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Methods and compositions for detecting transfusion-transmitted pathogens

Abstract

Probe sets capable of detecting pathogen nucleic acids in a sample are described. The probe set can be provided on a solid support, such as a microarray. Methods of detecting pathogen nucleic acids in a sample using the probe set are also provided. In some examples, the probes and methods are capable of detecting one or more RNA viruses, one or more DNA viruses, one or more bacterial nucleic acids, and/or one or more protozoan nucleic acids in a sample.

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Background/Summary

CROSS REFERENCE TO RELATED APPLICATIONS (1) This application is the U.S. National Stage of International Application No. PCT/US2020/016262, filed Jan. 31, 2020, which was published in English under PCT Article 21 (2), which in turn claims the benefit of U.S. Provisional Application No. 62/799,482, filed Jan. 31, 2019, which is incorporated herein by reference in its entirety.

FIELD

16:83-95, 2016).

- (1) This disclosure relates to compositions and methods for detecting pathogens in a sample, particularly probes and microarrays and methods of their use.

 BACKGROUND
- (2) Each year millions of blood donations are collected globally and millions of blood components are transfused to patients. Though screening of these blood units using serologic and nucleic acid testing (NAT) has greatly reduced the risk of some transfusion-transmitted infections (TTIs), the vast majority of bloodborne agents are not screened (Alter et al., *Semin. Hematol.* 44:32-41, 2007; Glynn et al., *Transfusion* 53:438-454, 2013; Leveton et al., *Transfusion* 36:919-927, 1996). The U.S. Food and Drug Administration-licensed methods for infectious disease screening of donor blood include: 1) nucleic acid testing (NAT) for Hepatitis B virus (HBV), Hepatitis C virus (HCV), HIV-1 and -2, *Babesia*, West Nile virus (WNV) and Zika virus (ZIKV); and 2) immunoassays for HBV, HCV, HIV-1 and -2, cytomegalovirus (CMV), human T-cell lymphotropic virus I and II (HTLV), *Treponema pallidum* (syphilis), and *Trypanosoma cruzi* (Chagas). HTLV, syphilis, and Chagas antibody testing fail to detect these pathogens during a window period and Chagas is screened only once on samples from first-time blood donors (Duncan et al., *Exp. Rev. Mol. Diagn*.
- (3) The American Association of Blood Banks Transfusion-Transmitted Diseases Committee produced a list of over 30 pathogens of concern for transmission via blood that included bacteria, parasites, prions and viruses (Stramer et al., *Transfusion* 49:1S-29S, 2009). Only prions cannot be detected by currently available technology. Nearly all the other agents currently require individual qPCR or serologic testing and it is logistically impractical and cost prohibitive to test all known and potential agents individually (Stramer *ISBT Science Series* 9:30-37, 2014; Atrey et al., *Transfusion* 51:1855-1871, 2011).

(4) Multiplex PCR-based devices for testing blood-borne pathogens are limited. FDA-approved blood donor screening assays that use transcription-mediated amplification for multiplex detection of HBV, HCV, and HIV 1 and 2 include the cobas TaqScreen MPX Test (Roche Molecular Systems, Inc.) and the Procleix Ultrio Plus (Gen-Probe, Inc.) (Duncan et al., *Exp. Rev. Mol. Diagn.* 16:83-95, 2016).

SUMMARY

- (5) A multiplex assay capable of detecting many, most, or all known pathogens of concern in a single small blood sample with high sensitivity and specificity could significantly increase the safety of the blood supply. Further, to counter emerging pathogens, the platform should be adaptable for rapid addition and validation of probes to detect new agents. Microarray-based technology offers the advantage of multiplex detection in a miniaturized format with high adaptability.
- (6) Disclosed herein are probe sets that include probes with at least 90% identity (such as at least 90%, at least 95%, at least 98%, or at least 99% identity) with the nucleic acid sequences of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769, or subsets thereof. In some examples, the probe set includes probes with the nucleic acid sequences of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769, or a subset thereof. In some embodiments, the probe set includes one or more probes (such as 30 or more probes) for one or more RNA viruses, such as one or more of Chikungunya virus, Dengue virus type 1, Dengue virus type 2, Dengue virus type 3, Dengue virus type 4, Hepatitis A virus, Hepatitis C virus type 1, Hepatitis C virus type 2, Hepatitis C virus type 3, Hepatitis E virus, Human immunodeficiency virus type 1, Human immunodeficiency virus type 2, Human Tlymphotropic virus type I, Human T-lymphotropic virus type II, West Nile virus, and Zika virus. (7) In other embodiments, the probe set includes one or more probes for one or more DNA viruses, such as one or more of cytomegalovirus (CMV, also known as HHV-5), Epstein Barr virus (EBV, also known as HHV-4, for example subtype B95-8 and/or AG876)), human herpes virus 8 (HHV-8), Hepatitis B virus (such as one or more of Hepatitis B virus subtype adw, subtype ayw, subtype adr, and subtype ayr), human parvovirus B19, and human papillomavirus (HPV, such as one or more of type 6, 11, 16, and 18). In some embodiments, the probe set includes probes with at least 90% identity (such as at least 90%, at least 95%, at least 98%, or at least 99% identity) with the nucleic acid sequences of SEQ ID NOs: 1770-2647, or a subset thereof. In some examples, the probe set includes probes with the nucleic acid sequences of SEQ ID NOs: 1770-2647, or a subset thereof.
- (8) Further disclosed are probe sets that include one or more probes for one or more bacterial or protozoan pathogens, such as one or more of *Treponema pallidum*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris*, *Borrelia burgdorferi*, *Coxiella burnetii*, *Trypanosoma brucei*, *Trypanosoma cruzi Leishmania major*, *Babesia microti*, *Plasmodium falciparum*, and *Plasmodium vivax*. In some embodiments, the probe set includes probes with at least 90% identity (such as at least 90%, at least 95%, at least 98%, or at least 99% identity) with the nucleic acid sequences of SEQ ID NOs: 2648-3207, or a subset thereof. In some examples, the probe set includes probes with the nucleic acid sequences of SEQ ID NOs: 2648-3207, or a subset thereof.
- (9) In some embodiments, the disclosed probe sets include at least one negative control probe and/or at least one positive control probe. In some examples the negative control probe is a probe with at least 90% identity (such as at least 90%, at least 95%, at least 98%, or at least 99% identity) with the nucleic acid sequences of any one of SEQ ID NOs: 1571-1690. In other examples the control probe is a probe with at least 90% identity (such as at least 90%, at least 95%, at least 98%, or at least 99% identity) with the nucleic acid sequences of any one of SEQ ID NOs: 3208-3628. (10) In one non-limiting embodiment, the probe set is a set of probes including each of SEQ ID NOs: 1-1769. In another non-limiting embodiment, the probe set is a set of probes including each of SEQ ID NOs: 1770-2647 and 3208-3628, each of SEQ ID NOs: 2648-3628, or each of SEQ ID NOs: 1770-3628. In a further non-limiting embodiment, the microarray includes probes including

each of SEQ ID NOs: 1-3628.

- (11) Also disclosed are microarrays that include a probe set described herein, for example, wherein the probes are covalently linked to a solid support. In one non-limiting example, the microarray includes probes with at least 90% identity (such as at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identity) with the nucleic acid sequences of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769, or subsets thereof. In another non-limiting example, the microarray includes probes with at least 90% identity (such as at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identity) with the nucleic acid sequences of SEQ ID NOs: 1770-2647, or subsets thereof. In a further non-limiting example, the microarray includes probes with at least 90% identity (such as at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identity) with the nucleic acid sequences of SEQ ID NOs: 2648-3207, or subsets thereof. In yet another nonlimiting embodiment, the microarray includes probes with at least 90% identity (such as at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identity) with the nucleic acid sequences of SEQ ID NOs: 1770-3207, or subsets thereof. The microarray may further include negative and/or positive control probes. In one non-limiting embodiment, the microarray includes probes including each of SEQ ID NOs: 1-1769. In other non-limiting embodiments, the microarray includes probes including each of SEQ ID NOs: 1770-2647 and 3208-3628, each of SEQ ID NOs: 2648-3628, each of SEQ ID NOs: 1770-3628. In a further non-limiting embodiment, the microarray includes probes including each of SEQ ID NOs: 1-3628.
- (12) Disclosed herein are methods of detecting one or more pathogen nucleic acids in a sample. In some examples, the methods include detecting nucleic acids from one or more RNA viruses, such as one or more of Chikungunya virus, Dengue virus type 1, Dengue virus type 2, Dengue virus type 3, Dengue virus type 4, Hepatitis A virus, Hepatitis C virus type 1, Hepatitis C virus type 2, Hepatitis C virus type 3, Hepatitis E virus, Human immunodeficiency virus type 1, Human immunodeficiency virus type 2, Human T-lymphotropic virus type I, Human T-lymphotropic virus type II, West Nile virus, and Zika virus in a sample. In other examples, the methods include detecting nucleic acids from one or more DNA viruses, such as one or more of cytomegalovirus, Epstein Barr virus, human herpes virus 8, Hepatitis B virus, human parvovirus B19, and human papillomavirus.
- (13) Also disclosed are methods of detecting one or more bacterial and/or protozoan nucleic acids in a sample. In some examples, the methods include detecting nucleic acids from one or more of *Treponema pallidum*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris*, *Borrelia burgdorferi*, *Coxiella burnetii*, *Trypanosoma brucei*, *Trypanosoma cruzi*, *Leishmania major*, *Babesia microti*, *Plasmodium falciparum*, and *Plasmodium vivax*.
- (14) In some examples, the methods include contacting a sample with a disclosed probe set or microarray under conditions sufficient to allow hybridization of pathogen nucleic acids present in the sample to the probes of the probe set or microarray and measuring hybridization of the sample to one or more of the probes, thereby detecting one or more nucleic acids in the sample. The sample may be a blood, serum, or plasma sample, or nucleic acids (such as RNA or cDNA) isolated from the sample. In particular examples, the sample is a blood donation sample or nucleic acids isolated from a blood donation sample. In particular examples, nucleic acids (such as RNA or cDNA) from the sample are labeled prior to contacting the probe set or microarray with the nucleic acids. In one example, the method includes preparing cDNA from the sample and labeling the cDNA. In some examples, the method does not include amplifying RNA from the sample prior to preparing the cDNA.
- (15) The foregoing and other features of the disclosure will become more apparent from the following detailed description, which proceeds with reference to the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

- (1) FIGS. **1**A-**1**C are a series of panels showing pathogen chip design (FIG. **1**A), sample preparation work flow (FIG. **1**B), and analysis strategy (FIG. **1**C) for pathogen detection microarrays.
- (2) FIGS. **2**A-**2**C are a series of graphs showing amplification method and Pathogen Chip assay performance assessed using positive control viral RNAs. FIG. **2**A shows SPIA amplification vs. standard (STD) method. cDNA concentration after amplification for four representative viral RNAs is shown. Starting RNA concentration was <10 ng/µl each. FIG. **2**B shows Pathogen chip assay performance 1. Bars are the mean of Cy3 signal for the Chikungunya and West Nile probes hybridized to test samples positive for CHIKV and WNV and a negative plasma sample. Only probes specific to target showed a specific hybridization signal. No signal was detected for negative plasma. FIG. **2**C shows Pathogen chip assay performance 2. Detection responses of four representative samples (Dengue-4) were measured over a dilution series from 10,000 to 10 genomic copies per sample. Bars are the mean of Cy3 signals for all probes to the indicated viruses hybridized to test samples.

SEQUENCE LISTING

- (3) Any nucleic acid and amino acid sequences listed herein or in the accompanying sequence listing are shown using standard letter abbreviations for nucleotide bases and amino acids, as defined in 37 C.F.R. § 1.822. In at least some cases, only one strand of each nucleic acid sequence is shown, but the complementary strand is understood as included by any reference to the displayed strand.
- (4) The Sequence Listing is submitted as an ASCII text file in the form of the file named Sequence_Listing.txt, which was created on Jul. 22, 2021, and is 676,876 bytes, which is incorporated by reference herein.
- (5) In the accompanying sequence listing: SEQ ID NOs: 1-110 are Hepatitis C virus genotype 1 probes SEQ ID NOs: 111-210 are Hepatitis C virus genotype 2 probes SEQ ID NOs: 211-310 are Hepatitis C virus genotype 3 probes SEQ ID NOs: 311-400 are Human Immunodeficiency virus 1 probes SEQ ID NOs: 401-510 are Human Immunodeficiency virus 2 probes SEQ ID NOs: 511-570 are Human T-lymphotropic virus I probes SEQ ID NOs: 571-660 are Human T-lymphotropic virus II probes SEQ ID NOs: 661-760 are West Nile virus NY99 probes SEQ ID NOs: 761-870 are West Nile virus 956 probes SEQ ID NOs: 871-900 are Chikungunya virus probes SEQ ID NOs: 901-1000 are Dengue virus 1 probes SEQ ID NOs: 1001-1100 are Dengue virus 2 probes SEQ ID NOs: 1101-1199 are Dengue virus 3 probes SEQ ID NOs: 1200-1300 are Dengue virus 4 probes SEQ ID NOs: 1301-1390 are GB virus C/Hepatitis G virus probes SEQ ID NOs: 1391-1500 are Hepatitis A virus probes SEQ ID NOs: 1501-1570 are Hepatitis E virus probes SEQ ID NOs: 1571-1580 are White clover cryptic virus 1 probes SEQ ID NOs: 1581-1620 are Broad bean wilt virus 1 probes SEQ ID NOs: 1621-1690 are Lettuce necrotic yellows virus probes SEQ ID NOs: 1691-1700 are Zika virus isolate Brazil-ZKV2015 probes SEQ ID NOs: 1701-1710 are Zika virus strain PRVABC59 probes SEQ ID NOs: 1711-1720 are Zika virus isolate Z1106033 probes SEQ ID NOs: 1721-1730 are Zika virus isolate SSABR1 probes SEQ ID NOs: 1731-1769 are Zika virus strain ZikaSPH2015 probes SEQ ID NOs: 1770-1852 are Cytomegalovirus probes SEQ ID NOs: 1853-1917 are Epstein Barr virus B95-8 probes SEQ ID NOs: 1918-2023 are Epstein Barr virus AG876 probes SEQ ID NOs: 2024-2108 are Human herpesvirus 8 probes SEQ ID NOs: 2109-2192 are Human papillomavirus subtype 6b probes SEQ ID NOs: 2193-2271 are Human papillomavirus subtype 11 probes SEQ ID NOs: 2272-2342 are Human papillomavirus subtype 16 probes SEQ ID NOs: 2343-2419 are Human papillomavirus subtype 18 probes SEQ ID NOs: 2420-2470 are Hepatitis B virus subtype adw probes SEQ ID NOs: 2471-2520 are Hepatitis B virus subtype ayw probes SEQ ID NOs: 2521-2556 are Hepatitis B virus subtype adr probes SEQ ID NOs: 2557-2602 are Hepatitis B virus subtype ayr probes SEQ ID NOs: 2603-2647 are Human parvovirus B19

probes SEQ ID NOs: 2648-2751 are *Treponema pallidum* probes SEQ ID NOs: 2752-2852 are *Ehrlichia chaffeensis* probes SEQ ID NOs: 2853-2861 are *Ehrlichia ewingii* probes SEQ ID NOs: 2862-2922 are *Ehrlichia muris* probes SEQ ID NOs: 2923-3001 are *Borrelia burgdorferi* probes SEQ ID NOs: 3002-3085 are *Coxiella burnetii* probes SEQ ID NOs: 3086-3097 are *Trypanosoma brucei* probes SEQ ID NO: 3098 is a *Trypanosoma cruzi* probe SEQ ID NOs: 3099-3113 are *Leishmania major* probes SEQ ID NOs: 3114-3154 are *Babesia microti* probes SEQ ID NOs: 3155-3185 are *Plasmodium falciparum* probes SEQ ID NOs: 3186-3207 are *Plasmodium vivax* probes SEQ ID NOs: 3208-3301 are human ACTB probes SEQ ID NOs: 3302-3385 are human ARL1 probes SEQ ID NOs: 3386-3519 are human CCDN1 probes SEQ ID NOs: 3520-3557 are *Aedes albopictus* densovirus 2 probes SEQ ID NOs: 3558-3598 are Maize streak virus probes SEQ ID NOs: 3599-3628 are Tomato pseudo-curly top virus probes

DETAILED DESCRIPTION

(6) Disclosed herein are customized sets of probes, including microarray-based pathogen chips, for simultaneous detection of nucleic acids from RNA viruses, DNA viruses, and/or bacteria or protozoan pathogens in blood samples (such as human plasma) that are designed to have the flexibility to expand to detect emerging agents in a relatively short time frame. The presence of multiple probes per target represents an advantage in comparison to traditional NAT or EIA assays since the pathogen(s) can be detected even in the case of failure of one of the probes due to mutation (Petrik *Vox Sanguinis* 80:1-11, 2001). The flexibility and high-throughput capability of microarrays hold great potential for pathogen detection and identification, but historically have had limitations in detecting the presence of the low viral levels (Chen et al., *J. Vis. Exp.* 50:e2536, 2011; Wang et al., *Proc. Natl. Acad. Sci. USA* 99:15687-15692, 2002; Eckburg et al., *Clin. Infect. Dis.* 43:e71-e76, 2006). Disclosed herein are probe sets and microarray assays that include: 1) a platform design that simultaneously detects and distinguishes multiple pathogens and closely related strains or subtypes; and 2) a combination of amplification and labeling protocols to detect multiple targets present at low levels in a sample.

I. Terms

- (7) Unless otherwise noted, technical terms are used according to conventional usage. Definitions of common terms in molecular biology may be found in *Lewin's Genes X*, ed. Krebs et al., Jones and Bartlett Publishers, 2009 (ISBN 0763766321); Kendrew et al. (eds.), *The Encyclopedia of Molecular Biology*, published by Blackwell Publishers, 1994 (ISBN 0632021829); Robert A. Meyers (ed.), *Molecular Biology and Biotechnology: a Comprehensive Desk Reference*, published by Wiley, John & Sons, Inc., 1995 (ISBN 0471186341); and George P. Rédei, *Encyclopedic Dictionary of Genetics, Genomics, Proteomics and Informatics*, 3.sup.rd Edition, Springer, 2008 (ISBN: 1402067534), and other similar references.
- (8) Unless otherwise explained, 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 disclosure belongs. The singular terms "a," "an," and "the" include plural referents unless the context clearly indicates otherwise. Similarly, the word "or" is intended to include "and" unless the context clearly indicates otherwise. Hence "comprising A or B" means including A, or B, or A and B. It is further to be understood that all base sizes or amino acid sizes, and all molecular weight or molecular mass values, given for nucleic acids or polypeptides are approximate, and are provided for description. (9) Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including explanations of terms, will control. In addition, the materials, methods, and examples are
- (10) In order to facilitate review of the various embodiments of the disclosure, the following explanations of specific terms are provided:

illustrative only and not intended to be limiting.

- (11) Array or Microarray: An arrangement of nucleic acids (such as DNA or RNA) or proteins (such as antibodies) in assigned locations on a matrix or substrate. In some examples, the nucleic acid molecules or proteins are attached covalently to the matrix or substrate.
- (12) *Babesia*: A tick-borne protozoan parasite that infects vertebrate red blood cells. In humans, *Babesia* species may cause asymptomatic infection or babesiosis, characterized by flu-like symptoms. Most cases of transmission between humans are attributed to a tick vector; however, it may also be transmitted through blood transfusion or organ donation. The most common pathogenic species in humans are *Babesia divergens* and *Babesia* microti. *Babesia* sequences are publicly available, and include GenBank Accession Nos. ASM107745v2 (*Babesia divergens*) and ASM69194v2 and ASM165006v1 (*Babesia microti*), which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.
- (13) *Borrelia*: A genus of tick-borne spirochete bacteria that cause Lyme disease. The major species of *Borrelia* that cause Lyme disease include *Borrelia burgdorferi*, *Borrelia afzelii*, *Borrelia garinii*, and *Borrelia mayonii*. *Borrelia* has been identified in blood stored for donation, though there is currently no evidence of Lyme disease linked to blood transfusion. *Borrelia* sequences are publicly available, and include GenBank Accession Nos. ASM868v2 (*Borrelia burgdorferi*), ASM30473v1 (*Borrelia afzelii*), ASM192254v1 (*Borrelia garinii*), and ASM194566v1 (*Borrelia mayonii*), which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020).
- (14) Chikungunya virus (CHIKV): A positive-sense single-stranded RNA virus of the alphavirus genus in the family Togaviridae. This virus is primarily transmitted by *Aedes* mosquitoes, particularly *A. albopictus* and *A. aegypti*. The symptoms of CHIKV infection include rash, high fever and joint pain. CHIKV was first isolated in Tanzania in 1952 and re-emerged in Kenya in 2004. The evolution and spread of this virus into new geographic areas, and the disease severity resulting from CHIKV infection, present a serious public health concern. CHIKV sequences are publicly available, and include GenBank Accession No. NC_004162 (gi|27754751)), which is incorporated by reference in its entirety as present in GenBank on Jan. 30, 2019.
- (15) *Coxiella burnetii*: A Gram-negative bacteria that causes Q fever. Symptoms are typically flulike and may be mild or severe, and a small percentage of infected individuals develop chronic Q fever. The bacteria infects livestock (such as cows, sheep, and goats) and is transmitted to humans by contact with feces, urine, milk, or other products from an infected animal, typically by breathing dust contaminated with the bacteria. *Coxiella burnetii* sequences are publicly available, and includes GenBank Accession No. ASM776v2, which is incorporated by reference in its entirety as present in GenBank on Jan. 30, 2020.
- (16) Cytomegalovirus (CMV): Also known as human herpesvirus 5. A common virus that infects up to 50% of adults by the age of 40. Most people show no symptoms of infection or only mild symptoms; however, babies born with congenital CMV infection may have long-term health problems. CMV is transmitted by body fluids, including blood transfusions. CMV sequences are publicly available, and include GenBank Accession No. NC_006273, which is incorporated by reference in its entirety as present in GenBank on Jan. 30, 2020.
- (17) Dengue virus (DEN): An RNA virus of the family Flaviviridae, genus *Flavivirus*. There are four serotypes of dengue virus, referred to as DEN1, DEN2, DEN3 and DEN4. All four serotypes can cause the full spectrum of dengue disease. Infection with one serotype can produce lifelong immunity to that serotype. However, severe complications can occur upon subsequent infection by a different serotype. Dengue virus is primarily transmitted by *Aedes* mosquitoes, particularly *A. aegypti*. Symptoms of dengue virus infection include fever, headache, muscle and joint pain and a skin rash similar to measles. In a small percentage of cases, the infection develops into a lifethreatening dengue hemorrhagic fever, typically resulting in bleeding, low platelet levels and blood plasma leakage, or into dengue shock syndrome, characterized by dangerously low blood pressure. DEN sequences are publicly available, and include GenBank Accession Nos. NC_001477 (gi|9626685) (DEN1), NC_001474 (gi|158976983) (DEN2), NC_001475 (gi|163644368) (DEN3),

- and NC_002640 (gi|12084822) (DEN4), which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2019.
- (18) Epstein-Barr virus (EBV): Also known as human herpesvirus 4. EBV is a common virus that is spread primarily through saliva, though it can also be spread by sexual contact, blood transfusion, and organ transplantation. EBV causes infectious mononucleosis, characterized by fatigue, fever, swollen lymph nodes, and sore throat; however, EBV infection may also be asymptomatic. EBV sequences are publicly available, and include GenBank Accession Nos. AJ278309 (EBV strain B95-8), DQ279927 (EBV strain AG876), and NC_009334, all of which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.
- (19) *Ehrlichia*: A genus of tick-borne bacteria that causes ehrlichiosis. In some cases, *Ehrlichia* has been transmitted through blood transfusion or organ transplantation. Symptoms can include rash, fever, headache, muscle aches, nausea, vomiting, and diarrhea. Severe, late stage illness can include neural damage, respiratory failure, and organ failure. Disease causing species include *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, and *Ehrlichia muris*. *Ehrlichia* sequences are publicly available, and include GenBank Accession Nos. NC_007799 (*E. chaffeensis*) and NC_023063 (*E. muris*), which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.
- (20) Hepatitis A virus (HAV): A single-stranded RNA virus in the order Picomavirales, family Picornaviridae. The virus is transmitted through fecal-oral and blood routes. HAV causes symptoms such as nausea, vomiting, diarrhea, jaundice, fever, and abdominal pain and typically lasts about 8 weeks. Acute liver failure may occur in some cases. HAV sequences are publicly available, and include GenBank Accession No. NC_001489 (gi|9626732), which is incorporated by reference in its entirety as present in GenBank on Jan. 30, 2019.
- (21) Hepatitis B virus (HBV): A DNA virus of the Hepadnaviridae family. HBV is transmitted through blood or bodily fluids and new infections are frequently asymptomatic in healthy adults. (22) Immunosuppressed adults and children less than 5 years of age more commonly exhibit symptoms, including flu-like symptoms and jaundice. HBV sequences are publicly available and include GenBank Accession Nos. AY518556 (subtype adw), NC_003977 (subtype ayw), AY123041 (subtype adr), and X04615 (subtype ayr), all of which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.
- (23) Hepatitis C virus (HCV): A single-stranded positive sense RNA virus of the family Flaviviridae. HCV is transmitted primarily through blood and acute infection typically causes mild or no symptoms. However, chronic infection frequently leads to liver disease, including cirrhosis, liver failure, and/or hepatocellular carcinoma. HCV type 1 sequences are publicly available, and include GenBank Accession No. NC_004102 (gi|22129792). HCV type 2 sequences are also publicly available, and include GenBank Accession No. NC_009823 (gi|157781212). HCV type 3 sequences are also publicly available, and include GenBank Accession No. NC_009824 (gi|157781216). Each of these sequences are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2019.
- (24) Hepatitis E virus (HEV): A single-stranded positive sense RNA virus that is currently classified in the Hepeviridae family, genus *Orthohepevirus*. HEV causes liver inflammation, and is typically an acute and self-limiting infection. However, it can cause chronic hepatitis in individuals with weakened immune systems, particularly organ transplant recipients. HEV sequences are publicly available, and include GenBank Accession No. NC_001434 (gi|9626440), which is incorporated by reference in its entirety as present in GenBank on Jan. 30, 2019.
- (25) Human Immunodeficiency virus (HIV): A single-stranded positive-sense RNA virus (retrovirus) that causes HIV infection and acquired immunodeficiency syndrome (AIDS). HIV is transmitted by blood or sexual contact. HIV type 1 sequences are publicly available, and include GenBank Accession No. NC_001802 (gi|9629357). HIV type 2 sequences are also publicly available and include GenBank Accession No. NC_001722 (gi|9628880). Each sequence is

