安捷倫6475A TQ應用在多維深度代謝體解決方案

The Proposal of Agilent Metabolomics and Lipidomics Solutions with Triple Quadrupole MS

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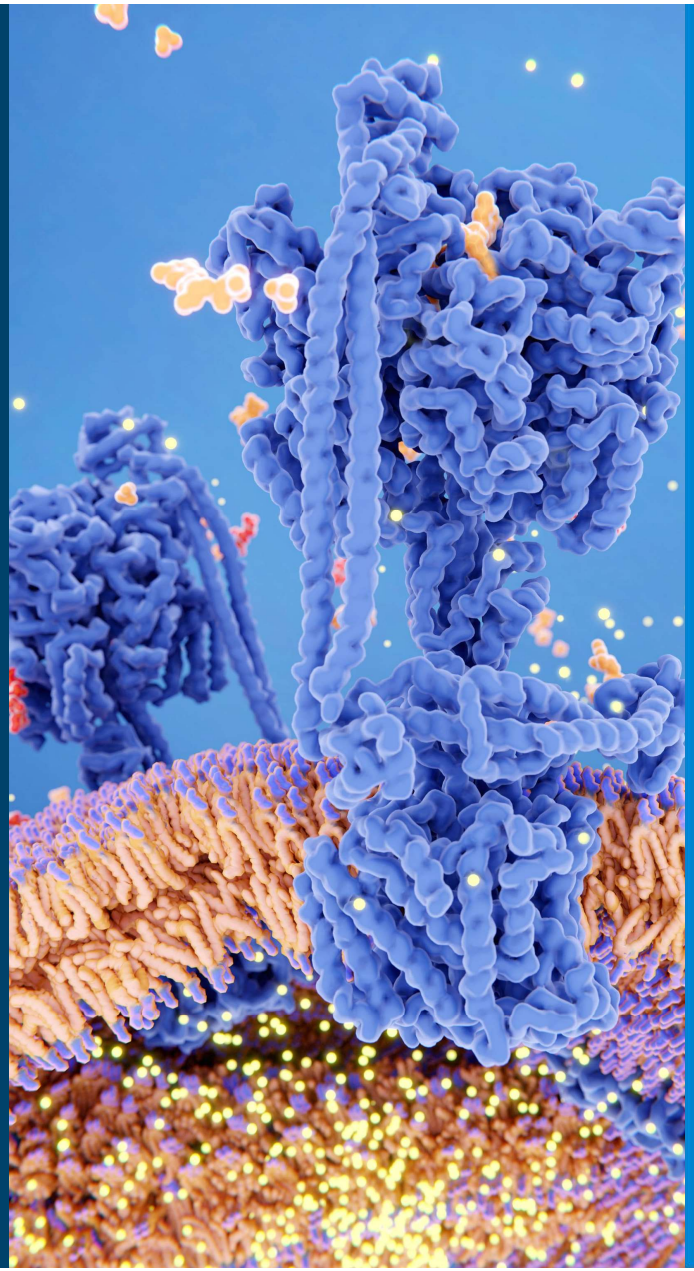
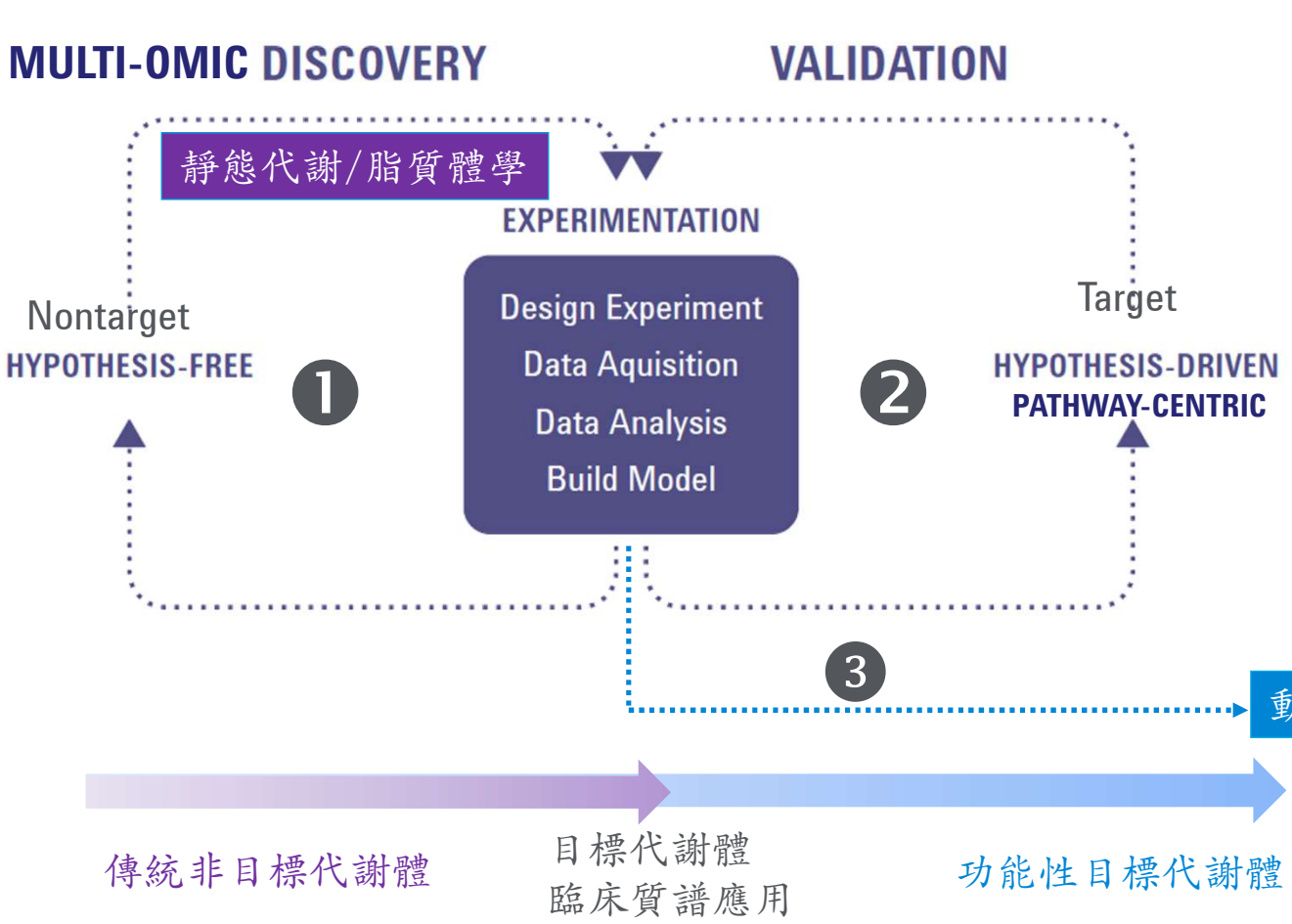
LCMS Product Specialist
Agilent Technology, Inc.



