癌症分子檢驗與治療之健保給付面面觀 論壇

健保給付與癌症分子檢驗之科技發展

俞松良 Sung-Liang Yu

Nat Taiwan University, Medicine College

Mar. 25, 2019

生醫產業推動方案 (科技會報)

► 行動方案 D. 推動特色重點產業

- ► 發展利基精準醫學
- ► 發展國際級特色醫療
- ► 推動健康福祉產業

連結國際

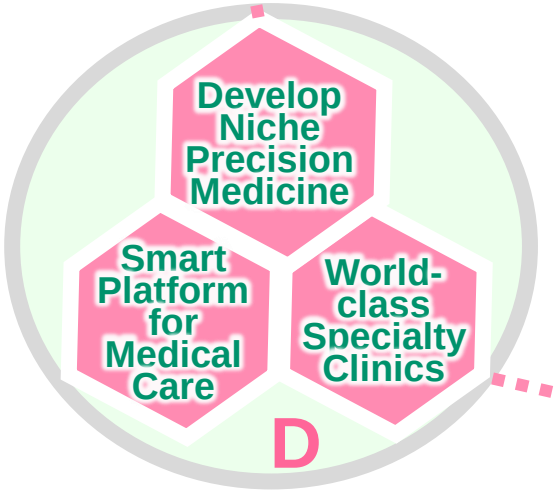
- 新穎技術平台
- 國人重大癌症蛋白基因體資料庫

- 精準醫療之依據 – 早期癌症、新藥臨床測試、先導藥物之標靶生物標記

- 檢測或癌症標靶可橋接生技製藥產業
- 提升台灣的生技產業能見度與研發能量
- 節省台灣單獨出資的成本，提高投資效益

Biomedical Industrial Innovation Program

CANCER MOONSHOT



Pass in Oct. 2016, Execute Yuan

- **A** Enhance Domestic Integrate Ecosystems
- **B** Innovative Business
- **C** Link global Market Resources
- **D** Promote Specialized Key Industries

Aim 1. Establishment of proteogenomics database
Aim 2. Development of proteogenomics analysis pipeline
Aim 3. Development of comprehensive bioinformatics
Aim 4. Identifying new drugs & IVD against early recurrence, drug resistance, metastasis

衛生福利部 Ministry of Health and Welfare 促進全民健康與福祉

科技部

行政院科技會報 BOST Board of Science and Technology

NGS Panel Survey – U.S. / E.U. / JP.

Panel test	No. of targeted genes	Enrichment approach	Liquid biopsy	TMB / MSI identification	FDA approval	Turnaround time (from receipt sample to result)	Cost
Oncomine Dx Target Test	23 genes	Amplicon	–	– / –	Yes	5 days	–
MSK-IMPACT	468 genes	Capture	–	Yes / Yes	Yes	< 21 days	–
FoundationOne CDx	324 genes	Capture	–	Yes / Yes	Yes	14 days	USD 5,800
FoundationOne Liquid	70 genes	Capture	Yes	– / Yes	–	14 days	USD 5,001
FoundationFocus CDxBRCA	2 genes	Capture	Yes	– / –	Yes	14 days	USD 5,002
Guardant 360	73 genes	Capture	Yes	Yes / Yes	–	7 days	USD 3,500
Caris Molecular Intelligence	>600 genes	Capture	–	Yes / Yes	–	14 days	USD 6,500
OncoDEEP	75 genes	Amplicon	–	Yes / Yes	–	7 days	USD 3,500
Todai OncoPanel	464 genes	Capture	–	Yes / Yes	–	–	915,000 円
PCDx	186 genes	Amplicon	–	– / Yes	–	5 days	USD 4,800

NGS Panel Survey - Taiwan

Panel test	No. of targeted genes	Enrichment approach	TMB / MSI identification	Clinical accredidation	Provider	Turnaround time (from receipt sample to result)	Cost
Oncomine Focus Test	52 genes	Amplicon	– / –	TAF-15189	NTUH	7 days	NTD 60,000
AVENIO Target panel	17 genes	Capture	– / –			14 days	–
AVENIO Expanded panel	77 genes	Capture	– / –	–	SOFIVA genimics	14 days	–
AVENIO Survelliance panel	197 genes	Capture	Yes / –			14 days	–
ACTOnco	440 genes	Capture	Yes / Yes	CAP	ACT genomics	14 days	NTD 60,000

