HMRF 2024 OPEN CALL
BRIEFING SESSION FOR GRANT APPLICATIONS

Sharing of experience

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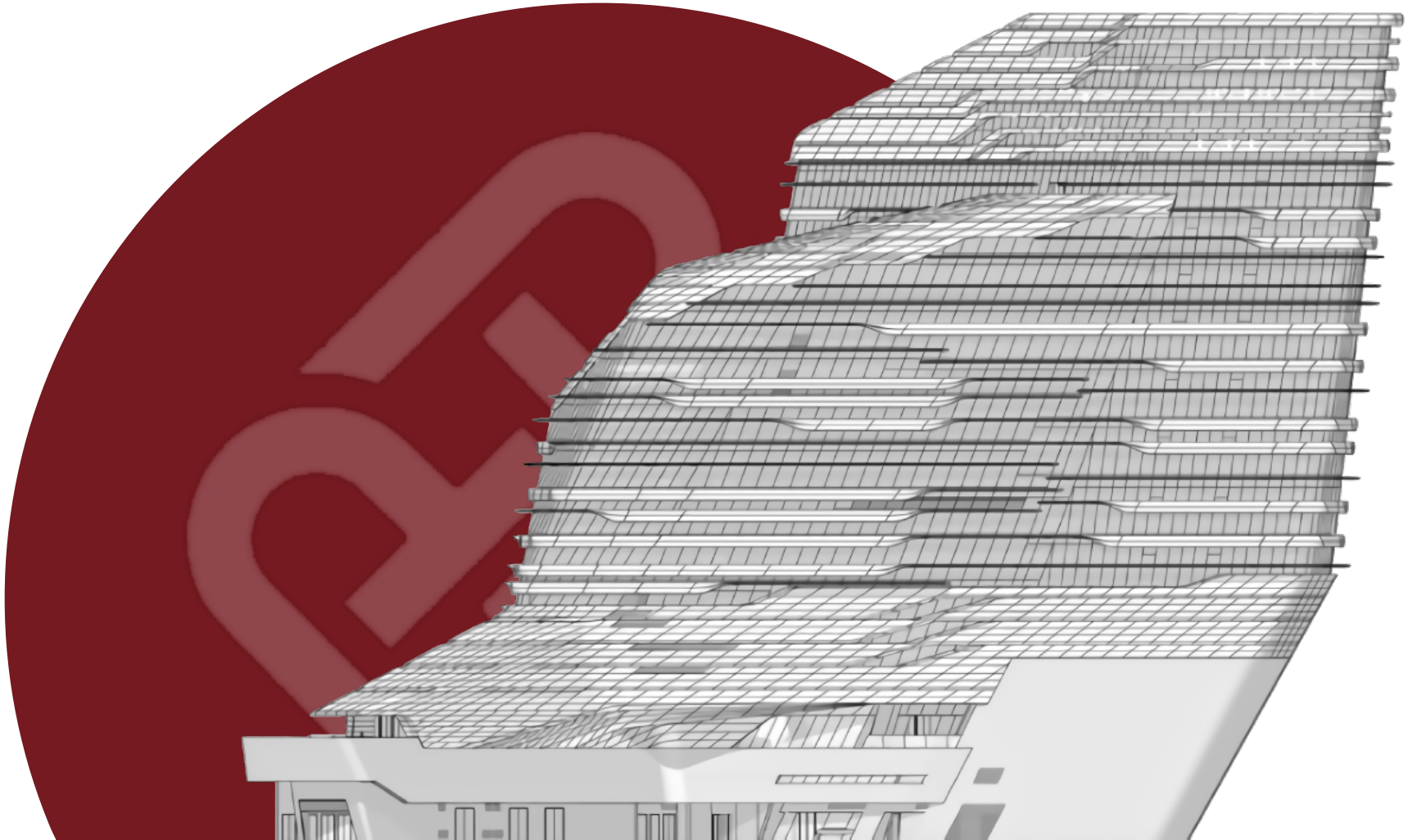


Outstanding Grant Applicant

≠

Outstanding Grant Recipient

I failed the first two rounds of application!!

Would I get fired?