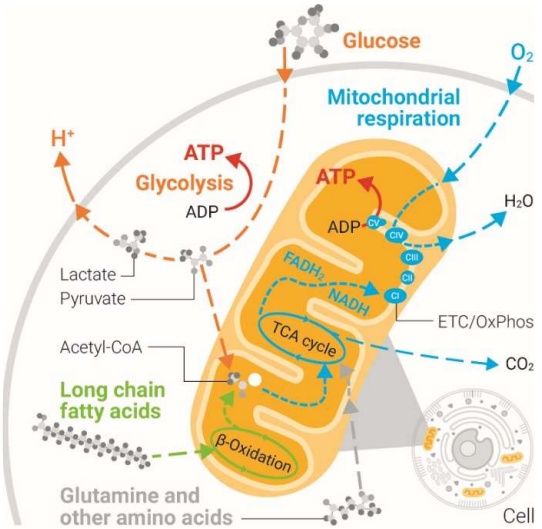
Agilent
Trusted Answers

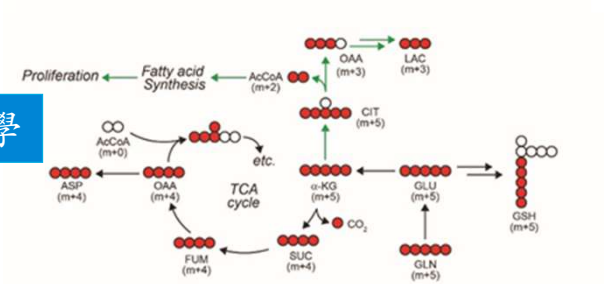
安捷倫多維深度代謝(脂質)體學構建理念

安捷倫多維深度代謝(脂質)體學加速生物學研究



生物體動態變化-時間

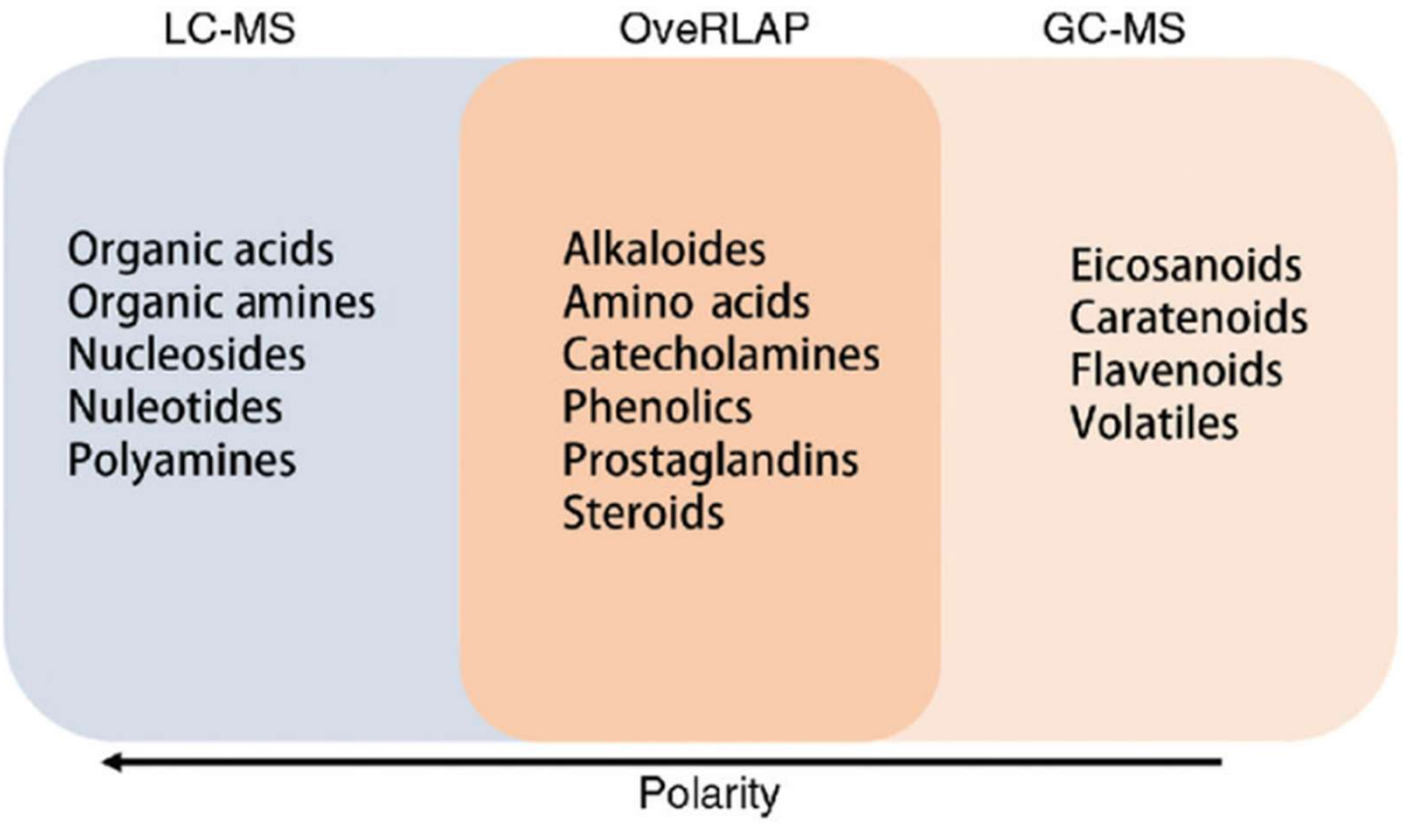




分子水平分析(穩定同位素代謝追蹤)