- incorporated by reference in their entirety as present in GenBank on Jan. 30, 2019
- (26) Human Herpesvirus 8 (HHV-8): Also known as Kaposi sarcoma-associated herpesvirus. HHV-8 is associated with Kaposi sarcoma and other cancers, including some lymphomas. It is transmitted through bodily fluids, including blood, saliva, and sexual contact. HHV-8 sequences are publicly available and include GenBank Accession No. NC_009333, which is incorporated by reference in its entirety as present in GenBank on Jan. 30, 2020.
- (27) Human parvovirus: A single-stranded DNA virus of the Parvoviridae family. Parvovirus B19 is the only parvovirus known to infect humans. B19 primarily causes disease in children, and causes what is sometimes called "fifth disease," a mild rash. Parvovirus B19 can be transmitted via respiratory secretions or through blood or blood products. Human parvovirus B19 sequences are publicly available and include GenBank Accession No. NC_000883, which is incorporated by reference in its entirety as present in GenBank on Jan. 30, 2020.
- (28) Human papillomavirus (HPV): A DNA virus of the family Papillomaviridae. HPV is a common sexually transmitted virus that can cause warts and cancers, including cervical cancer and head and neck cancer, in some individuals. HPV DNA can be detected in the blood in some cases; however, it is not clear whether it can be transmitted by blood transfusion. There are over 100 known types of HPV to date. HPV sequences are publicly available, and include GenBank Accession Nos. HG793809 (type 6), HE574701 (type 11), NC_001526 (type 16), and NC_001357 (type 18), each of which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.
- (29) Human T-lymphotropic virus (HTLV): A group of positive-sense RNA retroviruses that are implicated in cancer (for example, T-cell lymphomas) and myelopathy. HTLV type I sequences are publicly available, and include GenBank Accession Nos. AF033817 and NC_001436 (gi|9626453). HTLV type II sequences are also publicly available and include GenBank Accession No. NC_001488 (gi|9626726). Each sequence is incorporated by reference in their entirety as present in GenBank on Jan. 30, 2019
- (30) *Leishmania major*: A trypanosomatid parasite transmitted by sand flies. *L. major* causes cutaneous leishmaniosis. *L. major* sequences are publicly available, and include GenBank Accession No. ASM272v2, incorporated by reference in its entirety as present in GenBank on Jan. 30, 2020.
- (31) *Plasmodium*: A genus of mosquito-transmitted protozoan parasites that causes malaria in humans. The two major malaria causing *Plasmodium* species in humans are *P. falciparum* and *P. vivax*. *P. falciparum* is also associated with Burkitt's lymphoma. *Plasmodium* can be transmitted by blood transfusion, causing transfusion-transmitted malaria. *Plasmodium* sequences are publicly available and include GenBank Accession No. ASM276v2 (*P. falciparum*) and ASM241v2 (*P. vivax*), which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.
- (32) Probe: A probe typically comprises an isolated nucleic acid (for example, at least 10 or more nucleotides in length, such as 10-60, 15-50, 20-40, 20-50, 25-50, or 30-60 nucleotides in length). In some examples, a probe includes a detectable label, while in other examples a probe does not include a detectable label.
- (33) Sample (or biological sample): A biological specimen containing nucleic acids (for example, DNA, RNA, and/or mRNA), proteins, or combinations thereof, obtained from a subject. Examples include, but are not limited to, peripheral blood, serum, plasma, urine, saliva, tissue biopsy, fine needle aspirate, surgical specimen, and autopsy material. In some examples, a sample includes blood, serum, or plasma.
- (34) Subject: A living multi-cellular vertebrate organism, a category that includes human and non-human mammals. In one example, a subject is a blood donor.
- (35) *Treponema*: A genus of spirochete bacteria. The major pathogenic species in humans is *Treponema pallidum*, of which subspecies *T. pallidum pallidum* causes syphilis. The bacteria is

transmitted primarily by sexual contact. Nucleic acid sequences for *T. pallidum pallidum* are publicly available and include GenBank Accession Nos. NC_016844 and NC_00919, which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.

- (36) *Trypanosoma*: A genus of protozoan parasites transmitted by blood-feeding insects. *T. brucei* is transmitted by infected tsetse flies and causes sleeping sickness (trypanosomiasis) in humans. There are two types of trypanosomiasis: East African trypanosomiasis, caused by *Trypanosoma brucei gambiense*. *Trypanosoma brucei brucei* infects primarily cattle, and does not normally infect humans. *T. cruzi* causes Chagas disease and is transmitted by triatomine bugs. *Trypanosoma* sequences are publicly available and include GenBank Accession Nos. ASM21029v1 (*T. brucei* gambiense), and ASM20906v1 (*T. cruzi*), each of which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2020.
- (37) West Nile virus (WNV): A member of the virus family Flaviviridae and the genus *Flavivirus*. WNV was first isolated from a woman in the West Nile district of Uganda in 1937. The virus was later identified in birds in the Nile delta region in 1953. Human infections attributable to WNV have been reported in many countries for over 50 years. In 1999, a WNV circulating in Israel and Tunisia was imported into New York, producing a large and dramatic outbreak that spread throughout the continental United States in the following years. Human infection is most often the result of bites from infected mosquitoes, but may also be transmitted through contact with other infected animals, their blood or other tissues. Infection with WNV is asymptomatic in about 80% of infected people, but about 20% develop West Nile fever. Symptoms include fever, headache, fatigue, body aches, nausea, vomiting, swollen lymph glands and in some cases, a skin rash. Approximately 1 in 150 of infected individuals develop severe, neuroinvasive disease, such as encephalitis, meningitis, or poliomyelitis. WNV sequences are publicly available, and include GenBank Accession Nos. NC_009942 (gi|158516887) (NY99, lineage 1) and NC_001563 (gi|11528013) (956, lineage 2), which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2019.
- (38) Zika virus (ZKV or ZIKV): A member of the virus family Flaviviridae and the genus *Flavivirus*. ZIKV is spread by the daytime-active mosquitoes *Aedes aegypti* and *A. albopictus*. This virus was first isolated from a Rhesus macaque from the Zika Forest of Uganda in 1947. Since the 1950s, ZIKV has been known to occur within a narrow equatorial belt from Africa to Asia. The virus spread eastward across the Pacific Ocean in 2013-2014, resulting in ZIKV outbreaks in Oceania to French Polynesia, New Caledonia, the Cook islands, and Easter Island. In 2015, ZKV spread to Mexico, Central America, the Caribbean and South America, where ZKV has reached pandemic levels. Infection by ZIKV generally causes either no symptoms or mild symptoms, including mild headache, maculopapular rash, fever, malaise, conjunctivitis and joint pain. However, ZKV infection has been linked to the birth of microcephalic infants following maternal infection. Reports have also indicated that ZIKV has the potential for human blood-borne and sexual transmission. ZIKV sequences are publicly available, and include GenBank Accession Nos. KU497555 (gi|985578255) (isolate Brazil-ZK2015), KU501215 (gi|984874581) (strain PRVABC59), KU312312 (gi|973447404) (isolate Z1106033), KU707826 (gi|992324757) (isolate SSABR1), and KU321639 (strain ZikaSPH2015), which are incorporated by reference in their entirety as present in GenBank on Jan. 30, 2019.

II. Probes and Microarrays

(39) Disclosed herein is a nucleic acid probe set capable of detecting nucleic acid molecules from one or more RNA viruses, including Chikungunya virus (CHIKV), Dengue virus types 1, 2, 3, or 4, (DEN1, DEN2, DEN3, DEN4), Hepatitis A virus (HAV), Hepatitis C virus (HCV) types 1, 2, or 3, Hepatitis E virus (HEV), Human Immunodeficiency virus (HIV) types 1 or 2, Human T-lymphotropic virus (HTLV) types I or II, West Nile virus (WNV), and Zika virus (ZKV). In some embodiments, the probe set includes 30 or more probes for one or more of the viruses (such as 30

or more, 50 or more, 60 or more, 70 or more, 80 or more, 90 or more, 100 or more, 110 or more, or 120 or more), for example 30-120 probes, 50-100 probes, or 70-110 probes for one or more of CHIKV, DEN1, DEN2, DEN3, DEN4, HAV, HCV type 1, HCV type 2, HCV type 3, HEV, HIV type 1, HIV type 2, HTLV type 1, HTLV type 2, WNV, and ZIKV.

- (40) In some embodiments, the probe set includes nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769. In other embodiments, the probe set includes a subset of the probes of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769, such as at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 50%, at least 97%, at least 98%, at least 99%, or at least 99.9% of the probes of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769. In some examples, the subset includes at least one probe for each of CHIKV, DEN1, DEN2, DEN3, DEN4, HAV, HCV type 1, HCV type 2, HCV type 3, HEV, HIV type 1, HIV type 2, HTLV type 1, HTLV type 2, WNV, and ZKV, such as at least 1, at least 2, at least 5, at least 10, at least 20, at least 30, or more probes for each virus. In some examples, the subset includes at least 40 probes (such as at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, or at least 110 probes) for one or more of CHIKV, DEN1, DEN2, DEN3, DEN4, HAV, HCV type 1, HCV type 2, HCV type 3, HEV, HIV type 1, HIV type 2, HTLV type 1, HTLV type 2, WNV, and ZKV.
- (41) In one non-limiting example, the probe set includes or consists of each of the probes of SEQ ID NOs: 1-1769. In another non-limiting example, the probe set includes or consists of each of the probes of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769. In another example, the probe set includes or consists of each of the probes of SEQ ID NOs: 1-1300 and 1391-1769. In other embodiments, the probe set includes a subset of the probes of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769 or a subset of the probes of SEQ ID NOs: 1-1300 and 1391-1769.
- (42) Also disclosed herein is a nucleic acid probe set capable of detecting nucleic acid molecules from one or more DNA viruses, including one or more of cytomegalovirus, Epstein Barr virus (e.g., one or more of EBV subtype B95-8 and EBV subtype AG876), human herpes virus 8, Hepatitis B virus (e.g., one or more of HBV subtypes adw, ayw, adr, and ayr), human parvovirus B19, and human papillomavirus (e.g., one or more of HPV types 6, 11, 16, and 18). In some embodiments, the probe set includes 10 or more probes for one or more of the viruses (such as 15 or more, 20 or more, 30 or more, 50 or more, 60 or more, 70 or more, 80 or more, 90 or more, 100 or more, 110 or more, or 120 or more), for example 10-50 probes, 30-120 probes, 50-100 probes, or 70-110 probes for one or more of cytomegalovirus, Epstein Barr virus, human herpes virus 8, Hepatitis B virus, human parvovirus B19, and human papillomavirus.
- (43) In some embodiments, the probe set includes nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 1770-2647. In other embodiments, the probe set includes a subset of the probes of SEQ ID NOs: 1770-2647, such as 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 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 99.9% of the probes of SEQ ID NOs: 1770-2647. In some examples, the subset includes at least one probe for each of CMV, EBV subtype B95-8, EBV subtype AG876, human herpes virus 8, Hepatitis B virus subtype adw, Hepatitis B virus subtype ayw, Hepatitis B virus subtype adr, Hepatitis B virus subtype ayr, human parvovirus B19, HPV type 6, HPV type 11, HPV type 16, and HPV type 18, such as at least 1, at least 2, at least 5, at least 10, at least 20, at least 30, or more probes for each virus. In some examples, the subset includes at least 10 probes (such as 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 100, or at least 110 probes) for one or more of CMV, EBV subtype B95-8, EBV subtype AG876, human herpes virus 8, Hepatitis B virus subtype adw, Hepatitis B virus subtype ayw, Hepatitis B virus subtype adr, Hepatitis B virus subtype ayr, human parvovirus B19, HPV type 6, HPV type 11, HPV type 16, and HPV type 18. In

one non-limiting example, the probe set includes or consists of each of the probes of SEQ ID NOs: 1770-2647.

- (44) Further disclosed herein is a nucleic acid probe set capable of detecting nucleic acid molecules from one or more bacterial and/or protozoan pathogens, including one or more of *Treponema pallidum*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris*, *Borrelia burgdorferi*, *Coxiella burnetii*, *Trypanosoma brucei*, *Trypanosoma cruzi*, *Leishmania major*, *Babesia microti*, *Plasmodium falciparum*, and *Plasmodium vivax*. In some embodiments, the probe set includes 10 or more probes for one or more of the viruses (such as 10 or more, 20 or more, 30 or more, 50 or more, 60 or more, 70 or more, 80 or more, 90 or more, 100 or more, 110 or more, or 120 or more), for example 30-120 probes, 50-100 probes, or 70-110 probes for one or more of *Treponema pallidum*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris*, *Borrelia burgdorferi*, *Coxiella burnetii*, *Trypanosoma brucei*, *Leishmania major*, *Babesia microti*, *Plasmodium falciparum*, and *Plasmodium vivax*
- (45) In some embodiments, the probe set includes nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 2648-3207. In other embodiments, the probe set includes a subset of the probes of SEQ ID NOs: 2648-3207, such as 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 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 99.9% of the probes of SEQ ID NOs: 2648-3207. In some examples, the subset includes at least one probe for each of *Treponema* pallidum, Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris, Borrelia burgdorferi, Coxiella burnetii, Trypanosoma brucei, Trypanosoma cruzi, Leishmania major, Babesia microti, Plasmodium falciparum, and Plasmodium vivax, such as at least 1, at least 2, at least 5, at least 10, at least 20, at least 30, or more probes for each pathogen. In some examples, the subset includes at least 10 probes (such as at least 20, at least 30, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, or at least 110 probes) for one or more of Treponema pallidum, Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris, Borrelia burgdorferi, Coxiella burnetii, Trypanosoma brucei, Leishmania major, Babesia microti, Plasmodium falciparum, and Plasmodium vivax. In one non-limiting example, the probe set includes or consists of each of the probes of SEQ ID NOs: 2648-3207.
- (46) In further embodiments, one or more of the disclosed probe sets are combined. Thus, some embodiments, the probe set includes probes for detecting at least one RNA virus, at least one DNA virus, at least one bacterial pathogen, at least one protozoan pathogen, or combinations of two or more thereof. In one example, a probe set includes probes capable of detecting nucleic acid molecules from one or more DNA viruses and one or more bacterial and/or protozoan pathogens. In one non-limiting example, a probe set includes probes including or consisting of each of the probes of SEQ ID NOs: 1770-3207. In another example, a probe set includes probes capable of detecting nucleic acid molecules from one or more RNA viruses, one or more DNA viruses, and one or more bacterial and/or protozoan pathogens. In a non-limiting example, the probe set includes probes including or consisting of each of the probes of SEQ ID NOs: 1-1300, SEQ ID NOs: 1391-1570, SEQ ID NOs: 1691-1769, and SEQ ID NOs: 1770-3207.
- (47) In additional embodiments, a disclosed probe set further includes one or more control probes, such as one or more positive and/or negative control probes. For testing for validity of the run, intra-array reproducibility control and normalization. positive control probes may include one or more of: 1) one or more reference probes for intensity normalization, 2) one or more internal standards of known concentrations, and 3) one or more probes that are homologous to an internal control included in the hybridization mix. In some embodiments, positive control probes include one or more (such as 1, 10, 25, 50, 96, or more) ERCC probes (External RNA Controls Consortium) and one or more (such as 1, 10, 25, 50, 96, 250, 500, 900, or more) biological replicates targeting human genome sequences (for example, to define possible host contaminant).

- (48) Negative control probes may include one or more probes for a virus that is known not to be present in human or mammalian subjects. In some non-limiting examples, negative control probes are specific for a plant virus. In other examples, negative control probes can be a structural negative probe, such as a sequence that forms a hairpin and does not hybridize with nucleic acids from any species.
- (49) In some examples, the probe set includes 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 100, at least 110, or at least 120 control probes. In some examples, the control probes are for one or more one or more different negative control viruses (such as 1, 2, 3, 4, 5, or more negative control viruses). In some examples, the probe set includes 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 100, at least 110, at least 120, or more negative control probes. In some examples, the negative control probes are probes for one or more of White clover cryptic virus 1 (e.g. SEQ ID NOs: 1571-1580), Broad bean wilt virus 1 (e.g., SEQ ID NOs: 1582-1620), Lettuce necrotic yellows virus (e.g., SEQ ID NOs: 1621-1690), Aedes albopictus densovirus 2 (e.g., SEQ ID NOs: 3520-3557), Maize streak virus (e.g., SEQ ID NOs: 3558-3598), and/or Tomato pseudocurly top virus (e.g., SEQ ID NOs: 3599-3628). In additional examples, the probe set includes 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 100, at least 110, at least 120, or more positive control probes. In some examples, the positive control probes are probes for one or more housekeeping genes, such as one of more of ACTB (e.g., SEQ ID NOs: 3208-3301), ARL1 (e.g., SEQ ID NOs: 3302-3385), and/or CCDN1 (e.g., SEQ ID NOs: 3386-3519).
- (50) In some embodiments, the disclosed probes are between 30 and 80 nucleotides in length (for example 30-50, 40-60, 50-70, or 60-80 nucleotides in length). In some examples, the probes are 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, or 80 nucleotides in length and are capable of hybridizing to the disclosed pathogen (e.g., viral, bacterial, or protozoan) nucleic acid molecules. In some examples, the probes are 60 nucleotides in length. In some examples, each of the probes in the probe set has a Tm between about 72-89° C., such as about 74-88° C., about 75-85° C., or about 76-82° C. In one specific example, each of the probes in the probe set has a Tm between 74.4 and 87.8° C. Tm ranges for exemplary RNA virus probes are shown in Table 1.
- (51) In other embodiments the disclosed probe sets, or a subset thereof, are linked to a solid support. In some examples, the disclosed probe sets, or a subset thereof, are included on a microarray. In other examples, the solid support is a bead or plurality of beads, a microplate, column, or microfluidic device.
- (52) In some embodiments, the microarray is a solid support or substrate including the probe set (or subset thereof) covalently linked to the support or substrate. Within an array, each arrayed probe is addressable, in that its location can be reliably and consistently determined within at least two dimensions of the array. Addressable arrays usually are computer readable, in that a computer can be programmed to correlate a particular address on the array with information about the sample at that position (such as hybridization or binding data, including for instance signal intensity). (53) The microarray can include any of the probe sets described above, individually, or in combination. In some embodiments, the microarray includes nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769. In another embodiment, the microarray includes or consists of nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 1-1300 and 1391-1769. In one non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 1-1769. In another non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769. In a further non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 1-1300 and 1391-1769.

- (54) In another embodiment, the microarray includes nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 1770-2647. In one non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 1770-2647. In another non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 1170-2647 and 3250-3628.
- (55) In another embodiment, the microarray includes nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 2648-3207. In one non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 2648-3207. In another non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 2648-3519.
- (56) In a further embodiment, the microarray includes nucleic acid probes that are at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the nucleic acid sequences of SEQ ID NOs: 1770-3207. In one non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 1770-3207. In a further non-limiting example, the microarray includes or consists of each of the probes of SEQ ID NOs: 1770-3628.
- (57) In other embodiments, the microarray includes a subset of the probes of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769, such as 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 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 99.9% of the probes of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769. In some examples, the microarray includes at least one probe for each of CHIKV, DEN1, DEN2, DEN3, DEN4, HAV, HCV type 1, HCV type 2, HCV type 3, HEV, HIV type 1, HIV type 2, HTLV type 1, HTLV type 2, WNV, and ZKV, such as at least 1, at least 2, at least 5, at least 10, at least 20, at least 30, or more probes for each virus. In some examples, the microarray includes at least 40 probes (such as at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, or at least 110 probes) for one or more of CHIKV, DEN1, DEN2, DEN3, DEN4, HAV, HCV type 1, HCV type 2, HCV type 3, HEV, HIV type 1, HIV type 2, HTLV type 1, HTLV type 2, WNV, and ZKV.
- (58) In other embodiments, the microarray includes a subset of the probes of SEQ ID NOs: 1770-2647, such as 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 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 99.9% of the probes of SEQ ID NOs: 1770-2647. In some examples, the microarray includes at least one probe for each of CMV, EBV subtype B95-8, EBV subtype AG876, human herpes virus 8, Hepatitis B virus subtype adw, Hepatitis B virus subtype ayr, human parvovirus B19, HPV type 6, HPV type 11, HPV type 16, and HPV type 18, such as at least 1, at least 2, at least 5, at least 10, at least 20, at least 30, or more probes for each virus. In some examples, the microarray includes at least 20 probes (such as at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, or at least 110 probes) for one or more of CMV, EBV subtype B95-8, EBV subtype AG876, human herpes virus 8, Hepatitis B virus subtype adw, Hepatitis B virus subtype ayr, human parvovirus B19, HPV type 6, HPV type 11, HPV type 16, and HPV type 18.
- (59) In other embodiments, the microarray includes a subset of the probes of SEQ ID NOs: 2648-3207, such as 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 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 99.9% of the probes of SEQ ID NOs: 2648-3207. In some examples, the microarray includes at least one probe for each of *Treponema pallidum*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris*, *Borrelia burgdorferi*, *Coxiella burnetii*, *Trypanosoma brucei*,

Trypanosoma cruzi, Leishmania major, Babesia microti, Plasmodium falciparum, and *Plasmodium vivax*, such as at least 1, at least 2, at least 5, at least 10, at least 20, at least 30, or more probes for each virus. In some examples, the microarray includes at least 10 probes (such as at least 30, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, or at least 110 probes) for one or more of *Treponema pallidum, Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris, Borrelia burgdorferi, Coxiella burnetii, Trypanosoma brucei, Leishmania major, Babesia microti, Plasmodium falciparum, and <i>Plasmodium vivax*.

- (60) In additional embodiments, the microarray includes one or more control probes, such as one or more positive and/or negative control probes. In some examples, the microarray includes 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 100, at least 110, or at least 120 negative control probes. In some examples, the microarray includes one or more negative control probes selected from SEQ ID NOs: 1571-1580, SEQ ID NOs: 1582-1620, SEQ ID NOs: 1621-1690, and SEQ ID NOs: 3520-3628. In additional examples, the microarray includes 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 110, or at least 120 positive control probes. In some examples, the microarray includes one or more positive control probes selected from SEQ ID NOs: 3208-3519.
- (61) The solid support or substrate of the array can be formed from an organic polymer. Suitable materials for the solid support include, but are not limited to: polypropylene, polyethylene, polybutylene, polyisobutylene, polybutadiene, polyisoprene, polyvinylpyrrolidine, polytetrafluroethylene, polyvinylidene difluroide, polyfluoroethylene-propylene, polyethylenevinyl alcohol, polymethylpentene, polycholorotrifluoroethylene, polysulfornes, hydroxylated biaxially oriented polypropylene, aminated biaxially oriented polypropylene, thiolated biaxially oriented polypropylene, ethyleneacrylic acid, thylene methacrylic acid, and blends of copolymers thereof). (62) A wide variety of array formats can be employed in accordance with the present disclosure. One example includes a two-dimensional pattern of discrete cells (such as 4096 squares in a 64 by 64 array). Other array formats including, but not limited to slot (rectangular) and circular arrays are equally suitable for use. In some examples, the array is a multi-well plate. In one example, the array is formed on a polymer medium, which is a thread, membrane or film. An example of an organic polymer medium is a polypropylene sheet having a thickness on the order of about 1 mil. (0.001 inch) to about 20 mil., although the thickness of the film is not critical and can be varied over a fairly broad range. The array can include biaxially oriented polypropylene (BOPP) films, which in addition to their durability, exhibit low background fluorescence.
- (63) The array formats of the present disclosure can be included in a variety of different types of formats. A "format" includes any format to which the solid support can be affixed, such as microtiter plates (e.g., multi-well plates), test tubes, inorganic sheets, dipsticks, and the like. For example, membranes can be affixed to glass slides. The particular format is, in and of itself, unimportant. All that is necessary is that the solid support can be affixed thereto without affecting the functional behavior of the solid support or any biopolymer absorbed thereon, and that the format (such as the slide) is stable to any materials into which the device is introduced (such as clinical samples and hybridization solutions).
- (64) The arrays of the present disclosure can be prepared by a variety of approaches. In one example, oligonucleotides (e.g., probes) are synthesized separately and then attached to a solid support (see U.S. Pat. No. 6,013,789). In another example, probes are synthesized directly onto the support to provide the desired array (see U.S. Pat. No. 5,554,501). Suitable methods for covalently coupling oligonucleotides to a solid support and for directly synthesizing oligonucleotides on the support are known; a summary of suitable methods can be found in Matson et al., Anal. Biochem. 217:306-10, 1994. In one example, the oligonucleotides are synthesized onto the support using conventional chemical techniques for preparing oligonucleotides on solid supports (such as PCT applications WO 85/01051 and WO 89/10977, or U.S. Pat. No. 5,554,501).