ISO 15189 Certificated Ref Lab

TAF

Certificate No. : L2695-160531

財團法人全國認證基金會
Taiwan Accreditation Foundation

Certificate of Accreditation

This is to certify that

National Taiwan University Hospital
Pharmacogenomics Laboratory
8F., No17, Xu-Zhou Rd., Zhongzheng Dist., Taipei City 100, Taiwan

is accredited in respect of laboratory

Accreditation Criteria	:	ISO 15189: 2012
Accreditation Number	:	2695
Originally Accredited	:	April 08, 2013
Effective Period	:	May 31, 2016 to May 30, 2019
Accredited Scope	:	Medical Testing Field, see described in the Appendix

Jay-San Chen
President, Taiwan Accreditation Foundation
Date : May 31, 2016

P1, total 3 pages

The Appendix forms an integral part of this Certificate, which shall be invalid when use without the Appendix

TAF

Certificate No. : L2695-160531

財團法人全國認證基金會
Taiwan Accreditation Foundation

Accreditation Number : 2695
Laboratory Head : YU, Sung-Liang

HJ0199 BRAF Gene examination
Frozen tissue, Paraffin block sections, Pleural effusion, DNA, Lung lavage fluid
Standard inspection procedure for EGFR, KRAS, BRAF and HER2 gene testing in DNA MASS(TCL-SP-MS-001)

HJ0199 EGFR Gene examination
Frozen tissue, Paraffin block sections, Pleural effusion, DNA, Lung lavage fluid
Standard inspection procedure for EGFR, KRAS, BRAF and HER2 gene testing in DNA MASS(TCL-SP-MS-001)

HJ0199 HER2 Gene examination
Frozen tissue, Paraffin block sections, Pleural effusion, DNA, Lung lavage fluid
Standard inspection procedure for EGFR, KRAS, BRAF and HER2 gene testing in DNA MASS(TCL-SP-MS-001)

HJ0199 KRAS Gene examination
Frozen tissue, Paraffin block sections, Pleural effusion, DNA, Lung lavage fluid
Standard inspection procedure for EGFR, KRAS, BRAF and HER2 gene testing in DNA MASS(TCL-SP-MS-001)

HJ0199 NGS-based cancer-associated gene panel assay
Frozen tissue, Paraffin block sections, DNA/RNA, Whole blood
Standard inspection procedure for cancer-associated gene testing in next generation sequencer (TCL-SP-SE-003)
(NGS-based cancer-associated gene panel assay including: ABL1, AKT1, AKT3, ALK, AR, AXL, BRAF, CCND1, CDK4, CDK6, CTNNB1, DDR2, EGFR, ERBB2, ERBB3, ERBB4, ERG, ETV1, ETV4, ETV5, ESR1, FGFR1, FGFR2, FGFR3, FGFR4, GNA11, GNAQ, HRAS, IDH1, IDH2, JAK1, JAK2, JAK3, KIT, KRAS, MAP2K1, MAP2K2, MET, MTOR, MYC, MYCN, NRAS, NTRK1, NTRK2, NTRK3, PDGFRA, PIK3CA, PPARG, RAF1, RET, ROS1, SMO, BRCA1, BRCA2)

P2, total 3 pages

The Appendix forms an integral part of this Certificate, which shall be invalid when use without the Appendix

TAF

Certificate No. : L2695-160531

財團法人全國認證基金會
Taiwan Accreditation Foundation

HJ0199 Cancer Related Single Nucleotied Polymorphism Examination
Frozen tissue, Paraffin block sections, Pleural effusion, DNA, Lung lavage fluid, PBMC gDNA
Standard inspection procedure for cancer related SNPs identification by DNA Mass (TCL-SP-MS-006)
(Cancer Related Single Nucleotied Polymorphism Examination including: rs7086803, rs4488809, rs2395185, rs2736100, rs28366298, rs7216064, rs9387478, YAP1)

