



代謝物與個人健康

T-CHO	總膽固醇	<200	mg/dL
LDL-C	低密度脂蛋白 (壞膽固醇)	<130*	mg/dL
HDL-C	高密度脂蛋白 (好膽固醇)	>40	mg/dL
TG	三酸甘油酯	<150	mg/dL

今週刊

代謝體 (代謝組) 又是啥 ?



Roche Diabetes





大綱

🧬 代謝體/代謝組（學）是什麼？可以吃嗎？

🧬 Taiwan Biobank 提供了哪些代謝體學資源？

🧬 有什麼應用實例？





小小民調

🧠 您知道代謝體/代謝組 (學) 是什麼嗎？



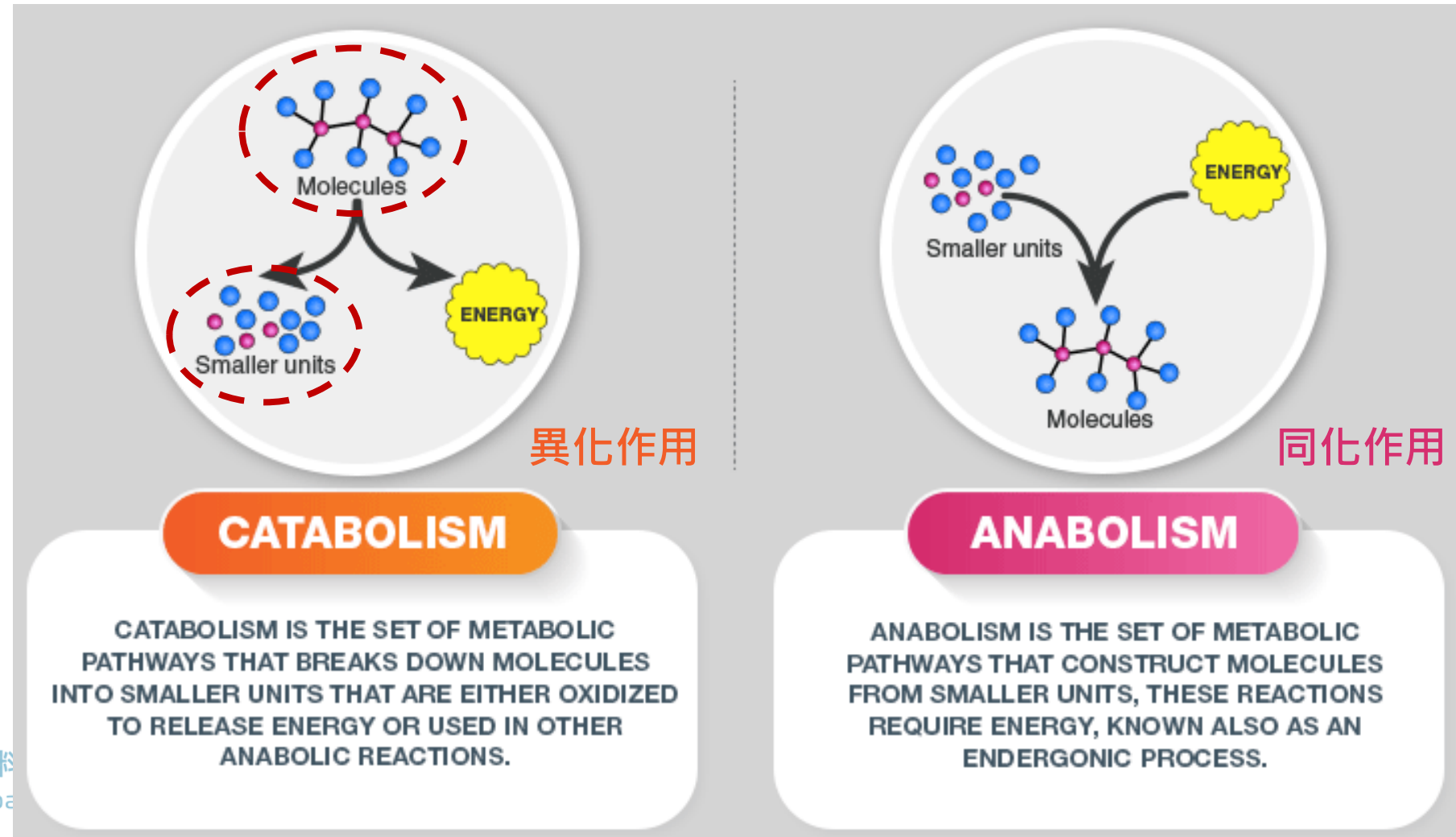
代謝是什麼？

<https://byjus.com/biology/differences-between-catabolism-and-anabolism/>

代謝物：“Made or used when the body breaks down food, drugs or chemicals, or its own tissue.”

NCI Cancer Dictionary

代謝體：所有代謝物。





觀念演進 – 小分子？大分子？

- 以前的代謝體：以各別小分子（分子量 < 1 kD）為主
- 現在的代謝體：打破分子大小的界線，例如醣綴合物（glycoconjugates）→ 看到「黏」在蛋白上的醣。



什麼是代謝體學（結論：不可以吃喔！）

Combining Genomics, Metabolome Analysis, and Biochemical Modelling to Understand Metabolic Networks. Oliver Fiehn. *Comp Funct Genom* 794(3), 155-68, 2001 **(Not indexed by JCR)**

Metabolomics: “comprehensive and quantitative analysis of all metabolites” “of the biological system under study”.

Metabonomics: Understanding The Metabolic Responses of Living Systems to Pathophysiological Stimuli via Multivariate Statistical Analysis of Biological NMR Spectroscopic Data. Jeremy K. Nicholson, John C. Lindon and Elaine Holmes. *Xenobiotica* 29(11), 1181-9, 1999 **(Impact factor: 1.9)**

Metabonomics: “the quantitative measurement of the dynamic multiparametric metabolic response of living systems to pathophysiological stimuli or genetic modification”.





小小民調 (二)

🧠 您曾在自己的研究課題中，用過（或收集過）代謝體學資料嗎？

ChatGPT 5.5 臆測 – 核心使用者：

全球 15,000 人

台灣約 150 人





為什麼要研究代謝體？

- 🧠 生物功能的直接 readout，反映實際的生理狀況。
- 🧠 連結各種 omics 的樞紐，例如：受到環境暨生活型態因子影響，對於了解 gene-environment interaction、personalized nutrition、exposomics 極為重要。
- 🧠 通常比臨床變化（甚至蛋白質體變化）更早顯現，可用於早期診斷。例如：糖尿病。
- 🧠 高轉譯價值，也可用於基礎的機轉研究。



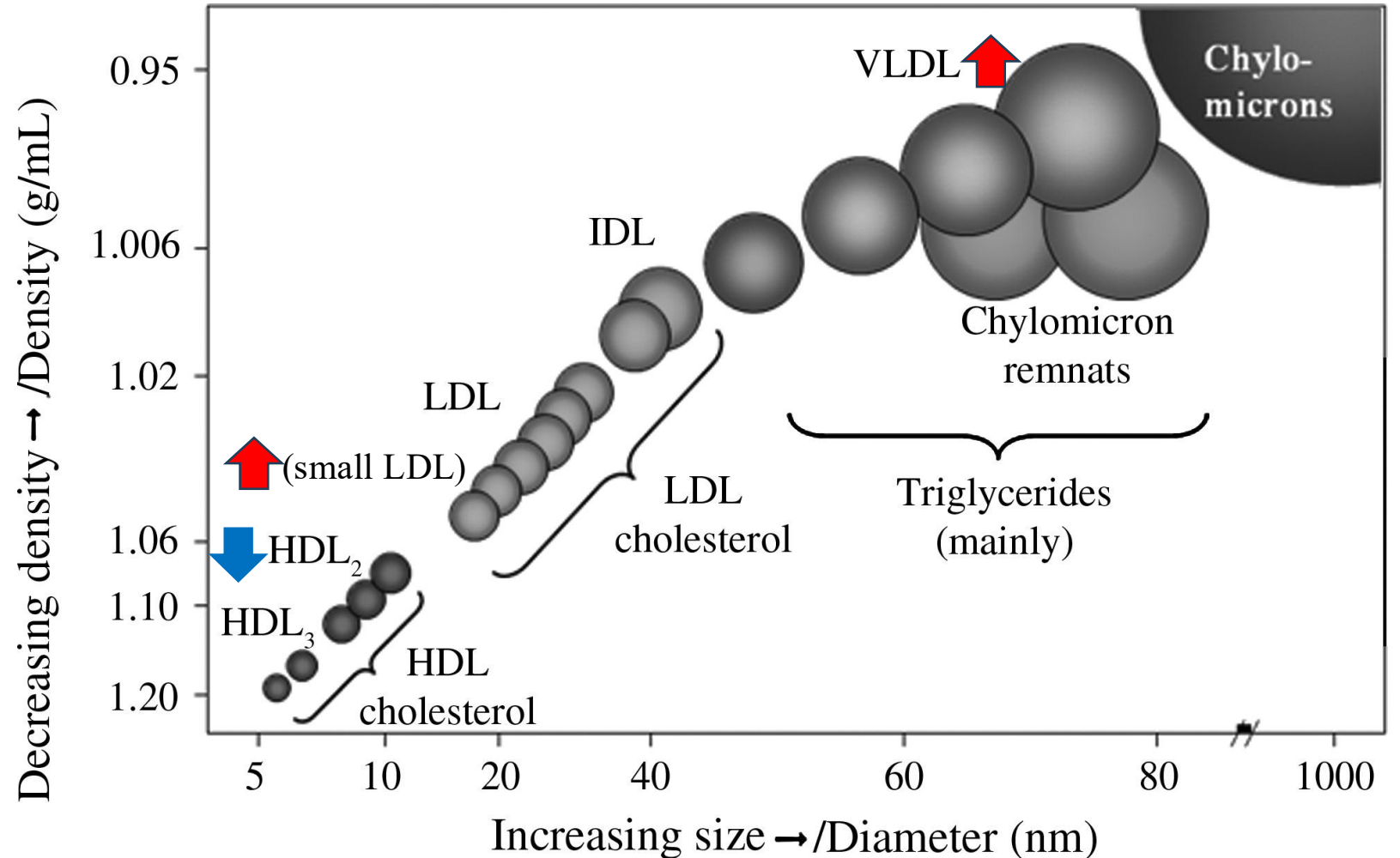


案例：脂蛋白分級

Frazier-Wood, A.C., et al. Metabolic Syndrome and Related Disorders, 2012, 10:4, 244-251

胰島素耐受性 (Insulin Resistance, IR)

- 與脂蛋白分級有關
- 與LDL-C、total cholesterol 無關
- 可預測 (!)



Understanding the NMR LipoProfile® Test Report

LDL-P

- LDL-P is the direct measure of low density lipoprotein particles - the causal link between high levels of LDL-P and development of cardiovascular disease (CVD) is well established.
- Studies have demonstrated per-particle cholesterol amount varies in patients with type II diabetes, statin-treated patients, and those with cardiometabolic risk factors (CMR) listed below:^{1,2,3}

Age: men ≥ 45 yrs, women ≥ 55 yrs)⁴
Elevated BP: ($\geq 130/\geq 85$ mmHg; on antihypertensive medication)⁵
Abdominal obesity/waist circumference: male $\geq 40"$ (Asian $\geq 35"$), female $\geq 35"$ (Asian $\geq 31"$)⁵
Elevated triglycerides: (≥ 150 mg/dL), low HDL (men < 40 mg/dL, women < 50 mg/dL), increased numbers of small dense LDL particles,^{2,5} on drug treatment for elevated triglycerides or HDL-C
Elevated fasting blood glucose: (≥ 100 mg/dL),⁵ on drug treatment for elevated glucose
Insulin resistance: (IR)³

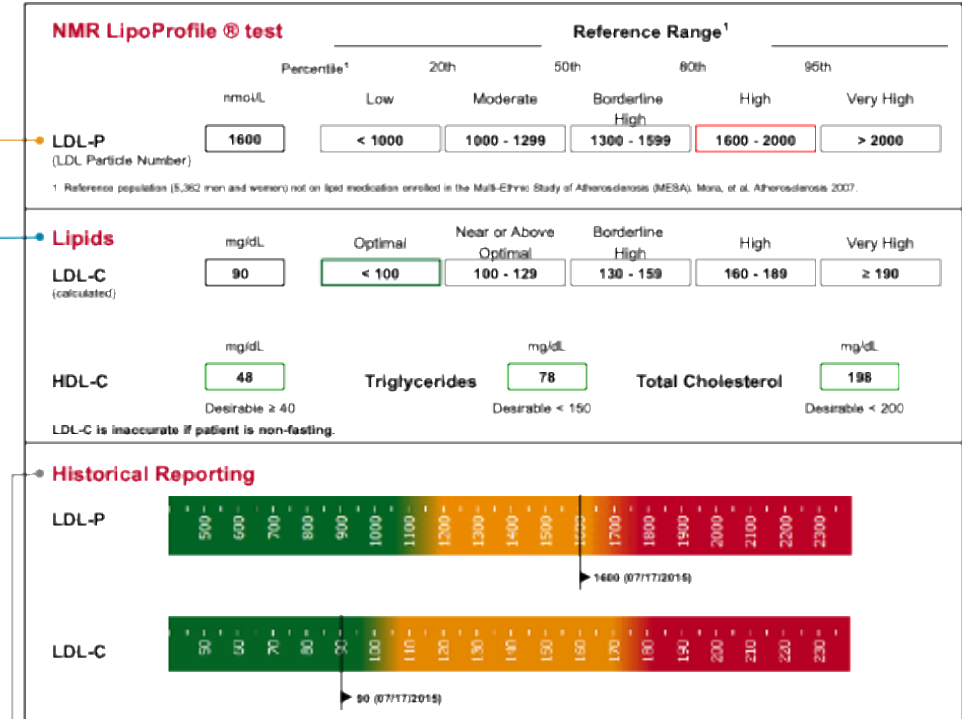
- Many expert panels recommend use of LDL-P values to optimize treatment decisions in these at-risk patients.^{1,6}
- NMR LipoProfile® Test is FDA cleared for use in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with CVD.⁷

