精準醫學的範疇與挑戰

(2017-9-1)

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Overview of this talk

1. Scope of Precision Medicine

2. Challenges of Precision Medicine

3. 台灣精準醫學學會 TPMS

(www.tpms.org.tw)

醫療常被認為是藝術，而不是科學？

“If it were not for the great variability among individuals, medicine might as well be a science and not an art”

Sir William Osler, 1892

現行的醫學診斷和治療大多是針對「標準化病人」設計，這種「標準診斷和治療策略」雖然在許多病人非常成功，但對某些病人卻無法奏效，因為這樣的概全式診斷和治療忽視了病人的個體差異和疾病的異質性。

「精準醫學」：在針對病人體質差異和疾病的異質性的特殊考慮下，所訂定出來的疾病診斷、預防和治療策略。

Precision Medicine: beyond the inflection point.

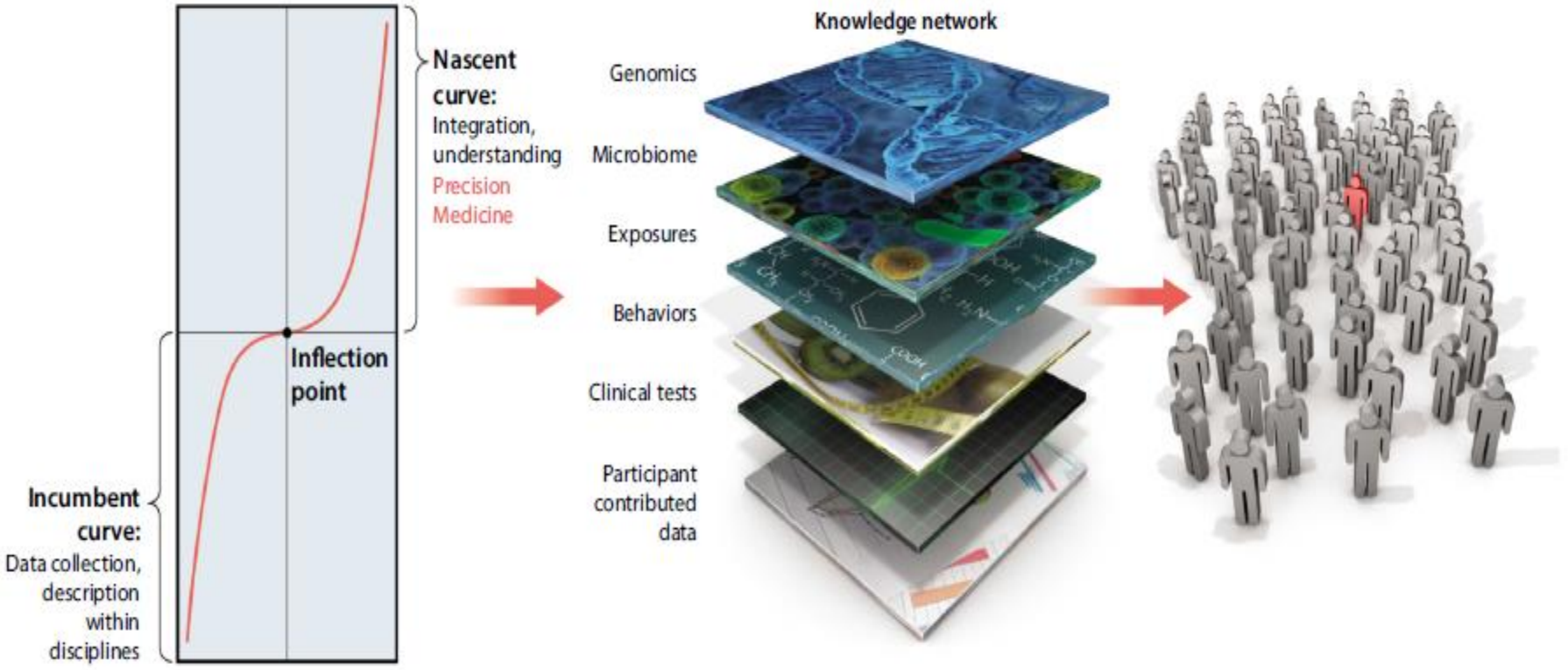


Fig. 1. Surpassing single-layer health care. An inflection point marks an opportunity or moment of dramatic change between the first, or incumbent, curve, marking steady progress, and a second, or nascent, curve, indicating transformation and accelerated progress. In biomedical research, health, and health care, we are at an inflection point, poised for precision medicine. Whereas Google Maps links layers of transportation, land use, and other data, precision medicine aims to integrate and apply data from biomedical research, clinical practice, social/behavioral studies, and participant-contributed observations toward better diagnosis, treatment, and preventative strategies.

Hawgood S et al. ***ScienceTranslationalMedicine (2015)*** Vol 7 Issue 300 p.300ps17

The Oncologist
Fundamentals In Cancer Medicine

(1999)

New Era of Personalized Medicine

Targeting Drugs For Each Unique Genetic Profile

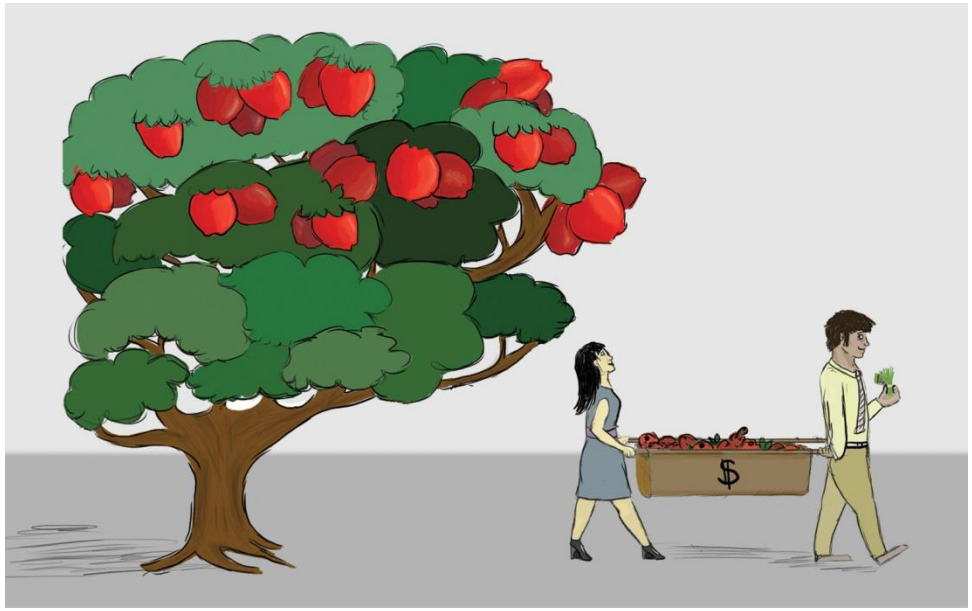
BY ROBERT LANGRETH And MICHAEL WALDHOLZ

Staff Reporters of THE WALL STREET JOURNAL

Precision Medicine

First coined by Clayton Christensen in a book
"***The Innovator's Prescription: a disruptive solution for health care***" (**2009**)

Better known in a US National Research Council (NRC) **2011** report "***Toward Precision Medicine: Building a knowledge network for biomedical research and a new taxonomy of disease***".



