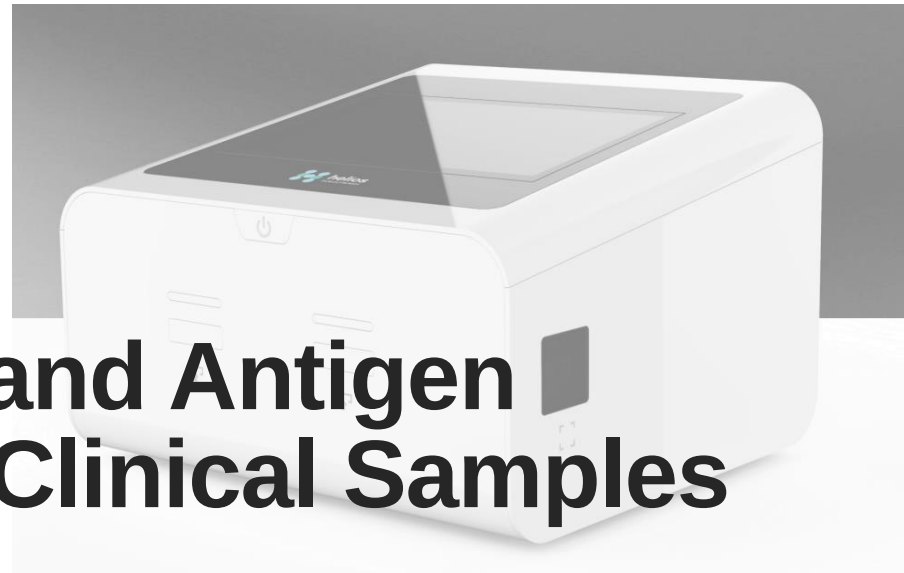
helios BIOELECTRONICS

2022國家級人體生物資料庫整合平台第二屆年會

國家衛生研究院人體生物資料庫
National Health Research Institutes Biobank



COVID-19 Serological Antibody and Antigen Assay by Immunopanel Sensor-Clinical Samples from NHRI BioBank

Ching-Wei Tsai (蔡經緯), PhD
Director of Biosensor Development, Helios Bioelectronics Inc. (瀚源生醫)

HBI Serves as a Global Hub

Bridging the gap between healthcare & electronic worlds by offering the **semiconductor biosensor solution** for biomedical applications.

Electrical Changes

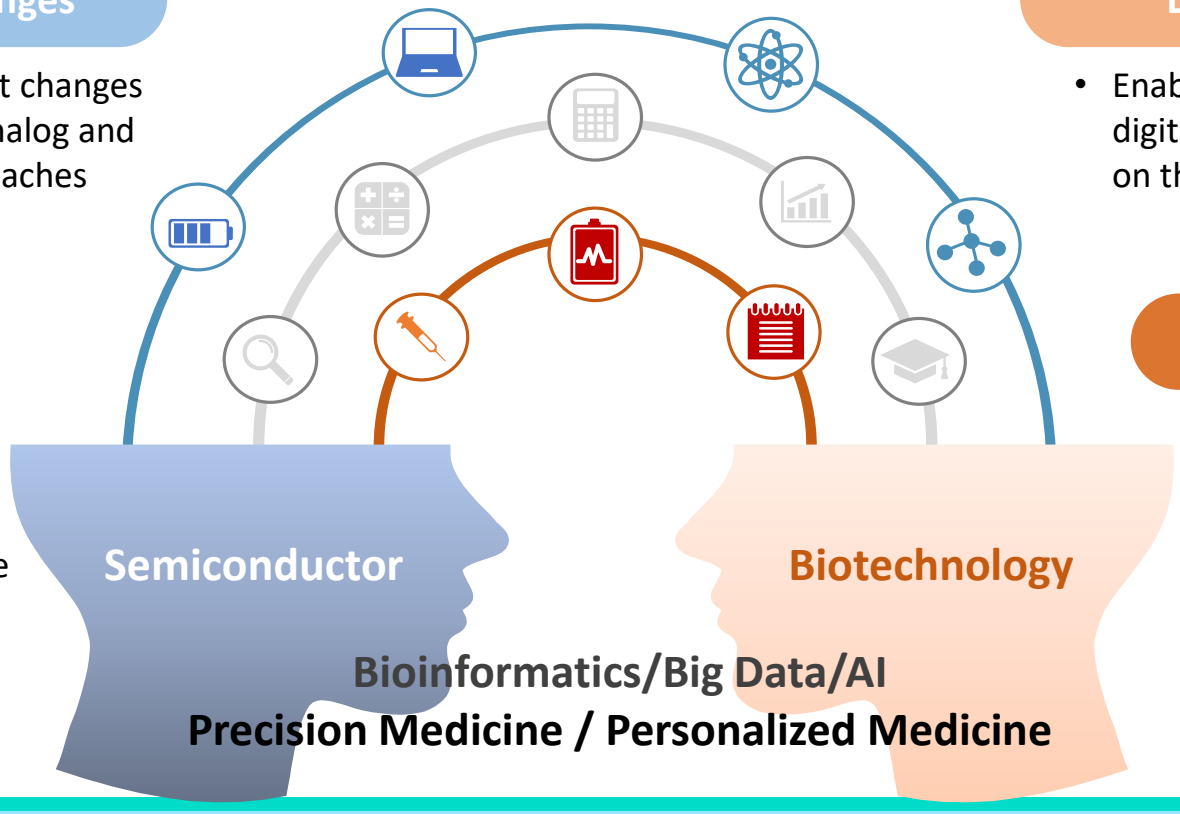
- Detecting the electrical current changes
- Different from conventional analog and optical based diagnostic approaches

Digital Data

- Enable the quantification and digitalization corresponding to charges on the biomarkers

Semiconductor Biochip

- Field-Effect Transistors (FETs)
- Fingertip-size fully integrated semiconductor biosensor
- Size and numbers of pixels are scalable
- Good surface-to-volume ratio

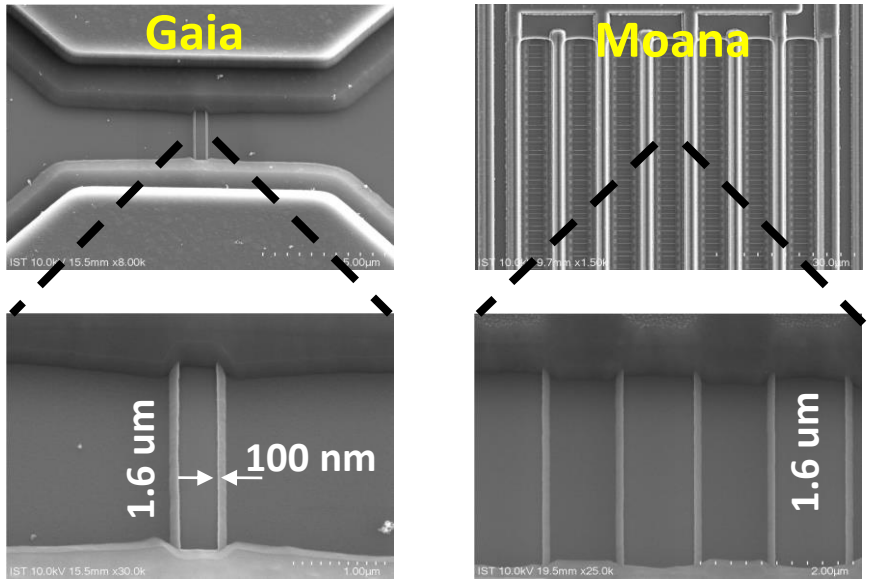


Biological/Clinical Application

- Concurrent detection of multiple biomarkers
- Hundreds of sensors per biomarker for statistical credence