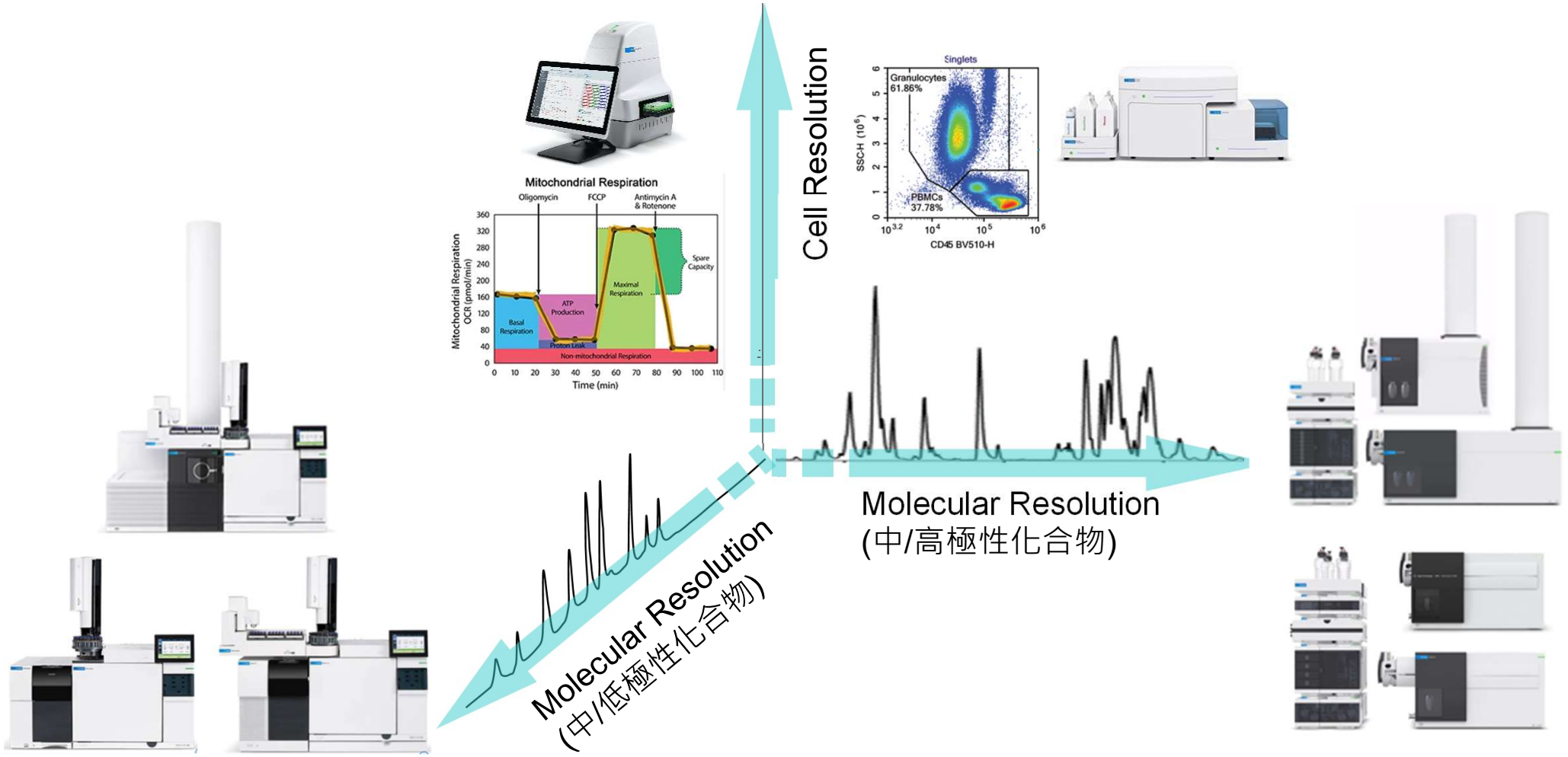
傳統代謝體研究需要非常廣的化合物覆蓋

Metabolite classes identify by LC-MS, GCMS or Both



Hormone Molecular Biology and Clinical Investigation. 2019; 20180045 (Review Article)