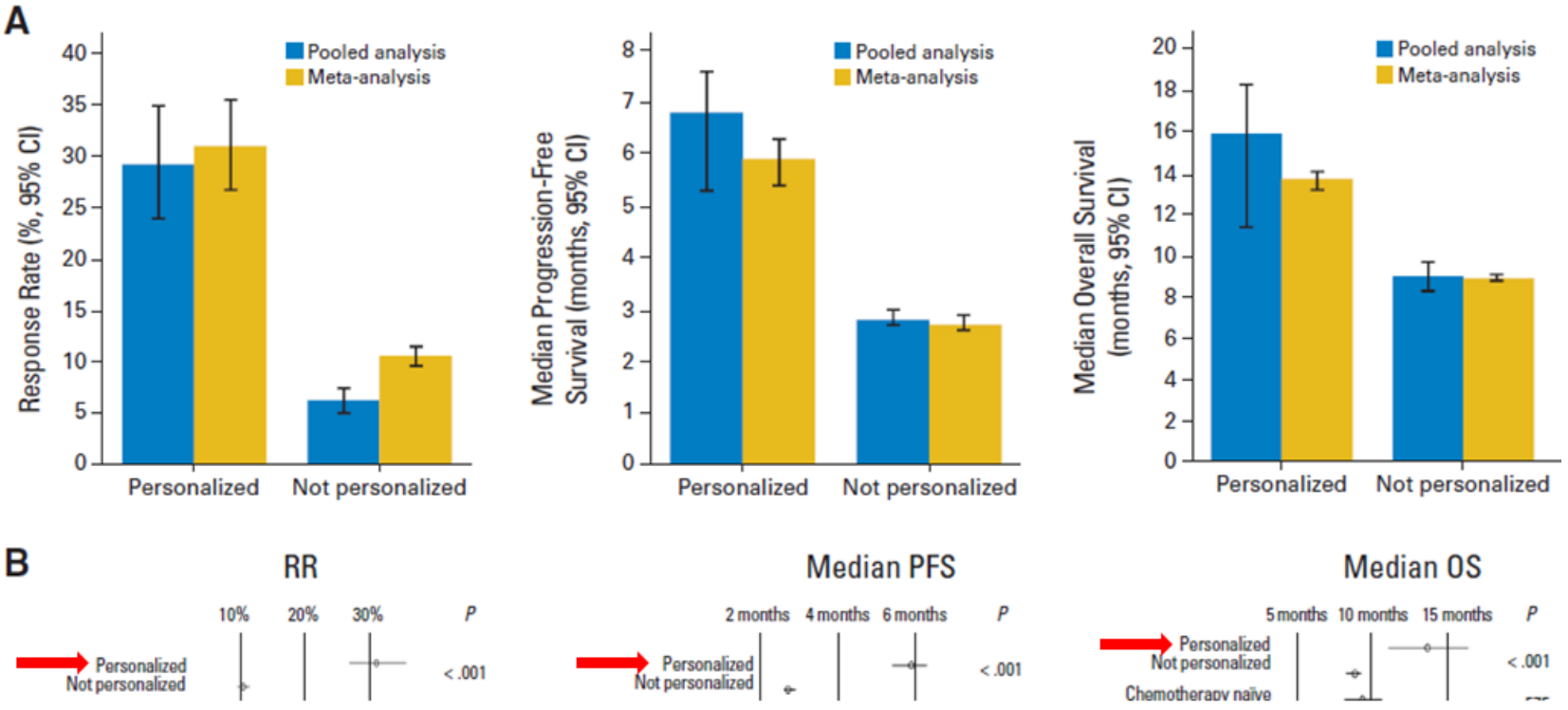
Targeted therapy

NIPT

Targeted therapy-1

Impact of Precision Medicine in Diverse cancers: a Meta-analysis **of Phase II clinical trials**

- Matching patients with drugs based on specific biomarker
- **570** phase II single-agent studies (**32,149 patients**)
- Published between Jan 1, 2010 to Dec 31, 2012
- End points: Response rate (RR), Progression-free survival (PFS), and overall survival (OS)



Schwaederle M et al. ***J Clinical Oncology (2015)*** 33: 3817-3825.

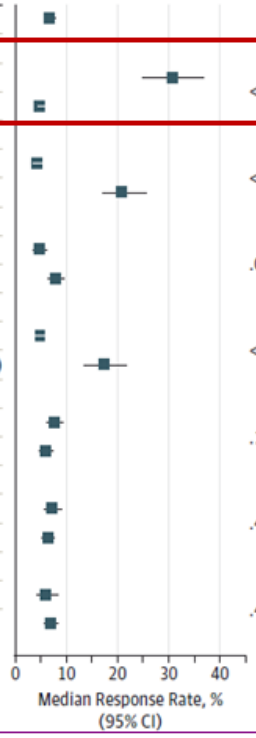
Targeted therapy-2

Impact of Precision Medicine in Diverse cancers: a Meta-analysis of Phase I clinical trials

- Comparing outcomes in patients that used a biomarker selection with those did not
- 351 arms in 346 phase I single-agent studies (13,203 patients): **58 arms (2655 cases) with personalized** vs. **293 arms (10548 cases) using a nonpersonalized strategy**
- Published between Jan 1, 2011 to Dec 31, 2013
- End points: Response rate (RR), Progression-free survival (PFS)

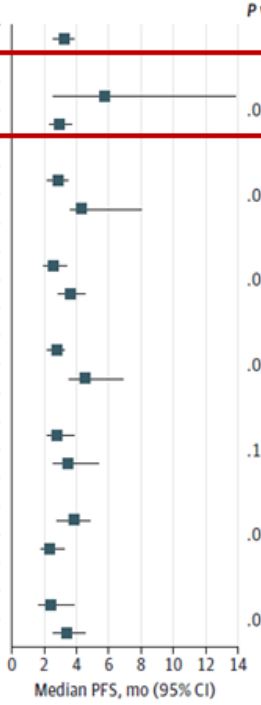
B Response rate (meta-analysis)

Variable	No. of Arms	Median Response Rate, % (95% CI)	P value
Overall	351	6.56 (5.57-7.72)	
Used a personalized strategy			
Yes	58	30.62 (25.0-36.90)	<.001[a]
No	293	4.89 (4.22-5.66)	
Tumor type			
Solid	272	4.25 (3.48-5.19)	<.001[a]
Hematologic	79	21.02 (17.0-25.71)	
Agent class			
Cytotoxic	117	4.72 (3.60-6.17)	.003
Targeted	234	7.84 (6.46-9.49)	
FDA/EMA approved			
No	267	4.83 (4.04-5.76)	<.001[a]
Yes	84	17.27 (13.60-21.69)	
No. of patients per arm			
≤30	182	7.67 (6.20-9.45)	.11
>30	169	5.94 (4.70-7.48)	
Administration route			
Oral	162	7.23 (5.68-9.16)	.41
Systemic	189	6.32 (5.13-7.76)	
No. of treating centers			
Single center	91	6.0 (4.3-8.2)	.48
Multiple centers	260	6.8 (5.7-8.2)	



Representation of Progression-Free Survival (PFS)

Variable	No. of Arms	Median PFS, mo (95% CI)	P value
Overall	45	3.23 (2.56-3.80)	
Used a personalized strategy			
Yes	7	5.70 (2.56-13.78)	.049[a]
No	38	2.95 (2.30-3.70)	
Tumor type			
Solid	35	2.80 (2.24-3.43)	.002[a]
Hematologic	10	4.30 (3.62-8.0)	
Agent class			
Cytotoxic	15	2.50 (2.0-3.36)	.09
Targeted	30	3.64 (2.83-4.43)	
FDA/EMA approved			
No	29	2.80 (2.20-3.23)	.007
Yes	16	4.51 (3.57-6.90)	
No. of patients per arm			
≤30	27	2.87 (2.10-3.80)	.13
>30	18	3.47 (2.56-5.31)	
Administration route			
Oral	29	3.80 (2.87-4.84)	.004
Systemic	16	2.34 (1.80-3.23)	
No. of treating centers			
Single center	11	2.40 (1.70-3.80)	.055
Multiple centers	34	3.44 (2.60-4.47)	



Schwaederle M et al. ***JAMA Oncology (2016)*** Advance Online Pub on June 6

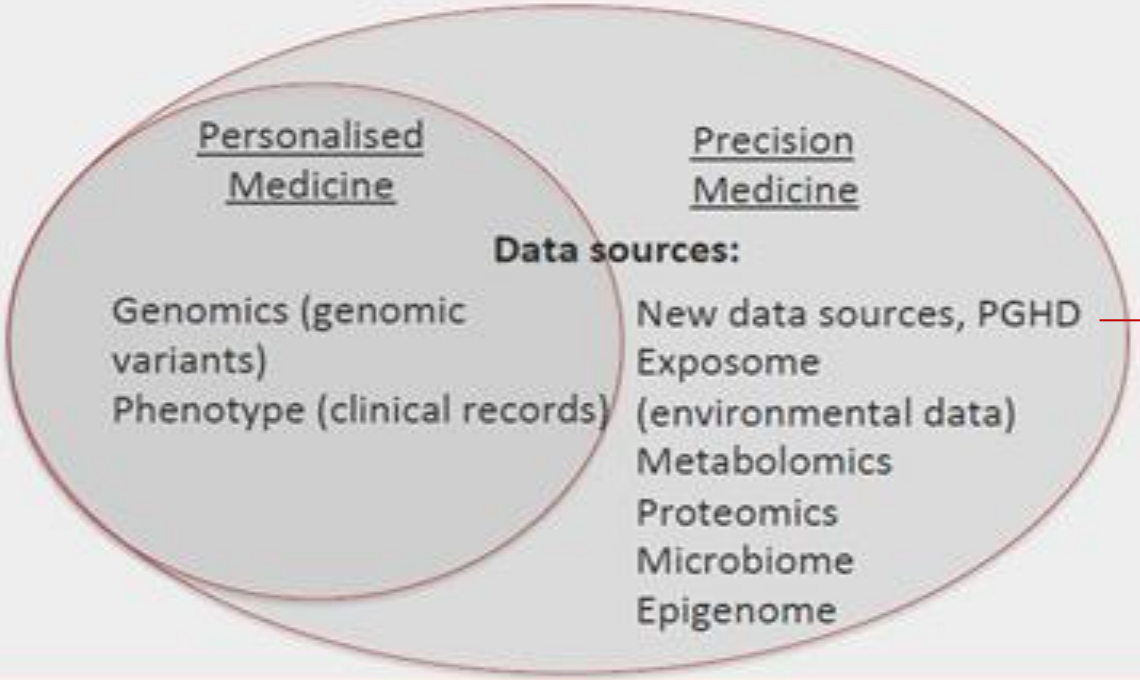
NIPT

Ch. Anomaly	Sensitivity	Specificity	Analyzed from case no.	The value of NIPT
Fetal sex	0.989	0.996	11,179	diagnostic
Rhesus D	0.993	0.984	10,290	diagnostic
Trisomy 21	0.994	0.999	148,344	screening
Trisomy 18	0.977	0.999	146,940	screening
Trisomy 13	0.906	1.0	134,691	screening

Mackie FL, et al. *BJOG (2017) 124*: 32-46.

2017年「英國婦產科期刊 (BJOG) 」整合性分析(meta-analysis)涵蓋了**117個獨立研究**，高達**472,935檢驗個案**的綜合結論：NIPT可當作胎兒性染色體異常和RhD基因狀態的診斷 (diagnostic)工具；而應該視為三染色體21(唐氏症)，18(愛德華症)和13(巴陶症)的篩檢(screening)工具。NIPT當作篩檢工具的意義，就是：一但NIPT檢查報告顯示有異常時，需要再用侵入性檢查- 羊膜穿刺來確認染色體異常的存在。

Personalised vs Precision Medicine



Patient-generated Health Data

PM combines the knowledge of the patient's characteristics with traditional medical records and environmental information to optimize health.