- (65) The oligonucleotides can be bound to the support or substrate by either the 3' end of the oligonucleotide or by the 5' end of the oligonucleotide. In one example, the oligonucleotides are bound to the solid support by the 3' end. In general, the internal complementarity of an oligonucleotide probe in the region of the 3' end and the 5' end determines binding to the support. III. Methods of Detecting Viral Nucleic Acids
- (66) Disclosed herein are methods of detecting one or more pathogen nucleic acids (such as one or more viral, bacterial, and/or protozoan nucleic acids) in a sample from a subject. In some embodiments, the methods include preparing or isolating nucleic acids (such as DNA, RNA, or cDNA) from a sample, labeling the nucleic acids, and contacting the probe set, or a microarray including the probe set, with the labeled nucleic acids under conditions sufficient to allow pathogen nucleic acids present in the sample to hybridize with one or more of the probes. The presence and/or identity of pathogen nucleic acids in the sample is determined by detecting hybridization. In one example, hybridization is detected by measuring presence of labeled nucleic acid at an addressable location in an array.
- (67) In particular embodiments, the methods include detecting one or more nucleic acids from RNA viruses in a sample, including one or more of CHIKV, DEN1, DEN2, DEN3, DEN4, HAV, HCV type 1, HCV type 2, HCV type 3, HEV, HIV type 1, HIV type 2, HTLV type I, HTLV type II, WNV, and ZKV. In other embodiments, the methods include detecting one or more nucleic acids from DNA viruses, including one or more of CMV, EBV subtype B95-8, EBV subtype AG876, human herpes virus 8, Hepatitis B virus subtype adw, Hepatitis B virus subtype ayw, Hepatitis B virus subtype adr, Hepatitis B virus subtype ayr, human parvovirus B19, HPV type 6, HPV type 11, HPV type 16, and HPV type 18. In still other embodiments, the methods include detecting one or more nucleic acids from bacteria and/or protozoans, including one or more of *Treponema pallidum*, Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris, Borrelia burgdorferi, Coxiella burnetii, Trypanosoma brucei, Trypanosoma cruzi, Leishmania major, Babesia microti, Plasmodium falciparum, and *Plasmodium vivax*. In further embodiments, the methods include detecting nucleic acids from at least one RNA virus, DNA virus, bacteria, and protozoan, such as at least one of the RNA viruses, DNA viruses, bacteria, and protozoans disclosed herein, or any combination thereof. (68) Exemplary samples include peripheral blood, serum, plasma, cerebrospinal fluid, urine, saliva, feces, mucus, nasal wash, tissue biopsy, fine needle aspirate, surgical specimen, placenta, autopsy material, semen, vaginal fluid or tissue, and environmental samples. In particular examples, the sample is a blood sample, such as plasma. In non-limiting examples, the sample is blood or plasma from a blood donor. Thus, in some examples, the methods disclosed herein are used to screen donated blood for one or more pathogens potentially present and/or transmitted through blood transfusions.
- (69) In some embodiments, the methods include isolating nucleic acids (such as RNA, cDNA, or a combination thereof) from the sample and contacting the probe set or microarray with the isolated nucleic acids. Methods of isolating RNA (e.g., viral RNA) from a sample are known and include commercially available kits, such as QIAGEN® RNeasy® mini-columns, MASTERPURE® Complete DNA and RNA Purification Kit (EPICENTRE® Madison, Wis.), Paraffin Block RNA Isolation Kit (Ambion, Inc.), and RNA Stat-60 (Tel-Test). cDNA is then prepared from the isolated RNA, and optionally labeled. In some examples, the methods include amplifying RNA prior to cDNA preparation and labeling, for example, using Quick Amp WT labeling kit (Agilent). Other methods of amplifying RNA include commercially available kits such as Ovation® RNA Amplification kit (Nugen), Arcturus™ RiboAmp™ HS kit (ThermoFisher), and Complete Whole Transcriptome Amplification Kit (WTA2, Sigma-Aldrich).
- (70) In some embodiments, the methods do not include isolating and/or amplifying RNA from a sample prior to labeling. In some examples, the methods include generating amplified cDNA from a sample, followed by labeling the cDNA (for example with a fluorescent label, such as CyTM3 dye). In one non-limiting example, amplified cDNA is prepared from the sample using single-

primer isothermal amplification (for example, Ribo-SPIA® amplification, NuGen) prior to labeling. Methods of labeling cDNA are known and include commercially available kits, such as Genomic DNA Enzymatic Labeling Kit (Agilent). In some examples, the methods generate amplified and labeled cDNA from about 250 pg of target viral RNA (such as about 500 pg, about 750 pg, about 1 ng, about 2 ng, or more of target viral RNA).

- (71) In other examples, the methods include isolating DNA from the sample and contacting the probe set or microarray with the isolated DNA. Methods of isolating DNA (such as viral DNA, bacterial DNA, or protozoan DNA) from a sample are known and include commercially available kits. In some examples, the methods include isolating viral DNA from a sample using a viral nucleic acid isolation kit. In one non-limiting example, the viral DNA is isolated using Dynabeads™ SILANE viral NA kit (Invitrogen). In other examples, bacterial or protozoan DNA is isolated from a sample using a DNA isolation kit. In one non-limiting example, bacterial or protozoan DNA is isolated using QIAamp® DNA Blood Mini kit (Qiagen). One of ordinary skill in the art can select appropriate methods or kits to isolate pathogen DNA from samples, for example, blood or plasma samples.
- (72) The sample (such as nucleic acids isolated and/or amplified from a sample) can be labeled with any suitable label. Generally, the label will be selected based on the intended use of the sample or the desired readout. In some examples, the sample or nucleic acids from the sample is labelled with a fluorescent or chemiluminescent compound. In other examples, the label is an enzyme, a fluorophore, or a radioactive isotope. In one specific non-limiting example, the label is $Cy^{TM}3$ or $Cy^{TM}5$.
- (73) Fluorophores suitable for use with the methods disclosed herein, include, but are not limited to, 6-carboxyfluorescein (FAM), tetrachlorofluorescein (TET), tetramethylrhodamine (TMR), hexachlorofluorescein (HEX), JOE, ROX, CAL Fluor™ dye, Pulsar™ dye, Quasar™ dye, Texas RedTM dye, CyTM3 dye and CyTM5 dye. Other examples of fluorophores that can be used with the methods provided herein include 4-acetamido-4'-isothiocyanatostilbene-2,2'disulfonic acid, acridine and derivatives such as acridine and acridine isothiocyanate, 5-(2'-aminoethyl)aminonaphthalene-1-sulfonic acid (EDANS), 4-amino-N-[3-vinylsulfonyl)phenyl]-naphthalimide-3,5 disulfonate (Lucifer Yellow VS), N-(4-anilino-1-naphthyl)-maleimide, anthranilamide, Brilliant Yellow, coumarin and derivatives such as coumarin, 7-amino-4-methylcoumarin (AMC, Coumarin 120), 7-amino-4-trifluoromethylcouluarin (Coumaran 151); cyanosine; 4',6-diaminidino-2phenylindole (DAPI); 5', 5"-dibromopyrogallol-sulfonephthalein (Bromopyrogallol Red); 7diethylamino-3-(4'-isothiocyanatophenyl)-4-methylcoumarin; diethylenetriamine pentaacetate; 4,4'-diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid; 4,4'-diisothiocyanatostilbene-2,2'disulfonic acid; 5-[dimethyl-amino]naphthalene-1-sulfonyl chloride (DNS, dansyl chloride); 4-(4'dimethyl-aminophenylazo)benzoic acid (DABCYL); 4-dimethylaminophenylazophenyl-4'isothiocyanate (DABITC); eosin and derivatives such as eosin and eosin isothiocyanate; erythrosin and derivatives such as erythrosin B and erythrosin isothiocyanate; ethidium; fluorescein and derivatives such as 5-carboxyfluorescein (FAM), 5-(4,6-dichlorotriazin-2-yl)aminofluorescein (DTAF), 2'7'-dimethoxy-4'5'-dichloro-6-carboxyfluorescein (JOE), fluorescein, fluorescein isothiocyanate (FITC), and QFITC (XRITC); fluorescamine; IR144; IR1446; Malachite Green isothiocyanate; 4-methylumbelliferone; ortho cresolphthalein; nitrotyrosine; pararosaniline; Phenol Red; B-phycoerythrin; o-phthaldialdehyde; pyrene and derivatives such as pyrene, pyrene butyrate and succinimidyl 1-pyrene butyrate; Reactive Red 4 (Cibacron Brilliant Red 3B-A); rhodamine and derivatives such as 6-carboxy-X-rhodamine (ROX), 6-carboxyrhodamine (R6G), lissamine rhodamine B sulfonyl chloride, rhodamine (Rhod), rhodamine B, rhodamine 123, rhodamine X isothiocyanate, sulforhodamine B, sulforhodamine 101 and sulfonyl chloride derivative of sulforhodamine 101 (Texas Red™ dye); N,N,N',N'-tetramethyl-6-carboxyrhodamine (TAMRA); tetramethyl rhodamine; tetramethyl rhodamine isothiocyanate (TRITC); riboflavin; rosolic acid and terbium chelate derivatives.

- (74) Other fluorophores that can be used include thiol-reactive europium chelates that emit at approximately 617 nm (Heyduk and Heyduk, *Analyt. Biochem.* 248:216-27, 1997; *J. Biol. Chem.* 274:3315-22, 1999). Other fluorophores that can be used include cyanine, merocyanine, styryl, and oxonyl compounds, such as those disclosed in U.S. Pat. Nos. 5,627,027; 5,486,616; 5,569,587; and 5,569,766, and in published PCT application no. US98/00475, each of which is incorporated herein by reference. Specific examples of fluorophores disclosed in one or more of these patent documents include Cy™3 and Cy™5, for instance, and substituted versions of these fluorophores. Additional fluorophores that can be used include GFP, Lissamine™, diethylaminocoumarin, fluorescein chlorotriazinyl, naphthofluorescein, 4,7-dichlororhodamine and xanthene (as described in U.S. Pat. No. 5,800,996 to Lee et al., herein incorporated by reference) and derivatives thereof. Other fluorophores are commercially available from known sources.
- (75) The methods include contacting the sample (such as labeled nucleic acids from a sample) with a probe set disclosed herein (or subset thereof), or a microarray including the probe set (or subset thereof), under conditions sufficient to allow hybridization of pathogen nucleic acids present in the sample to one or more probes and detecting presence of pathogen nucleic acids hybridized to the probe set or microarray.
- (76) Presence of one or more pathogen nucleic acids in the sample can be detected using any suitable means. For example, detection of hybridization can be accomplished by detecting nucleic acid molecules (such as RNA) using nucleic acid amplification methods (such as real-time RT-PCR) or array analysis. In a specific embodiment of the microarray technique, labeled cDNA prepared from a sample is applied to an array including a probe set disclosed herein. Labeled cDNA from the sample can hybridize specifically to one or more probes on the array. After washing to remove non-specifically bound probes, the chip is scanned by confocal laser microscopy or by another detection method, such as a CCD camera. Quantitation of hybridization of sample to each arrayed element allows for assessment of corresponding RNA abundance (e.g., if cDNA is analyzed). Microarray analysis can be performed by commercially available equipment, following manufacturer's protocols, such as are supplied with Affymetrix GeneChip® technology (Affymetrix, Santa Clara, CA), or Agilent's microarray technology (Agilent Technologies, Santa Clara, CA).
- (77) In some examples, a sample is determined to contain nucleic acids from a particular pathogen by detecting hybridization between the sample (nucleic acid) and one or more probes of the pathogen-specific probe set. In some examples, a sample is determined to be positive for a pathogen when the log ratio between the signal intensity mean for the pathogen-specific probe set and the mean of a control group probe set is ≥ 1.5 . In other examples, a sample is determined to be negative for a pathogen when the log ratio between the signal intensity mean for the pathogenspecific probe set and the mean of a control group probe set is <1. In further examples, the sample is determined to be borderline for the pathogen when the log ratio between the signal intensity mean for the pathogen-specific probe set and the mean of a control group probe set is ≥ 1.0 to ≤ 1.5 . In some examples, a sample that is determined to be borderline for one or more pathogens is retested (for example, retested with the assay disclosed herein and/or tested using a virus-specific nucleic acid based test). In other examples, a sample that is determined to be borderline is discarded (e.g., not administered to a subject). In additional examples, a sample is determined to be positive for a particular pathogen when ≥50% of the individual probes for the particular pathogen have a log ratio of >1.5. In some examples, a sample is determined to be positive for a particular pathogen when ≥50% of the individual probes for the particular pathogen have a log ratio of >1.5 and the log ratio between the signal intensity mean for the pathogen-specific probe set and the mean of a control group probe set is ≥ 1.5 .

EXAMPLES

(78) The following examples are provided to illustrate certain particular features and/or embodiments. These examples should not be construed to limit the disclosure to the particular

features or embodiments described.

Example 1

Materials and Methods

- (79) Microarray-Based Platform Design
- (80) Selection of transfusion-transmitted RNA viruses: Sequences of 16 RNA viruses of concern for transmission to blood recipients (released by AABB Transfusion-Transmitted Diseases Committee (Stramer et al., *Transfusion* 49:1S-29S, 2009)) were downloaded from GenBank at NCBI (available on the World Wide Web at ncbi.nlm.nih.gov/genbank).
- (81) The complete genome for each RNA virus was uploaded in FASTA format using Agilent eArray software (available on the World Wide Web at earray.chem.agilent.com/earray/, Agilent Technologies Inc., Santa Clara, CA). Design settings were chosen to select 60-mer sense probes with 3' bias from each viral gene, according to the base composition methodology, which considers fusion temperature, GC % and cross-hybridization potential for probes. To get the best quality level probes for viral genome detection the "best probe" (BP) was selected. The probes were checked for vector and low complexity masking. Entire viral genome sequences were covered to the extent possible with all available Agilent-designed probes. The microarray was supplemented with additional predesigned GE (gene expression) array probes for 906 genes from the human genome (replicated 10 times), ERCC probes (replicated 45 times) and probes covering plant virus sequences (negative control). The selected probes and their characteristics are provided in Table 1. (82) Oligonucleotide probe selection and methodology: Oligonucleotide probes were synthesized in situ from 3'-end base by base with Agilent SurePrint inkjet technology according to the manufacturer's protocol (Wolber et al., Meth. Enzymol. 410:28-57, 2006). The microarrays were manufactured with 60-mer oligonucleotides synthesized in 15,000 features on eight replicate arrays per slide.
- (83) Sample collection and processing: Specimens positive for CHIKV, DENV1-4, HIV1-2, WNV strain NY99, and ZIKV were prepared, validated, and supplied by the FDA Center for Biologics Evaluation and Research (CBER) (Dong et al., J. Appl. Microbiol. 120:1119-1129, 2016). (84) HCV genotypes 1a, 2a, and 3, and HEV RNA-positive plasma were purchased from Sera Care (Sera Care, Milford, MA). All positive specimens were diluted in negative plasma (Basematrix diluent, Sera Care) to create a range of concentrations. HAV RNA was obtained from Dr. Patrizia Farci, (National Institutes of Health, Bethesda, MD). HTLV types I and II NATtrol (Nucleic Acid Testing Control) were purchased from ZeptoMetrix (ZeptoMetrix, Buffalo, NY) (Table 2). (85) TABLE-US-00001 TABLE 1 Selected viral probes SEQ BP ID Probe Product Virus Target ID Start NO: Length 5 UTR Hepatitis C gi|22129792:1-341 243 1 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 194 2 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 193 3 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 173 4 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 172 5 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 171 6 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 170 7 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 169 8 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 168 9 60 genotype 1 5 UTR Hepatitis C gi|22129792:1-341 167 10 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 488 11 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 487 12 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 486 13 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 485 14 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 484 15 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 483 16 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 482 17 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 481 18 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 480 19 60 genotype 1 core protein Hepatitis C gi|22129792:342-914 479 20 60 genotype 1 E1 protein Hepatitis C gi|22129792:915-1494 342 21 60 genotype 1 E1 protein Hepatitis C gi|22129792:915-1494 341 22 60 genotype 1 E1 protein Hepatitis C gi|22129792:915-1494 340 23 60 genotype 1 E1 protein Hepatitis C gi|22129792:915-1494 339 24 60 genotype 1 E1 protein Hepatitis C gi|22129792:915-1494 504 25