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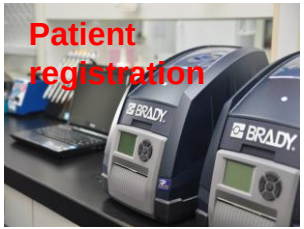
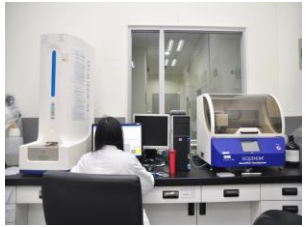
P3, total 3 pages

The Appendix forms an integral part of this Certificate, which shall be invalid when use without the Appendix





Summary of Acdemic & Industrial Cooperation

Routine Gene Test

a. EGFR acMut: AZ, Roche, BI
b. EGFR cfDNA: AZ
c. ALK fusion: Pfizer
d. PD-L1: MDS, Ono/Roche Diag
e. B-Raf: Novartis
f. BRCA: AZ

R&D Gene Test

a. Tumor mutation burden in lung ca & NHSCC: Roche Diag
b. BRCA large indel & CNV: AZ
c. cMet: PAREXEL International (Phase II)
d. iSeq100 beta-site Test and Cancer Panel development: Illumina, Power Chip
e. cfDNA T790M IVD: CBS
f. Mass mut Detection: Pharmigen
g. Tg lung cancer mouse model: immune modulator OBI Pharma

International Cooperation

a. Proteogenomics: Cancer Moonshot/NCI & 11 members
b. Protein Chip: ASU
c. Cancer Panel: Illumina & a US Biotech/Power Chip
d. Liquid Biopsy TMB: Roche Diag/ one of 8 labs worldwide
e. PD-L1: International RING study/ 7 countries
f. Single Cell Analysis: UCSD & Nanocellect Biomedical Inc.
g. Tg CLIA/ISO15189 Protein Mass Spec: US NCI

申請區

一、醫

二、黏
鐵

三、醫

四、切

五、國

六、臨
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八、學

九、臨

十、發

Analytical sens

Roche Cobas v2 | Cell line
dilution 8

Analyt

Roche Cobas

Roche Cobas

Interfer

Roche Cobas

Interfe

Roche Cobas

Roche Cobas

Roche Cobas

血漿樣品儲存溫度	≤ -70°C	2~8°C
保存時間	可達12個月	可達3天

Parallel comparison

Roche Cobas v2 | 74 NSCLC patients, compared to MiSeq. Presented by PPA, NPA,

	一致性百分比 (n)	95% CI
PPA)	80.0% (28/35)	70.3-83.7%

alidation

羅氏EGFR基因突變測試到的病人,所觀察到
未效益跟EURTAC population的比較。

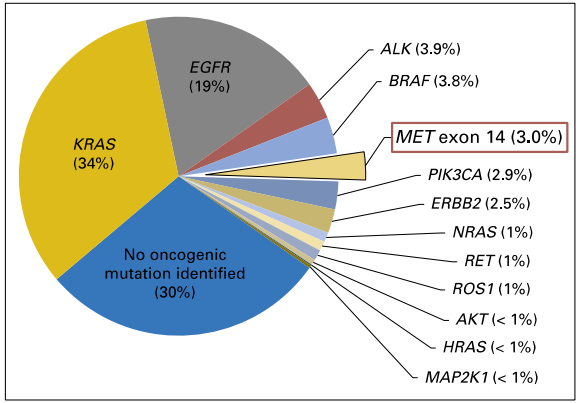
Parameter	cobas®-positive Population n = 116		EURTAC n = 173*	
	Chemotherapy	Erlotinib	Chemotherapy	Erlotinib