Success rate of HMRF Proposals

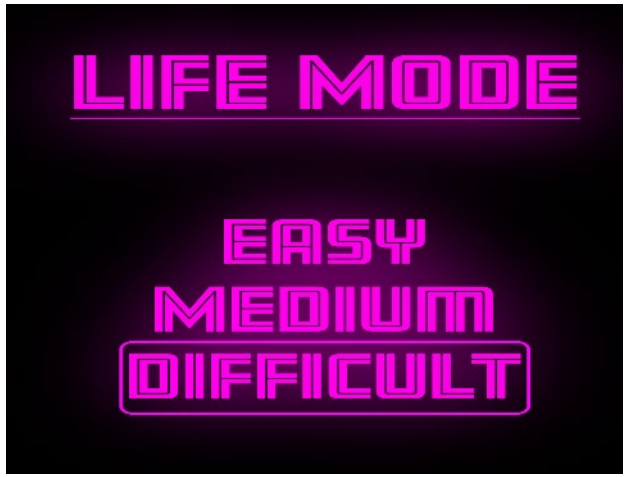
Number of Proposals

- Total: ~ 700 to ~800
- AMR>HHS>>ID>>HP
- ~350>~300>>~100>>~20

AMR : Advanced Medical Research
HHS : Health & Health Services
ID : Infectious Disease
HP : Health Promotion

Successful rate

- HMRF (2022 open call) : **~24%**
- GRF 23/24: ~ 33.31%
- ECS 23/24: ~ 35.62%
- GRF/ECS (Biology and Medicine Panel) : 25.81%



NOT an easy game at all!!

Step 1: Don't get disqualified – Study the project scope

HMRF emphasizes the importance of translational potential of research findings

Only clinical research and research on infectious diseases with public health implications will be supported.

Research proposals on infectious diseases should focus on those diseases which are prevalent in or pose threat to Hong Kong and neighbouring regions or areas in which the Hong Kong academic community has a competitive edge.
Research proposals on infectious diseases (i) with public health implications from bench to bedside and at community level, and (ii) with translational value are supported.

Step 2: Know the rules – Two-tier review system

First-tier

- External reviewers (ERs): Overseas, 2 for full proposals, 1 for seed grants
- Full proposals with single-low ER rating (e.g. 1) will not be carried forward for the second-tier review
- Seed grants with ER rating of 1 or 2: Not reviewed in the second-tier

Second-tier

- Local speakers together with a few oversea experts in some panel meetings
- First speaker reviews the proposal and present the case in the panel meeting
- Second speaker may submit written comments
- Final decision by consensus in the panel meeting (NOT by voting)

Step 2: Know the rules – Referee's assessment form

Both external reviewers and local speakers have to fill in the assessment form (with 9 items)

- Originality and Impact
- Research questions, aims and hypothesis
- Subjects and Study Methodology
- Outcomes and data analysis
- Research capability
- Budget
- Ethical and safety consideration
- Overall comments and conclusion (Strengths and Weaknesses)
- Confidential Comments to the Research Council

Step 3: Be strategic – Draft your proposal based on these items

Unlike publications, proposal will only be read by 3-4 people

- Senior researchers in the field – May not be an expert in your topic
- Grant assessment is an extra duty, taking up their personal time (and unpaid!)

Tailor-made a proposal for them!!

- Highlight these items in your proposal
- E.g. Use subheadings in the introduction to state clearly (i) Originality, (ii) clinical impact of your project
- Help the ERs/Speakers to find the answers for the assessment forms

- Originality and Impact
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Originality and Impact

What is the importance of the proposed research in terms of its **originality** and potential impact in the area under study?

Originality (Novelty)

State clearly in the "Research in Context"

- Indicate the problem to be addressed
- The pitfalls of the current practice (**Research gap**)
- Is the method you are proposing entirely novel?
- If not, how is your proposed study design different from the previous studies

  E.g. Relevance to Hong Kong context

  [Important for convincing ERs]

Funded HMRF project (2020): Establishment of clinical workflow for rapid identification of pathogens and antimicrobial resistance from infected body fluids – Metagenomic vs targeted amplicon sequencing approach

- Culture methods → long turnaround time for acute infection
- Nanopore sequencing → previous studies focused only on microbial ID, No AMR data
- Self-designed enrichment panel → higher sensitivity and rapid TAT
- Multicentre on-site evaluation → no previous study

Originality and Impact

What is the importance of the proposed research in terms of its originality and potential **impact** in the area under study?

