenes* species.

[00350] To expand beyond *L. monocytogenes* and cover other species within the genus additional species and subspecies variation was considered to select further strains for the panel. Again, focus was placed on the species and subspecies that are commonly identified in food processing plants. Ten (10) isolates representing each of the most common allelotypes of *L. welshmeri, L. innocua and L. selelingri* were selected. The panel as constructed covers 96% of the *L. innocua*, 98% of the *L. selelingri*, and 100% of the *L. welshmeri* ribotypes identified by Saunders *et al.* and provides an accurate representation of the *Listeria* genus. The Listeria host panel as assembled thus serves as a tool for the analysis of the host range of any bacteriophage against the *Listeria* genus. Accordingly, this panel can be used to define target bacteria of any given phage.

[00351] The genus, species, and subspecies of the members of the panel are provided in Table 13.

TABLE 13

Identifier	Strain Name	Genus/Species	Subspecies
NP1900	FSL R8-5085	Listeria innocua	sig B allelotype 11
NP1901	FSL R8-5091	Listeria innocua	sig B allelotype 11
NP1902	FSL R8-5098	Listeria innocua	sig B allelotype 11
NP1903	FSL R8-5255	Listeria innocua	sig B allelotype 11
NP1904	FSL R8-5293	Listeria innocua	sig B allelotype 11
NP1905	FSL R8-5295	Listeria innocua	sig B allelotype 11
NP1906	FSL R8-5306	Listeria innocua	sig B allelotype 11
NP1907	FSL R8-5440	Listeria innocua	sig B allelotype 11
NP1908	FSL R8-5442	Listeria innocua	sig B allelotype 11
NP1909	FSL R8-5448	Listeria innocua	sig B allelotype 11
NP1912	FSL R8-7061	Listeria innocua	sig B allelotype 22

NP1959	FSL S4-158	Listeria innocua	sig B allelotype 22
NP1960	FSL S10-784	Listeria innocua	sig B allelotype 22
NP1961	FSL F6-1168	Listeria innocua	sig B allelotype 22
NP1962	FSL R8-5961	Listeria innocua	sig B allelotype 22
NP1963	FSL R8-6922	Listeria innocua	sig B allelotype 22
NP1964	FSL R8-7352	Listeria innocua	sig B allelotype 22
NP1965	FSL R8-5598	Listeria innocua	sig B allelotype 22
NP1966	FSL R8-6733	Listeria innocua	sig B allelotype 22
NP1967	FSL R8-5942	Listeria innocua	sig B allelotype 22
NP1915	FSL R8-7548	Listeria innocua	sig B allelotype 37
NP1997	FSL R8-5764	Listeria innocua	sig B allelotype 37
NP1998	FSL R8-5802	Listeria innocua	sig B allelotype 37
NP1999	FSL R8-6012	Listeria innocua	sig B allelotype 37
NP2000	FSL R8-6355	Listeria innocua	sig B allelotype 37
NP2001	FSL R8-6369	Listeria innocua	sig B allelotype 37
NP2002	FSL R8-6476	Listeria innocua	sig B allelotype 37
NP2003	FSL R8-7175	Listeria innocua	sig B allelotype 37
NP2004	FSL R8-6888	Listeria innocua	sig B allelotype 37
NP2005	FSL R8-6672	Listeria innocua	sig B allelotype 37
NP1916	FSL R8-6667	Listeria innocua	sig B allelotype 56
NP2006	FSL S10-1311	Listeria innocua	sig B allelotype 56
NP2007	FSL F6-1159	Listeria innocua	sig B allelotype 56
NP2008	FSL F6-1126	Listeria innocua	sig B allelotype 56
NP2009	FSL S6-120	Listeria innocua	sig B allelotype 56
NP2010	FSL R8-5594	Listeria innocua	sig B allelotype 56
NP2011	FSL R8-7181	Listeria innocua	sig B allelotype 56
NP2012	FSL R2-632	Listeria innocua	sig B allelotype 56
NP2013	FSL L3-851	Listeria innocua	sig B allelotype 56
NP2014	FSL S10-1377	Listeria innocua	sig B allelotype 56
NP 1869	WSLC 3009	Listeria ivanovii	sig B allelotype 73
NP 1840	FSL J1-208	Listeria monocytogenes	ribotype DUP-10142
NP 1839	FSL F6-367	Listeria monocytogenes	ribotype DUP-1030A
NP2024	FSL F6-267	Listeria monocytogenes	ribotype DUP-1030A
NP2025	FSL F6-406	Listeria monocytogenes	ribotype DUP-1030A
NP2026	FSL H5-592	Listeria monocytogenes	ribotype DUP-1030A
NP2027	FSL H1-219	Listeria monocytogenes	ribotype DUP-1030A
NP2028	FSL H1-121	Listeria monocytogenes	ribotype DUP-1030A
NP2029	FSL W3-072	Listeria monocytogenes	ribotype DUP-1030A
NP2030	FSL N4-239	Listeria	ribotype DUP-

		monocytogenes	1030A
NP2031	FSL N3-293	Listeria monocytogenes	ribotype DUP-1030A
NP2032	FSL F3-319	Listeria monocytogenes	ribotype DUP-1030A
NP1879	FSL N4-221	Listeria monocytogenes	ribotype DUP-1030B
NP2033	FSL F2-738	Listeria monocytogenes	ribotype DUP-1030B
NP2034	FSL N3-881	Listeria monocytogenes	ribotype DUP-1030B
NP2035	FSL N4-048	Listeria monocytogenes	ribotype DUP-1030B
NP2036	FSL N4-696	Listeria monocytogenes	ribotype DUP-1030B
NP2037	FSL N4-242	Listeria monocytogenes	ribotype DUP-1030B
NP2038	FSL H4-364	Listeria monocytogenes	ribotype DUP-1030B
NP2039	FSL H4-147	Listeria monocytogenes	ribotype DUP-1030B
NP2040	FSL H4-946	Listeria monocytogenes	ribotype DUP-1030B
NP2041	FSL S4-461	Listeria monocytogenes	ribotype DUP-1030B
NP2042	FSL F6-206	Listeria monocytogenes	ribotype DUP-1038B
NP2043	FSL F6-224	Listeria monocytogenes	ribotype DUP-1038B
NP2044	FSL L3-739	Listeria monocytogenes	ribotype DUP-1038B
NP2045	FSL N3-008	Listeria monocytogenes	ribotype DUP-1038B
NP2046	FSL N3-022	Listeria monocytogenes	ribotype DUP-1038B
NP2047	FSL J1-108	Listeria monocytogenes	ribotype DUP-1038B
NP2048	FSL J1-119	Listeria monocytogenes	ribotype DUP-1038B
NP2049	FSL C1-122	Listeria monocytogenes	ribotype DUP-1038B
NP2050	FSL J1-126	Listeria monocytogenes	ribotype DUP-1038B
NP1880	FSL L3-159	Listeria monocytogenes	ribotype DUP-1039A
NP2051	FSL F3-285	Listeria monocytogenes	ribotype DUP-1039A

NP2052	FSL R6-288	Listeria monocytogenes	ribotype DUP-1039A
NP2053	FSL N1-021	Listeria monocytogenes	ribotype DUP-1039A
NP2054	FSL H1-208	Listeria monocytogenes	ribotype DUP-1039A
NP2055	FSL N3-034	Listeria monocytogenes	ribotype DUP-1039A
NP2056	FSL L5-072	Listeria monocytogenes	ribotype DUP-1039A
NP2057	FSL S6-131	Listeria monocytogenes	ribotype DUP-1039A
NP2058	FSL N3-278	Listeria monocytogenes	ribotype DUP-1039A
NP2059	FSL R2-282	Listeria monocytogenes	ribotype DUP-1039A
NP1881	FSL T1-323	Listeria monocytogenes	ribotype DUP-1039B
NP2060	FSL H5-770	Listeria monocytogenes	ribotype DUP-1039B
NP2061	FSL F6-207	Listeria monocytogenes	ribotype DUP-1039B
NP2062	FSL F6-236	Listeria monocytogenes	ribotype DUP-1039B
NP2063	FSL H5-795	Listeria monocytogenes	ribotype DUP-1039B
NP2064	FSL N3-246	Listeria monocytogenes	ribotype DUP-1039B
NP2065	FSL R2-062	Listeria monocytogenes	ribotype DUP-1039B
NP2066	FSL R2-437	Listeria monocytogenes	ribotype DUP-1039B
NP2067	FSL M1-004	Listeria monocytogenes	ribotype DUP-1039B
NP2068	FSL L4-352	Listeria monocytogenes	ribotype DUP-1039B
NP2069	FSL F6-605	Listeria monocytogenes	ribotype DUP-1039C
NP2070	FSL V1-001	Listeria monocytogenes	ribotype DUP-1039C
NP2071	FSL F6-464	Listeria monocytogenes	ribotype DUP-1039C
NP2072	FSL R8-2748	Listeria monocytogenes	ribotype DUP-1039C
NP2073	FSL R6-908	Listeria monocytogenes	ribotype DUP-1039C
NP2074	FSL L3-802	Listeria monocytogenes	ribotype DUP-1039C

NP2075	FSL F3-056	Listeria monocytogenes	ribotype DUP-1039C
NP2076	FSL J2-020	Listeria monocytogenes	ribotype DUP-1039C
NP2077	FSL S4-914	Listeria monocytogenes	ribotype DUP-1039C
NP1882	FSL H5-725	Listeria monocytogenes	ribotype DUP-1042A
NP2078	FSL F6-467	Listeria monocytogenes	ribotype DUP-1042A
NP2079	FSL F6-655	Listeria monocytogenes	ribotype DUP-1042A
NP2080	FSL F6-352	Listeria monocytogenes	ribotype DUP-1042A
NP2081	FSL H5-781	Listeria monocytogenes	ribotype DUP-1042A
NP2082	FSL K2-147	Listeria monocytogenes	ribotype DUP-1042A
NP2083	FSL V1-026	Listeria monocytogenes	ribotype DUP-1042A
NP2084	FSL H5-572	Listeria monocytogenes	ribotype DUP-1042A
NP2085	FSL K2-065	Listeria monocytogenes	ribotype DUP-1042A
NP2086	FSL H4-120	Listeria monocytogenes	ribotype DUP-1042A
NP2087	FSL F6-184	Listeria monocytogenes	ribotype DUP-1042B
NP2088	FSL F6-191	Listeria monocytogenes	ribotype DUP-1042B
NP2089	FSL H1-099	Listeria monocytogenes	ribotype DUP-1042B
NP2090	FSL J1-116	Listeria monocytogenes	ribotype DUP-1042B
NP2091	FSL R2-192	Listeria monocytogenes	ribotype DUP-1042B
NP2092	FSL J1-225	Listeria monocytogenes	ribotype DUP-1042B
NP2093	FSL R2-500	Listeria monocytogenes	ribotype DUP-1042B
NP2094	FSL R2-501	Listeria monocytogenes	ribotype DUP-1042B
NP2095	FSL E1-159	Listeria monocytogenes	ribotype DUP-1042B
NP2096	FSL F6-355	Listeria monocytogenes	ribotype DUP-1042C
NP2097	FSL F6-382	Listeria monocytogenes	ribotype DUP-1042C

NP2098	FSL F3-200	Listeria monocytogenes	ribotype DUP-1042C
NP2099	FSL K2-143	Listeria monocytogenes	ribotype DUP-1042C
NP2100	FSL N1-176	Listeria monocytogenes	ribotype DUP-1042C
NP2101	FSL N1-417	Listeria monocytogenes	ribotype DUP-1042C
NP2102	FSL L3-051	Listeria monocytogenes	ribotype DUP-1042C
NP2103	FSL T1-107	Listeria monocytogenes	ribotype DUP-1042C
NP2104	FSL T1-408	Listeria monocytogenes	ribotype DUP-1042C
NP1883	FSL T1-922	Listeria monocytogenes	ribotype DUP-1043A
NP2105	FSL F6-396	Listeria monocytogenes	ribotype DUP-1043A
NP2106	FSL H5-806	Listeria monocytogenes	ribotype DUP-1043A
NP2107	FSL F6-551	Listeria monocytogenes	ribotype DUP-1043A
NP2108	FSL F6-446	Listeria monocytogenes	ribotype DUP-1043A
NP2109	FSL F6-315	Listeria monocytogenes	ribotype DUP-1043A
NP2110	FSL V1-022	Listeria monocytogenes	ribotype DUP-1043A
NP2111	FSL R2-132	Listeria monocytogenes	ribotype DUP-1043A
NP2112	FSL R2-273	Listeria monocytogenes	ribotype DUP-1043A
NP2113	FSL N3-277	Listeria monocytogenes	ribotype DUP-1043A
NP1884	FSL H1-251	Listeria monocytogenes	ribotype DUP-1044A
NP2114	FSL F6-358	Listeria monocytogenes	ribotype DUP-1044A
NP2115	FSL F6-194	Listeria monocytogenes	ribotype DUP-1044A
NP2116	FSL R2-763	Listeria monocytogenes	ribotype DUP-1044A
NP2117	FSL R2-765	Listeria monocytogenes	ribotype DUP-1044A
NP2118	FSL R2-764	Listeria monocytogenes	ribotype DUP-1044A
NP2119	FSL N1-225	Listeria monocytogenes	ribotype DUP-1044A

NP2120	FSL N1-227	Listeria monocytogenes	ribotype DUP-1044A
NP2121	FSL N1-048	Listeria monocytogenes	ribotype DUP-1044A
NP2122	FSL K2-131	Listeria monocytogenes	ribotype DUP-1044A
NP1885	FSL L3-501	Listeria monocytogenes	ribotype DUP-1044B
NP2123	FSL F6-222	Listeria monocytogenes	ribotype DUP-1044B
NP2124	FSL F6-249	Listeria monocytogenes	ribotype DUP-1044B
NP2125	FSL N3-065	Listeria monocytogenes	ribotype DUP-1044B
NP2126	FSL H4-699	Listeria monocytogenes	ribotype DUP-1044B
NP2127	FSL L4-241	Listeria monocytogenes	ribotype DUP-1044B
NP2128	FSL S4-643	Listeria monocytogenes	ribotype DUP-1044B
NP2129	FSL R2-073	Listeria monocytogenes	ribotype DUP-1044B
NP2130	FSL F3-224	Listeria monocytogenes	ribotype DUP-1044B
NP2131	FSL N4-334	Listeria monocytogenes	ribotype DUP-1044B
NP1886	FSL R2-069	Listeria monocytogenes	ribotype DUP-1044E
NP2132	FSL R2-070	Listeria monocytogenes	ribotype DUP-1044E
NP1887	FSL H1-030	Listeria monocytogenes	ribotype DUP-1045B
NP2133	FSL F6-421	Listeria monocytogenes	ribotype DUP-1045B
NP2134	FSL F6-449	Listeria monocytogenes	ribotype DUP-1045B
NP2135	FSL J2-054	Listeria monocytogenes	ribotype DUP-1045B
NP2136	FSL S4-024	Listeria monocytogenes	ribotype DUP-1045B
NP2137	FSL H1-111	Listeria monocytogenes	ribotype DUP-1045B
NP2138	FSL K2-022	Listeria monocytogenes	ribotype DUP-1045B
NP2139	FSL S4-066	Listeria monocytogenes	ribotype DUP-1045B
NP2140	FSL R2-067	Listeria monocytogenes	ribotype DUP-1045B

NP2141	FSL R2-293	Listeria monocytogenes	ribotype DUP-1045B
NP2142	FSL F6-323	Listeria monocytogenes	ribotype DUP-1052A
NP2143	FSL F6-216	Listeria monocytogenes	ribotype DUP-1052A
NP2144	FSL F6-321	Listeria monocytogenes	ribotype DUP-1052A
NP2145	FSL V1-117	Listeria monocytogenes	ribotype DUP-1052A
NP2146	FSL H5-846	Listeria monocytogenes	ribotype DUP-1052A
NP2147	FSL L3-055	Listeria monocytogenes	ribotype DUP-1052A
NP2148	FSL T1-313	Listeria monocytogenes	ribotype DUP-1052A
NP2149	FSL R8-0875	Listeria monocytogenes	ribotype DUP-1052A
NP2150	FSL R2-317	Listeria monocytogenes	ribotype DUP-1052A
NP1888	FSL L4-019	Listeria monocytogenes	ribotype DUP-1053A
NP2151	FSL F6-335	Listeria monocytogenes	ribotype DUP-1053A
NP2152	FSL R6-653	Listeria monocytogenes	ribotype DUP-1053A
NP2153	FSL L3-135	Listeria monocytogenes	ribotype DUP-1053A
NP2154	FSL L3-143	Listeria monocytogenes	ribotype DUP-1053A
NP2155	FSL L3-167	Listeria monocytogenes	ribotype DUP-1053A
NP2156	FSL N3-031	Listeria monocytogenes	ribotype DUP-1053A
NP2157	FSL J1-101	Listeria monocytogenes	ribotype DUP-1053A
NP2158	FSL F6-154	Listeria monocytogenes	ribotype DUP-1053A
NP2159	FSL R2-499	Listeria monocytogenes	ribotype DUP-1053A
NP1889	FSL T1-027	Listeria monocytogenes	ribotype DUP-1062A
NP2160	FSL F6-325	Listeria monocytogenes	ribotype DUP-1062A
NP2161	FSL F6-220	Listeria monocytogenes	ribotype DUP-1062A
NP2162	FSL F6-319	Listeria monocytogenes	ribotype DUP-1062A

NP2163	FSL F6-365	Listeria monocytogenes	ribotype DUP-1062A
NP2164	FSL F6-360	Listeria monocytogenes	ribotype DUP-1062A
NP2165	FSL F6-313	Listeria monocytogenes	ribotype DUP-1062A
NP2166	FSL R2-031	Listeria monocytogenes	ribotype DUP-1062A
NP2167	FSL R2-050	Listeria monocytogenes	ribotype DUP-1062A
NP2168	FSL R2-078	Listeria monocytogenes	ribotype DUP-1062A
NP1890	FSL T1-041	Listeria monocytogenes	ribotype DUP-1062D
NP2169	FSL F6-264	Listeria monocytogenes	ribotype DUP-1062D
NP2170	FSL F3-146	Listeria monocytogenes	ribotype DUP-1062D
NP2171	FSL F3-194	Listeria monocytogenes	ribotype DUP-1062D
NP2172	FSL H4-122	Listeria monocytogenes	ribotype DUP-1062D
NP2173	FSL H4-286	Listeria monocytogenes	ribotype DUP-1062D
NP2174	FSL R6-646	Listeria monocytogenes	ribotype DUP-1062D
NP2175	FSL T1-041	Listeria monocytogenes	ribotype DUP-1062D
NP2176	FSL F7-002	Listeria monocytogenes	ribotype DUP-1062D
NP2177	FSL X1-005	Listeria monocytogenes	ribotype DUP-1062D
NP 1878	EGD-e	Listeria monocytogenes	
NP1911	FSL R8-7641	Listeria seeligeri	sig B allelotype 20
NP1950	FSL S10-030	Listeria seeligeri	sig B allelotype 20
NP1951	FSL S10-320	Listeria seeligeri	sig B allelotype 20
NP1952	FSL S10-1602	Listeria seeligeri	sig B allelotype 20
NP1953	FSL L5-075	Listeria seeligeri	sig B allelotype 20
NP1954	FSL L5-046	Listeria seeligeri	sig B allelotype 20
NP1955	FSL L5-104	Listeria seeligeri	sig B allelotype 20
NP1956	FSL R8-7575	Listeria seeligeri	sig B allelotype 20
NP1957	FSL S4-178	Listeria seeligeri	sig B allelotype 20
NP1958	FSL S4-135	Listeria seeligeri	sig B allelotype 20
NP1913	FSL R8-6826	Listeria seeligeri	sig B allelotype 24
NP1968	FSL S10-034	Listeria seeligeri	sig B allelotype 24
NP1969	FSL S10-1611	Listeria seeligeri	sig B allelotype 24

NP1970	FSL L5-054	Listeria seeligeri	sig B allelotype 24
NP1971	FSL L5-085	Listeria seeligeri	sig B allelotype 24
NP1972	FSL R8-6868	Listeria seeligeri	sig B allelotype 24
NP1973	FSL R8-6545	Listeria seeligeri	sig B allelotype 24
NP1974	FSL R8-6949	Listeria seeligeri	sig B allelotype 24
NP1975	FSL S4-167	Listeria seeligeri	sig B allelotype 24
NP1976	FSL S4-180	Listeria seeligeri	sig B allelotype 24
NP1891	FSL R8-5241	Listeria seeligeri	sig B allelotype 3
NP1892	FSL R8-5247	Listeria seeligeri	sig B allelotype 3
NP1893	FSL R8-5253	Listeria seeligeri	sig B allelotype 3
NP1894	FSL R8-5513	Listeria seeligeri	sig B allelotype 3
NP1895	FSL R8-6629	Listeria seeligeri	sig B allelotype 3
NP1896	FSL R8-6635	Listeria seeligeri	sig B allelotype 3
NP1897	FSL R8-6659	Listeria seeligeri	sig B allelotype 3
NP1898	FSL R8-6665	Listeria seeligeri	sig B allelotype 3
NP1899	FSL R8-6852	Listeria seeligeri	sig B allelotype 3
NP1990	FSL H6-027	Listeria seeligeri	sig B allelotype 35
NP1991	FSL H6-079	Listeria seeligeri	sig B allelotype 35
NP1992	FSL H6-185	Listeria seeligeri	sig B allelotype 35
NP1993	FSL R8-6874	Listeria seeligeri	sig B allelotype 35
NP1994	FSLR8-6880	Listeria seeligeri	sig B allelotype 35
NP1995	FSL R8-7629	Listeria seeligeri	sig B allelotype 35
NP1996	FSL S4-544	Listeria seeligeri	sig B allelotype 35
NP1910	FSL R8-7026	Listeria welshimeri	sig B allelotype 15
NP1945	FSL L5-079	Listeria welshimeri	sig B allelotype 15
NP1946	FSL S10-1450	Listeria welshimeri	sig B allelotype 15
NP1947	FSL S10-1451	Listeria welshimeri	sig B allelotype 15
NP1948	FSL S4-081	Listeria welshimeri	sig B allelotype 15
NP1949	FSL S4-101	Listeria welshimeri	sig B allelotype 15
NP1977	FSL N1-064	Listeria welshimeri	sig B allelotype 27
NP1978	FSL R8-8163	Listeria welshimeri	sig B allelotype 27
NP1979	FSL R8-7524	Listeria welshimeri	sig B allelotype 27
NP1980	FSL R8-7486	Listeria welshimeri	sig B allelotype 27
NP1981	FSL R8-6035	Listeria welshimeri	sig B allelotype 27
NP1982	FSL R8-5807	Listeria welshimeri	sig B allelotype 27
NP1983	FSL S4-182	Listeria welshimeri	sig B allelotype 27
NP1984	FSL R2-630	Listeria welshimeri	sig B allelotype 27
NP1985	FSL F6-1131	Listeria welshimeri	sig B allelotype 27
NP1914	FSL R8-7454	Listeria welshimeri	sig B allelotype 32
NP1986	FSL R8-7041	Listeria welshimeri	sig B allelotype 32
NP1987	FSL R8-5837	Listeria welshimeri	sig B allelotype 32
NP1988	FSL R8-6136	Listeria welshimeri	sig B allelotype 32
NP1989	FSL S4-289	Listeria welshimeri	sig B allelotype 32
NP1917	FSL R8-1903	Listeria welshimeri	sig B allelotype 89
NP2015	FSL S10-114	Listeria welshimeri	sig B allelotype 89
NP2016	FSL S10-115	Listeria welshimeri	sig B allelotype 89
NP2017	FSL S10-117	Listeria welshimeri	sig B allelotype 89

NP2018	FSL S10-119	Listeria welshimeri	sig B allelotype 89
NP2019	FSL S10-121	Listeria welshimeri	sig B allelotype 89
NP2020	FSL R8-0056	Listeria welshimeri	sig B allelotype 89
NP2021	FSL R8-1198	Listeria welshimeri	sig B allelotype 89
NP2022	FSL R8-7403	Listeria welshimeri	sig B allelotype 89
NP2023	FSL R2-631	Listeria welshimeri	sig B allelotype 89

Example 16: Plate-Based Phage Host Range Assay

[00352] In order to quantify the host range a given bacteriophage the plaque forming efficiency of the bacteriophage on a given isolate was standardized to a reference strain for the bacteriophage, normally the strain used for bacteriophage production. To determine the plaque forming efficiency a dilution series for the phage is generated and titered on each host. Before the work reported herein, this was the standard method of phage host range analysis. See, e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 3d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (2001).

[00353] The Listeria bacterial strain panel was used to determine the host range for a particular bacteriophage. To do this a culture of each Listeria strain to be tested was started in 5 ml of LBL1 and grown overnight at 30C in an orbital shaker and allowed to grow for 16 hours. For each bacterial host strain 30 µl of the 16-hour culture was mixed with 270 µl of fresh LBL1 medium. To each cell dilution, 4 ml of LBL1 soft agar was added and overlayed onto LBL1 agar in 100 mm petri dish. The soft agar overlay was allowed to cool and solidify at room temperature. Additionally, a reference strain (FSL F6-367 for A511 and P100) was treated in a similar manner to the host range isolates. A 10-fold dilution series of the bacteriophage in LBL1 medium was prepared from 10^{-1} to 10^{-8}. 5µl of each dilution of the bacteriophage was spotted onto the soft agar overlay and the liquid was allowed to adsorb and then the plate was incubated at 30C for 16 hours. After incubation the plaques present at each dilution series were counted and compared to the reference strain to provide an efficiency of plaquing for each host range isolate. The host range was represented as a percentage of the titer observed on the experimental host compared to the reference strain. Bacterial strains that showed a plaquing efficiency greater than 10% (Table 19, dark gray shading) of the reference strain were considered to be within the host range. Bacterial strains that showed a plaquing efficiency less than 10% but greater than .01% (Table 19, light gray shade) of the reference strain were considered to be weakly susceptible to the phage. Bacterial strains that showed a plaquing efficiency

less than .01 % (Table 19, unshaded) of the reference strain were considered to be outside of the host range for a phage. A phenomenon that was seen for many of the bacterial strains tested was what has been described in the literature and art as "extracellular killing" (ECK) (Table 19, black), see e.g. Shaw et al. (J Immunol Methods. 1983;56(1):75-83). A strain was defined as demonstrating ECK for a particular phage when at high phage concentration completely cleared the lawn, however, subsequent dilutions did not produce clearing.

[00354] The plate-based host range determination allowed for a rough approximation of the host range of A511 and P100 against the Listeria isolate library. Of the 272 strains tested in the bacterial strain library 67 and 120 strains supported plaque formation by A511 and P100, respectively (Table 19). The greatest limitations of this method were the length of time needed to process the entire library for a give bacteriophage and the inability to determine the entire host range due to the ECK phenomenon. For the bacteriophage A511 and P100, of the 272 bacterial strains in the host range panel tested, 117 and 42, respectively, showed ECK and hence provided no information about the host range for these strains. Additionally, in view of the ECK phenomenon and because of the general differences between bacteria growing on a plate and bacteria growing in a liquid culture, it was hypothesized that the plate-based method for determining host range may not represent the host range for a liquid-based application.

Example 17: A Liquid Culture Phage Host Range Assay

[00355] The prevalence of the extra-cellular killing (ECK) phenomenon demonstrated by both A511 and P100 in the plate-based host range method demonstrates that the plate based is not as useful as it could be for determining the host range for either phage. To overcome those deficiencies a novel liquid-based host range assay was developed. The liquid-based host range assay is an end point assay where the ability of a phage to infect a particular bacterial isolate is determined by comparing the optical density of a culture with or without bacteriophage.

[00356] The Listeria host panel strain collection (Table 13) was struck out on Brain Heart Infusion (BHI) agar plates and single colonies were inoculated in 1 ml BHI liquid in a 2-ml 96-deep well dish, covered with a sterile breathable sterile membrane and grown at 30C for 16 hours. Each of the 16-hour cultures from the 96-well plates were diluted 1:10,000 in 198 µl of LBL1 in a 300 µl flat-bottom optical 96-well plate and then either 1

X 10^5 pfu of the bacteriophage or an equivalent volume of LBL1 was added to each well of the 96-well plate. This concentration of bacteriophage and bacterial cell dilutions was to approximate a multiplicity of infection (MOI) of 1 in each well. After addition of the phage or control, the plates were incubated at 26C with shaking at 50 rpm for 16-hours. Plates were placed in a 96-well plate reader (Biotek Eon Microplate Reader) and agitated for 3 seconds with orbital shaking to resuspend cells that had settled out of culture. After the agitation, the optical density of each well was measure at 600 nm (OD600) wavelength light. The ratio of OD600 of the bacterial isolate in the presence of bacteriophage to the uninfected bacterial isolate culture was used as a metric to determine the efficiency of infection for a bacterial strain. A bacterial strain with a ratio of less than or equal to 0.4 (Table 2, dark gray shade) was considered to be sensitive to infection by the bacteriophage.

[00357] The liquid-based host range assay identified 192 and 153 bacterial strains sensitive to A511 and P100, respectively, of the 272 strains in the bacterial strain panel (Table 19). This data shows that A511 is capable of infecting approximately 70% and P100 is capable of infecting approximately 58% of the host range panel. In comparison to the liquid-based host range, the plate-based host range method identified 62 and 120 bacterial strains that demonstrated a plaquing-efficiency for A511 and P100, respectively. Of the strains identified in the plate-based host range methods, only 8 A511-sensitive bacterial strains and 3 P100-sensitive bacterial strains did not show clearance in the liquid-based clearance assay. Because the liquid-based assay is an endpoint assay and represents a kinetic interaction between bacteriophage infection and bacterial cell growth certain bacterial strains with increased cell growth rates may be able to saturate a culture even though the strain is susceptible to infection and this may explain the reason why a small number of strains identified in the plaque-based assay were not identified in the liquid assay.

[00358] The additional strains identified by the liquid-based host range assay were due to the ability to collect data on strains that demonstrated an ECK phenotype in the plate-based host range assay. The large number of strains that demonstrated this phenotype created a large amount of unknown information regarding the host range for A511 and P100. The liquid-based assay eliminated the ECK phenomenon, one of the large drawbacks of the plate-based host range method. Two factors contributed to the lack of ECK. First the concentration of phages used in the liquid-based assay is a set

concentration that is lower than the concentrations of phage that demonstrated ECK in the plate-based host range assay. Second, the delocalized concentration of bacteriophage within the liquid infection and the low MOI decreases the number of interactions between the bacterial cells and bacteriophage. The limited interaction decreases the possibility of non-productive encounters and lowers super-infection, or infection by multiple bacteriophages of a cell. By eliminating ECK, the sensitivity for measuring susceptibility of a particular bacterial cell to a bacteriophage was increased substantially and provided a more accurate representation of the host range of a bacteriophage across the Listeria species.

[00359] The liquid-based host range assay showed substantial advances over the prior method of using a plate-based system for determining host range of a bacteriophage. Previous literature did not report the ability of growing these bacteriophages in a format other than a plate-based method. The liquid format is also useful because the speed with which the liquid-based host range assay can be performed increases the speed of determining the host range of a bacteriophage from 7-10 days for the panel as it was assembled to several hours of hands on labor. Additionally, the high-throughput nature of the scoring of host susceptibility allowed for multiple bacteriophage host ranges to be determined concurrently, a possibility that did not exist previously. The ability to process multiple bacteriophages concurrently allowed for a more direct comparison of bacteriophages by minimizing variation between bacterial culture physiology and media lots. Together, the increased speed and direct bacteriophage characterizations allowed for rapid processing of multiple phages and prioritization for bacteriophage engineering described herein. Moreover, the liquid-based host range assay allowed for a more accurate representation of the functional determination of a potential bacteriophage in a predicted product compared to a plate-based host range assay. The combination of the increased speed, ability for more direct comparison and ability to assess functionality of a bacteriophage in a more direct method to the final product makes the liquid-based host range assay significantly more useful than the plate-based host range method in most contexts.

[00360] The efficacy of a cocktail of a P100 and A511 bacteriophage can be determined by the ability of each of the bacteriophages to infect a particular strain. Infections of the host panel with a cocktail of P100 and A511 show the additive host range

expected from the extrapolation of the individual host ranges. Based on observations regarding the bacteriophage concentration required for optimum luciferase production during the course of infection, the concentration of bacteriophage added was maintained at a constant total phage concentration of $1X10^7$ whether a single bacteriophage or multiple phage cocktail was used for infections. The cocktail of A511 and P100 shows coverage of 74% of the panel constructed, while the individual bacteriophages show 70% and 55% coverage, respectively. (Table 19) This increased coverage of the panel arises from the face that while the phages have largely overlapping coverage the subset of strains susceptible to P100 infection is not full encompassed within the A511 strains. The ability to extrapolate function of a bacteriophage cocktail from the individual liquid-based host range provides as a powerful tool to identify and prioritize new bacteriophages for engineering to build a more complete cocktail.

[00361] The function of a bacteriophage cocktail of P100 and A511 on samples collected from environmental samples cannot be strictly inferred from the host panel assembled. The sites sampled in environmental testing represent diverse populations of bacteria and often have more than one species or subspecies of Listeria present at an individual location. Environmental sampling at food processing plants with geographic and source diversity identified 31 samples that have been confirmed positive for Listeria using a culture based method of detection at a third-party laboratory. Of these 31 positive samples, 10 samples contained multiple Listeria species or subspecies. The A511 and P100 cocktail was capable of detecting 24 of the 31 (77%) of the positive samples. The correlation between the liquid-based host range results and the environmental samples collected allows for further iterations on the bacteriophage cocktail to be made in order to gain more complete coverage of the Listeria genus and validated the usefulness of the liquid-based host range method.

Example 18: Host Range Characterization of Additional Listeria Phages

[00362] Construction of a Listeria host strain panel and development of a rapid liquid-based host range assay allowed for the rapid screening of additional bacteriophages to identify those bacteriophages that would increase the breadth of coverage of the Listeria genus. Twenty five additional bacteriophages were screened against the host panel in the liquid-based host range assay and analyzed for host susceptibility based on clearance versus an uninfected control. The data are presented in Tables 21-23. Strains were

considered within host range if they demonstrated a ratio of 0.4 or less (shaded dark gray). During the determination of the OD600 of the cultures there was no correction for the absorbance of the growth medium or culture plate, therefore, a ratio of 0.09 constituted a completely cleared culture by infection. Because of variations in the maximum OD600 obtained by different Listeria strains a conservative ratio of 0.4 was chosen to denote Listeria strains that were sensitive to a given bacteriophage. Strains that had an OD600 ratio of greater than 0.4 were considered to be outside of host range (Tables 21-23, unshaded). From these twenty five bacteriophages assayed, seven (7) bacteriophages were selected to proceed into engineering based on the criteria that they provided useful host panel coverage, had genome sequence availability for development of phage targeting vectors and were capable of infecting *L. monocytogenes* strain EGD-e, the strain of Listeria most amenable to transformation.

[00363] The seven bacteriophages selected in addition to A511 and P100 were LP44, LP40, LP48, LP99, LP101, LP124, LP125, and LP143. No individual phage assayed covers more than 78% of the Listeria host strain panel. In combination, the bacteriophages cover approximately 92% of the host strain panel as assayed by liquid-based host range assay (Tables 21-23). This combinatorial approach allows for the construction of a bacteriophage cocktail that provides the necessary coverage of the Listeria species to provide a reliable determination of the presence of Listeria in environmental sample collection.

[00364] After engineering the genome of the phages with two different genetic payloads, Firefly Luciferase and Nanoluciferase, the host range of these phages was retested to ensure that the genome modifications did not affect the fitness of the phages or compromise their ability to infect the target bacteria. To examine the result of combining bacteriophages in an infection the liquid-based host range assay was used to test the combinatorial effects of phage infection. For these infections the final concentration of phage was maintained at a constant $1X10^5$ pfu consisting of equal amounts of each of the phage within the cocktail (i.e. – a two phage cocktail would consist of $5X10^4$ pfu of each of the two component phages.

Example 19: Engineering Listeria Phage

[00365] A novel phage engineering method was developed to create recombinant phage. This method is sometimes referred to herein as Phage Infective Engineering (PIE).

This method allows insertion of a heterologous nucleic acid sequence into any desired location of a phage genome. The initial site chosen for insertion was that used in *Loessner, et al.* (Appl. Environ Microbiol., 62:1133–1140), downstream of the major capsid protein gene *cps*. The coding sequence (SEQ ID NO: 1) for the firefly luciferase (SEQ ID NO: 2) or the coding sequence (SEQ ID NO: 3) for the nanoluc luciferase (SEQ ID NO: 4) was inserted at this location.

[00366] The PIE method uses Phage Targeting Vectors PTVs which include the luciferase gene sequence flanked by ~1KB of phage sequence directly upstream and downstream of the desired insertion site (referred to as an upstream homology region (UHR) and downstream homology region (DHR)). Each of these inserts was created using PCR primers that would amplify the desired amplicon, while adding 20bp of homology to facilitate assembly. Plasmids were assembled using the GeneArt Seamless Assembly Kit (Life Technologies). The 3 inserts (UHR, luc, DHR) were assembled into the gram positive/gram negative shuttle vector pMK4, which was restriction-digested with SmaI and PstI (NEB).

[00367] The A511 phage genome sequence is available in Genbank (NC_009811). A511 phage may be obtained from ATCC (PTA-4608™).

[00368] The PIE method was used to insert the firefly luciferase gene (SEQ ID NO: 1) directly after the stop codon of the *cps* gene of A511, between bases 46,695 and 46,696 of the genomic sequence. No sequence was deleted from the phage genome. A 16bp sequence containing a ribosome-binding site (GAGGAGGTAAATATAT) (SEQ ID NO: 67) was placed before the start (ATG) of the firefly luciferase gene.

[00369] To engineer phage A511, 1276 bases of the *cps* gene were amplified using oligos “pMAK upf” and “pMAK upr”, forming the fragment “A511 UHR”. The luciferase gene was amplified using primers “pMAK lucf” and “pMAK lucr”, creating the fragment “A511 luc”. The primer “pMAK lucf” also added a ribosome binding site (Shine-Dalgarno) upstream of the luciferase gene. The 1140bp immediately after the *cps* stop codon was amplified using “pMAK dnf” and “pMAK dnr”, named “A511 DHR”.

[00370] These 3 amplicons were recombineered into pMK4 which had been restriction digested with SmaI/PstI using the GeneArt Seamless Assembly Kit, according to the manufacturer’s instructions. Once isolated in *E.coli*, the plasmid was sequenced to verify correct amplification and assembly. Upon verification, the plasmid was transformed

into the L. monocytogenes strain EGD-e and selected on BHI-chloramphenicol (10µg/ml) agar plates.

[00371] Once the PTV was successfully transformed into EGD-e, the initial recombination was performed: An overnight culture of the A511::FF PTV-containing EGD-e was diluted 1:100 and allowed to grow to an OD600 of 0.1. This culture was then diluted back to an OD600 of 0.02 and mixed with 1e5 pfu/ml of wild-type A511 phage in a 2 ml volume. This infection was cultured at 30°C, shaken at 50rpm overnight.

[00372] To assess whether recombination had occurred, the infection was assayed on the following day. First, the lysate was mixed with chloroform to kill any remaining cells, and to destroy the background luciferase made by the PTV. The phage is chloroform-resistant, which is a common trait in bacteriophages. 4% v/v CHCl3 was added to the lysate, vortexed, spun down, and the supernatant was recovered. A test infection was done, adding a 1:10 dilution of an overnight culture of EGD-e was mixed with the recombinant lysate (90µl cell dilution, 10µl phage lysate). A control infection was set up without cells. The infections were incubated statically at 30°C for 3hr, then assayed for luminescence on the Glomax 20/20. 20µl of the infection was mixed with 100µl of Promega Luciferase Assay Reagent (20µl of lysate and 20µl of NanoGlo for the NanoLuc phages), then read using a 10 second integration (1s for NanoGlo). The recombinant lysate produced light, indicating that there were recombinant phage in the lysate.

[00373] In order to enrich and isolate the recombinant phage, it needed to be separated away from the wild-type phages present in the recombinant lysate. Successive rounds of dilution and division were employed. Lysates were made with 10-fold dilutions of input phages, and screened for the presence of recombinant phage by assaying the lysates for luciferase activity.

[00374] The recombination efficiency was estimated to be 1:1e5 to 1:1e6. In order to isolate a pure recombinant lysate, the methods described in (Appl. Environ Microbiol. 62:1133–1140) were modified as follows. The initial recombinant lysate was titered. 20 1-ml lysates were set up each with 1e6, 1e5, and 1e4 pfu/ml of the recombinant lysate: 1ml EGD-e @ OD 0.02, 1eX phages; O/N, 30C, 50rpm. On the following day, the CHCl3 treatment was done, as described above, for each lysate. The lysates were used to set up infections as above. Each lysate was assayed on the Glomax 20/20 (20µl infection, 100µl Reagent for FF, 20µl infection, 20µl NanoGlo for nluc). The goal was to locate the lysate

that was made with the fewest number of phages that exhibits luminescence upon infection. Once this lysate was identified, it was titered and used to set up lysates with 1e3, 1e2 and 1e1 pfu/ml. Once a luminescent lysate was isolated that had been made with 1e2 phages, this lysate was plated for single plaques. Plaques were picked into SM buffer. These "soakates" were diluted 1:10 in dH2O and assayed by PCR using "DBONO360" and "DBONO361" to look for the presence of recombinant junctions between the luciferase gene and phage sequence.

[00375] The P100 phage genomic sequence is available in Genbank (DQ004855). P100 may be obtained from ATCC (PTA-4383™).

[00376] The luciferase insertion site for P100 was also downstream of the same cps gene. The location of the firefly luciferase insertion in P100 is between base 13,196 and 13,197 of the P100 genomic sequence.

[00377] P100 was engineered in the same manner as A511 with the following exceptions: the "P100 DHR" fragment was amplified using the primers "pMAK dnf" and "pMAK dnr P100". The single recombinant plaque was identified by picking the plaque into 100µl SM buffer. 10µl of this soakate was mixed with 50µl of luciferin and luminescence was seen on the luminometer. This method of identifying positives was utilized in subsequent recombinant phage isolation.

[00378] The following phages were engineered using the firefly luciferase gene and the methods described for A511::ffluc: LP48, LP124, LP125, LP99, LP101, LP143.

[00379] The following phages were engineered using the NanoLuc gene: A511, P100, LP40, LP124 and LP125.

[00380] The PTV for A511::nluc was constructed by amplifying the following PCR fragments : Using an A511 lysate as the template, the UHR fragment was generated using oligos pMAK upf and DBONO356; the DHR fragment was amplified using oligos DBONO359 and pMAK dnr. Using the Promega plasmid pNL1.1 as a template, the NanoLuc fragment was amplified using oligos DBONO357 and DBONO358. The assembly and subsequent PIE methods were similar to those described.

[00381] The PTV and engineering for P100::nluc was performed in the same way as for A511::nluc, with the exception that the DHR fragment was amplified using the oligo pMAK dnr P100 rather than pMAK dnr.

[00382] The PTVs for LP124, LP125, and LP40 were constructed in the same way as A511::nluc, with the following changes. The DHR fragment amplified was shorter to allow for more efficient assembly of the plasmid, using oligos DBONO359 and DBONO382. Also, the insertion site was modified by adding two additional stop codons (TAATAA) directly downstream of the *cps* gene of these phages. These 6 bases were added by creating additional primers DBONO379 and DBONO380. The UHR fragments for these phages were amplified using oligos pMAK upf and DBONO380. The NanoLuc fragments were amplified using oligos DBONO379 and DBONO358.

[00383] The following oligonucleotides were used in the PIE methods:

[00384] pMAK upf:
TTACGCCAAGCTTGGCTGCAACGTGAGTTCCTAGACGACC (SEQ ID NO: 55)

[00385] pMAK upr:
ATGTTTTTGGCGTCTTCCATATATATTTACCTCCTCTTAGTTGCTATGAACGTTT T (SEQ ID NO: 68)

[00386] pMAK lucf:
AAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAA ACAT (SEQ ID NO: 69)

[00387] pMAK lucr:
ATTCAATTATCCTATAATTATTACAATTTGGACTTTCCGC (SEQ ID NO: 70)

[00388] pMAK dnf:
GCGGAAAGTCCAAATTGTAATAATTATAGGATAATTGAAT (SEQ ID NO: 71)

[00389] pMAK dnr:
ACGACGGCCAGTGAATTCCCAGTTACTAACTGCTCTAATG (SEQ ID NO: 72)

[00390] pMAK dnr P100:
ACGACGGCCAGTGAATTCCCAGTTACTAACTGTTCTAATG (SEQ ID NO: 73)

[00391] DBONO360: CCTCTAGCTCAAATTAACGCATCTGT (SEQ ID NO: 74)

[00392] DBONO361: TGGCTCTACATGCTTAGGGTTCC (SEQ ID NO: 75)

[00393] DBONO356:
TCTTCGAGTGTGAAGACCATATATATTTACCTCCTCTTAGTTGC (SEQ ID NO: 76)

[00394] DBONO357:
CTAAGAGGAGGTAAATATATATGGTCTTCACACTCGAAGATTT (SEQ ID NO: 77)

[00395] DBONO358:
ATTCAATTATCCTATAATTATTACGCCAGAATGCGTTCGC (SEQ ID NO: 78)
[00396] DBONO359:
GCGAACGCATTCTGGCGTAATAATTATAGGATAATTGAATAAA (SEQ ID NO: 79)
[00397] DBONO379:
AAAACGTTCATAGCAACTAATAATAAGAGGAGGTAAATATATATGGTCTTCAC ACTCGAAGATTT (SEQ ID NO: 80)
[00398] DBONO380:
ATATTTACCTCCTCTTATTATTAGTTGCTATGAACGTTTTTTACAGG (SEQ ID NO: 81)
[00399] DBONO382:
ACGACGGCCAGTGAATTCCCTCGTGGTGTTCTGACTCCCG (SEQ ID NO: 60).
[00400] In subsequent experiments some modifications were made to the method. During PTV construction it was discovered that the DHR fragment was often missing from the assembled plasmid. This was overcome by shortening the length of the fragment used, utilizing oligo DBONO382.
[00401] In a modified approach, following determining the titer of the recombinant lysate, the enrichment process was sometimes conducted as follows and was used to make the nanoluc phages.
[00402] 96-well microtiter plates were used to grow the PIE lysates at a 200µl volume. For the FF lysates, the initial step was making 96 lysates at 1e6 pfu/lysate (5e6 pfu/ml), 96 at 1e5, and 96 at 1e4. For the NanoLuc phages, it was found that the recombination efficiency of the recombinant lysate was significantly higher, and that dilutions down to 1e0 pfu/lysate could be used. These lysates were made by incubating at 30°C, shaking at 50rpm overnight. The lysates were assayed using the appropriate luciferase assay system (ff or nanoglo). Instead of using the lysates to infect fresh cells, it was found that the background signal of the lysate itself was an indication of the presence of recombinant phage.
[00403] Upon identification of a lysate made from the fewest number of phages, that lysate was used to set up new 96-well lysates using fewer phages. Once an approximate

recombinant frequency of 1:10-1:100 was reached, the phages were plated on agar plates to isolate single plaques as described above.