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60 genotype 1 E1 protein Hepatitis C gi|22129792:915-1494 503 26 60 genotype 1 E1 protein
Hepatitis C gi|22129792:915-1494 502 27 60 genotype 1 E1 protein Hepatitis C gi|22129792:915-
1494 501 28 60 genotype 1 E1 protein Hepatitis C gi|22129792:915-1494 500 29 60 genotype 1 E1
protein Hepatitis C gi|22129792:915-1494 379 30 60 genotype 1 E2 protein Hepatitis C
gi|22129792:1491-2579 703 31 60 genotype 1 E2 protein Hepatitis C gi|22129792:1491-2579 702
32 60 genotype 1 E2 protein Hepatitis C gi|22129792:1491-2579 701 33 60 genotype 1 E2 protein
Hepatitis C gi|22129792:1491-2579 700 34 60 genotype 1 E2 protein Hepatitis C
gi|22129792:1491-2579 699 35 60 genotype 1 E2 protein Hepatitis C gi|22129792:1491-2579 697
36 60 genotype 1 E2 protein Hepatitis C gi|22129792:1491-2579 696 37 60 genotype 1 E2 protein
Hepatitis C gi|22129792:1491-2579 695 38 60 genotype 1 E2 protein Hepatitis C
gi|22129792:1491-2579 694 39 60 genotype 1 E2 protein Hepatitis C gi|22129792:1491-2579 693
40 60 genotype 1 p7 protein Hepatitis C gi|22129792:2580-2768 56 41 60 genotype 1 p7 protein
Hepatitis C gi|22129792:2580-2768 55 42 60 genotype 1 p7 protein Hepatitis C gi|22129792:2580-
2768 54 43 60 genotype 1 p7 protein Hepatitis C gi|22129792:2580-2768 53 44 60 genotype 1 p7
protein Hepatitis C gi|22129792:2580-2768 52 45 60 genotype 1 p7 protein Hepatitis C
gi|22129792:2580-2768 51 46 60 genotype 1 p7 protein Hepatitis C gi|22129792:2580-2768 50 47
60 genotype 1 p7 protein Hepatitis C gi|22129792:2580-2768 49 48 60 genotype 1 p7 protein
Hepatitis C gi|22129792:2580-2768 48 49 60 genotype 1 p7 protein Hepatitis C gi|22129792:2769-
3419 47 50 60 genotype 1 NS2 protein Hepatitis C gi|22129792:2580-2768 366 51 60 genotype 1
NS2 protein Hepatitis C gi|22129792:2769-3419 194 52 60 genotype 1 NS2 protein Hepatitis C
gi|22129792:2769-3419 193 53 60 genotype 1 NS2 protein Hepatitis C gi|22129792:2769-3419
192 54 60 genotype 1 NS2 protein Hepatitis C gi|22129792:2769-3419 191 55 60 genotype 1 NS2
protein Hepatitis C gi|22129792:2769-3419 190 56 60 genotype 1 NS2 protein Hepatitis C
gi|22129792:2769-3419 189 57 60 genotype 1 NS2 protein Hepatitis C gi|22129792:2769-3419
188 58 60 genotype 1 NS2 protein Hepatitis C gi|22129792:2769-3419 187 59 60 genotype 1 NS2
protein Hepatitis C gi|22129792:2769-3419 186 60 60 genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 1812 61 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 1620 62 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 849 63 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 1744 64 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 1497 65 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 1294 66 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 1234 67 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:5313-5474 1092 68 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 1020 69 60 helicase genotype 1 NS3 protease/ Hepatitis C
gi|22129792:3420-5312 765 70 60 helicase genotype 1 NS4A protein Hepatitis C
gi|22129792:3420-5312 103 71 60 genotype 1 NS4A protein Hepatitis C gi|22129792:5313-5474
102 72 60 genotype 1 NS4A protein Hepatitis C gi|22129792:5313-5474 101 73 60 genotype 1
NS4A protein Hepatitis C gi|22129792:5313-5474 100 74 60 genotype 1 NS4A protein Hepatitis C
gi|22129792:5313-5474 99 75 60 genotype 1 NS4A protein Hepatitis C gi|22129792:5313-5474 98
76 60 genotype 1 NS4A protein Hepatitis C gi|22129792:5313-5474 97 77 60 genotype 1 NS4A
protein Hepatitis C gi|22129792:5313-5474 96 78 60 genotype 1 NS4A protein Hepatitis C
gi|22129792:5313-5474 95 79 60 genotype 1 NS4A protein Hepatitis C gi|22129792:5313-5474 94
80 60 genotype 1 NS4B protein Hepatitis C gi|22129792:5475-6257 133 81 60 genotype 1 NS4B
protein Hepatitis C gi|22129792:5475-6257 723 82 60 genotype 1 NS4B protein Hepatitis C
gi|22129792:5475-6257 702 83 60 genotype 1 NS4B protein Hepatitis C gi|22129792:5475-6257
456 84 60 genotype 1 NS4B protein Hepatitis C gi|22129792:5475-6257 416 85 60 genotype 1
NS4B protein Hepatitis C gi|22129792:5475-6257 226 86 60 genotype 1 NS4B protein Hepatitis C
gi|22129792:5475-6257 204 87 60 genotype 1 NS4B protein Hepatitis C gi|22129792:5475-6257
182 88 60 genotype 1 NS4B protein Hepatitis C gi|22129792:5475-6257 162 89 60 genotype 1
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NS4B protein Hepatitis C gi|22129792:5475-6257 113 90 60 genotype 1 NS5A protein Hepatitis C
gi|22129792:6258-7601 402 91 60 genotype 1 NS5A protein Hepatitis C gi|22129792:6258-7601
1138 92 60 genotype 1 NS5A protein Hepatitis C gi|22129792:6258-7601 1078 93 60 genotype 1
NS5A protein Hepatitis C gi|22129792:6258-7601 974 94 60 genotype 1 NS5A protein Hepatitis C
gi|22129792:6258-7601 826 95 60 genotype 1 NS5A protein Hepatitis C gi|22129792:6258-7601
578 96 60 genotype 1 NS5A protein Hepatitis C gi|22129792:6258-7601 515 97 60 genotype 1
NS5A protein Hepatitis C gi|22129792:6258-7601 342 98 60 genotype 1 NS5A protein Hepatitis C
gi|22129792:6258-7601 214 99 60 genotype 1 NS5A protein Hepatitis C gi|22129792:6258-7601
154 100 60 genotype 1 NS5B RNA- Hepatitis C gi|22129792:7602-9374 1560 101 60 dependent
RNA genotype 1 polymerase NS5B RNA- Hepatitis C gi|22129792:7602-9374 1559 102 60
dependent RNA genotype 1 polymerase NS5B RNA- Hepatitis C gi|22129792:7602-9374 1558
103 60 dependent RNA genotype 1 polymerase NS5B RNA- Hepatitis C gi|22129792:7602-9374
1557 104 60 dependent RNA genotype 1 polymerase NS5B RNA- Hepatitis C gi|22129792:7602-
9374 1556 105 60 dependent RNA genotype 1 polymerase NS5B RNA- Hepatitis C
gi|22129792:7602-9374 1391 106 60 dependent RNA genotype 1 polymerase NS5B RNA-
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NS3 protease/ Hepatitis C gi|157781216:3376-5328 1673 266 60 helicase genotype 3 NS3
protease/ Hepatitis C gi|157781216:3376-5328 1671 267 60 helicase genotype 3 NS3 protease/
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protein gp4-vpr HIV 2 gi|9628880:6239-6502 149 453 60 protein gp4-vpr HIV 2 gi|9628880:6239-
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gi|9628880:6239-6502 146 456 60 protein gp4-vpr HIV 2 gi|9628880:6239-6502 145 457 60
protein gp4-vpr HIV 2 gi|9628880:6239-6502 144 458 60 protein gp4-vpr HIV 2 gi|9628880:6239-
6502 143 459 60 protein gp4-vpr HIV 2 gi|9628880:6239-6502 142 460 60 protein gp5-tat HIV 2
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HIV 2 68 508 60 3 LTR HIV 2 38 509 60 3 LTR HIV 2 8 510 60 gag HTLV 1 gb|AF033817.1|:450-
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HTLV 1 gb|AF033817.1|:450-1739 923 515 60 gag HTLV 1 gb|AF033817.1|:450-1739 922 516 60
gag HTLV 1 gb|AF033817.1|:450-1739 921 517 60 gag HTLV 1 gb|AF033817.1|:450-1739 917
518 60 gag HTLV 1 gb|AF033817.1|:450-1739 916 519 60 gag HTLV 1 gb|AF033817.1|:450-1739
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gb|AF033817.1|:1718-2404 608 522 60 pro HTLV 1 gb|AF033817.1|:1718-2404 607 523 60 pro
HTLV 1 gb|AF033817.1|:1718-2404 606 524 60 pro HTLV 1 gb|AF033817.1|:1718-2404 605 525
60 pro HTLV 1 gb|AF033817.1|:1718-2404 604 526 60 pro HTLV 1 gb|AF033817.1|:1718-2404
603 527 60 pro HTLV 1 gb|AF033817.1|:1718-2404 602 528 60 pro HTLV 1
gb|AF033817.1|:1718-2404 583 529 60 pro HTLV 1 gb|AF033817.1|:1718-2404 582 530 60 Pol
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HTLV 1 gi|9626453:2245-4836 2202 533 60 Pol HTLV 1 gi|9626453:2245-4836 2051 534 60 Pol
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HTLV 1 gi|9626453:2245-4836 1475 537 60 Pol HTLV 1 gi|9626453:2245-4836 1333 538 60 Pol
HTLV 1 gi|9626453:2245-4836 1242 539 60 Pol HTLV 1 gi|9626453:2245-4836 1182 540 60 rex
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HTLV 1 gi|9626453:4829-6295 662 565 60 env HTLV 1 gi|9626453:4829-6295 621 566 60 env
HTLV 1 gi|9626453:4829-6295 454 567 60 env HTLV 1 gi|9626453:4829-6295 388 568 60 env
HTLV 1 gi|9626453:4829-6295 297 569 60 env HTLV 1 gi|9626453:4829-6295 257 570 60 5' LTR
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gi|9626726:1-763 257 575 60 5' LTR HTLV 2 gi|9626726:1-763 256 576 60 5' LTR HTLV 2
gi|9626726:1-763 255 577 60 5' LTR HTLV 2 gi|9626726:1-763 254 578 60 5' LTR HTLV 2
gi|9626726:1-763 253 579 60 5' LTR HTLV 2 gi|9626726:1-763 251 580 60 gp1-tax protein HTLV
2 gi|9626726:6-119 52 581 60 gp1-tax protein HTLV 2 gi|9626726:6-119 51 582 60 gp1-tax protein
HTLV 2 gi|9626726:6-119 50 583 60 gp1-tax protein HTLV 2 gi|9626726:6-119 48 584 60 gp1-tax
protein HTLV 2 gi|9626726:6-119 44 585 60 gp1-tax protein HTLV 2 gi|9626726:6-119 43 586 60
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588 60 gp1-tax protein HTLV 2 gi|9626726:6-119 40 589 60 gp1-tax protein HTLV 2
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gi|9626726:316-8751 7844 592 60 gs1 HTLV 2 gi|9626726:316-8751 7700 593 60 gs1 HTLV 2
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619 60 polyprotein gp2-gag HTLV 2 gi|9626726:807-2108 901 620 60 polyprotein gp4-rex 26 kD
HTLV 2 gi|9626726:5121-7663 2053 621 60 protein gp4-rex 26 kD HTLV 2 gi|9626726:5121-
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NY99 gi|158516887:4612-6468 1512 723 60 protein NS3 nonstructural WNV NY99
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NY99 gi|158516887:6469-6834 156 735 60 protein NS4A nonstructural WNV NY99
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gi|158516887:6916-7680 683 742 60 protein NS4B nonstructural WNV NY99 gi|158516887:6916-
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NY99 gi|158516887:6916-7680 140 747 60 protein NS4B nonstructural WNV NY99
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WNV 956 gi|11528013:967-2457 597 795 60 protein E envelope WNV 956 gi|11528013:967-2457
483 796 60 protein E envelope WNV 956 gi|11528013:967-2457 397 797 60 protein E envelope
WNV 956 gi|11528013:967-2457 337 798 60 protein E envelope WNV 956 gi|11528013:967-2457
123 799 60 protein E envelope WNV 956 gi|11528013:967-2457 63 800 60 protein E nonstructural
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gi|11528013:2458-3513 827 802 60 protein NS1 nonstructural WNV 956 gi|11528013:2458-3513
826 803 60 protein NS1 nonstructural WNV 956 gi|11528013:2458-3513 825 804 60 protein NS1
nonstructural WNV 956 gi|11528013:2458-3513 824 805 60 protein NS1 nonstructural WNV 956
gi|11528013:2458-3513 823 806 60 protein NS1 nonstructural WNV 956 gi|11528013:2458-3513
822 807 60 protein NS1 nonstructural WNV 956 gi|11528013:2458-3513 821 808 60 protein NS1
nonstructural WNV 956 gi|11528013:2458-3513 820 809 60 protein NS1 nonstructural WNV 956
gi|11528013:2458-3513 819 810 60 protein NS1 nonstructural WNV 956 gi|11528013:3514-4206
556 811 60 protein NS2A nonstructural WNV 956 gi|11528013:3514-4206 536 812 60 protein
NS2A nonstructural WNV 956 gi|11528013:3514-4206 516 813 60 protein NS2A nonstructural
WNV 956 gi|11528013:3514-4206 496 814 60 protein NS2A nonstructural WNV 956
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401 816 60 protein NS2A nonstructural WNV 956 gi|11528013:3514-4206 345 817 60 protein
NS2A nonstructural WNV 956 gi|11528013:3514-4206 325 818 60 protein NS2A nonstructural
WNV 956 gi|11528013:3514-4206 305 819 60 protein NS2A nonstructural WNV 956
gi|11528013:3514-4206 279 820 60 protein NS2A nonstructural WNV 956 gi|11528013:4207-4599
249 821 60 protein NS2B nonstructural WNV 956 gi|11528013:4207-4599 248 822 60 protein
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gi|11528013:4207-4599 245 825 60 protein NS2B nonstructural WNV 956 gi|11528013:4207-4599
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NS2B nonstructural WNV 956 gi|11528013:4207-4599 242 828 60 protein NS2B nonstructural
WNV 956 gi|11528013:4207-4599 241 829 60 protein NS2B nonstructural WNV 956
gi|11528013:4207-4599 240 830 60 protein NS2B nonstructural WNV 956 gi|11528013:4600-6456
1798 831 60 protein NS3 nonstructural WNV 956 gi|11528013:4600-6456 1729 832 60 protein
NS3 nonstructural WNV 956 gi|11528013:4600-6456 1668 833 60 protein NS3 nonstructural
WNV 956 gi|11528013:4600-6456 1597 834 60 protein NS3 nonstructural WNV 956
gi|11528013:4600-6456 1437 835 60 protein NS3 nonstructural WNV 956 gi|11528013:4600-6456
1212 836 60 protein NS3 nonstructural WNV 956 gi|11528013:4600-6456 1150 837 60 protein
NS3 nonstructural WNV 956 gi|11528013:4600-6456 1073 838 60 protein NS3 nonstructural
WNV 956 gi|11528013:4600-6456 1013 839 60 protein NS3 nonstructural WNV 956
gi|11528013:4600-6456 809 840 60 protein NS3 nonstructural WNV 956 gi|11528013:6457-6834
206 841 60 protein NS4A nonstructural WNV 956 gi|11528013:6457-6834 205 842 60 protein
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gi|11528013:6904-7671 505 860 60 protein NS4B nonstructural WNV 956 gi|11528013:7672-
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956 gi|11528013:7672-10386 2048 865 60 protein NS5 nonstructural WNV 956 gi|11528013:7672-
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956 gi|11528013:7672-10386 1170 870 60 protein NS5 gp1- Chikungunya gi|27754751:77-7501
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nonstructural polyprotein gp1- Chikungunya gi|27754751:77-7501 7166 873 60 nonstructural
polyprotein gp1- Chikungunya gi|27754751:77-7501 7088 874 60 nonstructural polyprotein gp1-
Chikungunya gi|27754751:77-7501 7016 875 60 nonstructural polyprotein gp1- Chikungunya
gi|27754751:77-7501 6874 876 60 nonstructural polyprotein gp1- Chikungunya gi|27754751:77-
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structural Chikungunya gi|27754751:7567-11313 3441 881 60 polyprotein gp2-structural
Chikungunya gi|27754751:7567-11313 3376 882 60 polyprotein gp2-structural Chikungunya
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11313 2945 884 60 polyprotein gp2-structural Chikungunya gi|27754751:7567-11313 2815 885 60
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structural Chikungunya gi|27754751:7567-11313 2552 887 60 polyprotein gp2-structural
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Chikungunya gi|27754751:7567-10040 1631 894 60 polyprotein gp3-truncated Chikungunya
gi|27754751:7567-10040 1568 895 60 polyprotein gp3-truncated Chikungunya gi|27754751:7567-
10040 1294 896 60 polyprotein gp3-truncated Chikungunya gi|27754751:7567-10040 1224 897 60
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Chikungunya gi|27754751:7567-10040 899 900 60 polyprotein anchored capsid DEN 1
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protein C anchored capsid DEN 1 gi|9626685:95-436 216 903 60 protein C anchored capsid DEN 1
gi|9626685:95-436 193 904 60 protein C anchored capsid DEN 1 gi|9626685:95-436 165 905 60
protein C anchored capsid DEN 1 gi|9626685:95-436 145 906 60 protein C anchored capsid DEN 1
gi|9626685:95-436 125 907 60 protein C anchored capsid DEN 1 gi|9626685:95-436 105 908 60
protein C anchored capsid DEN 1 gi|9626685:95-436 81 909 60 protein C anchored capsid DEN 1
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precursor M membrane DEN 1 gi|9626685:437-934 437 913 60 glycoprotein precursor M
membrane DEN 1 gi|9626685:437-934 436 914 60 glycoprotein precursor M membrane DEN 1
gi|9626685:437-934 435 915 60 glycoprotein precursor M membrane DEN 1 gi|9626685:437-934
434 916 60 glycoprotein precursor M membrane DEN 1 gi|9626685:437-934 433 917 60
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precursor M membrane DEN 1 gi|9626685:437-934 431 919 60 glycoprotein precursor M
membrane DEN 1 gi|9626685:437-934 430 920 60 glycoprotein precursor M envelope DEN 1
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protein E envelope DEN 1 gi|9626685:935-2419 1163 923 60 protein E envelope DEN 1
gi|9626685:935-2419 1082 924 60 protein E envelope DEN 1 gi|9626685:935-2419 954 925 60
protein E envelope DEN 1 gi|9626685:935-2419 892 926 60 protein E envelope DEN 1
gi|9626685:935-2419 820 927 60 protein E envelope DEN 1 gi|9626685:935-2419 734 928 60
protein E envelope DEN 1 gi|9626685:935-2419 674 929 60 protein E envelope DEN 1
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60 protein NS1 nonstructural DEN 1 gi|9626685:2420-3475 897 932 60 protein NS1 nonstructural
DEN 1 gi|9626685:2420-3475 837 933 60 protein NS1 nonstructural DEN 1 gi|9626685:2420-3475
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938 60 protein NS1 nonstructural DEN 1 gi|9626685:2420-3475 436 939 60 protein NS1
nonstructural DEN 1 gi|9626685:2420-3475 359 940 60 protein NS1 nonstructural DEN 1
gi|9626685:3476-4129 592 941 60 protein NS2A nonstructural DEN 1 gi|9626685:3476-4129 517
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946 60 protein NS2A nonstructural DEN 1 gi|9626685:3476-4129 309 947 60 protein NS2A
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gi|9626685:3476-4129 131 949 60 protein NS2A nonstructural DEN 1 gi|9626685:3476-4129 86
950 60 protein NS2A nonstructural DEN 1 gi|9626685:4130-4519 331 951 60 protein NS2B
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954 60 protein NS2B nonstructural DEN 1 gi|9626685:4130-4519 327 955 60 protein NS2B
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958 60 protein NS2B nonstructural DEN 1 gi|9626685:4130-4519 323 959 60 protein NS2B
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962 60 protein NS3 nonstructural DEN 1 gi|9626685:4520-6376 1213 963 60 protein NS3
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966 60 protein NS3 nonstructural DEN 1 gi|9626685:4520-6376 973 967 60 protein NS3
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gi|9626685:4520-6376 785 969 60 protein NS3 nonstructural DEN 1 gi|9626685:4520-6376 725
970 60 protein NS3 nonstructural DEN 1 gi|9626685:6377-6757 302 971 60 protein NS4A
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974 60 protein NS4A nonstructural DEN 1 gi|9626685:6377-6757 134 975 60 protein NS4A
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978 60 protein NS4A nonstructural DEN 1 gi|9626685:6377-6757 23 979 60 protein NS4A
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982 60 protein NS4B nonstructural DEN 1 gi|9626685:6827-7573 506 983 60 protein NS4B
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2425 994 60 protein NS5 nonstructural DEN 1 gi|9626685:7574-10270 2276 995 60 protein NS5
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1982 998 60 protein NS5 nonstructural DEN 1 gi|9626685:7574-10270 1919 999 60 protein NS5
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1002 60 protein C anchored capsid DEN 2 gi|158976983:97-438 279 1003 60 protein C anchored
capsid DEN 2 gi|158976983:97-438 278 1004 60 protein C anchored capsid DEN 2
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1006 60 protein C anchored capsid DEN 2 gi|158976983:97-438 275 1007 60 protein C anchored
capsid DEN 2 gi|158976983:97-438 274 1008 60 protein C anchored capsid DEN 2
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1010 60 protein C membrane DEN 2 gi|158976983:439-936 439 1011 60 glycoprotein precursor M
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gi|158976983:439-936 314 1015 60 glycoprotein precursor M membrane DEN 2
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gi|158976983:439-936 229 1017 60 glycoprotein precursor M membrane DEN 2
gi|158976983:439-936 60 1018 60 glycoprotein precursor M membrane DEN 2 gi|158976983:439-
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gi|158976983:3478-4131 550 1041 60 protein NS2A nonstructural DEN 2 gi|158976983:3478-
4131 508 1042 60 protein NS2A nonstructural DEN 2 gi|158976983:3478-4131 468 1043 60
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protein NS3 nonstructural DEN 2 gi|158976983:4522-6375 1246 1068 60 protein NS3
nonstructural DEN 2 gi|158976983:4522-6375 1186 1069 60 protein NS3 nonstructural DEN 2
gi|158976983:4522-6375 1126 1070 60 protein NS3 nonstructural DEN 2 gi|158976983:6376-6756
312 1071 60 protein NS4A nonstructural DEN 2 gi|158976983:6376-6756 311 1072 60 protein
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DEN 2 gi|158976983:6376-6756 309 1074 60 protein NS4A nonstructural DEN 2
gi|158976983:6376-6756 308 1075 60 protein NS4A nonstructural DEN 2 gi|158976983:6376-
6756 307 1076 60 protein NS4A nonstructural DEN 2 gi|158976983:6376-6756 306 1077 60
protein NS4A nonstructural DEN 2 gi|158976983:6376-6756 305 1078 60 protein NS4A
nonstructural DEN 2 gi|158976983:6376-6756 304 1079 60 protein NS4A nonstructural DEN 2
gi|158976983:6376-6756 303 1080 60 protein NS4A nonstructural DEN 2 gi|158976983:6826-
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protein NS4B nonstructural DEN 2 gi|158976983:6826-7569 532 1083 60 protein NS4B
nonstructural DEN 2 gi|158976983:6826-7569 491 1084 60 protein NS4B nonstructural DEN 2
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protein NS4B nonstructural DEN 2 gi|158976983:6826-7569 168 1088 60 protein NS4B
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DEN 2 gi|158976983:7570-10269 2379 1095 60 dependent RNA pol. NS5 RNA- DEN 2
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1102 60 protein C anchored capsid DEN 3 gi|163644368:95-436 281 1103 60 protein C anchored
capsid DEN 3 gi|163644368:95-436 280 1104 60 protein C anchored capsid DEN 3
gi|163644368:95-436 279 1105 60 protein C anchored capsid DEN 3 gi|163644368:95-436 278
1106 60 protein C anchored capsid DEN 3 gi|163644368:95-436 277 1107 60 protein C anchored
capsid DEN 3 gi|163644368:95-436 276 1108 60 protein C anchored capsid DEN 3
gi|163644368:95-436 275 1109 60 protein C anchored capsid DEN 3 gi|163644368:95-436 274
1110 60 protein C membrane DEN 3 gi|163644368:437-934 439 1111 60 glycoprotein precursor M
membrane DEN 3 gi|163644368:437-934 438 1112 60 glycoprotein precursor M membrane DEN 3
gi|163644368:437-934 437 1113 60 glycoprotein precursor M membrane DEN 3
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gi|163644368:437-934 431 1118 60 glycoprotein precursor M membrane DEN 3
gi|163644368:437-934 430 1119 60 glycoprotein precursor M membrane DEN 3
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1128 60 protein E envelope DEN 3 gi|163644368:935-2413 805 1129 60 protein E envelope DEN
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nonstructural DEN 3 gi|163644368:2414-3469 492 1137 60 protein NS1 nonstructural DEN 3
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320 1139 60 protein NS1 nonstructural DEN 3 gi|163644368:2414-3469 256 1140 60 protein NS1
nonstructural DEN 3 gi|163644368:3470-4123 592 1141 60 protein NS2A nonstructural DEN 3
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10264 2516 1192 60 protein NS5 nonstructural DEN 3 gi|163644368:7565-10264 2456 1193 60
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membrane DEN 4 gi|12084822:441-938 73 1218 60 glycoprotein precursor M membrane DEN 4
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DEN 4 gi|12084822:2424-3479 823 1232 60 protein NS1 non-structural DEN 4 gi|12084822:2424-
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NS1 non-structural DEN 4 gi|12084822:2424-3479 570 1235 60 protein NS1 non-structural DEN 4
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NS2B non-structural DEN 4 gi|12084822:4134-4523 324 1258 60 protein NS2B non-structural
DEN 4 gi|12084822:4134-4523 323 1259 60 protein NS2B non-structural DEN 4
gi|12084822:4134-4523 311 1260 60 protein NS2B non-structural DEN 4 gi|12084822:4524-6377
1780 1261 60 protein NS3 non-structural DEN 4 gi|12084822:4524-6377 1679 1262 60 protein
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structural DEN 4 gi|12084822:4524-6377 1088 1268 60 protein NS3 non-structural DEN 4
gi|12084822:4524-6377 1027 1269 60 protein NS3 non-structural DEN 4 gi|12084822:4524-6377
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NS4A non-structural DEN 4 gi|12084822:6378-6758 317 1276 60 protein NS4A non-structural
DEN 4 gi|12084822:6378-6758 316 1277 60 protein NS4A non-structural DEN 4
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314 1279 60 protein NS4A non-structural DEN 4 gi|12084822:6378-6758 313 1280 60 protein
NS4A non-structural DEN 4 gi|12084822:6828-7562 657 1281 60 protein NS4B non-structural
DEN 4 gi|12084822:6828-7562 536 1282 60 protein NS4B non-structural DEN 4
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DEN 4 gi|12084822:6828-7562 326 1287 60 protein NS4B non-structural DEN 4
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protein NS5 non-structural DEN 4 gi|12084822:7563-10262 2153 1295 60 protein NS5 non-
structural DEN 4 gi|12084822:7563-10262 2093 1296 60 protein NS5 non-structural DEN 4
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GB virus C/ gi|9628705:459-9080 8205 1301 60 precursor Hepatitis G polyprotein GB virus C/
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gi|9628705:459-1538 545 1311 60 protein Hepatitis G putative E1 GB virus C/ gi|9628705:459-
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protein Hepatitis G putative E1 GB virus C/gi|9628705:459-1538 924 1314 60 protein Hepatitis G
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virus C/ gi|9628705:459-1538 783 1316 60 protein Hepatitis G putative E1 GB virus C/
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1538 644 1318 60 protein Hepatitis G putative E1 GB virus C/gi|9628705:459-1538 601 1319 60
protein Hepatitis G putative E1 GB virus C/gi|9628705:459-1538 505 1320 60 protein Hepatitis G
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virus C/gi|9628705:1539-2474 847 1322 60 protein Hepatitis G putative E2 GB virus C/
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protein Hepatitis G putative E2 GB virus C/gi|9628705:1539-2474 611 1326 60 protein Hepatitis
G putative E2 GB virus C/gi|9628705:1539-2474 573 1327 60 protein Hepatitis G putative E2 GB
virus C/ gi|9628705:1539-2474 543 1328 60 protein Hepatitis G putative E2 GB virus C/
gi|9628705:1539-2474 502 1329 60 protein Hepatitis G putative E2 GB virus C/ gi|9628705:1539-
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Hepatitis G putative protein GB virus C/gi|9628705:2475-3233 532 1334 60 p7-NS2 Hepatitis G
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protein GB virus C/ gi|9628705:2475-3233 472 1336 60 p7-NS2 Hepatitis G putative protein GB
virus C/ gi|9628705:2475-3233 350 1337 60 p7-NS2 Hepatitis G putative protein GB virus C/
gi|9628705:2475-3233 320 1338 60 p7-NS2 Hepatitis G putative protein GB virus C/
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virus C/gi|9628705:7389-9077 1274 1382 60 RNA- Hepatitis G dependent RNA pol. putative
NS5B GB virus C/gi|9628705:7389-9077 856 1383 60 RNA- Hepatitis G dependent RNA pol.
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RNA pol. putative NS5B GB virus C/gi|9628705:7389-9077 373 1386 60 RNA- Hepatitis G
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9077 371 1388 60 RNA- Hepatitis G dependent RNA pol. putative NS5B GB virus C/
gi|9628705:7389-9077 74 1389 60 RNA- Hepatitis G dependent RNA pol. putative NS5B GB virus
C/gi|9628705:7389-9077 73 1390 60 RNA- Hepatitis G dependent RNA pol. 1A VP4b Hepatitis
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1392 60 mature peptide A virus 1A VP4b Hepatitis gi|9626732:1-805 568 1393 60 mature peptide
A virus 1A VP4b Hepatitis gi|9626732:1-805 513 1394 60 mature peptide A virus 1A VP4b
Hepatitis gi|9626732:1-805 466 1395 60 mature peptide A virus 1A VP4b Hepatitis gi|9626732:1-
805 426 1396 60 mature peptide A virus 1A VP4b Hepatitis gi|9626732:1-805 378 1397 60 mature
peptide A virus 1A VP4b Hepatitis gi|9626732:1-805 338 1398 60 mature peptide A virus 1A VP4b
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805 159 1400 60 mature peptide A virus 1B VP2 Hepatitis gi|9626732:804-1469 606 1401 60
mature peptide A virus 1B VP2 Hepatitis gi|9626732:804-1469 546 1402 60 mature peptide A virus
1B VP2 Hepatitis gi|9626732:804-1469 486 1403 60 mature peptide A virus 1B VP2 Hepatitis
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329 1405 60 mature peptide A virus 1B VP2 Hepatitis gi|9626732:804-1469 269 1406 60 mature
peptide A virus 1B VP2 Hepatitis gi|9626732:804-1469 203 1407 60 mature peptide A virus 1B
VP2 Hepatitis gi|9626732:804-1469 143 1408 60 mature peptide A virus 1B VP2 Hepatitis
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22 1410 60 mature peptide A virus 1C VP3 Hepatitis gi|9626732:1470-2207 679 1411 60 mature
peptide A virus 1C VP3 Hepatitis gi|9626732:1470-2207 619 1412 60 mature peptide A virus 1C
VP3 Hepatitis gi|9626732:1470-2207 559 1413 60 mature peptide A virus 1C VP3 Hepatitis
gi|9626732:1470-2207 499 1414 60 mature peptide A virus 1C VP3 Hepatitis gi|9626732:1470-
2207 439 1415 60 mature peptide A virus 1C VP3 Hepatitis gi|9626732:1470-2207 379 1416 60
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virus 1C VP3 Hepatitis gi|9626732:1470-2207 246 1418 60 mature peptide A virus 1C VP3
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virus 1D VP1 Hepatitis gi|9626732:2208-3107 594 1424 60 mature peptide A virus 1D VP1
Hepatitis gi|9626732:2208-3107 534 1425 60 mature peptide A virus 1D VP1 Hepatitis
gi|9626732:2208-3107 434 1426 60 mature peptide A virus 1D VP1 Hepatitis gi|9626732:2208-
3107 374 1427 60 mature peptide A virus 1D VP1 Hepatitis gi|9626732:2208-3107 314 1428 60
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virus 1D VP1 Hepatitis gi|9626732:2208-3107 189 1430 60 mature peptide A virus 2A mature
Hepatitis gi|9626732:3108-3674 494 1431 60 peptide A virus 2A mature Hepatitis
gi|9626732:3108-3674 452 1432 60 peptide A virus 2A mature Hepatitis gi|9626732:3108-3674
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136 1437 60 peptide A virus 2A mature Hepatitis gi|9626732:3108-3674 96 1438 60 peptide A
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1441 60 peptide A virus 2B mature Hepatitis gi|9626732:3675-3995 261 1442 60 peptide A virus
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1469 60 peptide A virus 3A mature Hepatitis gi|9626732:5001-5222 77 1470 60 peptide A virus 3B
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Hepatitis gi|9626732:5001-5291 226 1477 60 mature peptide A virus 3B (VPg) Hepatitis
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Hepatitis gi|9626732:5949-7415 1113 1495 60 peptide A virus 3D mature Hepatitis
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WCCV1 gi|52220883:75-1925 1290 1576 60 RNA pol. RNA1 RNA dependent WCCV1
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RNA 65 76.05 0 23.33 11.67 20 45 35 5 5' trailer RNA 73 75.88 0 23.33 11.67 21.67 43.33 35 5 5'
trailer RNA 74 76.29 0 23.33 11.67 23.33 41.67 35 5 5' trailer RNA 75 76.29 0 23.33 11.67 25 40
35 5 5' trailer RNA 76 76.39 0 25 11.67 25 38.33 36.67 5 NS5 protein 498 80.74 0 23.33 21.67
33.33 21.67 45 4 NS5 protein 559 81.87 0 25 20 35 20 45 5 NS5 protein 632 80.62 0 30 15 28.33
26.67 45 5 NS5 protein 872 82.48 0 20 25 28.33 26.67 45 4 NS5 protein 1080 81.39 0 28.33 16.67
40 15 45 4 NS5 protein 1140 81.31 0 26.67 16.67 23.33 33.33 43.33 3 NS5 protein 1284 81.05 0
31.67 13.33 28.33 26.67 45 2 NS5 protein 1350 81.53 0 23.33 21.67 31.67 23.33 45 5 NS5 protein
1411 78.37 0 23.33 15 43.33 18.33 38.33 5 NS5 protein 1506 81.82 0 25 20 36.67 18.33 45 3 NS5
protein 336 81.2 0 26.67 18.33 26.67 28.33 45 3 NS5 protein 399 81.27 0 25 20 33.33 21.67 45 4
NS5 protein 508 80.62 0 30 15 28.33 26.67 45 5 NS5 protein 748 82.48 0 20 25 28.33 26.67 45 4
NS5 protein 956 81.39 0 28.33 16.67 40 15 45 4 NS5 protein 1016 81.31 0 26.67 16.67 23.33
33.33 43.33 3 NS5 protein 1160 81.05 0 31.67 13.33 28.33 26.67 45 2 NS5 protein 1226 81.53 0
23.33 21.67 31.67 23.33 45 5 NS5 protein 1287 78.37 0 23.33 15 43.33 18.33 38.33 5 NS5 protein
1381 81.05 0 26.67 18.33 36.67 18.33 45 3 NS5 protein 101 81.2 0 26.67 18.33 26.67 28.33 45 3
NS5 protein 164 81.27 0 25 20 33.33 21.67 45 4 NS5 protein 273 80.62 0 30 15 28.33 26.67 45 5
NS5 protein 513 82.48 0 20 25 28.33 26.67 45 4 NS5 protein 721 81.39 0 28.33 16.67 40 15 45 4
NS5 protein 781 81.31 0 26.67 16.67 23.33 33.33 43.33 3 NS5 protein 925 81.05 0 31.67 13.33
28.33 26.67 45 2 NS5 protein 991 81.53 0 23.33 21.67 31.67 23.33 45 5 NS5 protein 1052 78.37 0
23.33 15 43.33 18.33 38.33 5 NS5 protein 1146 81.05 0 26.67 18.33 36.67 18.33 45 3 NS5 protein
375 80.74 0 23.33 21.67 33.33 21.67 45 4 NS5 protein 510 80.62 0 28.33 16.67 30 25 45 5 NS5
protein 749 82.48 0 20 25 28.33 26.67 45 4 NS5 protein 957 81.39 0 28.33 16.67 40 15 45 4 NS5
protein 1017 81.31 0 26.67 16.67 23.33 33.33 43.33 3 NS5 protein 1161 81.05 0 31.67 13.33 28.33
26.67 45 2 NS5 protein 1227 81.53 0 23.33 21.67 31.67 23.33 45 5 NS5 protein 1288 78.37 0
23.33 15 43.33 18.33 38.33 5 NS5 protein 1353 82.74 0 21.67 23.33 38.33 16.67 45 5 NS5 protein
1459 80.12 0 30 15 31.67 23.33 45 2 5UTR 60 78.39 0 25 15 30 30 40 4 5UTR 69 78.43 0 26.67
11.67 35 26.67 38.33 4 capsid 144 77.34 0 21.67 13.33 41.67 23.33 35 3 capsid 160 79.12 0 28.33
11.67 41.67 18.33 40 6 propeptide 174 80.99 0 23.33 21.67 28.33 26.67 45 3 propeptide 183 78.98
0 23.33 16.67 31.67 28.33 40 2 membrane 64 81.94 0 20 25 31.67 23.33 45 5 protein membrane 78
80.99 0 25 20 26.67 28.33 45 5 protein envelope 74 80.57 0 25 20 16.67 38.33 45 5 protein
envelope 194 81.61 0 26.67 15 26.67 31.67 41.67 5 protein envelope 447 80.6 0 21.67 23.33 33.33
21.67 45 4 protein envelope 960 79.05 0 23.33 18.33 23.33 35 41.67 4 protein envelope 1198 82.15
0 26.67 18.33 28.33 26.67 45 5 protein NS1 protein 64 79.96 0 21.67 21.67 31.67 25 43.33 2 NS1
protein 439 80.43 0 26.67 16.67 38.33 18.33 43.33 4 NS1 protein 608 77.05 0 26.67 13.33 26.67
33.33 40 3 NS1 protein 866 81.68 0 28.33 16.67 31.67 23.33 45 5 NS2A protein 148 80.85 0 25 20
28.33 26.67 45 4 NS2A protein 152 80.03 0 25 18.33 28.33 28.33 43.33 4 NS2A protein 451 80.55
0 23.33 21.67 25 30 45 3 NS2B protein 287 81.46 0 28.33 16.67 40 15 45 5 NS2B protein 292
80.68 0 28.33 15 40 16.67 43.33 5 NS2B protein 297 81.32 0 30 15 36.67 18.33 45 5 NS3 protein
192 81.23 0 26.67 18.33 36.67 18.33 45 3 NS3 protein 395 80.79 0 15 30 28.33 26.67 45 3 NS3
protein 797 82.73 0 28.33 16.67 28.33 26.67 45 5 NS3 protein 1131 81.83 0 18.33 26.67 33.33
21.67 45 3 NS4A protein 246 81.88 0 33.33 11.67 23.33 31.67 45 5 NS4A protein 204 87.21 0
33.33 21.67 18.33 26.67 55 4 NS4A protein 383 86.35 0 28.33 26.67 28.33 16.67 55 3 NS4B
protein 112 80.14 0 23.33 21.67 33.33 21.67 45 5 NS4B protein 819 80.74 0 23.33 21.67 28.33
26.67 45 3 NS4B protein 1082 80.52 0 26.67 16.67 33.33 23.33 43.33 3 NS4B protein 1506 80.98
0 31.67 13.33 38.33 16.67 45 3 NS5 protein 74 80.74 0 23.33 21.67 33.33 21.67 45 4 NS5 protein
716 81.31 0 26.67 16.67 23.33 33.33 43.33 3 NS5 protein 1172 79.51 0 30 15 35 20 45 3 3UTR 61
84.45 0 40 15 25 20 55 4 3UTR 70 84.24 0 33.33 21.67 23.33 21.67 55 4 WCCV - White clover
cryptic virus; BBWV - Broad bean wilt virus; LNYV - Lettuce necrotic yellows virus
(86) TABLE-US-00002 TABLE 2 Viral pathogens used in testing the Pathogen Chip Virus
Type/Strain Source References CHIKV R91064 FDA/CBER Lot Release Panels* HAV SD11 Dr.
Farci Lab HCV Genotype 1b Sera Care (Sera Care, Milford, MA) HCV Genotype 2a Sera Care
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(Sera Care, Milford, MA) HCV Genotype 3 Sera Care (Sera Care, Milford, MA) HEV Genotype 3a WHO Standard HIV-1 Group M, FDA/CBER Lot Release Panels 1, 2 Subtype B HIV-2 Subtype B FDA/CBER Lot Release Panels 3 DENGUE Serotype 1, *Aedes albopictus* 4 2, 3 and 4 C6/36 cell culture HTLV-I ZeptoMetrix HTLV-II ZeptoMetrix WEST NY99 Cell culture 5 NILE ZIKA PRVABC62 FDA/CBER Lot Release Panels ZIKA FSS13025 FDA/CBER Lot Release Panels *The FDA Center for Biologies Evaluation and Research (CBER), Division of Emerging and Transfusion Transmitted Diseases produces and makes available to blood donor screening test manufacturers panels which are sets of vialed human plasma containing virus particles that are carefully quantified for evaluating virus detection devices. Each set has several vials each one a different virus concentration and some with virus-free plasma. These panels are also used to test each new lot of a licensed blood donor screening device for release to the public, hence they are called Lot Release Panels. There are separate panels prepared for each type of virus. 1 Davis et al., *J Virol Methods*, 107: 37-44 (2003) 2 Lee et al., *J Virol Methods*, 137: 287-291 (2006) 3 Lee et al., *J Virol Methods*, 137: 287-291 (2006) 3 Lee et al., *J Virol Methods*, 137: 287-291 (2006). 5 Grinev et al., *J Virol Methods*, 154: 27-40 (2008).