Lipids

- Traditional lipid panel includes LDL-C, HDL-C, triglycerides and total cholesterol.
- Whether calculated or measured directly, LDL-C is an estimate of the amount of cholesterol contained within LDL-P.¹

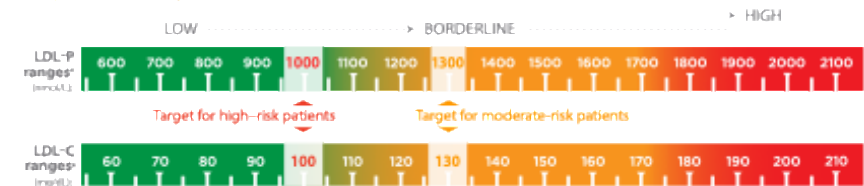
Historical Reporting

Patient LDL-P and LDL-C values and dates of services are tracked over time, providing opportunities for clinician/patient discussions regarding treatment strategies



Personalized LDL Management

Targets of Therapy (Adapted with permission from International Guidelines Center)



美國FDA許可之臨床檢測

評估心血管疾病風險之用





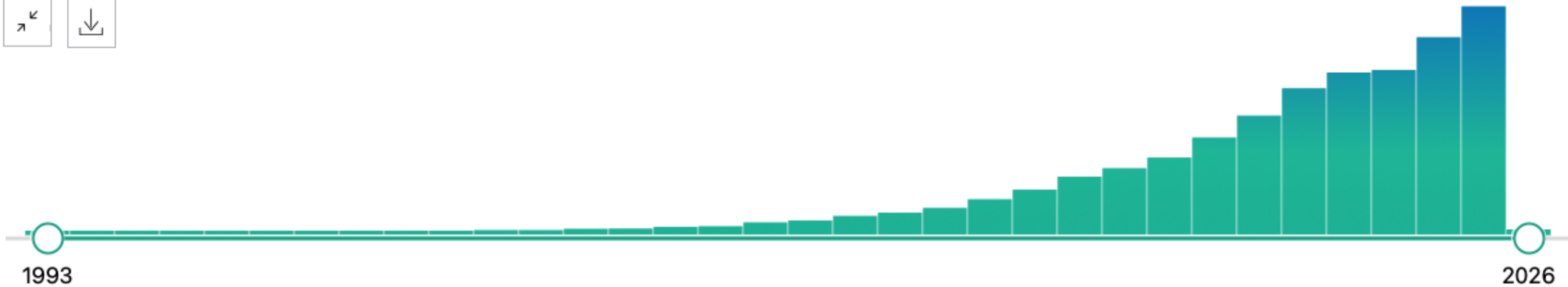
人體代謝體學研究方興未艾

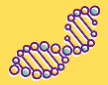
PubMed search: “(metabolomic OR metabolome OR metabolomics OR metabonomic OR metabonomics) AND clinical”

RESULTS BY YEAR

30,068 results

Page 1 of 3,007





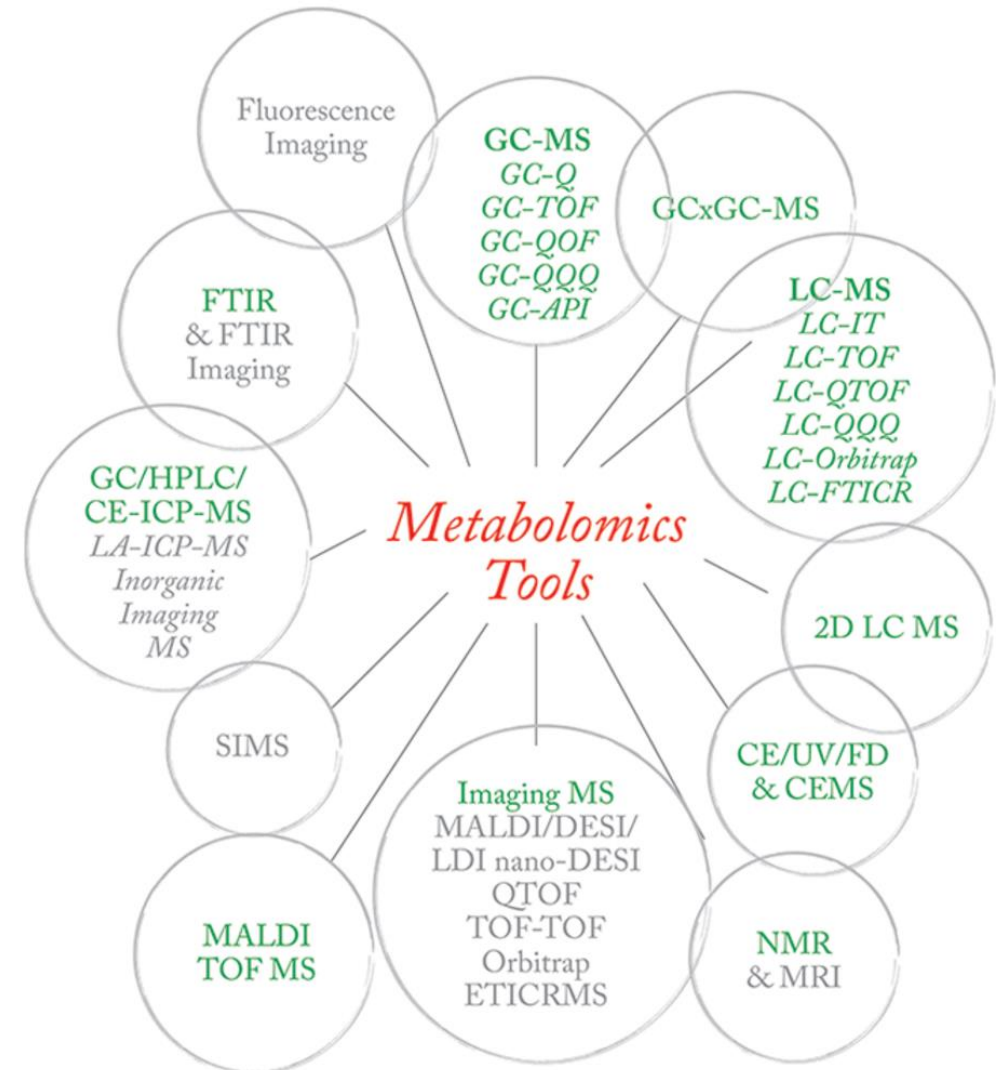
代謝體學資料的完整性？

- 「完整」的代謝體學資料需藉由多種互補的實驗技術方能達成。
- The invisible metabolome – 許多預期存在的代謝物尚未被偵測到。

(2023) ~ **20,000 detected metabolites**

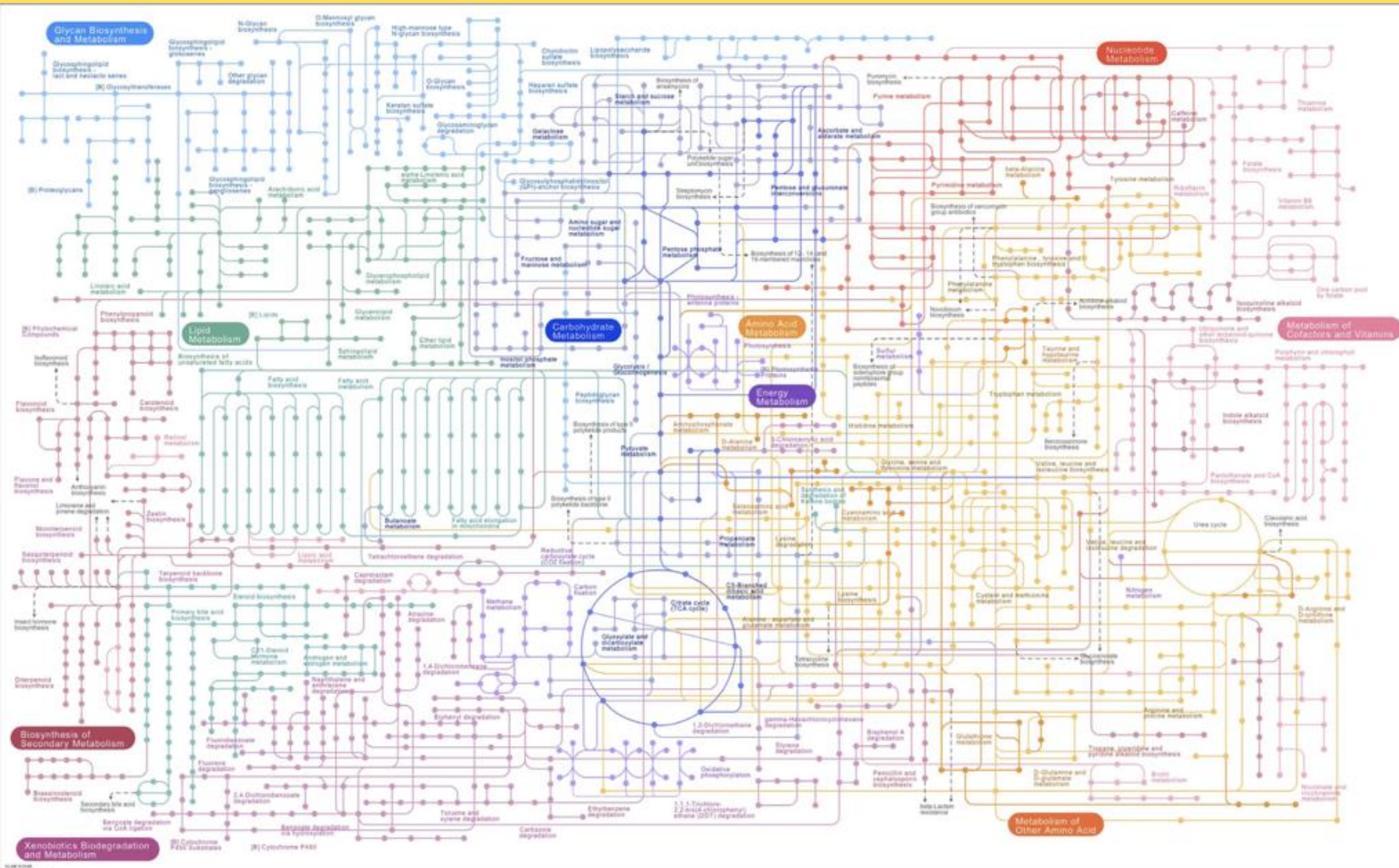
3,444 quantified metabolites

~ **100,000 expected metabolites**





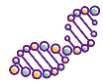
利用代謝路徑特性尋找「切入點」



變化會傳遞，可利用觀察得到的代謝物，反向設計研究方法。

Taiwan Biobank 提供「切入點」而非前面性的代謝體學資訊。

https://www.reddit.com/r/MapPorn/comments/pw8id/map_of_the_human_metabolic_pathways_2997x1849/