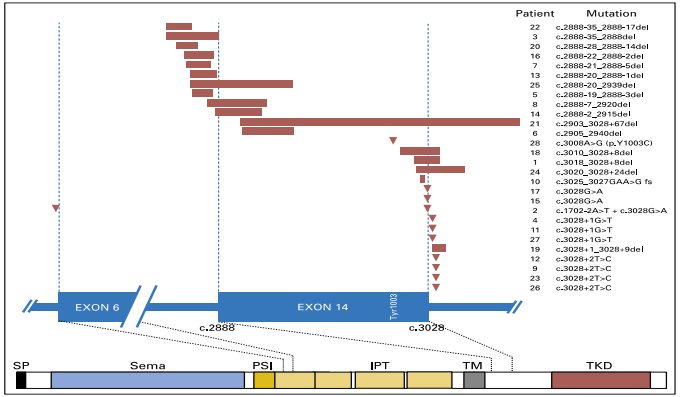
Batch Production

three batches

oduct (first in class)

Development of ddPCR-based c-MET Assay for Amplification & Exon 14 Skipping





Distribution of genotypes among 933 patients with nonsquamous non–small-cell lung cancer (NSCLC).

Table 3. Response of Patients with NSCLC with *METex14* to a MET TKI (Crizotinib)

Patient Case	Histologic Subtype	*METex14* Alteration	*MET* Amp	*MDM2* Amp	*CDK4* Amp	Biopsy Timing	Response to Crizotinib[a]
1	AdenoCA	3028+1_3028+1delG	Yes	No	Yes	After crizotinib	PR, 24 mo
2	AdenoCA	D1010Y	No	No	No	Before crizotinib	PR, 7 mo, ongoing
3	AdenoCA	3028+1delG	Yes	Yes	No	Before crizotinib	CR, 7 mo, ongoing
4	AdenoCA	D1010H	No	No	No	Before crizotinib	Stable disease, 4 mo, ongoing
5	AdenoCA	2888-16_2888-3del14	Yes	Yes	No	Before crizotinib	PR, 10 mo, ongoing
6	SqCC	2888-11_2904del28	No	No	No	Before crizotinib	PR
7	AdenoCA	2888-16_2888-13delTTCT	No	No	No	Before crizotinib	CR, 3 mo, ongoing
8	AdenoCA	3028 + 1G>A	No	No	No	Before crizotinib	Unresectable to resectable and NED after resection

[a]Investigator reported.
METex14, hepatocyte growth factor receptor gene exon 14 skipping; Amp, amplification; *MDM2*, murine double minute 2 gene; *CDK4*, cyclin-dependent kinase 4 gene; AdenoCA, adenocarcinoma; SqCC, squamous cell carcinoma; PR, partial resp