PM does not only rely on genomic medicine but also integrates any other relevant information such as non-genomic biological data, clinical data, environmental parameters and the patient's lifestyle.

Servant N et al. Front Genet. 2014; 5: 152.

Source: Fernando Martin-Sanchez' Talk on 2016-3-22

The Cancer Genome Atlas (TCGA)

- A NIH research program,
- launched by the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI) in 2006
- grew to include samples from 11,000 patients across 33 tumor types

  TCGA scientists had nearly completed sequencing protein-coding regions (exomes) for most tumor types, and completed whole-genome sequencing (WGS) for 1,000 tumor samples.
- Results from TCGA analyses to date have led to more than 2,700 articles in research journals.

http://cancergenome.nih.gov/

APPLICATIONS OF NEXT-GENERATION SEQUENCING

The human microbiome: at the interface of health and disease

Ilseung Cho[1,2] and Martin J. Blaser[1,2,3,4]

Metagenomics:
A frontier in human genetics

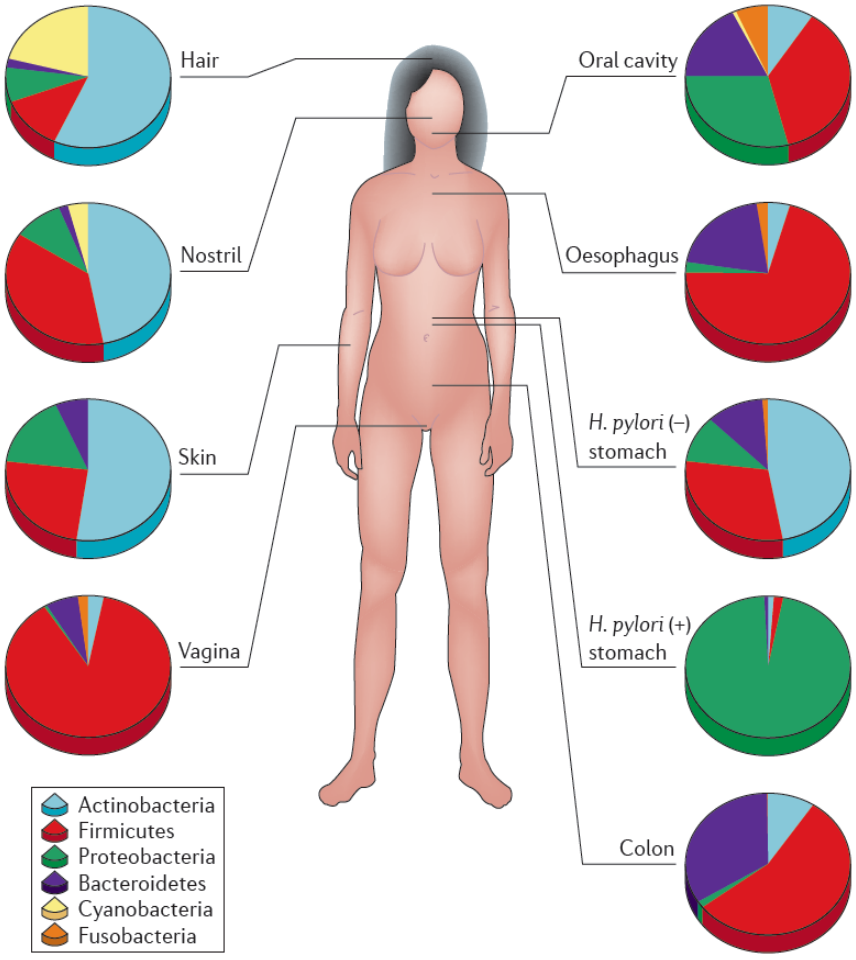


Figure 1 | **Compositional differences in the microbiome by anatomical site.**

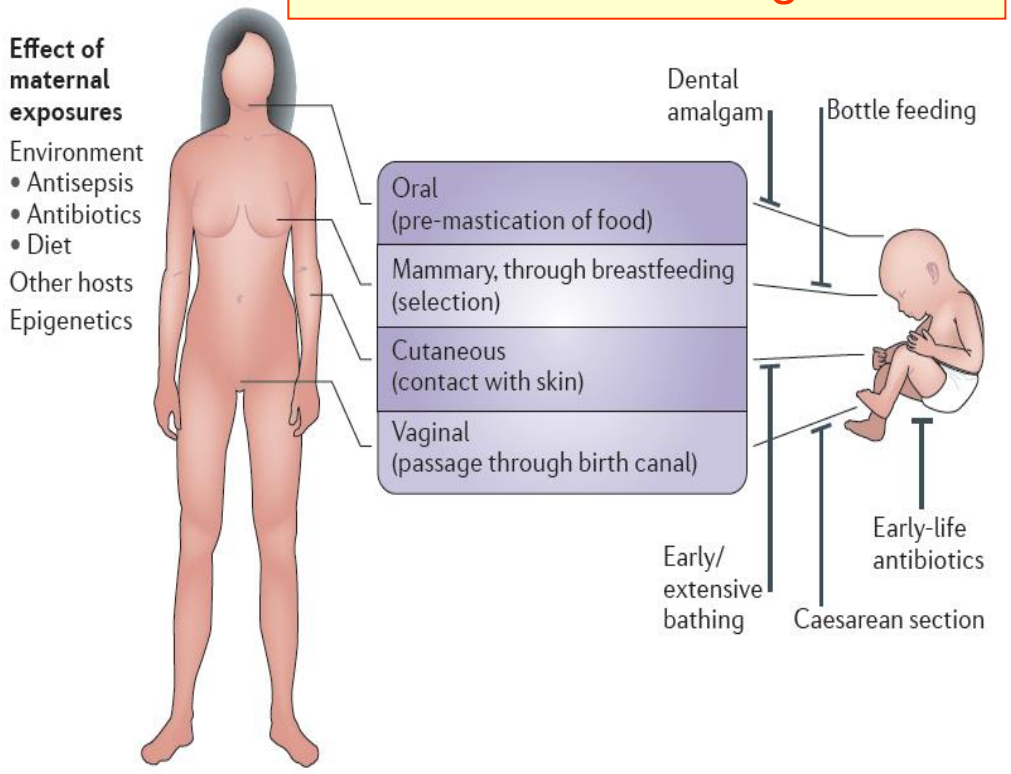
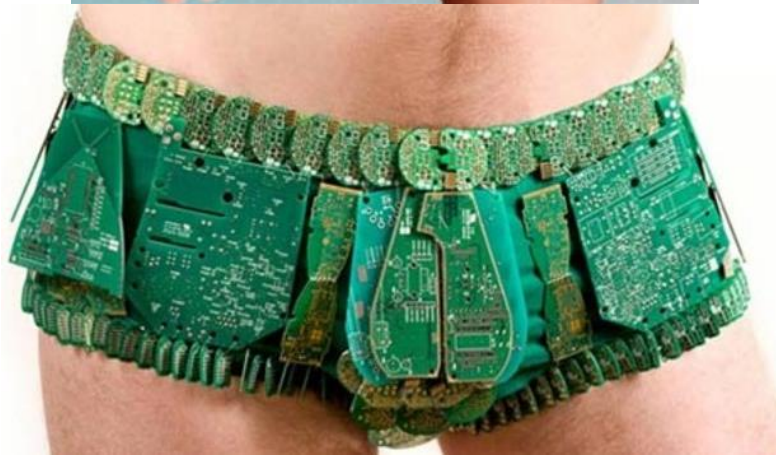