Taiwan Biobank 的代謝體學資源

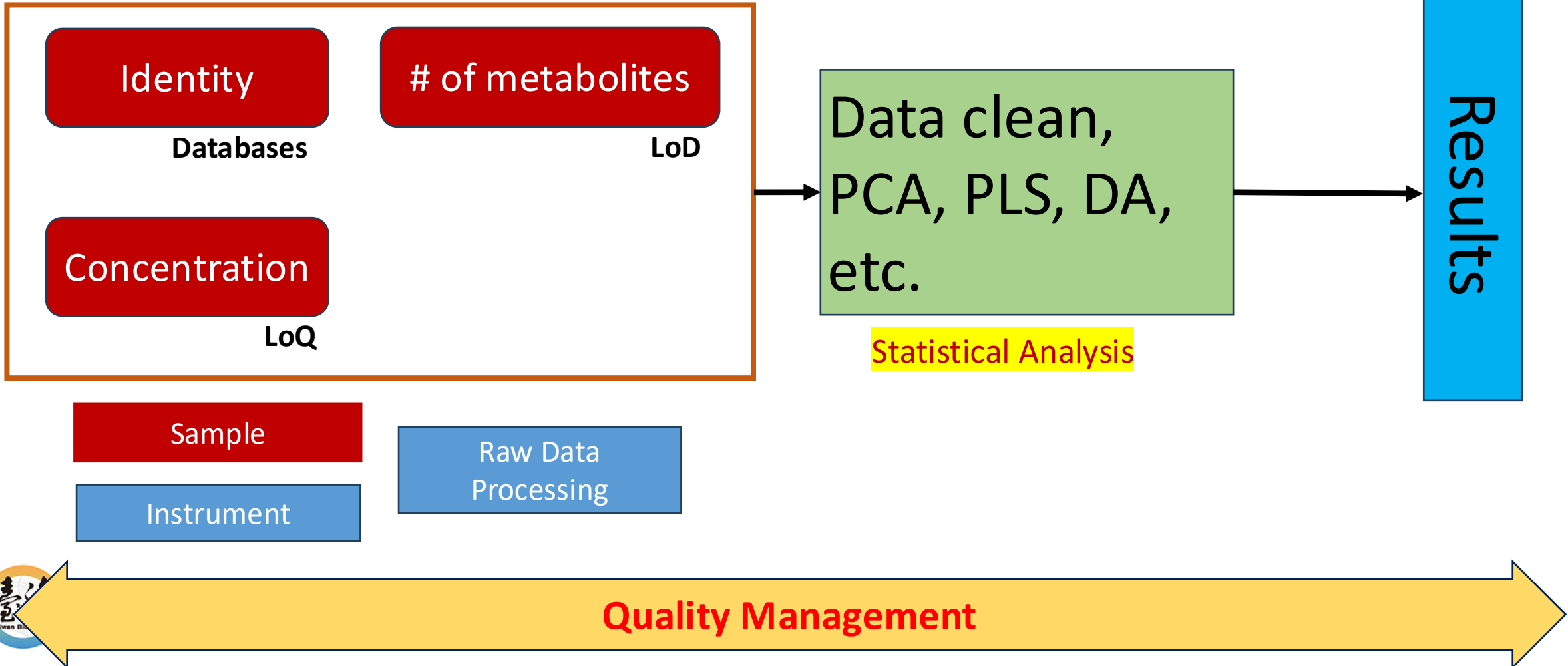
- 血漿資料為主
- 血漿塑化劑資料
- 少量測試用的尿液資料
- 檢體





代謝體資訊是怎樣收集的？

Design Experiments – **What do you want to see?**



Quality Management

科學重現性危機 – Replication Crisis

70%

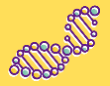
of researchers
can't reproduce
another scientist's
results



1 in 2

scientists say they've **failed to reproduce**
their own results





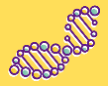
一個 biobank 的考量

🧠 很多人會用這些資料 → 資料的可重現性為最優先

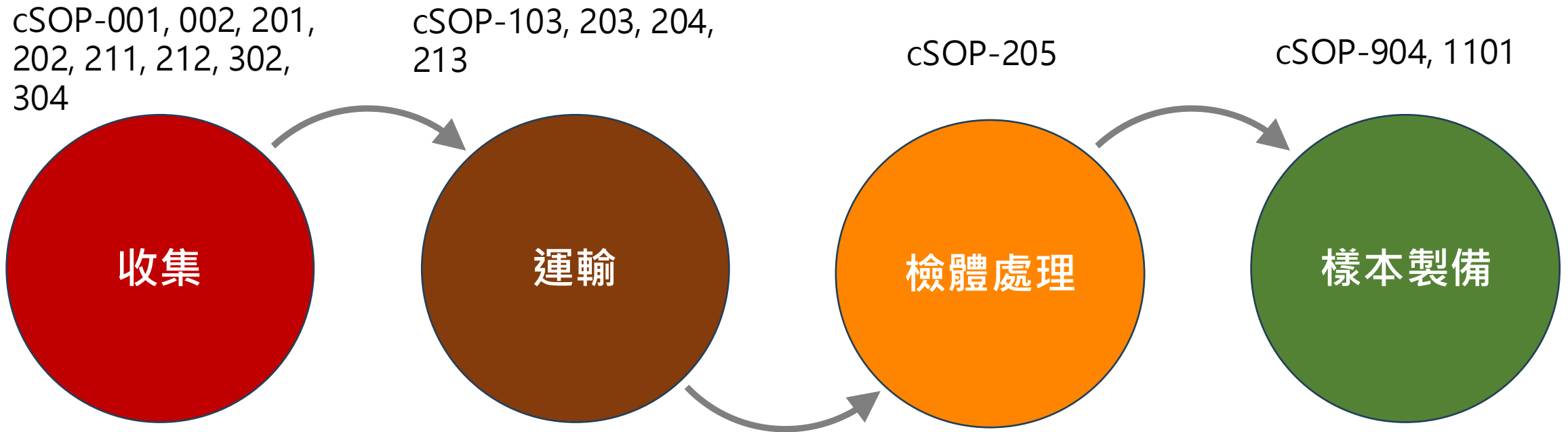
🧠 可重現性取決於檢體的品質、樣本製備的技術、量測儀器的特性、操作員的能力，缺一不可 → 了解各項環節，建立SOP、以技術為本位

🧠 高通量 → 低成本、快速的實驗、自動化的分析





源頭流程標準化



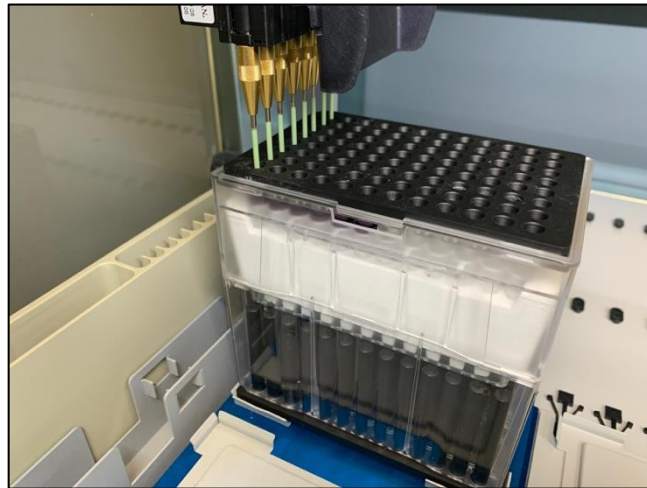
多駐站，單一標準

- 避免 garbage in, garbage out





樣本處理與資料收集自動化



Tecan Freedom EVO
Liquid Handler



Bruker IVDr-NMR system



中央研究院 · 臺灣人體生物資料庫
Academia Sinica · Taiwan Biobank

BRUKER

1 Alcohols and derivatives

Compound	Conc.	LOD	r	ρ	Δ	95% Range	Graphics (*)
	mmol/L	mmol/L	mmol/L	%	mmol/L	mmol/L	
Ethanol	< 0.10	0.10	0.000	0	2.971	≤ 0.82	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

2 Amines and derivatives

Compound	Conc.	LOD	r	ρ	Δ	95% Range	Graphics (*)
	mmol/L	mmol/L	mmol/L	%	mmol/L	mmol/L	
Trimethylamine-N-oxide	< 0.08	0.08	0.004	97	0.051	≤ 0.08	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

3 Amino acids and derivatives


Compound	Conc.	LOD	r	ρ	Δ	95% Range	Graphics (*)
	mmol/L	mmol/L	mmol/L	%	mmol/L	mmol/L	
2-Aminobutyric acid	< 0.05	0.05	0.000	0	0.725	≤ 0.10	
Alanine	0.35	0.02	0.353	100	0.010	0.29 - 0.64	
Asparagine	< 0.05	0.05	0.000	0	4.894	≤ 0.08	
Creatine	< 0.01	0.01	0.005	100	0.002	≤ 0.07	
Creatinine	0.09	0.01	0.090	100	0.002	0.06 - 0.14	
Glutamic acid	0.20	0.05	0.200	52	0.057	≤ 0.24	
Glutamine	0.55	0.02	0.550	84	0.075	0.30 - 0.83	
Glycine	0.21	0.01	0.211	100	0.002	0.17 - 0.44	
Histidine	0.16	0.02	0.163	99	0.007	0.07 - 0.16	
Isoleucine	0.04	0.03	0.041	94	0.008	0.03 - 0.11	
Leucine	0.08	0.01	0.083	96	0.012	0.07 - 0.20	
Lysine	0.22	0.04	0.223	78	0.057	≤ 0.29	
Methionine	< 0.05	0.05	0.011	97	0.001	0.05 - 0.13	
N,N-Dimethylglycine	< 0.01	0.01	0.001	96	0.000	≤ 0.01	
Ornithine	< 0.02	0.02	0.008	20	0.062	≤ 0.16	
Phenylalanine	0.06	0.03	0.056	98	0.003	≤ 0.07	
Proline	0.46	0.05	0.465	84	0.111	≤ 0.59	
Sarcosine	0.02	0.01	0.019	86	0.005	≤ 0.01	
Threonine	< 0.04	0.04	0.000	0	2.902	≤ 0.24	
Tyrosine	0.04	0.03	0.044	96	0.005	≤ 0.08	
Valine	0.21	0.03	0.213	100	0.005	0.15 - 0.35	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

Sample: 20210910D3-2,expno10,100000,10r 3 / 7

自動化的報告生成

為什麼不以 LC-MS 為主？-各項因素的妥協

 LC (液相管柱層析) 所用的管柱會髒、會更新換代，所以無法保證其分離結果的重現性。

 需要每次都做 calibration curve。

 MS (質譜) 過於靈敏，樣本保存的環境變化也會影響其結果。

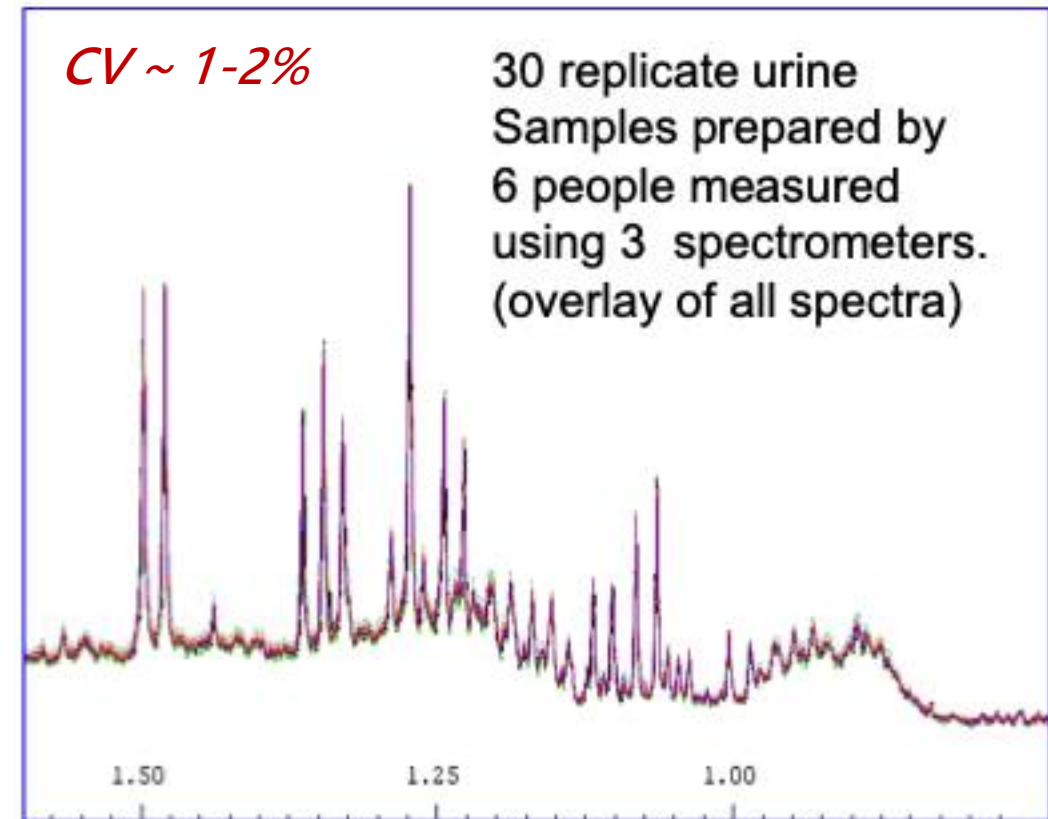
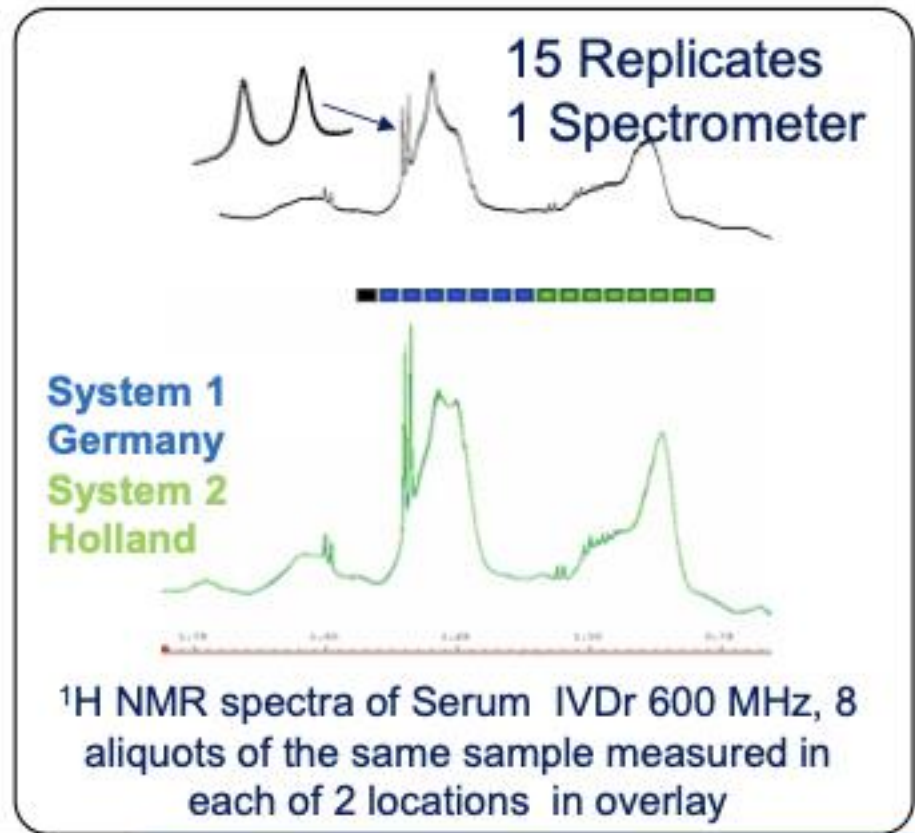
 人員：懂 NMR，不那麼懂 MS。