How will the research findings **benefit patients and/or the healthcare system**?

Will the research findings **improve patient care, population health, influence clinical practice** and/or **health services management**, or **inform health policy** in Hong Kong and elsewhere?

Have the potential facilitators and barriers to this impact being achieved been identified?

Impact (The spirit of HMRF)

State clearly in the introduction and the last paragraph of proposal

- Benefit the healthcare system – Addressing a major health problem / diseases prevalent in Hong Kong
- Improve patient care – Clinically effective /better treatment outcome
- Influence clinical practice – More cost-effective and shorter TAT
- Inform health policy – actionable and supported by government departments

Likely failed HMRF project

Establishment of clinical workflow for rapid identification of pathogens and antimicrobial resistance from infected Urine – Metagenomic vs targeted amplicon sequencing approach

Research questions, aims and hypothesis

How specific, clearly expressed and realistic are the research questions, aims and hypotheses?

Funded HMRF project (2022)

The second aim **is to develop surveillance and risk analysis tools for risk management of foodborne AMR in Hong Kong.**

Aim

To attain the project aims, **three objectives** are set for this study:

(i) **To delineate the association of microbiome and antimicrobial resistome shared by food and sewage samples.**

Objective

- The primary outcome is to identify the extent of overlap in microbial communities between food and sewage samples. This will help identify the taxonomic affiliations (at the species level) and antimicrobial resistance genes (ARGs) that can commonly shared between food and human microbiomes.
- The secondary outcome is to identify, based on metagenomic-assembled genomes, foodborne antimicrobial-resistant bacteria at the strain level that are consistently found in the human microbiome. This will help determine whether specific foodborne bacterial strains preferentially colonize and contribute to the microbiome and antimicrobial resistome in the human gut.

Outcome

(ii) **To characterize the phenotypic and genotypic AMR profile of foodborne AMR organisms and their phylogenetic relatedness with clinical MDRO strains.**

- The primary outcome is to characterize the phylogenetic relatedness between MDROs isolated from food and those found in clinical settings.
- The secondary outcome is to identify the transmission dynamics of foodborne AMR to human supported by epidemiological evidence.

(iii) **To develop surveillance and risk analysis tools for risk management of foodborne AMR in Hong Kong.**

- The primary outcome is to establish an active surveillance platform to monitor the trends and distribution of foodborne AMR in Hong Kong.
- The secondary outcome is to establish a Rapid Risk Assessment (RRA) framework that provides actionable evidence for policymakers. This framework will help evaluate whether risk management measures are required when critically important MDRO strains or key ARGs are detected in food.

Aims and Hypotheses to be tested

- Emphasize the major **research questions**
- **One project aim, 3-4 objectives** to achieve the project aim
- List out the objectives in **point forms (subheading)** to ensure that the reviewers will be able to see them and tick off from their checklist.
- State clearly the **hypotheses** and the **primary and secondary outcomes** for each objective
- Be realistic

Subjects and Study Methodology

Is the proposed **design and methodology appropriate** for the study?

Are **sample sizes** clear, justified, adequate and realistic??

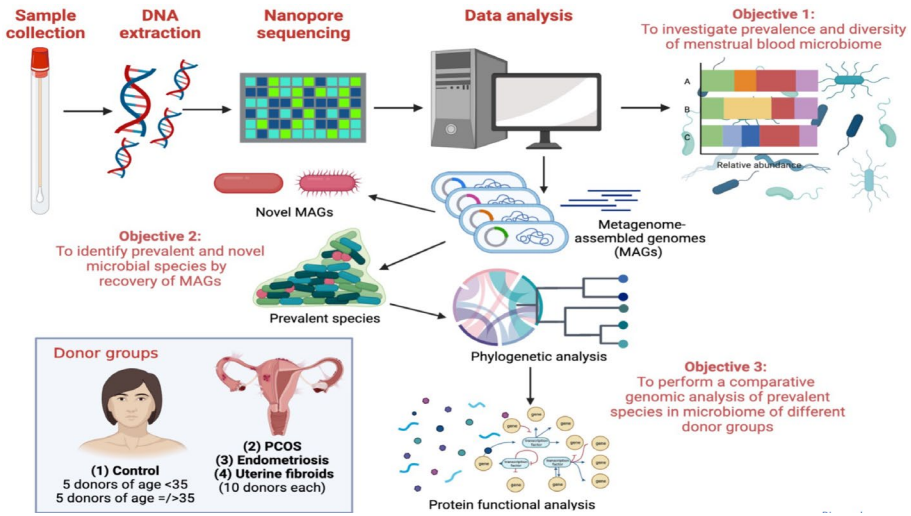
Are any **preliminary data** available?