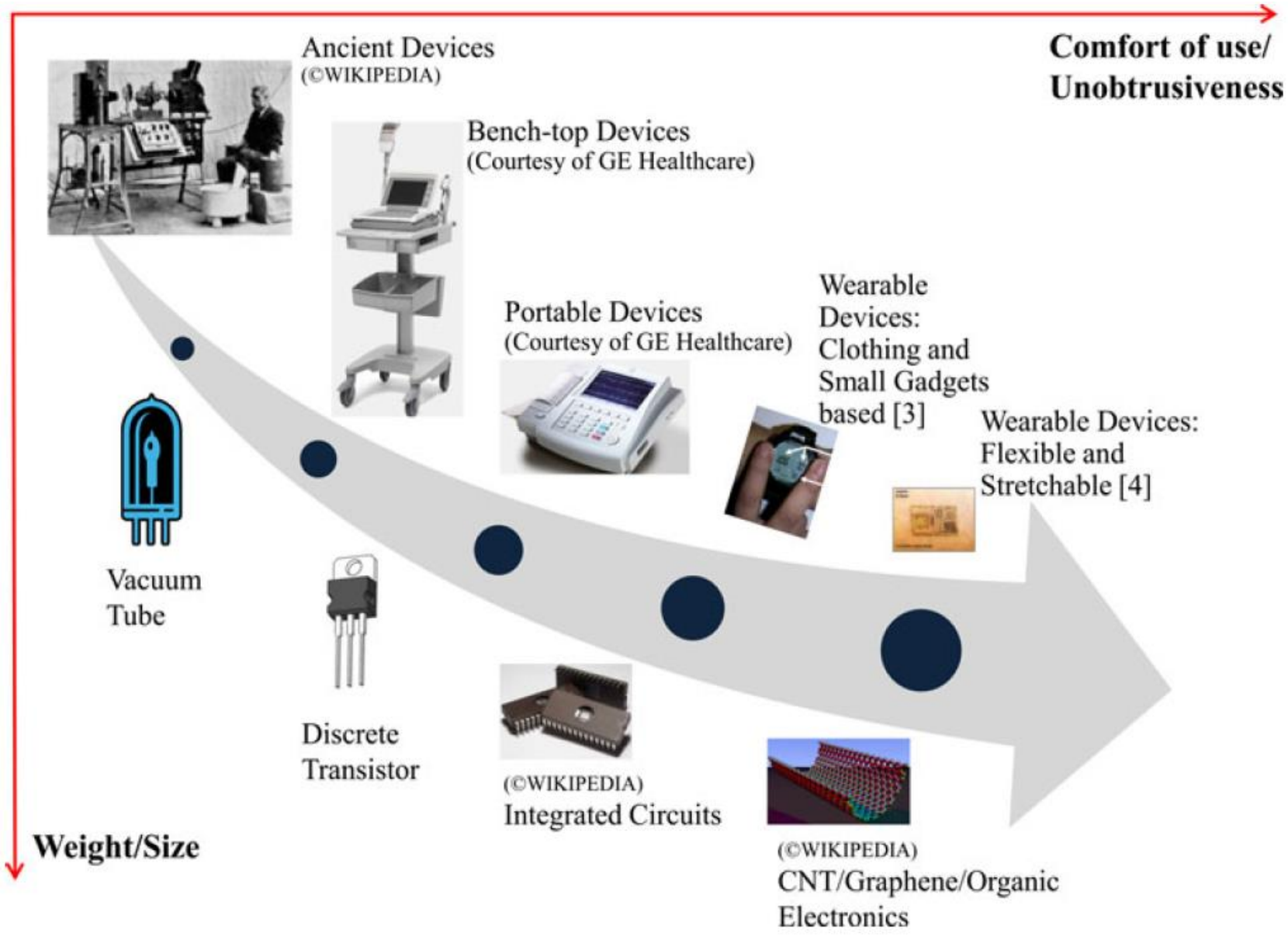
Figure 3 | **Acquisition of the microbiome in early life by vertical transmission, and factors modifying mother-to-child microbial transmission.** Through

(Nat Rev Genet 2012; 13: 260-270)

Mobile data from Wearable devices

> *"You can take pretty noisy data, but if you have enough of it, you can find a signal."*





Timelines of medical devices for ECG measurement with the evolution of electronic technology.

Zheng YL et al. ***IEEE Transactions on Biomedical Engineering*** (2014) 61: 1538-1554.

The essential roles of smartphones in wearable development

P4 Medicine

(by Leory Hood)

- **P**redictive,
- **P**reventive,
- **P**ersonalized,
- **P**articipatory

Institute for Systems Biology

P-Medicine

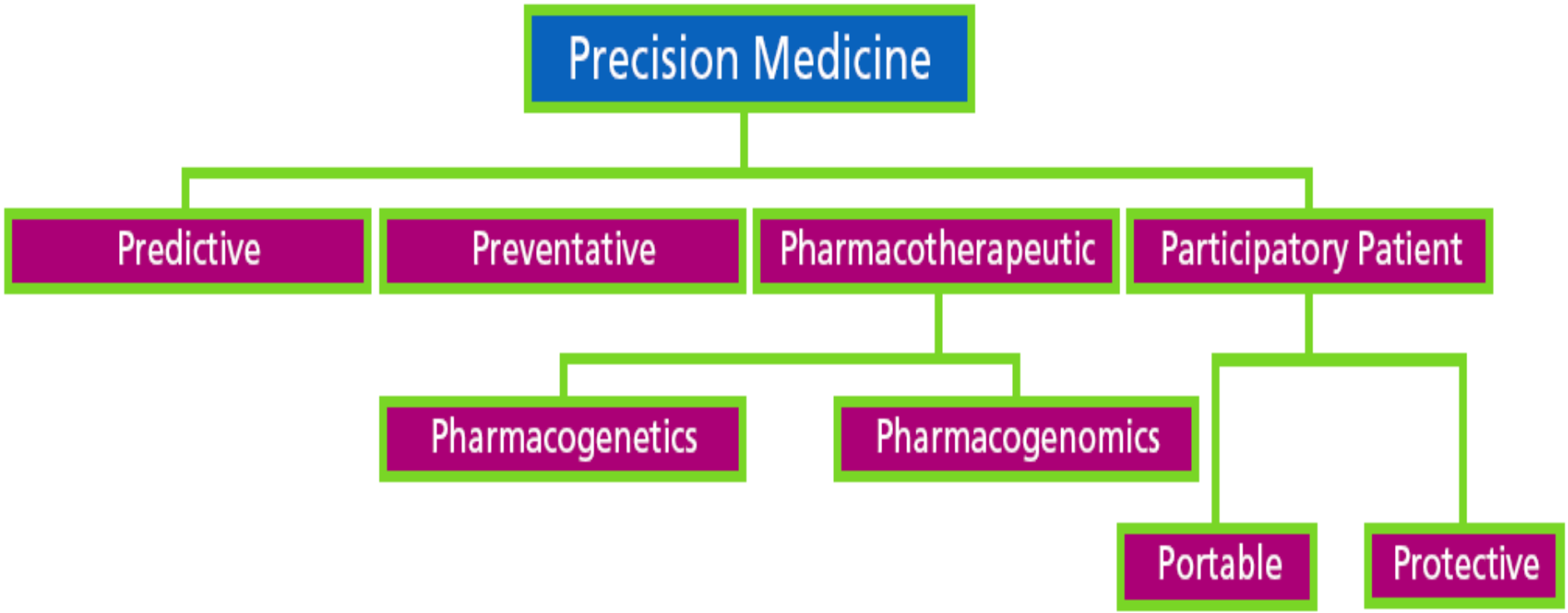
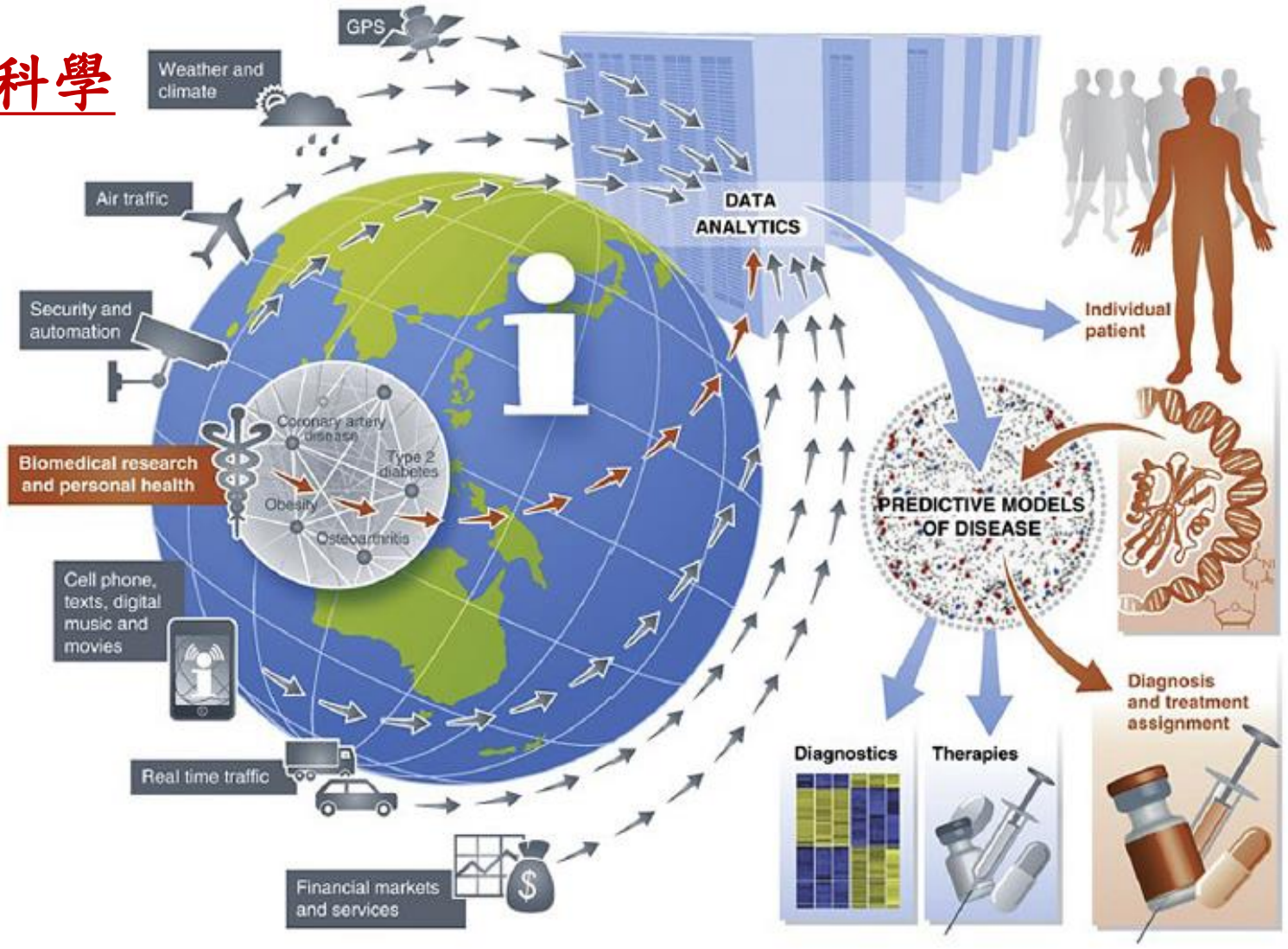


FIGURE 5. Component parts of Precision Medicine as it evolves from just being a genomic analysis of an individual patient. The "P-Medicine" Paradigm.