Awad MM *et al.*, *J Clin Oncol*, 2016

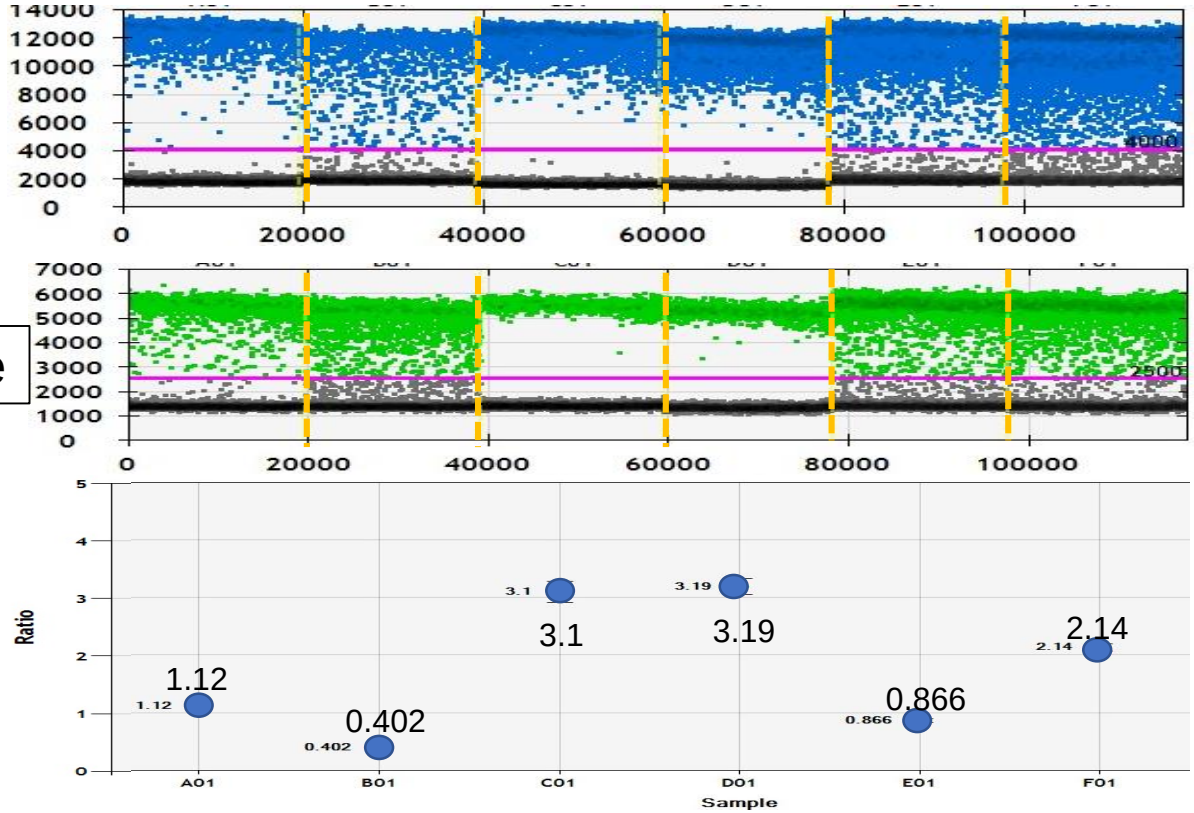
Schrock AB *et al.*, *J Thorac Oncol.*, 2016

healthy patient VL-386 VL-474 2882 N3524

c-Met

Reference Gene

Copy Number



藥物基因體實驗室 Pharmacogenomics Lab
8F., No.17, Xuzhou Rd., Zhongzheng Dist., Taipei City 100, Taiwan (R.O.C.)
TEL: 886-2-23123456 #88674, FAX: 886-2-2395-8341

GENE TESTING REPORT

CUSTOMER INFORMATION[#1]:

SPEC NO:	N3524	REF NO:	
HOSPITAL:	台中榮總	CLINICAL DIAGNOSIS:	
SPEC TYPE:			
DATE OF BIRTH (yyyy/mm/dd)		SEX	

REQUEST ITEM: MET exon 14 skipping, MET gene amplification, and MET mRNA Expression Examination

SAMPLING DATE[#2]:

RECEIVING DATE: 2018.11.05

TESTING DATE: 2018.11.06

ISSUE DATE: 2018.11.12

TURNOVER DAYS: 5 days

TESTING METHODS:

The DNA and RNA were extracted from the FFPE samples by RecoverAll™ Multi-Sample RNA/DNA Isolation Workflow. The quantity of extracted DNA and RNA was measured by Qubit and the MET DNA/RNA alterations were detected by droplet digital PCR (Bio-Rad). MET gene amplification was detected using DNA as material and MET exon 14 skipping was detected using cDNA, reverse transcribed from RNA, as material.

CLINICAL INTERPRETATION:

Patients with MET gene (NM_001127500.2) exon 14 skipping or gene amplification may have better response for MET-tyrosine kinase inhibitors target therapy.