[00404] These methods were used to create recombinant phage comprising either a heterologous open reading frame encoding the ff luciferase or an open reading frame encoding the nanoluc luciferase. In order to confirm the integrity of the inserted payload and the surrounding sequence in the recombinant phages, a fragment was amplified by PCR and sequenced. This fragment spanned the inserted sequence, beginning in the *cps* gene, crossing through the firefly or nanoluc gene, and crossing into the downstream sequence. The full cps gene was also PCR amplified using oligos DBONO398 and pMAK upr

[00405] DBONO398: TGCTATATTATAGGAACATGGGAA (SEQ ID NO: 82).

[00406] The gene was sequenced using oligos DBONO273, DBONO398, and pMAK upr.

[00407] The PCR fragment was amplified using primers:

[00408] DBONO273: TGCTTACATGCCAGTAGGGGT (SEQ ID NO: 83); and

[00409] DBONO382: ACGACGGCCAGTGAATTCCCTCGTGGTGTTCTGACTCCCG (SEQ ID NO: 60)

[00410] The nanoluc phages were sequenced using oligos:

[00411] DBONO273;

[00412] DBONO382;

[00413] DBONO361: TGGCTCTACATGCTTAGGGTTCC (SEQ ID NO: 75);

[00414] DBONO360: CCTCTAGCTCAAATTAACGCATCTGT (SEQ ID NO: 74);

[00415] DBONO362: GTATGAAGGTCTGAGCGGCG (SEQ ID NO: 84) and

[00416] DBONO363: GATCTGGCCCATTTGGTCGC (SEQ ID NO: 85).

[00417] The firefly phages were sequenced using oligos:

[00418] DBONO273;

[00419] DBONO382;

[00420] DBONO360;

[00421] DBONO361;

[00422] DBONO274: CGCATAGAACTGCCTGCGTC (SEQ ID NO: 86);

[00423] DBONO151: CACCCCAACATCTTCGACGC (SEQ ID NO: 87); and

[00424] DBONO152: GCGCAACTGCAACTCCGATA (SEQ ID NO: 88)

[00425] Sequencing was performed by Genewiz, Inc. Using the Geneious software package, alignments were made and a consensus sequence was generated for each phage.

[00426] The following recombinant phages have been created and the insertion site regions sequenced as described above:

[00427] Phages containing an inserted firefly luciferase:

[00428] LP48::ffluc (SEQ ID NO: 23);

[00429] LP99::ffluc (SEQ ID NO: 24);

[00430] LP101::ffluc (SEQ ID NO: 25);

[00431] LP124::ffluc (SEQ ID NO: 26);

[00432] LP125::ffluc (SEQ ID NO: 27);

[00433] LP143::ffluc (SEQ ID NO: 28);

[00434] A511::ffluc (SEQ ID NO: 29); and

[00435] P100::ffluc (SEQ ID NO: 30).

[00436] Phages containing an inserted nanoluc luciferase:

[00437] LP124::nluc (SEQ ID NO: 31);

[00438] LP125::nluc (SEQ ID NO: 32);

[00439] A511::nluc (SEQ ID NO: 33);

[00440] P100::nluc (SEQ ID NO: 34); and

[00441] LP40::nluc (SEQ ID NO: 35).

[00442] The insertion site regions of the phages comprising an inserted firefly luciferase coding sequence are aligned in Figure 28. The insertion site regions of the phages comprising an inserted firefly luciferase coding sequence contain the following parts as indicated in Table 14.

Table 14

	LP48	LP99	LP101	LP124	LP125	LP143	A511	P100
cps gene	1-1407	1-1407	1-1407	1-1407	1-1407	1-1404	1-1404	1-1407
RBS (inserted)	1408-1423	1408-1423	1408-1423	1408-1423	1408-1423	1405-1420	1405-1420	1408-1423
Firefly Luciferase	1424-3076	1424-3076	1424-3076	1424-3076	1424-3076	1421-3073	1421-3073	1424-3076
Downstream	3077-	3077-	3077-	3077-	3077-	3074-	3074-	3077-

genes	3729	3789	3789	3789	3729	3786	3786	3729

[00443] The insertion site regions of the phages comprising an inserted nanoluc luciferase coding sequence are aligned in Figure 29. The insertion site regions of the phages comprising an inserted nanoluc luciferase coding sequence contain the following parts as indicated in Table 15.

Table 15

	LP124::nluc	LP125::nluc	A511::nluc	P100::nluc	LP40::nluc
cps gene	1-1407	1-1407	1-1404	1-1407	1-1407
additional stop codons (inserted)	1408-1413	1408-1413	n/a	n/a	1408-1413
RBS (inserted)	1414-1429	1414-1429	1405-1420	1408-1423	1414-1429
NanoLuc	1430-1945	1430-1945	1421-1936	1424-1939	1430-1945
Downstream genes	1946-2658	1946-2598	1937-2649	1940-2592	1946-2613

[00444] The cps open reading frames and encoded proteins for each phage are listed in Table 16.

Table 16

Phage	Cps Gene Sequence	Cps Protein Sequence
LP40	5	6
LP48	7	8
LP99	9	10
LP101	11	12
LP124	13	14

LP125	15	16
LP143	17	18
A511	19	20
P100	21	22

[00445] The cps gene sequences are aligned in Figure 26 and the protein sequences in Figure 27. The cps genes of the engineered phage display a relatively high degree of homology.

[00446] All of the above phages were engineered using the methods described above. Partial genome sequences showed that the primers used for A511 could be used to create PTVs for LP48, LP124, and LP125. No genome sequence was available at the time for LP99, LP101 or LP143. Using the A511 PTV primers, it was possible to amplify the appropriate fragments for PTV construction in the same manner as A511. This reflects homology between the cps gene regions across those phages. The luciferase gene insertion site was at the same location (after the cps gene stop codon TAA) as in A511::ffluc.

[00447] Engineering of HIS-tagged phages

[00448] To allow for the concentration of signal produced by the infection of listeria by recombinant phages, alternate versions of recombinant phage were produced that included a HIS tag. The 6xHIS tag (SEQ ID NO: 89) is a commonly used affinity tag for concentrating and purifying recombinant proteins.

[00449] HIS tags are commonly placed at the N-terminus or C-terminus of a protein, as it is often unknown *a priori* which location is optimal. Depending on the structure of the protein being tagged, as well as interactions with substrates, the tag sequence can interfere with, inhibit, or enhance enzyme function. For this reason phages were engineered with the HIS tag at either the N- or C-terminus.

[00450] Further, often times a spacer sequence comprising a small number of amino acid residues is place between the HIS tag and the gene being tagged. The size, charge, and other characteristics of this spacer can effect interactions with the enzyme, substrate, or HIS-binding beads/resins/antibodies. For this reason 2 different spacer were used between the HIS tag and the Nanoluc protein.

[00451] The HIS-tagged nanoluc versions of A511, LP124, and LP40 were constructed using the same methods as the untagged phages. The HIS tag and spacer were introduced during PTV construction by adding sequence to the oligos used to amplify the various DNA fragments. The oligos used in constructing the PTVs for A511, LP124 and LP40 are common to all 3 phages.

[00452] 4 versions of each phage were constructed:

[00453] C-terminal long spacer

[00454] C-terminal short spacer

[00455] N-terminal long spacer

[00456] N-terminal short spacer

[00457] Oligos used to construct C-terminal long spacer PTV:

[00458] UHR fragment: pMAK upf and DBONO380

[00459] NLUC fragment: DBONO379 and DBONO400

[00460] DHR fragment: DBONO401 and DBONO382

[00461] Oligos used to construct C-terminal short spacer PTV:

[00462] UHR fragment: pMAK upf and DBONO380

[00463] NLUC fragment: DBONO379 and DBONO402

[00464] DHR fragment: DBONO401 and DBONO382

[00465] Oligos used to construct N-terminal long spacer PTV:

[00466] UHR fragment: pMAK upf and DBONO380

[00467] NLUC fragment: DBONO403 and DBONO358

[00468] DHR fragment: DBONO359 and DBONO382

[00469] Oligos used to construct N-terminal short spacer PTV:

[00470] UHR fragment: pMAK upf and DBONO380

[00471] NLUC fragment: DBONO404 and DBONO358

[00472] DHR fragment: DBONO359 and DBONO382

[00473] Once PTVs were constructed and verified, the rest of the PIE process was carried out as described above.

[00474] Oligo sequences:

[00475] DBONO400:
ATTCAATTATCCTATAATTATTAATGGTGATGGTGATGATGACCTCCACCTGCT
GCCGCCAGAATGCGTTCGCACA (SEQ ID NO: 90)

[00476] DBONO401: ATCATCACCATCACCATTAATAATTATAGGATAATTGAATAAAAAC (SEQ ID NO: 91)

[00477] DBONO402: ATTCAATTATCCTATAATTATTAATGGTGATGGTGATGATGTGCTGCCGCCAGA ATGCGTTCGCACA (SEQ ID NO: 92)

[00478] DBONO403: TAATAAGAGGAGGTAAATATATATGCATCATCACCATCACCATGGTGGAGGTG CAGCAGTCTTCACACTCGAAGATTTCG (SEQ ID NO: 93)

[00479] DBONO404: AGCAACTAATAATAAGAGGAGGTAAATATATATGCATCATCACCATCACCATG CAGCAGTCTTCACACTCGAAGATTTCG (SEQ ID NO: 94)

[00480] HIS tag amino acid sequence: HHHHHH (SEQ ID NO: 89)

[00481] HIS tag DNA sequence: CATCATCACCATCACCAT (SEQ ID NO: 95)

[00482] C-terminal HIS with long spacer amino acid sequence: AAGGGHHHHHH (SEQ ID NO: 96)

[00483] C-terminal HIS with long spacer DNA sequence: GCAGCAGGTGGAGGTCATCATCACCATCACCAT (SEQ ID NO: 97)

[00484] C-terminal HIS with short spacer amino acid sequence: AAHHHHHH (SEQ ID NO: 98)

[00485] C-terminal HIS with short spacer DNA sequence: GCAGCACATCATCACCATCACCAT (SEQ ID NO: 99)

[00486] N-terminal HIS with long spacer amino acid sequence: HHHHHHGGGAA (SEQ ID NO: 100)

[00487] N-terminal HIS with long spacer DNA sequence: CATCATCACCATCACCATGGTGGAGGTGCAGCA (SEQ ID NO: 101)

[00488] N-terminal HIS with short spacer amino acid sequence: HHHHHHAA (SEQ ID NO: 102)

[00489] N-terminal HIS with short spacer DNA sequence: CATCATCACCATCACCATGCAGCA (SEQ ID NO: 103)

[00490] The insertion locations for each of the twelve tagged enzymes are provided in Table D. The numbering is the same as in the preceding tables in this example.

Table D

Phage	Tag Location	Spacer	Inserted between bases
A511	C-terminal	Long	1933-1934
LP124	C-terminal	Long	1941-1942
LP40	C-terminal	Long	1941-1942
A511	C-terminal	Short	1933-1934
LP124	C-terminal	Short	1941-1942
LP40	C-terminal	Short	1941-1942
A511	N-terminal	Long	1423-1424
LP124	N-terminal	Long	1432-1433
LP40	N-terminal	Long	1432-1433
A511	N-terminal	Short	1423-1424
LP124	N-terminal	Short	1432-1433
LP40	N-terminal	Short	1432-1433

[00491] The recombinant phage described in this example were deposited on May 16, 2013, with the American Type Culture Collection (ATCC®). The deposits were made under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. The ATCC® Patent Deposit Designations for the deposits are provided in Table E.

Table E

Phage	**ATCC Patent Deposit Designation**
LP48::ffluc	PTA-120333
LP125::ffluc	PTA-120334
LP40::nluc	PTA-120335
A511::nluc	PTA-120336
P100::ffluc	PTA-120337
LP124::nluc	PTA-120338
LP101::ffluc	PTA-120339
LP99::ffluc	PTA-120340
LP143::ffluc	PTA-120341
A511::ffluc	PTA-120342
P100::nluc	PTA-120343

LP124:ffluc	PTA-120344
LP125::nluc	PTA-120345

Example 20: Host Range Characterization of Combinations of Listeria Phages

[00492] After engineering the genome of the phages with two different genetic payloads, Firefly Luciferase and Nanoluciferase, the host range of these phages was retested to ensure that the genome modifications did not affect the fitness of the phages or compromise their ability to provide coverage across the Listeria strain host panel. Engineered phages were tested in the liquid-based host range assay and compared to non-modified bacteriophages. The engineered bacteriophages did not show a change in their host range compared to the non-modified wild-type versions (Tables 24-25).

[00493] The identification of bacteriophages that, when their individual host range profiles were combined, provided the necessary coverage of the Listeria genus raised the question of whether the phages when used in a combinatorial infection would provide the additive coverage expected or whether the presence of additional bacteriophages in an infection would diminish the ability of a single bacteriophage to infect a susceptible strain. To test this, combinations of bacteriophages (cocktails) were tested for the ability of a bacteriophage cocktail to provide clearance in the liquid-based host range assay. For these infections the final concentration of phage was maintained at a constant $1X10^5$ pfu consisting of equal amounts of each of the phage within the cocktail (i.e. – a two phage cocktail would consist of $5X10^4$ pfu of each of the two component phages). The combination of bacteriophages in a cocktail (either a two, three or four bacteriophage cocktail) did not cause a loss of host range and provided the expected additive effects of the host range of the individual bacteriophages (Tables 24-25). The additive effect of the bacteriophages was independent of the genomic modifications as neither the engineered Firefly luciferase and Nanoluc luciferase expressing bacteriophages had an altered liquid-based host range compared to the unengineered bacteriophages.

Example 21: Comparison of Liquid-Based Host Range Versus Marker-Based Host Range

[00494] The ability of a bacteriophage to clear an actively growing culture is determined by a number of factors including the rate of growth of a particular strain and the rate of bacteriophage replication, in addition to the ability of the bacteriophage to infect

a specific strain. Therefore, the output of culture clearance measure used in the liquid culture method disclosed herein is potentially more restrictive than the host range that could be determined by exposing bacterial strains to an recombinant phage comprising a heterologous nucleic acid sequence encoding a marker and assaying for marker production. One example of such a marker is luciferase. Therefore, the host range was determined for phage LP124:nluc by both the liquid-based host range assay and by an infection based luciferase detection assay. To carry out the infection based assay, the Listeria host panel strain collection was struck out on Brain Heart Infusion (BHI) agar plates and single colonies were inoculated in 1 ml BHI liquid in a 2-ml 96-deep well dish, covered with a sterile breathable sterile membrane and grown at 30C for 16 hours. Each of the 16-hour cultures from the 96-well plates were diluted 1:10,000 in 198 µl of BHI. For the infection, 12.5 µl of the culture dilution were mixed added to 12.5 µl of LP124:nluc at a concentration of $1X10^7$ pfu/ml in an opaque luminescence reader plate and incubated at 30C for 3 hours. After three hours the level of luminescence was detected using a Promega Glomax 96-well plate reader using Promega NanoGlo reaction following manufacturer's recommendations.

[00495] Table 5 shows the host range determined by the two methods. A strain was considered to be within host range for the clearance assay if the ratio of infected culture OD600 to the uninfected culture OD600 was less than 0.4. For the luciferase detection-based host range assay strains were stratified in three categories, high RLU strains (Table 26, dark gray shading,), medium RLU strains (Table 26, light gray shading), and low RLU strains (Table 26, unshaded). Based on the performance of the assay a strain was considered to be within the host range of the bacteriophage if the RLU measurement was greater than 10,000 Random Light Units (RLU) (Table 26, light gray shading). This luciferase activity cut-off was used because it characterizes a useful level of sensitivity in bacterial assays. Based on these criteria the liquid-based host range clearance, LP124 shows a broad host range by clearing 50.5% (140 of 276) of the Listeria strains tested. By the luciferase detection assay, 78.2% (216 of 276) of the Listeria strains tested showed high RLU levels.

[00496] The comparison between the ability of LP124::nluc to clear cultures of the Listeria host-panel to the RLU output shows that the host range measured using marker expression is greater than that defined using the liquid-based host range. This could be for

several reasons. First, a bacterial strain that is not cleared by the infection but that produces light may have a growth rate that outpaces the ability of the bacteriophage to infect and replicate. In this case, the strain would never succumb completely to bacteriophage because the number of uninfected cells would outpace the bacteriophage in the culture. Second, the bacteriophage may be able to carry out the initial steps of infection (*i.e.* attachment, injection of DNA and translation of viral proteins) but be unable to complete the infection process (*i.e.* virion assembly, release from the cell). Because the bacteriophage life-cycle can be separated into discrete steps, a bacteriophage is capable to produce phage encoded proteins, in this case luciferase, without clearance of the culture or producing additional bacteriophage. While additional strains that produce luciferase without producing bacteriophage would not fall within the classical definition of host range for a bacteriophage, the strains do meet inclusion in the host range definition for the purpose of this disclosure because the host range that matters in methods of detecting target bacteria using a phage comprising a heterologous nucleic acid sequence encoding a marker is the types of bacteria that support marker production. This increased host-range observed when using the engineered bacteriophage is an advantageous byproduct of the engineering process and could not be determined *a priori* for the Listeria host panel.

[00497] One possible concern raised by the ability of a bacteriophage to produce light in a bacterial strain that it could not clear from a liquid-based culture is that other off-target bacterial genera may also produce luciferase in the presence of engineered phages. These bacterial species would not have been considered to be in host range of these phages because of an inability to produce bacteriophage in response to bacteriophage infections. However, the increased sensitivity for detecting early stages of infection with the engineered phages could, at least theoretically, result in production of marker (in this case luciferase—assayed by light production) in strains of bacteria not identified as hosts using the liquid culture method, for example. To address this issue, a panel of bacterial species closely related to Listeria was assembled (Table 27). This panel consisted of other Gram-positive organisms phylogenetically similar to Listeria. To determine if these strains were able to produce light in the presence of the engineered bacteriophage each of the species were grown for 16 hours under appropriate growth conditions (Table 27). The strains were diluted to a concentration of 10^5 cfu/ml and then 90 µl of cells were mixed with 10 µl of a bacteriophage cocktail at $1X10^7$ pfu/ml and incubated for 3 hours at 30C. The reactions

were then measured for the presence of luciferase using the standard protocol. None of the bacterial species tested had detectable levels of RLU (Table 27) demonstrating that the ability of the bacteriophages to show RLUs in strains that they do not clear is not a strictly off-target effect that will decrease the accuracy of a bacteriophage reporter based assay.

[00498] A second question was whether these bacteria species that were phylogenetically similar to Listeria would decrease the sensitivity of the engineered bacteriophages to detect Listeria when the Listeria and non-Listeria bacteria species were present together in an assay. To examine this possibility the related bacterial species were grown as above and diluted to a concentration of 10^5 cfu/ml. A Listeria strain was struck out on Brain Heart Infusion (BHI) agar plates and single colonies were inoculated in 5 ml BHI liquid and grown at 30C for 16 hours. The overnight culture was diluter 1:5 in fresh 0.5X BHI medium and grown for 2 hours at 30C shaking at 200 rpm in an orbital shaker. After two hours a 10-fold serial dilution of the culture was made. To perform the test 10 µl of the Listeria serial dilution that should represent ~10 cfu total was mixed with 20 µl of the potentially inhibitory bacterial species and 10 µl of the bacteriophage cocktail (A511::nluc/LP124::nluc/P100::nluc) and the mixture was incubated for 3 hours at 30C. After the incubation the reaction was assayed for the presence of luciferase using the Promega Glomax 20/20 luminometer and Promega NanoGlo reaction as suggested. These assays showed that there was no decrease in the ability to detect Listeria in the presence of 10^4 greater numbers of competing bacteria (Table 27) demonstrating the sensitivity of the assay is not affected by the presence of non-target bacteria in samples.

[00499] This selection of bacteria was a limited set and did not represent all of the bacteria that could be present during environmental sampling. To generate a more exhaustive sample of bacterial species that may decrease the sensitivity and accuracy of the bacteriophage cocktail, environmental samples were collected from food processing plants and bacterial species were isolated from environmental swabs to determine the effect of these species on performance of the assay. To isolate bacterial species that were present, environmental samples were plated onto both Brain Heart Infusion Agar or R2A agar and grown overnight at 30C. Bacteria that were present on the plates were identified based on colony morphology and struck to purity on BHI agar plates. Pure cultures of the bacterial species were grown in BHI medium at 30C for 16 hours. The cultures were diluted to a concentration of 10^5cfu/ml and tested for both the production of luciferase in the presence

of the bacteriophage cocktail and inhibition of Listeria infection by the bacteriophage cocktail as above. None of the bacterial species, consisting of both Gram-positive and Gram-negative bacteria, showed any luciferase production in the presence of the bacteriophage (Table 28). Additionally, incubation of Listeria in the presence of the collected samples failed to show any decrease in the production of luciferase, demonstrating that the environmentally collected bacteria do not decrease the sensitivity or accuracy of the assay.

Example 22: Design of Phage Compositions

[00500] The increased host range observed by the RLU-based luciferase detection assay compared to the liquid-based host range assay identified a novel method for distinguishing differences between the host range of bacteriophages. Additionally, the RLU-based luciferase detection assay as a means to assess phage host range allows for a highly accurate assessment of the target bacteria identified by an engineered bacteriophage under conditions similar to those of methods of detecting target bacteria. One way this information may be used is to identify useful combinations of phage that can be combined to make a combination of phage having a useful cumulative host range.

[00501] To determine the additive effect of including LP124::nluc in a bacteriophage cocktail a RLU-based luciferase detection assay was compared between A511::nluc and LP124::nluc for a portion of the Listeria host range panel. LP124::nluc had a larger RLU-based host range (detects 77 of 96 strains, 80.2%) compared to A511:nluc (detects 37 of 96 strains, 38.5%) (Table 29). Moreover, LP124:nluc produces greater than 100-times higher RLU values compared to A511:nluc in 73 of 96 strains (76%). This increased RLU output from LP124:nluc infections predicts that a bacteriophage cocktail that contains both A511 and LP124:nluc would have greater sensitivity and accuracy over a A511:nluc alone.

[00502] To test whether LP124::nluc would increase the levels of RLU produced in the presence of A511 and P100 the RLU values were compared between samples infected with both a two-phage cocktail (A511::nluc/P100::nluc) and a three-phage cocktail (A511::nluc/P100::nluc/LP124::nluc). To test this, 1 ml of complex environmental samples grown in UVM medium were pelleted by centrifugation. The supernatant was removed and the cells were resuspended in 100 µl of either the two-phage or three-phage cocktail at a total bacteriophage concentration of $1X10^7$ and incubated at 30C. RLU levels

were measured by using Promega NanoGlo reagent and the Promega 20/20 luminometer. As for the Listeria host panel, the environmental samples showed higher levels of RLU in the presence of the three-phage cocktail than the two-phage cocktail (Table 30). This increase in the RLU output of the infection demonstrates a clear advantage from having LP124::nluc present over P100::nluc and A511::nluc alone.

[00503] The increased host range and RLU output of the three-phage compared to the two-phage cocktail suggested that a cocktail of A511::nluc and LP124::nluc would provide useful coverage against environmental samples. To determine the ability of the cocktail to identify Listeria relevant to food processing plants environmental sampling was conducted in various food processing plants in the United States. These food processing plants represented seafood, dairy, meat and produce processing plants and were geographically diverse in their location. After environmental collection was performed, Listeria that were present in the environmental samples were isolated using a modified USDA isolation method. The Listeria were struck out on BHI agar plates and a single colony was used to inoculate 1 ml of 0.5X BHI medium in a 2 ml deep well dish and covered with a sterile breathable membrane and incubated for 16 hours at 30C. Each of the 16-hour cultures from the 96-well plated were diluted 1:10,000 in 198 µl of BHI. For the infection, 12.5 µl of the culture dilution were mixed added to 12.5 µl of a bacteriophage cocktail containing A511::nluc and LP124::nluc at a total bacteriophage concentration of $1X10^7$ pfu/ml in an opaque luminescence reader plate and incubated at 30C for 3 hours. After three hours the level of luminescence was detected using a Promega Glomax 96-well plate reader using Promega NanoGlo reaction following manufacturer's recommendations. Concurrently, a liquid-based host range assay was performed to compare the RLU output to culture clearance.

[00504] Based on the liquid-based host range assay the bacteriophage cocktail was able to clear the bacterial culture in 25 of 100 strains (25%). This decreased level of clearance is due to a greater growth rate for the environmentally isolated strains compared to common lab isolates tested in the Listeria host range panel. The RLU based host range assay identified 75 of 100 strains (75%) (Table 31). These environmental samples represented complex microbiological communities and had multiple Listeria isolates per environmental sample. The presence of multiple strains of Listeria within these microbiological communities improves the sensitivity of the assay. In this example the

environmental samples were collected using sponges and the sponges were incubated for up to 24h with media, after which an aliquot was removed and assayed for the presence or absence of the bacterial population to be detected. Based on the ability of the bacteriophage cocktail to identify individual Listeria strains identified from the same environmental samples it would have been predicted that the bacteriophage cocktail of A511 and LP124:nluc would be able to detect 48 of 57 (84.2%) Listeria positive sponges. When the environmental sponge was incubated in a growth medium and a sample of the enriched sample is tested using the assay the bacteriophage cocktail containing A511 and LP124:nluc was able to detect 49 of 57 (85.9%) Listeria-positive sponges. This increased sensitivity demonstrates that the presence of multiple Listeria strains, including those out of host range for the bacteriophage cocktail, does not diminish the sensitivity of the assay to detect Listeria strains that are sensitive to the bacteriophage cocktail.

TABLE 19

NP #	A511 Plate	P100 Plate	Avg A511	Avg P100	A511/P100 Cocktail
NP1900		0.00	0.09	1.03	0.29
NP1901	0.75	0.17	0.15	0.10	0.10
NP1902			0.10	1.04	0.30
NP1903	0.75	0.03	0.09	0.11	0.10
NP1904			0.09	0.11	0.11
NP1905			0.16	0.12	0.12
NP1906			0.10	1.08	0.79
NP1907		0.00	0.09	1.05	0.30
NP1908	0.45	0.17	0.19	0.10	0.11
NP1909		0.00	0.09	1.00	0.10
NP1912		0.00	0.10	0.93	0.28
NP1959	0.28	0.20	0.09	0.09	0.10
NP1960	0.00	0.00	0.09	0.91	0.15
NP1961		0.20	0.11	0.10	0.12
NP1962		0.00	0.09	0.91	0.34
NP1963	0.12	0.90	0.09	0.09	0.12
NP1964	0.80	1.40	0.09	0.09	0.10
NP1965	0.20	0.30	0.09	0.09	0.10
NP1966		0.20	0.09	0.10	0.11
NP1967	1.40	0.50	0.10	0.09	0.10
NP1915	0.10		0.77	0.10	0.11
NP1997	0.05	0.00	0.09	0.11	0.11
NP1998	0.10		0.09	0.10	0.11
NP1999	0.10	0.70	0.09	0.14	0.11
NP2000	0.10	0.00	0.09	0.10	0.11
NP2001	0.05	1.00	0.10	0.11	0.11
NP2002			0.10	0.98	0.28
NP2003		0.00	0.16	1.03	0.09
NP2004		0.00	0.13	1.00	0.10
NP2005		0.00	0.31	0.89	0.13
NP1916		0.00	0.41	0.90	1.01
NP2006		0.00	0.12	0.77	0.09
NP2007	0.06	10.00	0.09	0.09	0.11
NP2008	0.10	1.00	0.09	0.09	0.11
NP2009	0.25	0.90	0.09	0.11	0.11
NP2010		0.00	0.29	0.76	0.09

NP2011	[redacted]	0.00	0.45	0.78	1.00
NP2012	0.00	0.00	0.57	1.04	1.04
NP2013	0.00	0.00	0.49	1.00	1.04
NP2014	[redacted]	0.00	0.39	0.84	0.10
NP1869	0.10	1.71	0.13	0.21	0.13
NP1840	[redacted]		1.02	1.17	1.05
NP1839	1.00	1.00	0.24	0.35	0.14
NP2024	4.00	0.50	0.10	0.10	0.11
NP2025	1.20	0.33	0.09	0.09	0.11
NP2026	1.10	0.33	0.56	0.57	0.26
NP2027	0.00	0.27	0.10	0.12	0.12
NP2028	1.00	0.33	0.09	0.09	0.12
NP2029	[redacted]		0.21	0.98	0.12
NP2030	0.00	1.33	0.10	0.09	0.12
NP2031	0.10	0.27	0.09	0.09	0.11
NP2032	1.00	0.33	0.08	0.09	0.12
NP1879	0.20	0.50	1.05	0.13	0.20
NP2033	1.00	0.67	0.10	0.11	0.10
NP2034	0.90	3.33	0.10	0.11	0.11
NP2035	2.00	0.30	0.10	0.11	0.11
NP2036	1.00	0.33	0.09	0.09	0.12
NP2037	1.00	0.33	0.10	0.11	0.11
NP2038	[redacted]	1.00	1.04	0.11	0.23
NP2039	[redacted]	0.33	0.99	0.10	0.24
NP2040	[redacted]	0.33	0.89	0.10	0.23
NP2041	1.50	0.33	0.10	0.12	0.12
NP2042	[redacted]	0.17	0.15	0.09	0.13
NP2043	[redacted]	1.33	0.09	0.09	0.10
NP2044	[redacted]	0.00	0.09	0.09	0.26
NP2045	[redacted]	3.33	0.20	0.20	0.11
NP2046	0.00	0.07	0.09	0.09	0.11
NP2047	[redacted]	0.17	0.10	0.10	0.13
NP2048	[redacted]	0.33	0.13	0.10	0.17
NP2049	[redacted]	0.33	0.10	0.09	0.21
NP2050	[redacted]	0.27	0.10	0.09	0.12
NP1880	0.00	0.00	1.01	1.07	1.07
NP2051	[redacted]	0.33	0.90	0.09	0.19
NP2052	1.00	0.07	0.09	0.09	0.10
NP2053	0.30	0.33	0.09	0.09	0.12

NP2054	0.30	0.07	0.09	0.09	0.16
NP2055	2.00	0.43	0.09	0.09	0.10
NP2056	1.20	0.10	0.09	0.09	0.12
NP2057		0.33	0.97	0.09	0.28
NP2058		0.10	0.97	0.10	0.25
NP2059	0.09	0.17	0.12	0.13	0.14
NP1881	0.00	0.00	0.17	1.05	0.20
NP2060	0.00		0.44	0.95	0.98
NP2061			0.12	0.89	0.12
NP2062			0.12	0.90	0.13
NP2063			0.96	1.03	1.25
NP2064		0.01	0.09	0.09	0.25
NP2065			0.11	0.97	0.09
NP2066			0.49	1.02	0.96
NP2067	0.00	0.00	1.06	1.08	0.93
NP2068			1.12	1.11	1.05
NP2069			0.19	1.04	0.17
NP2070		0.27	0.45	0.10	0.11
NP2071	0.00	0.00	1.14	1.14	1.21
NP2072	0.60	0.33	0.10	0.11	0.12
NP2073			0.63	1.12	1.07
NP2074	0.10	0.33	0.18	0.11	0.16
NP2075		0.03	0.12	0.91	0.79
NP2076	1.20	0.27	0.09	0.10	0.11
NP2077	0.00	0.17	0.14	0.10	0.11
NP1882	0.95	0.58	0.93	0.11	0.12
NP2078			0.11	0.77	0.17
NP2079			1.04	1.07	1.04
NP2080	0.00	0.00	1.04	1.05	1.02
NP2081	0.00	0.00	1.00	0.98	1.01
NP2082	0.00	0.00	1.07	1.06	1.02
NP2083			0.13	0.36	0.89
NP2084			0.14	1.00	0.17
NP2085	0.00	0.00	1.01	1.00	0.95
NP2086			0.19	1.06	0.17
NP2087	0.00	0.00	0.96	0.96	1.16
NP2088	0.20	0.60	0.11	0.11	0.15
NP2089	0.00	0.00	0.90	1.00	1.06
NP2090	0.50	0.40	0.12	0.12	0.17

NP2091	0.01	0.01	0.10	0.16	0.49
NP2092	0.50	1.00	0.09	0.09	0.10
NP2093	[redacted]	1.00	0.25	0.09	0.10
NP2094	[redacted]	1.00	0.09	0.09	0.10
NP2095	1.00	0.20	0.14	0.18	0.22
NP2096	[redacted]	0.30	0.13	0.09	0.10
NP2097	0.00	0.70	0.12	0.10	0.11
NP2098	[redacted]	0.00	0.12	0.09	0.13
NP2099	0.00	0.20	0.12	0.09	0.11
NP2100	0.00	0.00	0.97	1.00	0.99
NP2101	[redacted]	0.00	0.91	1.02	1.04
NP2102	[redacted]	0.00	0.98	1.02	1.01
NP2103	0.00	0.00	1.02	1.01	0.98
NP2104	[redacted]	0.00	0.98	1.02	1.03
NP1883	0.00	0.00	0.40	0.94	1.00
NP2105	0.00	0.00	1.05	1.03	1.02
NP2106	[redacted]	[redacted]	0.79	1.04	1.01
NP2107	0.00	0.00	1.07	1.12	1.03
NP2108	0.00	0.00	1.05	1.11	1.01
NP2109	[redacted]	[redacted]	0.10	1.09	0.10
NP2110	0.00	0.00	0.92	0.84	1.06
NP2111	[redacted]	[redacted]	0.71	0.92	1.12
NP2112	0.00	0.00	1.00	0.92	1.05
NP2113	2.00	0.30	0.09	0.09	0.10
NP1884	0.00	[redacted]	0.10	1.09	0.20
NP2114	[redacted]	[redacted]	0.09	0.48	0.09
NP2115	[redacted]	[redacted]	0.09	0.97	0.09
NP2116	[redacted]	[redacted]	0.09	1.03	0.09
NP2117	[redacted]	[redacted]	0.10	0.88	0.10
NP2118	[redacted]	[redacted]	0.10	1.01	0.10
NP2119	[redacted]	[redacted]	0.09	0.86	0.09
NP2120	[redacted]	0.00	0.11	1.06	0.11
NP2121	[redacted]	[redacted]	0.09	0.98	0.09
NP2122	[redacted]	[redacted]	0.09	0.88	0.09
NP1885	1.50	0.50	0.94	0.11	0.12
NP2123	0.10	0.20	0.09	0.09	0.11
NP2124	0.60	1.00	0.09	0.09	0.11
NP2125	[redacted]	2.00	0.09	0.09	0.10
NP2126	[redacted]	1.00	0.52	0.10	0.22

NP2127	[redacted]		0.93	1.06	1.08
NP2128	0.09	0.10	**0.09**	**0.09**	**0.10**
NP2129	**0.20**	0.03	**0.09**	**0.09**	**0.10**
NP2130	**0.60**	0.10	**0.09**	**0.09**	**0.10**
NP2131	0.00	**0.11**	**0.09**	**0.09**	**0.10**
NP1886	0.00	0.00	0.47	0.96	1.04
NP2132	0.00	0.00	1.03	1.02	1.03
NP1887	[redacted]	0.00	1.02	0.99	1.00
NP2133	[redacted]	**0.40**	1.07	**0.09**	**0.12**
NP2134	[redacted]	0.00	1.06	1.12	1.16
NP2135	0.00	**0.30**	**0.12**	**0.08**	**0.18**
NP2136	[redacted]	**0.20**	0.86	**0.09**	**0.10**
NP2137	[redacted]	**0.20**	0.85	**0.09**	**0.10**
NP2138	[redacted]	0.00	0.98	1.01	1.00
NP2139	0.10	0.10	**0.09**	**0.10**	**0.12**
NP2140	[redacted]		0.96	0.97	1.08
NP2141	[redacted]		**0.14**	**0.10**	**0.18**
NP2142	[redacted]		0.71	1.06	1.02
NP2143	[redacted]		0.90	1.05	1.03
NP2144	0.00	0.00	**0.10**	**0.10**	**0.11**
NP2145	0.00	0.00	**0.09**	**0.10**	**0.11**
NP2146	**0.40**	**0.20**	0.94	0.94	1.12
NP2147	[redacted]	0.00	**0.09**	**0.09**	**0.15**
NP2148	0.00	**0.30**	**0.10**	**0.10**	**0.10**
NP2149	0.00	0.00	1.12	1.18	1.01
NP2150	0.00	0.00	0.73	1.12	1.11
NP1888	[redacted]		**0.09**	0.97	**0.19**
NP2151	0.00	0.00	1.13	1.07	1.04
NP2152	[redacted]	**1.00**	**0.10**	**0.10**	**0.14**
NP2153	[redacted]	0.00	0.81	1.01	1.05
NP2154	[redacted]	0.00	1.06	1.00	1.09
NP2155	0.00	0.00	0.74	1.00	1.10
NP2156	**0.20**	**0.20**	**0.11**	**0.10**	**0.13**
NP2157	**0.40**	**6.00**	**0.10**	**0.10**	**0.10**
NP2158	0.00	**0.50**	**0.13**	**0.12**	**0.12**
NP2159	0.00	0.00	1.11	1.10	1.23
NP1889	**0.80**	**0.17**	1.02	**0.10**	**0.10**
NP2160	**0.20**	0.00	**0.11**	**0.11**	**0.14**
NP2161	**0.20**	**1.50**	**0.10**	**0.10**	**0.17**

NP2162	0.40	1.00	0.10	0.10	0.12
NP2163	0.30	1.00	0.10	0.10	0.16
NP2164	0.14	1.00	1.05	1.11	0.96
NP2165	[redacted]	1.10	0.44	0.95	1.16
NP2166	0.00	0.00	0.09	0.09	0.13
NP2167	0.12	1.60	0.10	0.11	0.16
NP2168	0.80	1.30	0.11	0.11	0.14
NP1890	0.00	0.00	0.89	1.02	1.04
NP2169	0.04	1.00	0.10	0.10	0.14
NP2170	0.30	0.70	0.10	0.10	0.13
NP2171	0.60	0.60	0.09	0.10	0.11
NP2172	0.22	0.10	0.09	0.10	0.11
NP2173	0.40	0.10	0.10	0.10	0.11
NP2174	0.20	3.00	0.09	0.09	0.11
NP2175	0.00	0.00	1.08	1.05	1.05
NP2176	0.00	0.00	1.07	1.06	1.08
NP2177	[redacted]		1.08	1.06	0.91
NP1878	[redacted]		0.11	0.12	0.12
NP1911	0.00	[redacted]	0.15	0.54	0.15
NP1950	0.30	2.00	0.09	0.11	0.09
NP1951	0.20	1.40	0.10	0.10	0.23
NP1952	0.05	1.20	0.09	0.10	0.10
NP1953	[redacted]		0.10	0.10	0.10
NP1954	0.10	2.00	0.09	0.10	0.10
NP1955	[redacted]	1.30	0.14	0.09	0.10
NP1956	[redacted]	0.00	0.09	1.03	0.27
NP1957	0.00	0.70	0.10	0.09	0.10
NP1958	0.20	3.00	0.08	0.10	0.10
NP1913	[redacted]	0.00	0.09	0.78	0.15
NP1968	0.40	2.00	0.10	0.10	0.09
NP1969	1.00	2.00	0.09	0.10	0.09
NP1970	0.08	0.50	0.10	0.10	0.08
NP1971	0.40	0.60	0.12	0.10	0.09
NP1972	0.00	0.00	1.11	1.22	0.92
NP1973	[redacted]	0.00	0.22	0.73	0.21
NP1974	[redacted]	0.00	0.23	0.70	0.31
NP1975	[redacted]		0.95	1.03	1.12
NP1976	0.50	1.00	0.10	0.10	0.11
NP1891	0.00	0.00	0.99	1.03	0.95

NP1892	0.00	0.00	1.01	1.04	0.96
NP1893	0.00	0.00	1.00	1.04	0.97
NP1894	0.00	0.00	0.10	0.99	0.20
NP1895	3.00	0.67	0.16	0.11	0.12
NP1896	1.00	0.33	0.10	0.16	0.12
NP1897	1.00	0.25	0.09	0.10	0.10
NP1898	5.00	16.70	0.99	0.09	0.10
NP1899	0.00	0.00	0.12	1.04	0.40
NP1990	[redacted]	0.00	0.10	1.07	0.59
NP1991	[redacted]	0.00	0.10	1.03	0.09
NP1992	[redacted]	0.00	0.10	1.07	0.10
NP1993	[redacted]	0.00	0.10	1.04	0.10
NP1994	[redacted]	0.00	0.09	0.99	0.16
NP1995	[redacted]	0.00	0.10	0.93	0.13
NP1996	0.05	12.00	0.09	0.10	0.10
NP1910	0.55	[redacted]	0.09	0.09	0.11
NP1945	0.10	0.60	0.14	0.10	0.10
NP1946	0.00	1.90	0.12	0.10	0.17
NP1947	0.00	0.70	0.14	0.10	0.12
NP1948	0.00	0.20	0.09	0.14	0.47
NP1949	0.10	20.00	0.10	0.10	0.11
NP1977	0.06	2.00	0.09	0.09	0.11
NP1978	[redacted]	0.00	0.44	1.04	1.10
NP1979	0.00	0.00	0.52	1.01	1.04
NP1980	[redacted]	[redacted]	0.27	1.04	0.20
NP1981	[redacted]	0.00	0.39	0.84	0.39
NP1982	[redacted]	0.00	0.35	0.87	0.13
NP1983	[redacted]	0.20	0.11	0.10	0.16
NP1984	0.00	0.00	0.27	0.95	0.21
NP1985	[redacted]	0.00	0.63	1.05	1.01
NP1914	[redacted]	0.25	0.09	0.10	0.11
NP1986	[redacted]	0.70	0.09	0.10	0.11
NP1987	[redacted]	0.60	0.09	0.10	0.11
NP1988	0.00	0.40	0.10	0.10	0.11
NP1989	0.00	1.00	0.83	0.09	0.21
NP1917	[redacted]	0.00	0.10	1.00	0.20
NP2015	0.00	0.00	0.17	0.20	0.10
NP2016	0.00	0.00	0.12	0.20	0.12
NP2017	[redacted]	[redacted]	0.13	0.20	0.26

NP2018	[redacted]	0.00	0.10	0.25	0.25
NP2019	[redacted]	[redacted]	0.10	0.24	0.24
NP2020	0.00	0.20	0.12	0.27	0.83
NP2021	0.00	0.00	0.26	1.06	0.39
NP2022	[redacted]	0.00	0.30	1.07	0.13
NP2023	[redacted]	0.00	0.44	0.98	1.03

TABLE 20

NP #	LP14	LP20	LP30	LP34	LP39	LP40	LP44
1900	1.18	0.09	1.01	1.14	1.14	0.52	0.24
1901	1.11	0.18	1.00	0.12	1.14	0.98	0.09
1902	1.10	0.13	0.99	0.22	1.15	0.95	0.09
1903	1.10	0.11	1.01	0.13	1.13	0.95	0.09
1904	1.11	0.10	1.02	0.11	1.13	0.85	0.14
1905	1.12	0.10	1.01	0.19	1.12	0.87	0.13
1906	1.08	0.16	0.99	0.10	1.08	0.91	0.09
1907	1.14	0.10	1.02	1.11	1.12	0.22	0.25
1908	1.03	0.12	1.05	0.11	1.03	0.89	0.09
1909	1.08	0.09	0.95	1.05	1.07	0.21	0.16
1912	1.23	0.10	0.98	1.31	1.21	0.24	0.17
1959	1.02	0.22	1.04	0.10	0.99	0.97	0.22
1960	0.11	0.18	0.76	0.11	1.04	0.93	0.09
1961	0.94	0.09	0.88	0.12	1.25	0.87	0.10
1962	1.08	0.09	1.09	1.30	1.30	0.19	0.25
1963	0.97	0.09	1.02	0.13	1.22	0.78	0.23
1964	1.04	0.10	1.11	0.10	1.11	0.93	0.30
1965	1.04	0.11	0.97	0.10	1.13	0.87	0.23
1966	1.09	0.22	0.98	0.11	1.19	1.02	0.28
1967	1.00	0.42	1.16	0.11	1.16	0.95	0.18
1915	1.15	0.09	0.70	0.22	1.12	0.89	0.16
1997	1.08	0.09	0.11	0.10	1.06	0.93	0.18
1998	1.07	0.09	0.11	0.10	1.07	0.88	0.18
1999	1.06	0.09	0.16	0.10	1.05	0.91	0.25
2000	1.07	0.09	0.11	0.10	1.05	0.94	0.33
2001	1.08	0.10	0.14	0.11	1.06	0.89	0.19
2002	1.04	1.10	1.03	0.14	1.06	0.72	0.13
2003	1.05	0.09	0.73	0.10	1.05	0.80	0.22

