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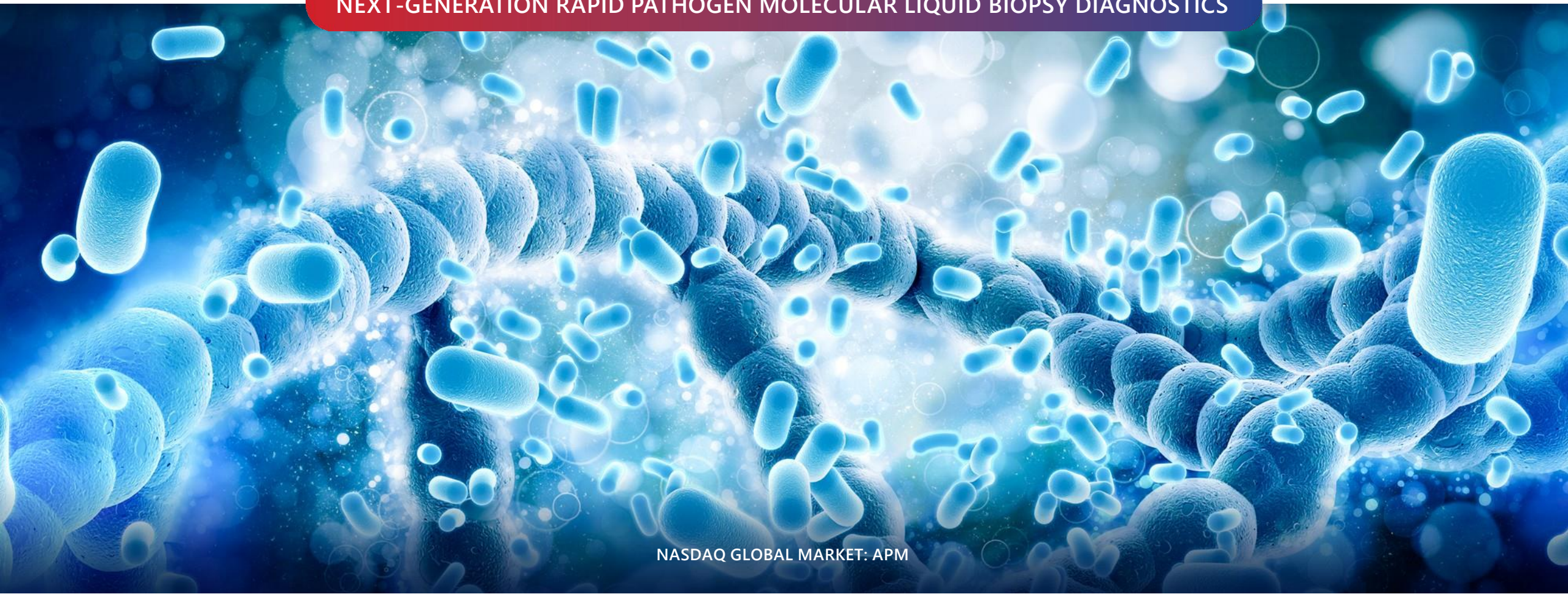
Facilitating Life Science Innovations to Serve Unmet Medical Needs

NEXT-GENERATION RAPID PATHOGEN MOLECULAR LIQUID BIOPSY DIAGNOSTICS



NASDAQ GLOBAL MARKET: APM

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Executive Summary

Infectious diseases have experienced major development in the past two decades and have had a devastating global impact on humanity and our economy. Within the past 20 years, the world has been affected by outbreaks such as the SARS (2004), Avian flu (2008), Swine flu (2010), MERS (2012), Ebola (2014/18), Zika (2016) and the recent COVID19 (2019/20). Despite the arsenal of antimicrobial therapeutics available, patients continue to suffer from significant rates of morbidity and mortality as evident by the COVID19 pandemic. If these issues are not adequately addressed by all stakeholders alike, a recent UK study presented by economist Jim O'Neill, which was further publicised by the BBC, has shown that, for example, by 2050 potentially drug resistant infections (such as that of MRSA, E.coli, malaria, tuberculosis) may cause more deaths than cancer globally (by an incremental 10 million deaths) and costs could spiral to $100 trillion[1].

At Aptorum Group and in line with WHO global action plans[2] and antimicrobial stewardship policies (ASPs) of healthcare providers, rapid diagnostics has been identified as one of the key first line of defenses against infectious diseases. By means of accurately identifying and tracking the pathogen(s) identity early on, "precision medicine" can then be applied so the patient is prescribed more appropriate and targeted antimicrobial treatment earlier on, thus reducing the risks of morbidity and mortality that is often caused by the inappropriate use of untargeted broad spectrum therapeutics and related antimicrobial resistance driven complications. For example, inappropriate initial antimicrobial therapy occurs in about 20% of patients with septic shock[3] and is associated with a fivefold reduction in survival; a US study in 2011 showed approximately 30% of 260 million antibiotic prescriptions in US outpatient pharmacies were also considered unnecessary[3].

We believe that rapid pathogen molecular diagnostics, coupled with next-generation sequencing platforms can accurately and more adequately address the medical needs of broader spectrum infectious diseases and has significant advantages over the more lengthy and inaccurate blood culture testing and (pathogen specific-only) polymerase chain reaction (PCR) testing. However, current molecular diagnostics are still too cost prohibitive (averaging USD$2,500 – 3,000+ per diagnosis in the US) due to the scientific and technical approaches. Consequently, such diagnostics do not achieve the necessary market penetration to be adopted as a first line of choice as means of diagnostics. On this basis, our molecular liquid biopsy based technology "RPIDD" is developed with the following targeted technical and economical objectives in mind in order to hasten the adoption of RPIDD in private service and public ASP policies:

- Based on a novel scientific approach to sample preparation, to achieve over 60% (or more) reduction in costs per sample compared to current infectious disease molecular diagnostic providers;
- Working collaboratively with major NGS platform providers, to achieve more than 99% analytical specificity and more than 95% analytical sensitivity;
- To identify on an unbiased basis of known pathogens whose genomic data is available and any emerging and previously unknown pathogen(s) whose genomic data is not yet available (e.g. the next coronavirus pandemic for example);
- To identify antimicrobial resistance properties associated to these known or emerging pathogens for further research and development purposes; and
- To collaborate with Key Opinion Leaders in the infectious disease space globally to carry out our research and validation on an ongoing basis.