 「名人效應」：UK Biobank 首選以 NMR 收集代謝體資料，而未選擇 LC-MS。

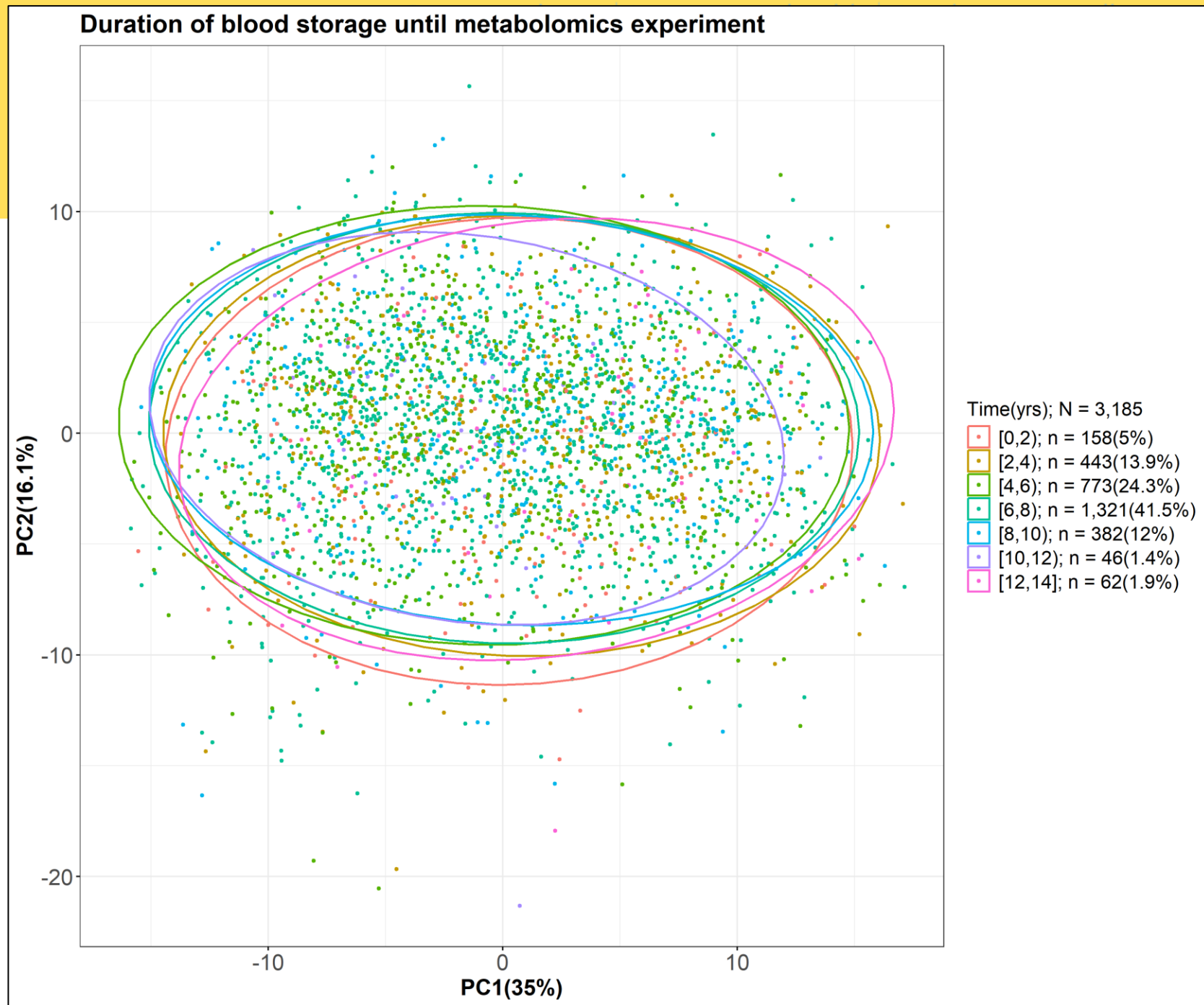


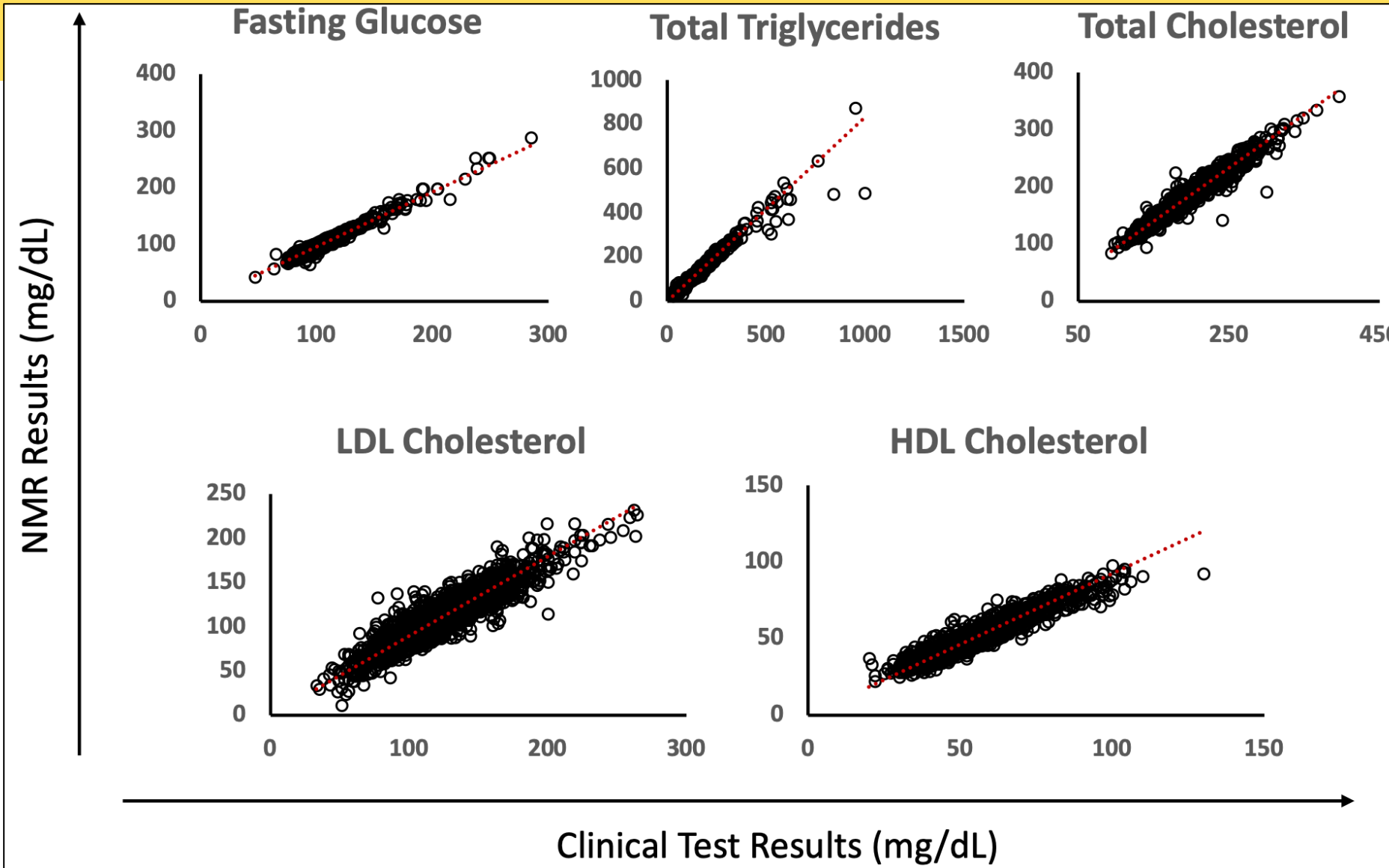


磁共振光譜具有高重現性



血漿檢體冷凍儲存時間對整體代謝物濃度的影響，相當小





🧠 以 NMR 量測數值
接近臨床檢驗數
值。

$N = 1,195$

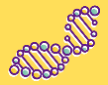


藥物合成及分析 – 核磁共振子核心

Bruker IVDr provides automatic identification on:

- 41 metabolites in **Plasma**/Serum
- 150 metabolites in **Urine**
- 115 Lipoprotein parameters in **Plasma**/Serum
- Analysis for CSF (腦脊髓液) is coming

🧪 若研究人員遵循同樣的收案與樣本處理 SOP，實驗結果可與 Taiwan Biobank 的資料直接比較。



代謝體學交付資料

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
2-Aminobutyric acid	< 0.05	0.05	0.021	0 ○	0.108	≤ 0.10	
Alanine	0.33	0.02	0.335	100 ●	0.010	0.29 - 0.64	
Asparagine	< 0.05	0.05	0.000	0 ○	4.510	≤ 0.08	
Creatine	< 0.01	0.01	0.005	99 ●	0.003	≤ 0.07	
Creatinine	0.07	0.01	0.074	99 ●	0.003	0.06 - 0.14	
Glutamic acid	0.08	0.05	0.076	15 ○	0.055	≤ 0.24	
Glutamine	0.58	0.02	0.575	90 ○	0.073	0.30 - 0.83	
Glycine	< 0.01	0.01	0.000	0 ○	0.235	0.17 - 0.44	

41 metabolite concentrations

- Alcohols and derivatives
- Amines and derivatives
- Amino acids and derivatives
- Carboxylic acids
- Essential nutrient
- Keto acids and derivatives
- Sugars and derivatives
- Sulfones
- Technical additives

115 Lipoprotein subclass analysis

- 6 VLDL subclasses, 6 LDL subclasses, 4 HDL subclasses, IDL
- Particle number, cholesterol, triglyceride content, free cholesterol content, Apo A1, Apo A2, Apo B100, various ratios





代謝體學交付資料 – 解讀

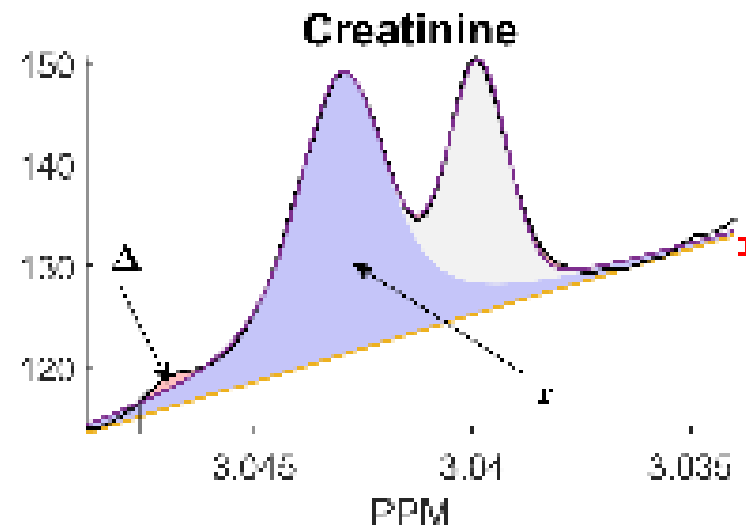
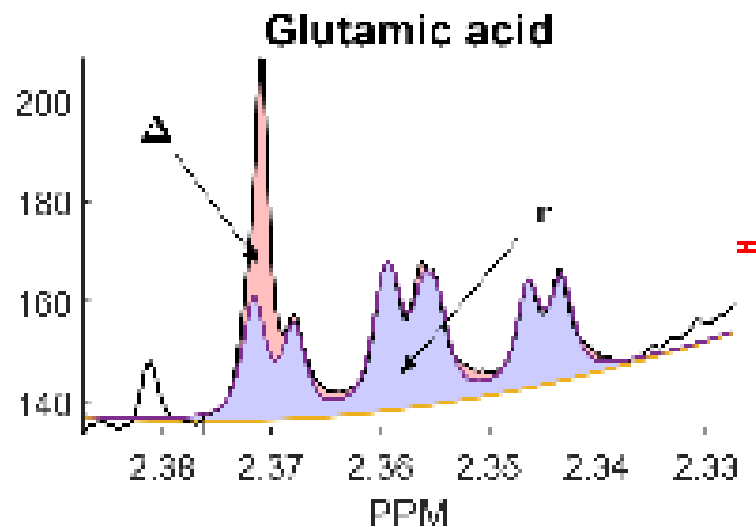
Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
2-Aminobutyric acid	< 0.05	0.05	0.021	0 ○	0.108	≤ 0.10	
Alanine	0.33	0.02	0.335	100 ●	0.010	0.29 - 0.64	
Asparagine	< 0.05	0.05	0.000	0 ○	4.510	≤ 0.08	
Creatine	< 0.01	0.01	0.005	99 ●	0.003	≤ 0.07	
Creatinine	0.07	0.01	0.074	99 ●	0.003	0.06 - 0.14	
Glutamic acid	0.08	0.05	0.076	15 ○	0.055	≤ 0.24	
Glutamine	0.58	0.02	0.575	90 ○	0.073	0.30 - 0.83	
Glycine	< 0.01	0.01	0.000	0 ○	0.235	0.17 - 0.44	