2004	1.03	0.09	0.20	0.12	1.00	1.10	0.16
2005	1.05	0.10	0.16	0.11	1.04	0.98	0.21
1916	1.17	0.47	1.02	0.14	1.04	0.44	0.18
2006	1.08	0.25	1.04	0.11	0.90	0.31	0.23
2007	0.10	0.27	0.11	0.13	1.00	0.47	0.09
2008	0.10	0.16	0.11	0.09	1.01	0.45	0.10
2009	1.08	0.40	0.10	0.10	1.07	0.86	0.09
2010	1.01	0.18	1.16	0.10	0.91	0.26	0.20
2011	1.04	0.31	0.97	0.11	0.92	0.40	0.22
2012	1.06	0.34	0.99	1.02	1.07	0.61	0.32
2013	1.06	0.36	0.98	1.05	1.07	0.67	0.30
2014	1.04	0.33	0.98	0.11	0.96	0.42	0.27
1869	0.83	0.22	1.01	0.21	0.15	0.13	0.13
1840	1.04	0.38	0.14	0.24	1.09	0.41	0.32
1839	1.16	1.56	1.02	1.12	0.16	0.21	0.95
2024	1.00	1.16	0.20	0.95	0.10	0.08	1.02
2025	1.04	1.13	0.20	1.02	0.33	0.08	1.05
2026	1.05	1.35	0.52	0.17	0.21	0.44	1.05
2027	1.04	1.06	0.63	1.01	0.27	0.08	1.01
2028	0.98	1.12	0.16	0.99	0.19	0.10	0.99
2029	1.10	1.17	0.97	1.09	0.16	0.10	0.94
2030	1.03	1.22	0.25	0.90	0.12	0.09	0.84
2031	1.00	1.06	0.94	1.03	0.11	0.08	0.89
2032	0.26	1.12	0.15	1.04	0.10	0.08	0.96
1878	1.15	1.18	1.08	1.15	0.15	0.08	1.03
2033	1.01	1.21	0.18	0.98	0.20	0.09	1.01
2034	1.04	1.10	0.16	1.06	0.15	0.09	0.96
2035	1.02	1.19	0.14	1.02	0.16	0.09	0.97
2036	1.01	1.11	0.23	1.02	0.12	0.09	0.98
2037	0.99	1.09	0.17	1.05	0.13	0.09	0.92
2038	1.02	1.07	1.08	1.05	0.19	0.11	0.94
2039	1.06	1.02	1.03	1.03	0.22	0.10	0.93
2040	0.99	1.09	1.02	1.25	0.23	0.11	0.91
2041	1.13	1.10	0.20	1.15	0.12	0.11	1.01
2042	1.08	0.94	0.10	1.03	1.04	0.81	0.12
2043	1.05	1.09	0.83	1.08	1.05	0.65	0.11
2044	1.08	1.00	0.28	1.10	1.08	0.48	0.10
2045	1.03	0.45	0.10	0.19	1.04	0.26	0.09
2046	1.03	0.75	0.10	0.27	1.03	0.35	0.09

2047	1.00	1.12	**0.10**	1.07	1.00	0.44	**0.09**
2048	1.01	**0.32**	**0.23**	**0.12**	1.01	**0.23**	**0.23**
2049	1.07	0.97	1.06	1.14	1.12	0.58	**0.12**
2050	1.04	0.86	0.99	1.13	1.08	0.43	**0.09**
1880	1.15	1.05	1.08	1.15	1.15	**0.09**	1.03
2051	1.05	1.10	1.00	1.13	**0.16**	**0.09**	0.93
2052	1.06	1.15	**0.18**	1.08	**0.15**	**0.10**	0.94
2053	1.00	1.15	**0.23**	1.04	0.45	**0.11**	1.04
2054	1.11	1.14	0.77	1.17	**0.18**	**0.11**	0.96
2055	0.98	1.09	**0.18**	1.06	**0.19**	**0.09**	0.97
2056	1.21	1.07	**0.25**	1.21	**0.12**	**0.10**	0.99
2057	1.17	1.04	1.03	1.06	**0.13**	**0.10**	1.02
2058	1.16	1.14	1.01	1.12	**0.16**	**0.10**	0.95
2059	0.92	1.08	**0.17**	1.00	**0.11**	**0.10**	1.11
1881	1.15	1.24	1.13	1.09	1.13	**0.08**	1.01
2060	1.13	1.14	1.06	1.08	**0.16**	**0.11**	1.06
2061	1.15	1.32	1.08	1.09	**0.20**	**0.10**	1.04
2062	1.14	1.10	0.98	1.06	**0.11**	**0.10**	1.06
2063	1.06	1.06	1.02	1.11	**0.21**	**0.10**	1.08
2064	0.95	1.09	1.03	1.21	**0.17**	**0.09**	1.00
2065	0.98	1.12	1.04	1.01	**0.13**	**0.11**	1.04
2066	0.88	1.19	1.07	0.95	**0.12**	**0.10**	0.96
2067	0.89	1.09	0.99	0.94	0.91	0.90	1.00
2068	0.88	1.06	1.08	0.97	0.93	**0.10**	1.03
2069	0.90	1.07	1.13	1.07	0.96	**0.12**	1.05
2070	0.93	1.19	1.20	1.08	**0.12**	**0.10**	1.06
2071	0.92	1.18	1.09	1.03	1.09	0.95	1.01
2072	0.96	1.18	**0.32**	1.09	**0.14**	**0.11**	1.08
2073	1.04	1.21	1.04	1.09	**0.29**	**0.11**	1.06
2074	1.11	1.10	1.00	1.01	**0.16**	**0.11**	0.49
2075	1.01	1.30	1.03	1.20	**0.17**	**0.11**	1.04
2076	1.07	1.05	**0.24**	0.77	**0.12**	**0.10**	1.01
2077	1.13	1.11	1.08	1.17	**0.13**	**0.09**	1.02
1882	1.06	1.04	1.03	1.02	**0.12**	**0.09**	1.00
2078	1.08	1.05	1.06	1.11	**0.14**	**0.09**	1.03
2079	1.04	1.10	1.09	1.07	1.00	**0.09**	1.03
2080	1.05	1.05	1.08	1.09	**0.16**	**0.10**	1.06
2081	1.05	1.06	1.08	1.11	1.02	1.10	1.08
2082	1.02	1.08	1.06	1.07	0.98	1.17	1.06

2083	1.02	1.08	1.04	1.07	**0.25**	**0.10**	1.04
2084	0.97	1.09	1.06	1.01	**0.14**	**0.09**	1.05
2085	1.04	1.07	1.08	1.06	**0.12**	**0.10**	1.10
2086	1.06	0.97	1.07	0.96	**0.12**	**0.11**	1.08
2087	1.03	1.21	1.22	1.05	1.12	1.12	1.03
2088	1.02	1.00	**0.22**	0.72	0.81	**0.35**	**0.10**
2089	1.05	1.03	1.22	1.02	0.91	0.98	1.04
2090	1.13	1.04	0.72	0.99	1.07	**0.37**	**0.11**
2091	1.07	1.09	1.10	1.04	**0.16**	**0.11**	1.05
2092	0.89	1.01	**0.18**	**0.11**	0.99	0.58	**0.10**
2093	1.05	0.98	1.05	1.08	1.01	0.82	**0.09**
2094	1.08	1.00	0.87	1.03	0.95	0.78	**0.09**
2095	1.09	1.08	**0.24**	1.08	1.02	**0.11**	1.07
2096	1.09	1.10	1.08	1.05	**0.24**	**0.09**	1.06
2097	0.93	1.04	1.11	1.05	**0.12**	**0.10**	1.04
2098	1.13	1.05	1.07	0.94	**0.18**	**0.10**	1.06
2099	0.98	1.15	0.97	1.16	**0.15**	**0.10**	0.99
2100	1.06	1.06	1.13	1.05	**0.12**	**0.10**	1.04
2101	1.07	1.09	1.09	1.07	1.15	0.71	1.09
2102	1.06	1.08	1.10	1.04	1.09	0.70	1.06
2103	1.10	1.07	1.08	1.07	**0.20**	**0.09**	1.06
2104	1.06	1.09	1.10	1.05	1.16	0.75	1.07
1883	1.13	1.08	1.04	1.06	1.11	0.90	1.07
2105	1.08	1.12	1.07	1.06	1.07	**0.10**	1.04
2106	1.13	1.11	1.07	1.11	**0.13**	**0.09**	1.05
2107	1.06	1.09	1.07	1.00	1.00	**0.10**	1.05
2108	1.09	1.13	1.03	1.04	1.11	1.09	1.05
2109	1.22	1.23	1.06	1.04	1.10	**0.13**	**0.09**
2110	1.00	1.17	1.12	0.94	1.02	1.04	1.04
2111	1.00	1.25	0.98	1.11	**0.24**	**0.10**	1.00
2112	1.00	1.14	1.07	1.01	0.99	0.92	1.01
2113	0.63	1.16	**0.18**	1.03	**0.14**	**0.09**	1.03
1884	1.00	1.02	1.01	0.94	1.04	0.50	**0.19**
2114	1.03	1.13	1.07	0.48	1.02	0.54	**0.09**
2115	1.03	1.15	0.91	0.95	0.96	0.53	**0.09**
2116	1.02	1.11	1.03	0.92	1.03	0.70	**0.10**
2117	1.06	1.10	1.02	0.98	1.07	0.60	**0.13**
2118	1.03	1.11	0.96	0.96	1.05	0.69	**0.11**
2119	1.05	1.19	0.89	0.51	1.02	**0.31**	**0.09**

2120	1.07	1.12	1.01	1.08	1.05	0.12	0.10
2121	1.00	1.16	1.05	0.99	1.02	0.51	0.10
2122	1.11	1.12	0.97	0.99	1.00	0.55	0.09
1885	1.13	0.96	1.05	1.12	0.11	0.10	1.04
2123	1.05	1.13	0.18	1.04	1.17	0.44	0.09
2124	1.08	1.03	0.15	0.10	1.05	0.28	0.09
2125	1.04	1.02	0.09	0.95	1.06	0.74	0.10
2126	1.04	1.12	1.07	1.08	0.13	0.10	1.03
2127	1.02	1.14	1.09	1.10	0.98	0.10	1.04
2128	1.07	1.01	0.10	1.05	1.08	0.74	0.09
2129	1.06	1.04	0.10	1.08	1.07	0.32	0.09
2130	1.10	1.03	0.13	1.12	1.10	0.26	0.09
2131	1.07	1.08	0.09	1.07	1.03	0.79	0.10
1886	1.02	1.06	0.95	1.13	0.17	0.09	0.92
2132	1.05	1.07	1.10	1.04	0.14	0.09	1.06
1887	0.99	1.20	1.01	1.05	0.22	0.09	0.94
2133	1.09	1.12	1.13	1.20	0.12	0.11	1.11
2134	1.11	1.12	1.18	0.83	0.84	0.45	1.15
2135	1.01	1.15	1.02	1.02	0.24	0.09	1.00
2136	0.93	1.02	1.07	0.95	0.09	0.10	1.01
2137	1.04	1.06	1.08	1.03	0.13	0.09	1.04
2138	1.15	1.12	0.98	1.15	1.07	1.07	0.96
2139	1.06	1.09	1.14	1.09	0.12	0.09	1.11
2140	1.00	1.06	1.27	1.00	1.00	0.10	1.05
2141	0.99	1.21	1.25	1.11	0.13	0.10	1.17
2142	1.08	1.14	1.19	1.12	0.14	0.10	1.11
2143	1.09	1.13	1.21	1.12	0.13	0.10	1.14
2148	1.13	1.10	0.20	1.09	0.24	0.10	1.00
2149	1.07	1.12	0.95	1.08	1.05	0.97	0.95
2150	1.13	1.16	1.11	1.09	0.17	0.11	1.11
2164	1.05	1.13	0.27	1.05	0.21	0.11	1.08
2165	1.04	1.12	0.16	1.11	0.20	0.10	1.14
2166	0.98	1.14	1.17	0.92	0.16	0.11	1.16
2167	1.12	1.15	0.31	1.25	0.17	0.09	1.03
1888	1.18	1.17	1.07	1.16	0.11	0.09	0.98
2151	1.12	1.24	1.09	1.06	0.18	0.11	1.07
2152	1.13	1.09	0.22	1.08	0.12	0.11	1.21
2153	1.12	1.06	1.03	1.06	0.17	0.11	1.01
2154	1.07	1.21	1.08	1.09	0.13	0.11	1.03

2155	1.09	1.11	0.96	1.05	**0.18**	**0.11**	1.03
2156	1.11	1.12	1.11	0.98	**0.21**	**0.09**	1.34
2157	1.16	1.24	**0.14**	1.15	**0.12**	**0.09**	0.94
2158	0.94	1.05	**0.29**	0.90	**0.12**	**0.10**	1.07
2159	0.90	1.11	1.10	0.99	**0.11**	**0.12**	1.09
1889	1.18	1.19	1.03	1.15	**0.19**	**0.09**	0.99
2144	1.09	1.11	1.11	1.10	**0.19**	**0.10**	1.09
2145	1.10	1.10	1.17	1.13	**0.12**	**0.10**	1.12
2146	1.07	1.13	**0.23**	1.10	**0.17**	**0.09**	1.10
2147	0.97	1.10	1.13	0.98	**0.18**	**0.12**	1.05
2160	0.99	1.11	**0.18**	1.10	**0.21**	**0.12**	1.11
2161	1.05	1.13	**0.18**	1.16	**0.25**	**0.11**	1.14
2162	1.10	1.10	**0.28**	1.15	**0.22**	**0.11**	1.12
2163	1.04	1.16	**0.27**	1.08	**0.30**	**0.11**	1.19
2168	0.96	1.17	**0.24**	0.97	**0.31**	**0.10**	0.99
1890	1.15	1.14	1.06	1.13	**0.19**	**0.09**	1.00
2169	1.13	1.16	0.46	1.11	**0.18**	**0.12**	1.09
2170	1.08	1.07	**0.16**	1.10	**0.19**	**0.10**	1.07
2171	1.04	1.10	**0.23**	1.14	**0.26**	**0.11**	1.07
2172	1.06	1.10	**0.20**	1.19	1.04	**0.11**	1.10
2173	1.11	1.16	**0.13**	1.16	0.68	**0.10**	1.05
2174	1.09	1.07	**0.23**	1.12	**0.10**	**0.11**	1.05
2175	1.05	1.08	1.06	1.12	**0.19**	**0.10**	1.10
2176	1.17	1.10	1.08	1.11	1.09	**0.10**	1.08
2177	1.13	1.12	1.03	1.14	1.12	1.07	1.04
1879	1.28	1.07	1.04	0.68	**0.13**	**0.08**	1.14
1911	1.10	**0.11**	1.02	1.06	1.10	**0.21**	**0.11**
1950	1.08	1.06	1.12	1.09	**0.10**	**0.09**	1.09
1951	1.33	1.00	1.02	0.80	0.78	1.05	1.00
1952	0.95	1.02	1.02	**0.10**	**0.12**	**0.10**	**0.11**
1953	**0.16**	**0.10**	1.01	**0.09**	0.94	0.73	**0.10**
1954	1.03	1.10	1.00	1.08	**0.11**	**0.09**	1.02
1955	0.79	**0.10**	1.02	**0.10**	0.94	0.74	**0.11**
1956	1.09	**0.10**	1.02	1.17	1.14	**0.14**	**0.10**
1957	0.99	0.99	1.14	1.06	**0.15**	**0.10**	1.12
1958	1.00	1.05	1.08	1.03	**0.10**	**0.09**	1.04
1913	1.05	**0.09**	1.15	1.09	1.03	**0.16**	**0.11**
1968	1.09	1.14	1.07	**0.11**	**0.14**	**0.10**	**0.11**
1969	1.17	1.05	1.02	1.19	1.30	**0.11**	1.02

1970	1.14	1.17	1.08	0.11	0.10	0.09	0.14
1971	1.07	1.10	1.00	1.08	0.13	0.09	1.06
1972	1.26	0.09	0.96	1.07	1.11	0.15	0.10
1973	1.25	0.10	1.15	0.81	1.24	0.21	0.11
1974	1.16	0.10	1.05	0.94	1.10	0.14	0.10
1975	0.88	1.01	1.00	0.87	0.92	0.09	0.92
1976	0.92	1.02	0.97	0.97	0.82	0.09	1.00
1891	1.16	1.12	1.03	1.16	1.13	1.02	1.12
1892	1.12	1.14	1.06	1.12	1.12	1.00	0.99
1893	1.12	1.09	1.04	1.14	0.23	0.09	1.00
1894	1.16	1.02	1.05	1.15	1.16	1.04	1.12
1895	1.08	1.13	1.04	1.00	0.19	0.09	1.09
1896	1.09	1.05	1.02	1.02	0.18	0.10	1.03
1897	1.11	1.03	1.05	0.37	0.17	0.10	0.99
1898	0.91	0.94	1.10	1.04	0.23	0.09	0.96
1899	1.09	1.00	1.04	0.99	1.00	0.97	1.05
1990	1.00	0.09	1.05	0.30	1.00	0.09	0.09
1991	1.03	0.09	1.02	0.26	1.01	0.09	0.09
1992	1.02	0.09	1.03	0.38	1.10	0.09	0.09
1993	1.13	0.10	0.92	0.11	0.10	0.10	0.08
1994	1.06	0.10	1.08	0.09	0.12	0.09	0.09
1995	1.04	0.10	1.14	0.10	0.10	0.09	0.09
1996	1.04	0.09	0.09	0.09	1.01	0.09	0.09
1910	0.11	0.09	0.23	0.11	1.13	0.62	0.09
1945	1.14	1.10	1.05	0.15	0.20	0.08	0.90
1946	0.10	0.23	1.04	0.10	1.10	0.89	0.09
1947	0.10	0.29	0.95	0.15	1.04	0.72	0.10
1948	0.16	0.18	0.72	0.11	1.13	0.89	0.11
1949	0.17	0.09	0.22	0.11	1.09	0.53	0.09
1977	0.13	0.79	1.05	0.10	0.96	1.00	0.09
1978	0.95	0.75	1.03	0.96	1.00	0.80	0.37
1979	0.95	0.70	1.06	0.85	0.98	0.78	0.32
1980	1.01	0.92	1.09	1.01	1.04	0.78	0.82
1981	0.98	0.70	1.14	0.93	0.94	0.78	0.37
1982	1.05	0.90	1.09	1.03	1.11	0.94	0.34
1983	0.95	1.14	0.96	0.94	0.12	0.10	0.10
1984	1.05	0.79	1.03	1.05	1.04	0.88	0.27
1985	0.11	1.00	0.98	0.09	1.02	0.85	0.09
1914	1.19	1.05	1.03	0.11	1.12	0.86	0.11

1986	1.04	0.85	1.04	**0.10**	1.02	0.81	**0.13**
1987	1.04	0.83	1.03	**0.09**	1.02	0.85	**0.12**
1988	1.03	0.58	1.07	**0.09**	1.01	0.88	**0.13**
1989	1.01	1.07	1.01	**0.11**	**0.22**	**0.08**	**0.15**
1917	1.14	0.78	1.05	1.16	1.16	0.89	0.68
2015	0.99	0.46	1.08	**0.10**	1.04	0.89	**0.10**
2016	0.72	0.46	1.00	**0.10**	0.99	0.77	**0.10**
2017	1.12	0.43	0.93	**0.12**	1.24	0.80	**0.10**
2018	1.10	**0.40**	1.07	**0.12**	1.19	0.77	**0.11**
2019	1.09	0.53	1.11	**0.11**	1.10	0.74	**0.11**
2020	1.10	0.65	1.12	**0.11**	1.09	0.87	0.43
2021	1.08	0.50	1.10	1.09	1.08	0.79	**0.36**
2022	1.05	0.55	1.08	1.06	1.06	0.84	**0.36**
2023	1.03	1.07	1.05	1.09	1.04	0.98	0.51

TABLE 21

NP #	LP48	LP49	LP54	LP56	LP95	LP99	LP101
1900	0.91	0.93	**0.09**	0.71	0.89	**0.37**	**0.20**
1901	**0.13**	0.95	**0.13**	1.01	**0.09**	**0.09**	**0.10**
1902	1.00	0.88	**0.12**	1.04	0.70	**0.09**	**0.13**
1903	**0.13**	0.88	**0.10**	1.02	**0.10**	**0.10**	**0.10**
1904	**0.19**	0.87	**0.10**	0.95	**0.10**	**0.09**	0.84
1905	**0.18**	0.94	**0.10**	1.01	**0.11**	**0.09**	0.90
1906	0.99	0.86	**0.11**	1.03	0.70	**0.09**	**0.12**
1907	0.94	0.79	**0.10**	0.77	0.98	**0.39**	**0.15**
1908	**0.13**	0.97	**0.11**	0.95	**0.09**	**0.09**	**0.16**
1909	0.91	0.82	**0.09**	0.72	0.97	0.40	**0.17**
1912	1.03	0.55	**0.17**	0.61	0.74	**0.29**	**0.17**
1959	**0.14**	1.01	**0.22**	0.93	**0.09**	**0.08**	**0.10**
1960	0.75	0.96	**0.11**	1.00	**0.10**	**0.10**	**0.10**
1961	**0.18**	0.97	**0.09**	0.89	**0.09**	**0.09**	**0.10**
1962	1.22	0.58	**0.09**	0.48	0.63	**0.17**	**0.27**
1963	**0.12**	0.89	**0.09**	0.93	**0.08**	**0.08**	**0.09**
1964	**0.12**	1.04	**0.09**	0.94	**0.08**	**0.08**	**0.09**
1965	**0.12**	0.92	**0.09**	1.02	**0.09**	**0.08**	**0.09**
1966	**0.19**	1.05	**0.13**	0.96	**0.08**	**0.08**	0.91
1967	**0.17**	1.08	**0.18**	1.00	**0.09**	**0.08**	0.49
1915	**0.09**	0.92	**0.09**	1.26	**0.12**	**0.09**	**0.09**

1997	0.10	0.95	0.09	0.99	0.10	0.09	0.09
1998	0.10	0.94	0.09	1.10	0.11	0.09	0.09
1999	0.11	0.94	0.09	1.11	0.10	0.09	0.10
2000	0.10	0.96	0.09	1.07	0.10	0.09	0.09
2001	0.10	0.97	0.10	1.04	0.10	0.09	0.09
2002	0.21	0.95	1.08	0.89	0.12	0.09	0.17
2003	0.83	0.94	0.09	1.04	0.22	0.09	0.09
2004	0.88	1.12	0.10	1.00	1.05	0.10	0.11
2005	0.92	0.90	0.10	1.07	1.08	0.12	0.11
1916	1.04	0.63	0.48	0.59	0.88	0.53	0.45
2006	0.94	0.72	0.13	0.86	0.95	0.46	0.22
2007	0.23	0.96	0.11	0.51	0.12	0.09	0.11
2008	0.25	0.89	0.11	0.65	0.12	0.10	0.11
2009	0.37	0.96	0.13	0.88	0.14	0.10	0.10
2010	0.82	0.72	0.12	0.86	1.24	0.59	0.20
2011	0.89	0.99	0.14	0.56	0.82	0.57	0.35
2012	0.85	0.96	0.20	0.87	0.96	0.41	0.41
2013	0.99	0.93	0.16	0.89	1.03	0.88	0.40
2014	0.95	0.83	0.14	0.59	0.70	0.63	0.44
1869	0.17	0.28	0.22	0.57	0.15	0.12	0.13
1840	1.00	0.99	0.85	0.85	1.05	0.48	0.26
1839	0.29	0.29	1.21	0.48	0.46	0.16	0.21
2024	0.09	0.54	1.10	0.10	0.10	0.11	0.08
2025	0.10	0.79	1.14	0.11	0.11	0.10	0.08
2026	0.46	0.50	1.32	0.60	0.60	0.32	0.45
2027	0.12	0.09	1.13	0.15	0.11	0.10	0.10
2028	0.10	0.10	1.07	0.10	0.09	0.09	0.11
2029	1.04	1.00	1.08	0.10	0.16	0.12	0.11
2030	0.09	0.49	1.21	0.10	0.09	0.10	0.09
2031	0.09	0.62	1.04	0.09	0.09	0.09	0.09
2032	0.10	0.69	1.11	0.10	0.09	0.09	0.08
1878	0.12	0.87	1.14	0.52	0.11	0.10	0.14
2033	0.10	0.72	1.10	0.10	0.10	0.11	0.09
2034	0.11	0.72	1.21	0.11	0.10	0.10	0.09
2035	0.10	0.73	1.09	0.11	0.10	0.09	0.09
2036	0.09	0.50	1.10	0.10	0.10	0.09	0.08
2037	0.10	0.77	1.10	0.11	0.10	0.10	0.09
2038	0.12	1.03	1.12	0.88	0.10	0.10	0.21
2039	0.11	0.88	1.03	0.15	0.10	0.10	0.12

2040	0.11	1.11	1.18	1.11	0.11	0.10	0.31
2041	0.10	0.52	1.21	0.11	0.10	0.10	0.12
2042	0.09	0.96	1.08	0.91	0.09	0.10	0.46
2043	0.09	0.98	1.01	0.94	0.10	0.09	0.33
2044	0.09	0.81	1.00	0.85	0.10	0.10	0.31
2045	0.10	0.86	0.35	0.57	0.10	0.10	0.21
2046	0.09	0.90	0.72	0.90	0.11	0.10	0.26
2047	0.11	1.02	1.11	0.95	0.11	0.11	0.26
2048	0.20	0.60	0.33	0.57	0.19	0.11	0.19
2049	0.09	1.07	1.01	0.97	0.10	0.10	0.39
2050	0.09	1.05	0.75	0.90	0.10	0.10	0.34
1880	1.13	0.87	1.16	1.01	0.73	0.10	0.94
2051	0.11	0.83	1.11	0.27	0.10	0.10	0.17
2052	0.09	0.41	1.08	0.10	0.10	0.11	0.11
2053	0.10	0.78	1.17	1.08	0.10	0.11	0.31
2054	0.11	0.12	0.99	0.13	0.10	0.10	0.15
2055	0.09	0.60	1.04	0.10	0.09	0.09	0.09
2056	0.09	0.09	1.10	0.10	0.09	0.11	0.10
2057	0.10	0.94	1.09	0.56	0.10	0.10	0.21
2058	0.11	1.02	1.16	1.02	0.10	0.11	0.53
2059	0.10	0.51	1.08	0.11	0.10	0.10	0.10
1881	0.91	0.78	1.11	1.11	0.96	0.10	0.85
2060	1.05	1.16	1.12	0.12	0.13	0.10	0.13
2061	0.96	1.09	1.21	0.12	0.13	0.10	0.13
2062	1.05	1.03	1.14	0.12	0.13	0.11	0.13
2063	0.94	1.05	1.14	0.14	1.05	0.41	0.12
2064	0.22	0.43	1.13	0.10	0.09	0.09	0.09
2065	0.98	1.10	1.13	0.12	0.13	0.12	0.13
2066	1.04	1.03	1.19	0.13	0.15	0.13	0.12
2067	1.01	1.03	1.08	1.15	1.13	0.99	1.02
2068	0.90	1.06	1.16	1.18	1.17	0.11	0.96
2069	0.93	1.01	1.10	1.13	0.30	0.11	1.02
2070	0.09	0.93	1.26	0.12	0.11	0.10	0.10
2071	0.85	1.01	1.19	1.21	1.12	1.09	1.03
2072	0.10	0.57	1.14	0.13	0.11	0.11	0.11
2073	0.95	0.46	1.15	1.06	1.06	0.09	0.99
2074	0.08	0.69	0.99	0.11	0.10	0.12	0.11
2075	1.05	1.12	1.29	0.13	0.13	0.10	0.13
2076	0.10	0.87	1.11	1.11	0.11	0.09	0.99

2077	0.09	0.75	1.14	0.12	0.11	0.09	0.09
1882	0.10	0.48	1.07	0.11	0.10	0.09	0.09
2078	1.04	1.09	1.08	0.13	0.16	0.09	0.11
2079	1.07	0.89	1.14	1.17	1.16	0.14	0.89
2080	1.04	1.01	1.14	0.12	1.05	0.94	0.11
2081	1.04	0.96	1.15	1.13	1.12	0.99	0.91
2082	1.09	0.98	1.13	1.11	1.10	1.08	0.95
2083	1.07	0.94	1.05	0.11	0.12	0.10	0.10
2084	1.10	0.95	1.10	0.11	0.12	0.09	0.11
2085	1.07	1.03	1.14	0.12	1.07	0.98	0.11
2086	1.04	0.99	1.10	0.11	0.12	0.10	0.12
2087	1.01	0.95	1.20	0.98	1.00	1.08	1.17
2088	0.20	0.97	0.92	0.76	0.12	0.11	0.28
2089	1.10	0.92	1.08	1.16	1.11	0.95	0.98
2090	0.19	0.84	1.01	0.58	0.12	0.12	0.31
2091	1.05	0.90	1.15	0.12	0.13	0.10	0.10
2092	0.10	0.92	1.08	0.92	0.10	0.09	0.35
2093	0.09	0.96	1.07	1.03	0.11	0.09	0.49
2094	0.10	0.91	1.13	1.06	0.11	0.09	0.42
2095	0.13	1.02	1.09	0.14	0.12	0.13	0.11
2096	0.10	0.94	1.15	0.12	0.11	0.09	0.09
2097	0.10	0.38	1.19	0.11	0.10	0.09	0.10
2098	0.09	0.82	1.14	0.10	0.10	0.09	0.11
2099	0.10	0.76	1.17	0.11	0.11	0.09	0.11
2100	1.04	0.99	1.10	0.13	1.15	0.96	0.11
2101	1.05	0.96	1.18	1.22	1.22	0.93	0.85
2102	1.07	1.05	1.08	1.27	1.16	0.92	1.10
2103	1.05	1.01	1.16	0.15	1.11	0.96	0.10
2104	1.10	0.83	1.09	1.25	1.22	0.96	0.92
1883	0.96	0.91	1.08	1.04	1.06	1.10	0.88
2105	1.04	1.08	1.19	1.16	1.11	0.96	1.00
2106	1.12	1.10	1.08	0.14	1.06	0.10	0.10
2107	1.07	1.01	1.11	1.05	1.01	0.97	0.93
2108	1.07	1.00	1.10	1.05	1.10	0.97	1.00
2109	1.05	0.94	1.23	0.65	1.09	0.10	0.11
2110	1.05	1.03	1.11	1.00	1.01	0.91	1.10
2111	0.94	0.95	1.28	0.11	0.35	0.09	0.10
2112	1.01	1.00	1.19	1.15	1.09	0.93	0.97
2113	0.09	0.96	1.17	0.10	0.10	0.09	0.09

1884	0.98	0.88	0.99	0.90	1.02	**0.09**	**0.34**
2114	1.02	0.97	1.14	1.01	1.05	**0.09**	**0.36**
2115	1.04	1.07	1.17	1.09	1.04	**0.09**	**0.36**
2116	1.02	1.00	1.19	1.06	1.04	**0.09**	0.50
2117	1.08	1.08	1.16	1.00	0.87	**0.09**	**0.32**
2118	1.02	0.99	1.22	1.00	1.03	**0.09**	**0.38**
2119	1.03	1.01	1.24	0.58	0.55	**0.10**	**0.20**
2120	0.97	1.01	1.16	0.66	0.99	**0.10**	**0.11**
2121	0.95	1.01	1.17	1.07	1.09	**0.09**	**0.32**
2122	0.99	1.00	1.14	0.95	1.01	**0.09**	**0.34**
1885	**0.09**	0.72	0.94	**0.10**	**0.10**	**0.09**	**0.09**
2123	**0.09**	1.03	1.08	0.95	**0.09**	**0.09**	**0.31**
2124	**0.10**	1.02	1.05	0.84	**0.10**	**0.09**	**0.22**
2125	**0.10**	0.97	0.99	0.86	**0.09**	**0.09**	**0.32**
2126	**0.11**	0.95	1.14	**0.26**	**0.10**	**0.10**	**0.16**
2127	1.08	0.94	1.17	1.02	0.96	**0.10**	1.16
2128	**0.10**	0.96	0.97	1.04	**0.11**	**0.09**	**0.29**
2129	**0.10**	0.95	0.98	0.95	**0.10**	**0.09**	**0.30**
2130	**0.10**	1.01	1.12	0.91	**0.11**	**0.09**	**0.25**
2131	**0.10**	1.10	1.05	1.03	**0.11**	**0.09**	**0.37**
1886	1.06	0.97	1.00	**0.11**	0.97	1.06	**0.10**
2132	1.20	0.94	1.09	**0.13**	1.18	0.98	**0.10**
1887	1.12	0.91	1.08	**0.11**	**0.31**	**0.11**	**0.09**
2133	**0.11**	0.65	1.15	**0.12**	**0.10**	**0.11**	**0.11**
2134	1.10	0.91	1.18	1.00	1.08	0.85	1.13
2135	**0.09**	0.75	1.11	**0.11**	**0.10**	**0.09**	**0.10**
2136	**0.09**	0.91	1.15	**0.11**	**0.10**	**0.09**	**0.10**
2137	**0.10**	0.79	1.13	**0.11**	**0.10**	**0.10**	**0.10**
2138	0.99	0.92	1.12	1.11	1.10	0.97	1.05
2139	**0.10**	0.56	1.09	**0.14**	**0.11**	**0.10**	**0.10**
2140	0.94	0.84	1.04	1.09	1.07	**0.10**	0.97
2141	**0.09**	0.47	1.13	**0.11**	**0.10**	**0.10**	**0.11**
2142	0.98	1.00	1.19	**0.12**	0.85	**0.10**	**0.11**
2143	0.99	1.05	1.17	**0.15**	0.99	**0.11**	**0.11**
2148	**0.10**	0.82	1.06	**0.11**	**0.09**	**0.09**	**0.10**
2149	1.06	0.99	1.04	1.01	1.02	0.95	1.00
2150	1.09	1.01	1.11	**0.12**	**0.25**	**0.09**	**0.12**
2164	**0.10**	0.51	1.17	**0.11**	**0.09**	**0.11**	**0.11**
2165	**0.10**	0.77	1.21	**0.10**	**0.09**	**0.10**	**0.11**

2166	0.95	1.02	1.06	0.11	1.01	1.10	0.12
2167	0.09	0.87	1.02	0.11	0.10	0.08	0.10
1888	0.98	0.95	1.12	0.11	0.18	0.12	0.09
2151	1.08	1.12	1.22	0.12	0.20	0.11	0.12
2152	0.10	1.03	1.14	0.11	0.10	0.09	0.11
2153	1.06	0.90	1.02	0.11	0.15	0.12	0.11
2154	1.07	1.16	1.17	0.13	0.20	0.09	0.12
2155	1.14	1.09	1.21	0.11	0.15	0.12	0.11
2156	0.10	0.87	0.95	0.11	0.10	0.10	0.10
2157	0.10	0.96	1.10	0.10	0.09	0.09	0.10
2158	0.09	0.98	1.06	0.11	0.10	0.09	0.11
2159	1.16	1.20	1.13	0.13	0.25	0.11	0.13
1889	0.10	0.63	1.08	0.10	0.09	0.11	0.10
2144	1.06	0.84	1.13	0.11	1.07	1.21	0.10
2145	0.77	0.90	1.14	1.04	0.94	0.10	0.94
2146	0.10	0.88	1.13	0.12	0.10	0.09	0.11
2147	0.12	1.03	1.11	0.14	0.10	0.10	0.13
2160	0.11	1.14	0.55	0.12	0.10	0.10	0.13
2161	0.10	1.06	1.17	0.11	0.10	0.10	0.11
2162	0.11	1.05	1.17	0.11	0.10	0.10	0.11
2163	0.11	1.00	1.17	0.11	0.10	0.10	0.12
2168	0.10	1.03	1.10	0.11	0.10	0.08	0.11
1890	0.90	0.87	1.10	0.81	1.00	1.06	0.19
2169	0.11	1.15	1.12	0.11	0.11	0.51	0.13
2170	0.10	1.01	1.16	0.38	0.11	0.09	0.18
2171	0.10	0.98	1.12	0.57	0.10	0.10	0.15
2172	0.11	0.95	1.16	1.20	0.11	0.09	1.07
2173	0.11	1.11	1.26	1.11	0.10	0.09	0.98
2174	0.09	0.88	1.15	0.11	0.10	0.30	0.10
2175	1.13	1.02	1.14	0.25	1.13	0.97	0.21
2176	1.09	1.05	1.15	1.09	0.75	0.09	1.05
2177	1.00	1.09	1.14	1.11	1.04	0.98	0.97
1879	0.11	0.66	1.03	0.10	0.10	0.10	0.09
1911	0.99	0.68	0.11	0.37	0.50	0.13	0.14
1950	0.10	1.00	0.98	0.09	0.09	0.08	0.09
1951	1.24	1.02	0.98	0.98	0.98	0.91	1.07
1952	0.10	0.97	1.00	0.09	0.09	0.09	0.10
1953	1.01	1.12	0.09	0.92	0.88	0.91	0.12
1954	0.09	0.92	1.05	0.10	0.10	0.09	0.09

1955	1.07	1.08	**0.10**	0.78	0.83	0.77	**0.12**
1956	1.09	0.62	**0.10**	**0.38**	0.56	**0.11**	**0.12**
1957	**0.09**	1.02	1.00	**0.10**	**0.10**	**0.09**	**0.09**
1958	**0.09**	0.98	1.07	**0.09**	**0.09**	**0.09**	**0.09**
1913	1.04	0.72	**0.11**	**0.23**	**0.39**	**0.12**	**0.11**
1968	**0.09**	0.96	1.02	**0.09**	**0.08**	**0.09**	**0.10**
1969	**0.10**	1.03	1.04	0.96	**0.08**	**0.09**	1.05
1970	**0.09**	0.88	1.05	**0.09**	**0.09**	**0.08**	**0.09**
1971	**0.09**	0.92	1.10	**0.09**	**0.09**	**0.08**	**0.09**
1972	1.01	**0.39**	**0.09**	**0.23**	**0.36**	**0.09**	**0.12**
1973	1.20	0.70	**0.09**	0.45	**0.40**	**0.10**	**0.19**
1974	1.08	0.76	**0.10**	**0.24**	**0.35**	**0.11**	**0.11**
1975	**0.09**	0.87	1.00	1.14	**0.10**	**0.12**	0.65
1976	**0.09**	0.87	0.97	1.03	**0.09**	**0.08**	0.92
1891	1.03	0.99	1.07	1.14	0.95	1.02	0.88
1892	0.95	0.96	1.07	1.08	0.99	1.04	0.88
1893	0.90	0.90	1.06	**0.11**	1.00	1.04	**0.09**
1894	0.97	0.99	1.02	1.09	1.09	1.03	0.89
1895	**0.11**	**0.28**	1.02	**0.13**	**0.14**	**0.10**	**0.10**
1896	**0.10**	**0.25**	1.00	**0.11**	**0.10**	**0.11**	**0.10**
1897	**0.09**	**0.32**	0.98	**0.09**	**0.09**	**0.09**	**0.10**
1898	**0.09**	**0.38**	0.90	**0.11**	**0.09**	**0.08**	**0.09**
1899	1.00	0.96	0.98	1.04	0.94	1.05	0.96
1990	0.74	0.63	**0.09**	**0.15**	0.90	**0.10**	**0.09**
1991	0.80	**0.32**	**0.10**	**0.15**	0.88	**0.10**	**0.09**
1992	0.80	**0.37**	**0.10**	**0.17**	1.05	**0.10**	**0.09**
1993	0.94	**0.22**	**0.09**	**0.12**	1.14	**0.10**	**0.10**
1994	0.93	**0.19**	**0.10**	**0.16**	1.08	**0.10**	**0.09**
1995	0.94	**0.27**	**0.10**	**0.14**	1.18	**0.10**	**0.09**
1996	0.88	0.82	**0.09**	0.48	**0.30**	**0.09**	**0.09**
1910	**0.24**	0.92	**0.10**	1.08	**0.12**	**0.09**	**0.09**
1945	**0.09**	**0.15**	0.73	**0.14**	**0.12**	**0.09**	**0.09**
1946	**0.11**	0.98	**0.13**	1.24	**0.11**	**0.09**	**0.08**
1947	**0.10**	0.83	**0.12**	1.16	**0.11**	**0.09**	**0.08**
1948	0.92	0.94	**0.30**	1.21	1.28	0.97	**0.09**
1949	**0.33**	0.89	**0.09**	0.88	**0.10**	**0.09**	**0.09**
1977	0.87	0.91	0.66	1.05	**0.27**	**0.19**	**0.09**
1978	0.90	0.88	0.43	1.10	1.15	1.10	0.79
1979	0.95	0.83	0.49	0.95	1.00	0.96	0.80

1980	1.02	0.77	0.80	1.09	1.05	1.00	0.80
1981	1.03	0.85	0.49	1.03	1.06	0.92	0.78
1982	0.98	0.96	0.64	1.19	1.11	0.97	0.90
1983	**0.10**	**0.16**	1.09	**0.13**	**0.11**	**0.09**	**0.11**
1984	0.97	0.94	0.48	1.08	1.10	0.83	0.81
1985	0.88	0.88	0.83	1.15	1.11	0.93	**0.08**
1914	**0.25**	0.93	1.05	1.18	**0.14**	**0.10**	**0.23**
1986	**0.27**	0.94	0.53	1.18	**0.15**	**0.10**	**0.28**
1987	**0.26**	0.94	0.59	1.13	**0.14**	**0.10**	**0.31**
1988	**0.28**	0.87	0.42	0.95	**0.12**	**0.10**	**0.31**
1989	**0.10**	**0.28**	1.05	**0.14**	**0.11**	**0.09**	**0.09**
1917	0.95	0.92	0.50	0.86	1.01	0.70	0.80
2015	0.86	0.95	**0.39**	0.88	0.80	**0.21**	**0.16**
2016	0.89	0.97	**0.32**	1.00	0.83	**0.22**	**0.24**
2017	0.97	0.77	**0.29**	0.97	0.85	**0.23**	**0.19**
2018	0.88	0.87	**0.36**	1.14	0.73	**0.21**	**0.13**
2019	1.09	0.79	0.44	1.10	0.72	**0.19**	**0.12**
2020	0.84	0.88	0.59	0.95	**0.22**	**0.15**	0.78
2021	0.94	0.95	**0.34**	1.06	0.93	0.45	0.69
2022	0.92	0.93	**0.37**	1.08	1.03	0.57	0.72
2023	1.04	1.05	0.99	1.15	1.10	**0.18**	0.97

TABLE 22

NP #	LP103	LP106	LP109	LP114	LP124	LP125
1900	1.25	1.16	1.06	0.97	0.66	1.18
1901	**0.10**	**0.16**	**0.12**	**0.09**	**0.10**	1.14
1902	1.14	1.20	**0.13**	**0.10**	**0.36**	1.17
1903	**0.10**	**0.28**	**0.12**	**0.10**	**0.11**	1.12
1904	**0.12**	**0.22**	0.77	**0.11**	**0.11**	1.09
1905	**0.11**	**0.23**	0.95	**0.11**	**0.11**	1.14
1906	1.17	0.98	**0.12**	**0.10**	0.76	1.08
1907	1.22	1.16	1.02	0.96	0.76	1.07
1908	**0.10**	**0.11**	**0.12**	**0.09**	**0.10**	0.73
1909	1.26	1.05	0.95	0.88	0.73	1.00
1912	1.08	1.27	1.15	1.08	0.71	1.13
1959	**0.09**	**0.10**	**0.09**	1.00	**0.09**	1.06
1960	**0.20**	**0.38**	**0.09**	**0.08**	**0.13**	0.94
1961	**0.16**	**0.16**	**0.08**	0.95	**0.12**	1.00

1962	0.91	1.21	1.01	1.15	0.25	1.06
1963	0.08	0.10	0.09	1.00	0.09	1.00
1964	0.08	0.11	0.09	1.08	0.09	1.06
1965	0.08	0.10	0.08	1.03	0.09	1.01
1966	0.10	0.12	0.08	0.97	0.10	1.06
1967	0.09	0.13	0.10	1.14	0.10	1.03
1915	0.09	0.23	0.09	0.12	0.10	0.10
1997	0.09	0.10	0.09	1.03	0.09	0.10
1998	0.09	0.11	0.09	1.03	0.10	0.10
1999	0.09	0.10	0.09	1.00	0.09	0.11
2000	0.09	0.10	0.09	1.02	0.09	0.09
2001	0.09	0.23	0.09	1.02	0.10	0.10
2002	0.10	0.12	0.09	0.97	0.10	0.77
2003	0.97	1.04	0.09	1.10	0.09	1.10
2004	1.06	1.06	0.09	0.96	0.09	1.06
2005	1.12	1.17	0.09	1.10	0.10	1.02
1916	1.08	1.04	1.14	1.11	0.73	1.07
2006	0.97	0.99	0.77	1.00	0.59	1.18
2007	0.14	0.23	0.10	0.10	0.11	1.11
2008	0.18	0.20	0.10	0.10	0.11	1.08
2009	0.28	0.45	0.09	0.09	0.14	1.05
2010	1.24	0.84	0.74	0.98	0.57	1.13
2011	0.94	0.86	0.88	1.02	0.59	1.14
2012	1.06	1.04	0.94	1.01	0.91	1.03
2013	1.06	1.04	0.92	0.98	0.89	1.03
2014	1.01	0.89	0.78	1.01	0.63	1.08
1869	0.13	0.14	0.13	0.13	0.22	0.62
1840	1.19	1.08	0.16	0.13	1.02	1.10
1839	0.17	0.15	1.07	1.23	0.21	0.17
2024	0.09	0.10	1.00	1.09	0.10	0.09
2025	0.09	0.18	1.04	1.14	0.09	0.09
2026	0.30	0.16	0.97	1.05	0.26	0.32
2027	0.10	0.20	1.09	1.11	0.09	0.09
2028	0.09	0.15	0.97	0.95	0.09	0.09
2029	0.47	0.29	1.11	0.99	0.15	0.11
2030	0.09	0.24	0.90	0.96	0.10	0.10
2031	0.08	0.11	0.92	0.91	0.10	0.10
2032	0.09	0.19	1.05	0.93	0.09	0.10
1878	0.10	0.11	0.95	0.98	0.11	0.11

2033	0.10	0.10	1.15	0.97	0.10	0.10
2034	0.09	0.15	0.95	0.99	0.10	0.12
2035	0.09	0.12	1.08	0.93	0.10	0.11
2036	0.09	0.15	1.14	0.95	0.09	0.11
2037	0.09	0.10	1.09	0.94	0.10	0.10
2038	0.09	0.28	0.96	0.91	0.09	0.10
2039	0.09	0.23	1.07	0.94	0.09	0.10
2040	0.09	0.12	0.90	1.07	0.10	0.11
2041	0.10	0.16	1.14	0.99	0.10	0.10
2042	0.09	0.16	0.91	0.98	0.10	0.10
2043	0.09	0.10	0.89	0.99	0.09	0.09
2044	0.09	0.14	1.01	1.03	0.09	0.10
2045	0.10	0.11	0.75	0.93	0.13	0.10
2046	0.09	0.10	0.94	1.08	0.10	0.09
2047	0.11	0.11	0.96	0.91	0.11	0.12
2048	0.10	0.10	0.30	0.95	0.13	0.12
2049	0.09	0.15	1.03	0.93	0.09	0.09
2050	0.10	0.13	0.98	0.90	0.10	0.10
1880	1.26	1.16	0.98	1.03	1.07	1.12
2051	0.10	0.11	0.98	0.91	0.10	0.10
2052	0.10	0.24	0.98	0.86	0.10	0.10
2053	0.11	0.34	1.12	1.07	0.10	0.10
2054	0.10	0.13	1.07	1.10	0.11	0.11
2055	0.09	0.23	1.02	1.15	0.09	0.09
2056	0.10	0.17	1.03	0.99	0.09	0.10
2057	0.10	0.11	1.03	0.98	0.09	0.10
2058	0.11	0.11	1.00	0.96	0.10	0.10
2059	0.10	0.16	1.10	1.09	0.10	0.22
1881	1.23	1.16	0.93	0.97	1.06	1.20
2060	0.51	0.19	1.07	1.04	0.14	0.11
2061	0.25	0.23	1.08	1.03	0.14	0.26
2062	0.28	0.18	1.06	1.25	0.13	0.12
2063	0.99	0.87	1.05	1.16	1.06	0.96
2064	0.14	0.30	1.05	1.24	0.09	0.09
2065	0.42	0.15	1.07	1.02	0.14	0.11
2066	0.38	0.11	1.00	1.11	0.17	0.10
2067	1.14	1.08	0.96	1.10	1.10	0.94
2068	0.98	1.17	1.03	1.12	1.17	0.97
2069	0.70	0.25	1.08	1.33	0.36	0.11