We believe that RPIDD has the potential to transform the world and further advance humanity's capabilities to counter rapidly evolving infectious disease pathogens. We are dedicated to developing RPIDD with these objectives in mind and in conjunction with our current and future collaborative partners. We believe that our technology can contribute towards the eventual eradication of unnecessary infectious disease complications and risks of the next major pandemic. We thank you for your support.

Dr Clark Cheng and Mr Darren Lui (Executive Directors of Aptorum Innovation)

1. https://www.bbc.co.uk/news/health-30416844; 2. https://www.who.int/bulletin/volumes/96/3/17-198614.pdf?ua=1 and https://www.who.int/bulletin/volumes/95/8/16-185314-ab/en/; 3. https://journal.chestnet.org/article/S0012-3692(19)31246-2/pdf;

* The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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Our Solution: Rapid Pathogen Identification and Detection Device Technology ("RPIDD")

Summary

OVERVIEW

- **RPIDD**: Next-generation molecular based diagnostics for "unbiased" detection of any foreign pathogens (virus, bacteria, fungus, parasites) in infected patients using DNA/RNA
- <24hours turn around time (improve further with NGS platforms) + cost effective
- Blood sample based
- Collaboration with Molecular Engineering Laboratory, A*Star Singapore
- Patented proprietary technology to prepare and enrich the pathogenic DNA/RNA and deplete the background human host DNA simultaneously + software analytics solution

TARGET

- Next generation technology to transform diagnostic procedures for infectious diseases
- To become a first line of diagnostics in line or ahead of traditional methods
- By 2023: Target to serve globally over 100 hospitals / clinics by Aptorum Innovation
- Market Size Target by 2026: over USD$1.2 billion sales per annum, over 3.5 million patients p.a.

OUR TECHNOLOGY

- ✓ Lower costs: target to reduce costs by over 60% of current USD$2500 molecular diagnostic services
- ✓ Unbiased and broad range of pathogen detection
- ✓ <24 hour turn-around time
- ✓ Support world wide tracking and research on pathogen genomic data

VS

TRADITIONAL

- × **Blood culture**: Slow (5 days) and inaccurate (c. 80% accuracy)
- × **PCR based diagnosis**: Biased only to specific pathogens (selective)

CAPABILITIES

Our technology can potentially detect or achieve the following, subject to further validation:

- majority known pathogenic DNA/RNA (estimated over 1300+ types) including coronavirus such as COVID19
- pathogen genes responsible for antimicrobial resistance properties (e.g. MRSA)
- previously unknown and novel mutated pathogens (e.g. new virus)
- genome database expansion with further detection of pathogens using software and AI driven analytics based on genome sequence

Targeted outcomes of our technology include:

- TO REDUCE diagnosis time within 24 hours (vs avg 3 – 5 days using blood culture)
- TO REDUCE cost of existing NGS based diagnosis by more than 60%
- TO ACHIEVE analytical specificity >99% per pathogen + analytical sensitivity >95%
- "Precision Medicine" approach to infections allowing clinicians to prescribe suitable and targeted treatment at an early stage of admission of the patient

	Blood Culture	PCR and Film Array	Existing NGS Technologies	Our Technology*
Rapid	No (5 days)	Yes (1 day)	Yes (2 days)	Yes (1 day)
Detect unknown pathogens	No	No (biased & specific to pathogen)	Yes	Yes
Detect antibiotic resistance	Yes (limited)	Yes (limited)	Yes	Yes
Average Costs	USD$100-150 per culture / pathogen BUT no broad range detection; specific only		>USD$2,500 avg cost per sample	Target to achieve below USD$1,000 avg cost per sample

***Subject to further human clinical validation and is no guarantee of any outcome.**

Technology Highlights and Origins of RPIDD

TECHNOLOGY HIGHLIGHTS*

- Ex-Nobel Prize Winner Sydney Brenner molecular diagnostics laboratory technology
- Current and ongoing validation of patient clinical samples in collaboration with A*STAR
- Targeted to overcome existing cost and outcome limitations of blood culture and PCR based diagnostics
- Untargeted approach for pathogen identification (potentially over 1300 pathogens can be screened)
- Detect pathogen DNA + RNA in single reaction + compatible with NGS platforms (e.g. Illumina platforms)
- Technology in principle can identify new emerging infectious disease events (e.g. coronavirus, drug resistant E.coli, tuberculosis, malaria etc), subject to further validation
- In principle, can track infectome landscape (e.g. tracking mutations), subject to further validation
- In principle, can identify antibiotic resistant properties of "super" pathogens (e.g. MRSA, VRSA), subject to further validation
- Targeted to lower cost by more than 60% than current molecular based infectious disease diagnostic provider

The rapid pathogen identification and detection device technology (RPIDD device) was developed by researchers in **A*Star's Molecular Engineering Laboratory**

The Molecular Engineering Lab was started by world-renowned molecular biologist **Dr. Sydney Brenner** (Nobel laureate in Physiology or Medicine) in 2009[2]

DR. SYDNEY BRENNER

- Since its operation in 2009, the **Molecular Engineering Lab** has attracted researchers from all over the world (e.g. Stanford University, University of Oxford, Imperial College London, etc) to develop technologies that have novel applications in areas such as nucleic acid amplification and detection, molecular diagnostics and high throughput sequencing assay development and analysis[1]
- **In 2020, Aptorum Group acquired exclusive rights to develop and commercialize the technology**

1. https://www.a-star.edu.sg/imcb/imcb-research/scientific-programmes/molecular-engineering-lab;; 2. https://research.a-star.edu.sg/articles/features/commemorating-the-life-of-sydney-brenner/

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Challenges Faced from Infectious Diseases

Significant Financial Burden to Society

- **7%** of deaths, **8%** of hospital bed days[1]
- Global infectious disease diagnostics market valued between **USD16bn – 26bn** in 2019, with CAGR **6.2%**[7]

Pathogens in Blood

- **1 in 4** hospital patients have an infection in their blood stream and at least **1 in 2** infectious disease patients are on 1 or more antibiotics or similar treatment[2]
- Estimated **2.8 million** of US based infections are caused by **antibiotic resistance**[5]
- Antimicrobial resistance is directly correlated to antibiotic consumption and economic costs are multiple times exceeding the direct treatment costs[6]
- Antimicrobial diagnostics is a core development theme of World Health Organisation's Global Antimicrobial Resistance action plan[8]

The Global Infectious Disease Threat

- Infectious diseases kill over **17 million people** a year according to the World Health Organisation[3]
- If action is not taken antimicrobial resistance could exceed mortality from other diseases by 2050[4]