- (87) Nucleic acids from positive plasma and from NATtrol were extracted using the Dynabeads™ SILANE Viral NA Kit (ThermoFisher Scientific, Waltham, MA) according to the manufacturer's protocol.
- (88) cDNA from random-primed, reverse-transcribed total RNA was performed with the Ovation® Pico WTA System (NuGEN, San Carlos, CA) using the manufacturer's recommended protocols and input amounts. For this study, the Agilent SureTag® Labeling Kit was used for generating $Cy^{TM}3$ dye labeled cDNA targets. Labeled cDNA was purified with SureTag® Kit spin columns and specific activities (degree of labeling) were calculated for use in hybridization reactions. A master mix containing $10\times$ blocking agent and $2\times$ GE hybridization buffer HI-RPM, was added to 3-5 µg of labeled cDNA, denatured, and hybridized to arrays under 8-chamber gasket slides at 65° C. with 20-rpm rotation for 24 hours in an Agilent hybridization oven. Arrays were processed using wash procedure A and scanned on an Agilent SureScan® G4900DA microarray scanner using 5-µm resolution.
- (89) Microarray-based platform data analysis: After scanning, microarray images were analyzed using Agilent Feature Extraction software (Agilent Technologies, Inc., Santa Clara, CA) with default protocols and settings. Average pixel intensity and subtraction of local background for each feature was calculated. Images were manually examined to note any arrays affected by high background, scratches, or other technical artifacts. Probe sets associated with low signal intensity or bad quality features were considered unreliable and excluded from the analysis. Feature intensities for CyTM3 dye channels were imported into the PartekTM Genomics SuiteTM software (Partek Inc., St. Louis, MO, USA).
- (90) First, microarray analysis was performed by ranking the highest signal intensity probes by the mean of the set of probes defining each pathogen on the platform. Next, an experimental threshold was defined as a log ratio of signal intensity mean for the set of probes defining each pathogen and the mean of the Agilent control probes set. The threshold was applied to all the arrays tested to define the final parameters for test validation.
- (91) RT-qPCR Validation
- (92) Altona RT-qPCR: CHIKV, DENV 1-4 and ZIKV positive specimens were quantified using the Altona RealStar RT-qPCR kit (Altona Diagnostic GmbH, Hamburg, Germany) according to the manufacturer's instructions. The positive control and the internal control were provided by the manufacturer. Serial dilutions of CHIKV (ATCC VR-3246SD), DENV (ATCC VR-3231SD), and ZIKV (ATCC VR-1843DQ) quantitative genomic RNA (specification range: 1×10.sup.5-1×10.sup.6 copies/4) obtained from ATCC (American Type Culture Collection Manassas, VA) were prepared to generate a standard curve for copy number quantification.
- (93) Primer Design (Genesig) RT-qPCR: HAV (target/5' NCR), HCV (5'UTR), HEV (ORF2), HIV-

- 1 (target/POL), HIV-2 (target/POL), HTLVI (target/POL), HTLVII (target/POL), and WNV (5'UTR) positive specimens were quantified using the Primer Design Genesig kit (Primerdesign Ltd, United Kingdom) according to the manufacturer's protocol (OneStep RT-qPCR protocol). Each kit contained a positive control template for the PCR set up and for copy number determination (generated serial dilutions for the standard curve).
- (94) The RT-qPCR assays were performed on a ViiA7 Applied Biosystems real-time PCR system (Thermo Fisher Scientific Inc., Waltham, MA, USA). Each sample was tested in duplicate and the mean C.sub.q value was calculated.

Example 2

Microarray Design, Specificity, and Validation

- (95) Microarray design: The pathogen chip design strategy was to cover all high priority bloodborne RNA viruses (retroviruses and both positive- and negative-strand RNA viruses) using multiple probes to independent targets sites in the genome of each species. In total, 1,769 unique viral oligonucleotides derived from 16 distinct viral genomes (Table 1) were included that allowed discrimination of pathogens at the level of species, subtypes and genotypes. The microarray was supplemented with an additional number of predesigned GE array probes for 906 genes from the human genome, 84 ERCC probes and 120 probes specific for plant viruses representing negative controls (Table 3).
- (96) TABLE-US-00003 TABLE 3 Probe distribution on pathogen chip Probe group Number of Number of type targets probes Purpose All spot 1010 14,716 RNA pathogens coverage and internal controls Pathogen Specific 17 1,769 Probes intensity analysis (not replicated) of pathogen specific genes Internal Control 902 902 Agilent requirement (replicated for probes normalization 10 times) ERCC probes 84 84 Determination of (replicated intra-probe variance 45 times) Negative Control 3 120 Determination of (not replicated) probes cross reactivity
- (97) The design included multiple gene targets for each pathogen genome in order to select the best probes for the final platform design. The design strategy was to balance the number of probes for each pathogen with a final count of 90-110 probes each. Probes selected in the final design generated a more intense signal and produced higher percentage coverage of the specific genome across the different experiments (FIG. **1**A).
- (98) Microarray specificity: One of the challenges impacting the sensitivity of microarray based multi-pathogen nucleic acid detection in blood specimens is the relatively small concentration of target nucleic acids compared to a high background concentration of human DNA. A novel workflow was designed, combining two different applications (Agilent and Nugen), that had not been previously combined, to address this challenge. Typically, the Agilent amplification WT kit (Oligo dT) is used to amplify total RNA, with a minimum nucleic acid requirement of 25 nanograms, and produces a cRNA final product that is labelled with Cy3 fluorophore. The workflow was modified using a method that generates amplified cDNA from as little as 500 picograms of target viral RNA. One single-primer isothermal amplification using Nugen Ribo-SPIA technology was combined with the Agilent Genomic DNA Enzymatic Labeling Kit for generating Cy3 labeled cDNA. This kit was not previously developed for single color RNA probes and produces 300% the amplified product compared to the standard methodology (FIG. 1B, FIG. **2**A). Nearly all samples were detected on the platform and all probes generated a strong signal specific for each positive plasma specimen analyzed. No specific signal was produced by negative control plasma (FIG. 2B). Random non-specific intensity signal was produced in only a few arrays. This indicated that the generation of cDNA instead of amplified RNA followed by Cy3 labelling and hybridization based on a DNA application was successful (FIG. 2C).
- (99) Analysis strategies: Quality of signals generated by probes for each species was assessed according to two experimental criteria: 1) defining a threshold able to distinguish a true signal from its background; and 2) defining true positives only when 50% of probes generated a signal above the set threshold. These two levels of data analysis were needed to detect positive probes in the

presence of multi-pathogen testing at the same time and at different concentrations.

- (100) The threshold was defined as the log ratio between the signal intensity mean for each pathogen specific probe set and the mean of the Agilent control group probe set. After comparing the results of the same set of probes across different arrays and selecting the probes showing an inter-array reproducibility, an experimental threshold value was defined as follows: Log Ratio \leq 1 negative; Log Ratio \geq 1.5 borderline; Log Ratio \geq 1.5 positive.
- (101) Data analysis at the individual probe level was also performed to assess if the tested samples were false positives. Only when at least 50% of specific probes had Log Ratio >1.5 was the test considered valid (FIG. 1C).
- (102) For nearly all borderline results, only 20-25% of the specific probes showed mean intensity in the correct range, so the test was defined negative. For positive results (Log Ratio >1.5) more than 50% of the specific probes set were in the correct range. One example was an HCV 1a positive plasma samples test that was detected by 110 out of 110 probes at a concentration of 10.sup.5 copies/mL, 90 out of 110 probes at a concentration of 10.sup.4 copies/mL, and 70 out of 110 probes at a concentration of 10.sup.3 copies/mL. On average, at 10.sup.2 copies/mL more than 50% of the probes were generating a fluorescence signal above the set threshold.
- (103) Data from more than 168 tested samples (one or multiple targets per array) showed consistent results. The mean of the probes specific for any positive plasma sample was always at least 10-fold higher than the mean of internal control probes (background), showing a wide probe population range of intensity. As shown in Table 4 and Table 5, the Log Ratio was above 1.5 for all the pathogens tested at a concentration of 10.sup.2 copies/mL and there were no cross reactions with other probes across the platform.
- (104) Microarray sensitivity: HAV, CHIKV, DENV1-4, HCV Genotypes 1a, 2b, and 3, HIV-1,2 and WNV strain NY99 had 10.sup.2 copies/mL limits of detection. The lowest detectable level for HEV was 10.sup.4 copies/mL. The analytical sensitivity for each assay was determined using a concentration range based on the clinical requirement for pathogen detection. There were no false negatives or false positives when testing the positive plasma. In the presence of very low pathogen concentrations, the log ratio was at the borderline level so the results were qualified according to double level analysis (at least 50% of the probes generated a fluorescence signal above the set threshold). In the presence of negative plasma samples, the log ratio value was always negative (Table 4).
- (105) A mix of different positive plasma samples at different concentrations was simultaneously tested in a single experiment. Four different combinations were generated. The multi-pathogens-mixes were composed of 8 (CHIKV, DEN3, DEN1, HAV, HCV1a, HEV, WNV and ZIKV), 4 (CHIKV, DEN1, ZKV, WNV), 4 (DENV3, HAV HCV1a HEV) and 3 (CHIKV, DEN1, ZIKV) different pathogens, respectively at a concentration range from 10.sup.5 to 10.sup.3 copies/mL. (Table 6).
- (106) TÁBLE-US-00004 TABLE 4 Test results based on Log ratio CK DEN1 DEN2 DEN3 DEN4 HAV HCV1a HCV2a CK 2.42 -1.15 -1.22 -0.04 -0.28 -0.50 -0.24 -0.35 DEN1 -0.12 1.60 -0.33 0.09 0.14 -0.08 -0.20 -0.31 DEN2 -0.24 -0.82 1.84 -0.30 -0.25 -0.24 -0.17 -0.28 DEN3 0.03 -0.19 -0.02 1.62 -0.24 -0.28 -0.24 -0.34 DEN4 0.07 -0.31 -0.64 0.18 1.80 -0.64 -0.17 -0.28 HAV -0.06 -0.97 -1.24 -0.25 -0.34 2.97 -0.21 -0.31 HCV1 0.46 -0.53 -0.55 0.63 0.56 0.26 2.91 2.80 HCV2 0.47 -0.60 -0.72 0.66 0.31 0.09 2.16 2.85 HCV3 0.39 -0.73 -0.77 0.06 0.06 -0.07 2.63 2.53 HEV 0.41 -0.62 -0.63 0.23 0.35 1.06 -0.14 -0.24 HIV1 0.96 0.55 0.08 0.77 0.56 0.01 0.05 -0.06 HIV2 -0.13 -0.90 -0.94 0.02 -0.29 -0.07 -0.09 -0.20 HTLVI -0.57 -1.29 -1.43 -0.35 -0.55 -0.51 -0.06 -0.17 HTLVII -0.21 -1.11 -1.19 -0.45 -0.40 -0.21 0.19 0.08 WNV 0.10 -0.50 -0.70 0.21 -0.34 -0.33 -0.19 -0.29 ZKV -0.29 -0.64 -0.92 -0.49 -0.41 -0.45 0.12 0.26 HCV3 HEV HIV-1 HIV-2 HTLVI HTLVII WNV ZKV NC CK -0.56 -0.02 -0.99 -0.68 -0.42 -0.96 -0.97 -0.20 -0.96 DEN1 -0.52 0.46 -0.76 -0.55 -0.28 -0.76 -0.53 0.00 -0.86 DEN2 -0.49 -0.11 -1.13 -0.89 -0.52 -0.84 -1.00 -0.28 -1.01 DEN3 -0.55 0.01 -0.95 -0.81

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-0.56 - 0.91 - 0.22 \ 0.05 - 0.96 \ DEN4 - 0.49 - 0.20 - 1.02 - 0.80 - 0.66 - 1.05 - 0.30 - 0.36 - 1.07
HAV -0.52 0.35 -0.78 -0.47 -0.35 -0.71 -1.22 -0.04 -0.69 HCV1 2.59 0.79 -0.30 0.94 0.44
-0.05 -0.43 0.60 -0.37 HCV2 1.84 0.76 -0.53 0.65 -0.10 -0.37 -0.05 0.50 -0.32 HCV3 2.32
0.34 -0.28 0.92 0.02 -0.51 -0.68 0.28 -0.46 HEV -0.45 1.89 -0.31 -0.17 0.10 -0.04 -0.51 0.54
-0.39 HIV1 -0.27 1.07 1.89 0.46 -0.22 0.06 0.13 0.92 0.23 HIV2 -0.41 0.23 0.91 1.68 -0.07
-0.44 -0.75 0.09 -0.66 HTLVI -0.38 -0.21 -1.08 -0.87 2.67 0.88 -1.47 -0.15 -0.99 HTLVII
-0.13 - 0.09 - 0.92 - 0.59 \ 0.38 \ 3.30 - 1.13 - 0.10 - 0.86 \ WNV - 0.51 \ 0.25 - 0.62 - 0.52 - 0.40 - 0.64
2.24 0.00 -0.82 ZKV 0.32 0.68 -0.96 -0.68 -0.52 -0.78 0.16 2.07 -0.83 CK, Chikungunya virus;
DEN, dengue; HAV, hepatitis A virus; HCV, hepatitis C virus; HEV, hepatitis E virus; HIV, human
immunodeficiency virus; HTLV, Human T-cell lymphotropic virus; WNV, West Nile Virus; ZKV,
Zika Virus; NC, negative control.
(107) TABLE-US-00005 TABLE 5 Multi-pathogen mix test results based on Log ratio MPM1
MPM2 MPM3 MPM4 CHIKV 3.42 3.37 0.24 2.25 DEN1 3.14 3.10 1.80 2.45 DEN2 1.11 1.10
-0.23 0.35 DEN3 2.72 1.19 3.00 0.51 DEN4 1.31 1.19 0.83 0.59 HAV 1.33 0.12 2.18 -1.13 HCV-
1a 2.53 0.61 2.72 -0.59 HCV-2a 2.16 0.66 2.44 -0.65 HCV-3 2.45 0.65 2.60 -0.72 HEV 1.64 0.67
1.21 -0.71 HIV-1 1.05 1.24 1.11 -0.36 HIV-2 0.13 0.24 0.17 -0.81 HTLV-I -0.17 0.06 -0.07
-1.37 HTLV-II -0.02 0.12 -0.09 -1.07 WNV 1.63 1.65 0.11 -0.03 ZKV 3.09 3.04 0.30 1.98
MPM1 = CHIKV, HAV, HCV-1a, HEV, DEN3, DEN1, ZKV, WNV MPM2 = CHIKV, DEN1, ZKV,
WNV MPM3 = HAV, HEV, DEN3, HCV-1a MPM4 = CHIKV, ZKV, DEN1
(108) TABLE-US-00006 TABLE 6 Pathogen Chip performance based plasma panel test results
Pathogen Copies/mL pos/total qPCR Validation Chikungunya 10{circumflex over ()}3 1/1 Y
Chikungunya 10{circumflex over ()}2 4/4 Y Dengue1 10{circumflex over ()}3 3/3 Y Dengue1
10{circumflex over ()}2 2/2 Y Dengue1 10{circumflex over ()}1 0/1 Y Dengue2 10{circumflex
over ()}3 3/3 Y Dengue2 10{circumflex over ()}2 3/3 Y Dengue2 10{circumflex over ()}1 0/1 Y
Dengue3 10{circumflex over ()}3 3/3 Y Dengue3 10{circumflex over ()}2 3/3 Y Dengue3
10{circumflex over ()}1 0/1 Y Dengue4 10{circumflex over ()}3 3/3 Y Dengue4 10{circumflex
over ()}2 3/3 Y Dengue4 10{circumflex over ()}1 0/1 Y HAV 10{circumflex over ()}3 2/2 Y HAV
10{circumflex over ()}2 2/2 Y HCV-1a 10{circumflex over ()}3 3/3 Y HCV-1a 10{circumflex
over ()}2 3/3 Y HCV-2a 10{circumflex over ()}2 2/2 Y HCV-3 10{circumflex over ()}2 2/2 Y
HEV 10{circumflex over ()}4 3/3 Y HEV 10{circumflex over ()}3 0/2 Y HEV 10{circumflex over
()}2 0/2 NA HIV-1 10{circumflex over ()}3 2/2 y HIV-1 10{circumflex over ()}2 2/2 y HIV-2
10{circumflex over ()}3 3/3 y HIV-2 10{circumflex over ()}2 3/3 y HTLV-I 10{circumflex over
()}3 2/2 y HTLV-I 10{circumflex over ()}2 2/2 y HTLV-II 10{circumflex over ()}3 2/2 y HTLV-II
10{circumflex over ( )}2 2/2 y WNV (NY99) 10{circumflex over ( )}5 1/1 y WNV (NY99)
10{circumflex over ()}4 1/1 y WNV (NY99) 10{circumflex over ()}3 3/3 y WNV (NY99)
10{circumflex over ()}2 4/4 y WNV (NY99) 10{circumflex over ()}1 0/2 NA ZIKA PRVABC60
10{circumflex over ()}3 3/3 Y ZIKA PRVABC61 10{circumflex over ()}2 3/3 Y ZIKA
PRVABC62 10{circumflex over ()}1 0/2 Y ZIKV FSS13025 10{circumflex over ()}3 3/3 Y ZIKV
FSS13025 10{circumflex over ()}2 3/3 Y ZIKV FSS13025 10{circumflex over ()}1 0/2 Y MPM1
10{circumflex over ()}5-10{circumflex over ()}3 3/3 y MPM2 10{circumflex over ()}5-
10{circumflex over ()}3 3/3 y MPM3 10{circumflex over ()}5-10{circumflex over ()}3 3/3 y
MPM4 10{circumflex over ()}5-10{circumflex over ()}3 3/3 y NA = not applicable
(109) Among the 99 positive samples tested at a concentration ranking from 10.sup.5 to 10.sup.2
copies/mL, 92 out 92 samples were correctly detected. Only HEV testing resulted correct detection
in 3 out of 7 positive samples (42%) at a final concentration of 10.sup.4 copies/mL. No specific
signal was detected below this value. There were 21 positive samples that were not detected
because the concentration was below the limit of detection of the platform (<10.sup.2 copies/mL).
In all four mix combinations all pathogens were detected without interference among the targets.
(110) All of the samples tested (single or multiple pathogens at the same time) were performed at
least 3 times each, with at least a week interval between the experiments, in order to test the
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reproducibility of the results. The consistency of positive results across the different arrays confirmed that the array design together with the double level analysis model performed well. (111) Validation of the limit of microarray data by RT-qPCR: Microarray-based pathogen chip results were confirmed by RT-qPCR of the RNA aliquots used for testing. All positive results were confirmed and the copy numbers for each pathogen were calculated to define the limit of the detection for each species on the array (Table 7).