2070	**0.09**	**0.20**	1.12	1.21	**0.11**	**0.11**
2071	0.93	0.92	1.06	0.94	1.05	0.97
2072	**0.11**	**0.16**	1.07	0.96	**0.11**	**0.10**
2073	0.90	**0.20**	1.14	0.89	1.09	**0.31**
2074	**0.11**	**0.12**	1.13	0.57	**0.09**	**0.11**
2075	**0.23**	**0.24**	1.13	1.14	**0.15**	**0.13**
2076	**0.08**	**0.21**	0.96	1.04	**0.09**	**0.10**
2077	**0.09**	**0.11**	0.97	1.01	**0.10**	**0.10**
1882	**0.09**	**0.10**	0.99	0.97	**0.10**	**0.10**
2078	**0.19**	**0.16**	1.10	1.02	**0.15**	**0.13**
2079	0.94	1.03	1.02	1.08	1.11	1.07
2080	0.93	1.03	1.04	1.06	1.03	1.07
2081	0.96	1.02	0.94	0.99	1.02	1.02
2082	1.03	0.99	1.01	1.07	1.09	0.98
2083	**0.15**	**0.12**	1.05	1.09	**0.13**	**0.09**
2084	**0.16**	**0.10**	1.05	1.04	**0.13**	**0.14**
2085	1.00	1.09	1.09	1.20	1.10	0.97
2086	**0.17**	**0.14**	1.12	1.19	**0.11**	**0.21**
2087	1.16	1.11	1.13	1.18	1.08	**0.11**
2088	**0.12**	**0.16**	0.96	1.07	**0.13**	**0.17**
2089	1.03	0.95	0.97	1.09	1.12	1.01
2090	**0.12**	**0.14**	1.10	1.04	**0.12**	**0.12**
2091	**0.13**	**0.23**	1.02	1.06	**0.15**	**0.10**
2092	**0.08**	**0.10**	1.04	1.07	**0.09**	**0.10**
2093	**0.08**	**0.09**	0.94	1.05	**0.09**	**0.10**
2094	**0.08**	**0.09**	1.01	1.05	**0.09**	**0.09**
2095	**0.11**	0.86	1.05	1.05	**0.11**	**0.10**
2096	**0.09**	**0.19**	1.05	1.19	**0.09**	**0.09**
2097	**0.09**	**0.13**	1.09	1.07	**0.09**	**0.09**
2098	**0.09**	**0.12**	1.12	1.13	**0.09**	**0.10**
2099	**0.09**	**0.28**	1.12	1.07	**0.10**	**0.09**
2100	1.07	1.07	1.08	1.08	1.10	1.09
2101	0.97	1.07	1.02	1.14	1.06	1.10
2102	0.97	0.97	0.96	1.07	1.11	1.02
2103	1.00	1.04	1.11	1.07	1.12	0.99
2104	0.99	1.03	0.95	1.15	1.14	1.08
1883	1.22	1.13	1.00	0.96	1.02	1.06
2105	1.02	1.06	0.99	1.15	1.18	0.94
2106	1.00	0.67	1.14	1.15	1.00	**0.12**

2107	0.98	1.02	1.02	1.25	1.11	0.92
2108	1.12	1.03	0.96	1.15	1.05	1.10
2109	0.92	1.04	1.06	1.16	1.10	0.93
2110	0.97	1.14	1.17	1.15	1.11	0.94
2111	1.05	**0.37**	1.05	1.12	**0.34**	**0.12**
2112	1.02	0.99	1.13	1.14	1.12	1.15
2113	**0.08**	**0.09**	1.07	1.10	**0.10**	**0.10**
1884	1.12	1.01	1.12	0.93	0.98	1.05
2114	0.97	0.92	1.01	1.20	1.06	1.09
2115	0.98	0.99	1.12	1.18	1.08	1.09
2116	1.13	0.87	1.00	1.15	1.10	1.14
2117	1.03	1.01	0.96	1.12	1.03	1.04
2118	1.06	1.05	1.03	1.11	1.13	1.01
2119	1.11	1.00	1.07	1.10	1.15	0.97
2120	0.99	1.05	1.02	1.18	1.04	0.95
2121	0.97	0.96	1.02	1.09	1.11	1.03
2122	0.86	1.09	1.21	1.13	1.12	0.92
1885	**0.10**	**0.16**	1.06	0.96	**0.09**	**0.09**
2123	**0.09**	**0.12**	1.01	0.98	**0.09**	**0.09**
2124	**0.09**	**0.10**	1.03	1.17	**0.09**	**0.10**
2125	**0.09**	**0.09**	1.03	**0.15**	**0.09**	**0.10**
2126	**0.09**	**0.15**	1.04	1.13	**0.10**	**0.09**
2127	1.03	1.03	1.03	1.14	1.01	0.97
2128	**0.09**	**0.09**	1.00	**0.14**	**0.09**	**0.09**
2129	**0.09**	**0.14**	1.01	**0.17**	**0.09**	**0.11**
2130	**0.09**	**0.19**	1.00	1.16	**0.10**	**0.11**
2131	**0.09**	**0.13**	1.02	**0.14**	**0.09**	**0.10**
1886	0.98	1.14	0.94	1.13	1.00	1.05
2132	0.92	1.05	1.04	1.10	1.01	1.04
1887	1.14	**0.12**	0.93	0.92	**0.36**	**0.10**
2133	**0.10**	**0.18**	1.02	1.03	**0.10**	**0.09**
2134	0.88	0.85	1.01	1.26	1.11	0.89
2135	**0.09**	**0.16**	1.05	1.15	**0.09**	**0.09**
2136	**0.09**	**0.13**	**0.11**	1.02	**0.09**	**0.08**
2137	**0.09**	**0.16**	1.21	1.20	**0.10**	**0.09**
2138	0.97	1.14	1.04	1.20	1.03	0.97
2139	**0.10**	**0.27**	1.03	1.17	**0.10**	**0.09**
2140	0.86	**0.18**	1.08	1.09	0.54	**0.17**
2141	**0.09**	**0.16**	1.18	1.25	**0.10**	**0.09**

2142	1.00	**0.13**	1.05	1.19	1.03	**0.10**
2143	1.06	0.50	1.03	1.32	0.98	**0.15**
2148	**0.09**	**0.23**	1.13	1.09	**0.10**	**0.10**
2149	0.92	1.07	1.08	1.00	0.96	1.06
2150	0.78	**0.32**	0.99	1.11	0.60	**0.19**
2164	**0.10**	**0.20**	1.07	1.20	**0.10**	**0.09**
2165	**0.10**	**0.15**	0.97	1.27	**0.10**	**0.08**
2166	1.12	0.93	1.03	1.37	1.06	1.03
2167	**0.08**	**0.11**	1.04	1.09	**0.10**	**0.10**
1888	1.13	**0.12**	1.02	0.97	**0.19**	**0.11**
2151	0.92	**0.15**	1.15	1.09	0.54	**0.11**
2152	**0.09**	**0.11**	1.11	1.18	**0.10**	**0.11**
2153	0.44	**0.23**	1.22	1.07	**0.14**	**0.10**
2154	0.90	**0.25**	1.39	1.12	**0.22**	**0.11**
2155	0.44	**0.13**	1.20	1.05	**0.15**	**0.12**
2156	**0.10**	**0.12**	1.16	1.06	**0.09**	**0.09**
2157	**0.09**	**0.11**	1.17	1.20	**0.09**	**0.09**
2158	**0.09**	**0.14**	1.22	1.17	**0.09**	**0.09**
2159	1.05	**0.20**	1.00	1.09	**0.21**	**0.13**
1889	**0.10**	**0.18**	0.99	0.97	**0.10**	**0.11**
2144	1.18	1.14	1.22	1.21	1.11	0.99
2145	**0.11**	0.85	1.02	1.26	0.71	**0.10**
2146	**0.09**	**0.14**	1.15	1.16	**0.10**	**0.09**
2147	**0.11**	**0.23**	1.10	1.15	**0.10**	**0.11**
2160	**0.11**	**0.18**	1.05	1.08	**0.10**	**0.09**
2161	**0.10**	**0.28**	1.05	1.15	**0.10**	**0.10**
2162	**0.10**	**0.23**	1.03	1.20	**0.10**	**0.09**
2163	**0.10**	**0.19**	1.07	1.22	**0.10**	**0.10**
2168	**0.08**	0.41	1.05	1.06	**0.10**	**0.09**
1890	1.20	1.10	1.00	0.97	1.04	1.13
2169	0.50	**0.11**	1.64	1.19	**0.10**	**0.10**
2170	**0.08**	**0.16**	1.09	1.08	**0.10**	**0.09**
2171	**0.10**	**0.30**	1.13	1.12	**0.10**	**0.09**
2172	**0.10**	**0.13**	1.12	1.06	**0.10**	**0.09**
2173	**0.09**	**0.11**	1.06	1.04	**0.11**	**0.09**
2174	**0.31**	**0.13**	1.04	1.02	**0.09**	**0.09**
2175	0.90	1.21	1.04	1.15	1.14	0.89
2176	0.84	0.43	1.15	1.13	0.65	**0.14**
2177	1.00	1.14	1.02	1.03	1.12	0.95

1879	**0.10**	0.43	0.99	1.01	**0.10**	**0.12**
1911	1.18	1.03	1.06	1.09	**0.27**	1.13
1950	**0.08**	**0.15**	1.01	1.18	**0.09**	**0.08**
1951	0.89	0.91	1.00	1.02	1.07	**0.09**
1952	**0.09**	**0.12**	**0.38**	**0.17**	**0.09**	**0.09**
1953	1.11	1.00	**0.14**	**0.09**	0.76	0.97
1954	**0.09**	**0.14**	0.92	0.98	**0.09**	**0.09**
1955	1.09	**0.10**	**0.14**	**0.09**	0.74	1.01
1956	1.10	0.95	0.90	1.02	**0.16**	0.98
1957	**0.09**	**0.23**	1.18	1.04	**0.09**	**0.09**
1958	**0.09**	**0.14**	1.03	1.07	**0.09**	**0.09**
1913	1.23	0.98	0.91	1.07	0.45	1.00
1968	**0.09**	**0.14**	**0.26**	**0.15**	**0.09**	**0.10**
1969	**0.09**	**0.14**	1.16	1.02	**0.10**	**0.10**
1970	**0.08**	**0.15**	**0.12**	**0.17**	**0.09**	**0.10**
1971	**0.07**	**0.13**	1.16	0.98	**0.09**	**0.09**
1972	0.89	**0.34**	0.93	0.94	**0.13**	1.00
1973	1.14	**0.30**	0.65	1.02	**0.17**	1.01
1974	0.98	0.96	0.76	0.82	**0.15**	1.05
1975	**0.11**	**0.13**	0.95	0.85	**0.09**	**0.10**
1976	**0.08**	**0.27**	0.83	0.85	**0.09**	**0.10**
1891	1.07	1.13	1.02	1.06	1.04	1.12
1892	1.12	1.13	1.17	1.02	1.03	1.06
1893	1.11	1.11	1.19	0.96	1.02	1.12
1894	1.13	1.14	1.04	1.01	1.05	1.03
1895	**0.10**	**0.15**	1.09	1.00	**0.11**	**0.11**
1896	**0.11**	**0.14**	1.13	1.03	**0.11**	**0.10**
1897	**0.08**	**0.12**	1.01	1.04	**0.09**	**0.09**
1898	**0.08**	**0.23**	0.97	1.00	**0.08**	**0.10**
1899	1.14	1.03	1.00	0.99	0.97	1.20
1990	0.94	1.01	0.95	0.90	0.46	1.00
1991	0.96	0.97	0.99	0.91	0.40	1.03
1992	0.92	1.08	0.82	0.94	**0.36**	1.03
1993	1.02	1.11	0.86	1.01	**0.11**	0.95
1994	1.13	0.98	1.05	0.98	**0.10**	1.08
1995	1.10	1.03	0.84	0.97	**0.10**	1.09
1996	0.76	**0.14**	**0.09**	**0.09**	**0.20**	1.07
1910	**0.14**	**0.36**	**0.09**	**0.09**	**0.09**	1.14
1945	**0.09**	**0.19**	0.97	1.04	**0.09**	**0.10**

1946	0.10	0.13	0.09	0.09	0.09	1.14
1947	0.09	0.10	0.10	0.10	0.10	1.14
1948	1.09	1.19	0.09	0.09	0.59	1.07
1949	0.15	0.70	0.09	0.09	0.11	1.07
1977	0.89	0.56	0.69	0.09	0.34	1.04
1978	1.12	1.15	0.99	0.90	1.03	1.06
1979	1.11	1.09	1.01	0.85	0.99	1.05
1980	1.00	1.18	0.94	1.01	1.01	1.08
1981	0.95	1.09	1.08	1.12	0.96	0.98
1982	1.07	1.19	1.08	1.10	1.08	1.02
1983	0.09	0.14	0.88	0.11	0.09	0.10
1984	1.05	1.07	0.83	1.02	0.98	1.03
1985	1.04	1.04	0.34	0.09	1.02	1.03
1914	0.17	0.16	0.09	0.12	0.16	1.16
1986	0.16	0.11	0.09	0.12	0.14	1.03
1987	0.15	0.12	0.09	0.11	0.12	1.06
1988	0.16	0.11	0.09	0.12	0.12	1.01
1989	0.09	0.15	0.12	0.31	0.10	0.09
1917	1.17	1.15	1.02	1.03	1.03	1.04
2015	0.98	0.98	0.12	0.10	0.83	1.02
2016	1.00	0.96	0.13	0.10	0.83	1.05
2017	0.97	1.11	0.14	0.10	0.81	0.98
2018	1.01	1.25	0.15	0.11	0.85	0.98
2019	1.05	1.05	0.13	0.11	0.94	0.98
2020	0.69	0.78	1.09	1.21	0.30	0.99
2021	1.05	1.10	1.05	1.19	0.96	1.06
2022	1.10	1.06	1.06	1.14	0.96	0.98
2023	1.10	1.03	1.01	0.99	1.11	0.95

TABLE 23

NP #	LP128	LP129	LP141	LP143	LP177
1900	0.54	1.01	1.10	0.30	0.79
1901	0.10	0.09	0.10	0.10	0.09
1902	0.10	0.09	0.10	0.36	0.55
1903	0.10	0.09	0.11	0.10	0.10
1904	0.10	0.10	0.10	0.11	0.10
1905	0.10	0.10	0.11	0.10	0.10
1906	0.09	0.10	0.10	0.20	0.48

1907	0.55	1.11	1.02	**0.28**	0.64
1908	**0.09**	**0.09**	**0.11**	**0.11**	**0.09**
1909	0.53	1.26	1.11	**0.17**	0.76
1912	0.56	0.75	1.10	0.62	0.61
1959	0.60	0.96	0.84	**0.09**	**0.09**
1960	**0.09**	**0.09**	**0.10**	**0.11**	**0.10**
1961	0.48	0.96	0.95	**0.12**	**0.09**
1962	0.44	0.62	0.85	**0.12**	0.52
1963	0.61	0.91	0.86	**0.09**	**0.08**
1964	0.72	0.97	0.95	**0.09**	**0.08**
1965	0.47	0.92	0.93	**0.09**	**0.08**
1966	0.63	0.79	0.98	**0.09**	**0.08**
1967	0.45	0.95	0.89	**0.09**	**0.09**
1915	0.67	0.75	1.04	**0.09**	**0.12**
1997	0.64	0.84	1.07	**0.09**	**0.10**
1998	0.76	0.95	0.74	**0.09**	**0.11**
1999	0.98	0.90	0.95	**0.09**	**0.10**
2000	0.77	1.02	0.94	**0.09**	**0.10**
2001	0.59	0.85	0.97	**0.10**	**0.11**
2002	0.59	1.07	1.14	**0.11**	**0.11**
2003	0.57	1.00	1.04	**0.10**	1.01
2004	0.54	**0.36**	1.16	**0.10**	**0.23**
2005	0.45	0.99	1.18	**0.11**	1.08
1916	**0.16**	0.65	**0.16**	0.68	0.72
2006	**0.20**	0.53	**0.29**	**0.39**	0.78
2007	**0.11**	**0.09**	**0.10**	**0.11**	**0.13**
2008	**0.11**	**0.09**	**0.10**	**0.11**	**0.13**
2009	**0.10**	**0.09**	**0.28**	**0.12**	**0.13**
2010	**0.20**	0.79	0.66	**0.30**	0.90
2011	**0.14**	0.65	0.46	0.44	0.56
2012	0.79	1.11	1.14	0.43	0.81
2013	0.86	1.02	1.10	0.44	0.89
2014	**0.13**	0.84	**0.25**	0.43	0.51
1869	**0.15**	**0.12**	**0.13**	**0.22**	**0.14**
1840	**0.10**	**0.10**	**0.11**	1.06	1.10
1839	1.21	0.98	1.28	**0.18**	0.47
2024	1.06	1.09	1.07	**0.10**	**0.10**
2025	1.13	1.18	1.07	**0.09**	**0.11**
2026	1.10	0.72	1.02	**0.28**	0.61

2027	1.09	1.09	1.06	**0.10**	**0.11**
2028	1.02	1.01	1.02	**0.10**	**0.09**
2029	1.04	1.11	1.12	**0.20**	**0.14**
2030	1.01	1.01	1.06	**0.10**	**0.09**
2031	1.00	1.02	1.01	**0.10**	**0.09**
2032	1.01	0.99	1.13	**0.10**	**0.09**
1878	1.14	1.22	1.20	**0.11**	**0.11**
2033	1.10	1.02	1.03	**0.10**	**0.10**
2034	1.09	0.98	1.01	**0.10**	**0.10**
2035	1.10	0.96	1.00	**0.10**	**0.10**
2036	1.07	0.95	1.09	**0.09**	**0.10**
2037	1.10	1.04	1.16	**0.10**	**0.10**
2038	1.09	0.98	1.00	**0.09**	**0.10**
2039	1.13	0.93	1.10	**0.09**	**0.10**
2040	1.27	0.96	1.02	**0.10**	**0.11**
2041	1.09	1.03	1.09	**0.10**	**0.10**
2042	**0.24**	1.07	1.09	**0.10**	**0.09**
2043	**0.23**	1.12	1.10	**0.09**	**0.10**
2044	**0.29**	1.24	1.17	**0.09**	**0.11**
2045	**0.19**	0.85	1.18	**0.14**	**0.10**
2046	**0.18**	1.09	1.20	**0.10**	**0.10**
2047	**0.25**	1.01	1.24	**0.11**	**0.11**
2048	**0.23**	0.44	0.95	**0.14**	**0.19**
2049	**0.28**	1.04	1.05	**0.09**	**0.10**
2050	**0.20**	1.07	1.05	**0.10**	**0.10**
1880	1.02	1.10	1.17	1.06	0.84
2051	1.11	1.03	0.98	**0.10**	**0.10**
2052	1.12	1.05	1.24	**0.10**	**0.10**
2053	1.07	1.11	1.21	**0.10**	**0.10**
2054	1.03	0.98	1.11	**0.12**	**0.09**
2055	1.02	1.02	1.17	**0.09**	**0.09**
2056	1.03	1.08	1.34	**0.10**	**0.09**
2057	1.00	1.05	1.13	**0.10**	**0.10**
2058	1.02	1.18	1.07	**0.10**	**0.10**
2059	1.09	1.00	1.05	**0.10**	**0.10**
1881	1.13	1.20	1.00	1.07	1.02
2060	1.07	0.97	1.10	**0.30**	**0.11**
2061	1.07	1.02	0.97	**0.18**	**0.11**
2062	1.09	0.99	0.93	**0.18**	**0.12**

2063	0.95	0.93	0.92	1.17	1.06
2064	0.99	0.82	1.00	**0.09**	**0.09**
2065	1.03	1.06	1.07	**0.16**	**0.11**
2066	1.00	0.99	1.04	**0.18**	**0.13**
2067	1.15	1.01	1.08	1.05	1.21
2068	1.14	1.07	1.02	1.27	1.21
2069	1.13	0.92	1.04	0.52	**0.25**
2070	1.13	1.02	0.93	**0.11**	**0.11**
2071	1.17	1.22	1.03	1.18	1.17
2072	1.11	1.32	1.03	**0.10**	**0.12**
2073	1.06	0.98	0.92	1.26	1.04
2074	1.08	1.03	1.48	**0.09**	**0.10**
2075	0.99	1.07	1.05	**0.18**	**0.12**
2076	1.06	0.97	1.02	**0.10**	**0.10**
2077	1.16	1.06	1.04	**0.09**	**0.11**
1882	1.07	1.22	0.99	**0.10**	**0.10**
2078	1.07	0.94	0.97	**0.14**	**0.14**
2079	1.21	0.84	0.98	1.09	1.14
2080	1.08	0.84	0.96	1.13	1.09
2081	1.26	0.99	1.03	1.06	1.23
2082	1.11	1.05	1.04	1.07	1.14
2083	1.05	1.18	1.02	**0.13**	**0.12**
2084	1.07	1.03	0.99	**0.13**	**0.12**
2085	1.09	1.02	0.99	1.17	1.12
2086	1.09	1.14	1.06	**0.11**	**0.12**
2087	0.92	1.02	0.95	1.22	1.00
2088	**0.32**	0.89	0.99	**0.14**	**0.12**
2089	1.09	1.01	0.97	1.09	1.14
2090	**0.36**	0.81	1.00	**0.12**	**0.11**
2091	1.11	1.00	1.02	**0.11**	**0.12**
2092	**0.33**	1.00	1.05	**0.09**	**0.11**
2093	**0.37**	1.08	1.03	**0.09**	**0.11**
2094	0.41	1.03	1.00	**0.09**	**0.11**
2095	1.17	1.01	1.08	**0.11**	**0.12**
2096	1.18	1.01	1.11	**0.09**	**0.11**
2097	1.12	0.98	0.98	**0.10**	**0.10**
2098	1.03	0.95	0.92	**0.09**	**0.09**
2099	1.16	0.91	0.99	**0.10**	**0.11**
2100	1.29	1.03	1.03	1.04	1.12

2101	1.29	1.04	1.00	1.07	1.18
2102	1.31	0.99	0.98	1.05	1.19
2103	1.18	0.99	0.99	1.05	1.12
2104	1.25	1.00	1.01	1.03	1.22
1883	1.04	1.11	0.90	1.16	1.06
2105	1.15	1.10	1.03	1.17	1.11
2106	1.25	1.09	1.16	0.92	1.01
2107	1.16	0.97	1.01	1.16	1.13
2108	1.12	1.00	1.03	1.10	1.09
2109	**0.21**	0.99	1.05	1.25	1.07
2110	1.03	1.05	0.96	1.17	1.00
2111	1.02	0.95	0.83	0.77	**0.35**
2112	1.12	1.00	0.99	1.19	1.10
2113	1.08	0.99	1.00	**0.10**	**0.10**
1884	**0.19**	1.05	0.84	0.98	0.97
2114	**0.27**	0.92	0.98	1.10	1.07
2115	**0.26**	0.95	0.97	1.10	1.02
2116	**0.26**	0.98	0.99	1.11	1.12
2117	**0.40**	1.03	1.00	1.11	0.84
2118	**0.21**	1.01	1.00	1.16	0.99
2119	**0.15**	1.04	1.11	1.10	0.47
2120	**0.22**	0.95	1.02	1.13	1.08
2121	**0.21**	0.97	1.17	1.17	1.04
2122	**0.15**	1.07	0.98	1.19	0.88
1885	1.01	1.09	1.02	**0.09**	**0.09**
2123	**0.10**	**0.14**	1.04	**0.09**	**0.09**
2124	**0.16**	0.86	1.09	**0.09**	**0.10**
2125	**0.10**	**0.13**	**0.32**	**0.09**	**0.09**
2126	1.14	1.10	1.20	**0.10**	**0.11**
2127	1.08	0.97	1.06	1.09	1.03
2128	**0.11**	**0.12**	**0.31**	**0.09**	**0.11**
2129	**0.11**	**0.13**	0.49	**0.09**	**0.10**
2130	**0.25**	0.85	1.15	**0.10**	**0.11**
2131	**0.12**	**0.12**	**0.32**	**0.09**	**0.11**
1886	1.01	0.98	0.95	1.01	0.99
2132	1.25	0.96	1.11	1.03	1.17
1887	1.08	1.04	0.99	1.17	**0.12**
2133	1.10	1.00	1.10	**0.10**	**0.10**
2134	1.00	0.94	1.03	1.24	1.07

2135	1.02	1.14	1.00	0.09	0.09
2136	1.05	1.10	0.97	0.09	0.10
2137	1.07	1.13	0.97	0.09	0.10
2138	1.09	1.03	0.84	1.08	1.09
2139	1.10	1.03	1.11	0.09	0.10
2140	1.08	1.00	0.93	0.88	1.08
2141	1.03	0.96	0.96	0.11	0.10
2142	1.08	1.05	1.18	0.83	0.96
2143	1.11	1.07	1.00	1.03	1.07
2148	1.08	1.08	1.00	0.09	0.10
2149	1.02	1.18	0.96	1.06	1.17
2150	1.10	1.00	0.86	0.71	0.31
2164	1.06	1.06	0.98	0.10	0.09
2165	1.04	1.03	0.97	0.10	0.09
2166	1.02	1.15	1.24	1.09	0.97
2167	1.07	0.80	0.92	0.10	0.10
1888	1.08	1.14	1.09	0.22	0.19
2151	1.15	0.94	0.90	0.36	0.28
2152	1.10	0.97	1.05	0.10	0.10
2153	1.09	1.03	0.95	0.16	0.15
2154	1.11	0.95	0.85	0.29	0.30
2155	1.06	1.07	1.18	0.19	0.17
2156	0.99	0.95	1.02	0.09	0.10
2157	1.01	1.07	0.99	0.09	0.09
2158	0.97	0.81	0.91	0.09	0.10
2159	1.06	0.93	1.09	0.40	0.35
1889	1.03	1.09	1.09	0.10	0.09
2144	1.10	1.11	1.04	1.07	1.08
2145	1.03	1.07	1.06	0.64	0.94
2146	1.05	1.04	1.05	0.10	0.10
2147	1.06	0.98	0.99	0.10	0.10
2160	1.01	0.89	1.05	0.10	0.10
2161	1.06	0.95	1.08	0.10	0.10
2162	1.02	0.96	1.05	0.10	0.09
2163	0.98	0.92	0.97	0.10	0.10
2168	1.13	0.93	0.93	0.10	0.10
1890	1.06	1.12	1.07	1.03	1.01
2169	1.12	0.90	1.11	0.10	0.10
2170	1.12	0.82	0.94	0.10	0.11

2171	1.10	0.86	0.91	**0.11**	**0.11**
2172	1.15	0.83	1.07	**0.10**	**0.12**
2173	1.03	0.84	0.95	**0.11**	**0.10**
2174	1.09	3.35	3.43	**0.10**	**0.10**
2175	1.14	0.91	0.97	1.11	1.11
2176	0.98	0.95	0.97	0.58	0.89
2177	1.02	1.01	1.08	1.18	1.05
1879	0.99	1.30	1.20	**0.10**	**0.09**
1911	**0.18**	0.94	1.23	**0.14**	**0.30**
1950	0.91	1.08	1.07	**0.09**	**0.09**
1951	0.98	0.89	0.98	1.00	0.98
1952	**0.10**	**0.11**	0.98	**0.09**	**0.09**
1953	**0.10**	**0.09**	**0.11**	**0.27**	0.79
1954	1.02	1.06	1.05	**0.09**	**0.10**
1955	**0.09**	**0.09**	**0.11**	**0.27**	0.81
1956	**0.19**	0.96	1.00	**0.10**	**0.28**
1957	1.09	0.92	0.96	**0.09**	**0.09**
1958	1.02	0.99	0.92	**0.09**	**0.09**
1913	**0.17**	0.97	1.18	**0.35**	**0.20**
1968	**0.09**	**0.11**	0.99	**0.09**	**0.08**
1969	0.92	0.99	0.86	**0.10**	**0.08**
1970	**0.11**	**0.20**	0.97	**0.09**	**0.08**
1971	0.98	0.84	0.87	**0.08**	**0.09**
1972	**0.17**	**0.21**	0.95	**0.11**	**0.20**
1973	**0.24**	0.79	0.95	**0.11**	**0.27**
1974	**0.18**	0.81	0.95	**0.11**	**0.20**
1975	1.14	1.26	1.27	**0.09**	**0.19**
1976	1.03	1.00	0.89	**0.09**	**0.09**
1891	1.07	1.06	1.02	1.06	1.14
1892	1.15	1.13	1.00	1.04	1.11
1893	1.09	1.11	0.95	1.13	1.09
1894	1.15	1.05	0.92	1.02	1.14
1895	1.11	1.08	0.95	**0.11**	**0.11**
1896	0.99	0.95	0.91	**0.09**	**0.10**
1897	0.98	1.01	0.97	**0.09**	**0.09**
1898	1.07	0.96	0.85	**0.08**	**0.09**
1899	0.99	0.99	1.07	1.00	1.03
1990	**0.12**	**0.27**	1.11	**0.09**	**0.20**
1991	**0.12**	**0.31**	1.12	**0.10**	**0.19**

1992	0.13	0.28	1.07	0.09	0.22
1993	0.11	0.21	1.16	0.10	0.58
1994	0.11	0.28	1.08	0.09	1.16
1995	0.13	0.22	1.05	0.10	0.71
1996	0.11	0.09	0.10	0.09	0.33
1910	0.11	0.09	0.10	0.09	0.12
1945	0.35	0.81	0.99	0.09	0.12
1946	0.11	0.09	0.09	0.09	0.11
1947	0.11	0.09	0.09	0.09	0.11
1948	0.11	0.09	0.09	0.31	1.04
1949	0.09	0.09	0.09	0.10	0.10
1977	0.09	0.10	0.10	0.31	0.26
1978	1.10	1.10	1.17	1.00	1.06
1979	0.95	1.10	0.97	0.87	0.85
1980	1.08	1.06	0.98	0.99	0.98
1981	1.01	0.97	0.93	0.87	0.93
1982	0.97	1.06	0.93	1.10	1.13
1983	0.11	1.02	0.91	0.10	0.11
1984	0.95	1.05	1.04	0.94	1.00
1985	0.10	0.08	0.09	1.00	1.01
1914	0.11	0.10	0.11	0.15	0.14
1986	0.11	0.09	0.13	0.14	0.15
1987	0.11	0.09	0.12	0.14	0.14
1988	0.10	0.09	0.11	0.13	0.12
1989	0.13	0.98	1.04	0.10	0.11
1917	0.81	1.20	0.90	1.05	0.71
2015	0.10	0.11	0.22	0.67	0.55
2016	0.11	0.11	0.21	0.61	0.58
2017	0.10	0.11	0.22	0.58	0.56
2018	0.11	0.10	0.27	0.66	0.70
2019	0.11	0.10	0.24	0.74	0.59
2020	0.30	1.11	0.13	0.25	0.22
2021	0.78	1.09	1.18	0.82	0.88
2022	0.82	1.16	1.11	0.79	0.96
2023	1.04	1.04	1.09	1.03	1.08

TABLE 24

NP #	A511:ff	P100:ff	LP48:ff	LP125:ff	A511:ff, P100:ff, LP48:ff	A511:ff, P100:ff, LP48:ff, LP125:ff
1839	**0.15**	**0.14**	**0.19**	**0.14**	**0.14**	**0.18**
1840	1.01	1.03	1.01	1.06	1.02	1.04
1869	**0.14**	**0.13**	**0.15**	0.90	**0.16**	**0.14**
1878	1.02	**0.19**	1.01	1.14	**0.26**	**0.22**
1879	**0.12**	**0.11**	**0.12**	**0.13**	**0.12**	**0.12**
1880	1.00	1.05	0.96	1.06	1.06	1.02
1881	1.07	1.09	1.04	1.16	1.08	1.04
1882	0.76	**0.11**	**0.22**	0.42	**0.14**	**0.15**
1883	1.08	1.09	1.08	1.08	1.02	1.04
1884	1.05	1.03	1.06	1.07	1.03	1.01
1885	**0.12**	**0.10**	**0.11**	**0.11**	**0.11**	**0.10**
1886	0.99	1.09	1.00	1.06	1.09	1.04
1887	1.02	1.07	1.17	0.98	1.11	1.05
1888	0.98	1.05	1.04	1.02	1.11	1.01
1889	**0.13**	**0.11**	**0.12**	**0.13**	**0.12**	**0.13**
1890	1.04	1.05	1.07	1.06	1.13	1.06
1891	1.01	1.02	1.00	1.06	1.08	1.03
1892	0.98	0.97	0.98	1.06	1.05	1.01
1893	1.01	1.00	1.02	1.07	1.06	1.01
1894	1.03	1.05	1.02	1.08	1.06	1.04
1895	**0.13**	**0.11**	**0.13**	**0.13**	**0.12**	**0.12**
1896	**0.12**	**0.11**	**0.12**	**0.17**	**0.11**	**0.12**
1897	**0.18**	**0.16**	**0.16**	**0.19**	**0.16**	**0.16**
1898	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
1899	1.07	1.07	1.05	1.04	1.08	0.98
1900	1.06	1.07	1.05	1.03	1.14	1.00
1901	**0.11**	**0.10**	**0.12**	1.01	**0.11**	**0.11**
1902	1.02	1.05	1.03	1.03	1.05	0.98
1903	**0.11**	**0.11**	**0.11**	1.03	**0.14**	**0.11**
1904	**0.11**	**0.12**	**0.16**	1.04	**0.12**	**0.12**
1905	**0.11**	**0.12**	**0.16**	1.05	**0.12**	**0.12**
1906	1.04	1.07	1.04	1.04	1.04	0.66
1907	1.04	1.09	1.03	1.05	1.05	0.98

1908	**0.11**	**0.10**	**0.12**	1.04	**0.11**	**0.11**
1909	0.99	1.01	1.00	1.01	1.00	0.94
1910	**0.17**	**0.14**	**0.25**	0.96	**0.19**	**0.18**
1911	1.06	1.02	1.06	1.07	1.20	1.01
1912	1.04	0.97	1.02	1.02	1.13	1.05
1913	0.99	0.98	0.96	0.95	1.13	0.96
1914	0.92	**0.13**	0.56	1.14	**0.27**	**0.20**
1915	**0.14**	**0.11**	**0.11**	**0.13**	**0.12**	**0.12**
1916	1.07	1.06	1.05	1.12	1.23	1.02
1917	1.02	0.99	1.06	1.09	1.09	1.02
1945	**0.12**	**0.10**	**0.11**	**0.16**	**0.10**	**0.10**
1946	0.75	**0.14**	0.85	1.09	**0.20**	**0.24**
1947	0.85	**0.15**	0.87	1.15	**0.21**	**0.20**
1948	0.43	0.99	1.05	1.04	0.43	0.85
1949	**0.13**	**0.13**	**0.17**	1.07	**0.14**	**0.12**
1950	**0.09**	**0.09**	**0.09**	**0.09**	**0.10**	**0.09**
1951	1.02	1.00	1.00	1.00	1.00	1.00
1952	**0.11**	**0.09**	**0.09**	**0.09**	**0.10**	**0.09**
1953	**0.11**	**0.10**	0.98	1.08	**0.13**	**0.12**
1954	**0.09**	**0.09**	**0.09**	**0.09**	**0.09**	**0.09**
1955	**0.11**	**0.10**	0.97	1.10	**0.12**	**0.12**
1956	0.97	0.87	0.97	1.02	0.98	0.94
1957	**0.13**	**0.10**	0.66	**0.17**	**0.10**	**0.10**
1958	**0.09**	**0.09**	**0.09**	**0.10**	**0.09**	**0.09**
1959	**0.10**	**0.10**	**0.12**	1.03	**0.10**	**0.10**
1960	**0.14**	0.93	**0.19**	1.00	**0.19**	**0.18**
1961	**0.12**	**0.16**	1.01	1.25	**0.12**	**0.12**
1962	1.10	1.17	1.13	1.21	1.17	1.10
1963	**0.13**	**0.10**	**0.13**	1.09	**0.12**	**0.12**
1964	**0.11**	**0.10**	**0.13**	1.09	**0.12**	**0.12**
1965	**0.12**	**0.10**	**0.13**	1.13	**0.12**	**0.12**
1966	**0.11**	**0.10**	**0.16**	1.00	**0.11**	**0.11**
1967	**0.12**	**0.10**	**0.23**	1.05	**0.12**	**0.12**
1968	**0.11**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
1969	**0.12**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
1970	**0.09**	**0.08**	**0.08**	**0.09**	**0.09**	**0.08**
1971	**0.09**	**0.08**	**0.09**	**0.09**	**0.08**	**0.08**
1972	1.08	1.02	1.10	1.46	1.10	1.14
1973	1.10	1.08	1.08	1.11	1.11	1.11

1974	1.14	1.15	1.15	1.14	1.27	1.14
1975	0.97	0.96	0.97	0.98	0.58	0.99
1976	**0.12**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
1977	**0.13**	**0.11**	0.90	1.03	**0.15**	**0.15**
1978	1.10	1.04	1.08	1.08	1.17	1.15
1979	1.14	1.12	1.11	1.16	1.26	1.21
1980	1.01	1.09	1.04	1.12	1.11	1.08
1981	1.16	1.21	1.09	1.14	1.18	1.15
1982	1.01	1.08	0.94	1.03	1.04	1.00
1983	0.43	**0.14**	**0.39**	**0.34**	**0.18**	**0.16**
1984	1.06	1.03	1.05	1.05	1.06	1.06
1985	1.00	1.03	1.02	1.01	1.04	1.02
1986	0.86	**0.12**	0.60	1.06	**0.14**	**0.14**
1987	0.81	**0.12**	0.61	1.02	**0.13**	**0.15**
1988	0.81	**0.12**	0.42	1.06	**0.14**	**0.15**
1989	0.96	**0.17**	0.76	0.71	**0.22**	**0.26**
1990	1.07	1.04	1.04	1.10	1.06	1.03
1991	1.03	1.03	1.00	1.06	1.01	0.98
1992	0.98	1.02	0.99	1.04	1.04	0.96
1993	1.00	1.02	1.12	1.20	1.36	1.04
1994	1.02	1.06	0.96	0.98	1.14	0.98
1995	1.03	1.00	1.02	1.02	1.07	1.01
1996	**0.10**	**0.09**	0.87	1.05	**0.09**	**0.09**
1997	**0.12**	**0.10**	**0.10**	**0.12**	**0.10**	**0.11**
1998	**0.12**	**0.10**	**0.10**	**0.11**	**0.10**	**0.10**
1999	**0.13**	**0.13**	**0.10**	0.51	**0.11**	**0.12**
2000	**0.13**	**0.10**	**0.10**	**0.12**	**0.11**	**0.11**
2001	**0.12**	**0.10**	**0.10**	**0.12**	**0.11**	**0.11**
2002	**0.30**	1.03	1.03	1.04	0.80	0.72
2003	1.00	1.01	1.01	1.03	1.01	0.95
2004	1.02	1.04	1.03	1.03	1.01	0.98
2005	0.98	1.00	1.02	1.00	1.12	1.00
2006	1.07	1.11	0.94	1.03	1.12	0.94
2007	**0.12**	**0.13**	**0.18**	1.01	**0.13**	**0.12**
2008	**0.12**	**0.13**	**0.19**	1.03	**0.13**	**0.12**
2009	**0.11**	**0.13**	**0.21**	0.98	**0.12**	**0.11**
2010	0.96	1.07	0.98	1.12	1.20	0.92
2011	0.97	1.01	0.95	0.98	1.09	0.90
2012	1.02	1.02	1.05	1.01	1.05	0.99

2013	0.96	1.01	1.01	0.97	1.02	0.95
2014	0.94	1.07	1.00	1.05	1.15	0.90
2015	0.98	1.03	1.03	1.01	0.99	0.96
2016	1.00	1.02	1.03	1.06	1.02	0.99
2017	0.95	0.93	0.98	0.99	1.04	0.96
2018	0.89	0.93	0.87	0.93	0.91	0.86
2019	1.00	0.99	0.97	1.03	1.06	0.98
2020	1.03	0.89	0.97	1.07	0.96	0.89
2021	0.98	1.01	0.98	1.01	1.04	0.98
2022	1.02	1.04	1.00	1.05	1.06	1.01
2023	1.12	1.05	1.03	1.06	1.10	1.11
2024	**0.11**	**0.10**	**0.10**	**0.11**	**0.10**	**0.10**
2025	**0.12**	**0.11**	**0.11**	**0.11**	**0.11**	**0.11**
2026	0.55	0.55	0.55	0.56	0.55	0.55
2027	**0.13**	**0.11**	**0.13**	**0.15**	**0.13**	**0.13**
2028	**0.11**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
2029	0.98	0.91	1.06	1.02	1.07	1.04
2030	**0.12**	**0.09**	**0.10**	**0.10**	**0.10**	**0.10**
2031	**0.21**	**0.10**	**0.16**	**0.23**	**0.11**	**0.12**
2032	**0.11**	**0.10**	**0.11**	**0.10**	**0.10**	**0.10**
2033	**0.11**	**0.10**	**0.10**	**0.10**	**0.11**	**0.10**
2034	**0.11**	**0.10**	**0.11**	**0.10**	**0.10**	**0.10**
2035	**0.10**	**0.09**	**0.10**	**0.10**	**0.10**	**0.10**
2036	**0.11**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
2037	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
2038	0.99	**0.18**	1.04	0.86	**0.22**	**0.19**
2039	1.04	**0.18**	0.96	0.75	**0.23**	**0.23**
2040	1.01	**0.15**	1.07	1.09	**0.25**	**0.24**
2041	**0.11**	**0.10**	**0.11**	**0.11**	**0.11**	**0.10**
2042	0.60	**0.10**	0.78	0.96	**0.25**	**0.20**
2043	1.02	**0.10**	0.65	0.95	**0.11**	**0.10**
2044	1.03	**0.11**	0.82	1.04	**0.19**	**0.13**
2045	1.00	**0.10**	**0.16**	1.01	**0.11**	**0.11**
2046	1.12	**0.11**	0.66	1.07	**0.12**	**0.12**
2047	0.99	**0.12**	0.84	0.99	**0.14**	**0.13**
2048	1.21	**0.22**	1.08	1.36	**0.25**	**0.27**
2049	0.97	**0.10**	0.79	1.00	**0.12**	**0.12**
2050	1.14	**0.11**	0.99	1.16	**0.12**	**0.13**
2051	0.99	**0.19**	1.02	0.90	**0.23**	**0.23**

2052	**0.12**	**0.10**	**0.11**	**0.10**	**0.10**	**0.10**
2053	**0.10**	**0.10**	**0.10**	**0.11**	**0.11**	**0.10**
2054	**0.14**	**0.13**	**0.14**	**0.16**	**0.14**	**0.14**
2055	**0.11**	**0.09**	**0.11**	**0.10**	**0.10**	**0.10**
2056	**0.13**	**0.11**	**0.12**	**0.12**	**0.12**	**0.12**
2057	1.06	**0.20**	1.07	1.07	**0.32**	**0.29**
2058	1.00	**0.24**	1.12	1.04	**0.28**	**0.29**
2059	**0.11**	**0.10**	**0.11**	**0.12**	**0.10**	**0.10**
2060	1.19	1.18	1.26	1.19	1.28	1.28
2061	1.03	0.91	1.07	0.98	1.01	0.95
2062	1.13	1.08	1.15	1.07	1.12	1.08
2063	1.00	1.00	1.06	1.04	1.17	1.04
2064	1.09	0.87	1.15	1.24	1.13	1.24
2065	0.96	0.97	0.94	0.86	0.93	0.96
2066	1.00	1.08	1.09	1.18	1.16	1.13
2067	1.14	1.09	1.18	1.18	1.13	1.15
2068	1.10	1.02	1.05	1.11	1.08	1.09
2069	1.11	1.13	1.08	1.26	1.09	1.16
2070	0.99	**0.10**	**0.20**	**0.21**	**0.11**	**0.11**
2071	1.13	1.12	1.03	1.20	1.21	1.15
2072	**0.14**	**0.12**	**0.13**	**0.12**	**0.12**	**0.12**
2073	1.01	0.99	0.98	1.11	1.08	1.05
2074	1.04	**0.12**	0.80	0.87	**0.14**	**0.15**
2075	1.00	1.00	1.04	1.17	1.04	1.07
2076	**0.11**	**0.10**	**0.11**	**0.10**	**0.10**	**0.10**
2077	**0.34**	**0.11**	**0.27**	**0.22**	**0.12**	**0.12**
2078	0.97	0.97	0.97	0.98	0.99	1.01
2079	1.06	1.06	1.07	1.07	1.04	1.06
2080	1.01	1.02	1.02	1.03	1.02	1.05
2081	1.03	1.03	1.07	1.05	1.02	1.04
2082	1.05	1.06	1.07	1.03	1.02	1.06
2083	1.08	1.07	1.05	1.04	1.03	1.09
2084	1.00	1.03	1.02	1.03	1.05	1.05
2085	1.09	1.06	1.02	1.09	0.97	1.11
2086	1.06	1.07	1.10	1.13	1.18	1.11
2087	1.01	1.30	0.94	0.97	1.08	1.01
2088	**0.18**	**0.13**	0.53	0.87	**0.16**	**0.16**
2089	1.09	1.19	1.12	1.08	1.11	1.07
2090	**0.15**	**0.11**	**0.34**	0.74	**0.13**	**0.14**