1. http://www.publichealthnetwork.cymru/files/4314/8525/4079/Infectious_Diseases.pdf; 2. Clinical Infectious Diseases, Volume 64, Issue suppl_2, 15 May 2017, Pages S61–S67, https://doi.org/10.1093/cid/cix103; 3. https://www.who.int/whr/1996/media_centre/press_release/en/; 4. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations The Review on Antimicrobial Resistance, Chaired by Jim O'Neill, December 2014; 5. https://www.cdc.gov/drugresistance/index.html; 6. https://aricjournal.biomedcentral.com/articles/10.1186/s13756-018-0384-3; 7. https://www.grandviewresearch.com/industry-analysis/ivd-infectious-disease-market; 8. https://apps.who.int/iris/handle/10665/193736

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Diagnostic Challenges Faced from Infectious Diseases

INFECTIOUS DISEASES OF UNKNOWN CAUSES REMAIN HIGH

Although hospitals have extensive laboratory testing for infectious diseases, it is estimated that etiology between 16 - 55% of infectious disease cases remained unknown[1]

Current most common clinical diagnostics for infectious disease:
Blood Culture

- ✗ Cheap (average $50 per test) but inaccurate
- ✗ Labour intensive
- ✗ Analytically insensitive
- ✗ Trial and error approach and takes up to 5 days to culture at which point the patient may already have worsened in condition

- ✓ Without early stage data, clinician typically is unable to prescribe appropriate medication or can only apply broad spectrum antibiotics or antivirals that may have limited efficacy on the patient

Other technology used in current clinical diagnosis for infectious disease:

Other diagnostic technologies including PCR is cost affordable (average $130 per test) but is biased to "known" specific pathogens only and unable to detect broad spectrum of both known and unknown pathogens. – It is not ready for **new emerging infectious diseases**

CONCLUSION

A new technology for a rapid, cost effective, sensitive and unbiased detection for ALL type of pathogens is needed

1. https://academic.oup.com/ofid/article/7/5/ofaa132/5828054

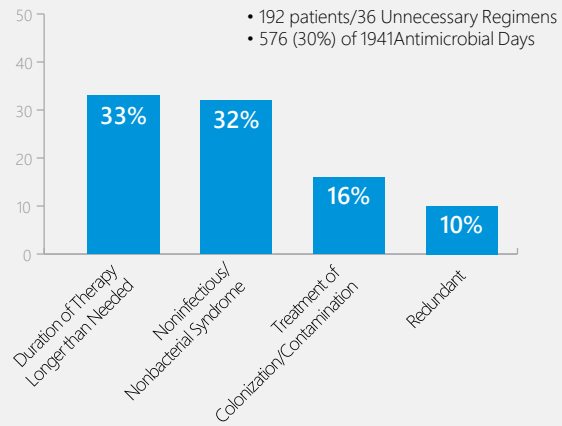
Appropriate Antibiotic Therapy in Favor of Inappropriate Antibiotic Therapy

Question Why Are Timely Precision Medicine Tests Important For Infectious Diseases?

Answer To Provide Crucial Information For Clinicians To Initiate The Appropriate Antibiotic Therapy

Today, up to 85% of antibiotics have a non-human use and up to 75% have a non-therapeutic use. Antibiotic use in hospitals and the community is common and often inappropriate [Figure 2]. In hospitals, up to 50% of antimicrobial use is inappropriate [Dellit et al., 2007][5]

Figure 2. "Unnecessary" Antimicrobial Therapy



Adapted from Hecker MT. et al. Arch Intern Med. 2003;162:972-978.

- RPIDD is a form of **Precision Medicine**
- Compared with "Appropriate Antibiotic Therapy", Inappropriate Antibiotic Therapy
  - Prolongs hospital and ICU duration of inpatient stay[1]; Longer lengths of stay lead to higher costs, as well as higher risks in acquiring **nosocomial infections**
  - Could lead to higher mortality rates[2]. High-risk patients with infections could see a **threefold increase** in mortality if they cannot get early appropriate antibiotic treatment[3]
  - Leading cause of antimicrobial resistance issues and complications
- Between 2008 - 2011, it is estimated that in the U.S. alone, over **70%** of cases was caused by unnecessary antimicrobial therapy[4]

1. Raman, G.; Avendano, E.; Berger, S.; Menon, V. Appropriate Initial Antibiotic Therapy In Hospitalized Patients With Gram-Negative Infections: Systematic Review And Meta-Analysis. BMC Infectious Diseases 2015, 15 (1); 2. Marquet, K., Liesenborgs, A., Bergs, J., Vleugels, A. and Claes, N., 2015. Incidence and outcome of inappropriate in-hospital empiric antibiotics for severe infection: a systematic review and meta-analysis. Critical Care, 19(1), p.63; 3. Andersson, M., Östholm-Balkhed, Å., Fredrikson, M., Holmbom, M., Hällgren, A., Berg, S. and Hanberger, H., 2019. Delay of appropriate antibiotic treatment is associated with high mortality in patients with community-onset sepsis in a Swedish setting. European Journal of Clinical Microbiology & Infectious Diseases, 38(7), pp.1223-1234; 4. Schultz, L., Lowe, T., Srinivasan, A., Neilson, D. and Pugliese, G., 2014. Economic Impact of Redundant Antimicrobial Therapy in US Hospitals. Infection Control & Hospital Epidemiology, 35(10), pp.1229-1235. 5. https://www.biomerieux.co.uk/sites/subsidiary_uk/files/antimicrobial-stewardship-booklet-final.pdf

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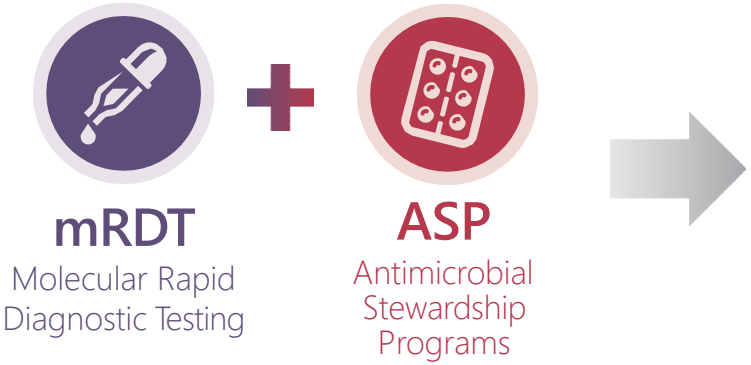
Economic Evaluation: Cost Effectiveness of General mRDT with ASP