HBI Owns Two Unique FET Biosensors

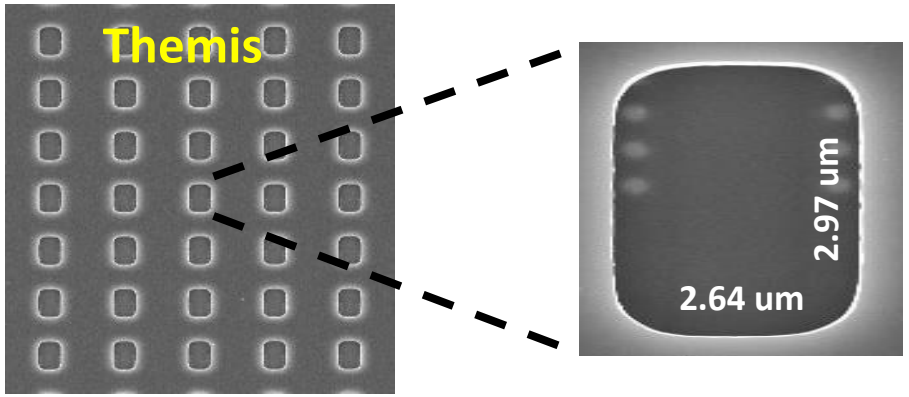
EPISIL



- Nanowire FET biosensor (tens of sensors)
- Ultra sensitive (fM)
- Lower cost, point of needs, on-site testing

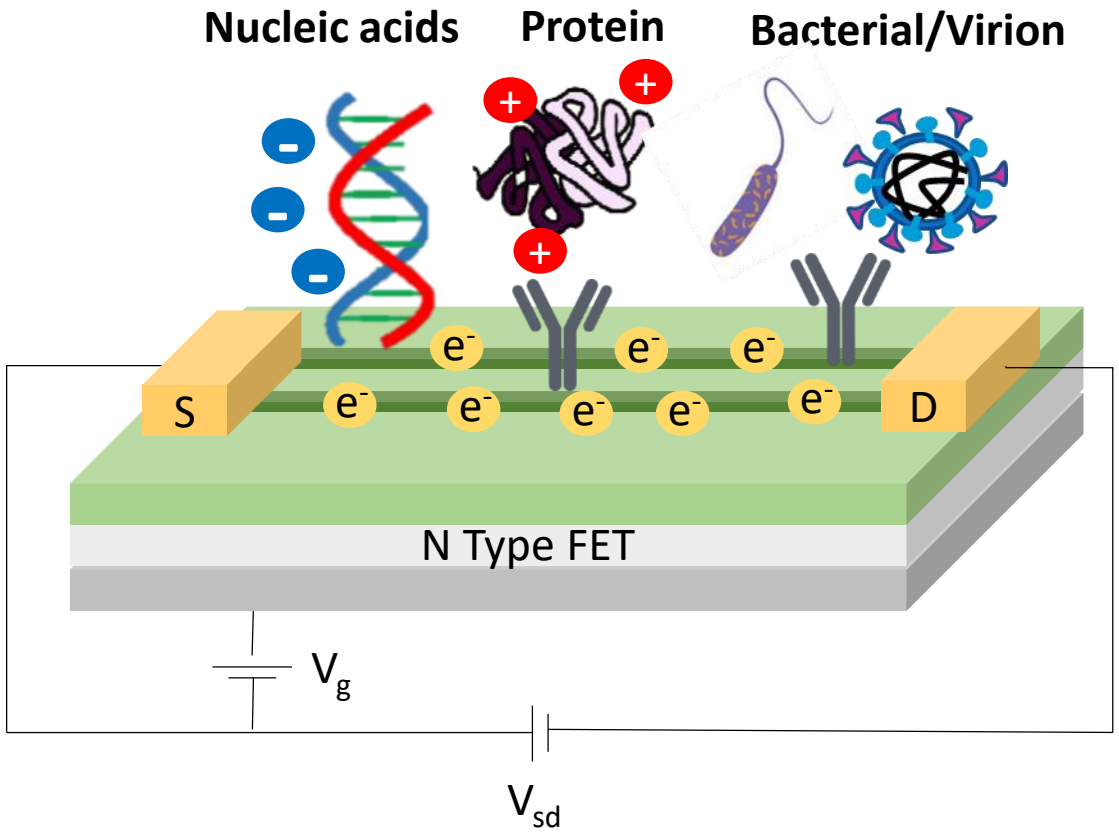
*Customized manufacturing processes for optimal results

tsmc



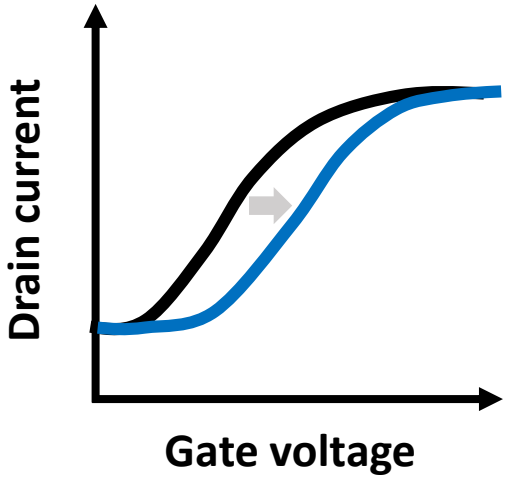
- Arrayed FET biosensor
- Highly integrated (16,384 sensors)
- Higher cost, upto mega-pixels, computing
- Multiplex detection

Detection Principle of FET Biosensor

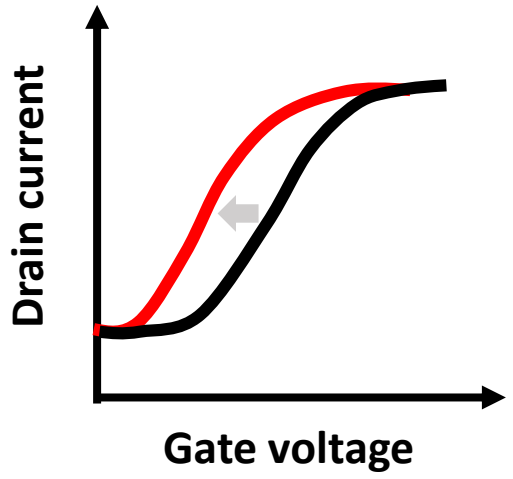


Vg: Gate Voltage
Vsd: Source-Drain Voltage

Negative charged Targets (i.e. nucleic acids)



Positively charged Targets (i.e. proteins)



Characteristics of BioFET

- Greater signal-to-noise ratio (highly sensitive)
- Fast measurement capabilities
- Compact or portable instrumentation