🧠 Taiwan Biobank 讓研究人員自行衡量數值的準確性與是否要採用。

🧠 各項數值的解釋，在報告的「10 Explanations」中。

🧠 建議：

- 🧠 低於 LOD – 不採用
- 🧠 低 ρ 與高 Δ – 不採用



也提供彙整後的資料集 CSV 檔


	A	B	C	D	E	F	G	H	I	J
1	MTBB_ID	Exp_Batch	Ethanol	Trimethylami	2-Aminobuty	Alanine	Asparagine	Creatine	Creatinine	Glutamic
2	MTBBxxxxx	20211005	0.75	0	0	0.28	0	0.02	0.09	0
3	MTBBxxxxx	20211006	1.5	0	0	0.42	0	0.05	0.06	
4	MTBBxxxxx	20211007	0	0	0	0.3	0	0.02	0.07	0
5	MTBBxxxxx	20211008	0	0	0	0.28	0	0.02	0.09	0
6	MTBBxxxxx	20211009	0	0	0	0.35	0	0.01	0.08	0
7	MTBBxxxxx	20211010	0.46	0	0	0.35	0	0.01	0.08	0
8	MTBBxxxxx	20211011	0.49	0	0	0.33	0	0	0.07	0
9	MTBBxxxxx	20211011	0	0	0	0.32	0.12	0	0.09	0
10	MTBBxxxxx	20211011	0	0	0	0.31	0	0.03	0.05	0
11	MTBBxxxxx	20211012	0	0	0	0.52	0	0.03	0.07	0
12	MTBBxxxxx	20211013	0	0	0.06	0.45	0	0.05	0.06	0
13	MTBBxxxxx	20211013	0	0	0.06	0.27	0	0.03	0.08	0
14	MTBBxxxxx	20211014	0	0	0.05	0.23	0	0.05	0.04	0
15	MTBBxxxxx	20211015	0	0	0	0.4	0.05	0.02	0.07	0

單位：mM



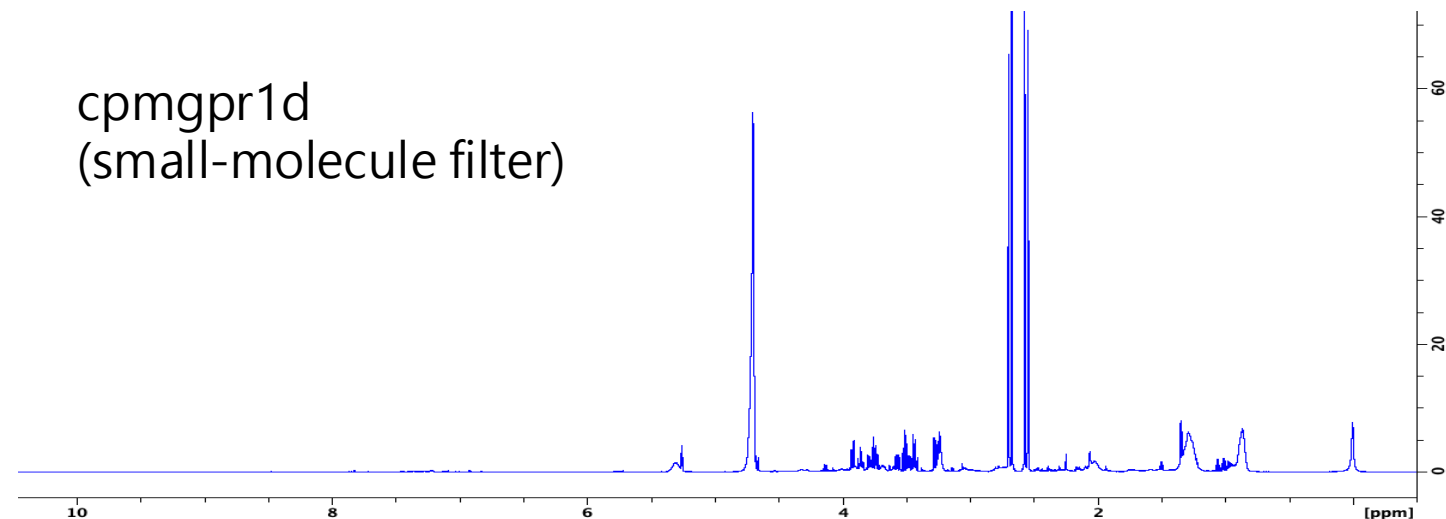
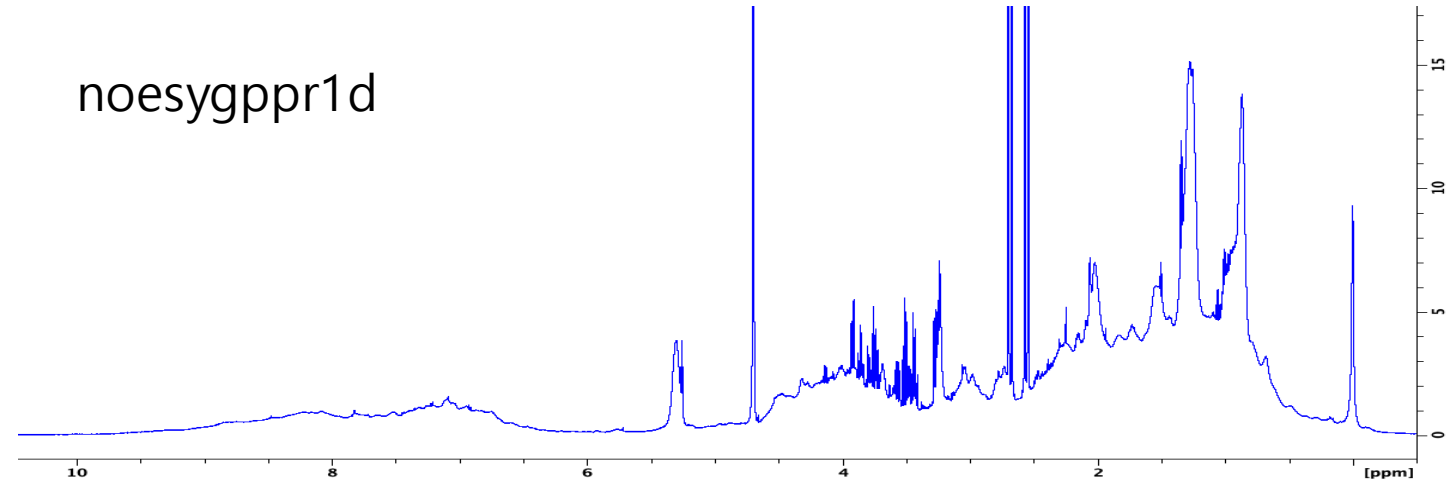
代謝體交付資料 – Raw Data (選用)

 可提供 raw data

 適用於：

 未知 (未確認) 的訊號分析

 方法學的开发





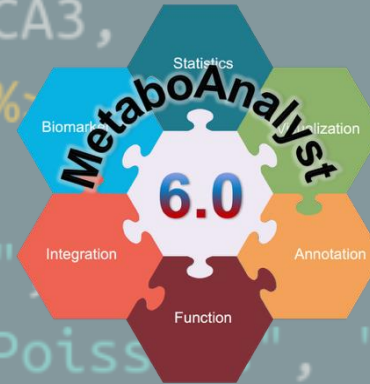
開放資料 – Taiwanview

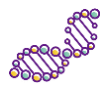
 <https://taiwanview.twbiobank.org.tw/metabolomeT.php>