2091	1.04	1.06	1.06	1.04	1.06	1.03
2092	**0.11**	**0.09**	**0.11**	**0.16**	**0.10**	**0.10**
2093	0.80	**0.09**	0.82	0.88	**0.09**	**0.09**
2094	0.77	**0.09**	0.78	0.85	**0.09**	**0.09**
2095	**0.15**	**0.12**	**0.14**	**0.14**	**0.14**	**0.14**
2096	0.67	**0.09**	**0.38**	0.67	**0.09**	**0.09**
2097	**0.39**	**0.10**	**0.28**	0.47	**0.10**	**0.10**
2098	0.57	**0.09**	0.43	0.61	**0.09**	**0.10**
2099	0.47	**0.10**	**0.23**	**0.26**	**0.10**	**0.10**
2100	1.02	1.03	1.00	1.03	1.02	1.01
2101	1.05	1.04	1.05	1.05	1.03	1.01
2102	1.00	0.98	1.00	0.99	0.99	0.98
2103	1.02	1.03	1.07	1.04	1.05	1.07
2104	0.98	0.99	0.99	0.98	0.98	0.99
2105	1.03	1.06	1.02	1.07	1.01	0.99
2106	1.00	0.98	1.01	1.00	1.00	1.02
2107	1.01	1.00	0.99	1.00	0.98	0.98
2108	1.00	0.98	1.01	0.96	1.01	1.01
2109	1.00	1.00	1.02	0.99	0.99	1.02
2110	1.01	0.96	1.02	0.98	1.04	1.00
2111	1.02	1.07	0.98	1.05	1.05	1.04
2112	1.00	1.03	1.06	1.03	1.01	1.04
2113	**0.12**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
2114	0.98	0.99	1.00	1.01	0.98	1.02
2115	1.00	1.06	1.03	1.06	1.01	1.03
2116	0.98	0.97	0.98	0.98	0.95	1.01
2117	0.99	1.04	1.05	1.02	1.01	0.92
2118	0.93	0.97	1.00	0.96	0.95	1.02
2119	1.08	1.05	1.07	1.06	1.03	0.95
2120	0.92	0.95	0.98	0.98	0.95	1.01
2121	1.13	1.16	1.18	1.22	1.12	1.20
2122	1.03	0.97	1.02	1.03	1.08	1.01
2123	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
2124	**0.11**	**0.09**	**0.10**	**0.10**	**0.10**	**0.10**
2125	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**	**0.10**
2126	1.00	**0.17**	1.06	0.86	**0.22**	**0.21**
2127	1.07	1.13	1.10	1.06	1.08	1.05
2128	**0.09**	**0.09**	**0.09**	**0.09**	**0.09**	**0.09**
2129	**0.10**	**0.10**	**0.10**	**0.10**	**0.09**	**0.10**

2130	0.09	0.09	0.10	0.10	0.09	0.09
2131	0.10	0.10	0.09	0.24	0.09	0.10
2132	0.93	1.00	1.00	0.95	1.00	0.98
2133	1.07	0.12	0.14	0.14	0.13	0.14
2134	1.09	0.96	0.97	0.99	1.06	0.98
2135	0.57	0.15	0.96	1.09	0.16	0.23
2136	1.07	0.10	0.11	0.12	0.10	0.11
2137	1.14	0.11	0.12	0.13	0.11	0.11
2138	1.11	1.06	1.02	1.04	1.05	1.04
2139	0.75	0.11	0.24	0.14	0.13	0.13
2140	1.02	1.05	1.05	1.05	0.98	1.05
2141	0.84	0.14	1.04	0.99	0.16	0.16
2142	0.99	1.02	1.06	1.03	0.94	0.95
2143	1.16	1.14	1.21	1.15	1.11	1.10
2164	0.10	0.10	0.11	0.11	0.10	0.10
2165	0.13	0.12	0.14	0.14	0.13	0.13
2166	1.04	1.00	1.09	1.09	1.10	1.08
2167	0.15	0.11	0.11	0.11	0.11	0.13
2148	0.11	0.10	0.11	0.12	0.10	0.10
2149	0.96	1.13	0.97	1.07	1.06	1.00
2150	0.93	1.05	0.95	1.03	1.02	1.04
2151	0.93	0.94	0.97	1.02	1.01	1.01
2152	0.10	0.09	0.09	0.10	0.10	0.09
2153	1.03	1.10	1.12	1.11	1.09	1.10
2154	0.93	1.03	1.12	1.02	1.01	1.10
2155	0.98	1.11	1.07	1.13	1.11	1.10
2156	0.12	0.09	0.09	0.10	0.09	0.09
2157	0.45	0.44	0.45	0.46	0.44	0.45
2158	0.12	0.10	0.11	0.11	0.10	0.11
2159	1.02	1.10	1.09	1.13	1.21	1.16
2160	0.17	0.12	0.13	0.14	0.13	0.13
2161	0.14	0.10	0.11	0.11	0.11	0.11
2162	0.14	0.10	0.11	0.11	0.12	0.11
2163	0.13	0.11	0.10	0.11	0.11	0.11
2144	1.03	1.00	1.03	1.07	1.13	1.14
2145	1.05	1.09	1.05	1.12	1.17	1.18
2146	0.12	0.10	0.11	0.11	0.10	0.10
2147	1.09	0.13	0.18	1.04	0.17	0.17
2168	0.13	0.12	0.13	0.13	0.12	0.11

2169	0.13	0.13	0.13	0.12	0.13	0.12
2170	0.11	0.09	0.11	0.10	0.10	0.11
2171	0.12	0.12	0.13	0.12	0.12	0.11
2172	0.11	0.13	0.21	0.20	0.12	0.12
2173	0.12	0.12	0.17	0.26	0.11	0.11
2174	0.11	0.10	0.11	0.11	0.11	0.10
2175	0.97	0.97	1.01	1.01	0.97	0.94
2176	1.03	1.01	1.00	1.02	1.00	1.00
2177	0.98	0.90	0.95	0.99	0.95	0.89

TABLE 25

NP #	P100 and A511:nluc	LP124:nluc	A511, P100, 124:nluc	LP124:nluc RLU
1839	0.14	0.27	0.31	4.14E+08
1840	1.05	1.11	1.04	5.68E+02
1869	0.13	0.20	0.17	4.63E+08
1878	0.20	0.55	0.65	2.43E+08
1879	0.12	0.10	0.10	
1880	1.07	1.01	1.09	1.16E+06
1881	1.00	0.96	1.08	2.41E+06
1882	0.12	0.20	0.23	8.90E+05
1883	1.00	1.12	1.03	8.22E+02
1884	1.05	1.04	1.01	1.14E+04
1885	0.12	0.09	0.09	9.07E+08
1886	1.04	1.02	0.96	4.83E+02
1887	1.00	0.94	1.08	5.87E+05
1888	0.94	0.88	1.00	3.72E+06
1889	0.10	0.10	0.10	7.50E+08
1890	1.04	0.96	1.01	1.32E+03
1891	0.95	0.90	1.13	4.48E+02
1892	0.96	1.00	1.04	5.21E+02
1893	0.97	1.03	1.07	5.34E+02
1894	0.96	0.90	1.05	4.04E+02
1895	0.12	0.11	0.15	1.18E+09

1896	0.12	0.10	0.15	1.18E+09
1897	0.10	0.11	0.10	1.20E+09
1898	0.10	0.13	0.10	1.18E+09
1899	0.98	1.16	1.09	7.88E+02
1900	0.94	0.88	1.06	6.40E+02
1901	0.10	0.09	0.10	5.17E+08
1902	1.02	1.00	0.57	2.88E+06
1903	0.10	0.11	0.10	4.89E+08
1904	0.11	0.13	0.10	1.03E+08
1905	0.12	0.16	0.11	1.12E+08
1906	0.79	0.91	1.06	3.11E+06
1907	0.98	0.98	1.07	6.91E+02
1908	0.11	0.11	0.12	4.99E+08
1909	1.10	0.98	1.02	6.89E+02
1910	0.11	0.11	0.13	1.36E+09
1911	1.05	0.92	1.10	4.16E+05
1912	1.08	1.07	1.11	4.00E+02
1913	1.15	1.59	0.97	6.22E+02
1914	0.11	0.17	0.11	3.71E+08
1915	0.11	0.10	0.11	2.25E+08
1916	1.01	0.89	0.99	1.88E+04
1917	1.10	0.89	1.05	1.18E+06
1945	0.10	0.12	0.09	1.07E+09
1946	0.17	0.30	0.79	8.28E+04
1947	0.12	0.31	0.54	1.08E+05
1948	0.47	0.79	0.56	1.68E+04
1949	0.11	0.14	0.13	9.51E+08
1950	0.09	0.11	0.12	1.14E+09
1951	1.02	1.00	1.02	8.32E+02
1952	0.10	0.14	0.10	1.26E+09
1953	0.10	1.22	0.10	1.31E+08
1954	0.10	0.13	0.11	7.70E+08
1955	0.10	1.04	0.10	1.15E+08
1956	1.07	1.08	1.01	1.50E+06
1957	0.10	0.14	0.10	3.15E+07
1958	0.10	0.13	0.11	8.58E+08
1959	0.10	0.12	0.11	4.59E+08
1960	0.15	0.14	0.14	6.09E+08
1961	0.12	0.12	0.13	1.49E+08

1962	1.04	0.97	1.41	9.90E+02
1963	0.12	0.10	0.11	1.13E+09
1964	0.10	0.10	0.11	1.24E+09
1965	0.10	0.10	0.09	1.31E+09
1966	0.11	0.09	0.10	8.83E+08
1967	0.10	0.10	0.10	5.14E+08
1968	0.09	0.12	0.12	1.08E+09
1969	0.09	0.12	0.12	1.19E+09
1970	0.08	0.09	0.10	9.52E+08
1971	0.09	0.10	0.10	1.17E+09
1972	0.92	0.75	1.68	2.46E+06
1973	1.10	1.02	1.80	1.27E+03
1974	1.11	0.96	1.08	5.58E+02
1975	1.12	0.10	0.12	2.05E+09
1976	0.11	0.11	0.12	1.01E+09
1977	0.11	0.78	0.13	9.36E+08
1978	1.10	1.04	1.17	4.25E+03
1979	1.04	0.90	1.08	8.68E+02
1980	0.99	0.93	1.14	1.01E+06
1981	1.59	0.78	1.18	8.87E+02
1982	1.03	1.02	0.98	2.26E+04
1983	0.16	0.26	0.25	1.10E+05
1984	1.01	1.14	0.99	5.70E+05
1985	1.01	1.07	1.00	3.71E+05
1986	0.11	0.17	0.11	4.42E+08
1987	0.11	0.16	0.11	4.19E+08
1988	0.11	0.16	0.12	5.10E+08
1989	0.21	0.35	0.70	7.94E+03
1990	0.59	1.05	1.03	5.21E+02
1991	0.97	1.08	0.97	7.81E+02
1992	0.98	1.06	0.98	5.54E+02
1993	1.10	1.05	1.08	5.49E+02
1994	0.99	1.12	1.05	6.11E+02
1995	1.05	1.07	1.07	6.58E+02
1996	0.10	0.40	0.09	9.57E+08
1997	0.11	0.10	0.11	1.03E+09
1998	0.11	0.10	0.11	7.04E+08
1999	0.11	0.10	0.13	7.03E+08
2000	0.11	0.12	0.12	7.44E+08

2001	0.11	0.85	0.20	7.40E+08
2002	0.28	0.14	0.55	2.40E+08
2003	1.06	1.08	1.07	2.97E+06
2004	1.06	1.00	1.12	2.48E+06
2005	1.09	1.02	1.07	1.91E+06
2006	1.01	1.39	1.08	2.27E+03
2007	0.11	0.15	0.11	1.03E+09
2008	0.11	0.15	0.12	1.49E+09
2009	0.11	0.14	0.10	7.14E+08
2010	1.00	1.16	1.15	1.41E+05
2011	1.00	1.18	1.18	9.53E+04
2012	1.04	1.06	1.04	1.96E+03
2013	1.04	1.05	1.05	4.57E+03
2014	0.95	1.18	1.18	6.58E+04
2015	0.98	1.04	1.00	9.04E+04
2016	1.01	1.17	0.93	1.18E+05
2017	1.05	0.91	1.32	1.27E+05
2018	1.12	1.15	0.99	1.63E+05
2019	1.00	1.15	1.02	5.09E+04
2020	0.83	0.67	0.74	1.33E+08
2021	1.05	1.05	1.04	8.08E+03
2022	1.04	1.12	1.05	1.60E+04
2023	1.03	1.06	0.96	2.05E+05
2024	0.11	0.10	0.09	2.00E+09
2025	0.11	0.10	0.10	9.29E+08
2026	0.26	0.42	0.41	8.12E+07
2027	0.12	0.13	0.10	2.18E+09
2028	0.12	0.10	0.09	5.25E+08
2029	1.12	1.06	0.98	8.97E+05
2030	0.12	0.11	0.10	4.29E+06
2031	0.11	0.15	0.20	3.22E+05
2032	0.12	0.11	0.09	8.40E+08
2033	0.10	0.10	0.09	8.34E+08
2034	0.11	0.10	0.09	9.17E+08
2035	0.11	0.09	0.09	1.02E+09
2036	0.12	0.10	0.09	1.25E+09
2037	0.11	0.10	0.09	8.85E+08
2038	0.23	0.57	0.26	8.38E+03
2039	0.24	0.57	0.37	1.71E+04

2040	0.23	0.38	0.56	2.20E+04
2041	0.12	0.10	0.10	7.90E+08
2042	0.13	0.29	0.56	2.60E+06
2043	0.10	0.15	0.25	1.51E+06
2044	0.26	0.15	0.31	1.54E+06
2045	0.11	0.71	0.38	1.85E+06
2046	0.11	0.19	0.34	3.69E+05
2047	0.13	0.16	0.29	5.60E+05
2048	0.17	0.91	0.73	5.59E+03
2049	0.21	0.13	0.33	5.39E+05
2050	0.12	0.16	0.28	6.97E+05
2051	0.19	0.52	0.48	2.43E+04
2052	0.10	0.10	0.10	5.51E+08
2053	0.12	0.12	0.11	2.63E+08
2054	0.16	0.13	0.11	2.25E+09
2055	0.10	0.10	0.10	1.79E+09
2056	0.12	0.09	0.10	1.24E+09
2057	0.28	0.53	0.54	1.38E+04
2058	0.25	0.69	0.65	2.17E+04
2059	0.14	0.10	0.10	1.94E+09
2060	0.98	0.88	0.97	1.62E+06
2061	1.00	0.69	0.93	2.51E+06
2062	1.03	0.39	1.01	3.04E+06
2063	1.25	0.96	0.99	8.85E+05
2064	0.25	0.12	0.13	1.21E+09
2065	0.90	0.35	0.95	2.52E+06
2066	0.96	0.19	1.12	1.77E+06
2067	0.93	1.48	1.42	5.81E+02
2068	1.05	1.02	1.07	1.34E+06
2069	0.92	0.95	1.15	1.63E+06
2070	0.11	0.13	0.16	6.71E+08
2071	1.21	1.40	1.07	2.29E+03
2072	0.12	0.12	0.11	8.04E+08
2073	1.07	0.94	1.13	1.32E+09
2074	0.16	0.22	0.51	7.06E+06
2075	0.79	0.40	0.51	3.07E+06
2076	0.11	0.09	0.10	2.65E+09
2077	0.11	0.19	0.41	7.24E+05
2078	1.01	0.39	1.05	4.00E+08

2079	1.04	1.06	1.09	2.89E+04
2080	1.02	1.02	1.11	6.69E+02
2081	1.01	1.15	1.58	5.28E+02
2082	1.02	1.05	1.11	5.89E+02
2083	0.89	**0.18**	0.99	**1.30E+09**
2084	1.02	0.49	1.04	**8.76E+08**
2085	0.95	1.11	0.98	4.66E+03
2086	1.17	**0.25**	0.99	**1.15E+09**
2087	1.16	1.13	1.09	9.13E+02
2088	**0.15**	**0.19**	**0.15**	**1.93E+09**
2089	1.06	1.15	1.08	1.55E+04
2090	**0.17**	**0.24**	**0.14**	**2.09E+09**
2091	0.49	**0.19**	0.68	**7.86E+08**
2092	**0.10**	**0.10**	**0.10**	**1.93E+09**
2093	**0.10**	0.42	0.54	5.39E+05
2094	**0.10**	0.43	0.64	6.93E+04
2095	**0.22**	**0.13**	**0.10**	**7.54E+08**
2096	**0.10**	**0.21**	**0.30**	2.01E+05
2097	**0.11**	**0.23**	**0.20**	**5.42E+06**
2098	**0.13**	**0.30**	**0.24**	1.89E+05
2099	**0.11**	**0.24**	0.41	1.80E+04
2100	0.99	1.13	1.06	9.19E+02
2101	1.04	1.05	1.06	2.03E+03
2102	1.01	1.09	1.03	7.52E+03
2103	0.98	1.26	1.07	1.80E+03
2104	1.03	1.02	1.06	2.07E+03
2105	1.02	1.09	1.02	8.50E+02
2106	1.01	1.19	1.03	**7.00E+06**
2107	1.03	1.34	1.02	1.20E+03
2108	1.01	1.09	0.98	7.31E+02
2109	1.04	1.15	1.06	1.35E+03
2110	1.06	0.99	1.05	1.23E+03
2111	1.12	0.99	1.05	4.33E+05
2112	1.05	1.09	1.01	9.46E+02
2113	**0.10**	**0.09**	**0.09**	**8.06E+08**
2114	1.06	0.94	1.02	3.13E+04
2115	1.08	0.99	0.94	9.25E+03
2116	1.04	1.01	1.05	1.23E+04
2117	1.04	0.78	1.03	3.64E+04

2118	1.05	1.00	1.02	1.31E+04
2119	1.08	0.48	0.72	2.41E+05
2120	1.05	0.48	0.78	1.13E+04
2121	1.03	0.62	1.04	6.97E+03
2122	1.10	0.39	1.05	7.79E+03
2123	0.11	0.09	0.10	1.19E+09
2124	0.11	0.09	0.10	1.84E+09
2125	0.10	0.10	0.09	1.04E+09
2126	0.22	0.50	0.66	1.52E+05
2127	1.08	1.05	1.08	1.40E+06
2128	0.10	0.10	0.09	9.27E+08
2129	0.10	0.10	0.09	9.59E+08
2130	0.10	0.10	0.09	1.10E+09
2131	0.10	0.10	0.09	8.76E+08
2132	1.03	1.21	1.01	8.98E+03
2133	0.12	0.12	0.10	7.24E+08
2134	1.16	1.07	1.10	4.11E+03
2135	0.18	0.33	0.32	6.59E+05
2136	0.10	0.09	0.09	1.73E+09
2137	0.10	0.09	0.09	1.13E+09
2138	1.00	1.16	0.99	2.04E+04
2139	0.12	0.09	0.10	7.09E+08
2140	1.08	0.85	1.02	8.74E+04
2141	0.18	0.19	0.72	2.03E+04
2142	1.02	0.88	1.01	1.19E+06
2143	1.03	0.54	1.02	2.61E+06
2164	0.11	0.11	0.09	3.17E+08
2165	0.11	0.11	0.09	3.67E+08
2166	1.12	0.56	1.04	2.34E+04
2167	0.15	0.13	0.10	9.74E+08
2148	0.10	0.12	0.10	2.01E+09
2149	1.01	1.06	1.12	9.57E+03
2150	1.11	1.09	1.06	8.18E+05
2151	1.04	1.07	1.05	8.33E+05
2152	0.14	0.09	0.10	6.38E+08
2153	1.05	0.85	1.06	1.12E+06
2154	1.09	0.98	1.09	1.31E+06
2155	1.10	0.50	1.12	9.99E+05
2156	0.13	0.11	0.09	9.04E+08

2157	0.10	0.37	0.17	7.10E+07
2158	0.12	0.10	0.10	6.65E+08
2159	1.23	0.87	1.10	1.01E+06
2160	0.14	0.12	0.13	6.33E+08
2161	0.17	0.15	0.11	3.43E+08
2162	0.12	0.12	0.11	6.64E+08
2163	0.16	0.10	0.12	1.23E+09
2144	0.96	1.09	1.13	8.40E+03
2145	1.16	0.55	1.17	1.41E+07
2146	0.13	0.11	0.11	1.48E+09
2147	0.16	0.15	0.17	1.08E+09
2168	0.14	0.09	0.11	7.92E+08
2169	0.14	0.11	0.12	1.49E+09
2170	0.13	0.10	0.11	2.46E+09
2171	0.11	0.09	0.11	1.83E+09
2172	0.11	0.10	0.24	1.23E+09
2173	0.11	0.10	0.11	1.68E+09
2174	0.11	0.09	0.10	1.48E+09
2175	1.05	1.04	1.08	1.44E+04
2176	1.08	0.97	1.03	1.51E+06
2177	0.91	1.30	1.02	1.31E+03

TABLE 26

NP #	LP124:nluc clearance	LP124:nluc RLU
1839	0.27	4.14E+08
1840	1.11	5.68E+02
1869	0.20	4.63E+08
1878	0.10	2.43E+08
1879	0.55	
1880	1.01	1.16E+06
1881	0.96	2.41E+06
1882	0.20	8.90E+05
1883	1.12	8.22E+02
1884	1.04	1.14E+04
1885	0.09	9.07E+08
1886	1.02	4.83E+02
1887	0.94	5.87E+05
1888	0.88	3.72E+06
1889	0.10	7.50E+08
1890	0.96	1.32E+03
1891	0.90	4.48E+02
1892	1.00	5.21E+02
1893	1.03	5.34E+02
1894	0.90	4.04E+02
1895	0.11	1.18E+09
1896	0.10	1.18E+09
1897	0.11	1.20E+09
1898	0.13	1.18E+09
1899	1.16	7.88E+02
1900	0.88	6.40E+02
1901	0.09	5.17E+08
1902	1.00	2.88E+06
1903	0.11	4.89E+08
1904	0.13	1.03E+08
1905	0.16	1.12E+09
1906	0.91	3.11E+06
1907	0.98	6.91E+02
1908	0.11	4.99E+08
1909	0.98	6.89E+02

1910	0.11	1.36E+09
1911	0.92	4.16E+05
1912	1.07	4.00E+02
1913	1.59	6.22E+02
1914	0.17	3.71E+08
1915	0.10	2.25E+08
1916	0.89	1.88E+04
1917	0.89	1.18E+06
1945	0.12	1.07E+09
1946	0.30	8.28E+04
1947	0.31	1.08E+05
1948	0.79	1.68E+04
1949	0.14	9.51E+08
1950	0.11	1.14E+09
1951	1.00	8.32E+02
1952	0.14	1.26E+09
1953	1.22	1.31E+08
1954	0.13	7.70E+08
1955	1.04	1.15E+08
1956	1.08	1.50E+06
1957	0.14	3.15E+07
1958	0.13	8.58E+08
1959	0.12	4.59E+08
1960	0.14	6.09E+08
1961	0.12	1.49E+08
1962	0.97	9.90E+02
1963	0.10	1.13E+09
1964	0.10	1.24E+09
1965	0.10	1.31E+09
1966	0.09	8.83E+08
1967	0.10	5.14E+08
1968	0.12	1.08E+09
1969	0.12	1.19E+09
1970	0.09	9.52E+08
1971	0.10	1.17E+09
1972	0.75	2.46E+06
1973	1.02	1.27E+03
1974	0.96	5.58E+02
1975	0.10	2.05E+09

1976	0.11	1.01E+09
1977	0.78	9.36E+08
1978	1.04	4.25E+03
1979	0.90	8.68E+02
1980	0.93	1.01E+06
1981	0.78	8.87E+02
1982	1.02	2.26E+04
1983	0.26	1.10E+05
1984	1.14	5.70E+05
1985	1.07	3.71E+05
1986	0.17	4.42E+08
1987	0.16	4.19E+08
1988	0.16	5.10E+08
1989	0.35	7.94E+03
1990	1.05	5.21E+02
1991	1.08	7.81E+02
1992	1.06	5.54E+02
1993	1.05	5.49E+02
1994	1.12	6.11E+02
1995	1.07	6.58E+02
1996	0.40	9.57E+08
1997	0.10	1.03E+09
1998	0.10	7.04E+08
1999	0.10	7.03E+08
2000	0.12	7.44E+08
2001	0.85	7.40E+08
2002	0.14	2.40E+08
2003	1.08	2.97E+06
2004	1.00	2.48E+06
2005	1.02	1.91E+06
2006	1.39	2.27E+03
2007	0.15	1.03E+09
2008	0.15	1.49E+09
2009	0.14	7.14E+08
2010	1.16	1.41E+05
2011	1.18	9.53E+04
2012	1.06	1.96E+03
2013	1.05	4.57E+03
2014	1.18	6.58E+04

2015	1.04	9.04E+04
2016	1.17	1.18E+05
2017	0.91	1.27E+05
2018	1.15	1.63E+05
2019	1.15	5.09E+04
2020	0.67	1.33E+08
2021	1.05	8.08E+03
2022	1.12	1.60E+04
2023	1.06	2.05E+05
2024	0.10	2.00E+09
2025	0.10	9.29E+08
2026	0.42	8.12E+07
2027	0.13	2.18E+09
2028	0.10	5.25E+08
2029	1.06	8.97E+05
2030	0.11	4.29E+06
2031	0.15	3.22E+05
2032	0.11	8.40E+08
2033	0.10	8.34E+08
2034	0.10	9.17E+08
2035	0.09	1.02E+09
2036	0.10	1.25E+09
2037	0.10	8.85E+08
2038	0.57	8.38E+03
2039	0.57	1.71E+04
2040	0.38	2.20E+04
2041	0.10	7.90E+08
2042	0.29	2.60E+06
2043	0.15	1.51E+06
2044	0.15	1.54E+06
2045	0.71	1.85E+06
2046	0.19	3.69E+05
2047	0.16	5.60E+05
2048	0.91	5.59E+03
2049	0.13	5.39E+05
2050	0.16	6.97E+05
2051	0.52	2.43E+04
2052	0.10	5.51E+08
2053	0.12	2.63E+08

2054	0.13	2.25E+09
2055	0.10	1.79E+09
2056	0.09	1.24E+09
2057	0.53	1.38E+04
2058	0.69	2.17E+04
2059	0.10	1.94E+09
2060	0.88	1.62E+06
2061	0.69	2.51E+06
2062	0.39	3.04E+06
2063	0.96	8.85E+05
2064	0.12	1.21E+09
2065	0.35	2.52E+06
2066	0.19	1.77E+06
2067	1.48	5.81E+02
2068	1.02	1.34E+06
2069	0.95	1.63E+06
2070	0.13	6.71E+08
2071	1.40	2.29E+03
2072	0.12	8.04E+08
2073	0.94	1.32E+09
2074	0.22	7.06E+06
2075	0.40	3.07E+06
2076	0.09	2.65E+09
2077	0.19	7.24E+05
2078	0.39	4.00E+08
2079	1.06	2.89E+04
2080	1.02	6.69E+02
2081	1.15	5.28E+02
2082	1.05	5.89E+02
2083	0.18	1.30E+09
2084	0.49	8.76E+08
2085	1.11	4.66E+03
2086	0.25	1.15E+09
2087	1.13	9.13E+02
2088	0.19	1.93E+09
2089	1.15	1.55E+04
2090	0.24	2.09E+09
2091	0.19	7.86E+08
2092	0.10	1.93E+09

2093	0.42	5.39E+05
2094	0.43	6.93E+04
2095	**0.13**	**7.54E+08**
2096	**0.21**	2.01E+05
2097	**0.23**	**5.42E+06**
2098	**0.30**	1.89E+05
2099	**0.24**	1.80E+04
2100	1.13	9.19E+02
2101	1.05	2.03E+03
2102	1.09	7.52E+03
2103	1.26	1.80E+03
2104	1.02	2.07E+03
2105	1.09	8.50E+02
2106	1.19	**7.00E+06**
2107	1.34	1.20E+03
2108	1.09	7.31E+02
2109	1.15	1.35E+03
2110	0.99	1.23E+03
2111	0.99	4.33E+05
2112	1.09	9.46E+02
2113	**0.09**	**8.06E+08**
2114	0.94	3.13E+04
2115	0.99	9.25E+03
2116	1.01	1.23E+04
2117	0.78	3.64E+04
2118	1.00	1.31E+04
2119	0.48	2.41E+05
2120	0.48	1.13E+04
2121	0.62	6.97E+03
2122	**0.39**	7.79E+03
2123	**0.09**	**1.19E+09**
2124	**0.09**	**1.84E+09**
2125	**0.10**	**1.04E+09**
2126	0.50	1.52E+05
2127	1.05	**1.40E+06**
2128	**0.10**	**9.27E+08**
2129	**0.10**	**9.59E+08**
2130	**0.10**	**1.10E+09**
2131	**0.10**	**8.76E+08**

2132	1.21	8.98E+03
2133	0.12	7.24E+08
2134	1.07	4.11E+03
2135	0.33	6.59E+05
2136	0.09	1.73E+09
2137	0.09	1.13E+09
2138	1.16	2.04E+04
2139	0.09	7.09E+08
2140	0.85	8.74E+04
2141	0.19	2.03E+04
2142	0.88	1.19E+06
2143	0.54	2.61E+06
2164	0.11	3.17E+08
2165	0.11	3.67E+08
2166	0.56	2.34E+04
2167	0.13	9.74E+08
2148	0.12	2.01E+09
2149	1.06	9.57E+03
2150	1.09	8.18E+05
2151	1.07	8.33E+05
2152	0.09	6.38E+08
2153	0.85	1.12E+06
2154	0.98	1.31E+06
2155	0.50	9.99E+05
2156	0.11	9.04E+08
2157	0.37	7.10E+07
2158	0.10	6.65E+08
2159	0.87	1.01E+06
2160	0.12	6.33E+08
2161	0.15	3.43E+08
2162	0.12	6.64E+08
2163	0.10	1.23E+09
2144	1.09	8.40E+03
2145	0.55	1.41E+07
2146	0.11	1.48E+09
2147	0.15	1.08E+09
2168	0.09	7.92E+08
2169	0.11	1.49E+09
2170	0.10	2.46E+09

2171	0.09	1.83E+09
2172	0.10	1.23E+09
2173	0.10	1.68E+09
2174	0.09	1.48E+09
2175	1.04	1.44E+04
2176	0.97	1.51E+06
2177	1.30	1.31E+03
2178	0.85	3.67E+04

TABLE 27

Species	Growth Medium	Growth Temperature	10^5 negative cfu	10^1 Listeria/10^5 negative cfu
Bacillus cereus	Nutrient Broth	30C	53	3756
Bacillus megaterium	Nutrient Broth	30C	74	4814
Bacillus subtilis	Nutrient Broth	30C	56	1982
Enterococcus durans	Brain Heart Infusion	37C	57	3507
Enterococcus faceium	Brain Heart Infusion	37C	55	8735
Enterococcus hirae	Brain Heart Infusion	37C	57	6145
Kocuria varians	Nutrient Broth	30C	52	6283
Kurthia gibsonii	Brain Heart Infusion	30C	44	4420
Kurthia zopfii	Nutrient Broth	26C	54	7226
Rhodococcus equi	Brain Heart Infusion	37C	61	4367
Staphylococcus aureus	Tryptic Soy Broth	37C	55	3575
Staphylococcus epidermidis	Tryptic Soy Broth	37C	51	4544
Staphylococcus saprophyticus	Nutrient Broth	37C	59	4434
Streptococcus equi	Brain Heart Infusion	37C	63	3368
Streptococcus galloyticus	Brain Heart Infusion	37C	64	5287
Lactobacillus casei	MRS	37C, 5% CO_2	59	5320
Lactobacillus buchneri	MRS	37C, 5% CO_3	53	6331
Lactobacillus lactus	MRS	37C, 5% CO_4	67	5065
Lactobacillus fermentum	MRS	37C, 5% CO_5	67	4318
Micrococcus lutues	Tryptic Soy Broth	30C	79	3322

TABLE 28

Sample #	Species	10^5 negative cfu	10^1 Listeria/10^5 negative cfu
2501-1	*Pseudomonas protogens*	253	3513
250-2	*Pseudomonas florescens*	285	1737
251(2)-1	*Pseudomonas florescens*	236	2903
251(2)-2	*Aeromonas* sp	240	1790
261(1)-1	*Serratia liquefaciens*	318	6165
261(1)-2	*Serratia proteamaculans*	260	4614
261(2)-1	*Serratia liquefaciens*	296	2421
261(2)-2	*Bacillaceae* bacterium	320	5289
289-1	*Serratia proteamaculans*	273	3487
289-2	*Pseudomonas florescens*	279	5161
289-3	*Pseudomonas poae*	241	1922
290(1)-1	*Pseudomonas* sp	241	1965
290(1)-2	*Pseudomonas* sp	271	2178
290(2)-1	*Pseudomonas fragi*	223	3052
290(3)-1	*Pseudomonas* sp	272	2560
291(1)-1	*Providencia alcalifaciens*	262	4963
291(1)-2	*Serratia* sp	272	3827
291(2)-1	*Serratia grimesii*	240	3302
291(2)-2	*Serratia* sp	213	3086
291-1	*Serratia* sp	270	2430
293-1	*Serratia* sp, *Hafnia* sp.	243	2989
293-2	*Serratia proteamaculans*	259	3254
296-4	*Serratia proteamaculans*	304	2314
304-1	*Pseudomonas florescens*	272	2639
304-2	*Chryseobacterium* sp.	269	2911
306-1	*Pseudomonas fragi*	266	3212
306-2	*Enterobacteriaceae*	273	4358

TABLE 29

NP #	A511: nluc	LP124:nluc	LP124/A511 RLU output
1997	5.13E+05	**1.03E+09**	2.01E+03
1998	4.47E+05	**7.04E+08**	1.58E+03
1999	4.15E+05	**7.03E+08**	1.69E+03
2000	4.60E+05	**7.44E+08**	1.62E+03
2001	3.76E+05	**7.40E+08**	1.97E+03
2002	4.39E+05	**2.40E+08**	5.47E+02
2003	1.25E+02	**2.97E+06**	2.38E+04
2004	1.69E+02	**2.48E+06**	1.47E+04
2005	8.90E+01	**1.91E+06**	2.15E+04
2006	1.90E+01	2.27E+03	1.20E+02
2007	**4.55E+06**	**1.03E+09**	2.27E+02

2008	**4.69E+06**	**1.49E+09**	3.18E+02
2009	**8.22E+06**	**7.14E+08**	8.68E+01
2010	5.70E+01	1.41E+05	2.48E+03
2011	1.20E+01	9.53E+04	7.94E+03
2012	1.50E+01	1.96E+03	1.31E+02
2013	1.20E+01	4.57E+03	3.81E+02
2014	9.00E+00	6.58E+04	7.31E+03
1869	**6.15E+06**	**4.63E+08**	7.52E+01
1840	4.20E+01	5.68E+02	1.35E+01
1839	**4.84E+06**	**4.14E+08**	8.54E+01
2024	**7.74E+06**	**2.00E+09**	2.58E+02
2025	**2.50E+06**	**9.29E+08**	3.71E+02
2026	9.99E+05	**8.12E+07**	8.13E+01
2027	**1.74E+06**	**2.18E+09**	1.25E+03
2028	**5.89E+06**	**5.25E+08**	8.91E+01
2029	3.46E+02	8.97E+05	2.59E+03
2030	**9.18E+06**	**4.29E+06**	4.68E-01
2031	3.36E+03	3.22E+05	9.57E+01
2032	**5.53E+06**	**8.40E+08**	1.52E+02
2033	**5.22E+06**	**8.34E+08**	1.60E+02
2034	**4.50E+06**	**9.17E+08**	2.04E+02
2035	**3.66E+06**	**1.02E+09**	2.78E+02
2036	**6.27E+06**	**1.25E+09**	2.00E+02
2037	**3.65E+06**	**8.85E+08**	2.42E+02
2038	4.60E+01	8.38E+03	1.82E+02
2039	3.10E+01	1.71E+04	5.50E+02
2040	4.40E+01	2.20E+04	4.99E+02
2041	**6.25E+06**	**7.90E+08**	1.26E+02
2042	1.38E+03	**2.60E+06**	1.89E+03
2043	3.65E+02	**1.51E+06**	4.13E+03
2044	7.03E+02	**1.54E+06**	2.19E+03
2045	4.52E+02	**1.85E+06**	4.10E+03
2046	7.35E+02	3.69E+05	5.02E+02
2047	2.18E+02	5.60E+05	2.57E+03
2048	2.01E+02	5.59E+03	2.78E+01
2049	3.10E+02	5.39E+05	1.74E+03
2050	5.27E+02	6.97E+05	1.32E+03
2051	7.00E+00	2.43E+04	3.47E+03
2052	**8.15E+06**	**5.51E+08**	6.76E+01

2053	**6.19E+06**	**2.63E+08**	4.25E+01
2054	**2.47E+06**	**2.25E+09**	9.13E+02
2055	**1.06E+07**	**1.79E+09**	1.69E+02
2056	**3.54E+06**	**1.24E+09**	3.52E+02
2057	4.40E+01	1.38E+04	3.14E+02
2058	8.00E+00	2.17E+04	2.72E+03
2059	**8.19E+06**	**1.94E+09**	2.37E+02
2060	1.13E+03	**1.62E+06**	1.43E+03
2061	1.20E+03	**2.51E+06**	2.08E+03
2062	8.02E+02	**3.04E+06**	3.79E+03
2063	1.49E+03	8.85E+05	5.96E+02
2064	1.02E+04	**1.21E+09**	1.19E+05
2065	1.01E+03	**2.52E+06**	2.50E+03
1973	4.40E+01	1.27E+03	2.88E+01
1974	9.00E+00	5.58E+02	6.20E+01
1975	1.40E+01	**2.05E+09**	1.47E+08
1976	**1.16E+07**	**1.01E+09**	8.72E+01
1990	1.40E+01	5.21E+02	3.72E+01
1991	6.00E+00	7.81E+02	1.30E+02
1992	1.00E+01	5.54E+02	5.54E+01
1993	8.00E+00	5.49E+02	6.86E+01
1994	9.00E+00	6.11E+02	6.79E+01
1995	8.00E+00	6.58E+02	8.23E+01
1996	**5.07E+06**	**9.57E+08**	1.89E+02
1977	**6.55E+06**	**9.36E+08**	1.43E+02
1978	2.00E+01	4.25E+03	2.12E+02
1979	8.00E+00	8.68E+02	1.09E+02
1980	1.45E+03	**1.01E+06**	7.00E+02
1981	1.00E+01	8.87E+02	8.87E+01
1982	3.30E+01	2.26E+04	6.85E+02
1983	1.47E+03	1.10E+05	7.52E+01
1984	2.07E+02	5.70E+05	2.75E+03
1985	5.78E+02	3.71E+05	6.42E+02
1986	**1.27E+06**	**4.42E+08**	3.49E+02
1987	**1.13E+06**	**4.19E+08**	3.72E+02
1988	**1.32E+06**	**5.10E+08**	3.87E+02
1989	5.02E+02	7.94E+03	1.58E+01
2015	1.00E+02	9.04E+04	9.04E+02
2016	1.49E+02	1.18E+05	7.90E+02

2017	1.18E+02	1.27E+05	1.08E+03
2018	1.34E+02	1.63E+05	1.22E+03
2019	1.46E+02	5.09E+04	3.48E+02
2020	1.40E+02	**1.33E+08**	9.48E+05
2021	8.20E+01	8.08E+03	9.86E+01
2022	3.60E+01	1.60E+04	4.45E+02
2023	4.40E+01	2.05E+05	4.67E+03

TABLE 30

Sample #	A511/P100 cocktail RLU	A511/P100/LP124 cocktail RLU	Signal Ratio of 3-phage/2-phage
398	1164	2212	1.9
399	11459	27183	2.4
401	2100	3058	1.5
402	113103	217389	1.9
403	46219	58768	1.3
405	9988	24151	2.4
407	2732	5329	2.0
426	64717	444121	6.9
427	75896	613358	8.1

TABLE 31

NP #	A511/LP124 Clearance	A511/LP124 RLU
2180	0.51	**9425355**
2181	0.91	**4829460**
2182	0.97	**22478532**
2183	**0.21**	**1178748672**
2184	0.95	8949
2185	1.08	3540
2186	0.93	**13285696**
2187	0.87	**1446053376**
2188	**0.11**	**1317144704**
2189	**0.15**	**1227835136**

2190	0.60	11299
2191	**0.09**	**1444555264**
2192	0.69	5535
2193	0.75	**1314372736**
2194	0.95	33425
2195	0.63	**483384224**
2196	**0.11**	**1402767616**
2197	0.97	**12005105**
2198	1.00	**4624066**
2199	1.05	**13923259**
2201	1.04	**17701700**
2200	1.09	**13959437**
2202	1.01	**18058374**
2203	1.19	**15579639**
2204	0.93	1058
2217	1.08	738479
2218	0.60	**3828983**
2222	0.89	3141
2234	1.47	111
2235	1.00	553
2236	1.18	1656
2237	**0.12**	624961
2238	0.56	25193
2239	0.97	39008
2242	0.96	152481
2243	0.97	1249
2244	**0.10**	**1478536320**
2246	0.93	12594
2248	0.43	**36580156**
2249	**0.17**	**43955716**
2250	0.60	236283
2251	1.02	1681
2253	1.05	**31609824**

2254	0.98	1130
2256	0.98	30291
2257	1.06	134811
2258	1.00	1072
2260	**0.17**	**38230508**
2262	1.03	6718
2263	0.67	**152658896**
2265	0.89	1923
2267	0.92	**86490696**
2269	**0.15**	**239873472**
2270	**0.13**	**1182304128**
2271	0.98	**9737881**
2272	**0.34**	**28609152**
2275	0.91	**22955124**
2278	**0.16**	**36394420**
2281	1.17	**8376739**
2282	**0.13**	**187224464**
2283	0.79	**4552574**
2284	**0.33**	**400019616**
2287	**0.12**	**334971200**
2290	**0.14**	**83818688**
2291	0.45	**11715284**
2293	1.05	457
2295	0.97	45340
2296	0.91	13112
2298	0.66	153830
2299	1.01	586
2301	1.13	567
2302	0.56	**3343962**
2303	**0.37**	**3420569**
2305	**0.15**	**331570720**
2306	1.12	1588
2307	1.10	12765

2308	1.10	4390
2309	1.17	6388
2310	1.20	3387
2311	1.06	**33898140**
2312	**0.19**	**19504462**
2313	1.12	1712
2314	1.04	6168
2316	**0.11**	**71091864**
2318	**0.11**	**33768470**4
2319	**0.11**	**47667123**2
2320	0.99	5048
2321	1.02	4614
2323	0.60	**10705072**
2325	0.79	**10092227**
2327	0.90	**17542488**0
2330	1.07	**23623790**4
2331	0.92	**3027250**
2333	1.06	19965
2334	1.03	11160
2335	**0.13**	**8174093**
2336	0.61	**38853036**
2337	0.75	**17568558**
2340	**0.16**	**92967936**
2341	0.69	**11054598**

INFORMAL SEQUENCE LISTING

SEQ ID NO: 1 - FF luc open reading frame
ATGGAAGACGCCAAAAACATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGA
GCAACTGCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACATATCG
AGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGCTATGAAACGATATGGG
CTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCTTCAATTCTTTATGCCGGTGTTGGGCGC
GTTATTTATCGGAGTTGCAGTTGCGCCCGCGAACGACATTTATAATGAACGTGAATTGCTCAACAGTATGA
ACATTTCGCAGCCTACCGTAGTGTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAA
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GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTTTGATCGTGACA
AAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAAGGGTGTGGCCCTTCCGCATAGA
ACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTATTTTTGGCAATCAAATCATTCCGGATACTGCGAT
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GAGTCGTCTTAATGTATAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGT
GCGTTGCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTTATCTAA
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GATGATAAACCGGGCGCGGTCGGTAAAGTTGTTCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGG
GAAAACGCTGGGCGTTAATCAGAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAA
ACAATCCGGAAGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTGG
GACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGGATATCAGGTGGC
CCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGACGCGGGCGTGGCAGGTCTTCCCG
ACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGTTTTGGAGCACGGAAAGACGATGACGGAAAAAGAG
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AGTACCGAAAGGTCTTACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGG
GCGGAAAGTCCAAATTGTAA

SEQ ID NO: 2 - FF luc amino acid sequence

MEDAKNIKKGPAPFYPLEDGTAGEQLHKAMKRYALVPGTIAFTDAHIEVNITYAEYFEMSVRLAEAMKRYG
LNTNHRIVVCSENSLQFFMPVLGALFIGVAVAPANDIYNERELLNSMNISQPTVVFVSKKGLQKILNVQKK
LPIIQKIIIMDSKTDYQGFQSMYTFVTSHLPPGFNEYDFVPESFDRDKTIALIMNSSGSTGLPKGVALPHR
TACVRFSHARDPIFGNQIIPDTAILSVVPFHHGFGMFTTLGYLICGFRVVLMYRFEEELFLRSLQDYKIQS
ALLVPTLFSFFAKSTLIDKYDLSNLHEIASGGAPLSKEVGEAVAKRFHLPGIRQGYGLTETTSAILITPEG
DDKPGAVGKVVPFFEAKVVDLDTGKTLGVNQRGELCVRGPMIMSGYVNNPEATNALIDKDGWLHSGDIAYW
DEDEHFFIVDRLKSLIKYKGYQVAPAELESILLQHPNIFDAGVAGLPDDDAGELPAAVVVLEHGKTMTEKE
IVDYVASQVTTAKKLRGGVVFVDEVPKGLTGKLDARKIREILIKAKKGGKSKL

SEQ ID NO: 3 - Nano luc open reading frame

ATGGTCTTCACACTCGAAGATTTCGTTGGGGACTGGCGACAGACAGCCGGCTACAACCTGGACCAAGTCCT
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TGAGCGGTGAAAATGGGCTGAAGATCGACATCCATGTCATCATCCCGTATGAAGGTCTGAGCGGCGACCAA
ATGGGCCAGATCGAAAAAATTTTTAAGGTGGTGTACCCTGTGGATGATCATCACTTTAAGGTGATCCTGCA
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CGCCTGATCAACCCCGACGGCTCCCTGCTGTTCCGAGTAACCATCAACGGAGTGACCGGCTGGCGGCTGTG
CGAACGCATTCTGGCGTAA