精準醫學是
生命資訊的科學



Heterogeneous and non-traditional sources of big data

Tenenbaum JD. ***Genomics Proteomics Bioinformatics (2016)*** 14: 31-41.

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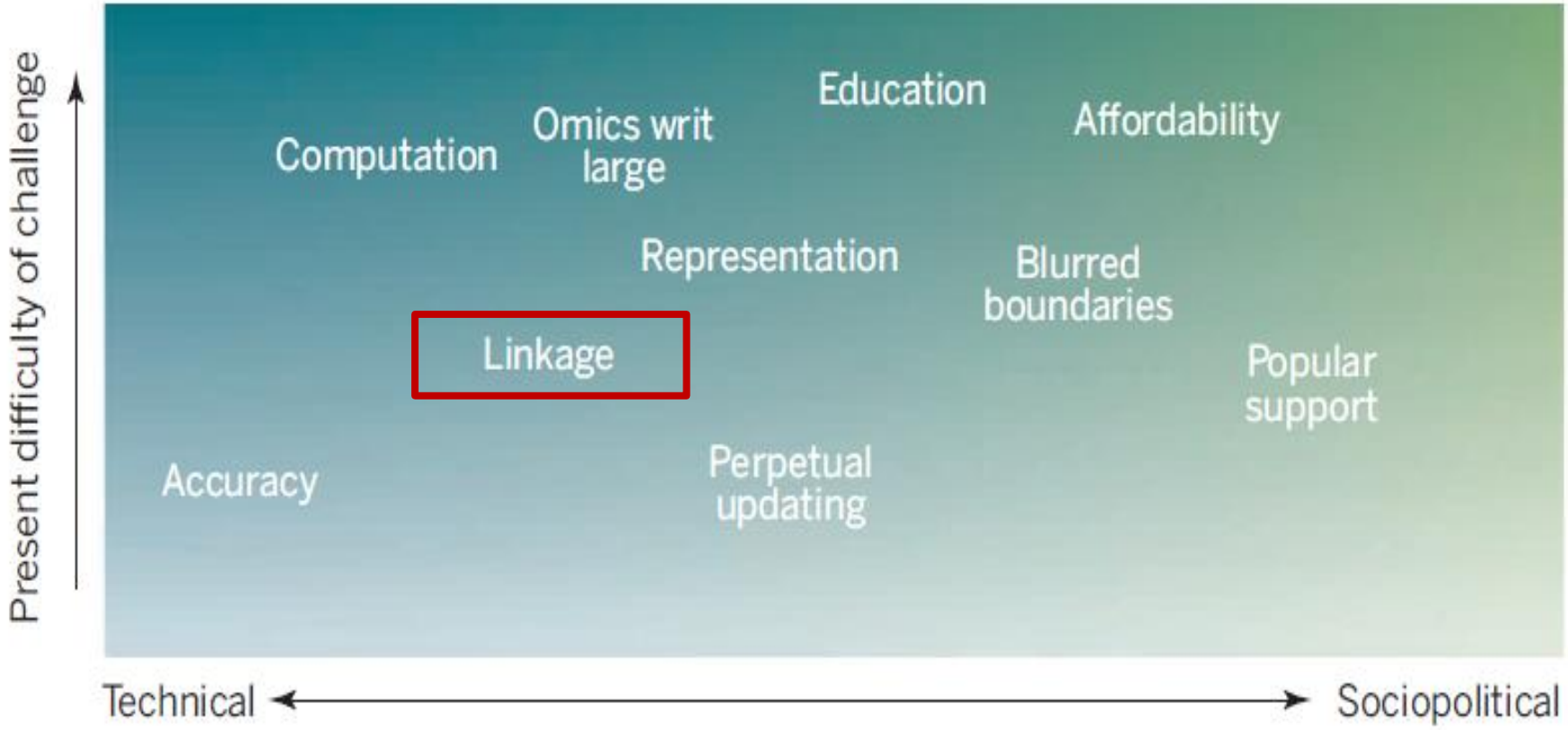


Moving toward precision medicine. Ten challenges for achieving precision medicine are qualitatively ordered on the *x* axis by how much they are intrinsically technical versus sociopolitical challenges. The *y* axis qualitatively orders the difficulty each challenge currently presents if we are to attain the widely articulated goals for precision medicine.

Kohane IS**.** Ten things we have to do to achieve precision medicine. ***Science (2015)*** 349: 37-8.

聯繫 (Linkage)：

由不同研究機構的研究計劃所得到的基因體學資料和每天生活資料，要如何能夠聯繫到正確的個體的正確年紀，是第一個必須克服的挑戰。

即使這些資料都能夠使用一套通用醫療識別碼(Universal health identifier)來串連，其他與個人健康相關的訊息例如：飲食、環境暴露、或社會網路活動，到現在都還無法聯繫到健康資料庫。

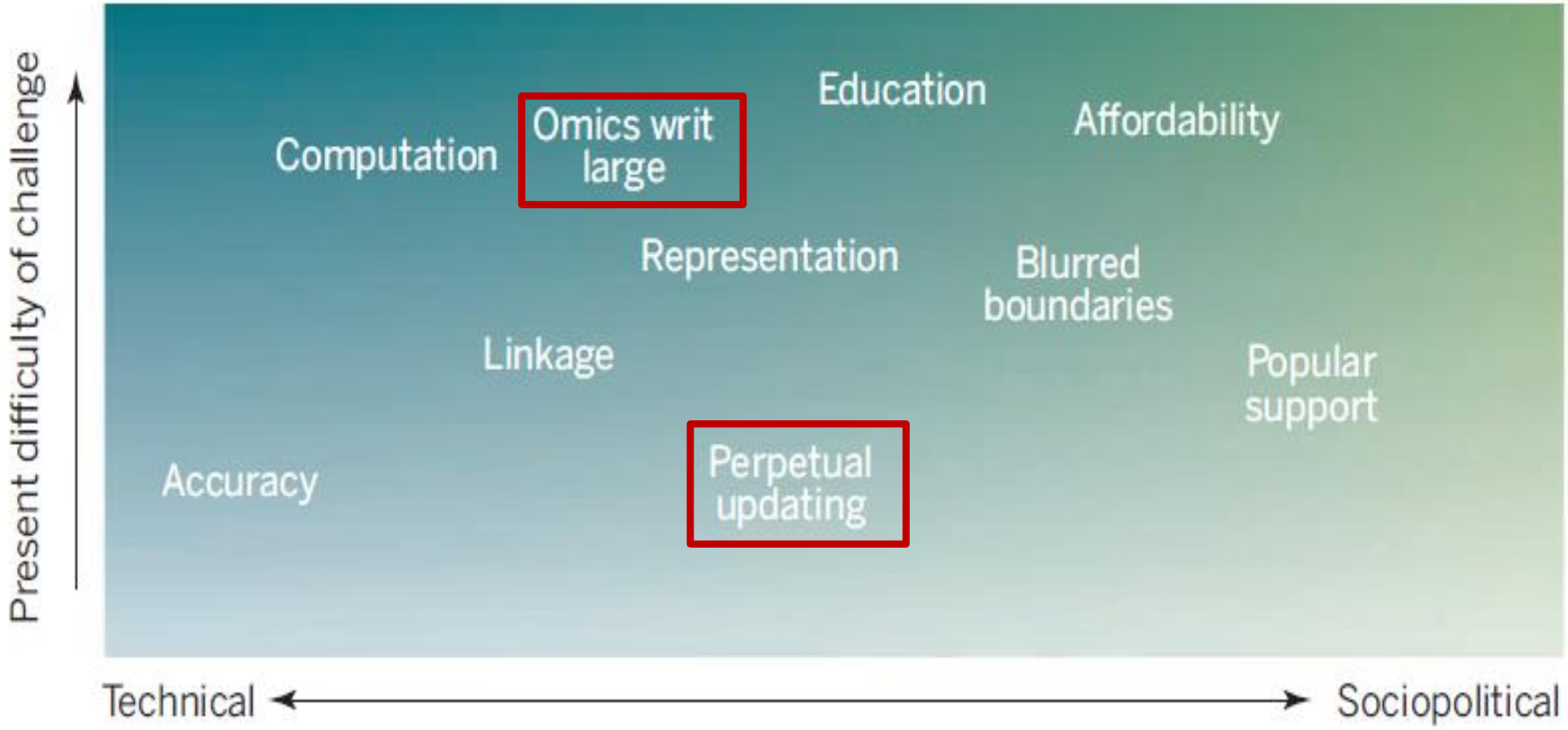
醫健通 ehealth 香港特別行政區政府 HKSAR GOVT

電子健康紀錄互通系統
Electronic Health Record Sharing System

Scope of eHR Sharable Data (First Phase)

- Personal Identification and Demographic Data
- Adverse Reactions and Allergies
- Diagnosis, Procedures & Medication
- Summary of Episodes and Encounters With Healthcare Providers
- Clinical Note Summary
- Birth and Immunisation Records
- Laboratory and Radiology Results
- Other Investigation Results
- Referral Between Providers

http://www.ehealth.gov.hk/



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推廣到更廣泛的體學資料 (Omics writ large)

雖然我們已經成功地整合各種分子層次的體學資料，但要瞭解多因子的常見疾病，我們還需要整合環境暴露因素，和一個人不同生命時期的各種生活模式等等。

隨時更新 (Perpetual updating)

不但資料挹注的過程必須更靈活，審理互相衝突的資料也要夠即時。什麼單位可以負責這個任務呢？也許需要一個類似國家標準科技局 (National Institute of Standards and Technologies)的新單位？

All of Us℠ Research Program

WHAT IS IT?