How feasible is the proposed **timeframe**?

CRITICAL comments mainly found here!

Study Design – Can it answer the research questions?

- A schematic figure to summarize the study design



Sample size – Seek help from statistician if you are not familiar

- Cite the references for the calculation method
- If each objective necessitates different subjects, calculate the sample size for each objective separately.

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Are any **preliminary data** available?

How feasible is the proposed **timeframe**?

Most CRITICAL comments found here!

Preliminary data – **Groundwork** and **pilot study**

Groundwork data

- Demonstrate that you are working on this topic.
- Better to be some published studies
- Describe in the introduction section

Funded HMRF project (2022): Risk assessment and surveillance of the transmission of foodborne antimicrobial resistance in Hong Kong

Since January 2022, **our team has been providing service to the Food and Environmental Hygiene Department of the Government of Hong Kong SAR for routine surveillance of antimicrobial Resistant microorganisms in food in Hong Kong**. In this programme, we are responsible for isolating MDROs, including (i) extended-spectrum beta-lactamases-producing Enterobacteriaceae (ESBL-PE), (ii) carbapenem-resistant Enterobacteriaceae (CRE), (iii) *Acinetobacter sp.* (CRA) and (iv) *Pseudomonas aeruginosa* (CRPA), and (v) vancomycin resistant Enterococci (VRE), from food samples collected at the import, wholesale and retail levels. As of March 2023, a total of 590 food samples, including 350 raw meat

Subjects and Study Methodology

Is the proposed **design and methodology appropriate** for the study?

Are **sample sizes** clear, justified, adequate and realistic??

Are any **preliminary data** available?

How feasible is the proposed **timeframe**?

Most CRITICAL comments found here!

Preliminary data – **Groundwork** and **pilot study**

Pilot study

- Prove the feasibility of the proposed methodologies
- Better to have pilot data for each objective
- But not too much
- Why additional grant money is needed

Funded HMRF project (2022): Risk assessment and surveillance of the transmission of foodborne antimicrobial resistance in Hong Kong

The microbiome and antimicrobial resistome in five different food types

Metagenomic sequencing was conducted for 50 food samples, including raw beef (n=10), raw pork (n=10), raw chicken (n=10), RTE-meat (sashimi) (n=10) and RTE vegetable (Salad) (n=10). The microbial taxonomic compositions of these food samples were uncovered (Figure 1A). The principal component analysis (PCA) revealed that the bacterial communities in the five food products were distinctively different, particularly in RTE-vegetables (Figure 1B). Among them, *Clostridium* (53.2%) and *Shewanella* (44.5%) were the dominant genera in beef, chicken and RTE-meat respectively (Figure 2). Curiously, the proportions of the dominant bacteria in both pork and RTE-vegetables were comparable. In pork, the dominant genus was *Staphylococcus* (18.5%), followed by *Clostridium* (17.1%) while in RTE-vegetables, *Rahnella* was the highest (22.1%), and then *Pantoea* (12.7%) (Figure 2).

For AMR profiles, the total abundance of genes related to aminoglycosides, beta-lactam, macrolide, quinolone, and tetracycline in the food products was illustrated (Figure 3A). It was highlighted that genes related to tetracycline were the most abundant in pork (45.2%). Importantly, the abundance of genes related to beta-lactams in chicken was the highest (10.7%), followed by pork (8%) and beef (3.8%) (Figure 3A). In the beta-lactam group, we identified five β-lactamase genes in the food products: TEM, SHV, NDM, CTX-M and ampC (Figure 3B). Of them, 34.0% (17/50) of food samples harboured at least one β-lactamase gene. **The findings demonstrated the utility of our metagenomic platform and analysis for investigating the relationship of microbial communities and AMR between different food types.**

Outcomes and data analysis

Are the primary and secondary outcomes clearly defined?