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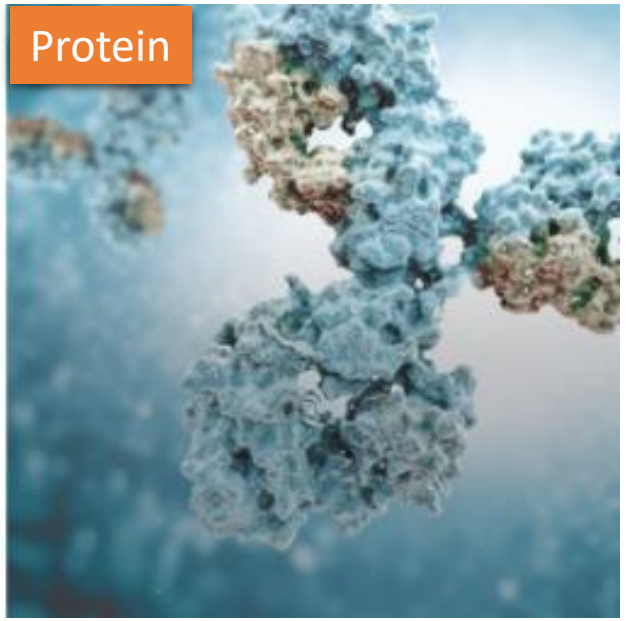
Performance Summary

Pathogens

- LOD: 5-10 CFU/Rxn
- TAT: 1-4 hr
- Qualitative
- Presence of bacteria, AST

Protein

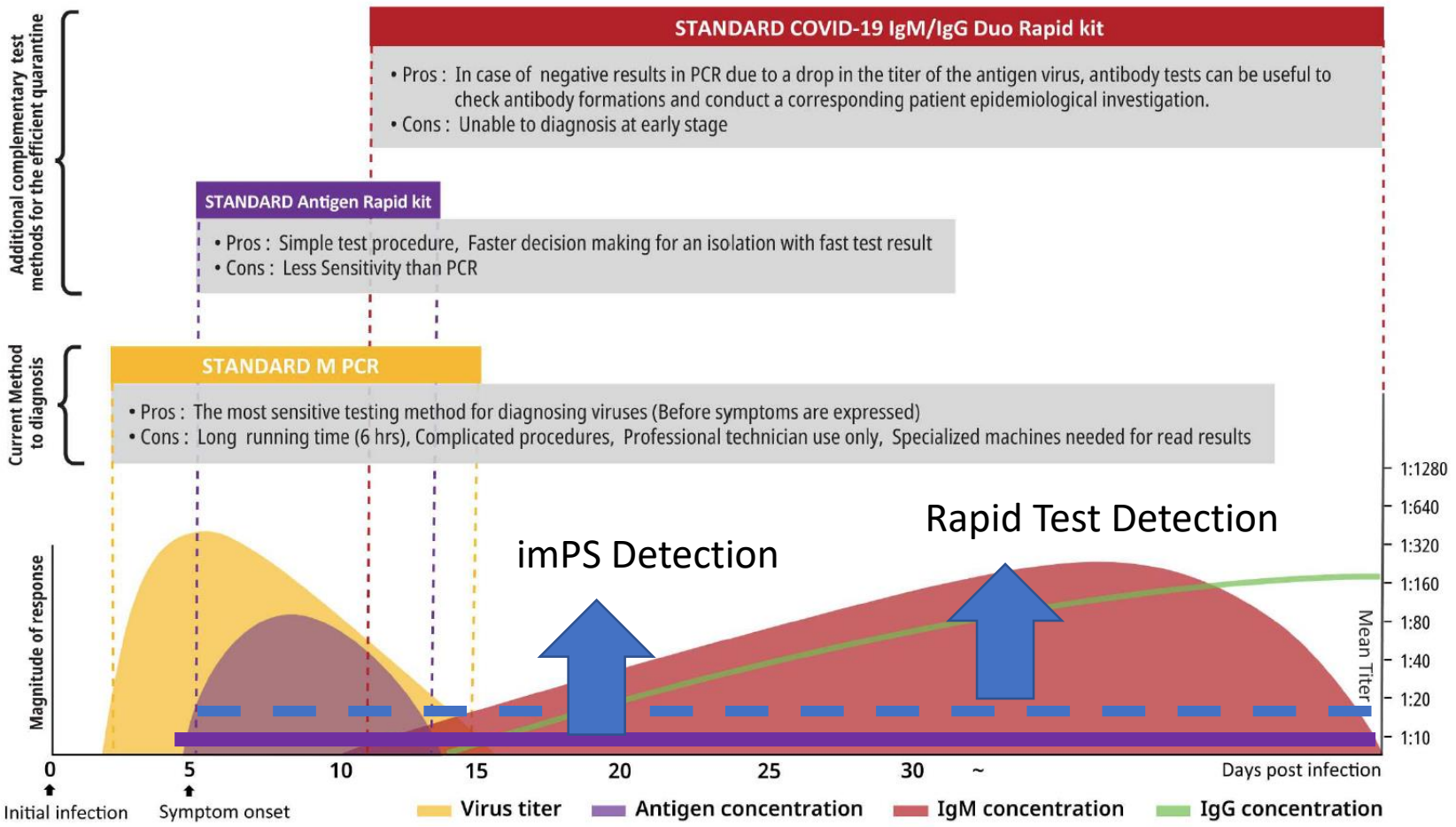


- LOD: 1-10 pg/ml
- TAT: 5-15 min
- Quantitative (10 -10^5 pg/mL)
- Cancer & Infectious diseases

Nucleic acids

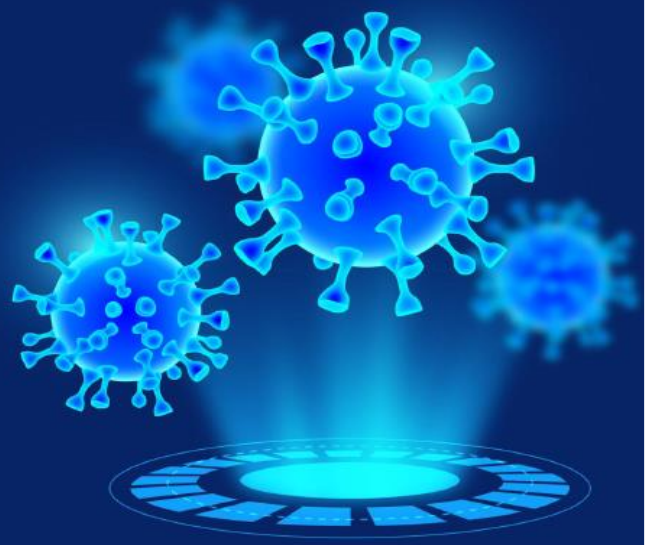
- LOD: 10-100 fM
- TAT: <40 min
- Quantitative (0.1 pM- 10^4 pM)
- Profiling, companion diagnosis

Whole Infection Spectrum of COVID-19 Diagnosis-ImmunoPanel Sensor (imPS)



SARS-CoV 2 Whole Infection Spectrum Blood Detection Technique by Arrayed bioFET

High Sensitivity to detect Ab& Ag



https://www.mdvip.com/about-mdvip/blog/igm-and-igg-antibody-tests-covid-19
https://eaglebio.com/wp-content/uploads/2020/07/SARS-CoV-2-whole-course-blood-detection-technology-%EF%BC%8820200812%EF%BC%89.pdf

Helios Platform for COVID-19 Assay

Chips Designed for your Desired Targets

Small chips, Big data

Helios offers an application driven and highly sensitive BioFET platform, enabling real-time monitoring of health status for precision medicine.