BETTER CLINICAL OUTCOMES

- In recent years, some molecular rapid diagnostic testing methods (e.g. PCR) have become available for rapid identification of pathogens and act as a precision medicine test for pathogens
- mRDT with an ASP: can prevent **1 death per 25 patients** tested compared to conventional laboratory methods without an ASP[2]
- With mRDT: the average length of stay in hospitals were shortened by **2.48 days**[1] and Mortality Risk is reduced compared to conventional methods. Reduction of use of inappropriate therapies

COST SAVINGS

Estimated to save > US$20,000 per infected patient per treatment[2]

Diagnostic Strategy	Average Cost (USD)[2]
1. Conventional method without ASP	55,932.02
2.Conventional method with ASP	41,723.98
3. mRDT with ASP*	**31,274.24**

ICER (cost per QALY) : -$45,764*

1. Timbrook, T.; Morton, J.; McConeghy, K.; Caffrey, A.; Mylonakis, E.; LaPlante, K. The Effect Of Molecular Rapid Diagnostic Testing On Clinical Outcomes In Bloodstream Infections: A Systematic Review And Meta-Analysis. Clinical Infectious Diseases 2016, 64 (1), 15-23; 2. Pliakos, E.; Andreatos, N.; Shehadeh, F.; Ziakas, P.; Mylonakis, E. The Cost-Effectiveness Of Rapid Diagnostic Testing For The Diagnosis Of Bloodstream Infections With Or Without Antimicrobial Stewardship. Clinical Microbiology Reviews 2018, 31 (3)

* Incremental Cost Effectiveness Ratio of mRDT in combination with effective antimicrobial stewardship programs (ASPs) is negative $45,764 per patient, indicating cost savings of $45k per 1 year of quality adjusted life year gained by patient.

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RPIDD Aims to Shift mRDT Methods to First-line Diagnosis

But Why Is Molecular Rapid Diagnostic Testing (mRDT) Currently Not First-line?

Current commercially available mRDT are **limited in scope** (often do not exceed 100 types of pathogens) and antimicrobial resistance marker due to a **lack of primers/probes**[1]

Emerging pathogens and known pathogens with new mutations **may not be detected**

High Costs: Average over USD$2500 per test in current molecular service provider

If a medical laboratory develops its own test using mRDT, the **quality of the results are significantly influenced by the manufacturing source** of the reagents used This limits the flexibility and adds extra cost to the labs

Therefore, A Technology For A Rapid, Cost Effective, Sensitive And Unbiased Detection For **ALL** Types Of Pathogens Is Urgently Needed: RPIDD

RPIDD is an **NGS based** (Next generation sequencing) molecular diagnostic technology

RPIDD employs an untargeted approach for **detection of all known and mutated pathogens**, as well as genes that cause antibiotic resistance in a single test. It provides valuable information in a timely manner and the appropriate antimicrobial therapy is initiated as rapidly as possible

Cost Efficient: target average <USD$1000 per test (long term target more than 60% cost reduction)

RPIDD is a **scaleable service integrated in hospitals** to support local and regional hospital service for blood-based rapid pathogen diagnostics

Karumaa, S.; Karpanoja, P.; Sarkkinen, H. PCR Identification Of Bacteria In Blood Culture Does Not Fit The Daily Workflow Of A Routine Microbiology Laboratory. Journal of Clinical Microbiology 2011, 50 (3), 1031-1033.

* The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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Our Market Overview

RPIDD targets to become first-line diagnosis, disrupting existing pathways for the Infectious Disease Diagnostic Market

PRECISION MEDICINE

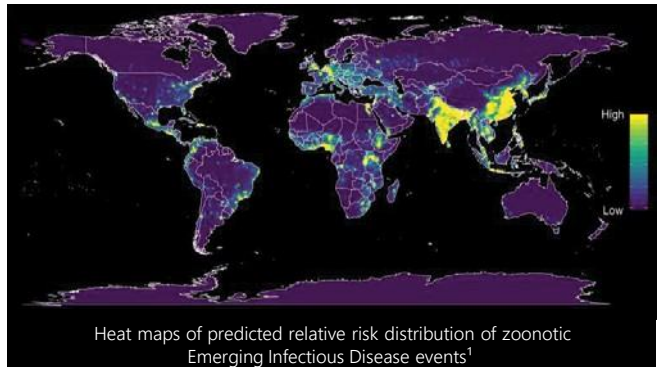
- Trend for precision medicine globally. Market for molecular diagnostics technique (e.g. NGS) will likely continue to expand

KEY TARGET MARKETS

South East Asia, China, US, UK, Europe, Australia:

Combination of:

- High risk zones for emerging infectious diseases
- Good healthcare systems and large markets



Heat maps of predicted relative risk distribution of zoonotic Emerging Infectious Disease events[1]

1. Allen, T.; Murray, K.; Zambrana-Torrelio, C.; Morse, S.; Rondinini, C.; Di Marco, M.; Breit, N.; Olival, K.; Daszak, P.Global Hotspots And Correlates Of Emerging Zoonotic Diseases. Nature Communications 2017, 8 (1).

BACKDROP MARKET SIZE

Total Population (S.E. Asia, China, US, Europe, Australia)[1]	**2.9 BILLION**
Inpatients Hospitalized (or discharged)[2]	**EST. > 427 MILLION** per year
Inpatients Hospitalized for Suspected Infectious Disease[3]	**EST. > 42 MILLION** per year
Estimated Market Share[4]	Target Market Size **3.5 MILLION PATIENTS** per year

1. https://www.worldometers.info/world-population/population-by-country/; 2. https://www.ncbi.nlm.nih.gov/books/NBK91986/; 3. Approximately 10% (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3021207/); 4. Assumed market penetration rate of 8% of inpatient hospitalized for suspected infectious disease

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RPIDD is integrated with NGS which is poised for widespread clinical adoption and will revolutionize precision medicine

DNA SEQUENCING REFERS TO **"READING"** DNA

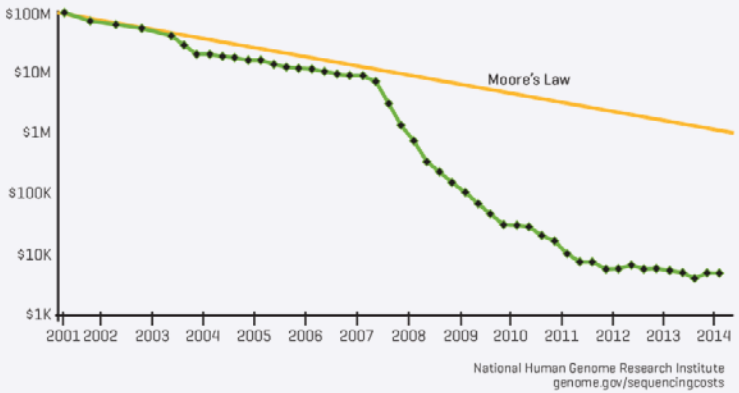
First generation (Sanger sequencing)