SEQ ID NO: 4 - Nano luc amino acid sequence

MVFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQNLGVSVTPIQRIVLSGENGLKIDIHVIIPYEGLSGDQ
MGQIEKIFKVVYPVDDHHFKVILHYGTLVIDGVTPNMIDYFGRPYEGIAVFDGKKITVTGTLWNGNKIIDE
RLINPDGSLLFRVTINGVTGWRLCERILA

SEQ ID NO: 5 - LP040 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGATGCGTTAAA
GTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGGGCACTAAGACGTGAGTTCC
TAGACGACCAAATCTCAATGCTTACTTGGACAGAAAATGATTTAACATTCTACAAAGACATCGCTAAAAAA
CCAGCTACATCTACAGTAGCAAAATACGATGTGTACATGCAACACGGTAAAGTAGGTCATACTAGATTTAC
TCGTGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTT
CTGATACTAAAAATATTAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCTATGCAAATTTTGACT
GATGATGCTATCGTAAATATCGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGA
TAGCCCAGAACCACAAGCAGGATTAGAATTTGATGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATG
ATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGT
ACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAAC
ACAACTTGTTCGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTG
GATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTA
CCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGG

CTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCT
CGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACC
TGCTAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACG
TATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTA
GCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAA
ATGGGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 6 - LP40 Cps protein

MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKK
PATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILT
DDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYG
TPTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILAL
PTAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSS
RPQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPL
AQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 7 - LP48 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGACGCGTTAAA
GTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCC
TAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAA
CCAGCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTAC
TCGTGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTT
CCGATACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACT
GACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGA
TAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATG
ATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGT
ACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAAC
ACAACTTGTTCGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTG
GATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTA
CCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGG
CTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCT
CGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACC
TGCTAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACG
TATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTA
GCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAA
ATGGGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 8 - LP48 protein

MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKK
PATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILT
DDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYG
TPTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILAL
PTAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSS
RPQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPL
AQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 9 - LP099 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGACGCGTTAAA
GTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCC
TAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAA
CCAGCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTAC
TCGTGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTT
CCGATACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACT
GACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGA
TAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATG
ATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGT
ACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAAC

ACAACTTGTTCGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTG
GATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTA
CCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGG
CTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCT
CGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACC
TGCTAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACG
TATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTA
GCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAA
ATGGGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 10 - LP099 Cps protein

MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKK
PATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILT
DDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYG
TPTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILAL
PTAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSS
RPQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPL
AQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 11 - LP101 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGACGCGTTAAA
GTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCC
TAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAA
CCAGCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTAC
TCGTGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTT
CCGATACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACT
GACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGA
TAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATG
ATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGT
ACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAAC
ACAACTTGTTCGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTG
GATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTA
CCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGG
CTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCT
CGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACC
TGCTAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACG
TATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTA
GCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAA
ATGGGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 12 - LP101 Cps protein

MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKK
PATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILT
DDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYG
TPTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILAL
PTAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSS
RPQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPL
AQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 13 - LP124 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGACGCGTTAAA
GTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCC
TAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAA
CCAGCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTAC
TCGTGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTT
CCGATACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACT

GACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGA
TAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATG
ATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGT
ACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAAC
ACAACTTGTTCGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTG
GATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTA
CCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGG
CTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCT
CGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACC
TGCTAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACG
TATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTA
GCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAA
ATGGGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 14 - LP124 Cps protein

MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKK
PATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILT
DDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYG
TPTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILAL
PTAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSS
RPQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPL
AQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 15 - LP125 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGACGCGTTAAA
GTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCC
TAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAA
CCAGCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTAC
TCGTGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTT
CCGATACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACT
GACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGA
TAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATG
ATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGT
ACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAAC
ACAACTTGTTCGTGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTG
GATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTA
CCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGG
CTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCT
CGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACC
TGCTAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACG
TATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTA
GCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAA
ATGGGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 16 - LP125 Cps protein

MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKK
PATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILT
DDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYG
TPTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILAL
PTAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSS
RPQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPL
AQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 17 - LP143 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGATGCGTTAAAGTC
CTTTACGACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCCTAG

ACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAACCA
GCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCG
TGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCG
ATACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACTGAC
GATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGATAG
CCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATGATG
CTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACA
CCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACA
ACTTGTTCGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTGGAT
TTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTACCA
ACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGAAGA
TTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTA
CAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGT
CCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGC
TAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACGTAT
TCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTAGCT
CAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAAATG
GGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 18 - LP143 Cps protein

MPKNNKEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKKP
ATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILTD
DAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYGT
PTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALP
TAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSR
PQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPLA
QINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 19 - A511 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGATGCGTTAAAGTC
CTTTACGACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCCTAG
ACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAACCA
GCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCG
TGAGATTGGGGTAGCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCG
ATACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACTGAC
GATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCAGATAG
CCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAGATAACGTTCATGATG
CTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACA
CCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACA
ACTTGTTCGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTGGAT
TTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTACCA
ACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGAAGA
TTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTA
CAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGT
CCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGC
TAGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACAGTAGACGTAT
TCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTAGCT
CAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAAATG
GGTACGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA

SEQ ID NO: 20 - A511 Cps protein

MPKNNKEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTENDLTFYKDIAKKP
ATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASDTKNISIAAGLVNNIQDPMQILTD
DAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLAKLINQDNVHDARGASLTESLLNQAAVMISKGYGT
PTDAYMPVGVQADFVNQQLSKQTQLVRDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALP
TAPQPAKVTATQEAGKKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSR
PQFVSIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLPMMRLPLA
QINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN

SEQ ID NO: 21 - P100 Cps open reading frame

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGACGCGTTAAA
GTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGCATTAAGACGTGAGTTCC
TAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAACATTCTATAAAGACATCGCTAAAAAA
CCAGCTACATCTACAGTAGCAAAATACGATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTAC
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SEQ ID NO: 22 – P100 Cps protein

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SEQ ID NO: 24 – LP99::ffluc

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SEQ ID NO: 25 – LP101::ffluc

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SEQ ID NO: 26 – LP124::ffluc

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SEQ ID NO: 33 – A511::nluc

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SEQ ID NO: 34 – P100::nluc

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SEQ ID NO: 35 – LP40::nluc

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SEQ ID NO: 36 – COP2 NanoLuc

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SEQ ID NO: 37—W40_VIP_MLi178 (COP3)

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SEQ ID NO: 38 - A511::COP2

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SEQ ID NO: 39 - LP124::COP2

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SEQ ID NO: 40 - LP40::COP2

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SEQ ID NO: 41 – COP2 NanoLuc

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SEQ ID NO: 42--A511::COP3

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SEQ ID NO: 43--LP124::COP3

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SEQ ID NO: 44 - LP40::COP3

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SEQ ID NO: 45 UTR1 (original)

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SEQ ID NO: 46 UTR2

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SEQ ID NO: 50 UTR6
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SEQ ID NO: 54 – Ribosome binding site
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SEQ ID NO: 55 - pMAK upf
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SEQ ID NO: 56 - dbono380
ATATTTACCTCCTCTTATTATTAGTTGCTATGAACGTTTTTTACAGG
SEQ ID NO: 57 - SO472
ATAAGAGGAGGTAAATATATATGGTATTCACATTAGAAGATTTTG
SEQ ID NO: 58 - SO473
ATTCAATTATCCTATAATTATTATGCTAGAATACGTTCACATAA
SEQ ID NO: 59 - SO474

GTGAACGTATTCTAGCATAATAATTATAGGATAATTGAATAAAAAC
SEQ ID NO: 60 - dbono382
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SEQ ID NO: 66 – SO672
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EQUIVALENTS

[00505] The details of one or more embodiments of the invention are set forth in the accompanying description above. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described. Other features, objects, and advantages of the invention will be apparent from the description and from the claims. In the specification and the appended claims, the singular forms include plural referents unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. All patents and publications cited in this specification are incorporated by reference.

[00506] The foregoing description has been presented only for the purposes of illustration and is not intended to limit the invention to the precise form disclosed, but by the claims appended hereto.

WHAT IS CLAIMED IS:

1. A composition comprising at least one recombinant phage capable of infecting a target microbe, said phage comprising at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker.

2. The composition of claim 1, further comprising at least two, three, four, five, or six recombinant phages capable of infecting a target microbe, each of said phage comprising at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker,.

3. The composition of claim 1, further comprising greater than six recombinant phage capable of infecting a target microbe, each of said phage comprising at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker.

4. The composition of any one of claims 1, 2, or 3 wherein the ribosome binding site of each phage is identical.

5. The composition of any one of claims 1, 2, or 3 wherein the ribosome binding site of each phage is SEQ ID NO: 54

6. The composition of any one of claims 1, 2, or 3, wherein the codon-optimized marker is a codon-optimized luciferase.

7. The composition of any one of claims 1-6, wherein the codon-optimized marker is SEQ ID NO: 36 (COP2).

8. The composition of any one of claims 1-6, wherein the codon-optimized marker is SEQ ID NO: 37 (COP3).

9. The composition of any one of claims 1-3, wherein at least one recombinant phage is selected from the group consisting of LP143, A511, LP101, LP124, LP99, LP48, LP125, P100, and LP40.

10. The composition of any one of claims 1-3, wherein at least one recombinant phage is A511, LP40 or LP124.

11. The composition of any one of claims 1-3, wherein the composition comprises A511, LP40 and LP124.

12. The composition of any one of claims 1-3, wherein the phage is A511.

13. The composition of any one of claims 1-3, wherein the phage is LP40.

14. The composition of any one of claims 1-3, wherein the phage is LP124.

15. The composition of claim 1, wherein the target microbe is selected from the group consisting of *coliform bacteria*, *Escherichia*, *Shigella*, *Listeria*, *Clostridium*, *Vibrio*, *Enterobacteriacae*, *Cronobacter*, *Mycobacterium*, *Staphylococcus*, *Bacillus*, *Campylobacter*, *Pseudomonas*, *Streptococcus*, *Acinetobacter*, *Klebsiella*, *Campylobacter*, and *Yersinia*.

16. The composition of claim 1, wherein the target microbe belongs to the genus *Listeria*.

17. The composition of claim 16, wherein the target microbe is *Listeria* selected from the group consisting of *Listeria innocua*, *Listeria monocytogenes*, *Listeria seeligeri*, *Listeria ivanovii, Listeria grayi, Listeria marthii, Listeria rocourti*, *Listeria welshimeri*, *Listeria floridensis, Listeria aquatic, Listeria cornellensis, Listeria riparia, Listeria weihenstephanensis, Listeria flieschmannii,* and *Listeria grandensis.*

18. The composition of claim 17, wherein the target microbe is *Listeria monocytogenes*.

19. The composition of any one of the preceding claims further comprising an aqueous solution, wherein the aqueous solution comprises:

a) at least one nutrient;

b) at least one selective agent suitable to inhibit growth of at least one non-target microbe in an environmental sample or an agricultural sample;

c) at least one vitamin;

d) at least one divalent metal;

e) at least one buffering agent capable of maintaining the composition at pH 7.0-7.5.

20. The composition of claim 19, further comprising at least one agent to prevent the decomposition of a marker substrate.

21. The composition of claim 20, wherein the at least one agent to prevent decomposition of a marker substrate comprises a compound to prevent the decomposition of luciferin.

22. The composition of claim 21, wherein the compound prevents decomposition of luciferin for between 5 and 10 hours.

23. The composition of claim 22, wherein the compound prevents decomposition of luciferin for less than 5 hours.

24. The composition of claim 23, wherein the compound prevents decomposition of luciferin for greater than 10 hours.

25. The composition of claim 21, wherein the at least one agent to prevent decomposition of the luciferin is selected from the group consisting of non-ionic detergents, oxygen scavengers and emulsifiers.

26. The composition of claim 25, wherein the at least one agent to prevent the decomposition of luciferin is selected from the group consisting of sodium metabisulfite, sodium thiosulfate, Tween-80, HEPES and lecithin.

27. The composition of claim 19, further comprising at least one agent suitable to neutralize a sanitizer present in an environmental sample.

28. The composition of claim 27, wherein the at least one agent suitable to neutralize a sanitizer is selected from the group consisting of sodium metabisulfite, sodium thiosulfate, Tween-80, HEPES and lecithin.

29. The composition of claim 19, wherein the at least one nutrient is selected from a culture medium, alcohol, sugar, sugar derivatives, and combinations thereof.

30. The composition of claim 29, wherein the at least one nutrient is selected from Brain Heart Infusion medium, Tryptic Soy Broth, glucose, glycerol, pyruvate, and combinations thereof.

31. The composition of claim 19, wherein the at least one selective agent suitable to inhibit growth of a non-target microbe is selected from LiCl, acriflavine, nalidixic acid, cycloheximide, and combinations thereof.

32. The composition of claim 19, wherein the at least one vitamin comprises yeast extract.

33. The composition of claim 19, wherein the at least one divalent metal is selected from $CaCl_2$, MgSO4, and combinations thereof.

34. The composition of claim 19, wherein the at least one buffering agent comprises HEPES buffer.

35. The composition of claim 19, wherein the aqueous solution comprises or consists of Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, and HEPES.

36. The composition of claim 19, wherein the aqueous solution comprises or consists of Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, HEPES, Tween-80, lecithin, and potassium phosphate.

37. The composition of any one of claim 1-3, further comprising a substrate for luciferase.

38. The composition of claim 37, wherein the substrate is luciferin.

39. The composition of any one of claims 1-3, further comprising a buffer to facilitate a light reaction.

40. A method of determining the presence or absence of a target microbe in an environmental sample, an agricultural sample or both, comprising:
a) contacting an environmental sample, an agricultural sample, or both with a composition of any one of claims 1-39 to form a test sample; and
b) detecting the presence or absence of light thereby determining the presence or absence of a target microbe in an environmental sample or an agricultural sample.

41. The method of claim 40, wherein the environmental sample is selected from the group consisting of an agricultural production facility, a food production facility, a container, a machine, a processing plant, a storage facility, a health care facility, an educational institution, a loading dock, a cargo hold, a sink, a vehicle, an airport, and a customs facility.

42. The method of claim 41, wherein the environmental sample is from a health care facility.

43. The method of claim 42, wherein the health care facility is a clinic, an emergency medical services location, a hospice, a hospital ship, a hospital train, a hospital, a military medical installation, a doctor's office, a long term care facility, respite care facility, or a quarantine station.

44. The method of claim 40, wherein the environmental sample is from a food production facility.

45. The method of claim 44, wherein the food production facility is a farm, a boat, a food distribution facility, a food processing plant, a food retail location, a home, or a restaurant.

46. The method of claim 40, wherein the agricultural sample is stock feed or food supply.

47. The method of 46, wherein the food supply is for human or non-human consumption.

48. The method of 47, wherein the food supply is plant or animal.

49. The method of 48, wherein the food supply is a dairy product, a fruit product, a grain product, a sweet, a vegetable product, a meat product, or a combination thereof.

50. The method of 49, wherein the dairy product is milk, butter, yogurt, cheese, ice cream, queso fresco, a derivative thereof or a combinations thereof.

51. The method of 49, wherein the fruit product is an apple, orange, banana, berry, lemon, or a combination thereof.

52. The method of 49, wherein the grain product is wheat, rice, oats, barley, bread, pasta, or a combination thereof.

53. The method of 49, wherein the sweet product is candy, soft drinks, cake, pie, or a combination thereof.

54. The method of 49, wherein the vegetable product is spinach, carrots, onions, peppers, avocado, broccoli, or a combination thereof.

55. The method of claim 54, wherein the vegetable product is guacamole.

56. The method of claim 49, wherein the meat product is chicken, fish, turkey, pork, beef, or a combination thereof.

57. The method of claim 56, wherein the meat product is whole muscle meat, ground meat, or a combination thereof.

58. The method of claim 56, wherein the meat product is selected from deli turkey, ground beef, or a combination thereof.

59. The method of any one of claims 49-58, wherein the food supply is a liquid or a solid.

60. A kit comprising a composition of any one of claims 1-39.

61. A kit comprising: a first container comprising at least one recombinant phage capable of infecting a target microbe, said phage comprising at least a capsid protein sequence, a ribosome binding site, and a codon-optimized marker; a second container comprising a aqueous solution composition comprising Tryptic Soy Broth, LiCl, nalidixic acid, yeast extract, glucose, $MgSO_4$, pyruvate, HEPES, Tween-80, lecithin, and potassium phosphate; a third container containing a substrate; and a fourth container containing a buffer to optimize light detection.

62. The kit of claim 60 or 61, further comprising a swab.

63. The kit of any one of claims 60-62, further comprising a container for facilitating detection of light.

FIGURE 1

A511::COP2

ATGCCAAAAAATAACAAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAGGAT
GCGTTAAAGTCCTTTACGACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGGAGC
ATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATTTAA
CATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATACGATGTATA
CATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTAGCACCAGTA
AGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCGATACTAAAAACAT
CAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACTGACGAT
GCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTTATCA
GATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAACCAAG
ATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGCAGTA
ATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAGCAG
ACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTTCGCGATAACGGAAACAACGTA
AGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTGGATTTATCAAACTTCACGGTTCT
ACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTACCAACAGCTCCACA
ACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGAAGA
TTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAAGTG
AAGTGGCTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATTAGC
TCCAATGTATAGCTCTCGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAGGTT
TATTCTACCTAATCGCTCGTGTACCTGCTAGCAAAGCAGAGAACAACGTAATCACTTTCTAC
GACTTAAACGACTCTATTCCTGAAACAGTAGACGTATTCGTTGGTGAAATGTCGGCTAACGT
AGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTAGCTCAAATTAACGCATCTG
TTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGT
ATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA***TAATAA*****GAGGAGG**
TAAATATATATGGTATTCACATTAGAAGATTTTGTAGGGGATTGGCGACAAACAGCGGGAT
ATAACTTAGATCAAGTTTTGGAACAGGGTGGAGTCTCAAGCCTCTTTCAAAATCTTGGAGTG
AGTGTTACTCCTATTCAAAGAATTGTACTATCTGGTGAAAATGGCTTAAAGATTGATATACA
TGTTATCATTCCATACGAAGGCTTATCGGGTGATCAAATGGGTCAAATTGAGAAAATCTTTA
AAGTAGTGTATCCTGTAGACGATCATCATTTCAAAGTTATTCTTCACTATGGTACGCTTGTGA
TAGACGGGGTTACACCAAATATGATTGATTACTTTGGTCGGCCGTATGAAGGCATTGCTGTT
TTTGACGGGAAAAAAATCACCGTCACTGGAACTTTATGGAATGGTAACAAAATCATTGATG
AACGTTTGATAAATCCAGATGGATCCTTACTTTTCCGCGTGACAATCAACGGAGTAACGGGC
TGGAGATTATGTGAACGTATTCTAGCATAA*TAATTATAGGATAATTGAATAAAAACAGTATAGAG*
AGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAG
CTAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTCTAATGAC
TTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATATTAAGACAGAACAGA
AAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGA
AAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTACAGAAAATGAATTAGACAGCTTCTTAGC
TAAAGAGCCTTCAATCAAAGAATTAAAAGAATTTGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTA
AGAAAAATGATATAATTGAAGAACTAAAGAGAGGGTAATGTATAATGTATGGAGGTTATGA

Legend:
A511 cps sequence (SEQ ID NO: 19)
Additional Stop Codons (Added by Sample6)
Ribosome Binding Site (Added by Sample6) (SEQ ID NO: 54)
COP2 NanoLuc Sequence (Added by Sample6) (SEQ ID NO: 36)
A511 downstream sequence (500bp) (SEQ ID NO: 61)

FIGURE 2

LP124::COP2

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG
GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGG
AGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAATGATT
TAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATACGATGT
ATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTAGCACCA
GTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGATACTAAAA
ACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATTTTGACTGAC
GATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTT
ATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCTAAACTTATTAAC
CAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGC
AGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAG
CAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTTCGCGATAACGGAAACAAC
GTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTGGATTTATCAAACTTCACGGT
TCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTACCAACAGCTCC
ACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAA
GTGAAGTGGCTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATT
AGCTCCAATGTATAGCTCTCGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAG
GTTTATTCTACCTAATCGCTCGTGTACCTGCTAGCAAAGCAGAGAACAACGTAATCACTTTC
TACGACTTAAACGACTCTATTCCTGAAACAGTAGACGTATTCGTTGGTGAAATGTCGGCTAA
CGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTAGCTCAAATTAACGCAT
CTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTA
CGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA***TAATAA***<u>**GAGGA**</u>
<u>**GGTAAATATAT**</u>ATGGTATTCACATTAGAAGATTTTGTAGGGGATTGGCGACAAACAGCGGG
ATATAACTTAGATCAAGTTTTGGAACAGGGTGGAGTCTCAAGCCTCTTTCAAAATCTTGGAG
TGAGTGTTACTCCTATTCAAAGAATTGTACTATCTGGTGAAAATGGCTTAAAGATTGATATA
CATGTTATCATTCCATACGAAGGCTTATCGGGTGATCAAATGGGTCAAATTGAGAAAATCTT
TAAAGTAGTGTATCCTGTAGACGATCATCATTTCAAAGTTATTCTTCACTATGGTACGCTTGT
GATAGACGGGGTTACACCAAATATGATTGATTACTTTGGTCGGCCGTATGAAGGCATTGCTG
TTTTTGACGGGAAAAAAATCACCGTCACTGGAACTTTATGGAATGGTAACAAAATCATTGAT
GAACGTTTGATAAATCCAGATGGATCCTTACTTTTCCGCGTGACAATCAACGGAGTAACGGG
CTGGAGATTATGTGAACGTATTCTAGCATAA*TAATTATAGGATAATTGAATAAAAACAGTATAGA*
GAGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTA
GCTAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTCTAATGA
CTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATATTAAGACAGAACAG
AAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAG
AAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTACAGAAAATGAATTAGACAGCTTCTTAG
CTAAAGAGCCTTCAATCAAAGAATTAAAAGAATTTGCGAGTAAAAAAGGCATTAAAATTGAAAAAACT
AAGAAAAATGATATAATTGAAGAACTAAAGAGAGGGTAATGTATAATGTATGGAGGTTATGA

Legend:
LP124 cps sequence (SEQ ID NO: 13)
Additional Stop Codons (Added by Sample6)
<u>**Ribosome Binding Site (Added by Sample6)**</u> (SEQ ID NO: 54)
<u>COP2 NanoLuc Sequence (Added by Sample6)</u> (SEQ ID NO: 36)
LP124 downstream sequence (500bp) (SEQ ID NO: 62)

FIGURE 3

LP40::COP2

ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG
GATGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCAGG
GGCACTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAAAATGATT
TAACATTCTACAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATACGATGT
GTACATGCAACACGGTAAAGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTAGCACCA
GTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCTGATACTAAAA
ATATTAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCTATGCAAATTTTGACTGAT
GATGCTATCGTAAATATCGCTAAAACAATTGAGTGGGCTTCATTCTTTGGAGATTCTGACTT
ATCAGATAGCCCAGAACCACAAGCAGGATTAGAATTTGATGGCTTGGCTAAACTTATTAACC
AAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTGTTAAACCAAGCAGC
AGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATGCCAGTAGGGGTTCAAG
CAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTTCGCGATAACGGAAACAAC
GTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGTGGATTTATCAAACTTCACGGT
TCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGTATTCTTGCTTTACCAACAGCTCC
ACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGTAAAAAAGGACAATTTAGAGCAGA
AGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGTTCTGACGATGCAGAGTCTATTGCAA
GTGAAGTGGCTACAGCTACAGTTACTGCAAAAGATGACGGCGTTAAACTAGAAATCGAATT
AGCTCCAATGTATAGCTCTCGTCCACAATTCGTTTCAATCTATAGAAAAGGTGCAGAAACAG
GTTTATTCTACCTAATCGCTCGTGTACCTGCTAGCAAAGCAGAGAACAACGTAATCACTTTC
TACGACTTAAACGACTCTATTCCTGAAACAGTAGACGTATTCGTTGGTGAAATGTCGGCTAA
CGTAGTACACTTGTTTGAATTACTACCAATGATGAGATTACCTCTAGCTCAAATTAACGCAT
CTGTTACATTTGCAGTTTTATGGTATGGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTA
CGTATTAGAAACGTTAAATATATTCCTGTAAAAAACGTTCATAGCAACTAA***TAATAA*****GAGGA**
GGTAAATATATATGGTATTCACATTAGAAGATTTTGTAGGGGATTGGCGACAAACAGCGGG
ATATAACTTAGATCAAGTTTTGGAACAGGGTGGAGTCTCAAGCCTCTTTCAAAATCTTGGAG
TGAGTGTTACTCCTATTCAAAGAATTGTACTATCTGGTGAAAATGGCTTAAAGATTGATATA
CATGTTATCATTCCATACGAAGGCTTATCGGGTGATCAAATGGGTCAAATTGAGAAAATCTT
TAAAGTAGTGTATCCTGTAGACGATCATCATTTCAAAGTTATTCTTCACTATGGTACGCTTGT
GATAGACGGGGTTACACCAAATATGATTGATTACTTTGGTCGGCCGTATGAAGGCATTGCTG
TTTTTGACGGGAAAAAAATCACCGTCACTGGAACTTTATGGAATGGTAACAAAATCATTGAT
GAACGTTTGATAAATCCAGATGGATCCTTACTTTTCCGCGTGACAATCAACGGAGTAACGGG
CTGGAGATTATGTGAACGTATTCTAGCATAA*TAATTATAGGATAATTGAATAAAAACAGTATAGA*
GAGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTA
GCTAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTCTAATGA
CTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATATTAAGACAGAACAG
AAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTACAGAA
AATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATTTGCGAGTAAAAA
AGGCATTAAAATTGAAAAAACTAAGAAAAACGATATAATTGAAGAACTAAAGAGAGGGTAATGTATA
ATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCCTTACTCACATGGGAACCCTAA

Legend:
LP40 cps sequence (SEQ ID NO: 5)
Additional Stop Codons (Added by Sample6)
Ribosome Binding Site (Added by Sample6) (SEQ ID NO: 54)
COP2 NanoLuc Sequence (Added by Sample6) (SEQ ID NO: 36)
LP40 downstream sequence (500bp) (SEQ ID NO: 63)

FIGURE 4

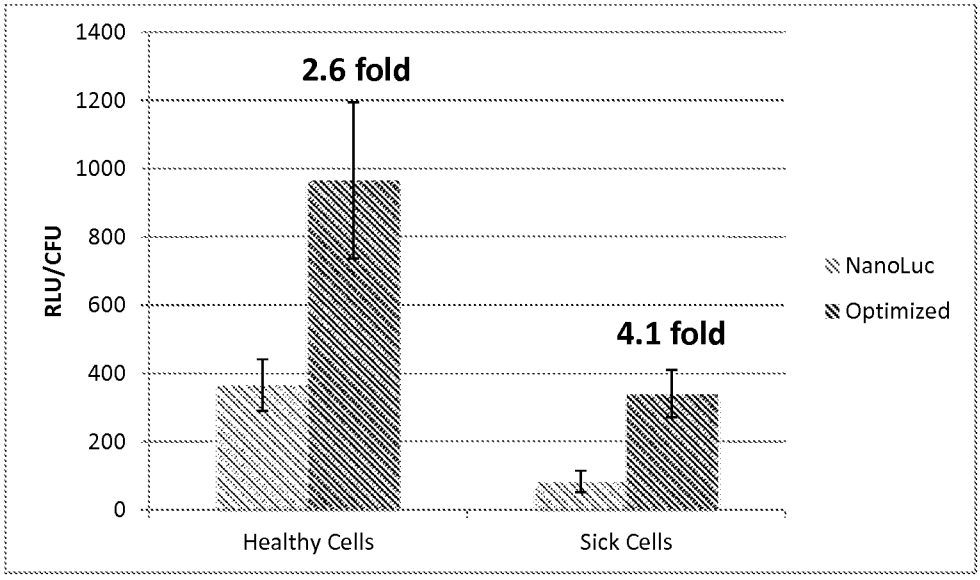

1400
1200
1000
800
600
400
200
0
RLU/CFU
2.6 fold
4.1 fold
Healthy Cells
Sick Cells
NanoLuc
Optimized

FIGURE 5

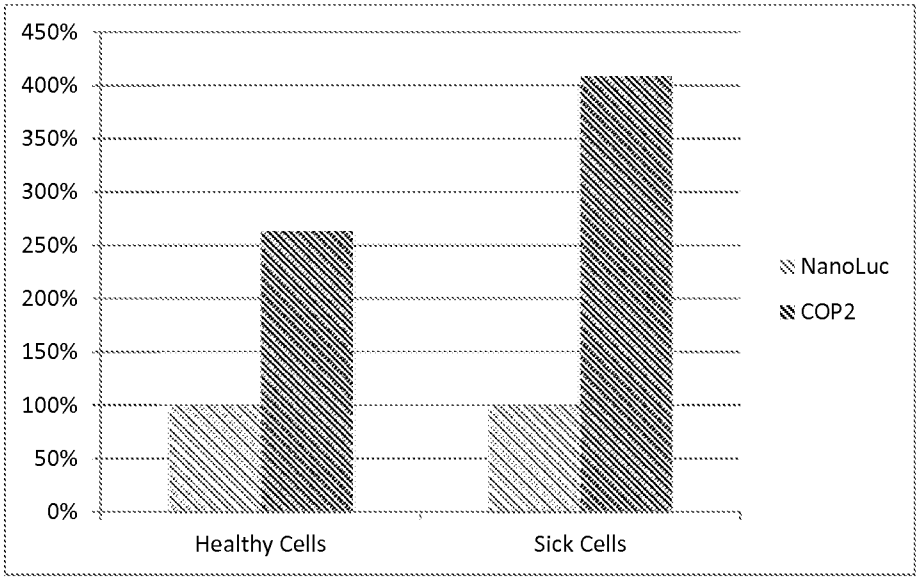

450%
400%
350%
300%
250%
200%
150%
100%
50%
0%
Healthy Cells
Sick Cells
NanoLuc
COP2

FIGURE 6

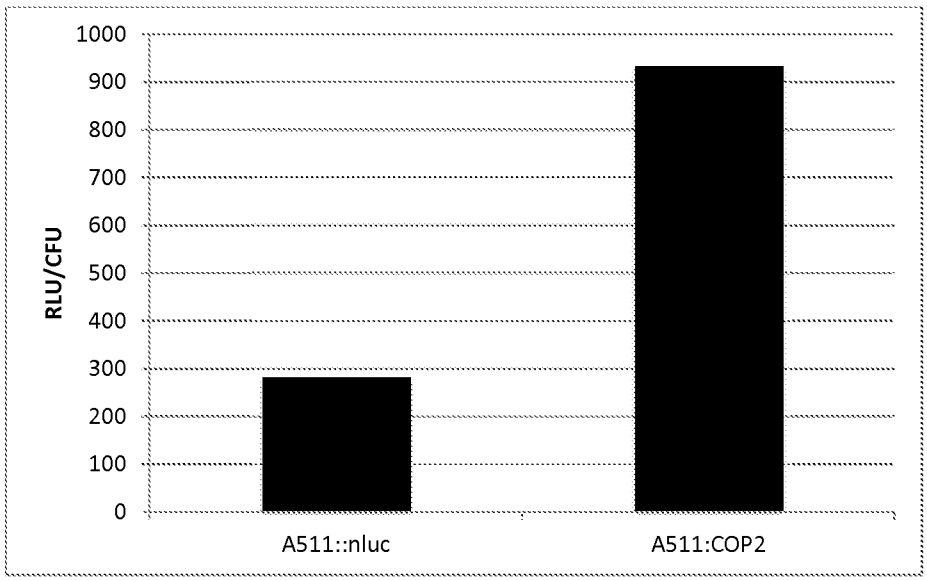

1000
900
800
700
600
500
400
300
200
100
0
RLU/CFU
A511::nluc
A511:COP2

FIGURE 7

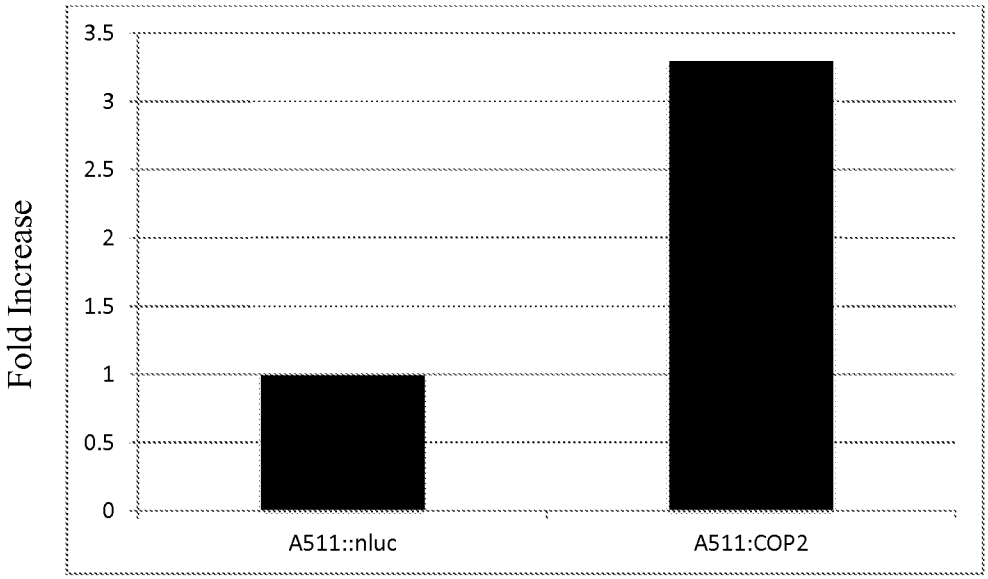


FIGURE 8

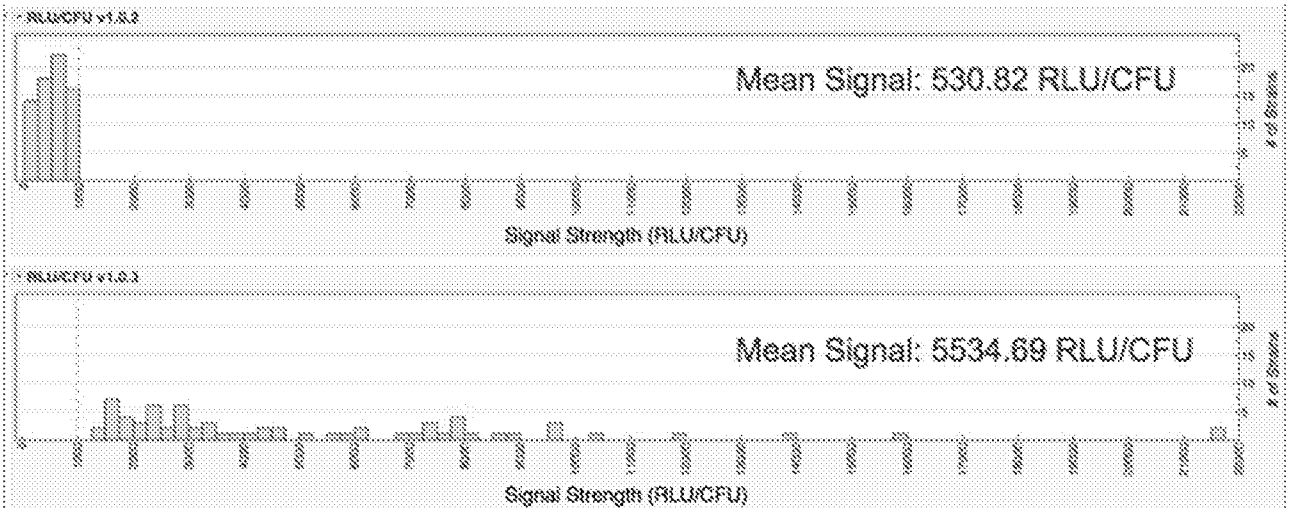

Mean Signal: 530.82 RLU/CFU
Signal Strength (RLU/CFU)
Mean Signal: 5534.69 RLU/CFU
Signal Strength (RLU/CFU)

FIGURE 9

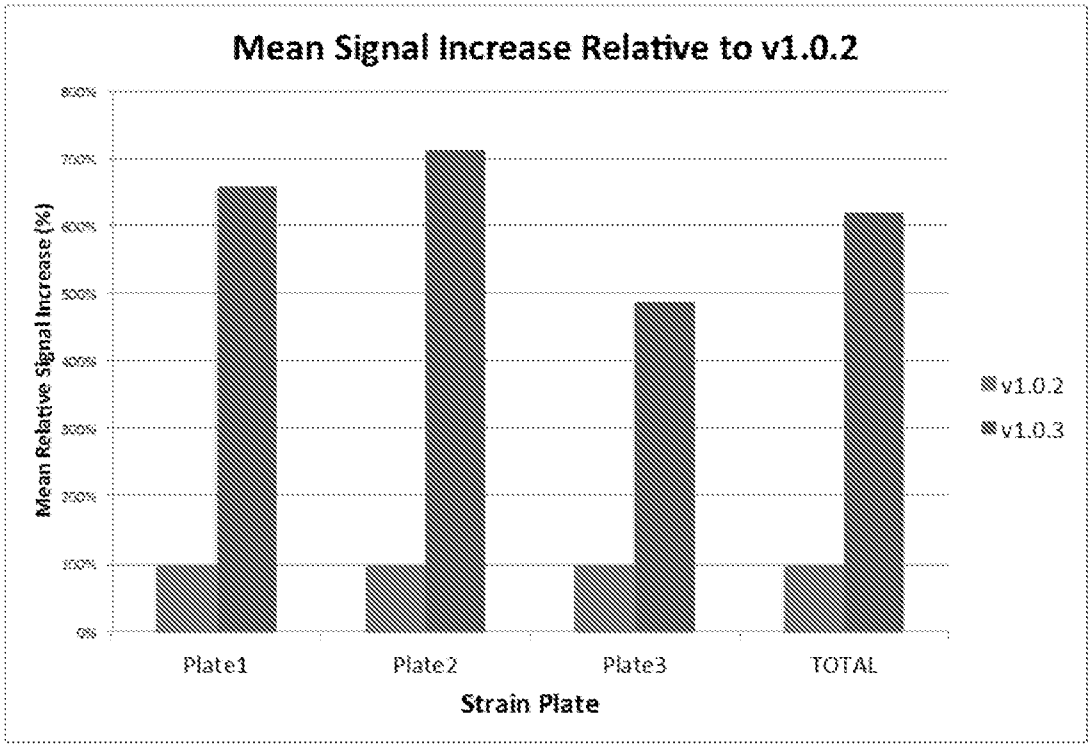

Mean Signal Increase Relative to v1.0.2
Mean Relative Signal Increase (%)
800%
700%
600%
500%
400%
300%
200%
100%
0%
Plate1
Plate2
Plate3
TOTAL
Strain Plate
v1.0.2
v1.0.3

FIGURE 10

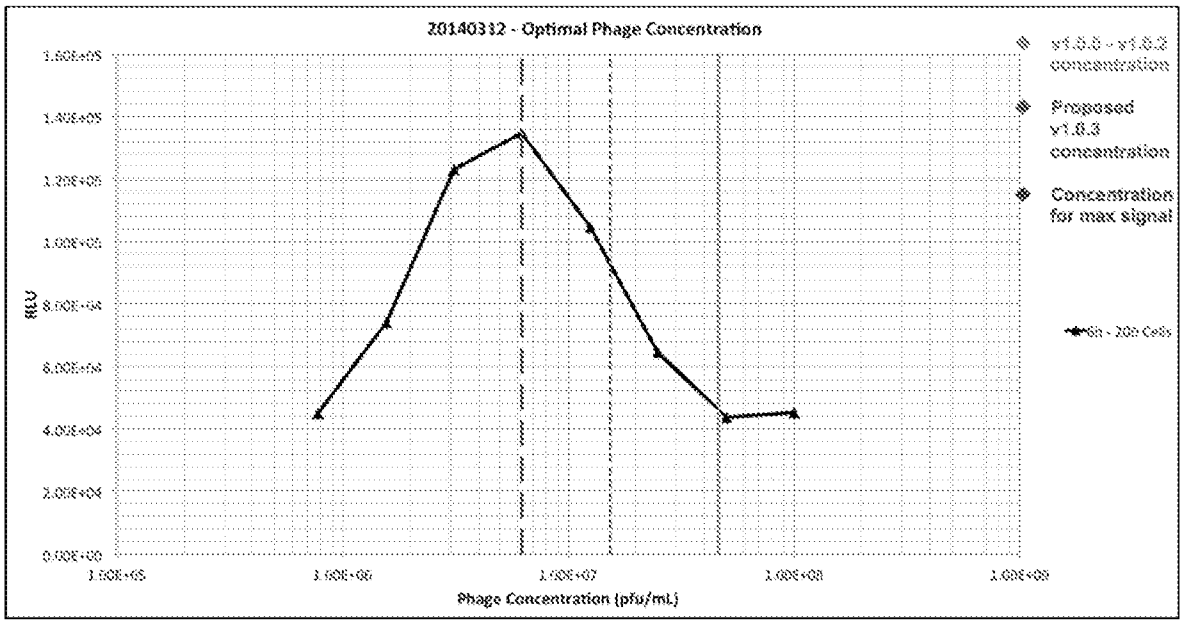

20140312 - Optimal Phage Concentration
RLU
Phage Concentration (pfu/mL)
v1.0.0 - v1.0.2 concentration
Proposed v1.0.3 concentration
Concentration for max signal
6h - 200 Cells

Figure 11

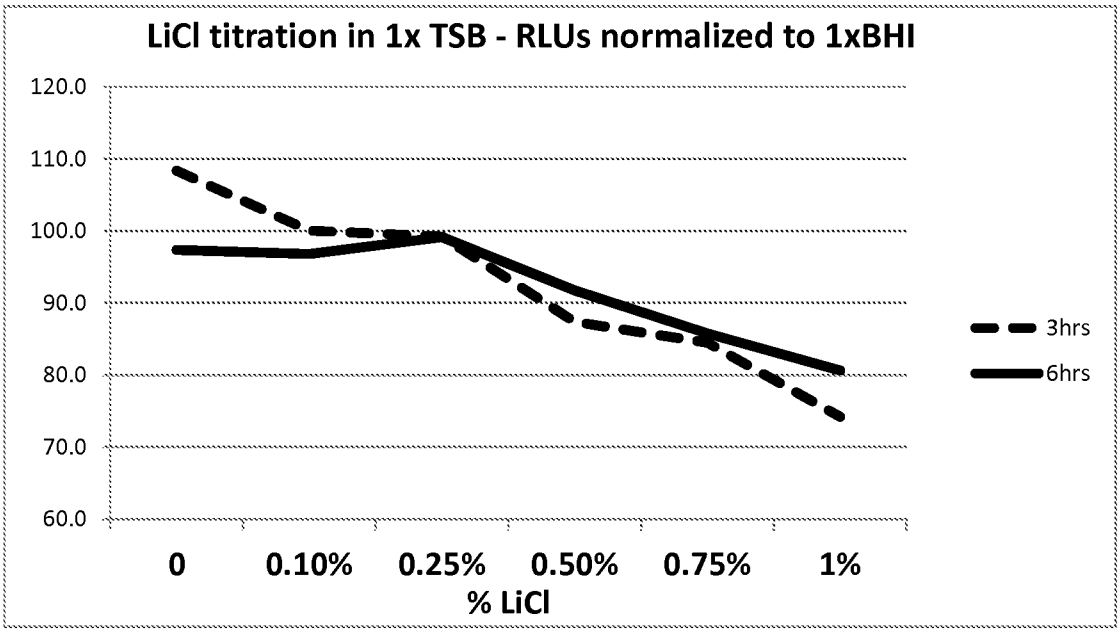

LiCl titration in 1x TSB - RLUs normalized to 1xBHI
120.0
110.0
100.0
90.0
80.0
70.0
60.0
0
0.10%
0.25%
0.50%
0.75%
1%
% LiCl
3hrs
6hrs

Figure 12

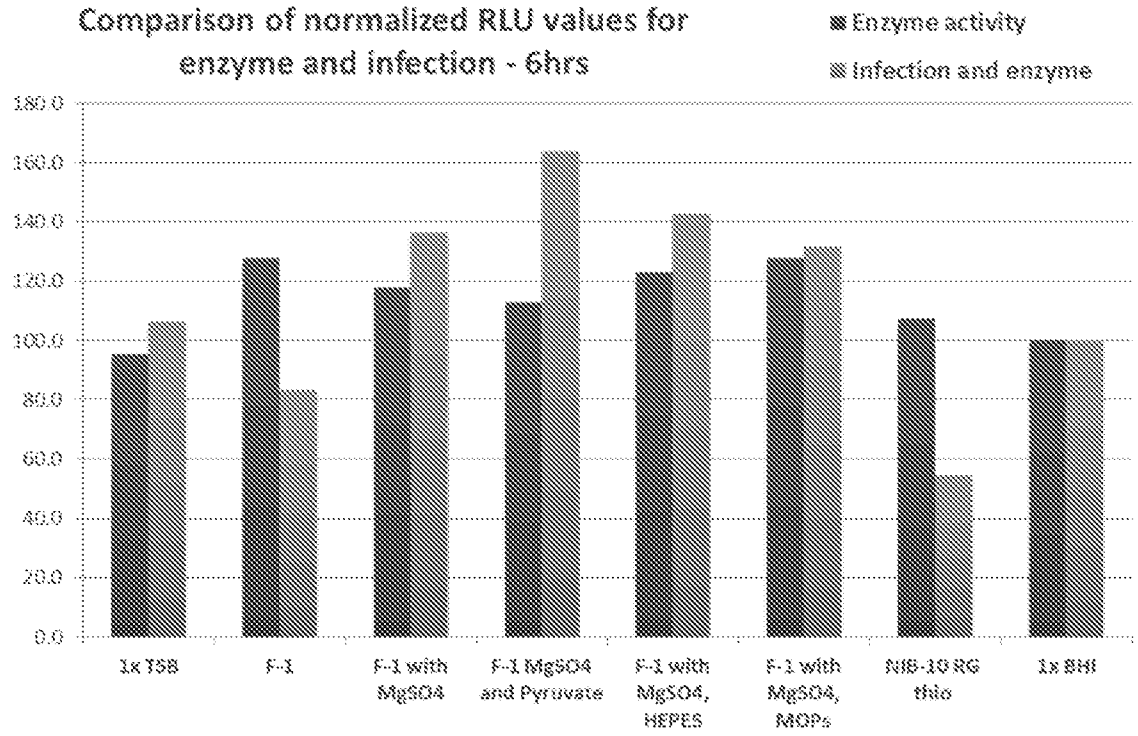

Comparison of normalized RLU values for enzyme and infection - 6hrs
Enzyme activity
Infection and enzyme
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
1x TSB
F-1
F-1 with MgSO4
F-1 MgSO4 and Pyruvate
F-1 with MgSO4, HEPES
F-1 with MgSO4, MOPs
NIB-10 RG thio
1x BHI