(112) TABLE-US-00007 TABLE 7 Validation of Pathogen Chip detection results Pathogen Chip qPCR Ct Virus Virus Results Value Copy No. CHIKV POS 26.9 3.1 × 10.sup.3 CHIKV POS 31.6 1.4 × 10.sup.2 CHIKV POS 31.5 1.6 × 10.sup.2 CHIKV POS 29.4 6.3 × 10.sup.2 CHIKV POS 29.7 5.8 × 10.sup.2 DENGUE-1 POS 31.1 2.3 × 10.sup.3 DENGUE-1 POS 34.4 3.0 × 10.sup.2 DENGUE-1 NEG 38.7 41 DENGUE-2 POS 29.1 8.4 × 10.sup.3 DENGUE-2 POS 35.9 1.2 × 10.sup.2 DENGUE-2 NEG 38.9 18 DENGUE-3 POS 29.3 7.1 × 10.sup.3 DENGUE-3 POS 32.7 8.4 × 10.sup.2 DENGUE-3 NEG 37.3 31 DENGUE-4 POS 30.3 3.3 × 10.sup.3 DENGUE-4 POS 34.2 2.6 × 10.sup.2 DENGUE-4 NEG 37.0 79 HAV POS 28.4 3.2 × 10.sup.3 HAV POS 39.1 2.8 × 10.sup.3 HAV POS 29.2 8.2 \times 10.sup.2 HAV POS 32.2 1.2 \times 10.sup.2 HCV-1a POS 26.2 4.1 \times 10.sup.3 HCV-1a POS 31.4 1.6 × 10.sup.2 HCV-2a POS 27.4 3.8 × 10.sup.3 HCV-2a POS 32.1 1.8 × 10.sup.2 HCV-3 POS 33.1 1.4 × 10.sup.2 HEV POS 25.4 1.9 × 10.sup.4 HEV NEG 28.4 1.8 × 10.sup.3 HIV-1 POS 27.3 4.6 × 10.sup.3 HIV-1 POS 32.8 1.6 × 10.sup.2 HIV-2 POS 27.4 4.3 × 10.sup.3 HIV-2 POS 30.7 1.8 × 10.sup.2 HTLV-I POS 28.7 3.9 × 10.sup.3 HTLV-I POS 28.3 2.9 × 10.sup.2 HTLV-II POS 25.574 2.7 × 10.sup.3 HTLV-II POS 29.289 2.4 × 10.sup.2 WNV (NY99) POS 21.5 1.9 × 10.sup.5 WNV (NY99) POS 24.5 1.5 × 10.sup.4 WNV (NY99) POS 27.6 2.1 × 10.sup.3 WNV (NY99) POS 31.4 1.0 × 10.sup.2 ZIKA PRVABC60 POS 26.2 1.5 × 10.sup.3 ZIKA PRVABC60 POS 30.1 1.2 × 10.sup.2 ZIKA PRVABC60 NEG 31.8 41 ZIKA FSS13025 POS 25.3 2.4 × 10.sup.3 ZIKA FSS13025 POS 29.1 1.3 × 10.sup.2 ZIKA FSS13025 NEG 33.0 17 Example 3

Microarray for Detection of DNA Viruses, Bacteria, and Protozoan Pathogens

(113) A microarray for DNA viruses, bacteria, and protozoan pathogens was developed. The design included multiple gene targets for each pathogen genome in order to select the best probes for the final platform design. The design strategy was to choose the probes with the best "scores" (homology, thermodynamics, secondary structure and sequence complexity) balancing the cross-hybridization with the host genome and with other pathogens' genomes. The second design strategy was to balance the number of probes for each pathogen with a final count of 50-110 probes each. Probes selected in the final design generated a more intense signal and produced higher percentage coverage of the specific genome across the different experiments.

(114) The final design was supplemented with predesigned DNA array probes (577 control probes, 225 replicates, and 11,620 backbone) specific for the reagents and the assay performance. These are used specifically for image orientation, to assess whether the samples are labeled, for the orientation of the platform during the scan process, and for measuring on element background. These probes form a hairpin and do not hybridize well with labeled sample of any species. In addition, 312 probes specific for three human housekeeping genes (ACTB, ARL1, CCDN1) and 109 probes specific for one Mosquito-specific virus and two plant viruses (*Aedes albopictus* densovirus 2, Maize streak virus, Tomato pseudo-curly top virus) were added to the design. (115) The microarray includes probes for cytomegalovirus (CMV; also known as HHV-5), Epstein Barr virus (EBV; also known as HHV-4), human herpesvirus 8 (HHV-8), human papilloma virus (HPV) type 6b HPV6, HPV11, HPV 16, HPV 17, hepatitis B virus (HBV) subtype adw, HBV subtype ayw, HBV subtype adr, HBV subtype ayr, and human parvovirus B19. Exemplary probes provided in Table 8 and include SEQ ID NOs: 1770-1852 (CMV), SEQ ID NOs: 1853-1917 (EBV B95-8), SEQ ID NOs: 1918-2023 (EBV AG876), SEQ ID NOs: 2024-2108 (HHV-8), SEQ ID NOs: 2109-2192 (HPV 6b), SEQ ID NOs: 2193-2271 (HPV 11), SEQ ID NOs: 2272-2342 (HPV 16), SEQ ID NOs: 2343-2419 (HPV 18), SEQ ID NOs: 2420-2470 (HBV subtype adw), SEQ ID