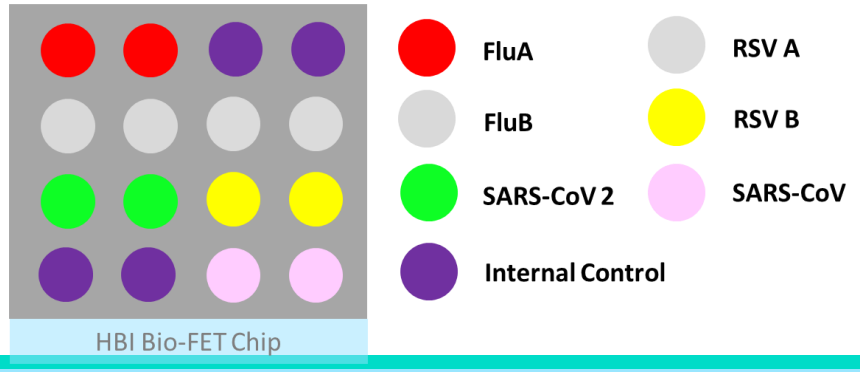
immunopanel assay (imPS)

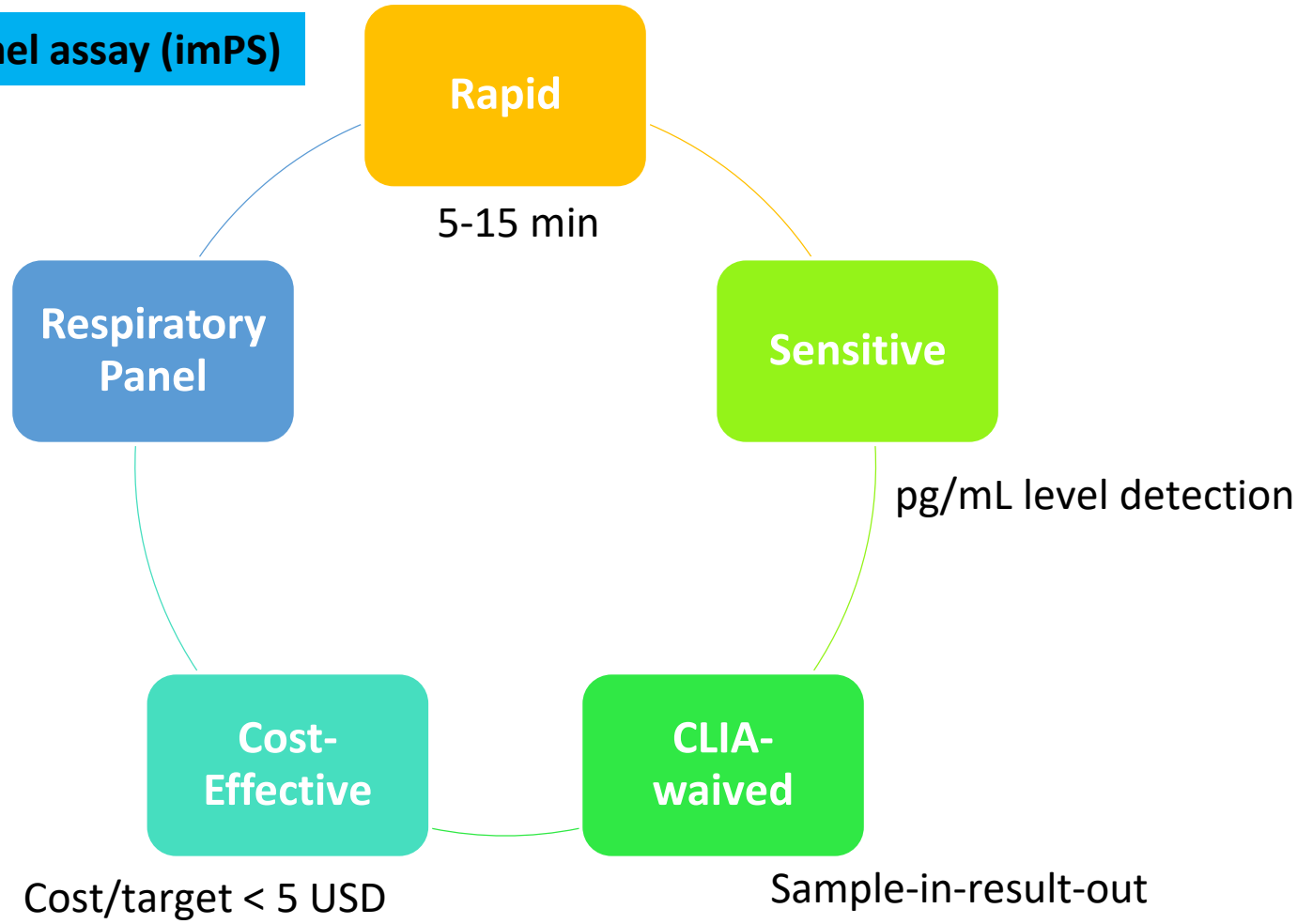
Viral Antigen assay

IgG/IgM assay

nAb assay

For Respiratory Panel Diagnosis

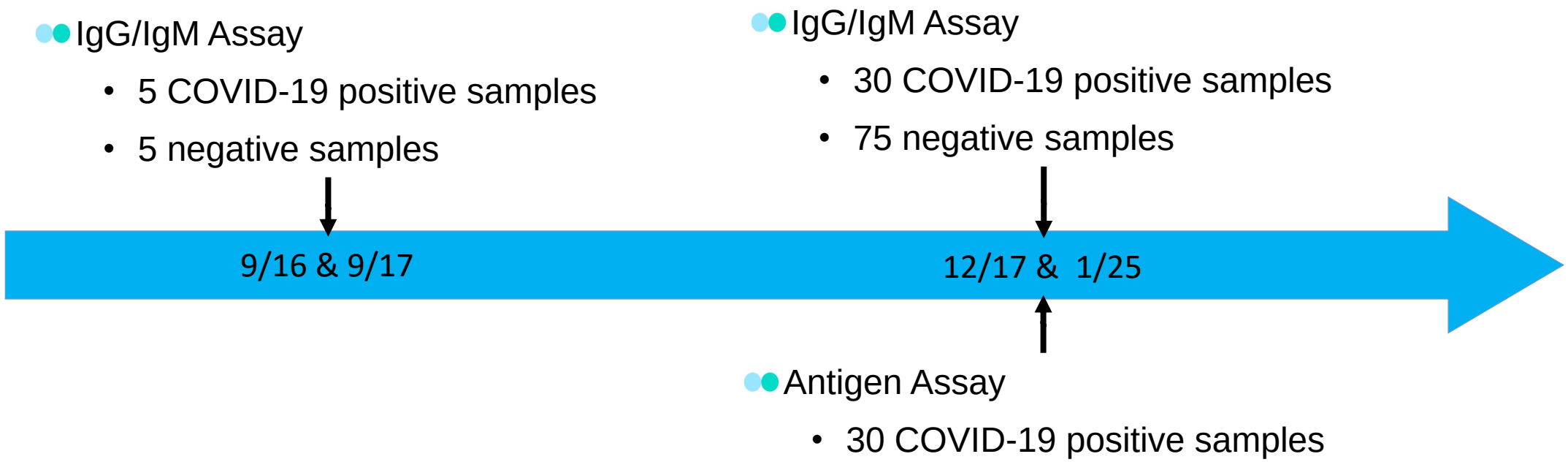




Intended use

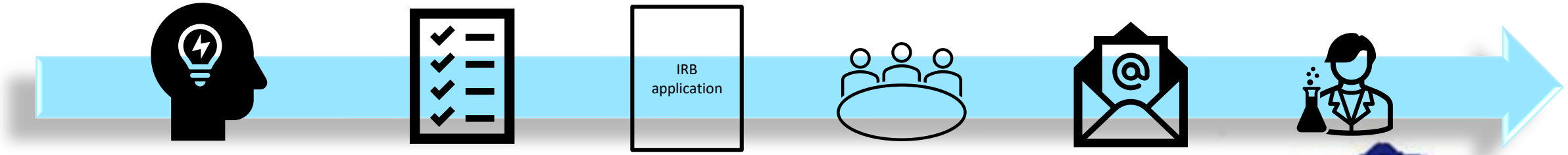
imPS COVID-19 Assay performed on the imPS Instrument is a rapid molecular ***in vitro*** diagnostic test utilizing the **immunoassay by semiconductor-based biosensor technology** intended for the **qualitative** detection of specific **COVID-19 antigen and antibody** in the **serum or blood** from individuals who are suspected of COVID-19 by their healthcare provider after onset of symptoms. Results should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