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TEL: 886-2-23123456 #88674, FAX: 886-2-2395-8341

CUSTOMER INFORMATION[#1]:

SPEC NO:	N3524	REF NO:	
HOSPITAL:	台中榮總	CLINICAL DIAGNOSIS:	
SPEC TYPE:			
DATE OF BIRTH (yyyy/mm/dd)		SEX	

RESULTS:

a. DNA quality

260 OD Value:		280 OD Value:		260/280 Ratio:		Concentration:	5.6 ng/ul

b. RNA quality

260 OD Value:		280 OD Value:		260/280 Ratio:		Concentration:	20 ng/ul

c. Alteration status[#5]

- ☐ MET exon 14 skipping: **unfound**
- ☐ MET gene amplification: **found**

台灣癌症次世代基因檢測共識聯盟

建立 NGS 基因檢測需求共識會議

會議時間：2018 年 9 月 27 日(星期四)中午 12:00~13:20

會議地點：台大醫院國際會議中心 205 包廂(100 臺北市中正區徐州

會議主持人：楊泮池 榮譽理事長/台灣基因體暨遺傳學會

與會學會：中華民國癌症學會，台灣肺癌學會，台灣病理學會，台灣
加護醫學會，台灣基因體暨遺傳學會，台灣臨床腫瘤醫學

議題討論：

(一). 共識會議背景:

癌症基因 NGS 檢測於現今腫瘤診斷及藥物治療所扮演之角色日益重
內現況，臨床端除採用國外廠商(如 FoundationOne CDx)代檢方案
也委託 精策會(TJCPM，台灣精準醫療品質策進會) 推動“精準醫
實驗試行查核計畫”。然而，從滿足臨床腫瘤醫療需求及維護腫瘤患
醫療權益的視角出發，現今國內現況尚有急需待改進之處，包含：(
床醫療的角度提供各項癌症合規的多基因檢測標的，協助提供各項癌
組規模及檢測成本上最大的效益評估依據？ (2).如何從臨床品質管
保檢測的品質，協助各項檢測於臨床確效的品質管制並維護病人權

台灣癌症次世代基因檢測共識聯盟第二次會議

會議時間：2018 年 10 月 29 日(星期一)中午 12:00~13:00

會議地點：台大醫院國際會議中心 205 包廂

會議主持人：楊泮池 榮譽理事長/台灣基因體暨遺傳學會

台灣癌症次世代基因檢測共識聯盟與會學會：中華民國癌症學會，
台灣肺癌學會，台灣病理學會，台灣胸腔暨重症加護醫學會，台
灣基因體暨遺傳學會，台灣臨床腫瘤醫學會

議題討論：

(一). 臨床及相關資源及現況更新:

國際藥廠（包括並不限於 Novartis, BMS, Ono, Pfizer, Roche, Bayer, Astra Zeneca 等七家藥廠）在台灣申請藥證的過程中，往往受限於個案基因變異資訊之不易取得而影響臨床試驗的收案規劃及執行。為了改善並加速新藥在台之臨床使用，上述藥廠擬在台灣聯合贊助進行 umbrella trail, 透過 NGS 之試驗方式，藉由 NGS 檢測套組所報告之個別基因變異進行個案分群，用以協助每一臨床個案能根據各自獨特的分子標記變異進行不同藥物的臨床試驗安排，而達到加速臨床試驗執行及協助每一臨床個案能獲得適合的臨床試驗規劃之目的。

International Cancer Proteogenomics Consortium

Establish proteogenomic technology; Share big data

- Transcend the genome to the proteome to **better manage an individual's cancer**
- Validate the potential of proteogenomic analyses to **facilitate novel combination therapies** as next generation standard of care
- Accelerate the **search for disease-associated processes** and better target drug development inefficiencies
- Provide a new level of **molecular analysis for better cancer patient treatment decisions**

Deep **genome** and **proteome** profiling of **patient tissues**, to understand **cancer** development, progression, and identify targets for diagnosis and therapies.