Precision medicine is a groundbreaking approach to disease prevention and treatment based on people's individual differences in environment, genes and lifestyle.

The *All of Us* Research Program will lay the foundation for using this approach in **clinical practice.**

WHY NOW?

The **time is right** because:

We have a greater understanding of human genes

People are more engaged in healthcare and research

We have the tools to track health information and use large databases

Research technologies have improved

WHAT ARE THE GOALS?

Engage a group of **1 million or more U.S. research participants** who will share biological samples, genetic data and diet/lifestyle information, all linked to their electronic health records. This data will allow researchers to develop more precise treatments for **many diseases and conditions**.

Pioneer a new model of research that emphasizes **engaged research participants, responsible data sharing and privacy protection.**

Research based on the cohort data will:

- Lay **scientific foundation** for precision medicine
- Help identify new ways to **treat and prevent disease**
- Test whether **mobile devices**, such as phones and tablets, can encourage healthy behaviors
- Help develop the **right drug** for the **right person** at the **right dose**

PORTABLE GENOMICS

OUR OFFICE

Janssen Labs Incubator
3210 Merryfield Row
San Diego, CA, 92121
(858) 242.1553

Our Vision

As the digitization of healthcare records, the development of inexpensive genomic mapping and the growing popularity of wireless health sensors continues to grow, individuals need a solution to control and organize their personal health information. Portable Genomics is uniquely positioned to provide individuals control of their personal health data in order to facilitate sharing with healthcare providers, payers and life science organizations leading to improved healthcare and smarter health discovery.

Founder

Patrick Merel, Ph.D.
President

Dr. Merel, an expert in molecular diagnostics and an early developer of robotics for the automation of molecular diagnostics from forensics to transplantations, is the founder of Portable Genomics' technology.

Read More ▾

PORTABLE GENOMICS

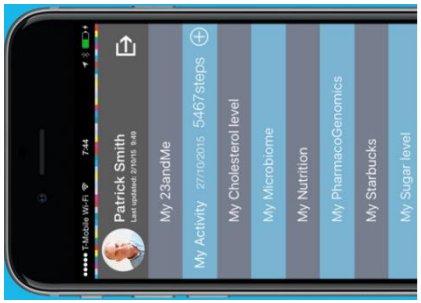
Platform

Collect Your Personal Health Data

Build and collect your personal collection of genomic, medical, behavior, and lifestyle data into one, user-friendly platform anywhere, anytime.

Gain a 360° View of Your Health

Access and monitor all of your personal health and lifestyle information, including the Internet of medical things from one integrated platform. Add notes and reminders on the go.



Share Health Information Real-Time

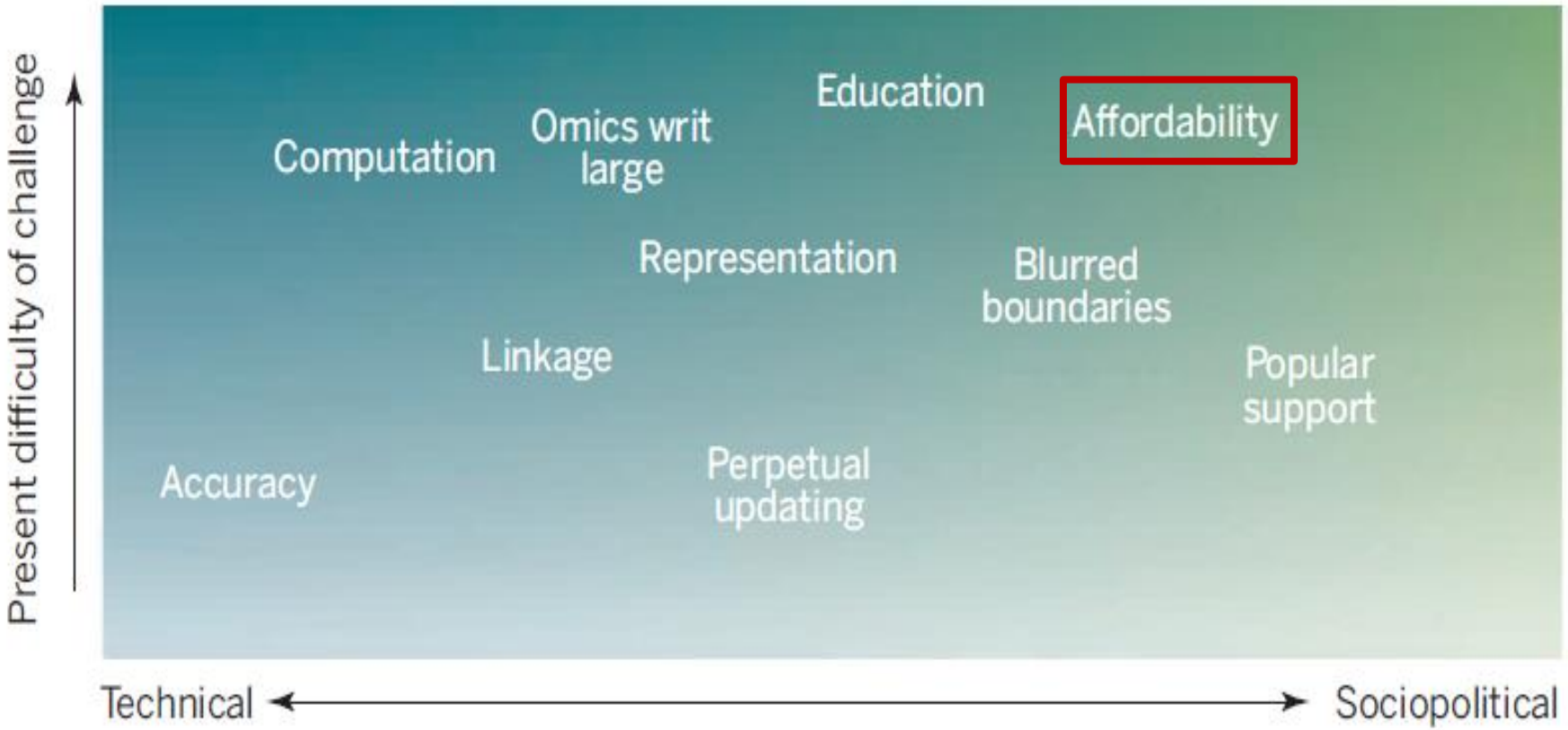
You decide and control who receives your personal health data – your family, caregivers or healthcare providers via text, email or hard copy.

Exchange Your Raw Health Data

Share all or part of your personal health data with non-profit or for profit organizations via a secure Personal Health Data Market Exchange. Indicate your willingness to share your data. You may opt-in or opt-out at anytime. When a request for raw data is received, you will be asked to confirm your willingness to share your data.

Create Value from Your Data

You control the personal health data you share and can be compensated with the revenue generated from the commercial use of that information. Your information will help for profit and non-profit organizations develop improved therapies for specific diseases.



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Precision medicine: Now, not when.

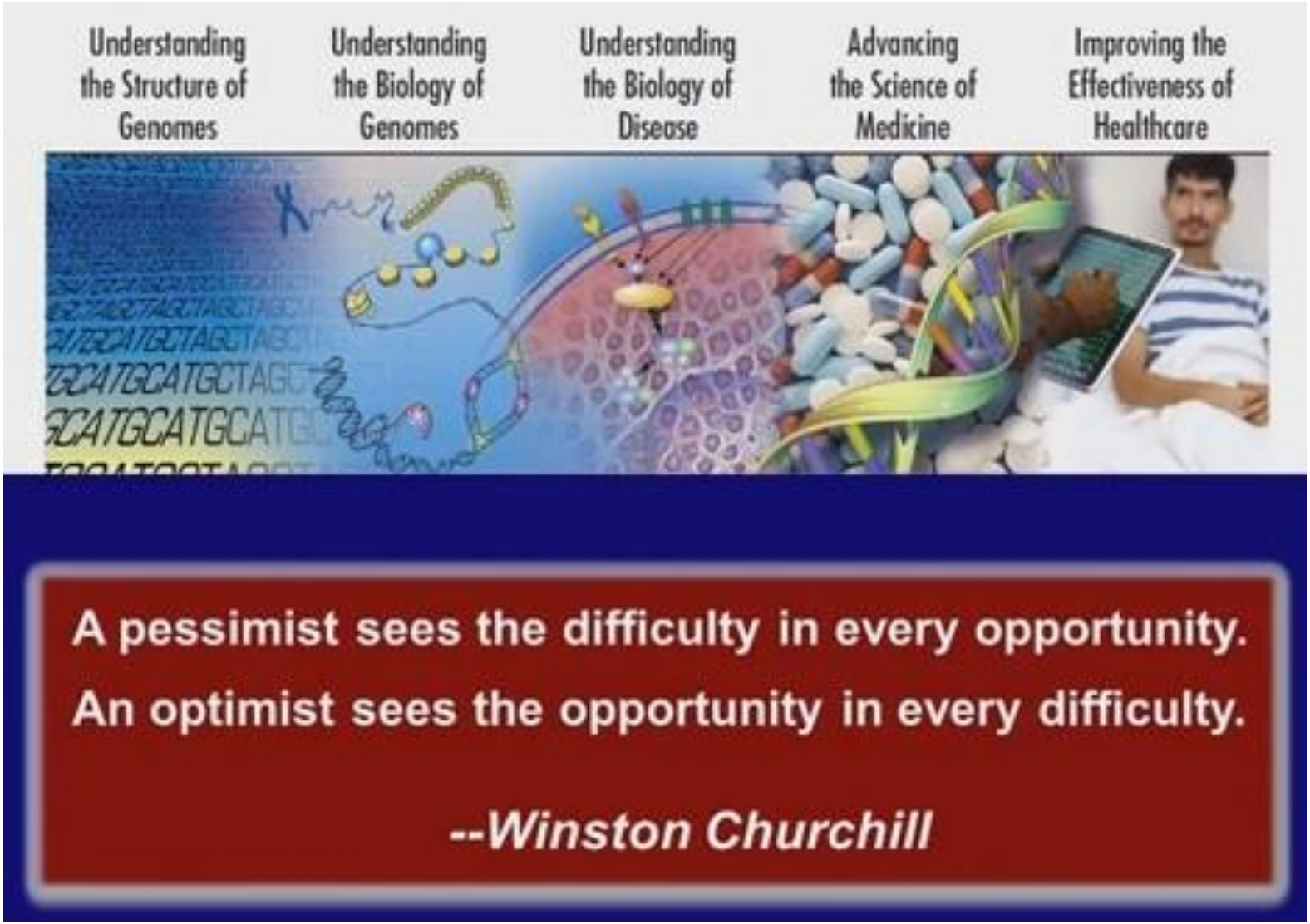
Precision medicine aims to fix what is wrong with today's healthcare: a lack of targeted interventions tailored to the person. It encompasses many aspects of health; chief among these is **one's genetic profile**.