Clinical Investigation Using BioBank Serum Retrospective Sample



Sample types:
Before 2019 FluA/B infection
COVID-19: Different days after onset

NHRI Biobank Application Process



Step 1
Submit proposal to the office of NHRI Biobank
1. Application form
2. Biosample request list

Step 2
1. Administration check up
2. Scientific review

Step 3
Inform the applicant the submit
1. IRB approval form or proof of IRB application
2. Business registration certificate

Step 4
Review by the EGC committee (one month)

Step 5
Inform the applicant of the decision
1. Approved
2. Need revision
3. Do not agree

Step 6
The applicant needs to submit
1. IRB approval
2. Sign the agreement form

Biobank starts to prepare the samples for the applicant

- ✓ **Consultant**
- ✓ **Biosample integrator**
- ✓ **Biosample supplier**

Clinical Investigation Document

正本

檔　號：
保存年限：

財團法人國家衛生研究院醫學研究倫理委員會
函

受文者：翰源生醫股份有限公司

發文日期：中華民國109年9月7日
發文字號：衛研倫字第1090008711號
速別：普通件
密等及解密條件或保密期限：
附件：

主旨：檢送貴公司林明瑜技術整晶片檢測COVID-19 血清號EC1090803-F-E）」之

說明：

一、本案經簡易審查通過，核議核備。若會議中之決

二、隨函附上「計畫主持人注理計畫後續事宜。

三、本計畫核准執行期程為2021年12月6日前繳交結展延「人體研究計畫同意2021年6月7日前繳交期中

正本：翰源生醫股份有限公司 林明瑜技術
副本：翰源生醫股份有限公司、本院人體

正本

檔　號：
保存年限：

財團法人國家衛生研究院醫學研究倫理委員會
書函

地址：35053 苗栗縣竹南鎮科研路35號
聯絡人：戴淑芬
電話：(037)206-166　分機：38602
傳真：(037)583-109
電子信箱：NIRB@nhri.edu.tw

受文者：瀚源生醫股份有限公司 蔡經緯生化感測開發總監

發文日期：中華民國109年12月2日
發文字號：衛研倫字第1090011695號
速別：普通件
密等及解密條件或保密期限：
附件：

主旨：檢送貴公司蔡經緯生化感測開發總監主持之「以半導體生物感測晶片檢測COVID-19 血清檢體中蛋白質可行性評估」變更研究計畫案（本會編號EC1090803-F-E-R1）之本會研究計畫變更許可書乙份。

說明：

一、此變更案經本會審查通過，同意核發許可書，並提醒計畫主持人須提供本院人體生物資料庫同意出庫之相關文件至本會備查。

二、本會同意內容如下：
(一)研究計畫申請表（版本日期：Version 2, 2020/11/3）
(二)計畫書（版本日期：Version 2,2020/11/2）

三、本計畫核准執行期程為2020/12/2~2021/9/6。另本項計畫請2021年12月6日前繳交結案報告，以利本會進行審查。如欲展延「人體研究計畫同意函」之有效期限，計畫主持人需在2021年6月7日前繳交期中報告以延長同意函之有效期限。

正本：瀚源生醫股份有限公司 蔡經緯生化感測開發總監
副本：瀚源生醫股份有限公司、本院人體生物資料庫、本院醫學研究倫理委員會

台灣新型嚴重性肺炎研究網
Taiwan Severe Pneumonia Network

Dear Doctor Lin,

We are pleased to inform you that your application (TSPN No.20-012) for biosamples: Serum of 5 COVID-19 positive patients, 5 COVID-19 negative patients and related clinical information from TSPN has been approved by the Scientific Review Committee. Since TSPN is now belonged to the NHRI Biobank, all applications need to be approved by the Ethic and Governance Committee of NHRI Biobank, too. Please provide the following documents to our office for further processing:

1. The Institutional Reviewing Board (IRB) approval form or the proof of IRB application to conduct the project (pdf file).
2. The approval form of the funding agency to sponsored the project (pdf file).

After we receive the above documents, your application will be reviewed and discussed in the regular meeting of the Ethic and Governance Committee to get the final approval.

Please be noted that, though the biosample itself is free, we do charge "processing fee" to cover the expense for specimen preparation. If you have any concern or question, please feel free to contact us.

Taiwan Severe Pneumonia
Network Office

台灣新型嚴重性肺炎研究網
2020.08.11
Taiwan Severe Pneumonia Network

國家衛生研究院 苗栗縣竹南鎮科研路 35 號 國家衛生研究院行政大樓 A-3120 室
National Health Research Institutes, 35, Keyan Road, Zhunan Town, Miaoli County, Taiwan 350
Telephone: 886-37-206166 ext 33327, Fax: 886-37-583109

正本

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傳真：(037)580-784
電子信箱：fckuo@nhri.edu.tw

30261
新竹縣竹北市生醫路2段2號3樓R307
受文者：翰源生醫股份有限公司

發文日期：中華民國109年9月26日
發文字號：衛研學字第1090009036號
速別：普通件
密等及解密條件或保密期限：
附件：詳如說明三

主旨：為辦理貴我雙方「人體生物資料庫商業運用利益回饋契約書」簽約事宜，詳如說明段，請查照。

說明：

一、貴司林明瑜博士因研究需求向本院人體生物資料庫提出檢體申請案。

二、經本院人體生物資料庫倫理委員會討論，鑑於上開申請案之經費來源為產業界，故視為已有商業運用利益，需依本院人體生物資料庫「商業運用利益回饋作業須知」，向貴司收取商業運用利益回饋金。

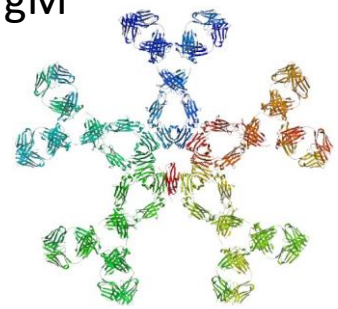
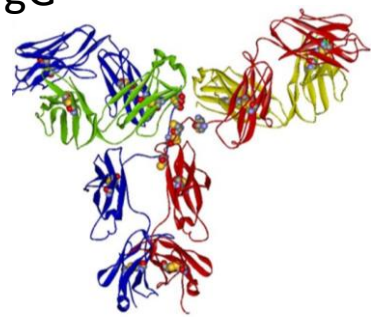
三、爰上，本院與貴司共同簽署商業運用利益回饋契約書，以保障雙方權利義務。檢附本院鈐印之「人體生物資料庫商業運用利益回饋契約書」1份。