- Single site reads
- Slow, costly

NGS

- Massively parallel reads
- Fast, cheap

Drastic Drop in cost and time anticipated to create commercialization opportunities*



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Blood Culture vs Next-Generation Sequencing (NGS)

Blood cultures are time-consuming, labor intensive and cannot detect all infectious organisms

BLOOD CULTURE

NGS[1]

STRENGTHS

- ✓ Cheap (USD$100-150 per culture)

- ✓ Untargeted approach – ready for **new emerging infectious diseases**
- ✓ **Simultaneously** detects genes causing **antibiotic resistance**
- ✓ ~**24hr** turnaround time

WEAKNESSES

- ✗ Cannot detect **all infectious pathogens** - NOT ready for the **next pandemic**
- ✗ Takes up to **5 days for 1 culture**
- ✗ A **trial-and-error** approach

- ✗ More expensive, with costs dropping rapidly **with process optimization (RPIDD is targeted to be more than 60% cheaper than existing NGS technologies)**

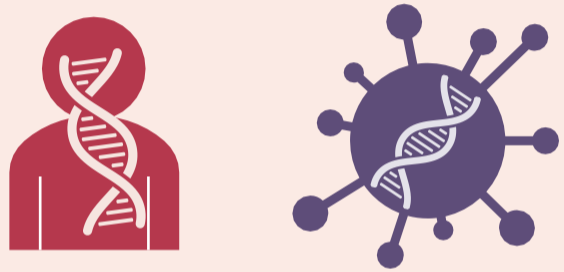
1. https://www.tandfonline.com/doi/pdf/10.1586/14737159.2015.1111140 and https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-017-0461-x

RPIDD Device Targets to Improve Sensitivity

RPIDD device can efficiently and selectively deplete human background DNA

(subject to ongoing clinical validation)*

BLOODSTREAM INFECTION



99% HUMAN DNA

<1% NON-HUMAN DNA

RPIDD DEVICE HUMAN DNA DEPLETION

Lowers human background by **100x** with **no significant loss** in signal of microbes

Improved Sensitivity = Lower Sequencing Cost Less reads will be required to give detectable signal

Target to achieve >99.99% specificity and >95% sensitivity, subject to ongoing clinical validation

Source: https://www.nature.com/articles/s41576-019-0113-7

* The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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RPIDD Device Workflow Overview

PROPRIETARY DIAGNOSIS WORKFLOW (24 HOURS)

Proprietary method in DNA/RNA extraction

1

Biofluid collection

- **~0.5ml of blood** is used in the current generation of method

2 6 hrs

Sample extraction

- Host **DNA** depletion
- Microbial **DNA/RNA** enrichment
- One-pot DNA & RNA library preparation
- Both **targeted** and **untargeted** workflows

Proprietary Method

3 8-14 hrs

Next-generation sequencing (NGS)

- Designed to be compatible with Illumina platforms (e.g. MiniSeq, NexSeq, HiSeq, MiSeq and iSeq100)
- Easy adapted to Nanopore workflow
- Compatible with other faster next generation sequencing machines (e.g Nanopore)

4 <2 hrs

Secure cloud-based artificial intelligence driven bioinformatics analysis & report generation

- Refined workflow for rapid diagnosis of infectious disease

Proprietary Software

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RPIDD Device : Untargeted Workflow Overview

Untargeted sequencing enables the detection of, in principle, majority DNA & RNA-based organisms*

Biofluid collection

Third Party Tubes

Host Depletion:

Both host DNA and RNA will be deleted

Proprietary Method

Nucleic Acid Purification

Adapted with our proprietary protocols

One-pot Unbiased Amplification

Proprietary Method

DNA Fragmentation

Proprietary Method

DNA Library preparation & barcoding

Proprietary Method

DNA Sequencing

- Compatible with all Illumina sequencing platforms: HiSeq, NextSeq, MiSeq, iSEQ 100 and MiniSeq

* The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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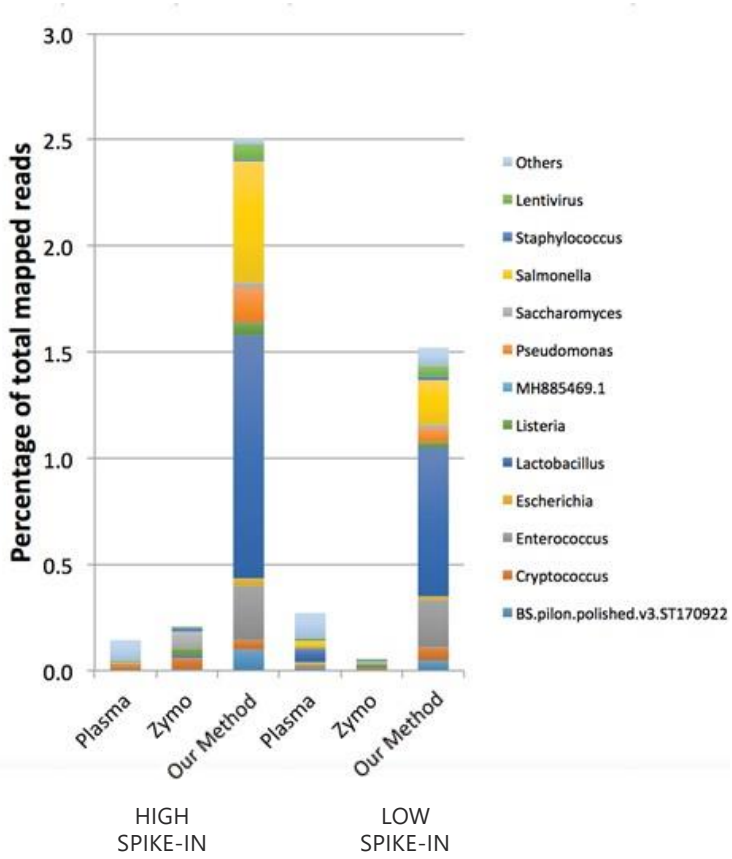
RPIDD DEPLETION OF HOST NUCLEIC ACIDS IS MORE SUPERIOR THAN COMMERCIAL KIT:

Controls : Zymo microbial standards, lentivirus and HCV in human plasma

- Left untreated or treated with Zymo Host-Zero* or our proprietary method host depletion
- DNA / RNA sequenced in similar fashion and reads mapped to microbes / viruses
- Remainder mapped to human



* Host-Zero was not designed for use with plasma, but a host depletion kit for plasma does not exist on the market at the moment. Host-Zero is the closest approximation.