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NOs: 2471-2520 (HBV subtype ayw), SEQ ID NOs: 2521-2556 (HBV subtype adr), SEQ ID NOs:
2557-2602 (HBV subtype ayr), and SEQ ID NOs: 2603-2647 (human parvovirus B19).
(116) The microarray also includes probes for Treponema pallidum, Ehrlichia chaffeensis,
Ehrlichia ewingii, Ehrlichia muris, Borrelia burgdorferi, Coxiella burnetii, Trypanosoma brucei,
Trypanosoma cruzi, Leishmania major, Babesia microti, Plasmodium falciparum, and Plasmodium
vivax. Exemplary probes provided in Table 9 and include SEQ ID NOs: 2648-2751 (Treponema
pallidum), SEQ ID NOs: 2752-2852 (Ehrlichia chaffeensis), SEQ ID NOs: 2853-2861 (Ehrlichia
ewingii), SEQ ID NOs: 2862-2922 (Ehrlichia muris), SEQ ID NOs: 2923-3001 (Borrelia
burgdorferi), SEQ ID NOs: 3002-3085 (Coxiella burnetii), SEQ ID NOs: 3086-3097
(Trypanosoma brucei), SEQ ID NO: 3098 (Trypanosoma cruzi), SEQ ID NOs: 3099-3113
(Leishmania major), SEQ ID NOs: 3114-3154 (Babesia microti), SEQ ID NOs: 3155-3185
(Plasmodium falciparum), and SEQ ID NOs: 3186-3207 (Plasmodium vivax).
(117) Finally, the microarray includes housekeeping and negative control probes (Table 10).
Exemplary probes include SEQ ID NOs: 3208-3301 (housekeeping gene ACTB), SEQ ID NOs:
3302-3385 (housekeeping gene ARL1), SEQ ID NOs: 3386-3519 (housekeeping gene CCDN1),
SEQ ID NOs: 3520-3557 (Aedes albopictus densovirus 2), SEQ ID NO: 3558-3598 (Maize streak
virus), and SEQ ID NOs: 3599-3628 (Tomato pseudo-curly top virus).
(118) For sample analysis, viral DNA from plasma specimens was extracted with the Invitrogen
Dynabeads™ SILANE viral NA kit. The kit is designed for highly predictable and consistent
isolation of viral nucleic acids. Beads and buffers are optimized for sensitive isolation of viral
DNA. DNA from bacteria and protozoans was extracted from whole blood with the QIAamp®
DNA Blood Mini kit (Qiagen) according to the manufacturer's protocol.
(119) SureTag® Labeling Kit (Agilent technology) was used to enzymatically label DNA from
plasma and blood. A modified protocol was developed and optimized for efficient sample
fragmentation, enzymatic labeling, and clean up. A master mix containing 10×aCGH blocking
agent and 2×HI-RPM hybridization buffer, was added to 2.5-3 µg of labeled DNA, denatured, and
hybridized to arrays under 8-chamber gasket slides at 67° C. with 20-rpm rotation for 24 hours in
an Agilent hybridization oven. Arrays were processed using wash procedure A and scanned on an
Agilent SureScan® G4900DA microarray scanner using 5-µm resolution.
(120) CMV, Trypanosoma, Parvovirus B19, HBV, EBV (HHV-4), Treponema, Babesia,
Leishmania, Coxiella, Borrelia, Papilloma Virus (HPV 6, 11, 16, 18), and P. falciparum had
10.sup.4-10.sup.3 copies/mL limits of detection. There were no false negatives or false positives
when testing the positive plasma. All the results were confirmed by RT-qPCR of the DNA aliquots
used for testing. All positive results were confirmed and the copy numbers for each pathogen were
calculated to define the limit of the detection for each species on the array.
(121) TABLE-US-00008 TABLE 8 Exemplary DNA virus probes SEQ ID Genomic ProbeID Start
End NO: Virus Region Product CUST_P10000630 45812 45860 1770 CMV (HHV-5)
Cytomegalovirus UL34 protein CUST_P10000631 45872 45916 1771 CMV (HHV-5)
Cytomegalovirus UL34 protein CUST P10000638 46336 46384 1772 CMV (HHV-5)
Cytomegalovirus UL34 protein CUST P10001082 78547 78591 1773 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST_P10001099 79469 79514 1774 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST_P10001109 80183 80227 1775 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST_P10001111 80253 80301 1776 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST_P10001120 80933 80979 1777 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST_P10001123 81072 81116 1778 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST_P10001126 81245 81289 1779 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST P10001131 81599 81643 1780 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST P10001132 81738 81782 1781 CMV (HHV-5)
Cytomegalovirus UL54 DNA rep CUST_P10001140 82327 82375 1782 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST_P10001146 82856 82901 1783 CMV (HHV-5)
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Cytomegalovirus UL55 envelop CUST_P10001152 83347 83399 1784 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST P10001154 83475 83525 1785 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST P10001155 83645 83701 1786 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST P10001156 83677 83724 1787 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST_P10001158 83744 83797 1788 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST_P10001160 83961 84012 1789 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST_P10001161 83993 84052 1790 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST_P10001162 84021 84073 1791 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST_P10001164 84223 84275 1792 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST P10001165 84398 84442 1793 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST P10001169 84665 84716 1794 CMV (HHV-5)
Cytomegalovirus UL55 envelop CUST_P10001175 85014 85071 1795 CMV (HHV-5)
Cytomegalovirus UL56 encapsi CUST_P10001177 85085 85132 1796 CMV (HHV-5)
Cytomegalovirus UL56 encapsi CUST P10001179 85221 85272 1797 CMV (HHV-5)
Cytomegalovirus UL56 encapsi CUST_P10001183 85645 85693 1798 CMV (HHV-5)
Cytomegalovirus UL56 encapsi CUST P10001189 86404 86461 1799 CMV (HHV-5)
Cytomegalovirus UL56 encapsi CUST P10001198 87249 87308 1800 CMV (HHV-5)
Cytomegalovirus UL56 encapsi CUST P10001603 117602 117650 1801 CMV (HHV-5)
Cytomegalovirus UL80 capsid CUST_P10001618 118112 118156 1802 CMV (HHV-5)
Cytomegalovirus UL80 capsid CUST_P10001622 118567 118615 1803 CMV (HHV-5)
Cytomegalovirus UL80 capsid CUST_P10001664 121437 121483 1804 CMV (HHV-5)
Cytomegalovirus UL83 tegumen CUST_P10001665 121470 121522 1805 CMV (HHV-5)
Cytomegalovirus UL83 tegumen CUST_P10001666 121493 121543 1806 CMV (HHV-5)
Cytomegalovirus UL83 tegumen CUST P10001675 122579 122623 1807 CMV (HHV-5)
Cytomegalovirus UL83 tegumen CUST P10001945 141984 142028 1808 CMV (HHV-5)
Cytomegalovirus UL97 core CUST P10001948 142100 142144 1809 CMV (HHV-5)
Cytomegalovirus UL97 core CUST_P10001960 142742 142789 1810 CMV (HHV-5)
Cytomegalovirus UL97 core CUST_P10001965 143122 143180 1811 CMV (HHV-5)
Cytomegalovirus UL97 core CUST_P10001966 143159 143203 1812 CMV (HHV-5)
Cytomegalovirus UL97 core CUST_P10002353 170852 170896 1813 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002359 171207 171256 1814 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002362 171393 171444 1815 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002371 171811 171858 1816 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002377 172241 172300 1817 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002378 172286 172345 1818 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002379 172307 172366 1819 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002381 172506 172559 1820 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002382 172633 172678 1821 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002384 172987 173046 1822 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002385 173023 173082 1823 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002386 173044 173097 1824 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002389 173134 173193 1825 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002390 173156 173215 1826 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002391 173191 173239 1827 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002392 173374 173433 1828 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002393 173395 173454 1829 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002394 173432 173489 1830 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002395 173456 173514 1831 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002396 173503 173553 1832 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002397 173520 173579 1833 CMV (HHV-5)
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Cytomegalovirus UL122 Beta Ge CUST_P10002398 173555 173613 1834 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002399 173596 173649 1835 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002400 173621 173679 1836 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002401 173674 173731 1837 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002402 173693 173746 1838 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002403 173735 173780 1839 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002404 173766 173812 1840 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST_P10002406 174051 174095 1841 CMV (HHV-5)
Cytomegalovirus UL122 Beta Ge CUST P10002407 174065 174109 1842 CMV (HHV-5)
Cytomegalovirus UL123 Prot E CUST P10002408 174215 174259 1843 CMV (HHV-5)
Cytomegalovirus UL123 Prot E CUST P10002411 174671 174726 1844 CMV (HHV-5)
Cytomegalovirus UL124 Prot E CUST_P10002466 178473 178527 1845 CMV (HHV-5)
Cytomegalovirus UL132 Glyco CUST_P10002470 178801 178851 1846 CMV (HHV-5)
Cytomegalovirus UL132 Glyco CUST P10002471 178825 178870 1847 CMV (HHV-5)
Cytomegalovirus UL132 Glyco CUST P10002474 178926 178974 1848 CMV (HHV-5)
Cytomegalovirus UL132 Glyco CUST P10002475 178954 179000 1849 CMV (HHV-5)
Cytomegalovirus UL132 Glyco CUST P10002927 211545 211592 1850 CMV (HHV-5)
Cytomegalovirus US17 protein CUST P10002930 211944 211988 1851 CMV (HHV-5)
Cytomegalovirus US17 protein CUST_P10002934 212083 212127 1852 CMV (HHV-5)
Cytomegalovirus US17 protein CUST_P10003273 1 60 1853 Human herpesvirus 4 (EBV), B95-8
LMP-2A transmembrane protein CUST_P10003278 444 503 1854 Human herpesvirus 4 (EBV),
B95-8 LMP-2A transmembrane protein CUST_P10003289 1435 1487 1855 Human herpesvirus 4
(EBV), B95-8 LMP-2A transmembrane protein CUST_P10003301 2062 2106 1856 Human
herpesvirus 4 (EBV), B95-8 BNFR1 tegument protein CUST_P10003303 2221 2265 1857 Human
herpesvirus 4 (EBV), B95-8 BNFR1 tegument protein CUST_P10003307 2620 2664 1858 Human
herpesvirus 4 (EBV), B95-8 BNFR1 tegument protein CUST P10003313 3104 3148 1859 Human
herpesvirus 4 (EBV), B95-8 BNFR1 tegument protein CUST_P10003322 3928 3972 1860 Human
herpesvirus 4 (EBV), B95-8 BNFR1 tegument protein CUST_P10003342 5201 5245 1861 Human
herpesvirus 4 (EBV), B95-8 BNFR1 tegument protein CUST_P10003349 5834 5893 1862 Human
herpesvirus 4 (EBV), B95-8 BNFR1 tegument protein CUST_P10003351 5931 5985 1863 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003352 6010 6069 1864 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003367 7289 7347 1865 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003369 7409 7468 1866 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003372 7520 7579 1867 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003375 7605 7664 1868 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003376 7635 7694 1869 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003377 7706 7765 1870 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003378 7731 7790 1871 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003379 7786 7845 1872 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003380 7821 7880 1873 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003381 7871 7930 1874 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003382 7901 7960 1875 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003383 7941 8000 1876 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003384 8000 8051 1877 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003390 8236 8291 1878 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003398 8631 8690 1879 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003399 8659 8716 1880 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003400 8690 8737 1881 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003404 9006 9063 1882 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003405 9052 9111 1883 Human
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herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003406 9110 9166 1884 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003408 9301 9350 1885 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003409 9349 9399 1886 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST P10003412 9759 9811 1887 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003413 9788 9841 1888 Human
herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003418 9961 10012 1889
Human herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003427 10915 10966
1890 Human herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003429 10994
11046 1891 Human herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen CUST_P10003432
11304 11362 1892 Human herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear antigen
CUST P10003721 35383 35442 1893 Human herpesvirus 4 (EBV), B95-8 EBNA-1 Nuclear
antigen CUST_P10003725 35654 35708 1894 Human herpesvirus 4 (EBV), B95-8 EBNA-1
Nuclear antigen CUST_P10005257 152676 152720 1895 Human herpesvirus 4 (EBV), B95-8
BALF5 Binding Protein CUST P10005266 153637 153681 1896 Human herpesvirus 4 (EBV),
B95-8 BALF5 Binding Protein CUST P10005267 153658 153702 1897 Human herpesvirus 4
(EBV), B95-8 BALF5 Binding Protein CUST P10005275 154346 154393 1898 Human
herpesvirus 4 (EBV), B95-8 BALF5 Binding Protein CUST P10005279 154462 154516 1899
Human herpesvirus 4 (EBV), B95-8 BALF5 Binding Protein CUST P10005291 155318 155362
1900 Human herpesvirus 4 (EBV), B95-8 BALF5 Binding Protein CUST_P10005293 155583
155627 1901 Human herpesvirus 4 (EBV), B95-8 BALF5 Binding Protein CUST_P10005300
155914 155958 1902 Human herpesvirus 4 (EBV), B95-8 BALF5 Binding Protein
CUST_P10005304 156254 156306 1903 Human herpesvirus 4 (EBV), B95-8 BALF5 Binding
Protein CUST P10005325 157914 157963 1904 Human herpesvirus 4 (EBV), B95-8 BALF4
Binding Protein CUST P10005327 158072 158121 1905 Human herpesvirus 4 (EBV), B95-8
BALF4 Binding Protein CUST P10005329 158133 158183 1906 Human herpesvirus 4 (EBV),
B95-8 BALF4 Binding Protein CUST P10005332 158230 158286 1907 Human herpesvirus 4
(EBV), B95-8 BALF4 Binding Protein CUST_P10005334 158408 158453 1908 Human
herpesvirus 4 (EBV), B95-8 BALF4 Binding Protein CUST_P10005335 158572 158625 1909
Human herpesvirus 4 (EBV), B95-8 BALF4 Binding Protein CUST_P10005336 158595 158644
1910 Human herpesvirus 4 (EBV), B95-8 BALF4 Binding Protein CUST_P10005340 158865
158916 1911 Human herpesvirus 4 (EBV), B95-8 BALF4 Binding Protein CUST P10005355
160486 160545 1912 Human herpesvirus 4 (EBV), B95-8 BALF4 Binding Protein
CUST P10005356 160515 160574 1913 Human herpesvirus 4 (EBV), B95-8 BALF3 Binding
Protein CUST_P10005367 161267 161318 1914 Human herpesvirus 4 (EBV), B95-8 BALF3
Binding Protein CUST_P10005380 162040 162086 1915 Human herpesvirus 4 (EBV), B95-8
BALF3 Binding Protein CUST_P10005381 162117 162161 1916 Human herpesvirus 4 (EBV),
B95-8 BALF3 Binding Protein CUST_P10005382 162322 162366 1917 Human herpesvirus 4
(EBV), B95-8 BALF3 Binding Protein CUST_P10005496 1 60 1918 Human herpesvirus 4 (EBV),
AG876 LMP-2B latency and B cell survival CUST P10005503 903 961 1919 Human herpesvirus
4 (EBV), AG876 LMP-2B latency and B cell survival CUST P10005506 1162 1221 1920 Human
herpesvirus 4 (EBV), AG876 LMP-2B latency and B cell survival CUST_P10005507 1290 1345
1921 Human herpesvirus 4 (EBV), AG876 LMP-2B latency and B cell survival CUST_P10005515
1658 1717 1922 Human herpesvirus 4 (EBV), AG876 LMP-2B latency and B cell survival
CUST_P10005567 5833 5892 1923 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA
replication CUST_P10005568 5869 5928 1924 Human herpesvirus 4 (EBV), AG876 EBER-1
DNA replication CUST_P10005571 6014 6073 1925 Human herpesvirus 4 (EBV), AG876 EBER-
1 DNA replication CUST P10005581 6584 6635 1926 Human herpesvirus 4 (EBV), AG876
EBER-1 DNA replication CUST P10005585 6912 6967 1927 Human herpesvirus 4 (EBV),
AG876 EBER-1 DNA replication CUST_P10005589 7293 7348 1928 Human herpesvirus 4
(EBV), AG876 EBER-1 DNA replication CUST_P10005592 7417 7476 1929 Human herpesvirus
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4 (EBV), AG876 EBER-1 DNA replication CUST_P10005593 7470 7529 1930 Human
herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST P10005594 7520 7579 1931
Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST P10005595 7590 7649
1932 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST P10005596 7615
7674 1933 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST_P10005597
7645 7704 1934 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication
CUST_P10005598 7701 7760 1935 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA
replication CUST P10005599 7740 7799 1936 Human herpesvirus 4 (EBV), AG876 EBER-1
DNA replication CUST P10005600 7770 7829 1937 Human herpesvirus 4 (EBV), AG876 EBER-
1 DNA replication CUST P10005601 7799 7858 1938 Human herpesvirus 4 (EBV), AG876
EBER-1 DNA replication CUST P10005602 7835 7894 1939 Human herpesvirus 4 (EBV),
AG876 EBER-1 DNA replication CUST_P10005604 7910 7969 1940 Human herpesvirus 4
(EBV), AG876 EBER-1 DNA replication CUST_P10005605 7940 7999 1941 Human herpesvirus
4 (EBV), AG876 EBER-1 DNA replication CUST P10005606 7972 8031 1942 Human
herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST P10005617 8432 8486 1943
Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST_P10005619 8501 8560
1944 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST P10005620 8536
8590 1945 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication CUST P10005622
8614 8673 1946 Human herpesvirus 4 (EBV), AG876 EBER-1 DNA replication
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Human papillomavirus type 6b E1 Regulatory (HPV 11) Protein CUST_P10009768 1962 2017
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2062 2216 Human papillomavirus type 6b E1 Regulatory (HPV 11) Protein CUST_P10009770
2127 2186 2217 Human papillomavirus type 6b E2 Regulatory (HPV 11) Protein
CUST_P10009771 2265 2316 2218 Human papillomavirus type 6b E2 Regulatory (HPV 11)
Protein CUST_P10009772 2303 2362 2219 Human papillomavirus type 6b E2 Regulatory (HPV
11) Protein CUST P10009773 2327 2384 2220 Human papillomavirus type 6b E2 Regulatory
(HPV 11) Protein CUST_P10009774 2370 2420 2221 Human papillomavirus type 6b E2
Regulatory (HPV 11) Protein CUST_P10009775 2422 2481 2222 Human papillomavirus type 6b
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E2 Regulatory (HPV 11) Protein CUST_P10009776 2458 2517 2223 Human papillomavirus type
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type 6b E2 Regulatory (HPV 11) Protein CUST P10009778 2625 2684 2225 Human
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CUST_P10009795 4408 4458 2242 Human papillomavirus type 6b E5 Regulatory (HPV 11)
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CUST P10009815 5819 5875 2258 Human papillomavirus type 6b L1 PolyA (HPV 11)
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CUST P10009833 221 280 2274 Human papillomavirus type 6b E6 Regulatory (HPV 16) Protein
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Protein CUST_P10009842 1131 1190 2282 Human papillomavirus type 6b E1 Regulatory (HPV
16) Protein CUST_P10009843 1269 1316 2283 Human papillomavirus type 6b E1 Regulatory
(HPV 16) Protein CUST_P10009844 1296 1346 2284 Human papillomavirus type 6b E1
Regulatory (HPV 16) Protein CUST P10009845 1461 1520 2285 Human papillomavirus type 6b
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E2 Regulatory (HPV 16) Protein CUST_P10009858 2974 3033 2298 Human papillomavirus type
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(HPV 16) CUST_P10009872 4347 4406 2309 Human papillomavirus type 6b L2 Capsid (HPV 16)
CUST_P10009873 4510 4566 2310 Human papillomavirus type 6b L2 Capsid (HPV 16)
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CUST_P10009881 4931 4990 2317 Human papillomavirus type 6b L2 Capsid (HPV 16)
CUST_P10009882 5068 5125 2318 Human papillomavirus type 6b L2 Capsid (HPV 16)
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Protein CUST_P10009926 1134 1187 2358 Human papillomavirus type 6b E1 Regulatory (HPV
18) Protein CUST_P10009927 1302 1357 2359 Human papillomavirus type 6b E1 Regulatory
(HPV 18) Protein CUST_P10009928 1663 1722 2360 Human papillomavirus type 6b E1
Regulatory (HPV 18) Protein CUST_P10009929 1691 1750 2361 Human papillomavirus type 6b
E1 Regulatory (HPV 18) Protein CUST_P10009930 1719 1778 2362 Human papillomavirus type
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18) Protein CUST P10009939 2558 2617 2371 Human papillomavirus type 6b E1 Regulatory
(HPV 18) Protein CUST_P10009940 2606 2665 2372 Human papillomavirus type 6b E1
Regulatory (HPV 18) Protein CUST_P10009941 2642 2701 2373 Human papillomavirus type 6b
E1 Regulatory (HPV 18) Protein CUST_P10009942 2808 2852 2374 Human papillomavirus type
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type 6b E2 Regulatory (HPV 18) Protein CUST P10009944 2858 2917 2376 Human
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L2 Capsid (HPV 18) CUST_P10009956 4357 4414 2386 Human papillomavirus type 6b L2
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78 126 2421 Hepatitis B virus subtype adw S surface protein CUST_P10010006 158 202 2422
Hepatitis B virus subtype adw S surface protein CUST_P10010008 230 281 2423 Hepatitis B virus
subtype adw S surface protein CUST_P10010009 267 311 2424 Hepatitis B virus subtype adw S
surface protein CUST_P10010010 328 372 2425 Hepatitis B virus subtype adw S surface protein
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CUST_P10010076 851 907 2486 Hepatitis B virus subtype ayw X x-protein CUST_P10010077
983 1033 2487 Hepatitis B virus subtype ayw X x-protein CUST_P10010078 1028 1087 2488
Hepatitis B virus subtype ayw X x-protein CUST_P10010079 1091 1147 2489 Hepatitis B virus
subtype ayw X x-protein CUST_P10010080 1161 1205 2490 Hepatitis B virus subtype ayw X x-
protein CUST_P10010081 1218 1262 2491 Hepatitis B virus subtype ayw X x-protein
CUST_P10010082 1265 1309 2492 Hepatitis B virus subtype ayw X x-protein CUST_P10010083
1319 1374 2493 Hepatitis B virus subtype ayw X x-protein CUST_P10010084 1384 1429 2494
Hepatitis B virus subtype ayw X x-protein CUST P10010085 1446 1490 2495 Hepatitis B virus
subtype ayw X x-protein CUST P10010086 1476 1520 2496 Hepatitis B virus subtype ayw X x-
protein CUST_P10010087 1528 1572 2497 Hepatitis B virus subtype ayw X x-protein
CUST_P10010088 1552 1596 2498 Hepatitis B virus subtype ayw X x-protein CUST_P10010089
1610 1654 2499 Hepatitis B virus subtype ayw X x-protein CUST_P10010090 1636 1685 2500
Hepatitis B virus subtype ayw X x-protein CUST_P10010092 1815 1870 2501 Hepatitis B virus
subtype ayw C Core CUST_P10010093 2042 2088 2502 Hepatitis B virus subtype ayw C Core
CUST_P10010094 2133 2192 2503 Hepatitis B virus subtype ayw C Core CUST_P10010095 2162
2221 2504 Hepatitis B virus subtype ayw C Core CUST_P10010096 2210 2269 2505 Hepatitis B
virus subtype ayw C Core CUST P10010097 2343 2387 2506 Hepatitis B virus subtype ayw C
Core CUST_P10010098 2390 2434 2507 Hepatitis B virus subtype ayw C Core CUST_P10010099
2427 2477 2508 Hepatitis B virus subtype ayw C Core CUST_P10010100 2535 2594 2509
Hepatitis B virus subtype ayw C Core CUST_P10010101 2577 2636 2510 Hepatitis B virus
subtype ayw P Pol CUST_P10010102 2641 2700 2511 Hepatitis B virus subtype ayw P Pol
CUST_P10010103 2698 2757 2512 Hepatitis B virus subtype ayw P Pol CUST_P10010104 2756
2815 2513 Hepatitis B virus subtype ayw P Pol CUST_P10010105 2794 2845 2514 Hepatitis B
virus subtype ayw P Pol CUST P10010106 2824 2872 2515 Hepatitis B virus subtype ayw P Pol
CUST_P10010107 2856 2900 2516 Hepatitis B virus subtype ayw P Pol CUST_P10010108 2885
2929 2517 Hepatitis B virus subtype ayw P Pol CUST_P10010109 2915 2963 2518 Hepatitis B
virus subtype ayw P Pol CUST_P10010110 3046 3090 2519 Hepatitis B virus subtype ayw P Pol
CUST_P10010111 3121 3165 2520 Hepatitis B virus subtype ayw P Pol CUST_P10010112 8 55
2521 Hepatitis B virus, subtype adr P Pol CUST_P10010113 79 125 2522 Hepatitis B virus,
subtype adr P Pol CUST_P10010114 112 156 2523 Hepatitis B virus, subtype adr P Pol
CUST_P10010119 325 370 2524 Hepatitis B virus, subtype adr P Pol CUST_P10010122 451 497
2525 Hepatitis B virus, subtype adr P Pol CUST_P10010123 477 521 2526 Hepatitis B virus,
subtype adr P Pol CUST_P10010124 638 682 2527 Hepatitis B virus, subtype adr P Pol
CUST_P10010125 667 714 2528 Hepatitis B virus, subtype adr P Pol CUST_P10010126 705 754
2529 Hepatitis B virus, subtype adr P Pol CUST_P10010127 839 894 2530 Hepatitis B virus,
subtype adr P Pol CUST_P10010128 971 1022 2531 Hepatitis B virus, subtype adr P Pol
CUST_P10010129 1088 1145 2532 Hepatitis B virus, subtype adr P Pol CUST_P10010131 1160
1204 2533 Hepatitis B virus, subtype adr P Pol CUST_P10010132 1203 1247 2534 Hepatitis B
virus, subtype adr P Pol CUST P10010133 1315 1361 2535 Hepatitis B virus, subtype adr P Pol
CUST_P10010134 1458 1502 2536 Hepatitis B virus, subtype adr P Pol CUST_P10010136 1556
1600 2537 Hepatitis B virus, subtype adr P Pol CUST_P10010137 1635 1683 2538 Hepatitis B
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virus, subtype adr P Pol CUST_P10010138 1679 1729 2539 Hepatitis B virus, subtype adr C Core
CUST_P10010139 1810 1864 2540 Hepatitis B virus, subtype adr C Core CUST_P10010140 1999
2043 2541 Hepatitis B virus, subtype adr C Core CUST_P10010141 2109 2153 2542 Hepatitis B
virus, subtype adr C Core CUST P10010142 2220 2279 2543 Hepatitis B virus, subtype adr C
Core CUST_P10010143 2247 2294 2544 Hepatitis B virus, subtype adr C Core CUST_P10010144
2295 2346 2545 Hepatitis B virus, subtype adr C Core CUST_P10010145 2365 2409 2546
Hepatitis B virus, subtype adr C Core CUST_P10010148 2545 2604 2547 Hepatitis B virus,
subtype adr P Pol CUST_P10010149 2575 2634 2548 Hepatitis B virus, subtype adr P Pol
CUST_P10010150 2618 2677 2549 Hepatitis B virus, subtype adr P Pol CUST_P10010151 2646
2705 2550 Hepatitis B virus, subtype adr P Pol CUST_P10010152 2672 2731 2551 Hepatitis B
virus, subtype adr P Pol CUST P10010153 2699 2758 2552 Hepatitis B virus, subtype adr P Pol
CUST_P10010154 2735 2794 2553 Hepatitis B virus, subtype adr P Pol CUST_P10010156 2928
2972 2554 Hepatitis B virus, subtype adr S1 surface protein CUST_P10010157 2976 3020 2555
Hepatitis B virus, subtype adr S1 surface protein CUST_P10010158 3063 3107 2556 Hepatitis B
virus, subtype adr S1 surface protein CUST_P10010159 42 86 2557 Hepatitis B virus, subtype ayr
P Pol CUST_P10010160 79 126 2558 Hepatitis B virus, subtype ayr P Pol CUST_P10010161 133
177 2559 Hepatitis B virus, subtype ayr S surface protein CUST_P10010162 158 202 2560
Hepatitis B virus, subtype ayr S surface protein CUST P10010163 190 238 2561 Hepatitis B virus,
subtype ayr S surface protein CUST_P10010164 227 280 2562 Hepatitis B virus, subtype ayr S
surface protein CUST_P10010165 272 316 2563 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010166 328 372 2564 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010167 366 414 2565 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010168 390 447 2566 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010169 452 500 2567 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010170 477 521 2568 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010171 598 642 2569 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010172 659 707 2570 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010173 839 898 2571 Hepatitis B virus, subtype ayr P Pol CUST_P10010174 971 1023
2572 Hepatitis B virus, subtype ayr P Pol CUST_P10010175 1087 1146 2573 Hepatitis B virus,
subtype ayr P Pol CUST_P10010176 1116 1163 2574 Hepatitis B virus, subtype ayr P Pol
CUST_P10010177 1151 1195 2575 Hepatitis B virus, subtype ayr P Pol CUST_P10010179 1318
1366 2576 Hepatitis B virus, subtype ayr P Pol CUST_P10010180 1356 1400 2577 Hepatitis B
virus, subtype ayr X x-protein CUST_P10010181 1388 1432 2578 Hepatitis B virus, subtype ayr X
x-protein CUST_P10010182 1419 1463 2579 Hepatitis B virus, subtype ayr X x-protein
CUST_P10010183 1472 1516 2580 Hepatitis B virus, subtype ayr X x-protein CUST_P10010185
1565 1609 2581 Hepatitis B virus, subtype ayr X x-protein CUST_P10010187 1643 1690 2582
Hepatitis B virus, subtype ayr X x-protein CUST_P10010188 1675 1725 2583 Hepatitis B virus,
subtype ayr X x-protein CUST_P10010189 1808 1856 2584 Hepatitis B virus, subtype ayr X x-
protein CUST_P10010190 1941 1996 2585 Hepatitis B virus, subtype ayr C Core
CUST_P10010191 2001 2045 2586 Hepatitis B virus, subtype ayr C Core CUST_P10010192 2111
2155 2587 Hepatitis B virus, subtype ayr C Core CUST_P10010193 2210 2266 2588 Hepatitis B
virus, subtype ayr C Core CUST_P10010194 2290 2335 2589 Hepatitis B virus, subtype ayr C
Core CUST_P10010195 2365 2409 2590 Hepatitis B virus, subtype ayr C Core CUST_P10010196
2410 2456 2591 Hepatitis B virus, subtype ayr C Core CUST_P10010197 2430 2484 2592
Hepatitis B virus, subtype ayr C Core CUST_P10010198 2516 2571 2593 Hepatitis B virus,
subtype ayr C Core CUST_P10010199 2577 2636 2594 Hepatitis B virus, subtype ayr C Core
CUST_P10010200 2629 2688 2595 Hepatitis B virus, subtype ayr C Core CUST_P10010201 2675
2734 2596 Hepatitis B virus, subtype ayr C Core CUST_P10010202 2702 2761 2597 Hepatitis B
virus, subtype ayr C Core CUST_P10010203 2742 2801 2598 Hepatitis B virus, subtype ayr C
Core CUST_P10010204 2890 2936 2599 Hepatitis B virus, subtype ayr S surface protein
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CUST_P10010205 2955 3001 2600 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010206 2978 3022 2601 Hepatitis B virus, subtype ayr S surface protein
CUST_P10010207 3012 3056 2602 Hepatitis B virus, subtype ayr S surface protein
CUST P10010208 57 104 2603 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010209 227 271 2604 Human parvovirus B19 NS non-structural protein NS2
CUST_P10010211 637 693 2605 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010212 685 744 2606 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010214 973 1032 2607 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010215 1065 1124 2608 Human parvovirus B19 NS non-structural protein NS1
CUST P10010216 1165 1210 2609 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010217 1220 1279 2610 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010218 1258 1317 2611 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010219 1357 1416 2612 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010220 1408 1467 2613 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010221 1542 1601 2614 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010222 1628 1687 2615 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010223 1767 1812 2616 Human parvovirus B19 NS non-structural protein NS1
CUST P10010224 1845 1902 2617 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010225 1911 1970 2618 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010226 2041 2096 2619 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010227 2257 2301 2620 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010228 2351 2399 2621 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010229 2395 2446 2622 Human parvovirus B19 NS non-structural protein NS1
CUST_P10010230 2426 2478 2623 Human parvovirus B19 NS non-structural protein NS1
CUST P10010231 2552 2607 2624 Human parvovirus B19 NS non-structural protein NS1
CUST P10010232 2787 2846 2625 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010233 2836 2895 2626 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010234 2868 2915 2627 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010235 2914 2973 2628 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010236 3081 3140 2629 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010237 3252 3297 2630 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010238 3276 3330 2631 Human parvovirus B19 VP1 minor capsid protein
CUST P10010239 3422 3481 2632 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010240 3524 3583 2633 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010241 3652 3711 2634 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010242 3801 3856 2635 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010243 3826 3885 2636 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010244 3864 3923 2637 Human parvovirus B19 VP1 minor capsid protein
CUST P10010245 3996 4042 2638 Human parvovirus B19 VP1 minor capsid protein
CUST P10010246 4097 4156 2639 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010247 4334 4393 2640 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010248 4463 4522 2641 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010249 4587 4646 2642 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010250 4723 4782 2643 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010251 4820 4864 2644 Human parvovirus B19 VP1 minor capsid protein
CUST_P10010252 4915 4960 2645 Human parvovirus B19 VP1 minor capsid protein
CUST P10010254 5087 5146 2646 Human parvovirus B19 VP2 major capsid protein
CUST P10010257 5492 5539 2647 Human parvovirus B19 VP2 major capsid protein
(122) TABLE-US-00009 TABLE 9 Exemplary bacterial and protozoan probes SEQ ID Genomic
NO: ProbeID Start End Pathogen Region Product 2648 CUST_P10011833 115100 115153
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Treponema pallidum polA Polymerase 2649 CUST_P10011835 115167 115219 Treponema
pallidum polA Polymerase 2650 CUST P10011836 115187 115237 Treponema pallidum polA
Polymerase 2651 CUST P10011838 115259 115314 Treponema pallidum polA Polymerase 2652
CUST P10011840 115554 115613 Treponema pallidum polA Polymerase 2653 CUST P10011841
115579 115638 Treponema pallidum polA Polymerase 2654 CUST_P10011842 115605 115664
Treponema pallidum polA Polymerase 2655 CUST_P10011843 115667 115716 Treponema
pallidum polA Polymerase 2656 CUST P10011844 115696 115740 Treponema pallidum polA
Polymerase 2657 CUST_P10011845 115755 115807 Treponema pallidum polA Polymerase 2658
CUST_P10011847 116076 116126 Treponema pallidum polA Polymerase 2659 CUST_P10011848
116171 116223 Treponema pallidum polA Polymerase 2660 CUST P10011849 116242 116294
Treponema pallidum polA Polymerase 2661 CUST P10011850 116332 116384 Treponema
pallidum polA Polymerase 2662 CUST_P10011851 116352 116396 Treponema pallidum polA
Polymerase 2663 CUST_P10011852 116408 116459 Treponema pallidum polA Polymerase 2664
CUST_P10011853 116430 116488 Treponema pallidum polA Polymerase 2665 CUST_P10011854
116601 116649 Treponema pallidum polA Polymerase 2666 CUST_P10011855 116623 116674
Treponema pallidum polA Polymerase 2667 CUST P10011856 116654 116713 Treponema
pallidum polA Polymerase 2668 CUST P10011857 116677 116736 Treponema pallidum polA
Polymerase 2669 CUST P10011858 116707 116760 Treponema pallidum polA Polymerase 2670
CUST_P10011860 116852 116906 Treponema pallidum polA Polymerase 2671 CUST_P10011862
116903 116962 Treponema pallidum polA Polymerase 2672 CUST_P10011863 116925 116978
Treponema pallidum polA Polymerase 2673 CUST_P10011864 116987 117032 Treponema
pallidum polA Polymerase 2674 CUST P10011865 117028 117077 Treponema pallidum polA
Polymerase 2675 CUST P10011866 117128 117176 Treponema pallidum polA Polymerase 2676
CUST_P10011867 117270 117329 Treponema pallidum polA Polymerase 2677 CUST_P10011868
117441 117488 Treponema pallidum polA Polymerase 2678 CUST P10011870 117516 117575
Treponema pallidum polA Polymerase 2679 CUST P10011871 117570 117620 Treponema
pallidum polA Polymerase 2680 CUST_P10011872 117777 117836 Treponema pallidum polA
Polymerase 2681 CUST_P10011873 117806 117865 Treponema pallidum polA Polymerase 2682
CUST_P10011874 117873 117932 Treponema pallidum polA Polymerase 2683 CUST_P10011875
118152 118211 Treponema pallidum polA Polymerase 2684 CUST_P10011876 118181 118240
Treponema pallidum polA Polymerase 2685 CUST_P10011877 118281 118340 Treponema
pallidum polA Polymerase 2686 CUST P10011878 118302 118361 Treponema pallidum polA
Polymerase 2687 CUST P10011880 118541 118600 Treponema pallidum polA Polymerase 2688
CUST_P10011882 118756 118810 Treponema pallidum polA Polymerase 2689 CUST_P10018873
622214 622258 Treponema pallidum TP0576 protein 2690 CUST_P10018877 622589 622637
Treponema pallidum TP0576 protein 2691 CUST_P10018878 622725 622775 Treponema pallidum
TP0576 protein 2692 CUST P10018881 622908 622961 Treponema pallidum TP0576 protein
2693 CUST_P10018882 622953 622997 Treponema pallidum TP0576 protein 2694
CUST_P10018883 622978 623030 Treponema pallidum TP0576 protein 2695 CUST_P10018884
623033 623087 Treponema pallidum TP0576 protein 2696 CUST_P10018887 623258 623302
Treponema pallidum TP0576 protein 2697 CUST_P10024966 1067780 1067830 Treponema
pallidum aspS aspartate-tRNA ligase 2698 CUST_P10024967 1067910 1067970 Treponema
pallidum aspS aspartate-tRNA ligase 2699 CUST_P10024968 1067940 1067990 Treponema
pallidum aspS aspartate-tRNA ligase 2700 CUST_P10024969 1068070 1068120 Treponema
pallidum aspS aspartate-tRNA ligase 2701 CUST P10024970 1068180 1068230 Treponema
pallidum aspS aspartate-tRNA ligase 2702 CUST P10024971 1068330 1068380 Treponema
pallidum aspS aspartate-tRNA ligase 2703 CUST P10024972 1068410 1068470 Treponema
pallidum aspS aspartate-tRNA ligase 2704 CUST P10024976 1068840 1068900 Treponema
pallidum aspS aspartate-tRNA ligase 2705 CUST_P10024981 1069090 1069140 Treponema
pallidum aspS aspartate-tRNA ligase 2706 CUST_P10024984 1069200 1069260 Treponema
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pallidum aspS aspartate-tRNA ligase 2708 CUST P10024991 1069740 1069790 Treponema
pallidum aspS aspartate-tRNA ligase 2709 CUST P10024994 1069890 1069940 Treponema
pallidum aspS aspartate-tRNA ligase 2710 CUST P10024996 1070010 1070060 Treponema
pallidum aspS aspartate-tRNA ligase 2711 CUST_P10024997 1070040 1070080 Treponema
pallidum aspS aspartate-tRNA ligase 2712 CUST_P10024998 1070090 1070130 Treponema
pallidum aspS aspartate-tRNA ligase 2713 CUST_P10024999 1070140 1070190 Treponema
pallidum aspS aspartate-tRNA ligase 2714 CUST_P10025000 1070250 1070300 Treponema
pallidum aspS aspartate-tRNA ligase 2715 CUST_P10025003 1070380 1070430 Treponema
pallidum aspS aspartate-tRNA ligase 2716 CUST P10025005 1070670 1070710 Treponema
pallidum aspS aspartate-tRNA ligase 2717 CUST_P10025006 1070800 1070850 Treponema
pallidum TP0986 protein 2718 CUST_P10025009 1071210 1071260 Treponema pallidum TP0986
protein 2719 CUST_P10025010 1071230 1071290 Treponema pallidum TP0986 protein 2720
CUST_P10025018 1071990 1072040 Treponema pallidum TP0986 protein 2721
CUST_P10025019 1072210 1072260 Treponema pallidum TP0989 protein 2722
CUST_P10025024 1072490 1072540 Treponema pallidum TP0989 protein 2723
CUST_P10025027 1072660 1072710 Treponema pallidum TP0989 protein 2724
CUST P10025028 1072870 1072910 Treponema pallidum TP0989 protein 2725
CUST_P10025029 1072990 1073040 Treponema pallidum TP0989 protein 2726
CUST_P10025030 1073010 1073060 Treponema pallidum TP0989 protein 2727
CUST_P10025044 1074070 1074120 Treponema pallidum TP0990 protein 2728
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CUST_P10025047 1074310 1074360 Treponema pallidum TP0992 protein 2730
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CUST P10025051 1074520 1074560 Treponema pallidum TP0994 protein 2732
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CUST_P10025061 1075310 1075360 Treponema pallidum TP1001 protein 2739
CUST P10025062 1075380 1075430 Treponema pallidum TP1002 protein 2740
CUST_P10025063 1075540 1075600 Treponema pallidum TP1003 protein 2741
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CUST_P10025065 1075670 1075720 Treponema pallidum TP1005 protein 2743
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CUST_P10025084 1077230 1077280 Treponema pallidum TP0992 protein 2748
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CUST_P10025097 1077980 1078030 Treponema pallidum TP0993 protein 2750
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CUST_P10025104 1078320 1078370 Treponema pallidum TP0993 protein 2752
CUST_P10025934 479 538 Ehrlichia chaffeensis ECH_RS00020 protein 2753 CUST_P10026529
69254 69313 Ehrlichia chaffeensis argF protein 2754 CUST_P10026957 118031 118090 Ehrlichia
chaffeensis ECH RS00525 protein 2755 CUST P10027106 133725 133784 Ehrlichia chaffeensis
ECH_RS00595 protein 2756 CUST_P10027296 155652 155711 Ehrlichia chaffeensis
ECH_RS00695 protein 2757 CUST_P10027314 158001 158060 Ehrlichia chaffeensis
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ECH RS01035 protein 2759 CUST P10027973 235768 235827 Ehrlichia chaffeensis
ECH RS01035 protein 2760 CUST P10028360 279872 279931 Ehrlichia chaffeensis
ECH RS01185 protein 2761 CUST P10028636 313330 313389 Ehrlichia chaffeensis
ECH_RS01325 protein 2762 CUST_P10028976 353675 353734 Ehrlichia chaffeensis groL
chaperonin GroEL 2763 CUST_P10028977 353852 353911 Ehrlichia chaffeensis groL chaperonin
GroEL 2764 CUST_P10028978 354008 354067 Ehrlichia chaffeensis groL chaperonin GroEL
2765 CUST_P10028979 354044 354103 Ehrlichia chaffeensis groL chaperonin GroEL 2766
CUST P10028980 354207 354266 Ehrlichia chaffeensis groL chaperonin GroEL 2767
CUST_P10028981 354405 354464 Ehrlichia chaffeensis groL chaperonin GroEL 2768
CUST_P10028982 354433 354492 Ehrlichia chaffeensis groL chaperonin GroEL 2769
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CUST_P10028986 354646 354694 Ehrlichia chaffeensis groL chaperonin GroEL 2773
CUST_P10028987 354808 354867 Ehrlichia chaffeensis groL chaperonin GroEL 2774
CUST_P10028988 354995 355054 Ehrlichia chaffeensis groL chaperonin GroEL 2775
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CUST_P10028991 355454 355508 Ehrlichia chaffeensis groL chaperonin GroEL 2778
CUST_P10029114 369147 369206 Ehrlichia chaffeensis groL chaperonin GroEL 2779
CUST_P10029290 392046 392105 Ehrlichia chaffeensis sppA signal peptide 2780
CUST_P10029649 429284 429343 Ehrlichia chaffeensis ECH_RS01865 Protein 2781
CUST_P10029666 431631 431690 Ehrlichia chaffeensis ECH_RS01866 Protein 2782
CUST_P10029696 434789 434848 Ehrlichia chaffeensis ECH_RS01867 Protein 2783
CUST P10029724 437453 437512 Ehrlichia chaffeensis ECH RS01868 Protein 2784
CUST_P10030575 531280 531339 Ehrlichia chaffeensis ECH_RS01869 Protein 2785
CUST_P10030591 532929 532988 Ehrlichia chaffeensis ECH_RS01870 Protein 2786
CUST_P10030711 547792 547851 Ehrlichia chaffeensis ECH_RS01871 Protein 2787
CUST_P10030738 551432 551491 Ehrlichia chaffeensis ECH_RS01872 Protein 2788
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transposase 3059 CUST_P10058823 502868 502915 Coxiella burnetii IS1111A transposase
IS1111A transposase 3060 CUST_P10058824 502908 502953 Coxiella burnetii IS1111A
transposase IS1111A transposase 3061 CUST_P10058825 502925 502974 Coxiella burnetii
IS1111A transposase IS1111A transposase 3062 CUST_P10058826 502960 503012 Coxiella
burnetii IS1111A transposase IS1111A transposase 3063 CUST P10058827 503069 503113
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transposase 3086 CUST_P10079271 1019 1078 Trypanosoma brucei kinetoplast apocy kinetoplast
apocy 3087 CUST_P10079269 471 530 Trypanosoma brucei kinetoplast apocy kinetoplast apocy
3088 CUST_P10079274 1363 1414 Trypanosoma brucei kinetoplast apocy kinetoplast apocy 3089
CUST_P10079272 1279 1334 Trypanosoma brucei kinetoplast apocy kinetoplast apocy 3090
CUST_P10079270 628 687 Trypanosoma brucei kinetoplast apocy kinetoplast apocy 3091
CUST_P10079273 1329 1373 Trypanosoma brucei kinetoplast apocy kinetoplast apocy 3092
CUST_P10079280 687 746 Trypanosoma brucei kinetoplast DNA m kinetoplast DNA m 3093
CUST_P10079276 478 526 Trypanosoma brucei kinetoplast DNA m kinetoplast DNA m 3094
CUST_P10079277 547 601 Trypanosoma brucei kinetoplast DNA m kinetoplast DNA m 3095
CUST_P10079275 1 60 Trypanosoma brucei kinetoplast DNA m kinetoplast DNA m 3096
CUST_P10079279 677 736 Trypanosoma brucei kinetoplast DNA m kinetoplast DNA m 3097
CUST P10079278 554 610 Trypanosoma brucei kinetoplast DNA m kinetoplast DNA m 3098
CUST P10079281 23 67 Trypanosoma Cruzi Mini satellite Mini satellite 3099 CUST P10079284
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Leishmania major kinetoplast DNA kinetoplast DNA 3101 CUST_P10079286 360 404 Leishmania
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kinetoplast DNA kinetoplast DNA 3103 CUST P10079287 382 426 Leishmania major kinetoplast
DNA kinetoplast DNA 3104 CUST P10079282 1 60 Leishmania major kinetoplast DNA
kinetoplast DNA 3105 CUST P10079294 504 548 Leishmania major kinetoplast DNA kinetoplast
DNA 3106 CUST_P10079292 333 377 Leishmania major kinetoplast DNA kinetoplast DNA 3107
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CUST P10079288 116 168 Leishmania major kinetoplast DNA kinetoplast DNA 3113
CUST_P10079293 462 507 Leishmania major kinetoplast DNA kinetoplast DNA 3114
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CUST_P10079327 140 189 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3116
CUST P10079328 168 227 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3117
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CUST P10079336 771 825 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3125
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CUST P10079346 1239 1298 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3135
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CUST P10079353 1758 1802 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3142
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CUST_P10079362 2125 2174 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3151
CUST_P10079363 2266 2322 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3152
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CUST P10079365 2363 2418 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3154
CUST P10079366 2389 2446 Babesia microti 18S ribosomal RNA 18S ribosomal RNA 3155
CUST P10079478 328 375 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA
3156 CUST_P10079479 433 492 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal
RNA 3157 CUST_P10079480 517 566 Plasmodium falciparum 18S ribosomal RNA 18S
ribosomal RNA 3158 CUST P10079481 612 671 Plasmodium falciparum 18S ribosomal RNA
18S ribosomal RNA 3159 CUST_P10079482 820 879 Plasmodium falciparum 18S ribosomal
RNA 18S ribosomal RNA 3160 CUST P10079483 945 1003 Plasmodium falciparum 18S
ribosomal RNA 18S ribosomal RNA 3161 CUST P10079484 971 1030 Plasmodium falciparum
18S ribosomal RNA 18S ribosomal RNA 3162 CUST P10079485 1018 1077 Plasmodium
falciparum 18S ribosomal RNA 18S ribosomal RNA 3163 CUST_P10079486 1211 1257
Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA 3164 CUST_P10079487 1284
1343 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA 3165 CUST P10079488
1386 1445 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA 3166
CUST_P10079489 1673 1727 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA
3167 CUST P10079490 1817 1876 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal
RNA 3168 CUST P10079491 1852 1911 Plasmodium falciparum 18S ribosomal RNA 18S
ribosomal RNA 3169 CUST_P10079492 70 129 Plasmodium falciparum 18S ribosomal RNA 18S
ribosomal RNA 3170 CUST_P10079493 321 373 Plasmodium falciparum 18S ribosomal RNA
18S ribosomal RNA 3171 CUST_P10079494 460 519 Plasmodium falciparum 18S ribosomal
RNA 18S ribosomal RNA 3172 CUST_P10079495 489 548 Plasmodium falciparum 18S
ribosomal RNA 18S ribosomal RNA 3173 CUST_P10079496 519 569 Plasmodium falciparum
18S ribosomal RNA 18S ribosomal RNA 3174 CUST_P10079497 599 658 Plasmodium
falciparum 18S ribosomal RNA 18S ribosomal RNA 3175 CUST P10079498 800 859
Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA 3176 CUST P10079499 826
885 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA 3177 CUST_P10079500
990 1046 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA 3178
CUST_P10079501 1014 1073 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal RNA
3179 CUST_P10079502 1053 1112 Plasmodium falciparum 18S ribosomal RNA 18S ribosomal
RNA 3180 CUST_P10079503 1264 1310 Plasmodium falciparum 18S ribosomal RNA 18S
ribosomal RNA 3181 CUST_P10079504 1332 1391 Plasmodium falciparum 18S ribosomal RNA
18S ribosomal RNA 3182 CUST_P10079505 1450 1509 Plasmodium falciparum 18S ribosomal
RNA 18S ribosomal RNA 3183 CUST_P10079506 1721 1770 Plasmodium falciparum 18S
ribosomal RNA 18S ribosomal RNA 3184 CUST_P10079507 1742 1801 Plasmodium falciparum
18S ribosomal RNA 18S ribosomal RNA 3185 CUST_P10079508 1890 1949 Plasmodium
falciparum 18S ribosomal RNA 18S ribosomal RNA 3186 CUST_P10079572 2 61 Plasmodium
vivax SSU rRNA external transcribed spacer 3187 CUST_P10079573 38 89 Plasmodium vivax
SSU rRNA external transcribed spacer 3188 CUST P10079574 68 127 Plasmodium vivax SSU
rRNA external transcribed spacer 3189 CUST_P10079575 112 171 Plasmodium vivax SSU rRNA
external transcribed spacer 3190 CUST_P10079576 249 308 Plasmodium vivax SSU rRNA
external transcribed spacer 3191 CUST_P10079577 279 338 Plasmodium vivax SSU rRNA
external transcribed spacer 3192 CUST_P10079578 319 372 Plasmodium vivax SSU rRNA
external transcribed spacer 3193 CUST_P10079579 421 480 Plasmodium vivax SSU rRNA
external transcribed spacer 3194 CUST_P10079580 590 645 Plasmodium vivax SSU rRNA
external transcribed spacer 3195 CUST_P10079581 671 719 Plasmodium vivax SSU rRNA
external transcribed spacer 3196 CUST_P10079582 783 842 Plasmodium vivax SSU rRNA
external transcribed spacer 3197 CUST_P10079583 803 862 Plasmodium vivax SSU rRNA
external transcribed spacer 3198 CUST_P10079584 829 888 Plasmodium vivax SSU rRNA
external transcribed spacer 3199 CUST_P10079585 849 899 Plasmodium vivax SSU rRNA
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(123) TABLE-US-00010 TABLE 10 Exemplary control probes SEQ ID Genomic NO: ProbeID Start End Type Region 3208 CUST P10079594 1561 1605 Housekeeping Gene ACTB 3209 CUST_P10079595 1703 1750 Housekeeping Gene ACTB 3210 CUST_P10079596 2220 2264 Housekeeping Gene ACTB 3211 CUST_P10079597 2242 2286 Housekeeping Gene ACTB 3212 CUST_P10079598 2276 2320 Housekeeping Gene ACTB 3213 CUST_P10079599 2402 2446 Housekeeping Gene ACTB 3214 CUST P10079600 2489 2533 Housekeeping Gene ACTB 3215 CUST P10079601 2659 2703 Housekeeping Gene ACTB 3216 CUST P10079602 2696 2740 Housekeeping Gene ACTB 3217 CUST P10079603 2823 2867 Housekeeping Gene ACTB 3218 CUST P10079604 2847 2891 Housekeeping Gene ACTB 3219 CUST P10079605 2874 2918 Housekeeping Gene ACTB 3220 CUST_P10079606 3005 3049 Housekeeping Gene ACTB 3221 CUST_P10079607 3046 3090 Housekeeping Gene ACTB 3222 CUST_P10079608 3213 3257 Housekeeping Gene ACTB 3223 CUST_P10079609 3338 3382 Housekeeping Gene ACTB 3224 CUST_P10079610 3376 3420 Housekeeping Gene ACTB 3225 CUST_P10079611 3393 3437 Housekeeping Gene ACTB 3226 CUST P10079612 3438 3482 Housekeeping Gene ACTB 3227 CUST P10079613 3545 3593 Housekeeping Gene ACTB 3228 CUST P10079614 3568 3622 Housekeeping Gene ACTB 3229 CUST P10079615 3601 3645 Housekeeping Gene ACTB 3230 CUST P10079616 3744 3788 Housekeeping Gene ACTB 3231 CUST P10079617 3858 3902 Housekeeping Gene ACTB 3232 CUST_P10079618 3973 4017 Housekeeping Gene ACTB 3233 CUST_P10079619 4130 4177 Housekeeping Gene ACTB 3234 CUST_P10079620 4223 4267 Housekeeping Gene ACTB 3235 CUST_P10079621 4280 4324 Housekeeping Gene ACTB 3236 CUST_P10079622 4304 4348 Housekeeping Gene ACTB 3237 CUST_P10079623 4315 4359 Housekeeping Gene ACTB 3238 CUST P10079624 4459 4503 Housekeeping Gene ACTB 3239 CUST P10079625 4592 4636 Housekeeping Gene ACTB 3240 CUST P10079626 4906 4950 Housekeeping Gene ACTB 3241 CUST P10079627 4932 4978 Housekeeping Gene ACTB 3242 CUST_P10079628 4972 5016 Housekeeping Gene ACTB 3243 CUST_P10079629 5024 5068 Housekeeping Gene ACTB 3244 CUST_P10079630 5040 5084 Housekeeping Gene ACTB 3245 CUST_P10079631 5076 5120 Housekeeping Gene ACTB 3246 CUST_P10079632 5110 5154 Housekeeping Gene ACTB 3247 CUST P10079633 5200 5244 Housekeeping Gene ACTB 3248 CUST P10079634 5357 5401 Housekeeping Gene ACTB 3249 CUST P10079635 5390 5434 Housekeeping Gene ACTB 3250 CUST P10079636 5415 5459 Housekeeping Gene ACTB 3251 CUST P10079637 5453 5497 Housekeeping Gene ACTB 3252 CUST P10079638 5474 5518 Housekeeping Gene ACTB 3253 CUST_P10079639 5622 5666 Housekeeping Gene ACTB 3254 CUST_P10079640 5662 5706 Housekeeping Gene ACTB 3255 CUST_P10079641 5691 5736 Housekeeping Gene ACTB 3256 CUST_P10079642 5712 5756 Housekeeping Gene ACTB 3257 CUST_P10079643 5760 5804 Housekeeping Gene ACTB 3258 CUST_P10079644 5783 5827 Housekeeping Gene ACTB 3259 CUST P10079645 5817 5861 Housekeeping Gene ACTB 3260 CUST P10079646 5963 6007 Housekeeping Gene ACTB 3261 CUST P10079647 6004 6048 Housekeeping Gene ACTB 3262 CUST P10079648 6106 6150 Housekeeping Gene ACTB 3263 CUST P10079649 6310 6354 Housekeeping Gene ACTB 3264 CUST P10079650 6421 6465 Housekeeping Gene ACTB 3265 CUST_P10079651 6507 6553 Housekeeping Gene ACTB 3266 CUST_P10079652 6696 6740 Housekeeping Gene ACTB 3267 CUST_P10079653 6722 6769