四、本案聯絡人：本院人體生物資料庫蘇美枝女士，聯絡電話：(037)206-166分機33332。

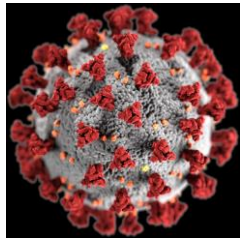
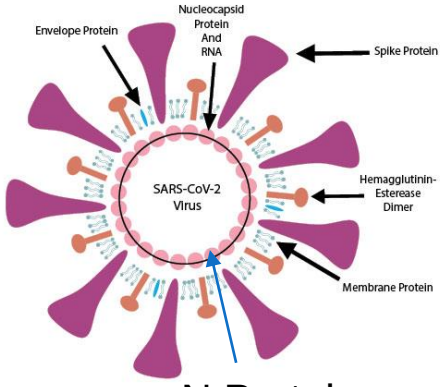
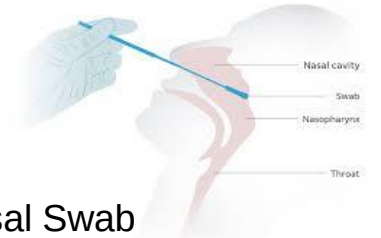
正本：瀚源生醫股份有限公司
副本：本院人體生物資料庫

院長 梁慶義

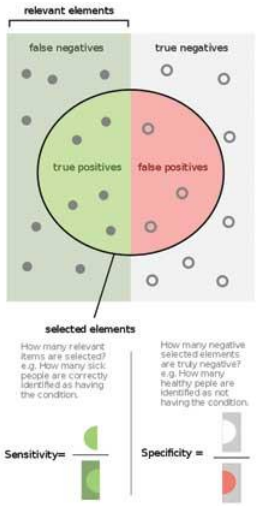
imPS COVID-19 IgG/IgM Assay

Target	Sample	Detection	Diagnosis
IgM  IgG 	Finger-Pricked Whole Blood  **Serum**/blood Saliva	  5-15 min	**Negative** / **IgG/IgM**: Signal* / -; Control / + **Positive** / **IgG/IgM**: Signal* / +; Control / + *Signal > Cutoff: + Singla < Cutoff: -

imPS COVID-19 Antigen Assay

Target	Sample	Detection	Diagnosis
  N Protein	Finger-Pricked Whole Blood **Serum**/blood/Saliva   Nasal Swab Nasopharyngeal swab	  5-15 min	**Negative** / **N protein** Signal* / - Control / + **Positive** / **N protein** Signal* / + Control / + *Signal > Cutoff: + Singla < Cutoff: -

Study Design of Clinical Investigation



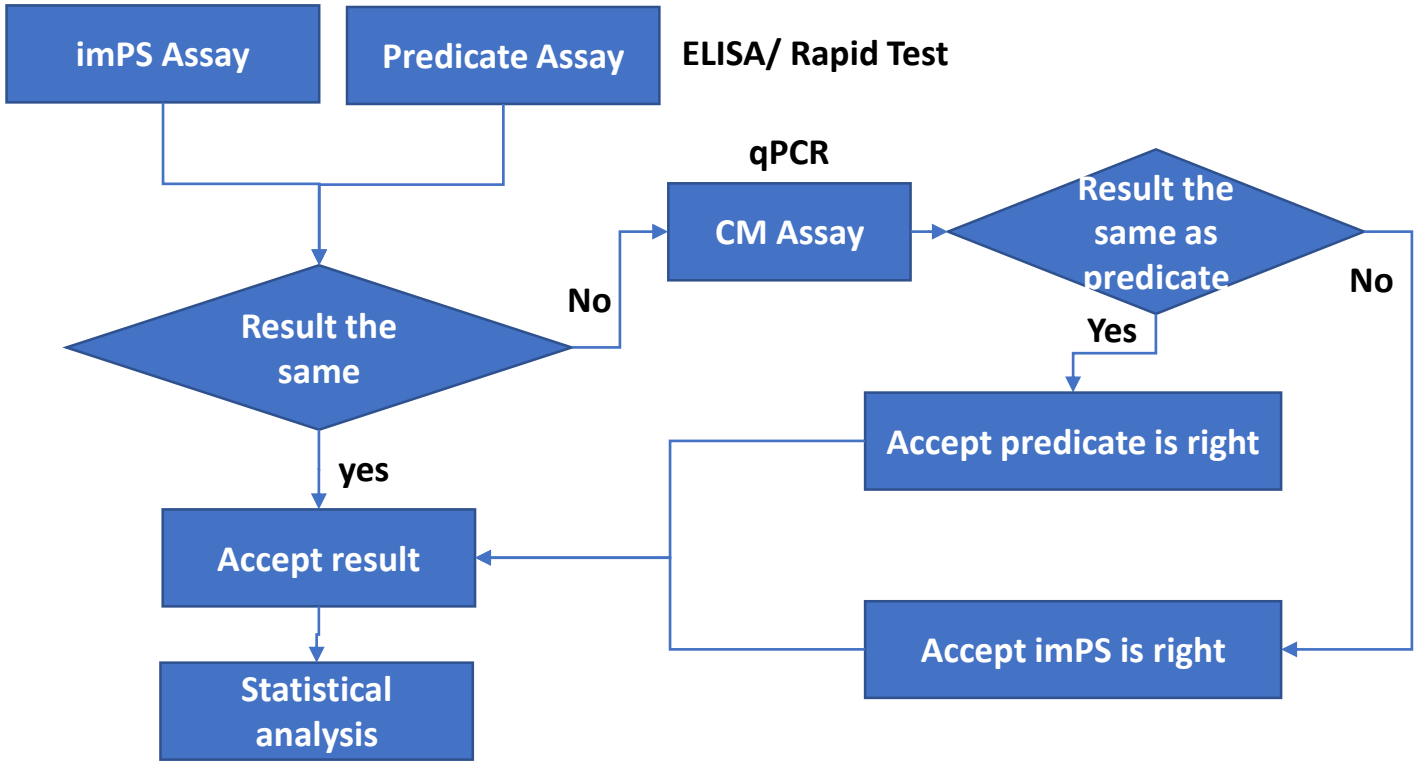
Sensitivity and Specificity

$$Sensitivity = \frac{Number\ of\ true\ positives}{(Number\ of\ true\ positives\ +\ Number\ of\ false\ negatives)}$$

$$= \frac{Number\ of\ true\ positives}{Total\ number\ of\ individuals\ with\ the\ illness}$$

$$Specificity = \frac{Number\ of\ true\ negatives}{(Number\ of\ true\ negatives\ +\ number\ of\ false\ positives)}$$

$$= \frac{Number\ of\ true\ negatives}{Total\ number\ of\ individuals\ without\ the\ illness}$$