分析用的軟體與網站





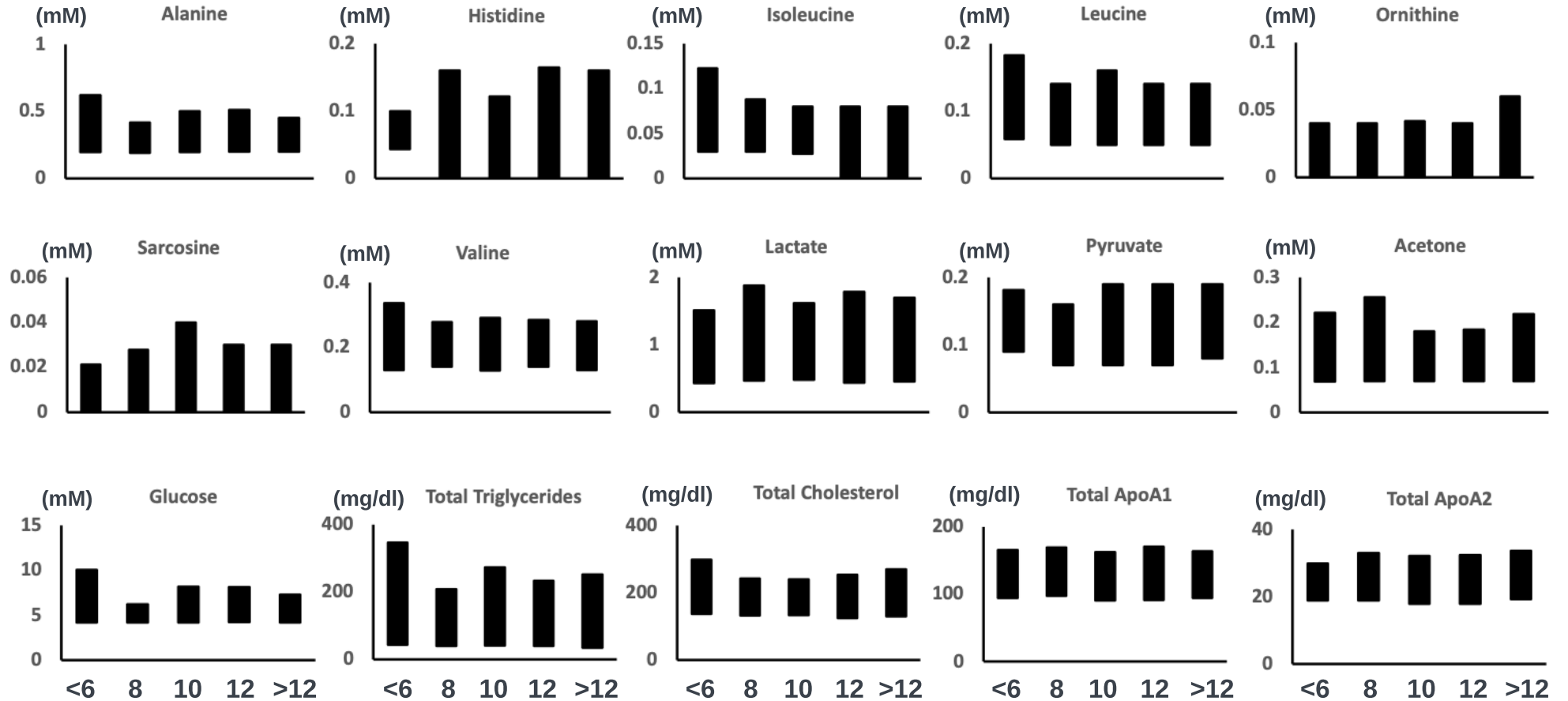
磁振代謝體學資料集應用實例

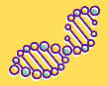




血漿代謝物濃度 vs. 禁食時間

N = 1,195

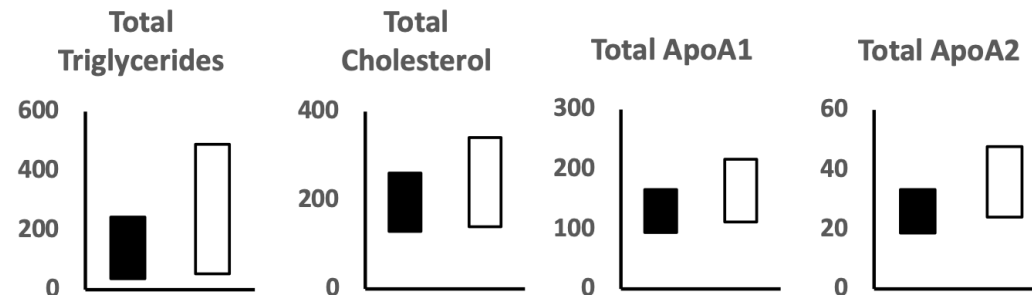
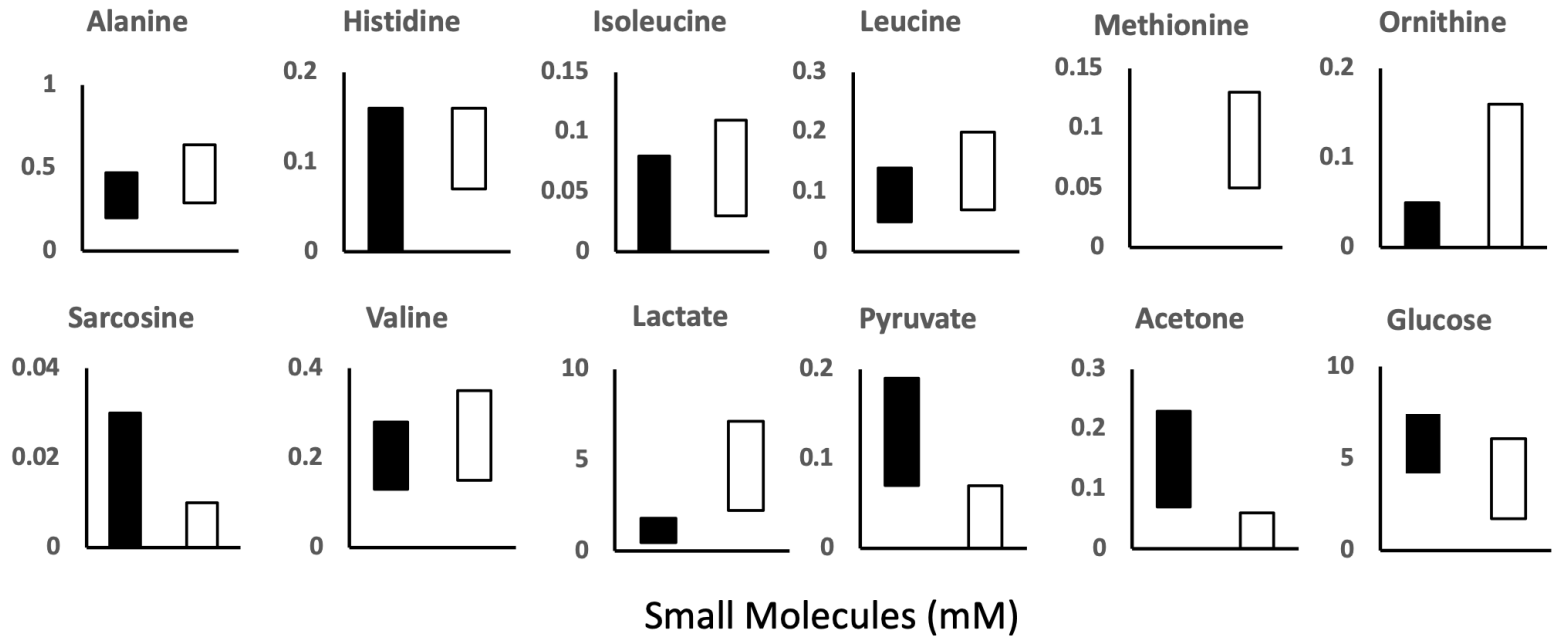




人口群代謝狀況與特色

不同人種的血漿代謝物濃度範圍不同

95% concentration range of blood plasma metabolites from Taiwan Biobank participants compared to vendor-provided Caucasian data.



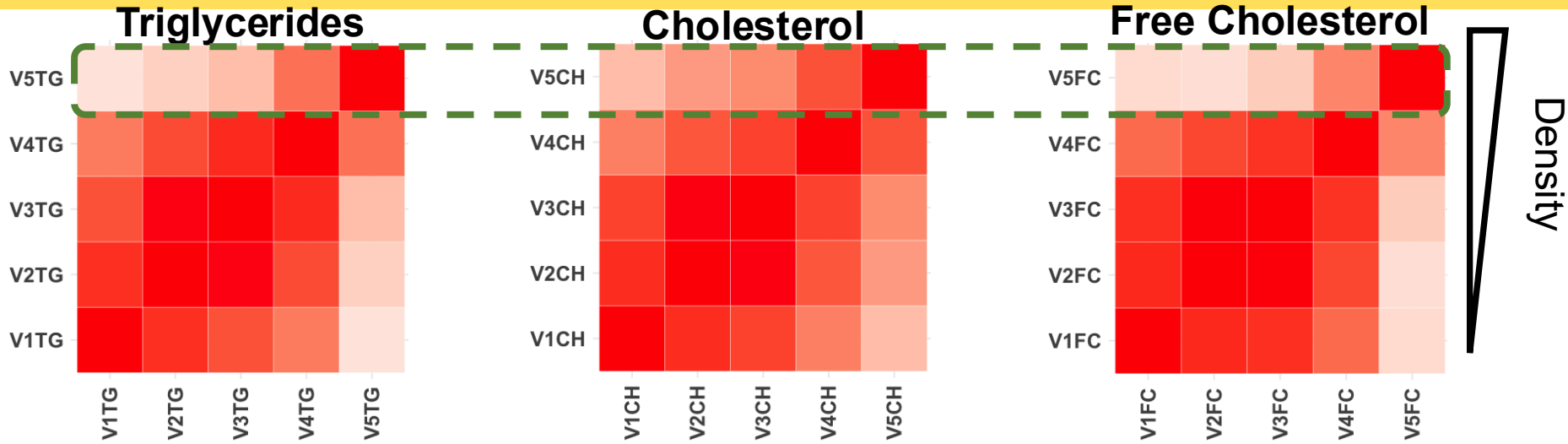
■ Taiwan Biobank data (N = 1195)
□ Caucasian data from vendor report



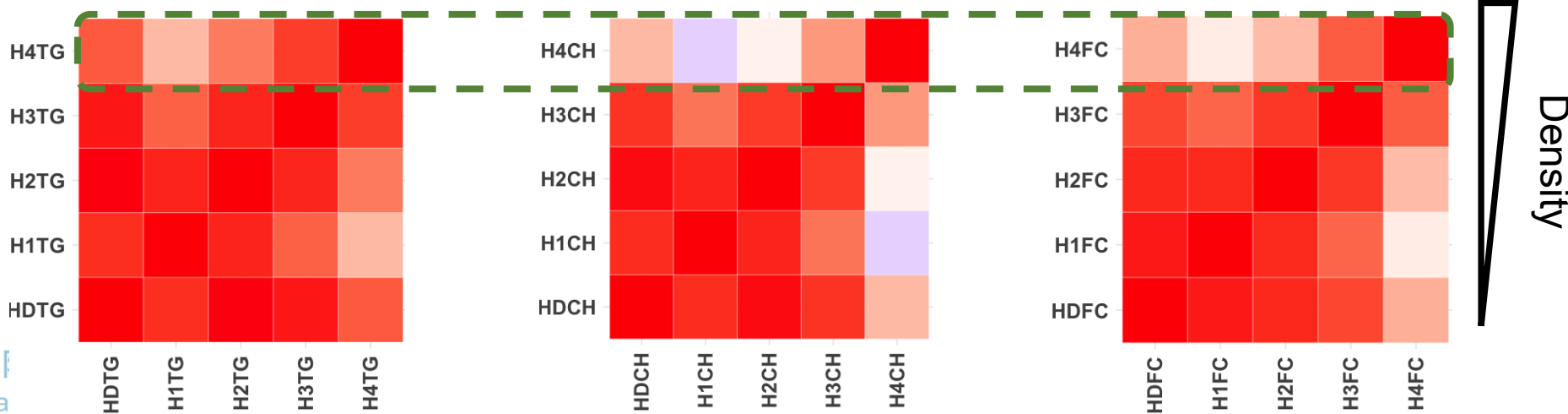


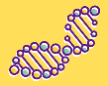
脂蛋白分型觀察

VLDL

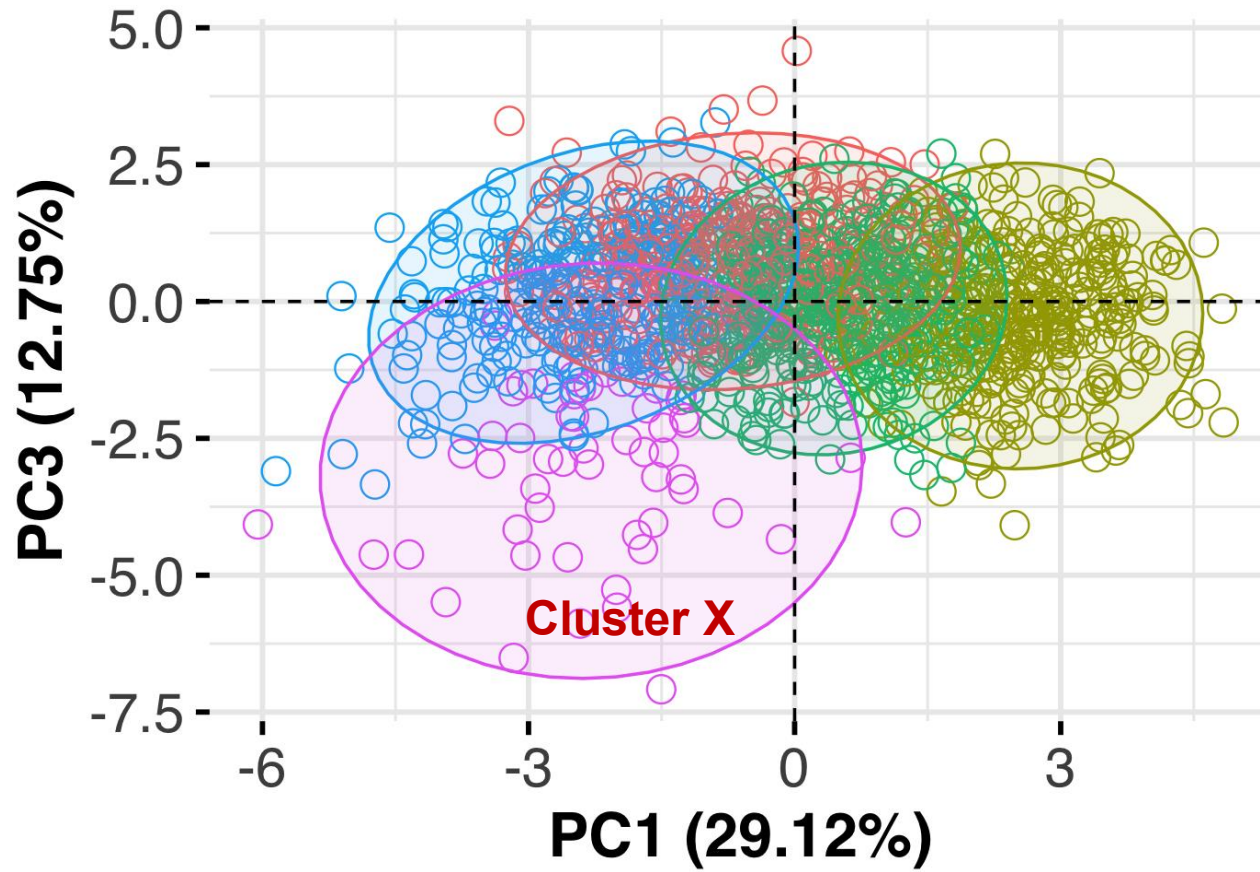


HDL





代謝型研究 (metabotyping)