Our Enrichment Protocol*:

- Host DNA/RNA depletion allows for more on-target sequencing, improving sensitivity and lowering cost
- Lowers human background by 100x with no significant loss in signal of microbes
- Depletion protocol effectively depletes dominant human signal across different regions:

  (i) Chromosome Mitochondria
  (ii) Hemoglobin Gene HBB
  (iii) Housekeeping Genes

* The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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Unique Features of RPIDD Device : One-pot DNA & RNA Library Preparation

DNA FRAGMENTATION METHOD

A DNA library prepared by our proprietary fragmentation method. The distribution sizes become **progressively clustered around the 300-500nt size suitable for Illumina sequencing** with increasing amount of different amount of methylated C (mC) incorporated*

1. Our Proprietary DNA/RNA library preparation allow the use of commercially available enzymes by any manufacturers, leading to greater flexibility and reduction of the operation cost

2. Library preparation performance between commercially available kit and our library preparation method is **comparable**

LIBRARY PREPARATION

* The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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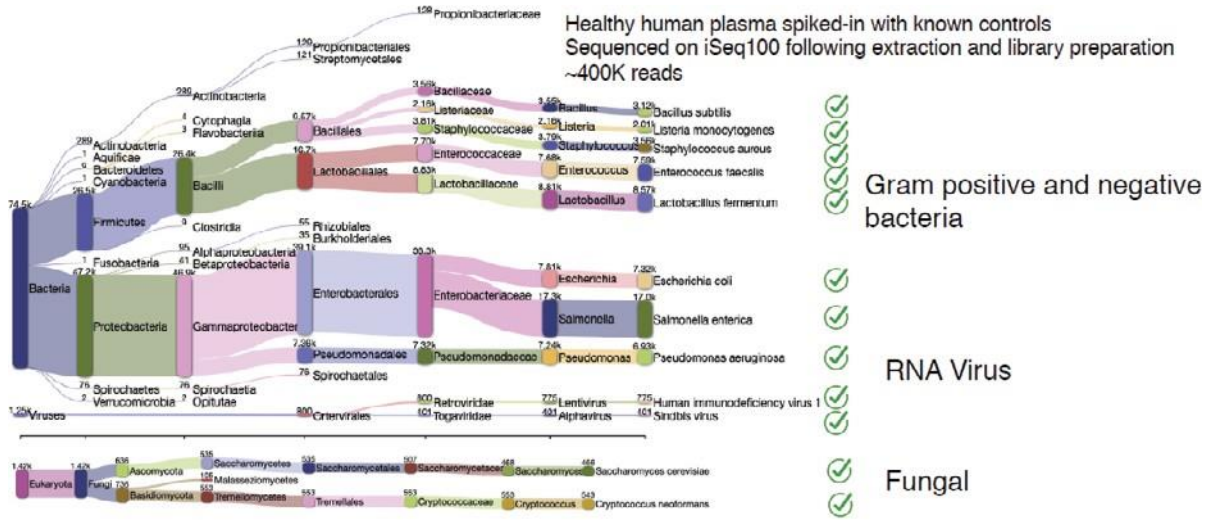
RPIDD device detected organisms ranging from bacteria, RNA virus and fungi in ONE TEST[1]

Sensitivity	1.25 copies of DNA/RNA per µl plasma
Specificity	Controls: ZymoBIOMICS Microbial Community Standard, Lentivirus and Seracare AccuSpan recombinant virus

- 8 species of bacteria,
- 2 species of RNA virus, and
- 2 fungal samples were spiked into human plasma

All 12 species identified in ONE TEST



1. The above experiments were conducted in-house and have not been verified by third parties.

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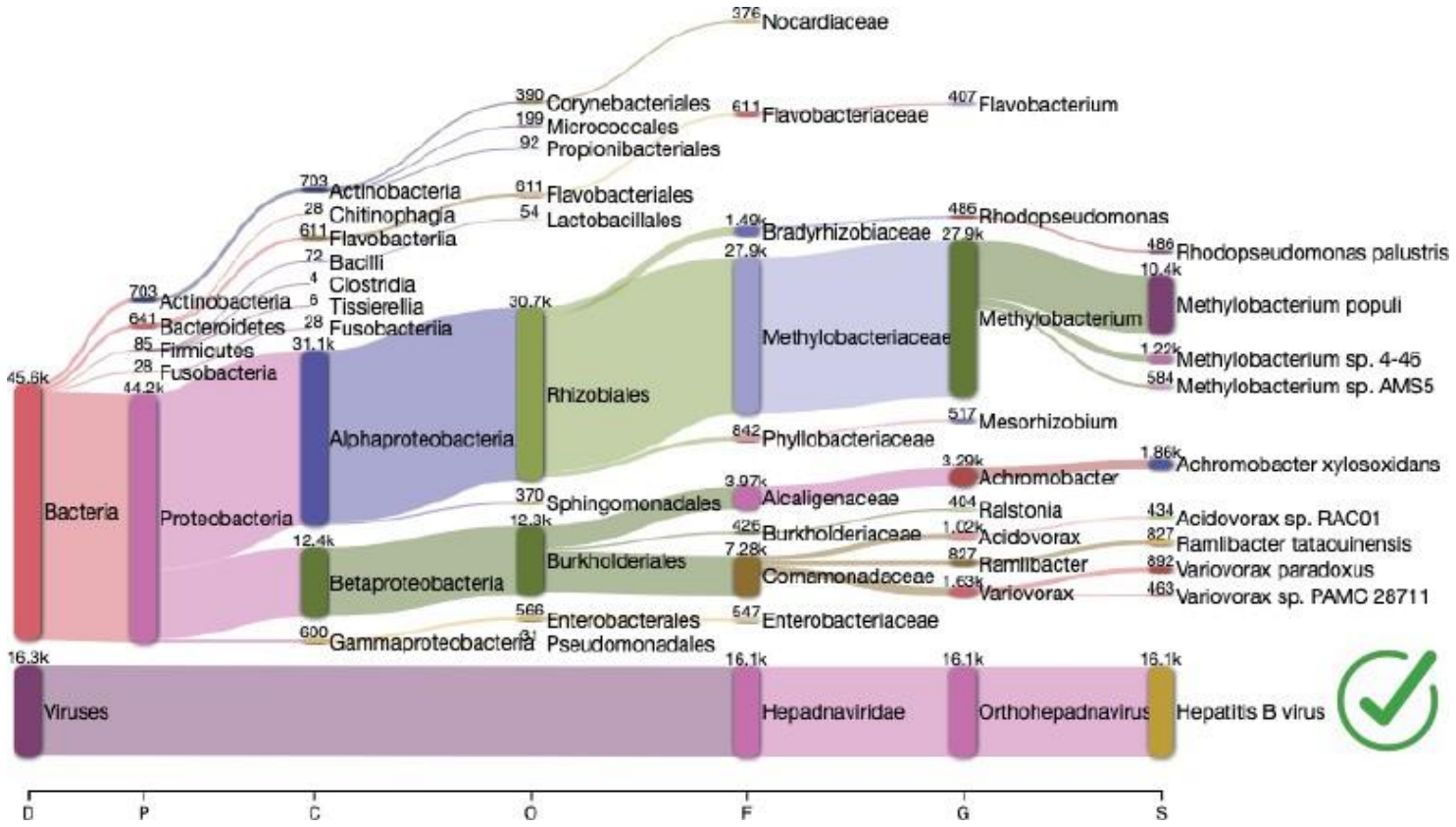
SAMPLE PROCESSED AT NUH WITH OUR PROTOCOLS AND REAGENTS[1]