…

Despite these barriers, **precision medicine** is **the only way forward**.

Roberts S and Julius M. ***Healthcare Management Forum (2016) 29: 158-61.***

實踐「精準醫療」有千頭萬緒，絕非易事，
誠如邱吉爾所說的：
「**悲觀者只看到困難重重，樂觀者卻覺得充滿契機**。」



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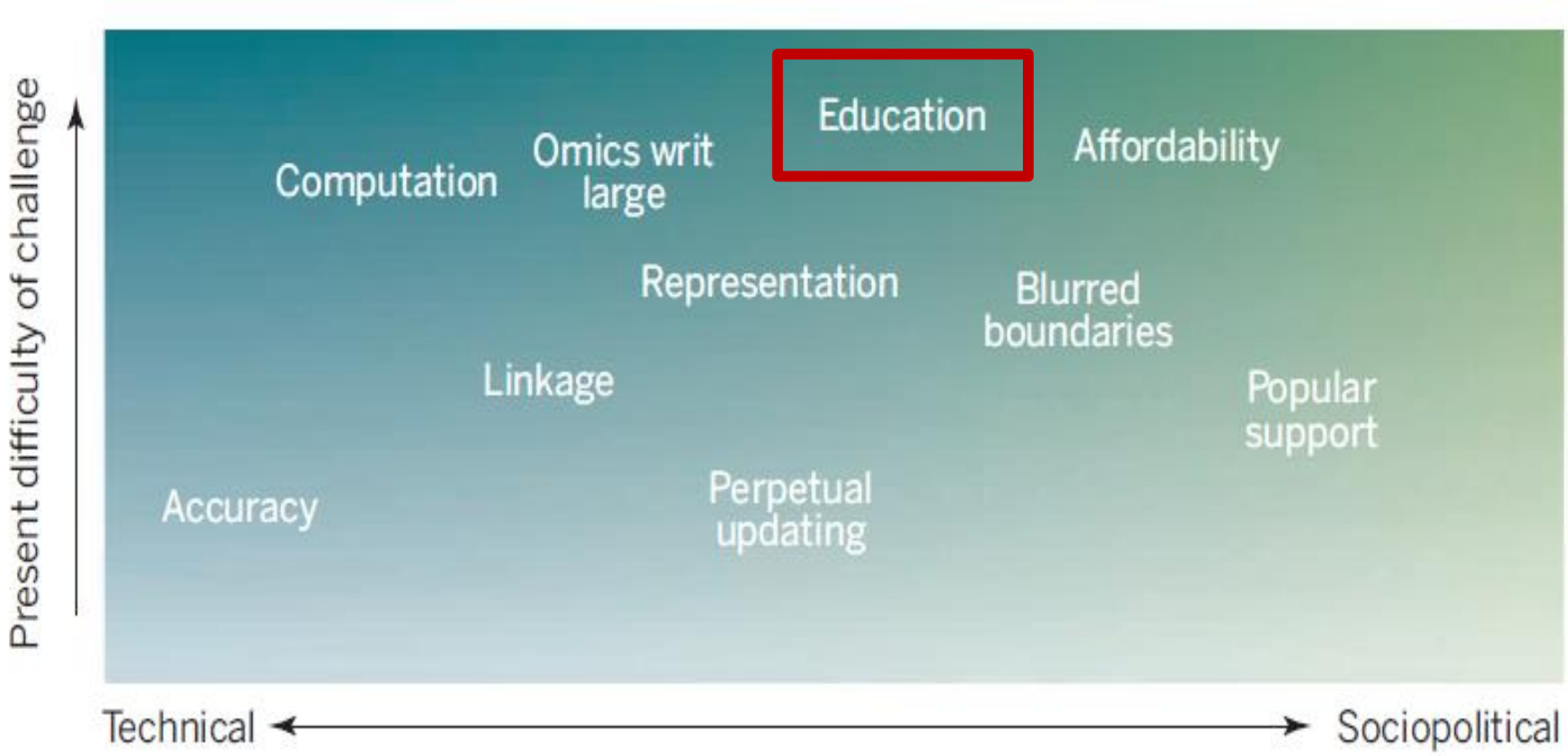
(www.tpms.org.tw)



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THE NEW YORKER

SCIENCE & TECH BUSINESS HUMOR CARTOONS MAGAZINE

FEBRUARY 5, 2015

THE PROBLEM WITH PRECISION MEDICINE

BY CYNTHIA GRABER

Many doctors are simply not qualified to make sense of genetic tests, or to communicate the results accurately to their patients.

台灣精準醫學學會
Taiwan Precision Medicine Society

Redefining Medicine
with Precise Mechanisms,
Promoting Health
with Proactive Tools.

有效鎖定個人基因組合的醫學
Redefining Cancer and Its Treatments

「精準醫學」的成果已經顯示於強大的新發現和針對個人「量身訂製」的新治療方法。例如，因為我們逐漸了解每個人的遺傳組成和解析了腫瘤遺傳變異性，所以對治療腫瘤的方法已產生了革命性的改變。

台灣精準醫學學會的任務

- ✓舉辦精準醫學之學術演講與討論會。
- ✓發行精準醫學之學術論文或出版有關雜誌刊物。
- ✓聯繫公私立醫療及研究機構，從事精準醫學之研究發展及應用。
- ✓參加國際學術活動，藉以促進國際間交流，提高我國在精準醫學的臨床應用與世界接軌。
- ✓舉辦精準醫學教育訓練課程，藉以提高臨床診療應用，以期促進國民健康。

參與「台灣精準醫學學會」跟上快速脈動的精準醫學資訊洪流

「精準醫學」更可以改善我們的健康照護，並加速新穎治療的發展。這些最新進展的快速，雖然令人振奮，也讓我們深感目不暇給，難以跟上快速脈動的資訊洪流。讓我們更加體認到：有必要建立一個「精準醫學」的臨床和學術團體，藉以凝聚參與人員的專長，經由資料流通、經驗分享、和活潑討論，讓「台灣精準醫學學會」的會員不但能獲得最即時和必要的醫學資訊，並能夠將我們的轉譯研究迅速接軌於國際最新水準。

相關科技介紹-1

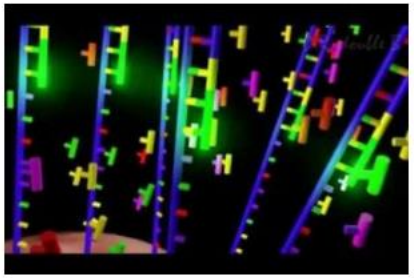
精準醫學科技：醫療大數據分析

Big Data: Biomedicine

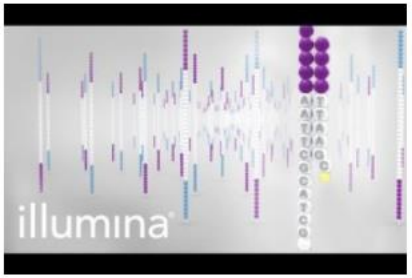
Big Data:The Promise and the Challenge for Personalized Medicine

The Big Data Opportunity in Medicine

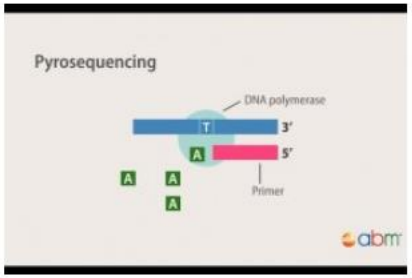
精準醫學科技：次世代定序



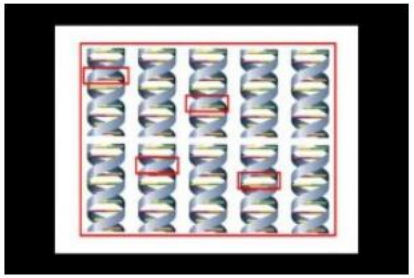
Next Generation Sequencing Animation



Illumina Sequencing by Synthesis (Now in 3D)