安捷倫多維深度代謝(脂質)體學: 三向大利器



安捷倫多維深度代謝(脂質)體學三向重要利器(硬體)
(細胞研究、液相層析質譜、氣相層析質譜)

安捷倫細胞研究產品

Seahorse XF
海馬生物能量分析儀

xCelligence RTCA
實時細胞行為分析儀

NovoCyte
流式細胞分析儀

BioTek
自動化影像系統與檢測儀

安捷倫液相層析智慧質譜更聰明、更自動的軟體控制(LCMS)

QTOF

Global Metabolomics &
Targeted Metabolomics

人工智能儀器校正
AI-based Tuning & Calibration
SWARM autotune

即時系統監控
Active System Monitoring
Early Maintenance Feedback

排成保養和校正
Maintenance and Method Automation
Scheduled Autotune/Checktune

智能反進樣系統
Reflexive Injection Logic
Intelligent Reflex (iReflex)

New 6475A
Targeted Quantitation

安捷倫豐富的多維度分離技術

❖ LC/MS (1290 Infinity II LC, 1290 BioLC)-多種層析分離針對不同類型代謝物

- C18 reverse phase (non-polar compounds, lipids…)
- HILIC or normal phase for polar compounds (nucleotides, amino acids, sugar phosphates, organic acids, class-based separation of lipids)

❖ SFC/MS (1260 Infinity II SFC or 1260 Infinity II SFC/UHPLC Hybrid System)- 特定代謝物的優勢技術

- Can be a combination of reverse and normal phases columns (Hybrid優勢特色)
- Excellent for fast and high-resolution lipids analysis and class separation (脂質體學)

❖ GC/MS (8890 or 8860 GC)

- Need to derivatize samples (TBDMS, TMS) prior to analysis
- Fatty acids, organic acids, amino acids…

❖ MD-LC/MS- 多維度、全訊息覆蓋分離

- Reducing sample complexity
- Multiple heart-cutting/Separation
- Coupling HILIC and reversed-phase separations

❖ CE/MS (7100 CE System)-特殊分離的優勢

- Highly polar and charged metabolites
- High-throughput, can be multiplexed

Intelligence that Inspires

Start building your lab of the future today

Introducing the New 6475 LC/TQ

Agilent's most intelligent highest performance LC/TQ system ever produced

"Excellent sensitivity combined with robustness, and onboard intelligence delivers meaningful and reportable results on time."