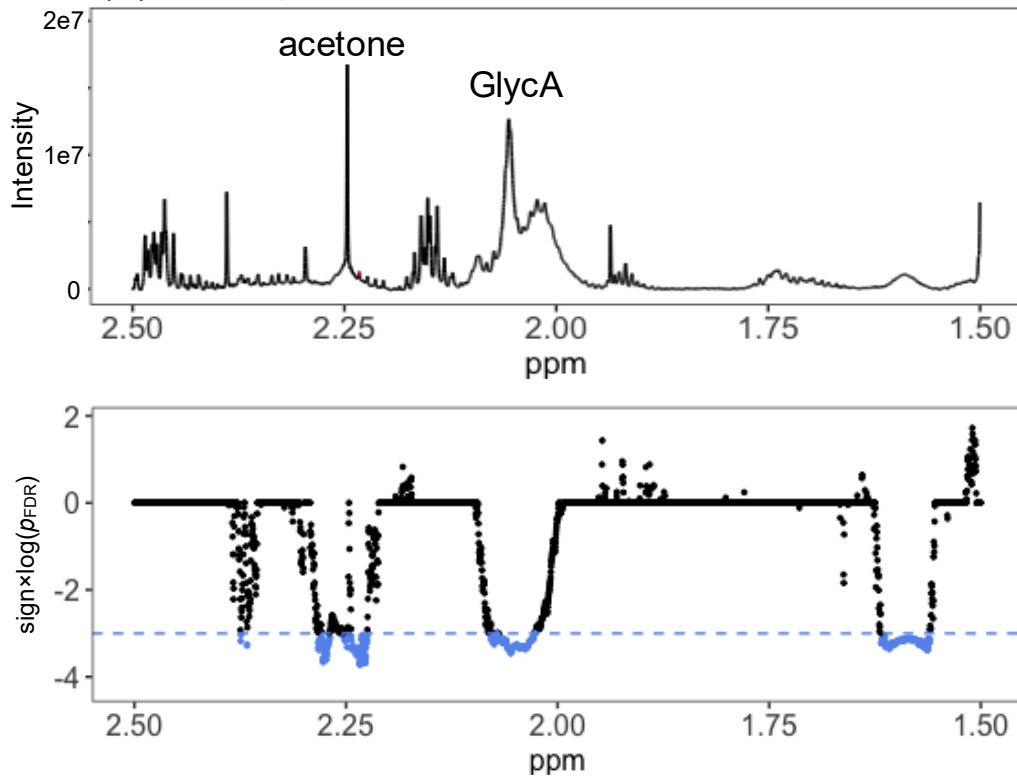


- 我們的人口群當中，有多少種「代謝型」？
- Cluster X 主要影響的指標：
 - IDL、LDL1、VLDL5 triglycerides
- Cluster X 有什麼特殊之處？當 N 變多，又會出現幾個 cluster？

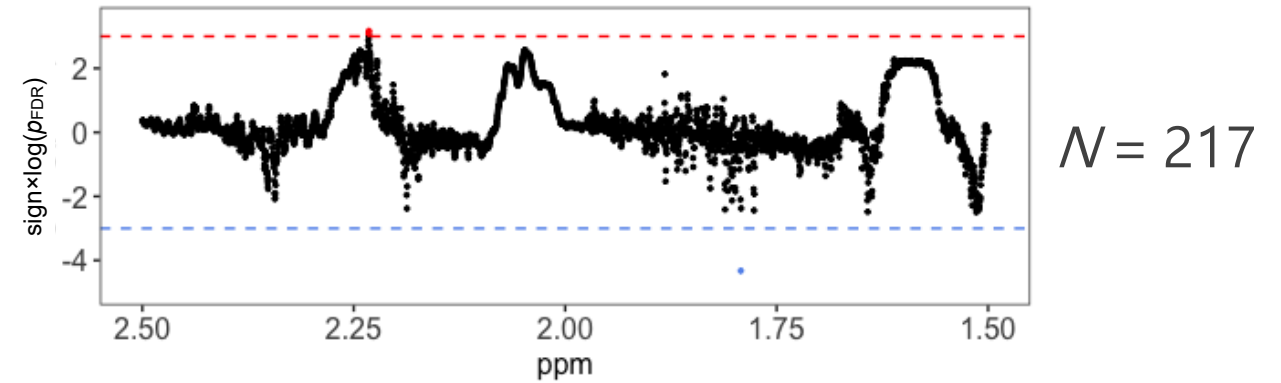




User 研究篇 I – 代謝體 to 基因體



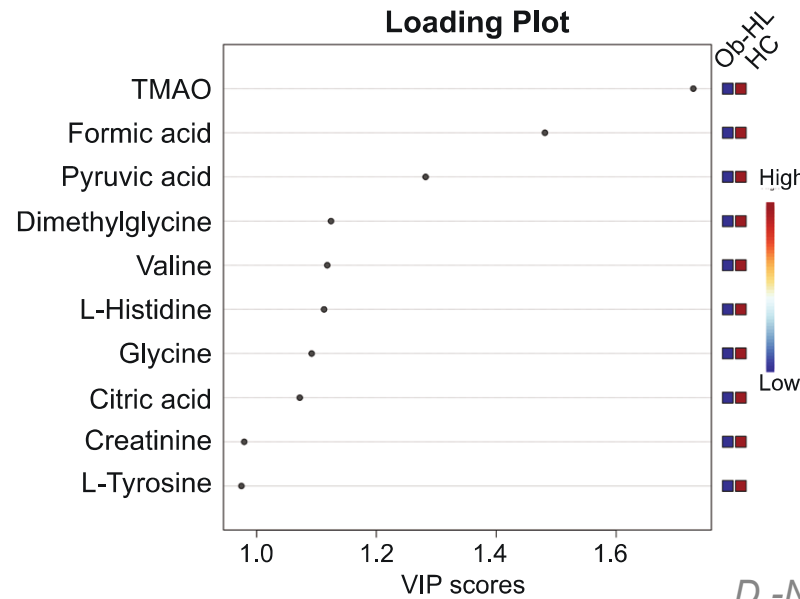
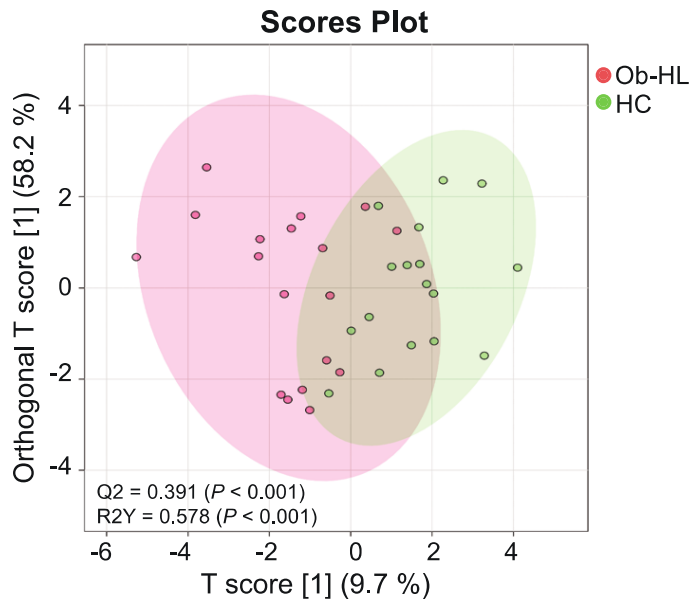
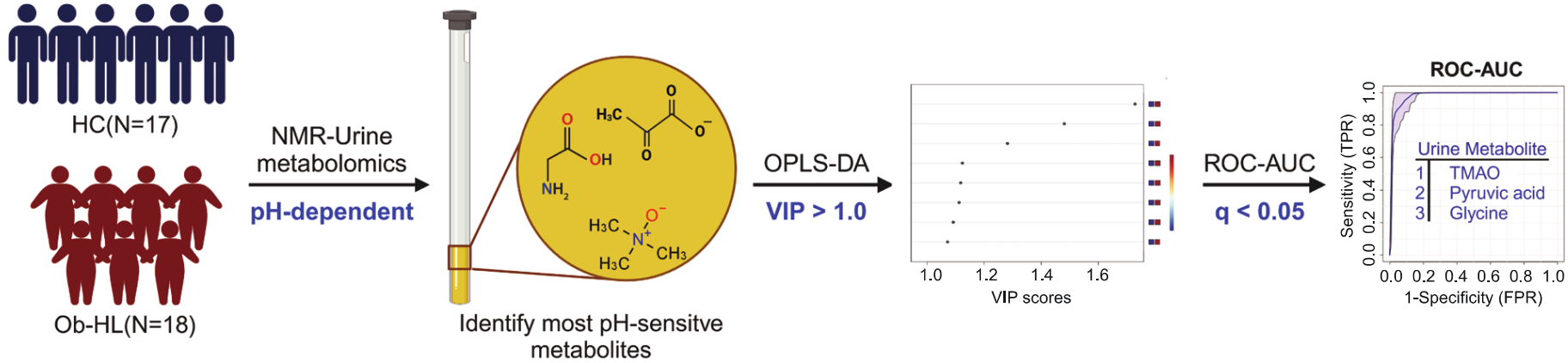
APO A5 rs651821C risk allele



- 「三高」的人在血漿氫譜的特定區域，有特別的型態 (pattern)。
- 氫譜特定訊號的強弱與基因型有關聯 (MWAS)



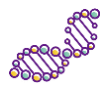
User 研究篇 II – 檢體應用



尿液 TMAO 含量是肥胖性高血脂的生物標記。

TMAO 不需要調整尿液 pH 即可量測。





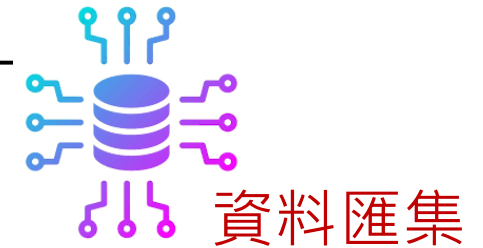
未來挑戰





Metabolomics (2025) 21:66
<https://doi.org/10.1007/s11306-025-02259-7>

REVIEW ARTICLE



Recommendations for sample selection, collection and preparation for NMR-based metabolomics studies of blood

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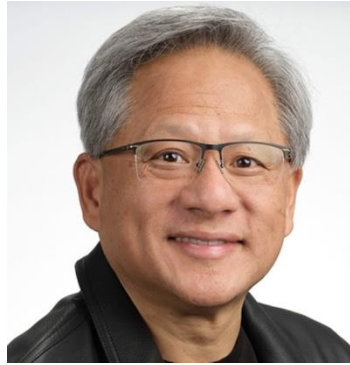
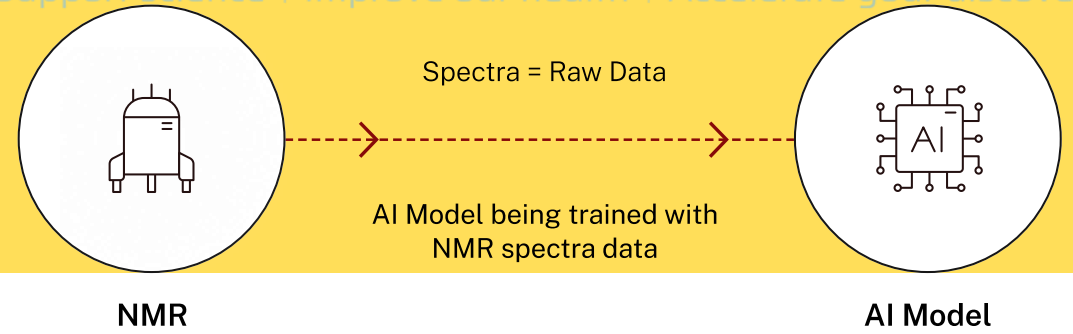


中央研究院 · 臺灣人體生物資料庫
Academia Sinica · Taiwan Biobank

廣告



人工智慧 (AI) 應用

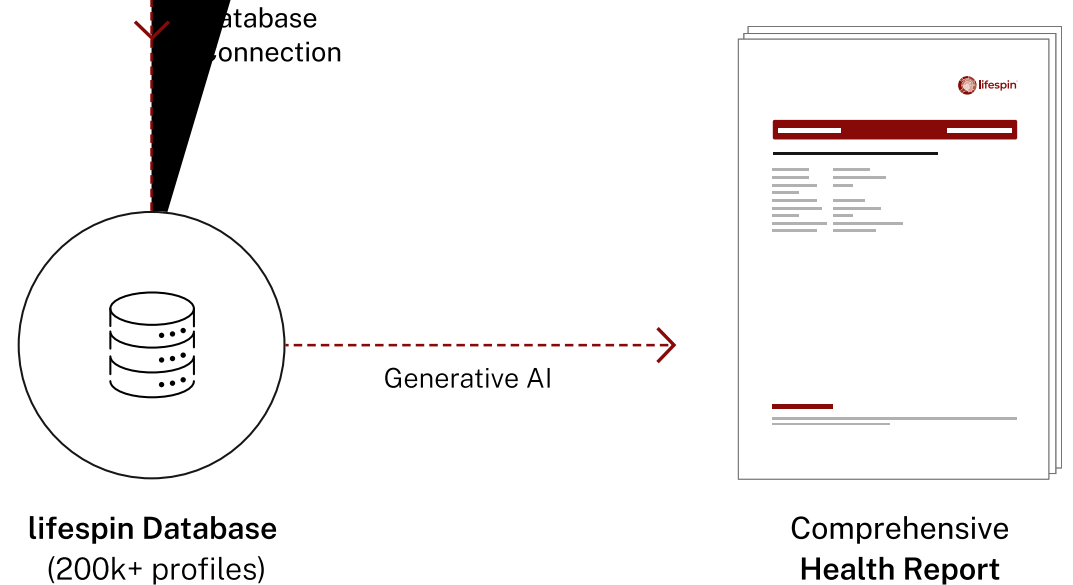


lifespin®

- AI Task:
- 1 Substance Quantification
 - 2 Health Assessment
 - 3 Diagnosis



TECHPOWERUP



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Taiwan Biobank for the Health of Future Generations