Have potential problems been anticipated and addressed?

Is the statistical/analytical design appropriate and clearly explained?

Funded HMRF project (2020): Establishment of clinical workflow for rapid identification of pathogens and antimicrobial resistance from infected body fluids – Metagenomic vs targeted amplicon sequencing approach

Potential pitfalls and contingency plans

If default setting of MegaPath-nano does not demonstrate superior sensitivity than other tools. We will reduce stringency of the alignment algorithm and filter settings. If the performances still could not be improved. We will compare the performance of existing bioinformatic tools, e.g WIMP and SURPI*rt(22)*, using our data set and choose the optimal one for subsequent milestones.

Most proposals did not state clearly the outcomes

Outcomes

- Align the primary and secondary outcomes with the research questions and objectives in the Aims section
- Help the reviewers to catch them!

Potential problems

- Leave a place in the proposal (e.g at end of each objective) to specifically mention potential problems, e.g., subject recruitment and bias
- Suggest possible solutions , i.e. contingent methods

Analysis

- Define what parameters you will measures
- Provides details on your analysis method
- Include statisticians or bioinformatians as co-A

Research capability

Comment on (i) the research team's expertise and track record (incl. principal investigator / project team members / collaborators) ?

Comment on the existing facilities of the Institution where the research will be conducted.

Define the roles of the Co-A of the research team

Determine what expertise are needed for the project

- Clinical partners in appropriate speciality (Physicians for subject recruitment; Pathologists for lab data etc.)
- Statisticians or bioinformatians for data analysis
- If you are junior researcher, good to have senior colleagues with relevant track records
- BUT define the role of each co-A clearly
- Avoid adding many Co-As with overlapping expertise

Supporting letter

- For public health study that can inform health policy, it is crucial to have supporting letter or any written evidence to show that you are supported by relevant **Government Departments**

Budget

Is the request for research personnel, consumables, equipment and overall budget justified and reasonable?

Be reasonable

Make the budget breakdown carefully

- E.g. calculate how many tests will be conducted in each year, and how much is the unit cost?
- How many manpower (FT + PT) required in each year?
- For lab consumables, no need to specify the brands
- Application of change request is needed for budget allocation

Ethical and safety consideration

Is the proposed research ethically sound?

Outline any safety or ethical issues that arise from the proposed research and comment on whether these have been adequately addressed in the proposal. Has ethical approval been sought?

Apply as soon as possible

- For projects involved invasive specimen collection which is not a routine medical procedure, better to obtained ethical approval before grant application.

- Take longer time to get centralized HA IRB approval

Overall comments and conclusion (Strengths and Weaknesses)

What are the specific strengths and weaknesses of this proposal?

Highlight the strengths of your proposed study at the end

- Try to leave one paragraph at the last pages to conclude the innovation, uniqueness and impact of your proposed study

Funded HMRF project (2020): Establishment of clinical workflow for rapid identification of pathogens and antimicrobial resistance from infected body fluids – Metagenomic vs targeted amplicon sequencing approach

IV. The clinical translation and the impact on diagnosis/ treatment.

The nanopore sequencing test is intended to use (1) for identification of culture-negative or slow-growing pathogens, (2) for diagnosis of rare or unusual infections with indistinguishable clinical manifestations, (3) as a first-line test in critically ill patients and (4) as an early alternative to the large number of send-out tests that would otherwise be ordered as part of the diagnostic workup.

Through extensive evaluation in this study, the bioinformatics should be able to report (i) the most likely pathogen(s) based on optimal normalized read per million (nRPM) threshold, and (ii) the source bacteria of the identified AMR genes based on the ratio of pathogen reads and AMR reads. In addition, a clinical advisory panel, which is composed of consultant microbiologists (who are the Co-I of this project, and are the Head of clinical microbiology laboratories of the respective public hospitals), will review the nanopore sequencing results. The clinical adjudication is based on the microbial taxonomy and the AMR genes reported by the bioinformatics together with demographic and clinical information, e.g. (i) age, (ii) signs and symptoms, (iii) orthogonal clinical testing (biochemical tests, haematological tests, and immunological tests) of other sample types collected concurrently from the patients, (iv) imaging result, (v) clinical history of recent infection.
With the rapid sequencing protcol and fast bioinformatic analysis, the sample-to-result turnaround time is expected less than 8 hours. Same day reporting of genetic information of pathogenic organisms and AMR in infected body fluids facilitates timely initiation of appropriate antimicrobial treatment for the patients before the availability of the culture results.