Sensitivity + Precision & Speed with Intelligence

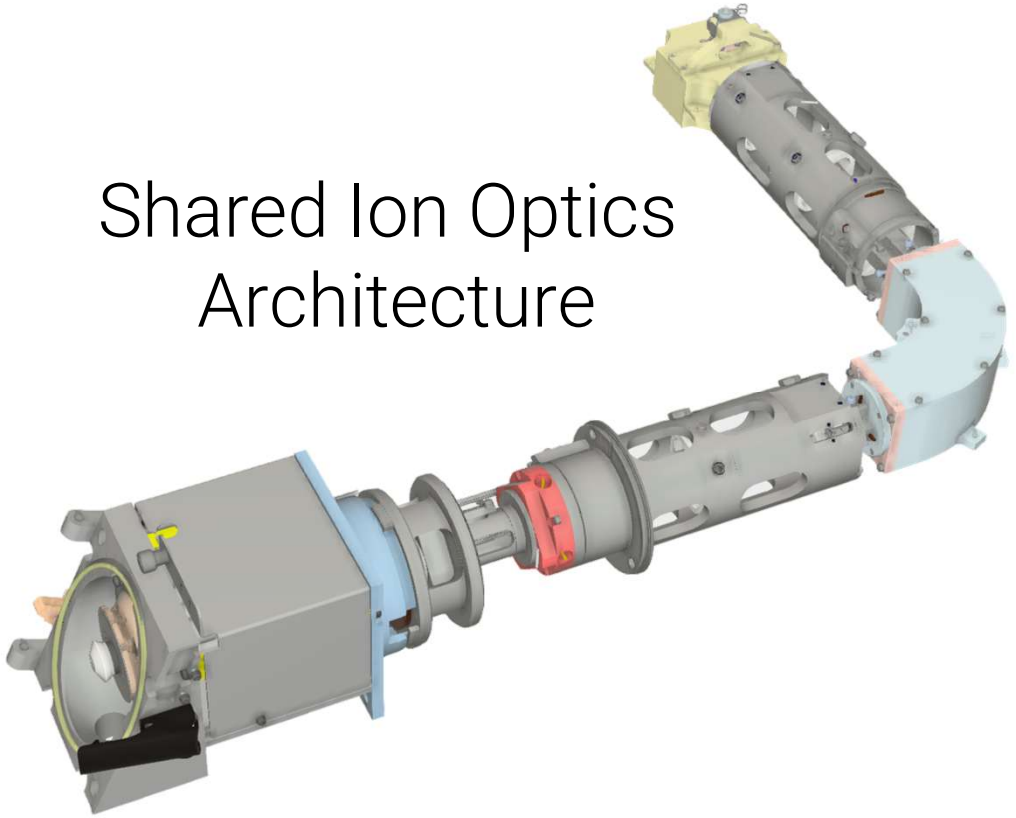
Meets the Needs of High-Throughput Labs Analyzing Large Numbers of Complex Samples at Trace Levels

Consistently robust and versatile hardware

6475 LC/TQ

Core Routine & Research

Shared Ion Optics Architecture



Consistently robust and versatile hardware

Less downtime, increased throughput

VacShield allows you to routinely maintain the instrument without venting. (低儀器汙染, 減少清潔時間,增加儀器效能)

Analyze a wide range of analytes and ions

The **octupole ion guide** allows you to transmit a wide m/z range to cover small molecules, peptides, oligonucleotides, and other polymers. (八極桿Q0設計,可提供最大離子傳輸與聚焦效率)

Confidently quantitate target compounds

Heated hyperbolic quadrupoles isolate and transmit ions efficiently, cleanly, with high precision and high instrument stability. (加熱式四極桿設計減少污染和更穩定的質量分析)

Reduce noise with improved signal

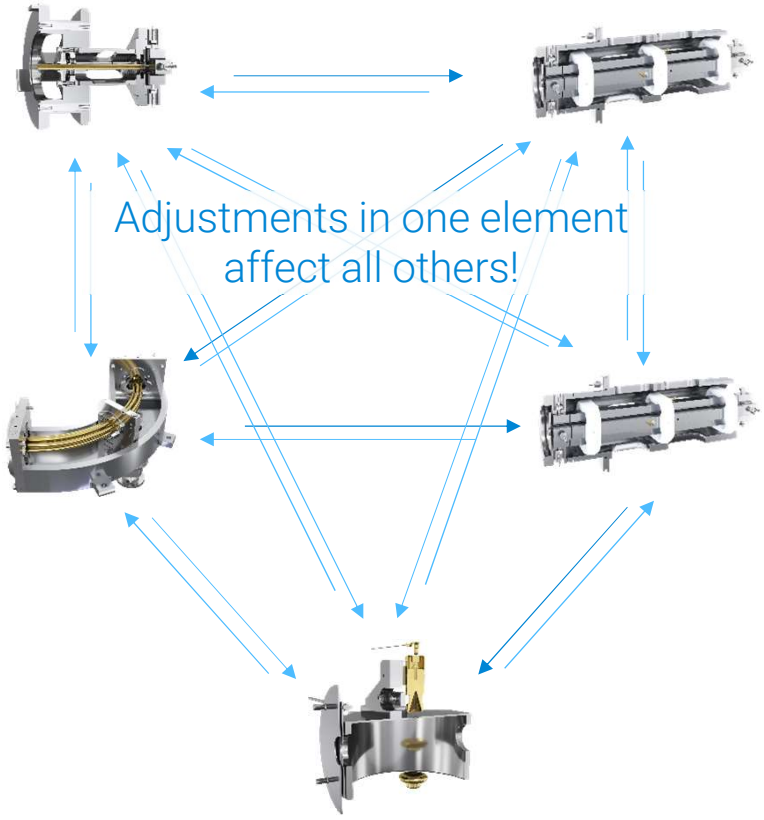
The **tapered and curved hexapole collision cell** refocuses fragment ions and substantially decreases noise by eliminating neutrals (彎曲式碰撞池設計, 降低噪音,提升S/N比靈敏度)