致謝

- 薛宜安
- 廖克霖
- 其他同仁

BioReC

- 羅元超



- 張七鳳

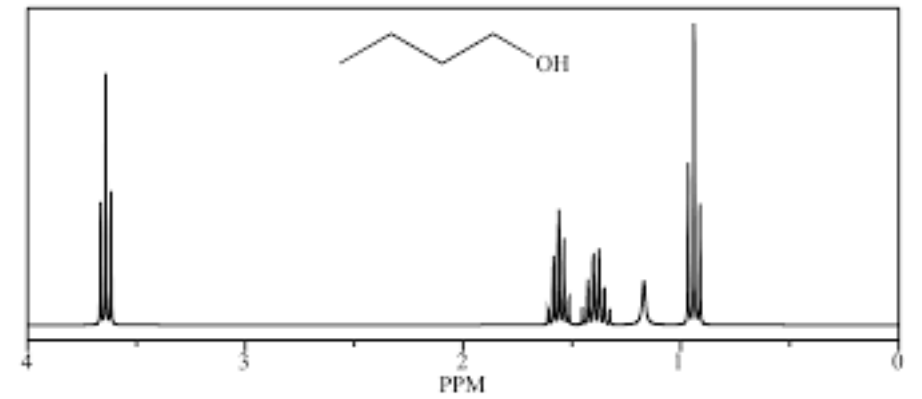
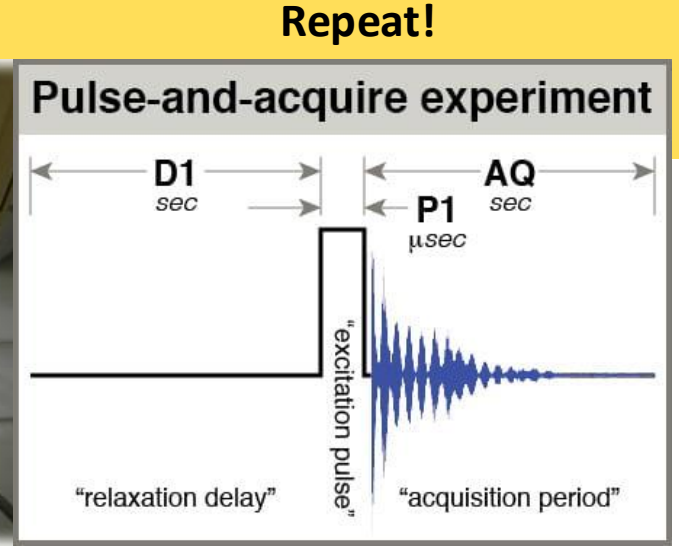
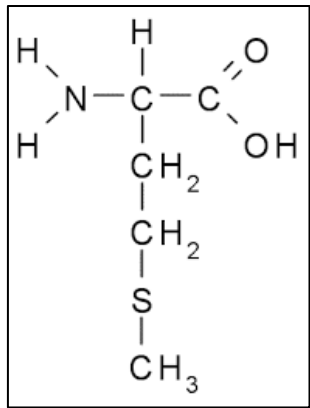
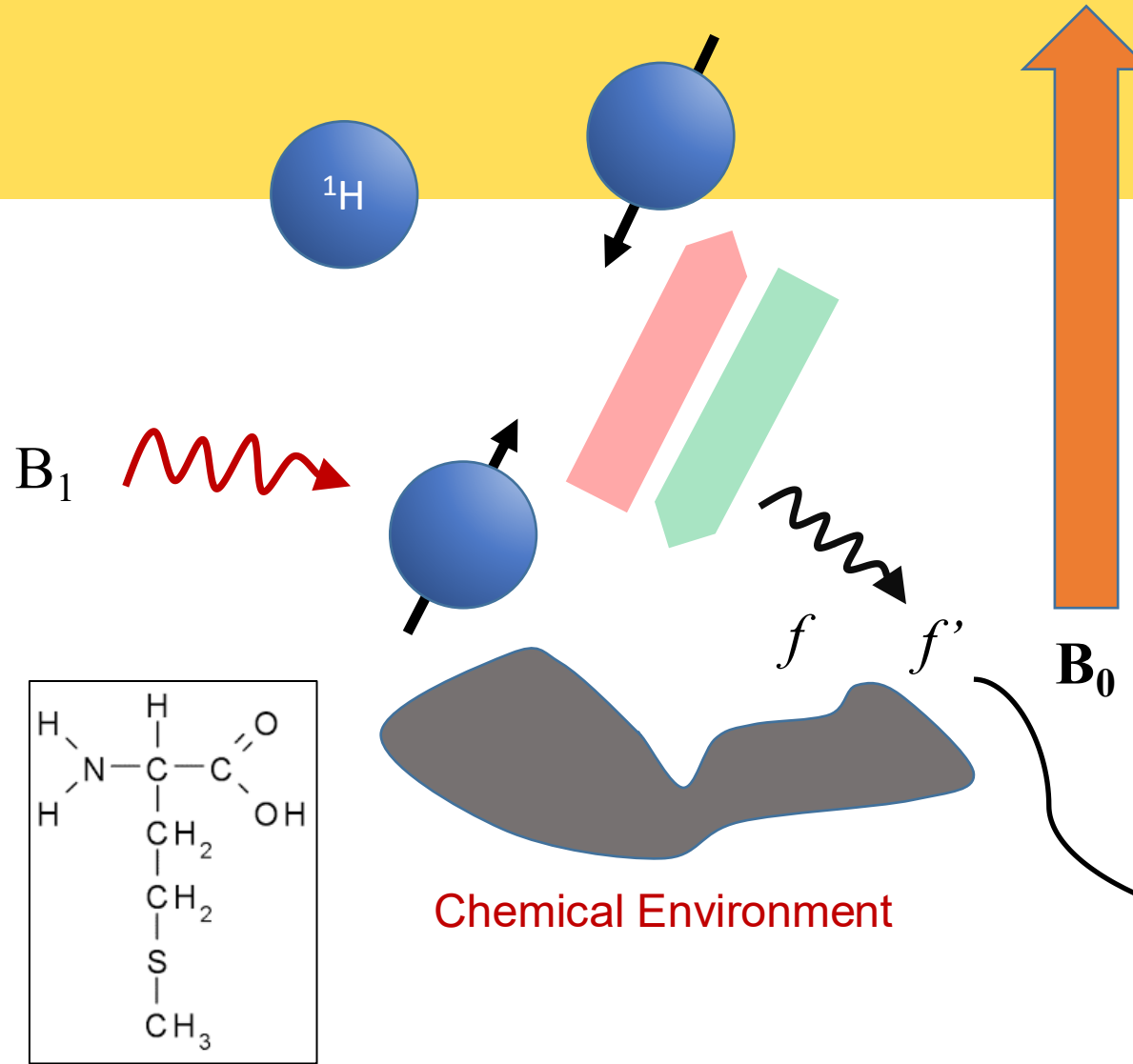


Thank you for listening!







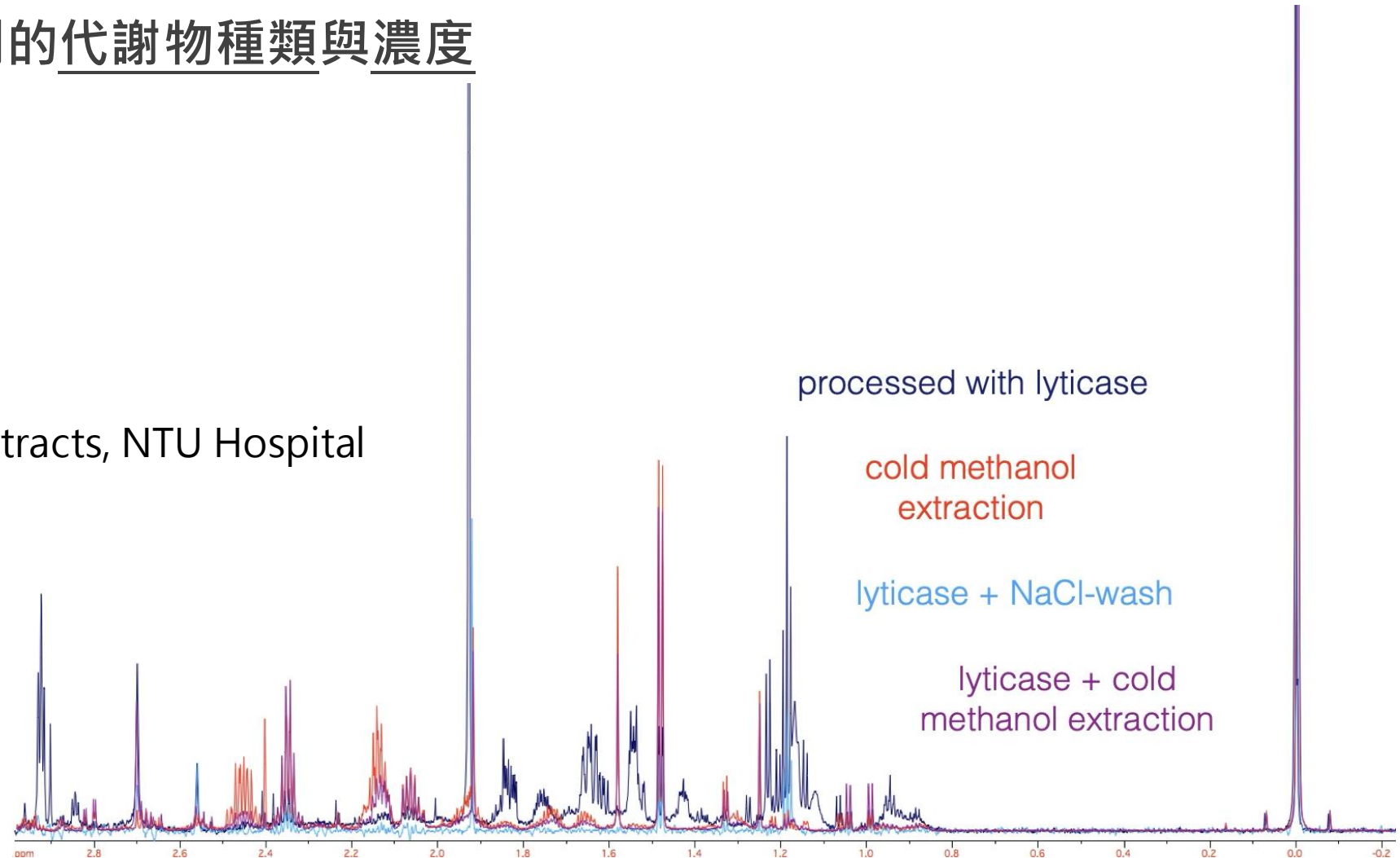




代謝體學資料集簡介 – 樣品處理的影響 I

樣品處理方式影響量測到的代謝物種類與濃度

C. albicans culture extracts, NTU Hospital



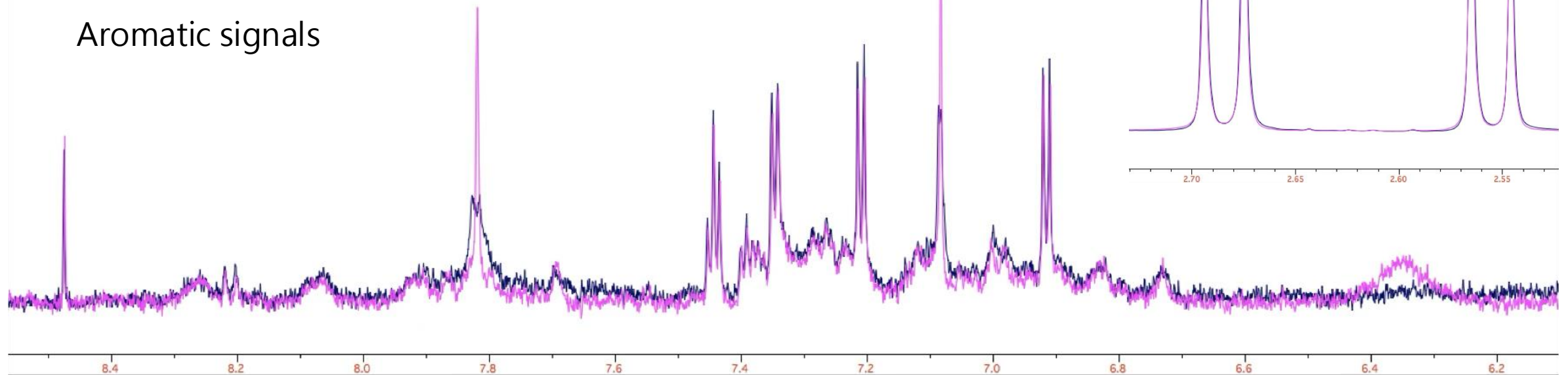


代謝體學資料集簡介 – 樣品處理的影響 II

反覆凍融對血漿 NMR 代謝體量測的影響

凍融前

凍融後





代謝體學資料集簡介 – 換磁場可不可以？

Field dependence of human blood plasma metabolite quantification at HFNMRC, Academia Sinica