- Banked sample with known Hepatitis B infection
- **Hepatitis B, a DNA virus was successfully identified**



Additional microorganisms were also identified

1. The above experiments were conducted in-house and have not been verified by third parties.

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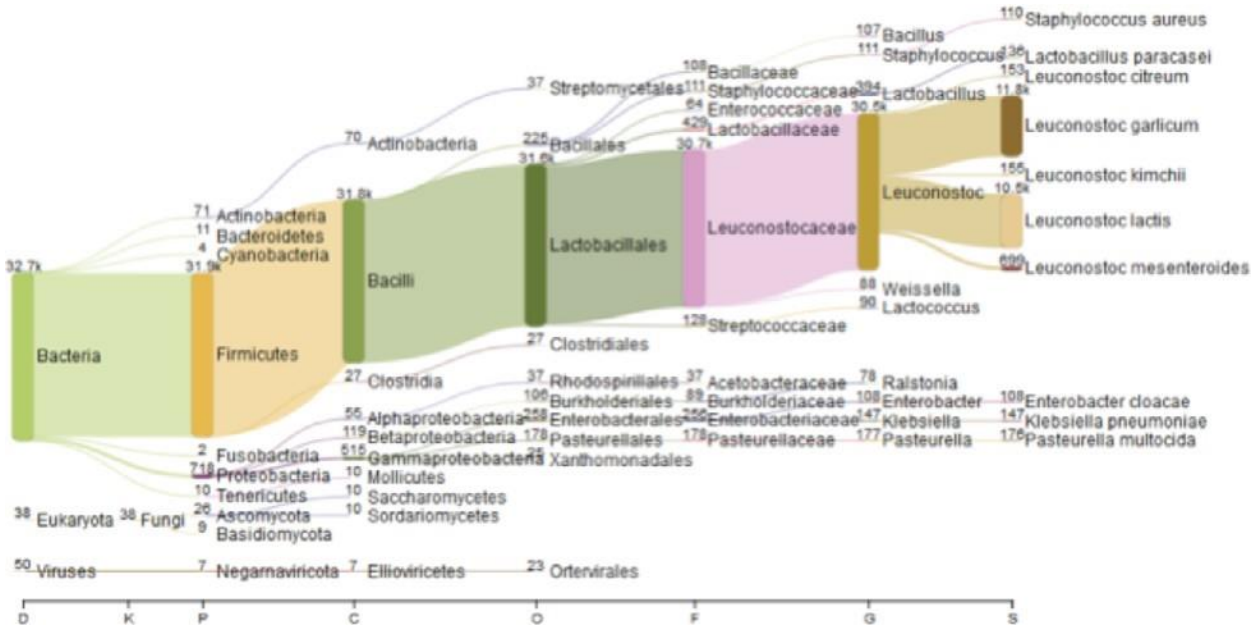
SAMPLE PROCESSED AT NUH WITH OUR PROTOCOLS AND REAGENTS[1]

- Undergoing chemotherapy with severe lung infection
- Refractory to first-line antibiotic
- Eventually responded to a combination of 2nd line antibiotics and antifungal medication

Traditional trial and error approach

- **Leuconostoc, a Gram+ bacteria was identified by RPIDD device , which was not previously considered by clinicians**
- **Leuconostoc was found to make up 10% of reads after host depletion**



1. The above experiments were conducted in-house and have not been verified by third parties.

- Part of Clinical validation with hospitals is also to profile healthy or background samples so that we can identify the background microbial sequences in samples from specific hospitals or are part of the “kitnome” that we can filter out from our report
- Public databases for different pathogens will be used for the matching
- We can also work with clinicians to curate a list of priority organisms that are clinically actionable. Rare but important pathogens could also be included because of our untargeted approach

FUTURE DEVELOPMENT FOR REPORT GENERATION:

- **Symptomatic way:** Using the host RNA details, for understanding host response to provide a wholistic picture of the different tissues and clinical correlates to infection related symptoms
- **Bioinformatics AI way:** Training an anomaly detector, learns what is a common endemic profile of organisms found in the biofluid using the initial training datasets and flags the sample when anomaly is detected