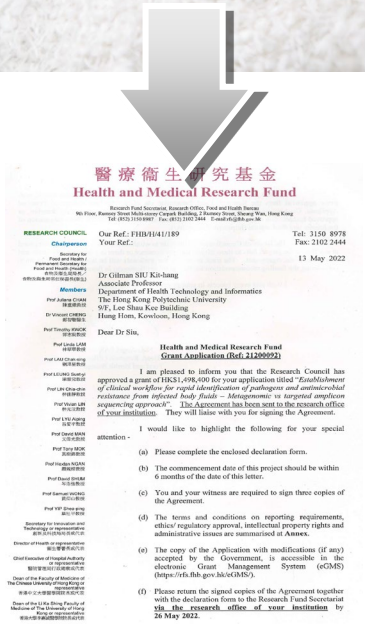
Step 4: Response to reviewers' comments

If your project is rated 3 or 4,

- You will have 3 week to address the comments and revise the proposal
- Point by point response to ALL comments from GRB and ALL reviewers
  (Just like how you respond to reviewers' comments in a point-by point manner during manuscript submission)
- Revise the proposal accordingly and indicate where and what you have amended in the response to reviewers' comments

Step 5: Increase Your Luck

2016



醫療衞生研究基金
Health and Medical Research Fund

Research Fund Secretariat, Research Office, Food and Health Bureau
9th Floor, Ruttonjee Street Multi-storey Carpark Building, 2 Ruttonjee Street, Sheung Wan, Hong Kong
Tel: (852) 3150 8987 Fax: (852) 2102 2444 E-mail:rfs@fhb.gov.hk

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Our Ref.: FHB/H/41/189
Your Ref.:
Tel: 3150 8978
Fax: 2102 2444
13 May 2022

Dr Gilman SIU Kit-lang
Associate Professor
Department of Health Technology and Informatics
The Hong Kong Polytechnic University
9/F, Lee Shau Kee Building
Hung Hom, Kowloon, Hong Kong

Dear Dr Siu,

Health and Medical Research Fund
Grant Application (Ref: 21200092)

I am pleased to inform you that the Research Council has approved a grant of HK$1,498,400 for your application titled *"Establishment of clinical workflow for rapid identification of pathogens and antimicrobial resistance from infected body fluids – Metagenomic vs targeted amplicon sequencing approach"*. The Agreement has been sent to the research office of your institution. They will liaise with you for signing the Agreement.

I would like to highlight the following for your special attention -

(a) Please complete the enclosed declaration form.

(b) The commencement date of this project should be within 6 months of the date of this letter.

(c) You and your witness are required to sign three copies of the Agreement.

(d) The terms and conditions on reporting requirements, ethics/ regulatory approval, intellectual property rights and administrative issues are summarised at **Annex**.

(e) The copy of the Application with modifications (if any) accepted by the Government, is accessible in the electronic Grant Management System (eGMS) (https://rfs.fhb.gov.hk/eGMS/).

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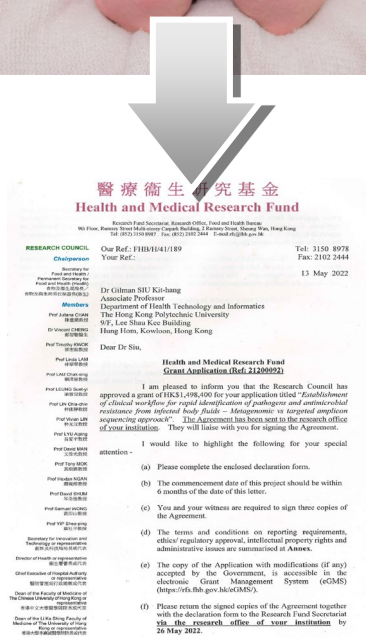
2018



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THANK YOU

Prof. SIU Kit Hang, Gilman

gilman.siu@polyu.edu.hk