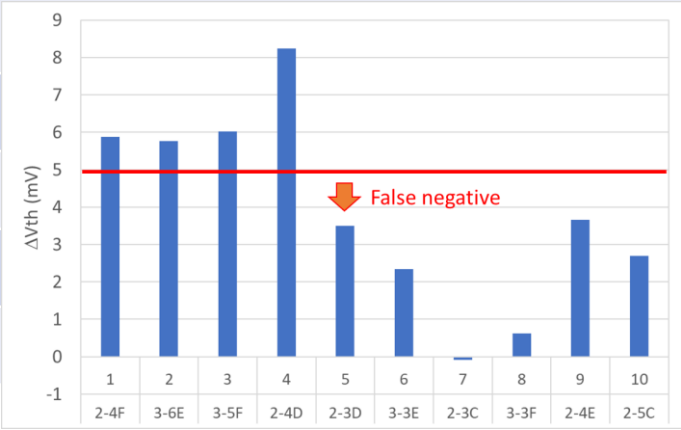


$$Accuracy = \frac{True\ positive + true\ negative}{Total\ Assay}$$

imPS Serological IgG/IgM Assay by 5 COVID-19 Positive & 5 Negative Samples

Sample ID	Biobank (qPCR)	Rapid Test Result	imPS	Day after onset
1	+	+	+	3
2	+	-	+	7
3	+	+	+	6
4	+	+	+	12
5	+	-	- (false negative)	1 (Low possibility to have antibody)
6	-	-	-	
7	-	-	-	
8	-	-	-	
9	-	-	-	
10	-	-	-	

imPS for COVID-19 IgG/IgM
Sensitivity=80%
Specificity=100%
Accuracy = 90%



Positive Sample Dilution Test by imPS

Rapid Test

Dilution	#4 (IgG/IgM)
10X	+ (IgG/IgM)
100X	+ (IgG/IgM)
1000X	+ (IgG)
10000X	-
100000X	-

Dilution	imPS
10X	+
10000X	+
100000X	+

imPS assay is more sensitive than rapid test by two orders of magnitude.

Summary

- imPS has higher clinical sensitivity than lateral flow (EUA approved).
- Detection sensitivity of imPS is at least two orders of magnitude higher than lateral flow

Clinical Performance of imPS IgG/IgM Assay (105 Samples)

Antibody Assay

COVID-19 Positive Patients		imPS		Total
		Positive	Negative	
ELISA	Positive*	24	1	25
	Negative*	4	76	80
*CM by qPCR				

Sensitivity: 96 %
Specificity: 95 %
Accuracy= 95.2 %

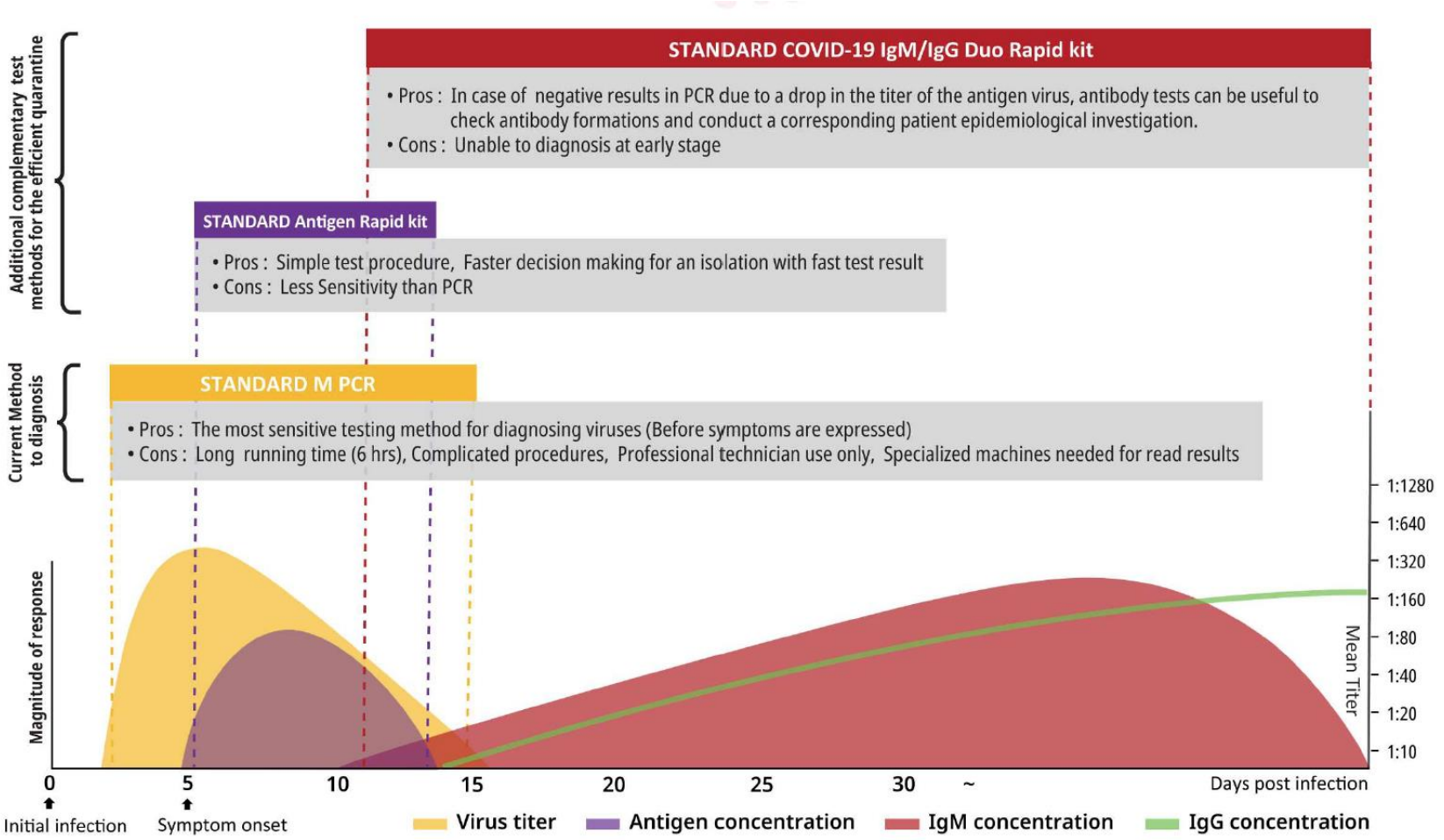
Clinical Performance of imPS Antigen Assay (30 Samples)

Antigen Assay

		imPS		Total
		Positive	Negative	
ELISA	Positive*	14	1 (No.9)	15
	Negative	0	15	15
*CM by qPCR, patient 4 should be negative				