Figure 13A

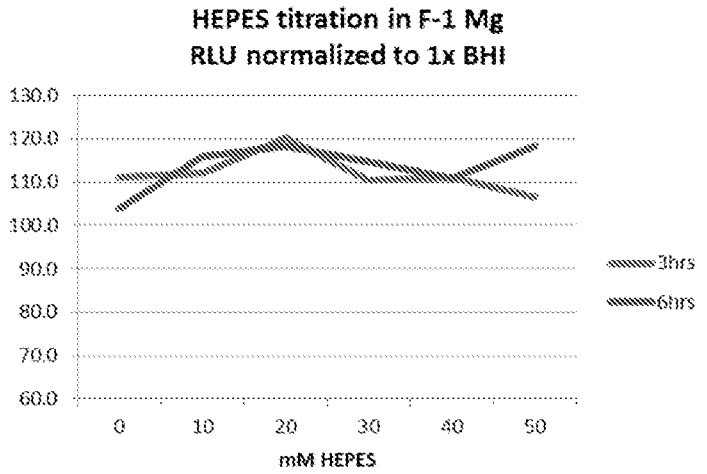


Figure 13B

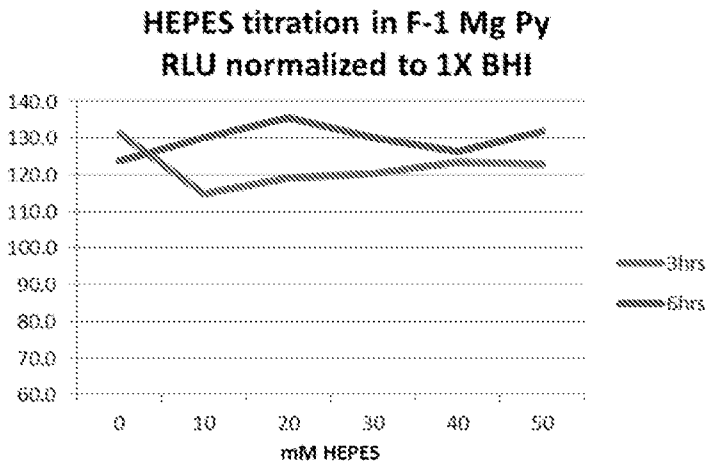


Figure 14

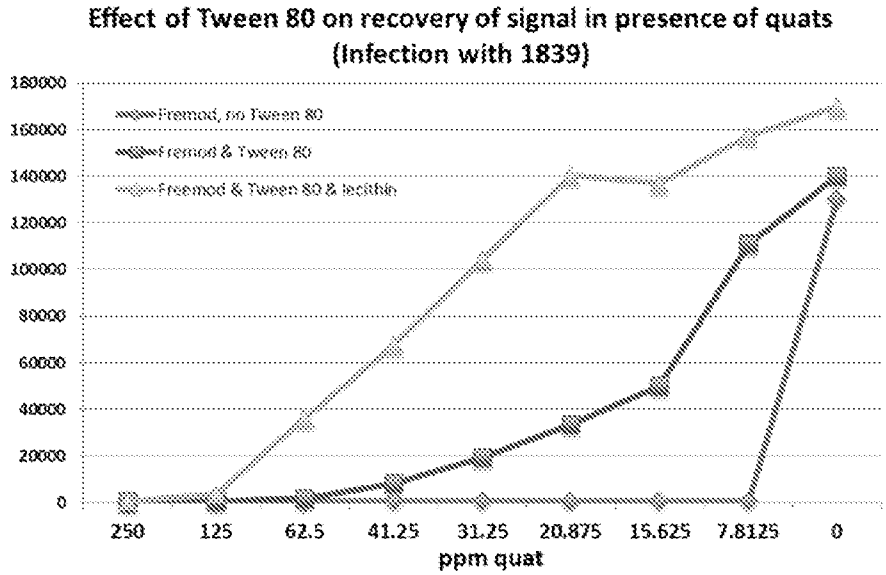

Effect of Tween 80 on recovery of signal in presence of quats
(Infection with 1839)
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
Freemod, no Tween 80
Freemod & Tween 80
Freemod & Tween 80 & lecithin
250
125
62.5
41.25
31.25
20.875
15.625
7.8125
0
ppm quat

Figure 15

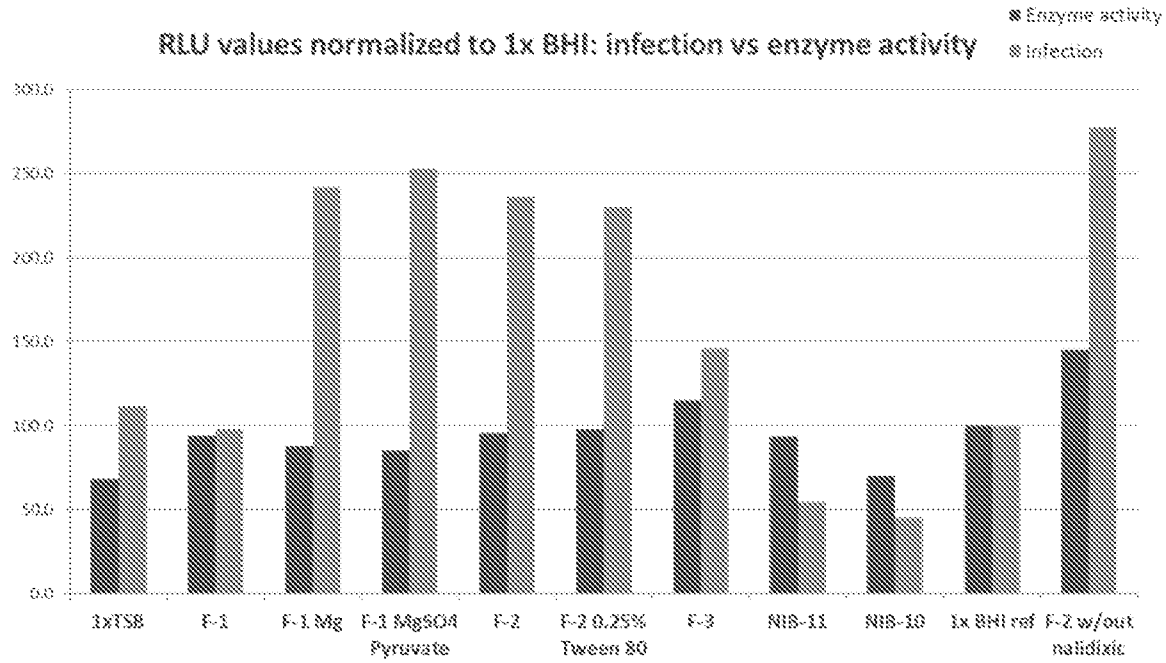

RLU values normalized to 1x BHI: infection vs enzyme activity
Enzyme activity
Infection
300.0
250.0
200.0
150.0
100.0
50.0
0.0
1xTSB
F-1
F-1 Mg
F-1 MgSO4 Pyruvate
F-2
F-2 0.25% Tween 80
F-3
NIB-11
NIB-10
1x BHI ref
F-2 w/out nalidixic

Figure 16

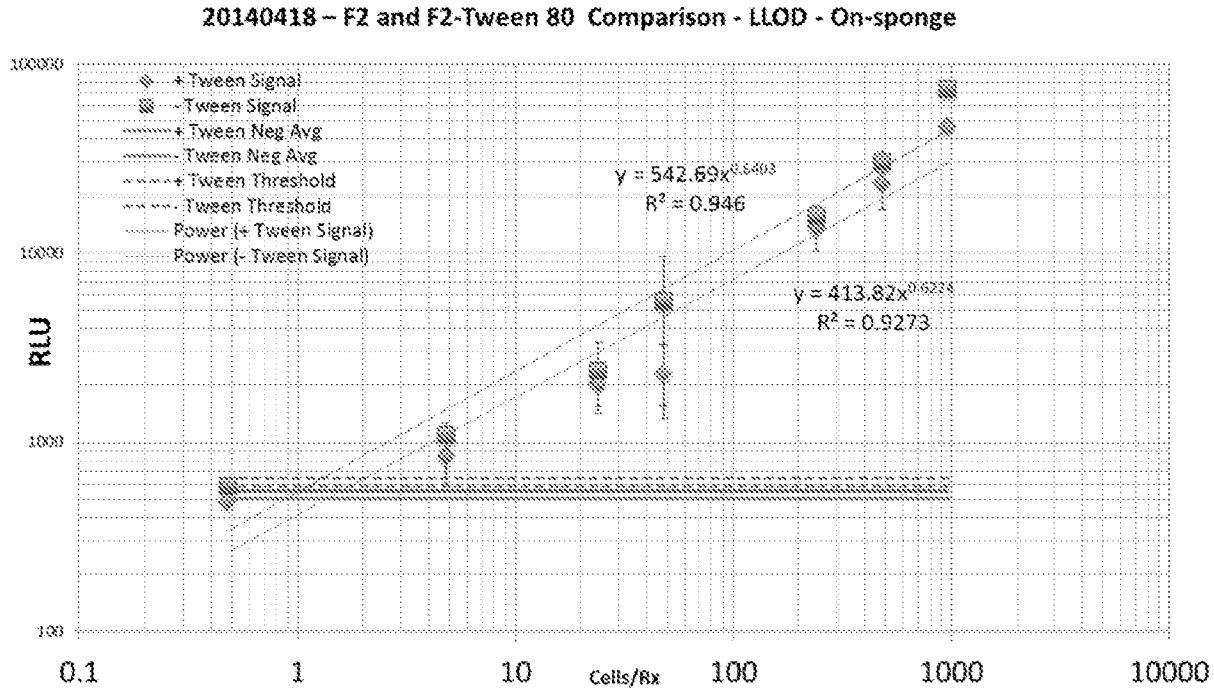

20140418 – F2 and F2-Tween 80 Comparison - LLOD - On-sponge
+ Tween Signal
- Tween Signal
+ Tween Neg Avg
- Tween Neg Avg
+ Tween Threshold
- Tween Threshold
Power (+ Tween Signal)
Power (- Tween Signal)
y = 542.69x^0.5403
R² = 0.946
y = 413.82x^0.6218
R² = 0.9273
RLU
100000
10000
1000
100
0.1
1
10
100
1000
10000
Cells/Rx

Figure 17A

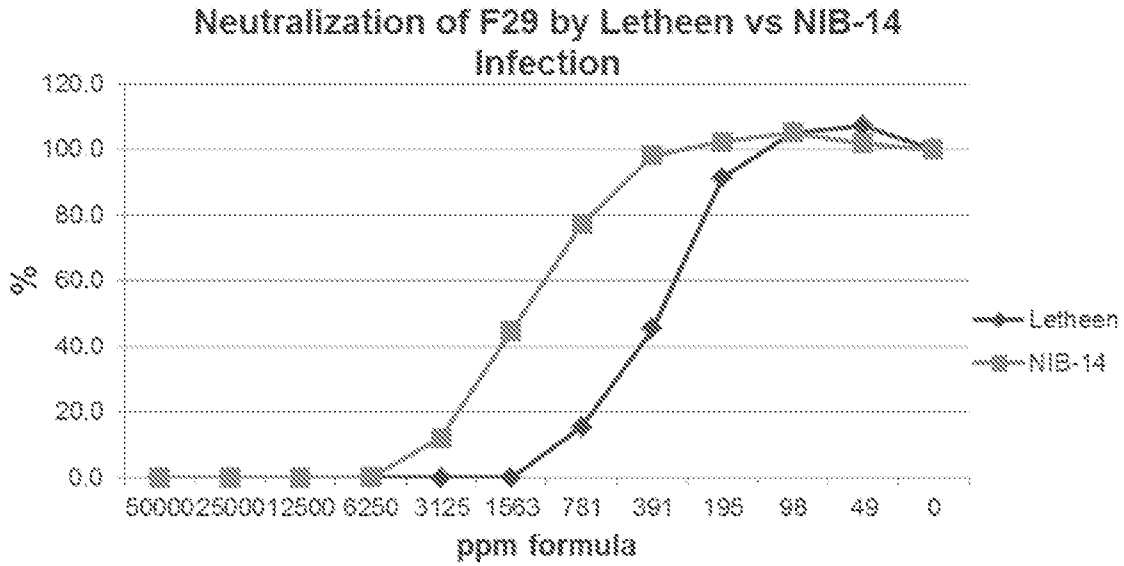


Figure 17B

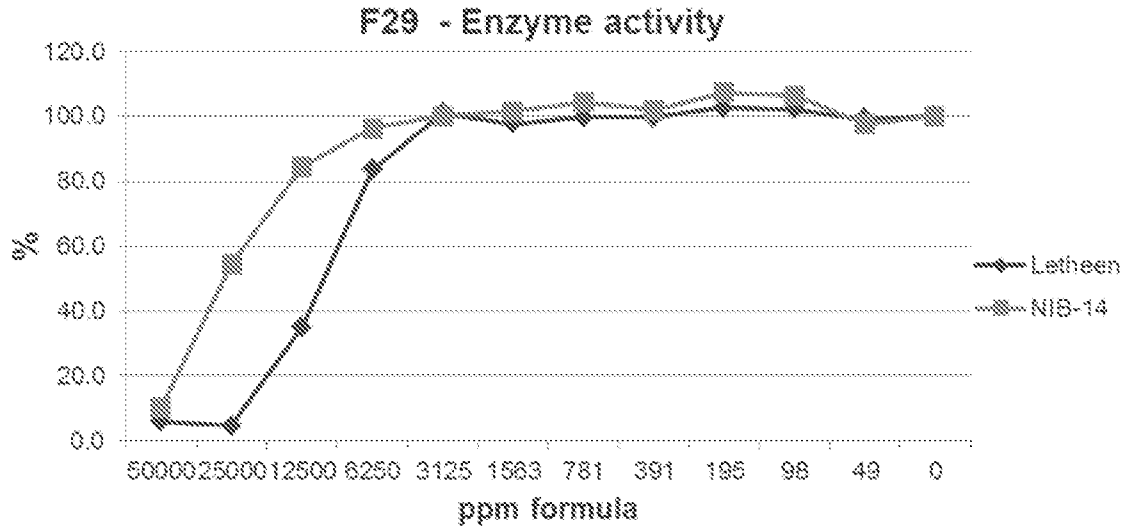


Figure 17C

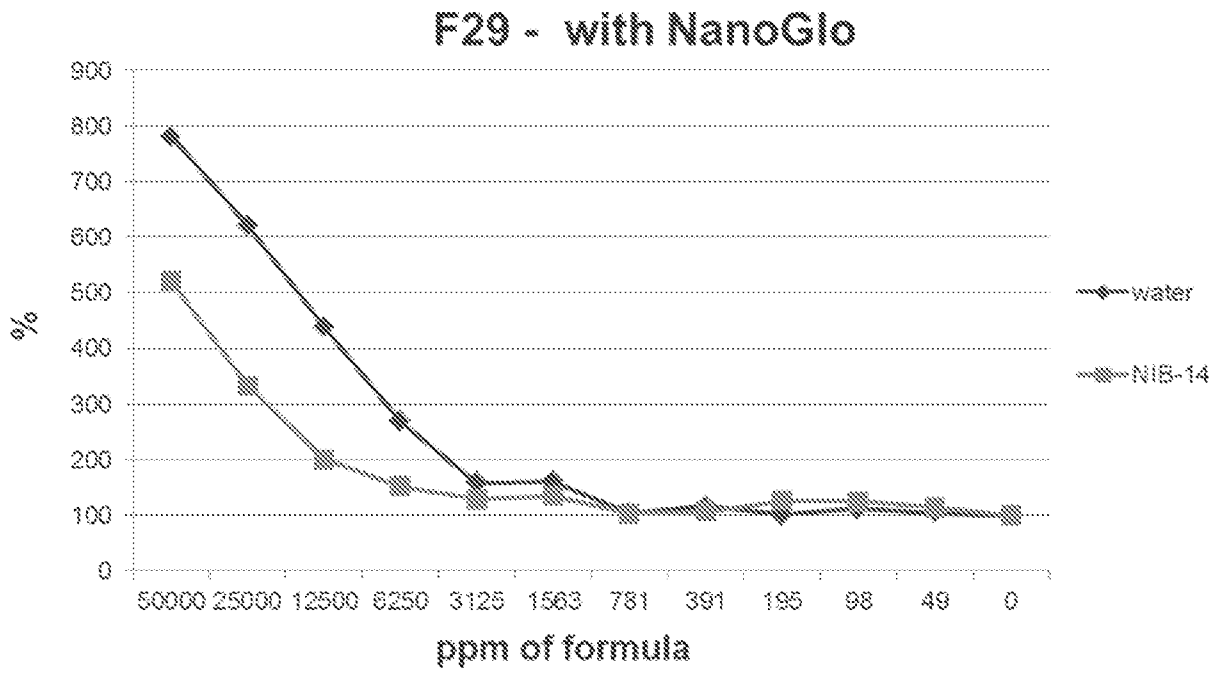


Figure 7D

Sanitizer	Recommended use	% of recommended amount to give 50% infection activity	% of recommended amount to give 50% Enzyme activity
F29	0.26%	54%	385%

Figure 18A

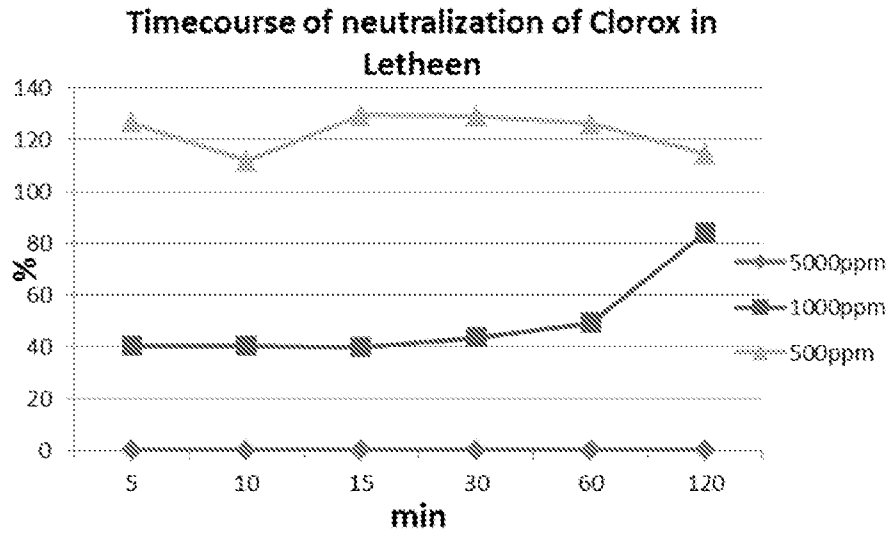


Figure 18B

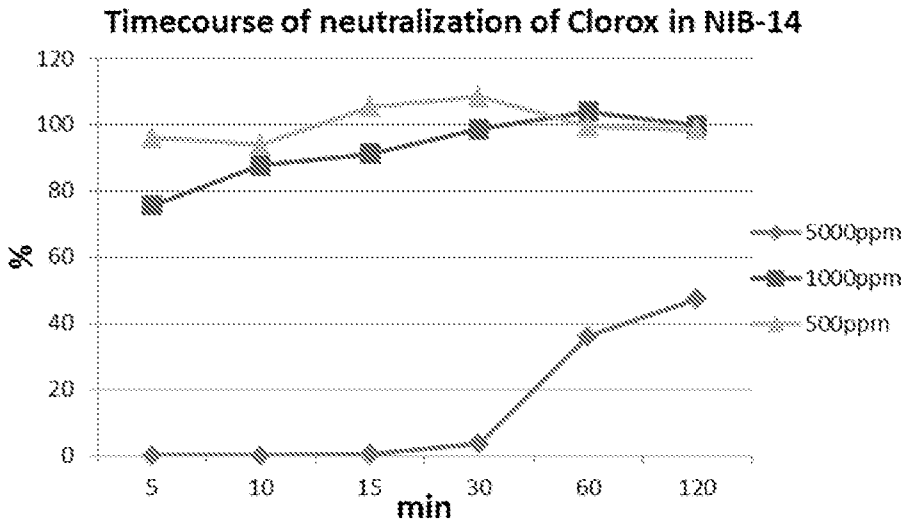


Figure 19

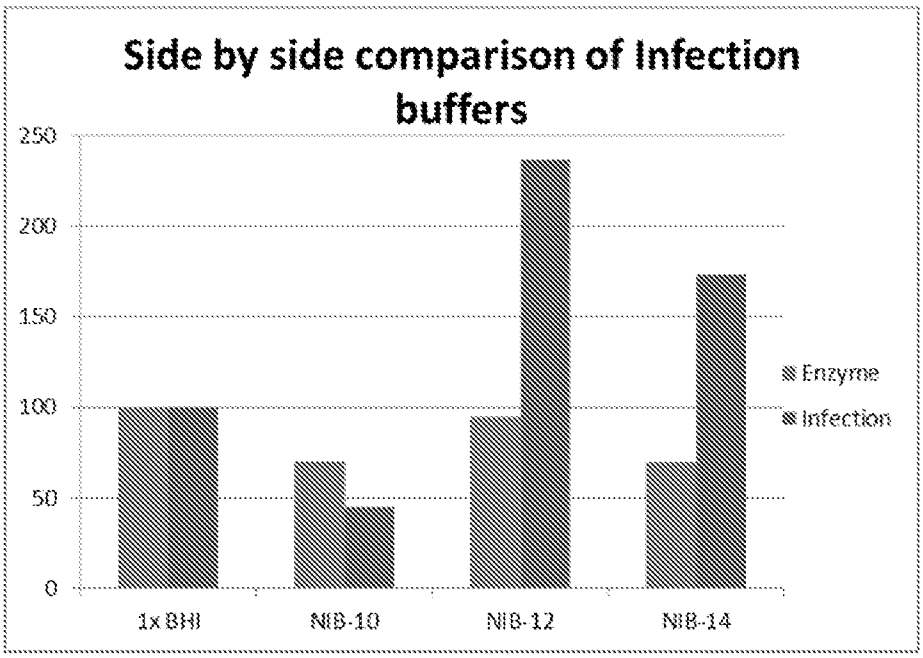

Side by side comparison of Infection buffers
250
200
150
100
50
0
1x BHI
NIB-10
NIB-12
NIB-14
Enzyme
Infection

Figure 20A

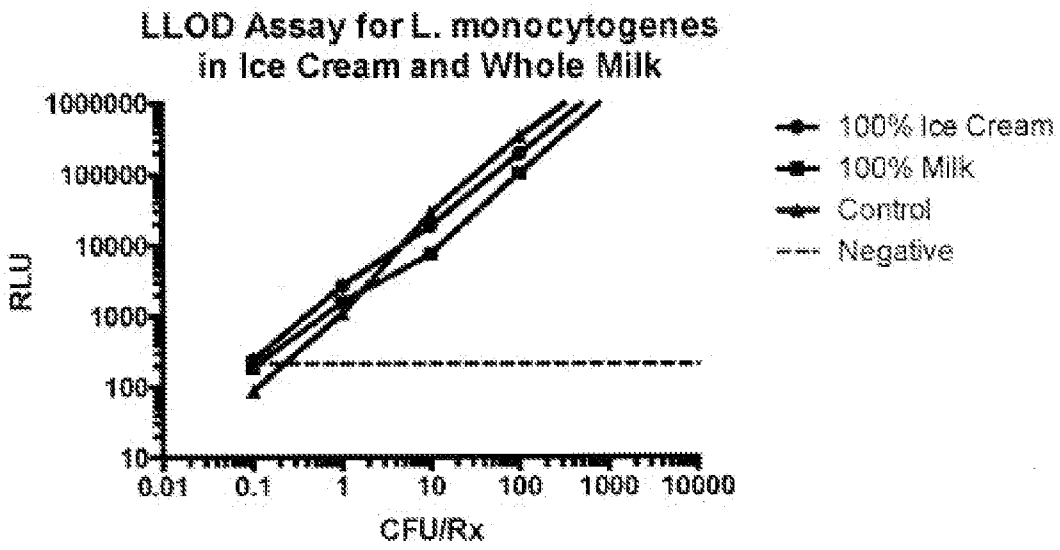


Figure 20B

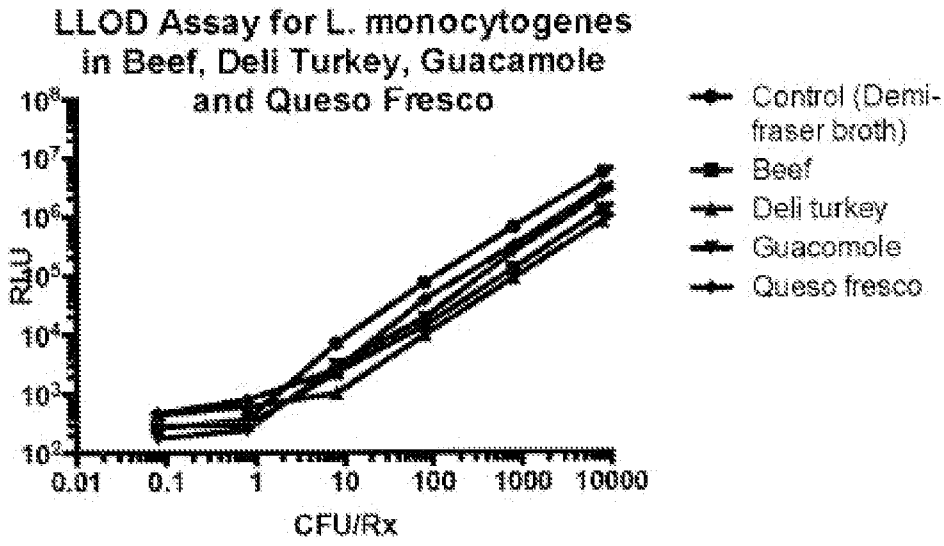


Figure 21A

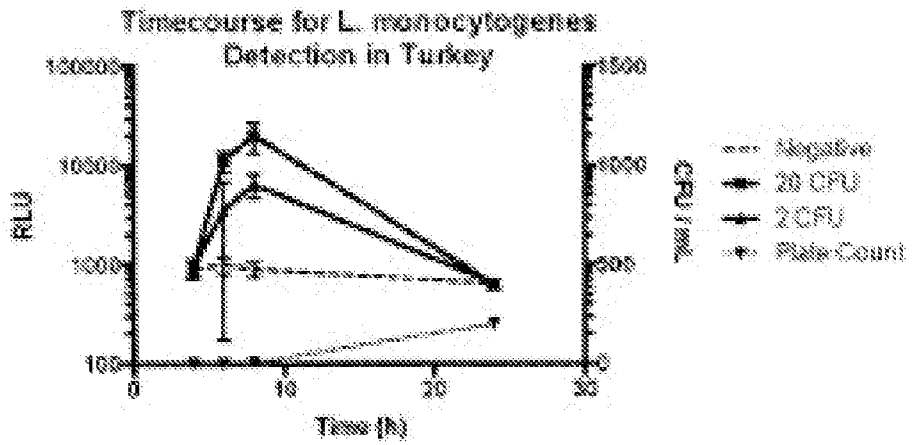


Figure 21B

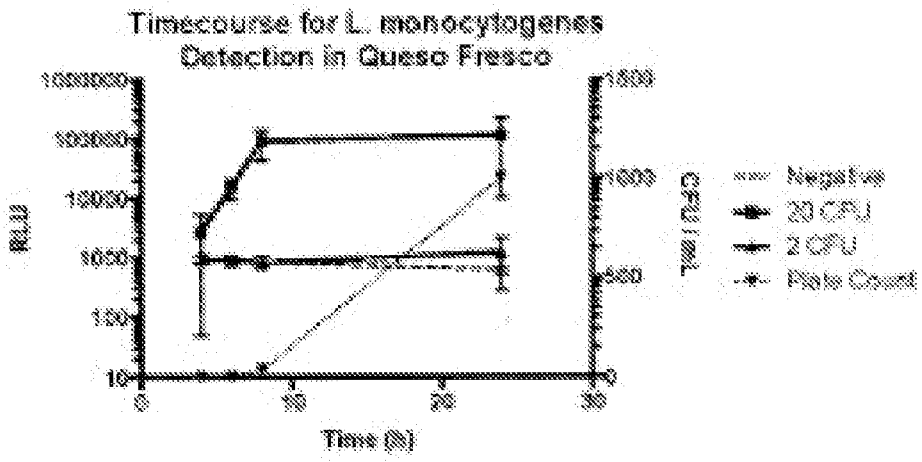


Figure 21C

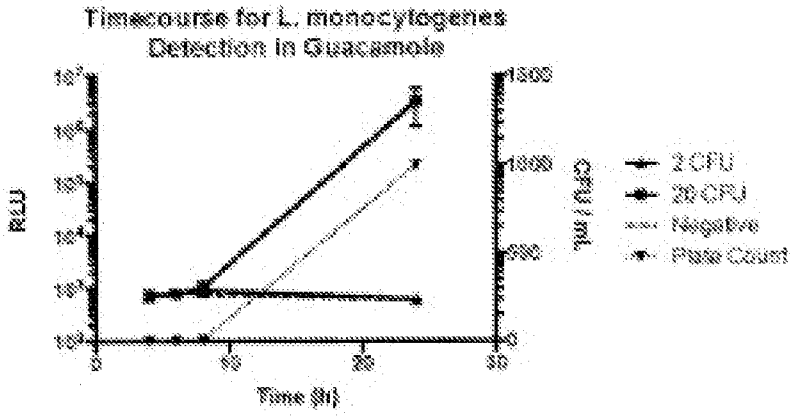


Figure 21D

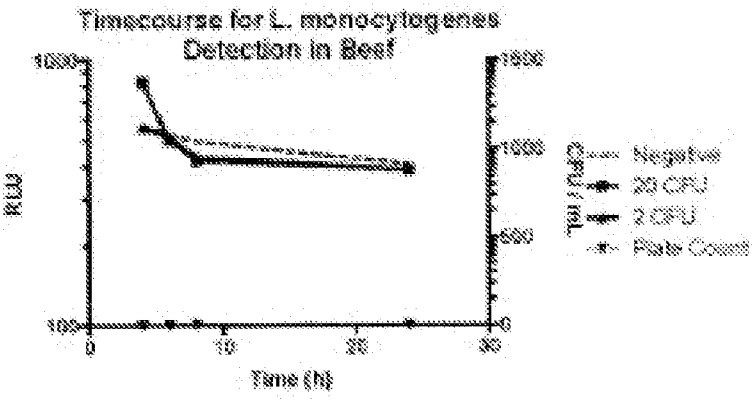


Figure 22A

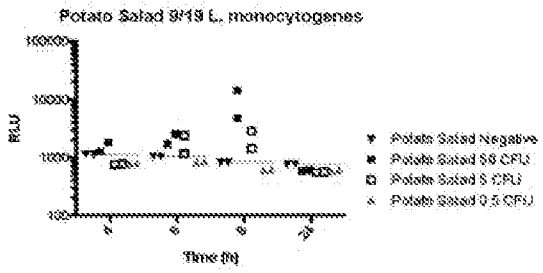


Figure 22B

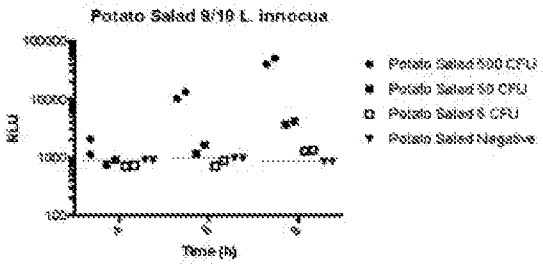


Figure 22C

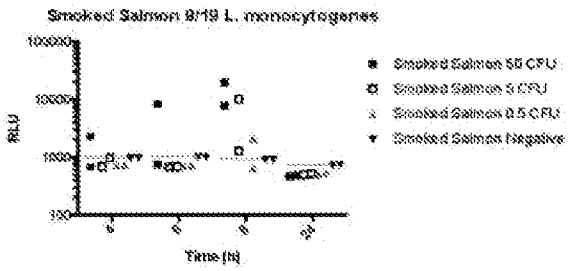


Figure 22D

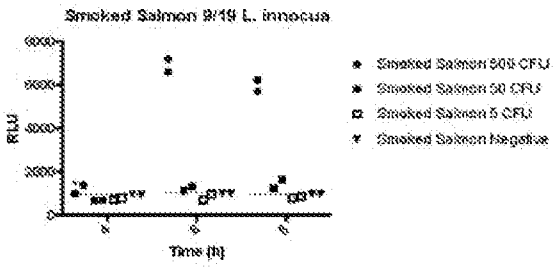


Figure 22E

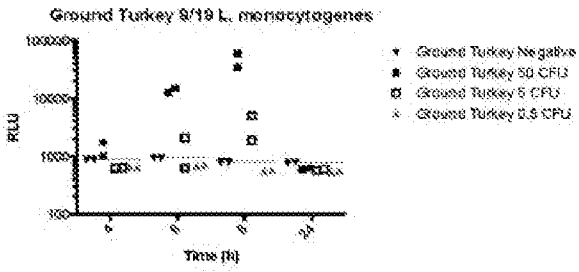


Figure 22F

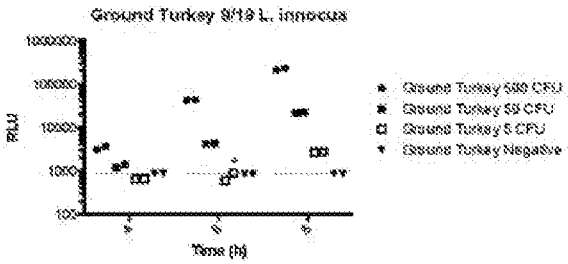


Figure 22G

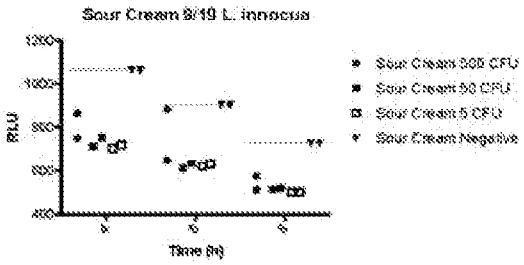


Figure 22H

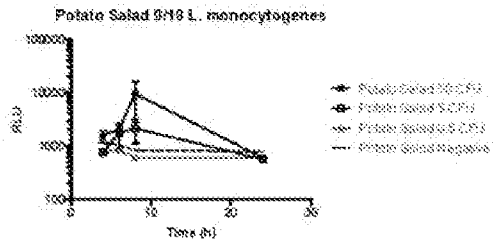


Figure 22I

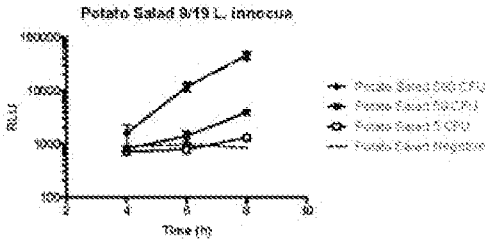


Figure 22J

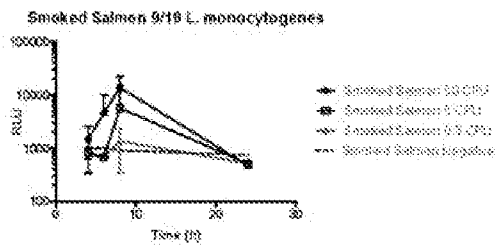


Figure 22K

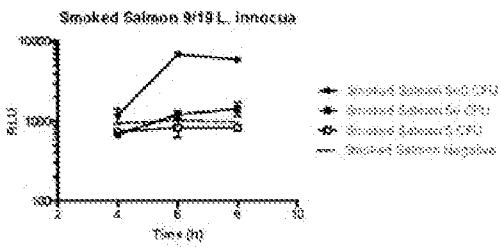


Figure 22L

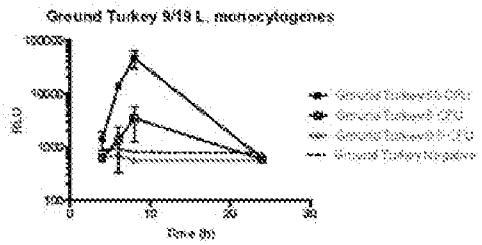


Figure 22M

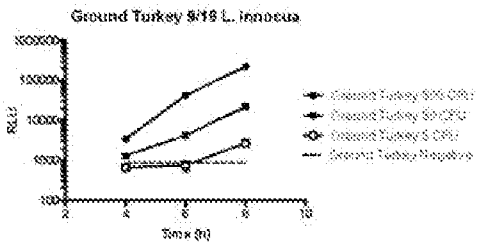


Figure 23A

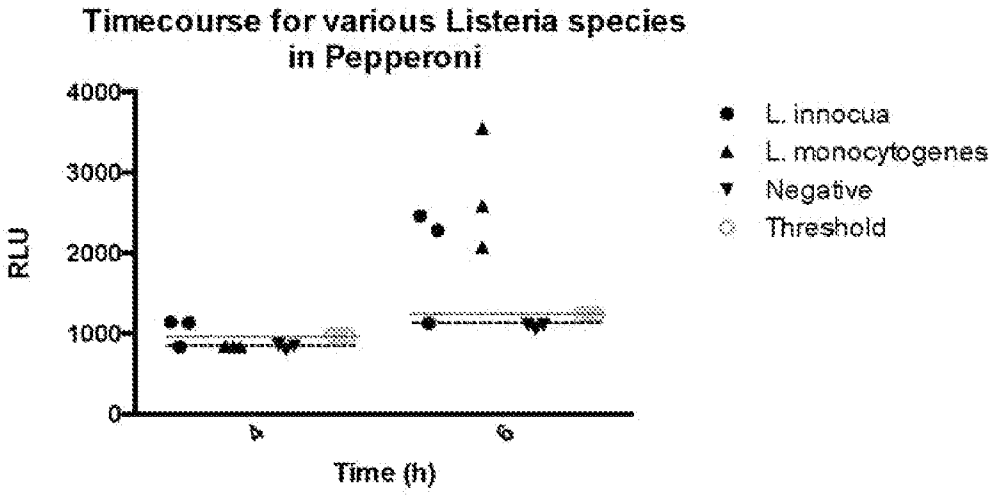


Figure 23B

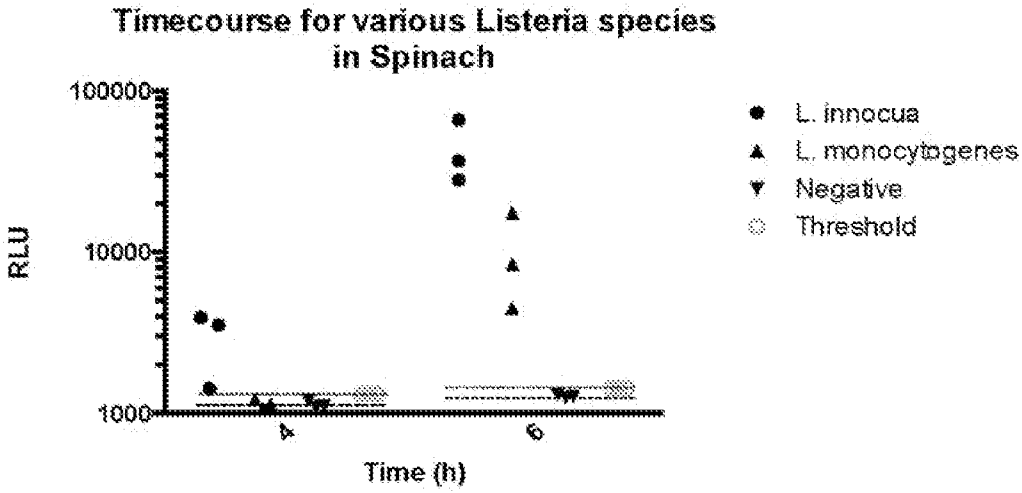


Figure 24A

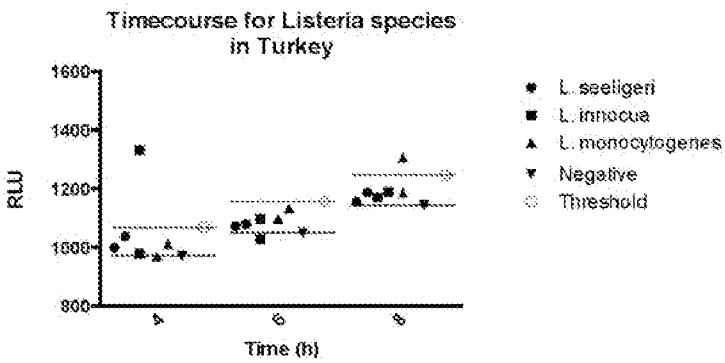


Figure 24B

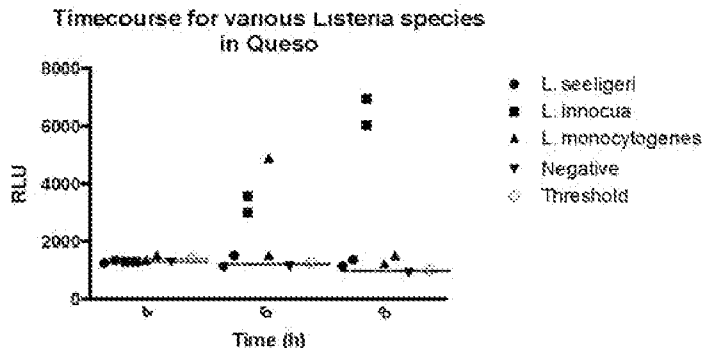


Figure 24C

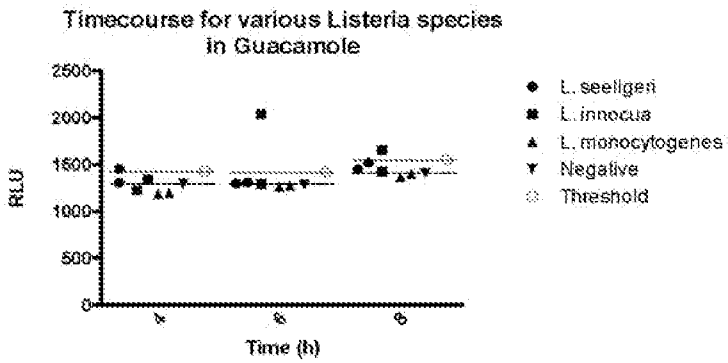


Figure 25A

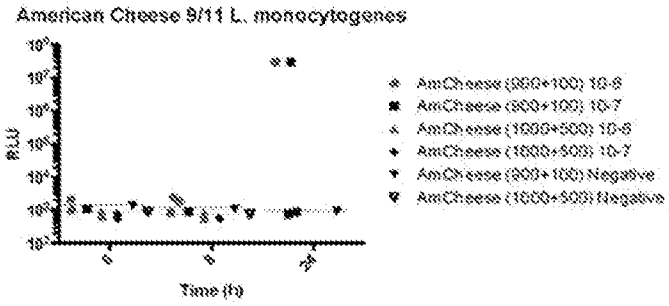


Figure 25B

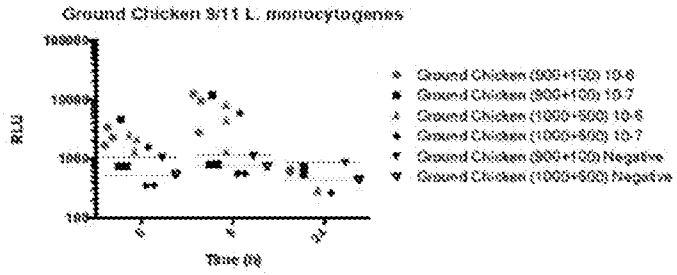


Figure 25C

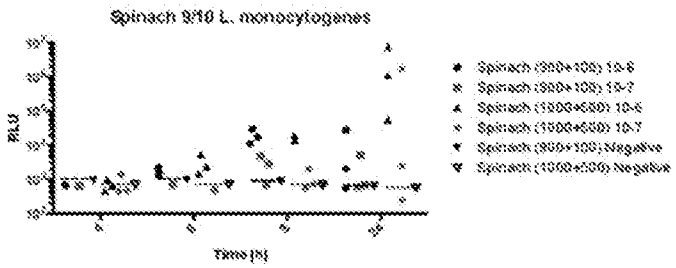


Figure 25D

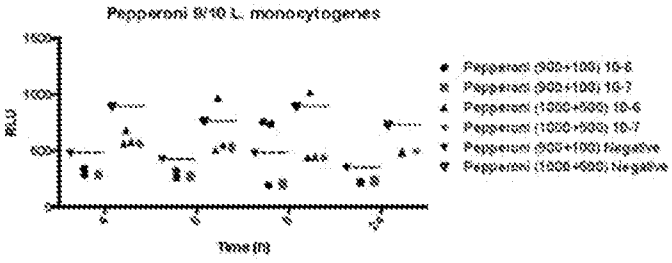


FIGURE 26

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LP124_cps       ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
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LP48_cps        ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
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LP124_cps       GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
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LP48_cps        GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
LP125_cps       GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
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LP124_cps       GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
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LP101_cps       TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
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LP101_cps       AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
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LP40_cps        AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
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A511_cps        TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 657
LP101_cps       TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP124_cps       TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP99_cps        TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP48_cps        TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP125_cps       TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
P100_cps        TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP40_cps        TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
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LP143_cps       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 717
A511_cps        CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 717
LP101_cps       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP124_cps       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP99_cps        CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP48_cps        CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP125_cps       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
P100_cps        CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAGCTTGTT 720
LP40_cps        CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
                ************************************************** ******

LP143_cps       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 777
A511_cps        CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 777
LP101_cps       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP124_cps       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP99_cps        CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP48_cps        CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP125_cps       CGTGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
P100_cps        CGTGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP40_cps        CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
                ** ********************************************************

LP143_cps       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 837
A511_cps        GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 837
LP101_cps       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP124_cps       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP99_cps        GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP48_cps        GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP125_cps       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
P100_cps        GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP40_cps        GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
                ************************************************************