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CUST P10079658 7000 7044 Housekeeping Gene ACTB 3273 CUST P10079659 7321 7365
Housekeeping Gene ACTB 3274 CUST_P10079660 7418 7462 Housekeeping Gene ACTB 3275
CUST_P10079661 7554 7598 Housekeeping Gene ACTB 3276 CUST_P10079662 7683 7727
Housekeeping Gene ACTB 3277 CUST P10079663 7777 7821 Housekeeping Gene ACTB 3278
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Housekeeping Gene ACTB 3280 CUST P10079666 8033 8077 Housekeeping Gene ACTB 3281
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Housekeeping Gene ACTB 3283 CUST P10079669 8459 8503 Housekeeping Gene ACTB 3284
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Housekeeping Gene ACTB 3286 CUST_P10079672 8574 8618 Housekeeping Gene ACTB 3287
CUST_P10079673 8628 8672 Housekeeping Gene ACTB 3288 CUST_P10079674 8732 8776
Housekeeping Gene ACTB 3289 CUST P10079675 8941 8985 Housekeeping Gene ACTB 3290
CUST P10079676 8962 9006 Housekeeping Gene ACTB 3291 CUST P10079677 8987 9031
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Housekeeping Gene ACTB 3301 CUST P10079687 10193 10245 Housekeeping Gene ACTB
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3314 Housekeeping Gene ARL1 3304 CUST P10079727 5957 6016 Housekeeping Gene ARL1
3305 CUST P10079741 10779 10838 Housekeeping Gene ARL1 3306 CUST P10079759 13558
13604 Housekeeping Gene ARL1 3307 CUST_P10079701 934 979 Housekeeping Gene ARL1
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Housekeeping Gene ARL1 3310 CUST_P10079730 6728 6787 Housekeeping Gene ARL1 3311
CUST_P10079746 11349 11397 Housekeeping Gene ARL1 3312 CUST_P10079744 11307 11354
Housekeeping Gene ARL1 3313 CUST_P10079732 7235 7286 Housekeeping Gene ARL1 3314
CUST P10079733 7270 7314 Housekeeping Gene ARL1 3315 CUST P10079760 13597 13641
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CUST_P10079742 10939 10998 Housekeeping Gene ARL1 3321 CUST_P10079696 746 796
Housekeeping Gene ARL1 3322 CUST_P10079703 1025 1079 Housekeeping Gene ARL1 3323
CUST_P10079688 137 181 Housekeeping Gene ARL1 3324 CUST_P10079755 12703 12762
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CUST_P10079745 11327 11379 Housekeeping Gene ARL1 3342 CUST_P10079712 3205 3264
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Housekeeping Gene ARL1 3349 CUST P10079699 861 910 Housekeeping Gene ARL1 3350
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CUST P10079731 7083 7139 Housekeeping Gene ARL1 3369 CUST P10079723 5093 5152
Housekeeping Gene ARL1 3370 CUST_P10079704 1198 1257 Housekeeping Gene ARL1 3371
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CUST_P10079771 14283 14342 Housekeeping Gene ARL1 3384 CUST_P10079737 8984 9043
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Housekeeping Gene CCDN1 3388 CUST P10079774 297 341 Housekeeping Gene CCDN1 3389
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1557 Housekeeping Gene CCDN1 3397 CUST_P10079783 1553 1597 Housekeeping Gene
CCDN1 3398 CUST P10079784 1811 1855 Housekeeping Gene CCDN1 3399 CUST P10079785
1936 1980 Housekeeping Gene CCDN1 3400 CUST P10079786 2041 2085 Housekeeping Gene
CCDN1 3401 CUST P10079787 2206 2250 Housekeeping Gene CCDN1 3402 CUST P10079788
2233 2277 Housekeeping Gene CCDN1 3403 CUST_P10079789 2279 2323 Housekeeping Gene
CCDN1 3404 CUST_P10079790 2321 2365 Housekeeping Gene CCDN1 3405 CUST_P10079791
2346 2390 Housekeeping Gene CCDN1 3406 CUST_P10079792 2376 2420 Housekeeping Gene
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Claims

- 1. A probe set comprising: (a) probes having at least 90% identity with the nucleic acid sequences of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769; (b) probes having at least 95% identity with the nucleic acid sequences of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769; (c) probes comprising the nucleic acid sequence of SEQ ID NOs: 1-1300, 1391-1570, and 1691-1769; or (d) probes comprising the nucleic acid sequence of SEQ ID NOs: 1-1769, wherein each of the probes is covalently linked to a solid support and each of the probes is 60 nucleotides in length.
- 2. The probe set of claim 1, wherein the probe set comprises probes for each of Chikungunya virus, Dengue virus type 1, Dengue virus type 2, Dengue virus type 3, Dengue virus type 4, Hepatitis A virus, Hepatitis C virus type 1, Hepatitis C virus type 2, Hepatitis C virus type 3, Hepatitis E virus, Human immunodeficiency virus type 1, Human immunodeficiency virus type 2, Human T-lymphotropic virus type II, West Nile virus, and Zika virus.
- 3. The probe set of claim 1, further comprising at least one negative control probe and/or further comprising at least one positive control probe.
- 4. The probe set of claim 3, wherein the at least one negative control probe comprises a set of probes with at least 90% identity with each of the nucleic acid sequences of SEQ ID NOs: 1571-1690 and wherein each of the probes is 60 nucleotides in length.
- 5. The probe set of claim 1, further comprising: (a) probes having at least 90% identity with the nucleic acid sequences of SEQ ID NOs: 1770-2647; (b) probes having at least 95% identity with the nucleic acid sequences of SEQ ID NOS: 1770-2647; or (c) probes comprising the nucleic acid sequence of SEQ ID NOs: 1770-2647; wherein each of the probes is covalently linked to a solid support and each of the probes is 40-60 nucleotides in length.
- 6. The probe set of claim 5, wherein the probe set comprises probes for each of cytomegalovirus, Epstein Barr virus subtype B95-8, Epstein Barr virus subtype AG876, human herpes virus 8, Hepatitis B virus subtype adw, Hepatitis B virus subtype adr,

- Hepatitis B virus subtype ayr, human parvovirus B19, human papillomavirus type 6, human papillomavirus type 11, human papillomavirus type 16, and human papillomavirus type 18.
- 7. The probe set of claim 5, further comprising at least one negative control probe and/or further comprising at least one positive control probe.
- 8. The probe set of claim 7, wherein the at least one negative control probe comprises a set of probes with at least 90% identity with the nucleic acid sequences of each of SEQ ID NOs: 3520-3628 and each of the probes is 45-60 nucleotides in length.
- 9. The probe set of claim 1, further comprising: (a) probes having at least 90% identity with the nucleic acid sequences of SEQ ID NOs: 2648-3207; (b) probes having at least 95% identity with the nucleic acid sequences of SEQ ID NOs: 2648-3207; or (c) probes comprising the nucleic acid sequence of SEQ ID NOs: 2648-3207; wherein each of the probes is covalently linked to a solid support and each of the probes is 45-60 nucleotides in length.
- 10. The probe set of claim 9, wherein the probe set comprises at least one probe for each of *Treponema pallidum*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris*, *Borrelia burgdorferi*, *Coxiella burnetii*, *Trypanosoma brucei*, *Trypanosoma cruzi Leishmania major*, *Babesia microti*, *Plasmodium falciparum*, and *Plasmodium vivax*.
- 11. The probe set of claim 9, further comprising at least one negative control probe and/or further comprising at least one positive control probe.
- 12. The probe set of claim 11, wherein the at least one positive control probe comprises a set of probes with at least 90% identity with the nucleic acid sequences of each of SEQ ID NOs: 3208-3519 and each of the probes is 45-60 nucleotides in length.
- 13. A microarray comprising the probe set of claim 1.
- 14. The microarray of claim 13, wherein the probe set comprises probes comprising the nucleic acid sequence of each of SEQ ID NOs: 1-1769.
- 15. A method of detecting one or more pathogen nucleic acids in a sample, comprising: contacting the sample with the probe set of claim 1 under conditions sufficient to allow hybridization of pathogen nucleic acids present in the sample to the probes of the probe set; and measuring hybridization of the sample to one or more of the probes, thereby detecting one or more pathogen nucleic acids in the sample.
- 16. The method of claim 15, wherein the sample comprises a blood, serum, or plasma sample or nucleic acids isolated from a blood, serum, or plasma sample.
- 17. The method of claim 16, further comprising isolating nucleic acids from the sample prior to contacting the sample with the probe set.
- 18. The method of claim 17, further comprising labeling the isolated nucleic acids from the sample.
- 19. The method of claim 18, wherein the isolated nucleic acids are isolated DNA, isolated RNA, isolated cDNA, or a combination of two or more thereof.
- 20. The method of claim 19, wherein labeling the isolated nucleic acids comprises labeling the nucleic acids with one or more fluorescent labels.
- 21. The method of claim 17, wherein the isolated nucleic acids are cDNA.
- 22. The method of claim 17, wherein isolating the nucleic acids does not comprise amplifying total RNA from the sample prior to preparing cDNA.
- 23. The method of claim 15, wherein measuring hybridization comprises detecting \geq 50% of the probes for the virus have a log ratio of >1.5 and/or the log ratio between the signal intensity mean for the probe set and the mean of a control group probe set is \geq 1.5.
- 24. The method of claim 15, wherein the pathogen nucleic acids comprise nucleic acids from one or more of Chikungunya virus, Dengue virus types 1, 2, 3, or 4, Hepatitis A virus, Hepatitis C virus types 1, 2, or 3, Hepatitis E virus, Human immunodeficiency virus types 1 or 2, Human T-lymphotropic virus types I or II, West Nile virus, and Zika virus.