Next Generation Sequencing (NGS) – An Introduction



Clinical exome sequencing explained

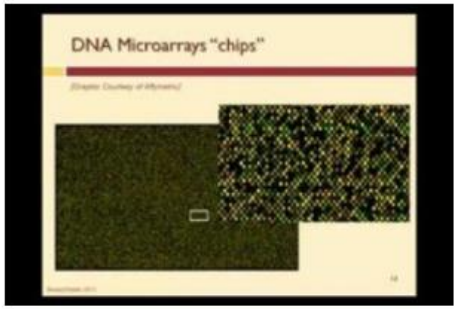
精準醫學科技：定量PCR

相關科技介紹-2

精準醫學科技：基因晶片

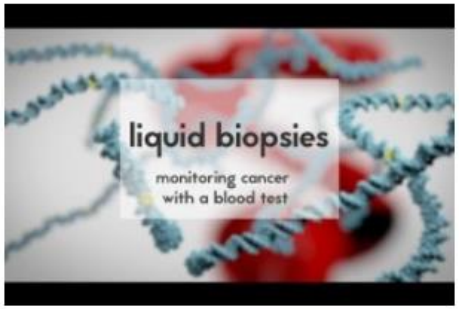
Microarrays vs RNA Sequencing

Microarray Method for Genetic Testing

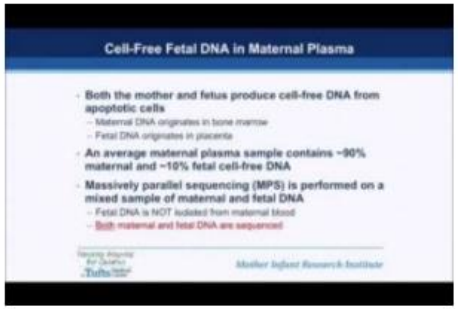


DNA Microarray

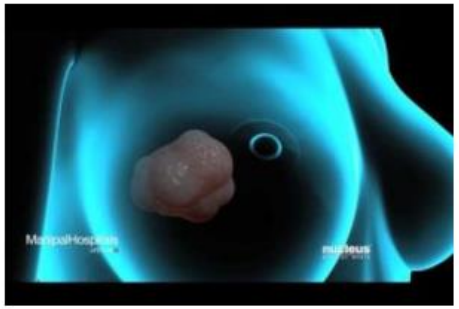
精準醫學科技：應用



Liquid biopsies to monitor cancer



Non-invasive Prenatal Testing (NIPT)



Targeted Cancer Therapy

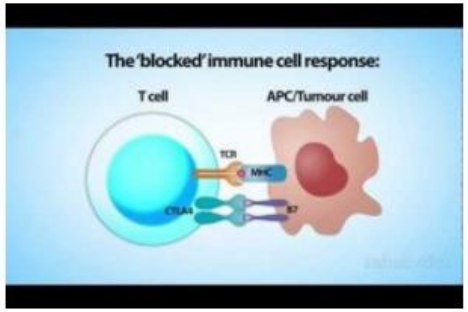
精準醫學科技：蛋白質體學

相關科技介紹-3

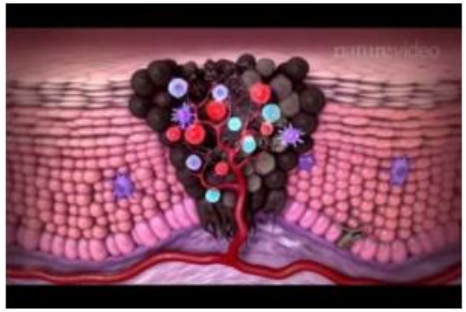
精準醫學科技：表觀遺傳學

Epigenetics

精準醫學科技：免疫治療

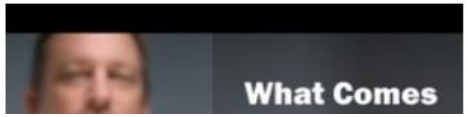


Nature | Cancer Immunotherapy – medical animation



Tumour immunology and immunotherapy

精準醫學科技：穿戴式醫療器具



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台灣精準醫學學會2016年會暨國際研討會

*研討會教育積分 (請於報到處簽到)：

中華民國癌症醫學會
- 腫瘤內科A類3學分
- 腫瘤外科A類3學分

時間 2016/08/14(日) 上午 08:30~下午17:30

地點 財團法人張榮發基金會國際會議中心10F-1001會議室
台北市中正區中山南路11號

Workshop on Immune Oncology
癌症免疫治療學術會議 -2016/12/18(日)

主辦單位: TPMS 台灣精準醫學學會 Taiwan Precision Medicine Society

2017 液態切片研討會
-Workshop on Liquid Biopsy

2017/04/16(日)

地點:台灣大學醫學院102講堂

主辦單位: TPMS 台灣精準醫學學會 Taiwan Precision Medicine Society









「2017.04.23 精準醫學專家會議 」，多項重大議題獲得媒體傳播

會員專屬繼續教育

台灣精準醫學學會
Taiwan Precision Medicine Society

首頁 關於學會 最新消息 精準醫學科技 新知分享 各界迴響 推薦影片 成為會員 相關連結 會員專區 團體會員資訊服務

會員名錄

2017 液態切片研討會演講影片

2016 癌症免疫治療學術會議演講影片

2016 台灣精準醫學學會年會暨國際研討會演講影片

2016 台灣精準醫學論壇演講影片

2015 台灣精準醫學論壇演講影片

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台灣精準醫學學會2017年會暨國際研討會

時間 2017/08/20（日） 08:30~17:00

地點 台灣大學公共衛生學院101講堂
台北市中正區徐州路17號

研討會教育積分 (請於報到處簽到)：
- 台灣臨床病理檢驗醫學會-5.5分
- 台灣放射腫瘤學會-5分

各學會積分陸續申請中，
積分申請更新請見台灣精準醫學學會官網

時間	講題	講者
08:30-08:50	報到	
08:50-09:00	Opening	張廷彰理事長 台灣精準醫學學會
09:00-09:50	Opportunities and Challenges of Precision Medicine Industry in Taiwan	Johnsee Lee, PhD Chairman, Taiwan Biotech Industry Organization
09:50-10:40	Precision cancer management: experience and challenges in Taiwan	Sue-Jen Chen, PhD. Chief Scientific Officer, ACT Genomics
10:40-11:00	Coffee break	
11:00-11:30	Next Generation Sequencing: Precision Medicine's Secret Weapon in Winning the Fight Against Cancer	Jee Hian Lim, Senior Manager, Market Development Oncology, Illumina, Singapore
11:30-12:00	Circulating tumor DNA - From bench to bedside	Eric Yu, PhD. Medical Science Liaison, Roche-Foundation Medicine,Hong Kong
12:00-12:30	Special Lecture New Frontier of Ovarian Cancer Treatment : PARP inhibitors	張志隆 主任 馬偕醫院婦產部婦科癌症學科

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台灣精準醫學學會2017年會暨國際研討會

時間 2017/08/20 (日) 08:30~17:00

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各學會積分陸續申請中，
積分申請更新請見台灣精準醫學學會官網

12:30-13:30	Lunch and Annual meeting of TPMS	
海峽兩岸精準醫學交流		
13:30-14:00	Clinical impact of Circulating tumor cells (CTC) detection	劉東戈 教授 衛生部北京醫院
14:00-14:30	Mutational analysis of hematological disorders by next generation sequencing	汝昆 教授 中國醫學科學院血液病醫院
14:30-15:00	Coffee break	
Clinical applications		
15:00-15:20	Precision Maternal-Fetal Medicine in Taiwan	蕭慶華 醫師 台灣母胎醫學會理事長
15:20-15:40	Gene expression prognostic and predictive profiles in early-stage NSCLC	吳玉琮 主任 台北榮總胸腔外科
15:40-16:00	21-gene Recurrence Score assay	王明暘 醫師 臺大醫院乳房外科
16:00-16:20	Application of precision medicine in the management of hematological malignancies	葉士芃 主任 中國醫藥大學附設醫院血液腫瘤科
16:20-16:40	Application of PDX in Nasopharygneal carcinoma research	徐正龍 醫師 林口長庚醫院腫瘤科
16:40-16:50	Panel Discussion	
16:50-17:00	Closing	

The Applications of Mass Spectrometry in Precision Medicine

預告

Taiwan Precision Medicine Society (2017-10-1)

(Tentative agenda)

Time	Topic	Speaker	Moderator
08:10-08:30	報到		
08:30-08:40	Opening	張廷彰教授 台灣精準醫學學會理事長 長庚醫院婦產部部長	
08:40-09:40	Keynote Lecture Mass Spectrometry in Clinical Care: about Drugs, Biomarkers and Proteomics	Erik van Maarseveen PhD. PharmD. University Medical Center Utrecht	和信癌症醫院 方麗華藥師
09:40-10:00	休息時間(coffee break)		
10:00-10:50	The use of metabolomics in management of heart failure patients (tentative)	王兆弘 MD. 基隆長庚醫院 心臟衰竭中心主任	基隆長庚醫院 吳俊德副院長
10:50-11:40	The use of metagenomics and metabolomics in management of pediatric asthma (tentative)	邱志勇 MD. 基隆長庚醫院 兒科主治醫師	台北病理中心 顧文輝醫師
11:40-11:50	Closing		

邀請您點閱

台灣精準醫學學會網頁:

www.tpms.org.tw

感謝聆聽

歡迎指正