Sensitivity: 93.3 %
Specificity: 100 %
Accuracy: 96.7 %

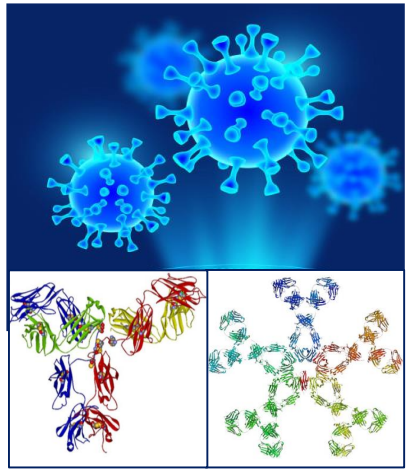
Whole Spectrum of COVID-19 Diagnosis



https://www.mdvip.com/about-mdvip/blog/igm-and-igg-antibody-tests-covid-19

Characteristics of HBI Platform

SARS-CoV 2 Whole Infection Spectrum Blood Detection

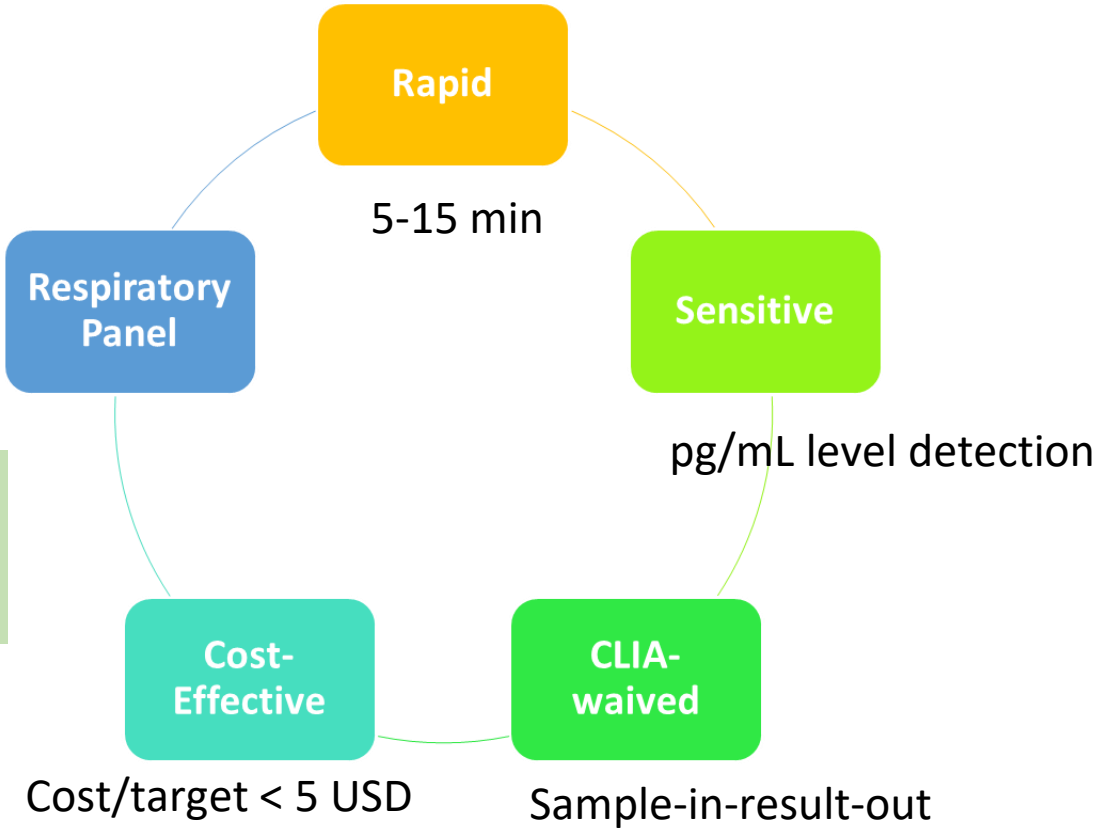


Antigen Assay

Sensitivity: 93.3 %
Specificity: 100 %
Accuracy: 96.7 %

Antibody Assay

Sensitivity: 96 %
Specificity: 95 %
Accuracy= 95.2 %

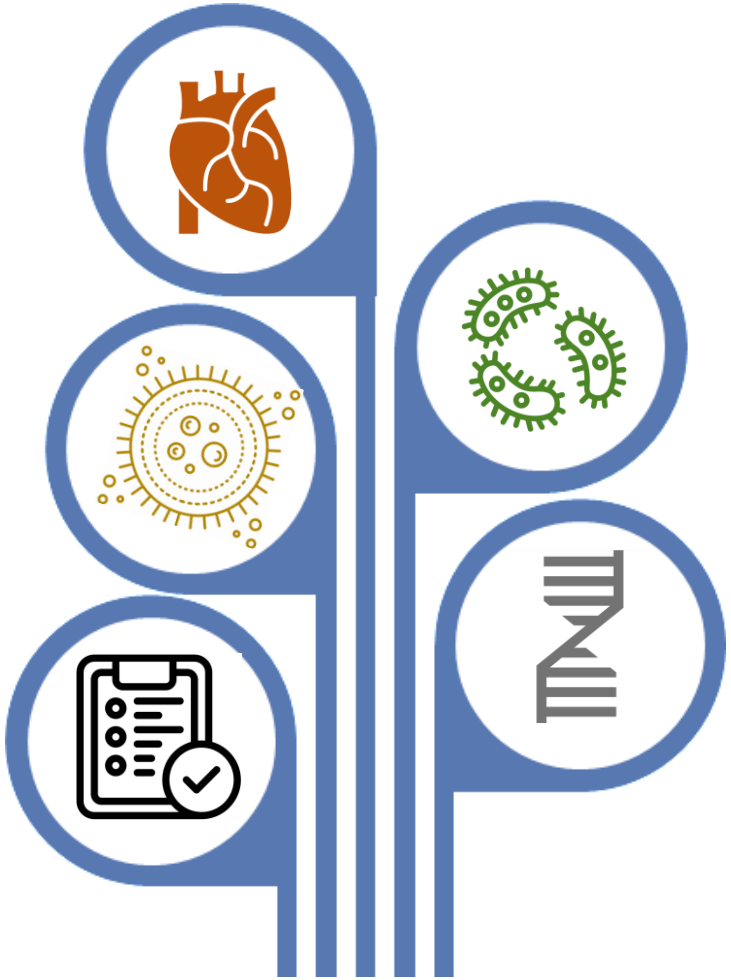


Clinical and Non-Clinical Applications

Cardiovascular Biomarker:
Troponin I Assay:
- Dynamic monitoring
- High sensitivity
- POCT

Sepsis: Cytokine Panel
- Cytokine: Protein
- Multiplexing
- POCT

Wafer Manufacturing Material QC:
- Advanced semiconductor process
- Detection of the ultra-low concentration of metal ions
- Quality control (QC)

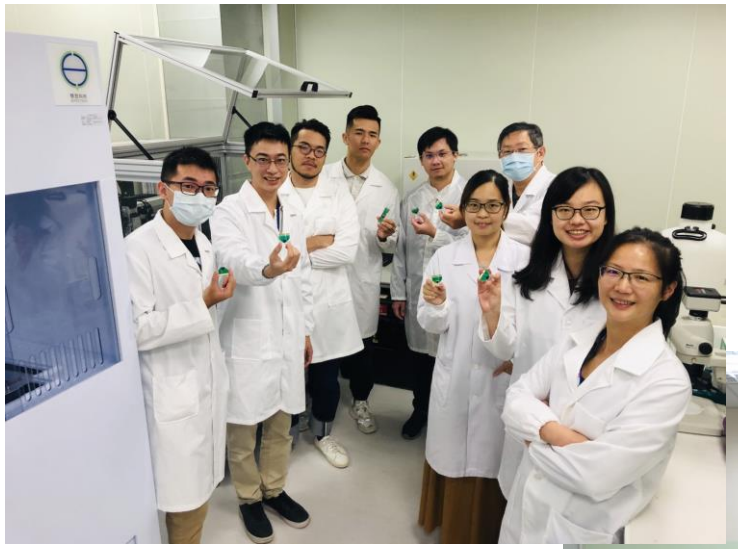


Infectious Disease and Microbiomes:
- Sepsis assay
- Antibiotic susceptibility testing (AST)
- Minimum inhibitory concentration (MIC)
- Phage therapy

Prostate Cancer miRNA Panel:
Diagnosis and Precision Medicine
- miRNA profiling
- Companion diagnosis
- Big data/AI

Acknowledgment

- HBI Team
- 國衛院人體生物資料庫
  - 黃秀芬 執行長
  - 鄭朝元
  - 蘇美枝
- 國衛院
  - 陳信偉 副所長 團隊
- 台積電團隊



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Innovation for a healthier future

Thank you