LP143_cps       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 897
A511_cps        ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 897
LP101_cps       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP124_cps       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP99_cps        ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP48_cps        ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP125_cps       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
P100_cps        ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP40_cps        ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
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LP143_cps       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 957
A511_cps        AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 957
LP101_cps       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP124_cps       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP99_cps        AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP48_cps        AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP125_cps       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
P100_cps        AAAAAAGGACAATTTAGAGCAGAAGACTTAGCAGCACACGAATACAAAGTTGTTGTAAGT 960
LP40_cps        AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
                ************************** *********** ***** ***************

LP143_cps       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1017
A511_cps        TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1017
LP101_cps       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP124_cps       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP99_cps        TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP48_cps        TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP125_cps       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
P100_cps        TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP40_cps        TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
                ************************************************************

LP143_cps       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1077
A511_cps        GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1077
LP101_cps       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP124_cps       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP99_cps        GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP48_cps        GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP125_cps       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
P100_cps        GACGGCGTTAAACTAGAAATCGAGTTAGCTCCAATGTACAGCTCCCGTCCACAATTCGTT 1080
LP40_cps        GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
                ********************** ************** ***** ***************

LP143_cps       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1137
A511_cps        TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1137
LP101_cps       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP124_cps       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP99_cps        TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP48_cps        TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP125_cps       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
P100_cps        TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP40_cps        TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
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LP143_cps       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1197
A511_cps        AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1197
LP101_cps       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP124_cps       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP99_cps        AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP48_cps        AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP125_cps       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
P100_cps        AGCAAAGCAGAGAACAACGTAATCACTTTCTATGACTTAAACGACTCTATTCCTGAAACA 1200
LP40_cps        AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
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LP143_cps       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1257
A511_cps        GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1257
LP101_cps       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP124_cps       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP99_cps        GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP48_cps        GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP125_cps       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
P100_cps        GTAGACGTATTCGTTGGTGAAATGTCTGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP40_cps        GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
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LP143_cps       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1317
A511_cps        ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1317
LP101_cps       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP124_cps       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP99_cps        ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP48_cps        ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP125_cps       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
P100_cps        ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP40_cps        ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
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LP143_cps       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1377
A511_cps        GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1377
LP101_cps       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP124_cps       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP99_cps        GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP48_cps        GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP125_cps       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
P100_cps        GGAGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
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LP40_cps        GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
                ** ********************************************************

LP143_cps       CCTGTAAAAAACGTTCATAGCAACTAA 1404
A511_cps        CCTGTAAAAAACGTTCATAGCAACTAA 1404
LP101_cps       CCTGTAAAAAACGTTCATAGCAACTAA 1407
LP124_cps       CCTGTAAAAAACGTTCATAGCAACTAA 1407
LP99_cps        CCTGTAAAAAACGTTCATAGCAACTAA 1407
LP48_cps        CCTGTAAAAAACGTTCATAGCAACTAA 1407
LP125_cps       CCTGTAAAAAACGTTCATAGCAACTAA 1407
P100_cps        CCTGTAAAAAACGTTCATAGCAACTAA 1407
LP40_cps        CCTGTAAAAAACGTTCATAGCAACTAA 1407
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FIGURE 27

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LP143_cps       MPKNNK-EEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 59
A511_cps        MPKNNK-EEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 59
LP40_cps        MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 60
LP48_cps        MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 60
LP99_cps        MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 60
LP101_cps       MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 60
LP124_cps       MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 60
P100_cps        MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 60
LP125_cps       MPKNNKEEEVKEVNLNSVQEDALKSFTTGYGITPDTQTDAGALRREFLDDQISMLTWTEN 60
                ****** **************************************************

LP143_cps       DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 119
A511_cps        DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 119
LP40_cps        DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 120
LP48_cps        DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 120
LP99_cps        DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 120
LP101_cps       DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 120
LP124_cps       DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 120
P100_cps        DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 120
LP125_cps       DLTFYKDIAKKPATSTVAKYDVYMQHGKVGHTRFTREIGVAPVSDPNIRQKTVNMKFASD 120
                ************************************************************

LP143_cps       TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 179
A511_cps        TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 179
LP40_cps        TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 180
LP48_cps        TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 180
LP99_cps        TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 180
LP101_cps       TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 180
LP124_cps       TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 180
P100_cps        TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 180
LP125_cps       TKNISIAAGLVNNIQDPMQILTDDAIVNIAKTIEWASFFGDSDLSDSPEPQAGLEFDGLA 180
                ************************************************************

LP143_cps       KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 239
A511_cps        KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 239
LP40_cps        KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 240
LP48_cps        KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 240
LP99_cps        KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 240
LP101_cps       KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 240
LP124_cps       KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 240
P100_cps        KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 240
LP125_cps       KLINQDNVHDARGASLTESLLNQAAVMISKGYGTPTDAYMPVGVQADFVNQQLSKQTQLV 240
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LP143_cps       RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 299
A511_cps        RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 299
LP40_cps        RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 300
LP48_cps        RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 300
LP99_cps        RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 300
LP101_cps       RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 300
LP124_cps       RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 300
P100_cps        RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 300
LP125_cps       RDNGNNVSVGFNIQGFHSARGFIKLHGSTVMENEQILDERILALPTAPQPAKVTATQEAG 300
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LP143_cps       KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 359
A511_cps        KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 359
LP40_cps        KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 360
LP48_cps        KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 360
LP99_cps        KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 360
LP101_cps       KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 360
LP124_cps       KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 360
P100_cps        KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 360
LP125_cps       KKGQFRAEDLAAHEYKVVVSSDDAESIASEVATATVTAKDDGVKLEIELAPMYSSRPQFV 360
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LP143_cps       SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 419
A511_cps        SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 419
LP40_cps        SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 420
LP48_cps        SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 420
LP99_cps        SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 420
LP101_cps       SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 420
LP124_cps       SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 420
P100_cps        SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 420
LP125_cps       SIYRKGAETGLFYLIARVPASKAENNVITFYDLNDSIPETVDVFVGEMSANVVHLFELLP 420
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LP143_cps       MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 467
A511_cps        MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 467
LP40_cps        MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 468
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LP48_cps        MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 468
LP99_cps        MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 468
LP101_cps       MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 468
LP124_cps       MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 468
P100_cps        MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 468
LP125_cps       MMRLPLAQINASVTFAVLWYGALALRAPKKWVRIRNVKYIPVKNVHSN 468
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FIGURE 28

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LP48__ffluc       ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
LP125__ffluc      ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
LP143__ffluc      ATGCCAAAAAATAACAAA---GAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 57
A511__ffluc       ATGCCAAAAAATAACAAA---GAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 57
LP124__ffluc      ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
lp101__ffluc      ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
LP99__ffluc       ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
P100__ffluc       ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
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LP48__ffluc       GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
LP125__ffluc      GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
LP143__ffluc      GATGCGTTAAAGTCCTTTACGACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 117
A511__ffluc       GATGCGTTAAAGTCCTTTACGACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 117
LP124__ffluc      GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
lp101__ffluc      GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
LP99__ffluc       GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
P100__ffluc       GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
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LP48__ffluc       GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
LP125__ffluc      GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
LP143__ffluc      GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 177
A511__ffluc       GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 177
LP124__ffluc      GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
lp101__ffluc      GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
LP99__ffluc       GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
P100__ffluc       GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
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LP48__ffluc       GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
LP125__ffluc      GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
LP143__ffluc      GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 237
A511__ffluc       GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 237
LP124__ffluc      GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
lp101__ffluc      GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
LP99__ffluc       GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
P100__ffluc       GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
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LP48__ffluc       GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
LP125__ffluc      GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
LP143__ffluc      GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 297
A511__ffluc       GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 297
LP124__ffluc      GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
lp101__ffluc      GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
LP99__ffluc       GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
P100__ffluc       GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
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LP48__ffluc       GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGAT 360
LP125__ffluc      GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGAT 360
LP143__ffluc      GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCGAT 357
A511__ffluc       GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCGAT 357
LP124__ffluc      GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGAT 360
lp101__ffluc      GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGAT 360
LP99__ffluc       GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGAT 360
P100__ffluc       GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCGAT 360
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LP48__ffluc       ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
LP125__ffluc      ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
LP143__ffluc      ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 417
A511__ffluc       ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 417
LP124__ffluc      ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
lp101__ffluc      ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
LP99__ffluc       ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
P100__ffluc       ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
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LP48__ffluc       TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
LP125__ffluc      TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
LP143__ffluc      TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 477
A511__ffluc       TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 477
LP124__ffluc      TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
lp101__ffluc      TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
LP99__ffluc       TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
P100__ffluc       TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
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LP48__ffluc       GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
LP125__ffluc      GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
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LP143__ffluc      GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 537
A511__ffluc       GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 537
LP124__ffluc      GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
lp101__ffluc      GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
LP99__ffluc       GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
P100__ffluc       GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
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LP48__ffluc       AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
LP125__ffluc      AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
LP143__ffluc      AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 597
A511__ffluc       AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 597
LP124__ffluc      AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
lp101__ffluc      AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
LP99__ffluc       AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
P100__ffluc       AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
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LP48__ffluc       TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP125__ffluc      TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP143__ffluc      TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 657
A511__ffluc       TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 657
LP124__ffluc      TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
lp101__ffluc      TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP99__ffluc       TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
P100__ffluc       TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
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LP48__ffluc       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP125__ffluc      CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP143__ffluc      CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 717
A511__ffluc       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 717
LP124__ffluc      CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
lp101__ffluc      CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP99__ffluc       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
P100__ffluc       CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAGCTTGTT 720
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LP48__ffluc       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP125__ffluc      CGTGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP143__ffluc      CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 777
A511__ffluc       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 777
LP124__ffluc      CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
lp101__ffluc      CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP99__ffluc       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
P100__ffluc       CGTGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
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LP48__ffluc       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP125__ffluc      GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP143__ffluc      GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 837
A511__ffluc       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 837
LP124__ffluc      GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
lp101__ffluc      GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP99__ffluc       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
P100__ffluc       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
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LP48__ffluc       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP125__ffluc      ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP143__ffluc      ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 897
A511__ffluc       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 897
LP124__ffluc      ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
lp101__ffluc      ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP99__ffluc       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
P100__ffluc       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
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LP48__ffluc       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP125__ffluc      AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP143__ffluc      AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 957
A511__ffluc       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 957
LP124__ffluc      AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
lp101__ffluc      AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP99__ffluc       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
P100__ffluc       AAAAAAGGACAATTTAGAGCAGAAGACTTAGCAGCACACGAATACAAAGTTGTTGTAAGT 960
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LP48__ffluc       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP125__ffluc      TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP143__ffluc      TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1017
A511__ffluc       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1017
LP124__ffluc      TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
lp101__ffluc      TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP99__ffluc       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
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P100__ffluc       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
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LP48__ffluc       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP125__ffluc      GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP143__ffluc      GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1077
A511__ffluc       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1077
LP124__ffluc      GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
lp101__ffluc      GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP99__ffluc       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
P100__ffluc       GACGGCGTTAAACTAGAAATCGAGTTAGCTCCAATGTACAGCTCCCGTCCACAATTCGTT 1080
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LP48__ffluc       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP125__ffluc      TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP143__ffluc      TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1137
A511__ffluc       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1137
LP124__ffluc      TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
lp101__ffluc      TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP99__ffluc       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
P100__ffluc       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
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LP48__ffluc       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP125__ffluc      AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP143__ffluc      AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1197
A511__ffluc       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1197
LP124__ffluc      AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
lp101__ffluc      AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP99__ffluc       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
P100__ffluc       AGCAAAGCAGAGAACAACGTAATCACTTTCTATGACTTAAACGACTCTATTCCTGAAACA 1200
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LP48__ffluc       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP125__ffluc      GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP143__ffluc      GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1257
A511__ffluc       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1257
LP124__ffluc      GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
lp101__ffluc      GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP99__ffluc       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
P100__ffluc       GTAGACGTATTCGTTGGTGAAATGTCTGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
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LP48__ffluc       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP125__ffluc      ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP143__ffluc      ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1317
A511__ffluc       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1317
LP124__ffluc      ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
lp101__ffluc      ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP99__ffluc       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
P100__ffluc       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
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LP48__ffluc       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP125__ffluc      GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP143__ffluc      GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1377
A511__ffluc       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1377
LP124__ffluc      GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
lp101__ffluc      GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP99__ffluc       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
P100__ffluc       GGAGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
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LP48__ffluc       CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1440
LP125__ffluc      CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1440
LP143__ffluc      CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1437
A511__ffluc       CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1437
LP124__ffluc      CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1440
lp101__ffluc      CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1440
LP99__ffluc       CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1440
P100__ffluc       CCTGTAAAAAACGTTCATAGCAACTAAGAGGAGGTAAATATATATGGAAGACGCCAAAAA 1440
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LP48__ffluc       CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1500
LP125__ffluc      CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1500
LP143__ffluc      CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1497
A511__ffluc       CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1497
LP124__ffluc      CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1500
lp101__ffluc      CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1500
LP99__ffluc       CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1500
P100__ffluc       CATAAAGAAAGGCCCGGCGCCATTCTATCCTCTAGAGGATGGAACCGCTGGAGAGCAACT 1500
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LP48__ffluc       GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1560
LP125  ffluc      GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1560
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LP143__ffluc      GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1557
A511__ffluc       GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1557
LP124__ffluc      GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1560
lp101__ffluc      GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1560
LP99__ffluc       GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1560
P100__ffluc       GCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACA 1560
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LP48__ffluc       TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1620
LP125__ffluc      TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1620
LP143__ffluc      TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1617
A511__ffluc       TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1617
LP124__ffluc      TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1620
lp101__ffluc      TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1620
LP99__ffluc       TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1620
P100__ffluc       TATCGAGGTGAACATCACGTACGCGGAATACTTCGAAATGTCCGTTCGGTTGGCAGAAGC 1620
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LP48__ffluc       TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1680
LP125__ffluc      TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1680
LP143__ffluc      TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1677
A511__ffluc       TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1677
LP124__ffluc      TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1680
lp101__ffluc      TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1680
LP99__ffluc       TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1680
P100__ffluc       TATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCT 1680
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LP48__ffluc       TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1740
LP125__ffluc      TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1740
LP143__ffluc      TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1737
A511__ffluc       TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1737
LP124__ffluc      TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1740
lp101__ffluc      TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1740
LP99__ffluc       TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1740
P100__ffluc       TCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAA 1740
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LP48__ffluc       CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1800
LP125__ffluc      CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1800
LP143__ffluc      CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1797
A511__ffluc       CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1797
LP124__ffluc      CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1800
lp101__ffluc      CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1800
LP99__ffluc       CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1800
P100__ffluc       CGACATTTATAATGAACGTGAATTGCTCAACAGTATGAACATTTCGCAGCCTACCGTAGT 1800
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LP48__ffluc       GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1860
LP125__ffluc      GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1860
LP143__ffluc      GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1857
A511__ffluc       GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1857
LP124__ffluc      GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1860
lp101__ffluc      GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1860
LP99__ffluc       GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1860
P100__ffluc       GTTTGTTTCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAATTACCAATAAT 1860
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LP48__ffluc       CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1920
LP125__ffluc      CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1920
LP143__ffluc      CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1917
A511__ffluc       CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1917
LP124__ffluc      CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1920
lp101__ffluc      CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1920
LP99__ffluc       CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1920
P100__ffluc       CCAGAAAATTATTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACAC 1920
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LP48__ffluc       GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1980
LP125__ffluc      GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1980
LP143__ffluc      GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1977
A511__ffluc       GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1977
LP124__ffluc      GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1980
lp101__ffluc      GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1980
LP99__ffluc       GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1980
P100__ffluc       GTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACGATTTTGTACCAGAGTCCTT 1980
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LP48__ffluc       TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2040
LP125__ffluc      TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2040
LP143__ffluc      TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2037
A511__ffluc       TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2037
LP124__ffluc      TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2040
lp101__ffluc      TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2040
LP99__ffluc       TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2040
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P100__ffluc       TGATCGTGACAAAACAATTGCACTGATAATGAATTCCTCTGGATCTACTGGGTTACCTAA 2040
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LP48__ffluc       GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2100
LP125__ffluc      GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2100
LP143__ffluc      GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2097
A511__ffluc       GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2097
LP124__ffluc      GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2100
lp101__ffluc      GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2100
LP99__ffluc       GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2100
P100__ffluc       GGGTGTGGCCCTTCCGCATAGAACTGCCTGCGTCAGATTCTCGCATGCCAGAGATCCTAT 2100
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LP48__ffluc       TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2160
LP125__ffluc      TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2160
LP143__ffluc      TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2157
A511__ffluc       TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2157
LP124__ffluc      TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2160
lp101__ffluc      TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2160
LP99__ffluc       TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2160
P100__ffluc       TTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCCATCACGG 2160
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LP48__ffluc       TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2220
LP125__ffluc      TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2220
LP143__ffluc      TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2217
A511__ffluc       TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2217
LP124__ffluc      TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2220
lp101__ffluc      TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2220
LP99__ffluc       TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2220
P100__ffluc       TTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAATGTA 2220
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LP48__ffluc       TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2280
LP125__ffluc      TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2280
LP143__ffluc      TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2277
A511__ffluc       TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2277
LP124__ffluc      TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2280
lp101__ffluc      TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2280
LP99__ffluc       TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2280
P100__ffluc       TAGATTTGAAGAAGAGCTGTTTTTACGATCCCTTCAGGATTACAAAATTCAAAGTGCGTT 2280
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LP48__ffluc       GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2340
LP125__ffluc      GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2340
LP143__ffluc      GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2337
A511__ffluc       GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2337
LP124__ffluc      GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2340
lp101__ffluc      GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2340
LP99__ffluc       GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2340
P100__ffluc       GCTAGTACCAACCCTATTTTCATTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTT 2340
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LP48__ffluc       ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2400
LP125__ffluc      ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2400
LP143__ffluc      ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2397
A511__ffluc       ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2397
LP124__ffluc      ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2400
lp101__ffluc      ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2400
LP99__ffluc       ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2400
P100__ffluc       ATCTAATTTACACGAAATTGCTTCTGGGGGCGCACCTCTTTCGAAAGAAGTCGGGGAAGC 2400
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LP48__ffluc       GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2460
LP125__ffluc      GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2460
LP143__ffluc      GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2457
A511__ffluc       GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2457
LP124__ffluc      GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2460
lp101__ffluc      GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2460
LP99__ffluc       GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2460
P100__ffluc       GGTTGCAAAACGCTTCCATCTTCCAGGGATACGACAAGGATATGGGCTCACTGAGACTAC 2460
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LP48__ffluc       ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2520
LP125__ffluc      ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2520
LP143__ffluc      ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2517
A511__ffluc       ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2517
LP124__ffluc      ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2520
lp101__ffluc      ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2520
LP99__ffluc       ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2520
P100__ffluc       ATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGT 2520
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LP48__ffluc       TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2580
LP125  ffluc      TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2580
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LP143__ffluc      TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2577
A511__ffluc       TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2577
LP124__ffluc      TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2580
lp101__ffluc      TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2580
LP99__ffluc       TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2580
P100__ffluc       TCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCA 2580
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LP48__ffluc       GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2640
LP125__ffluc      GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2640
LP143__ffluc      GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2637
A511__ffluc       GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2637
LP124__ffluc      GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2640
lp101__ffluc      GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2640
LP99__ffluc       GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2640
P100__ffluc       GAGAGGCGAATTATGTGTCAGAGGACCTATGATTATGTCCGGTTATGTAAACAATCCGGA 2640
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LP48__ffluc       AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2700
LP125__ffluc      AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2700
LP143__ffluc      AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2697
A511__ffluc       AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2697
LP124__ffluc      AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2700
lp101__ffluc      AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2700
LP99__ffluc       AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2700
P100__ffluc       AGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTG 2700
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LP48__ffluc       GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2760
LP125__ffluc      GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2760
LP143__ffluc      GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2757
A511__ffluc       GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2757
LP124__ffluc      GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2760
lp101__ffluc      GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2760
LP99__ffluc       GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2760
P100__ffluc       GGACGAAGACGAACACTTCTTCATAGTTGACCGCTTGAAGTCTTTAATTAAATACAAAGG 2760
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LP48__ffluc       ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2820
LP125__ffluc      ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2820
LP143__ffluc      ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2817
A511__ffluc       ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2817
LP124__ffluc      ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2820
lp101__ffluc      ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2820
LP99__ffluc       ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2820
P100__ffluc       ATATCAGGTGGCCCCCGCTGAATTGGAATCGATATTGTTACAACACCCCAACATCTTCGA 2820
                  ************************************************************

LP48__ffluc       CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCAGCCGCCGTTGTTGT 2880
LP125__ffluc      CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCAGCCGCCGTTGTTGT 2880
LP143__ffluc      CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGT 2877
A511__ffluc       CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGT 2877
LP124__ffluc      CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGT 2880
lp101__ffluc      CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGT 2880
LP99__ffluc       CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGT 2880
P100__ffluc       CGCGGGCGTGGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGT 2880
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LP48__ffluc       TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2940
LP125__ffluc      TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2940
LP143__ffluc      TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2937
A511__ffluc       TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2937
LP124__ffluc      TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2940
lp101__ffluc      TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2940
LP99__ffluc       TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2940
P100__ffluc       TTTGGAGCACGGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGT 2940
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LP48__ffluc       AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 3000
LP125__ffluc      AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 3000
LP143__ffluc      AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 2997
A511__ffluc       AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 2997
LP124__ffluc      AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 3000
lp101__ffluc      AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 3000
LP99__ffluc       AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 3000
P100__ffluc       AACAACCGCGAAAAAGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCT 3000
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LP48__ffluc       TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3060
LP125__ffluc      TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3060
LP143__ffluc      TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3057
A511__ffluc       TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3057
LP124__ffluc      TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3060
lp101__ffluc      TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3060
LP99__ffluc       TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3060
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P100__ffluc       TACCGGAAAACTCGACGCAAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGG 3060
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LP48__ffluc       AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3120
LP125__ffluc      AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3120
LP143__ffluc      AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3117
A511__ffluc       AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3117
LP124__ffluc      AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3120
lp101__ffluc      AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3120
LP99__ffluc       AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3120
P100__ffluc       AAAGTCCAAATTGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAGAGCAGATAA 3120
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LP48__ffluc       ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3180
LP125__ffluc      ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3180
LP143__ffluc      ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3177
A511__ffluc       ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3177
LP124__ffluc      ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3180
lp101__ffluc      ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3180
LP99__ffluc       ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3180
P100__ffluc       ATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATACAAACTTAGC 3180
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LP48__ffluc       TAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTC 3240
LP125__ffluc      TAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTC 3240
LP143__ffluc      TAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTC 3237
A511__ffluc       TAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTC 3237
LP124__ffluc      TAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTC 3240
lp101__ffluc      TAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTC 3240
LP99__ffluc       TAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAAAGGTATTTC 3240
P100__ffluc       TAATTATAAAAAAGTGAATACACGATTTGGAAATCTTAGTTTTGATGATAAAGGTATTTC 3240
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LP48__ffluc       TAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATAT 3300
LP125__ffluc      TAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATAT 3300
LP143__ffluc      TAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATAT 3297
A511__ffluc       TAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATAT 3297
LP124__ffluc      TAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATAT 3300
lp101__ffluc      TAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATAT 3300
LP99__ffluc       TAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATTCGAATATAT 3300
P100__ffluc       TAATGACCTAACGGAAGAGCAGCAAAAAGAATTAGGTAAGCTTAGAGGATTCGAATATAT 3300
                  ******* ********** ************************ ****************

LP48__ffluc       TAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAA----- 3355
LP125__ffluc      TAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAA----- 3355
LP143__ffluc      TAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACC 3357
A511__ffluc       TAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACC 3357
LP124__ffluc      TAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACC 3360
lp101__ffluc      TAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACC 3360
LP99__ffluc       TAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACC 3360
P100__ffluc       TAAGACAGAACAGAAAACGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAA----- 3355
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LP48__ffluc       ----------------------------------------------------------AGTAC 3360
LP125__ffluc      ----------------------------------------------------------AGTAC 3360
LP143__ffluc      TAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTAC 3417
A511__ffluc       TAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTAC 3417
LP124__ffluc      TAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTAC 3420
lp101__ffluc      TAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTAC 3420
LP99__ffluc       TAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAAGTAC 3420
P100__ffluc       ----------------------------------------------------------AGTAC 3360
                                                                           *****

LP48__ffluc       AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATT 3420
LP125__ffluc      AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATT 3420
LP143__ffluc      AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATT 3477
A511__ffluc       AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATT 3477
LP124__ffluc      AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATT 3480
lp101__ffluc      AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATT 3480
LP99__ffluc       AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATTAAAAGAATT 3480
P100__ffluc       AGAAAATGAATTAGACAGCTTCTTAGCTAAAGAACCTTCAATCAAAGAATTAAAAGAATT 3420
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LP48__ffluc       TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3480
LP125__ffluc      TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3480
LP143__ffluc      TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3537
A511__ffluc       TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3537
LP124__ffluc      TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3540
lp101__ffluc      TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3540
LP99__ffluc       TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3540
P100__ffluc       TGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAATTGAAGAACT 3480
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LP48__ffluc       AAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3540
LP125__ffluc      AAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3540
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LP143__ffluc      AAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3597
A511__ffluc       AAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3597
LP124__ffluc      AAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3600
lp101__ffluc      AAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3600
LP99__ffluc       AAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3600
P100__ffluc       AAAGAGAGGGTAATGTACAATGTATGGAGGTTATGAAGGACAAGATTCTTACGAATACCC 3540
                  ***************** ****************************************

LP48__ffluc       TTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3600
LP125__ffluc      TTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3600
LP143__ffluc      TTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3657
A511__ffluc       TTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3657
LP124__ffluc      TTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3660
lp101__ffluc      TTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3660
LP99__ffluc       TTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3660
P100__ffluc       TTACTCACACGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATATGTTCTTTC 3600
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LP48__ffluc       TGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3660
LP125__ffluc      TGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3660
LP143__ffluc      TGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3717
A511__ffluc       TGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3717
LP124__ffluc      TGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3720
lp101__ffluc      TGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3720
LP99__ffluc       TGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3720
P100__ffluc       TGATTATGGCTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCGTGTAGTAGA 3660
                  ********* ************************************************

LP48__ffluc       CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3720
LP125__ffluc      CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3720
LP143__ffluc      CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3777
A511__ffluc       CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3777
LP124__ffluc      CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3780
lp101__ffluc      CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3780
LP99__ffluc       CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3780
P100__ffluc       CCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGAGGTTGCCGT 3720
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LP48__ffluc       TGATAAGGC 3729
LP125__ffluc      TGATAAGGC 3729
LP143__ffluc      TGATAAGGC 3786
A511__ffluc       TGATAAGGC 3786
LP124__ffluc      TGATAAGGC 3789
lp101__ffluc      TGATAAGGC 3789
LP99__ffluc       TGATAAGGC 3789
P100__ffluc       TGATAAGGC 3729
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FIGURE 29

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LP124__nluc     ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
A511__nluc      ATGCCAAAAAATAACAAA---GAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 57
LP125__nluc     ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
LP40__nluc      ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
P100__nluc      ATGCCAAAAAATAACAAAGAAGAAGAAGTTAAAGAAGTAAACCTTAATTCAGTACAAGAG 60
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LP124__nluc     GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
A511__nluc      GATGCGTTAAAGTCCTTTACGACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 117
LP125__nluc     GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
LP40__nluc      GATGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
P100__nluc      GACGCGTTAAAGTCCTTTACAACTGGTTATGGTATCACACCTGATACACAAACAGATGCA 120
                ** ***************** ****************************************

LP124__nluc     GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
A511__nluc      GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 177
LP125__nluc     GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
LP40__nluc      GGGGCACTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAAAAT 180
P100__nluc      GGAGCATTAAGACGTGAGTTCCTAGACGACCAAATCTCAATGCTTACTTGGACAGAGAAT 180
                ** *** ************************************************** ***

LP124__nluc     GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
A511__nluc      GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 237
LP125__nluc     GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
LP40__nluc      GATTTAACATTCTACAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
P100__nluc      GATTTAACATTCTATAAAGACATCGCTAAAAAACCAGCTACATCTACAGTAGCAAAATAC 240
                ************** ************************************************

LP124__nluc     GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
A511__nluc      GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 297
LP125__nluc     GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
LP40__nluc      GATGTGTACATGCAACACGGTAAAGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
P100__nluc      GATGTATACATGCAACATGGTAAGGTAGGTCATACTAGATTTACTCGTGAGATTGGGGTA 300
                ***** *********** ***** ************************************

LP124__nluc     GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGAT 360
A511__nluc      GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCGAT 357
LP125__nluc     GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCCGAT 360
LP40__nluc      GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAACATGAAATTTGCTTCTGAT 360
P100__nluc      GCACCAGTAAGTGACCCTAACATCCGTCAAAAAACAGTAAATATGAAATTTGCTTCCGAT 360
                ****************************************** ************** ***

LP124__nluc     ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
A511__nluc      ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 417
LP125__nluc     ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
LP40__nluc      ACTAAAAATATTAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCTATGCAAATT 420
P100__nluc      ACTAAAAACATCAGTATCGCAGCAGGTCTAGTAAACAACATTCAAGACCCAATGCAAATT 420
                ******** ** ************************************ *********

LP124__nluc     TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
A511__nluc      TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 477
LP125__nluc     TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
LP40__nluc      TTGACTGATGATGCTATCGTAAATATCGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
P100__nluc      TTGACTGACGATGCTATCGTAAATATTGCTAAAACAATTGAGTGGGCTTCATTCTTTGGA 480
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LP124__nluc     GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
A511__nluc      GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 537
LP125__nluc     GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
LP40__nluc      GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGATTAGAATTTGATGGCTTGGCT 540
P100__nluc      GATTCTGACTTATCAGATAGCCCAGAACCACAAGCAGGACTAGAATTTGACGGCTTGGCT 540
                ************************************** ********** *********

LP124__nluc     AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
A511__nluc      AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 597
LP125__nluc     AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
LP40__nluc      AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
P100__nluc      AAACTTATTAACCAAGATAACGTTCATGATGCTCGTGGAGCTAGCTTGACTGAAAGCTTG 600
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LP124__nluc     TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
A511__nluc      TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 657
LP125__nluc     TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
LP40__nluc      TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
P100__nluc      TTAAACCAAGCAGCAGTAATGATTAGTAAAGGTTATGGTACACCTACAGATGCTTACATG 660
                ************************************************************

LP124__nluc     CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
A511__nluc      CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 717
LP125__nluc     CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
LP40__nluc      CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAACTTGTT 720
P100__nluc      CCAGTAGGGGTTCAAGCAGACTTTGTTAACCAACAACTTTCTAAACAAACACAGCTTGTT 720
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LP124__nluc      CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
A511__nluc       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 777
LP125__nluc      CGTGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
LP40__nluc       CGCGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
P100__nluc       CGTGATAACGGAAACAACGTAAGCGTTGGTTTCAACATCCAAGGTTTCCATTCAGCTCGT 780
                 ** ************************************************** ******

LP124__nluc      GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
A511__nluc       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 837
LP125__nluc      GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
LP40__nluc       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
P100__nluc       GGATTTATCAAACTTCACGGTTCTACAGTAATGGAAAACGAACAAATCTTAGATGAACGT 840
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LP124__nluc      ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
A511__nluc       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 897
LP125__nluc      ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
LP40__nluc       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
P100__nluc       ATTCTTGCTTTACCAACAGCTCCACAACCAGCTAAGGTAACTGCAACACAAGAAGCAGGT 900
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LP124__nluc      AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
A511__nluc       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 957
LP125__nluc      AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
LP40__nluc       AAAAAAGGACAATTTAGAGCAGAAGATTTAGCAGCACATGAATATAAAGTTGTTGTAAGT 960
P100__nluc       AAAAAAGGACAATTTAGAGCAGAAGACTTAGCAGCACACGAATACAAAGTTGTTGTAAGT 960
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LP124__nluc      TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
A511__nluc       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1017
LP125__nluc      TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
LP40__nluc       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
P100__nluc       TCTGACGATGCAGAGTCTATTGCAAGTGAAGTGGCTACAGCTACAGTTACTGCAAAAGAT 1020
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LP124__nluc      GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
A511__nluc       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1077
LP125__nluc      GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
LP40__nluc       GACGGCGTTAAACTAGAAATCGAATTAGCTCCAATGTATAGCTCTCGTCCACAATTCGTT 1080
P100__nluc       GACGGCGTTAAACTAGAAATCGAGTTAGCTCCAATGTACAGCTCCCGTCCACAATTCGTT 1080
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LP124__nluc      TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
A511__nluc       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1137
LP125__nluc      TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
LP40__nluc       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
P100__nluc       TCAATCTATAGAAAAGGTGCAGAAACAGGTTTATTCTACCTAATCGCTCGTGTACCTGCT 1140
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LP124__nluc      AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
A511__nluc       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1197
LP125__nluc      AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
LP40__nluc       AGCAAAGCAGAGAACAACGTAATCACTTTCTACGACTTAAACGACTCTATTCCTGAAACA 1200
P100__nluc       AGCAAAGCAGAGAACAACGTAATCACTTTCTATGACTTAAACGACTCTATTCCTGAAACA 1200
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LP124__nluc      GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
A511__nluc       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1257
LP125__nluc      GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
LP40__nluc       GTAGACGTATTCGTTGGTGAAATGTCGGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
P100__nluc       GTAGACGTATTCGTTGGTGAAATGTCTGCTAACGTAGTACACTTGTTTGAATTACTACCA 1260
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LP124__nluc      ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
A511__nluc       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1317
LP125__nluc      ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
LP40__nluc       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
P100__nluc       ATGATGAGATTACCTCTAGCTCAAATTAACGCATCTGTTACATTTGCAGTTTTATGGTAT 1320
                 ************************************************************

LP124__nluc      GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
A511__nluc       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1377
LP125__nluc      GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
LP40__nluc       GGCGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
P100__nluc       GGAGCATTAGCTCTAAGAGCACCTAAGAAATGGGTACGTATTAGAAACGTTAAATATATT 1380
                 ** ********************************************************

LP124__nluc      CCTGTAAAAAACGTTCATAGCAACTAATAATAAGAGGAGGTAAATATATATGGTCTTCAC 1440
A511__nluc       CCTGTAAAAAACGTTCATAGCAACTAA------GAGGAGGTAAATATATATGGTCTTCAC 1431
LP125__nluc      CCTGTAAAAAACGTTCATAGCAACTAATAATAAGAGGAGGTAAATATATATGGTCTTCAC 1440
LP40__nluc       CCTGTAAAAAACGTTCATAGCAACTAATAATAAGAGGAGGTAAATATATATGGTCTTCAC 1440
P100__nluc       CCTGTAAAAAACGTTCATAGCAACTAA------GAGGAGGTAAATATATATGGTCTTCAC 1434
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LP124__nluc       ACTCGAAGATTTCGTTGGGGACTGGCGACAGACAGCCGGCTACAACCTGGACCAAGTCCT 1500
A511__nluc        ACTCGAAGATTTCGTTGGGGACTGGCGACAGACAGCCGGCTACAACCTGGACCAAGTCCT 1491
LP125__nluc       ACTCGAAGATTTCGTTGGGGACTGGCGACAGACAGCCGGCTACAACCTGGACCAAGTCCT 1500
LP40__nluc        ACTCGAAGATTTCGTTGGGGACTGGCGACAGACAGCCGGCTACAACCTGGACCAAGTCCT 1500
P100__nluc        ACTCGAAGATTTCGTTGGGGACTGGCGACAGACAGCCGGCTACAACCTGGACCAAGTCCT 1494
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LP124__nluc       TGAACAGGGAGGTGTGTCCAGTTTGTTTCAGAATCTCGGGGTGTCCGTAACTCCGATCCA 1560
A511__nluc        TGAACAGGGAGGTGTGTCCAGTTTGTTTCAGAATCTCGGGGTGTCCGTAACTCCGATCCA 1551
LP125__nluc       TGAACAGGGAGGTGTGTCCAGTTTGTTTCAGAATCTCGGGGTGTCCGTAACTCCGATCCA 1560
LP40__nluc        TGAACAGGGAGGTGTGTCCAGTTTGTTTCAGAATCTCGGGGTGTCCGTAACTCCGATCCA 1560
P100__nluc        TGAACAGGGAGGTGTGTCCAGTTTGTTTCAGAATCTCGGGGTGTCCGTAACTCCGATCCA 1554
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LP124__nluc       AAGGATTGTCCTGAGCGGTGAAAATGGGCTGAAGATCGACATCCATGTCATCATCCCGTA 1620
A511__nluc        AAGGATTGTCCTGAGCGGTGAAAATGGGCTGAAGATCGACATCCATGTAATCATCCCGTA 1611
LP125__nluc       AAGGATTGTCCTGAGCGGTGAAAATGGGCTGAAGATCGACATCCATGTCATCATCCCGTA 1620
LP40__nluc        AAGGATTGTCCTGAGCGGTGAAAATGGGCTGAAGATCGACATCCATGTCATCATCCCGTA 1620
P100__nluc        AAGGATTGTCCTGAGCGGTGAAAATGGGCTGAAGATCGACATCCATGTCATCATCCCGTA 1614
                  ********************************************** ***********

LP124__nluc       TGAAGGTCTGAGCGGCGACCAAATGGGCCAGATCGAAAAAATTTTTAAGGTGGTGTACCC 1680
A511__nluc        TGAAGGTCTGAGCGGCGACCAAATGGGCCAGATCGAAAAAATTTTTAAGGTGGTGTACCC 1671
LP125__nluc       TGAAGGTCTGAGCGGCGACCAAATGGGCCAGATCGAAAAAATTTTTAAGGTGGTGTACCC 1680
LP40__nluc        TGAAGGTCTGAGCGGCGACCAAATGGGCCAGATCGAAAAAATTTTTAAGGTGGTGTACCC 1680
P100__nluc        TGAAGGTCTGAGCGGCGACCAAATGGGCCAGATCGAAAAAATTTTTAAGGTGGTGTACCC 1674
                  ************************************************************

LP124__nluc       TGTGGATGATCATCACTTTAAGGTGATCCTGCACTATGGCACACTGGTAATCGACGGGGT 1740
A511__nluc        TGTGGATGATCATCACTTTAAGGTGATCCTGCACTATGGCACACTGGTAATCGACGGGGT 1731
LP125__nluc       TGTGGATGATCATCACTTTAAGGTGATCCTGCACTATGGCACACTGGTAATCGACGGGGT 1740
LP40__nluc        TGTGGATGATCATCACTTTAAGGTGATCCTGCACTATGGCACACTGGTAATCGACGGGGT 1740
P100__nluc        TGTGGATGATCATCACTTTAAGGTGATCCTGCACTATGGCACACTGGTAATCGACGGGGT 1734
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LP124__nluc       TACGCCGAACATGATCGACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGG 1800
A511__nluc        TACGCCGAACATGATCGACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGG 1791
LP125__nluc       TACGCCGAACATGATCGACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGG 1800
LP40__nluc        TACGCCGAACATGATCGACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGG 1800
P100__nluc        TACGCCGAACATGATCGACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGG 1794
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LP124__nluc       CAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCT 1860
A511__nluc        CAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCT 1851
LP125__nluc       CAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCT 1860
LP40__nluc        CAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCT 1860
P100__nluc        CAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCT 1854
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LP124__nluc       GATCAACCCCGACGGCTCCCTGCTGTTCCGAGTAACCATCAACGGAGTGACCGGCTGGCG 1920
A511__nluc        GATCAACCCCGACGGCTCCCTGCTGTTCCGAGTAACCATCAACGGAGTGACCGGCTGGCG 1911
LP125__nluc       GATCAACCCCGACGGCTCCCTGCTGTTCCGAGTAACCATCAACGGAGTGACCGGCTGGCG 1920
LP40__nluc        GATCAACCCCGACGGCTCCCTGCTGTTCCGAGTAACCATCAACGGAGTGACCGGCTGGCG 1920
P100__nluc        GATCAACCCCGACGGCTCCCTGCTGTTCCGAGTAACCATCAACGGAGTGACCGGCTGGCG 1914
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LP124__nluc       GCTGTGCGAACGCATTCTGGCGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAG 1980
A511__nluc        GCTGTGCGAACGCATTCTGGCGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAG 1971
LP125__nluc       GCTGTGCGAACGCATTCTGGCGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAG 1980
LP40__nluc        GCTGTGCGAACGCATTCTGGCGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAG 1980
P100__nluc        GCTGTGCGAACGCATTCTGGCGTAATAATTATAGGATAATTGAATAAAAACAGTATAGAG 1974
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LP124__nluc       AGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATAC 2040
A511__nluc        AGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATAC 2031
LP125__nluc       AGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATAC 2040
LP40__nluc        AGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATAC 2040
P100__nluc        AGCAGATAAATACTGCTCTCTATTTTACTAATAAGGAGGATTTAAATTGCTAAAAAATAC 2034
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LP124__nluc       AAACTTAGCTAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAA 2100
A511__nluc        AAACTTAGCTAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAA 2091
LP125__nluc       AAACTTAGCTAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAA 2100
LP40__nluc        AAACTTAGCTAATTATAAAAAAGTGAATACACGGTTTGGAAATCTTAGTTTTGACGACAA 2100
P100__nluc        AAACTTAGCTAATTATAAAAAAGTGAATACACGATTTGGAAATCTTAGTTTTGATGATAA 2094
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LP124__nluc       AGGTATTTCTAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATT 2160
A511__nluc        AGGTATTTCTAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATT 2151
LP125__nluc       AGGTATTTCTAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATT 2160
LP40__nluc        AGGTATTTCTAATGACTTAACGGAAGAACAGCAAAAAGAATTAGGTAAGCTTCGAGGATT 2160
P100__nluc        AGGTATTTCTAATGACCTAACGGAAGAGCAGCAAAAAGAATTAGGTAAGCTTAGAGGATT 2154
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LP124__nluc      CGAATATATTAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAA 2220
A511__nluc       CGAATATATTAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAA 2211
LP125__nluc      CGAATATATTAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAA 2220
LP40__nluc       CGAATATATTAAGACAGAACAGAAAACAAAAGAAGAACCTAAGAAAGAAGAACCTAAGAA 2220
P100__nluc       CGAATATATTAAGACAGAACAGAAAACGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAA 2214
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LP124__nluc      AGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAA 2280
A511__nluc       AGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAAAGAAGAACCTAAGAA 2271
LP125__nluc      AGAA---------------------------------------------------------- 2224
LP40__nluc       AGAA-----------------------------------------GAACCTAAGAA 2235
P100__nluc       AGAA---------------------------------------------------------- 2218
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LP124__nluc      AGAAAGTACAGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATT 2340
A511__nluc       AGAAAGTACAGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATT 2331
LP125__nluc      ----AGTACAGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATT 2280
LP40__nluc       AGAAAGTACAGAAAATGAATTAGACAGCTTCTTAGCTAAAGAGCCTTCAATCAAAGAATT 2295
P100__nluc       ----AGTACAGAAAATGAATTAGACAGCTTCTTAGCTAAAGAACCTTCAATCAAAGAATT 2274
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LP124__nluc      AAAAGAATTTGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAAT 2400
A511__nluc       AAAAGAATTTGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAAT 2391
LP125__nluc      AAAAGAATTTGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAAT 2340
LP40__nluc       AAAAGAATTTGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAACGATATAAT 2355
P100__nluc       AAAAGAATTTGCGAGTAAAAAAGGCATTAAAATTGAAAAAACTAAGAAAAATGATATAAT 2334
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LP124__nluc      TGAAGAACTAAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTA 2460
A511__nluc       TGAAGAACTAAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTA 2451
LP125__nluc      TGAAGAACTAAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTA 2400
LP40__nluc       TGAAGAACTAAAGAGAGGGTAATGTATAATGTATGGAGGTTATGAAGGACAAGATTCTTA 2415
P100__nluc       TGAAGAACTAAAGAGAGGGTAATGTACAATGTATGGAGGTTATGAAGGACAAGATTCTTA 2394
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LP124__nluc      CGAATACCCTTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATA 2520
A511__nluc       CGAATACCCTTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATA 2511
LP125__nluc      CGAATACCCTTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATA 2460
LP40__nluc       CGAATACCCTTACTCACATGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATA 2475
P100__nluc       CGAATACCCTTACTCACACGGGAACCCTAAGCATGTAGAGCCAGAAAAAGTTGACGAATA 2454
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LP124__nluc      TGTTCTTTCTGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCG 2580
A511__nluc       TGTTCTTTCTGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCG 2571
LP125__nluc      TGTTCTTTCTGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCG 2520
LP40__nluc       TGTTCTTTCTGATTATGGTTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCG 2535
P100__nluc       TGTTCTTTCTGATTATGGCTGGACTGCGGAAACAATTAAAGCATACATGTATGGTGTTCG 2514
                 ****************** ****************************************

LP124__nluc      TGTAGTAGACCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGA 2640
A511__nluc       TGTAGTAGACCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGA 2631
LP125__nluc      TGTAGTAGACCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGA 2580
LP40__nluc       TGTAGTAGACCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGA 2595
P100__nluc       TGTAGTAGACCCTGAAACAGGAGAGGAAATGGGAGACACCTTCTACAATCATATTATAGA 2574
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LP124__nluc      GGTTGCCGTTGATAAGGC 2658
A511__nluc       GGTTGCCGTTGATAAGGC 2649
LP125__nluc      GGTTGCCGTTGATAAGGC 2598
LP40__nluc       GGTTGCCGTTGATAAGGC 2613
P100__nluc       GGTTGCCGTTGATAAGGC 2592
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2015/029992

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K35/76 C12N7/00 C12Q1/04
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 2014/160818 A2 (SAMPLE TECHNOLOGIES INC [US]) 2 October 2014 (2014-10-02) paragraph [0024] - paragraph [0031] paragraphs [0037], [0043], [0059], [0061], [0063], [0121] paragraph [0137] - paragraph [0154] paragraphs [0201], [0202]; claims 1, 36-45, 51, 59, 60, 80-86; examples 5, 8 ----- -/--	1-3,6,7, 9,10,12, 14-18, 37-50, 56,57, 59,60

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 July 2015	28/07/2015

Name and mailing address of the ISA/	Authorized officer
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	WO 2009/140375 A2 (GUILD ASS INC [US]; SCHOFIELD DAVID A [US]) 19 November 2009 (2009-11-19) page 5, line 27 - page 7, line 7 page 10, line 22 - page 12, line 25 page 14, line 18 - page 16, line 9	1-63
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2015/029992

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