計畫重要時程及里程碑

引進產業研發

宏碁 acer

In Silica Medicine

GRAPHEN

ACT GENOMICS 行動基因 Turn Genomics into Action

技術平台技轉

MERIDIGEN

DOB

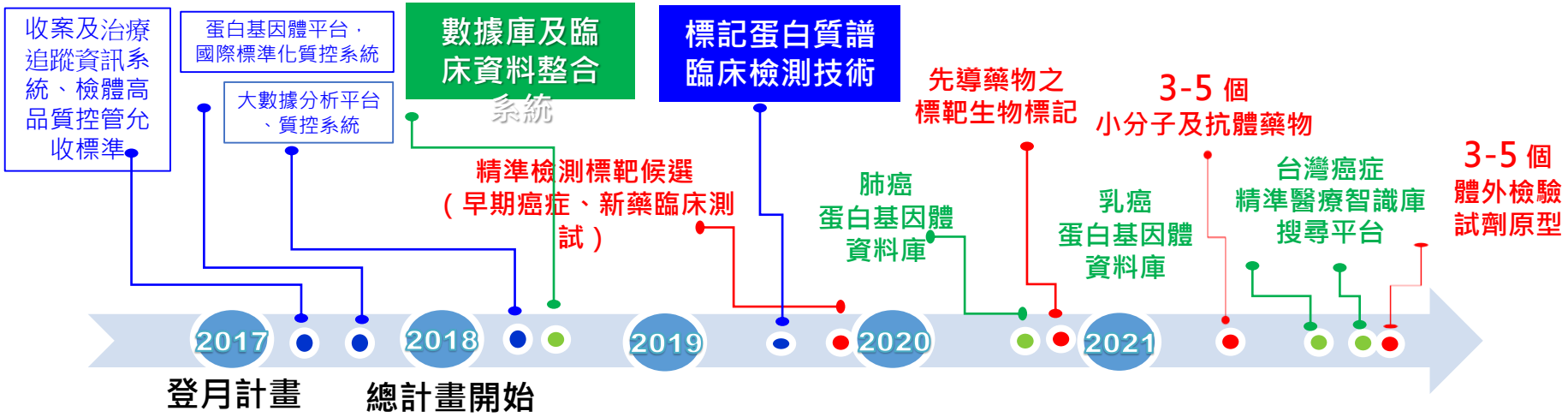
AstraZeneca

國際合作

日本京都/東京大學 (jPOST、KEGG)

美國NCI/FDA (TG 檢測, CLIA 實驗室)

馬來西亞 Taylor's University (CRC)



● 架構多體學巨量數據暨智識庫　● 檢測及新藥標靶

精準醫療分子檢測實驗室檢測與服務指引草案

►107年度委辦【分子檢測先期計畫-建立精準醫療分子檢測產業實驗室服務管理指引(LDTS)及其輔導試行計畫】

■ 計畫執行重點

- ➢ 分子檢測產業實驗室輔導試行查核
- ➢ 管理指引草案研擬

■ 現況

- ➢ 完成辦理專家會議2場、說明會3場、輔導試行查核專家共識營1場、輔導課程2場。
- ➢ 107年6-8月進行分子檢測產業實驗室試行輔導查核(12家)
- ➢ **107年9月27日公開「精準醫療分子檢測實驗室檢測與服務(LDTS)指引」草案，蒐集各界意見，目前完成彙整各界意見，刻正辦理草案公告程序。**

■ 重要期程

- ➢ **預計於107年底前公告LDTS指引**

LDTS草案管理架構

1. LDT Service 定義
2. LDTS 指引適用範圍
3. LDTS 列冊
4. LDTS實驗室品質管理系統
5. LDTS 檢測項目確效

落實精準醫療相關政策，促進生技相關產業發展

分子檢測納入健保給付

健保法第41條第1項

- 醫療服務給付項目及支付標準，由保險人與相關機關、專家學者、被保險人、雇主及保險醫事服務提供者等代表共同擬訂，報主管機關核定發布。

健保法第42條第2項

- 前項醫療服務給付項目及支付標準之訂定，保險人得先辦理醫療科技評估 ，並應考量人體健康、醫療倫理、醫療成本效益及本保險財務；藥物給付項目及支付標準之訂定，亦同。

■ 現行支付標準新增診療項目作業規範，申請檢驗項目須：

1. 具備食藥署核發之「醫療器材許可證」，
2. 執行單位須為健保特約醫事機構，
3. 並具備合格檢驗實驗室認證且具檢驗品質。

More Than EGFR Testing

1. Single gene test
2. Multiple gene test (NGS, microarray)
3. Tumor mutation burden
4. CART
5. Neoantigen (peptide vaccine)