* The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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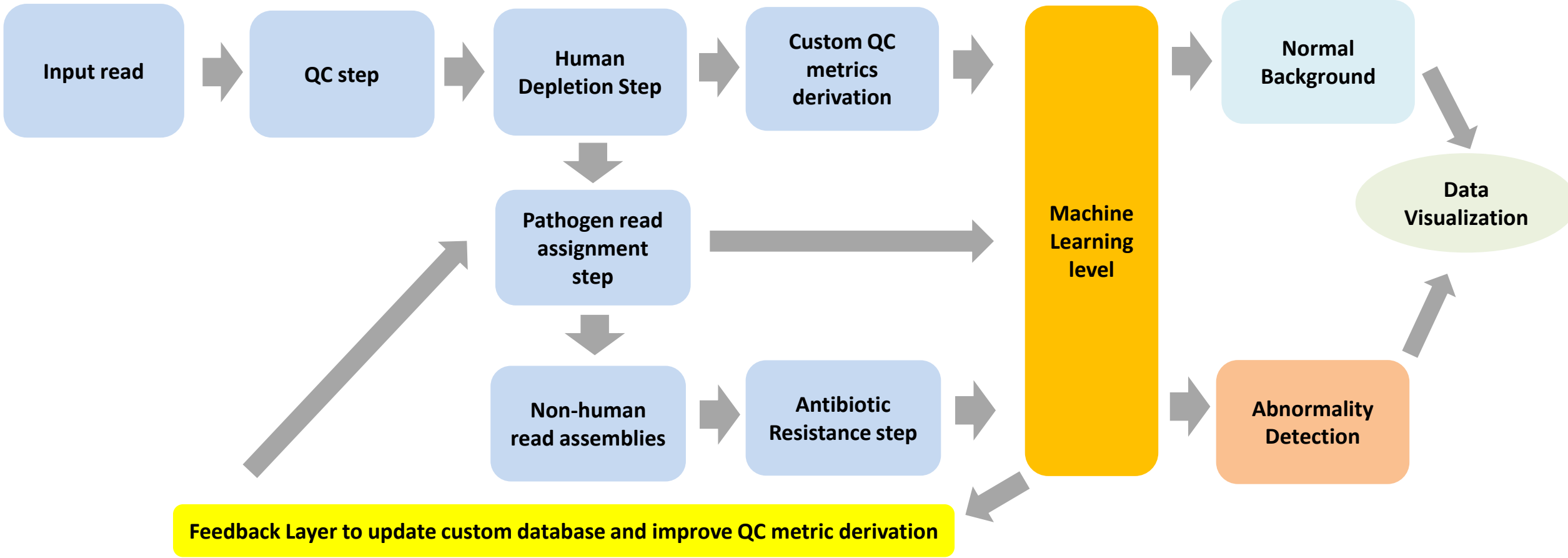
Pseudocode for Bioinformatics Pipeline



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- **Laboratory Device Test model:** Providing RPIDD device and workflow as a private pathological laboratory service integrated inside private hospitals and clinics, targeting majority in-patient market
- **Build out of self-controlled diagnostics laboratory (ISO standard)** to provide accredited diagnostics services and high-complexity clinical laboratory testing
- **Target customers:** private market including private hospitals, clinics, corporates, insurance companies
- **A combination of standalone diagnostic laboratories and collaboration sites** at selected private hospitals

Conclusion

- When dealing with an individual patient with an infectious disease or responding to a worldwide pandemic (such as SARS, COVID19, MERS etc), it is fundamental to provide quality care and treatment through the rapid and accurate identification of microbials.
- Despite advances in diagnostic technologies, many patients with suspected infections receive only empiric antimicrobial therapy[1] rather than appropriate "precision based" therapy dictated by the rapid identification of the infectious agent.
- New tests are needed that can identify a specific pathogen or at a minimum, distinguish between fungal, bacterial and DNA/RNA viral infections, and also provide information on susceptibility to antimicrobial agents.
- We believe our technology* enables the detection and quantification of pathogen burden with new speed, sensitivity, affordability and simplicity of use.
- Subject to ongoing validation of our workflow process, our technology aims to effectively communicate the clinical diagnostic results to the healthcare provider or public health practitioner in a timely manner and will have a positive impact on clinical decision making.
- We believe the availability of our technology will lead to improvements in clinical outcomes for patients, antimicrobial stewardship, detection and tracking of disease outbreaks, and investigation of unknown pathogens (such as COVID-19).

The need for diagnostics that advance clinical care and public health has never been greater, and there is a critical window of opportunity to harness new technologies, such as our RPIDD.

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4358713/ ; * The technology is subject to ongoing clinical validation. There is no guarantee of any outcome.

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Appendix: Bloodstream and Non-Bloodstream Infections Impact

	Can be Bloodstream or Non-Bloodstream Infections	Respiratory Diseases		Sexually Transmitted and Blood-borne Infections
	Sepsis	**Influenza**	**Tuberculosis ("TB")[8,9]**	**Hepatitis B and C**
Description / Related Notes	Defined as a Life-threatening organ dysfunction caused by a dysregulated host response to infection. The prompt administration of appropriate antibiotics is crucial in the survival of sepsis patients.	Advantage of Whole-genome sequencing (WGS) of influenza virus VS traditional method[5]: • WGS can detect drug resistance mutations more comprehensibly. • Detection of the emergence of antiviral resistance at an early stage. • Enable tracking of the origin of outbreaks and to forecast the spread of disease. • Valuable information to public health surveillance		Common Blood-borne Infections where many of the carriers do not know they have the disease.
Statistics:				
Global	**48.9M cases**, and **11.0M** sepsis-related deaths annually[1]	Approximately **1Bn** people are affected each year, and there will be up to **3 to 5 million** severe cases, and **300,000 to 500,000 deaths** annually[6]. 2018–2019 influenza season CDC estimated **35.5M** people getting sick with influenza, around **490,600** hospitalizations, and **34,200** deaths from influenza[7].	Around **10M** people infected with TB in 2018.	Approx. **325M worldwide** are chronic HBV or HCV carriers[10]; Many carriers do not know they are infected (Estimated by CDC, in US, About **66.7%** of HBV carriers and about **50%** of HCV carriers do not know they are infected[11].)
U.S.	At least **1.7M** adults develop sepsis[2] each year.		Approx. **9000 new cases** in 2018.	Estimated **71,900 new cases** of HBV and HCV annually in 2018. It is estimated that around **862,000** and **2.4M** people living with HBV and HCV respectively[12].
Europe (EU)	More than **3.4M** individuals develop sepsis annually[3]		Reported **0.3M new cases** in 2018.	About **62,100 new cases** of HBV and HCV annually in 2018. The population of chronic HBV and HCV estimated to be **4.7M** and **3.9M** respectively.
China	**5.7M** cases annually[4].		Approx. **0.9M** new cases in 2018	Approx. **86M** HBV carriers and **9M** HCV carriers[13]
South East Asia	In some countries, the **incidence rate high as 1.6%** of the population[1]		Approx. **4.4M** new cases in 2018.	Estimated **1.9M** of new cases of HBV and HCV annually. Around **100M** HBV carriers and **30M** HCV carriers[14]

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