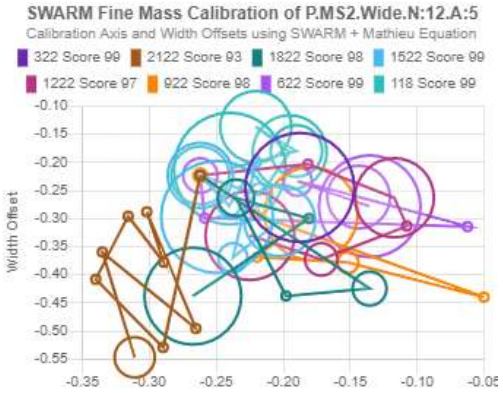
Achieve exceptional linear range

A **20kV high energy dynode (HED) and electron multiplier (EM)** detector system consistently produces linear results for a small, large, positive ions, and negative ions within the same analytical run. (高效能檢測器, 同時有市場最大的線性動態範圍)

AI-based Tuning & Calibration (人工智能儀器校正,保證穩定性)

SWARM Autotune results in improved performance and reduced instrument-to-instrument variability





"We developed SWARM Autotune to leverage a self-learning algorithm called Particle Swarm Optimization…SWARM repeatedly varies multiple optic elements and self-learns from each change."

Method Development Automation (全自動質譜優化系統)

Fully Automated MRM and Ion Source optimizer helps develop new methods or fine-tune existing methods quickly

Create new or load existing method

Input chemical formulas

Select optimization parameters

Select “Guided” or “Automated”

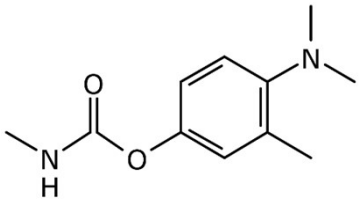
Execute workflow

Review Results

Finalize and Save to database

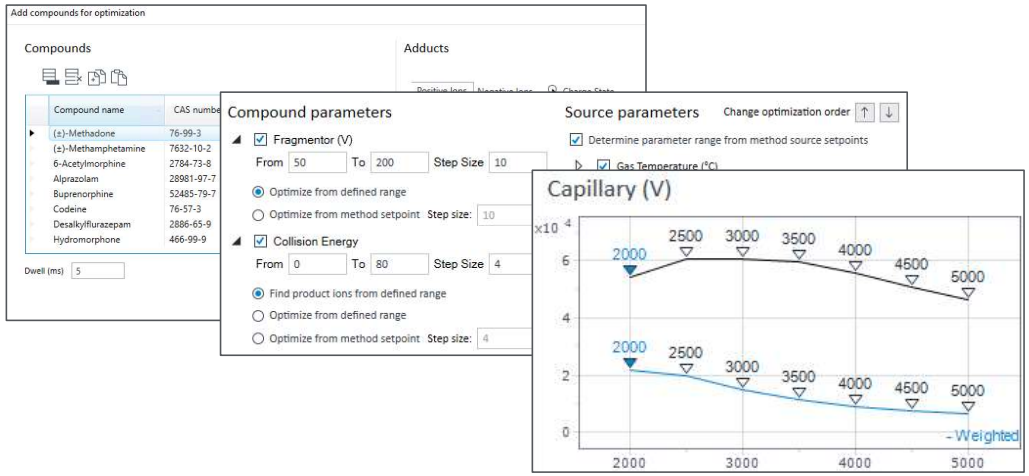
Define Target:

Aminocarb



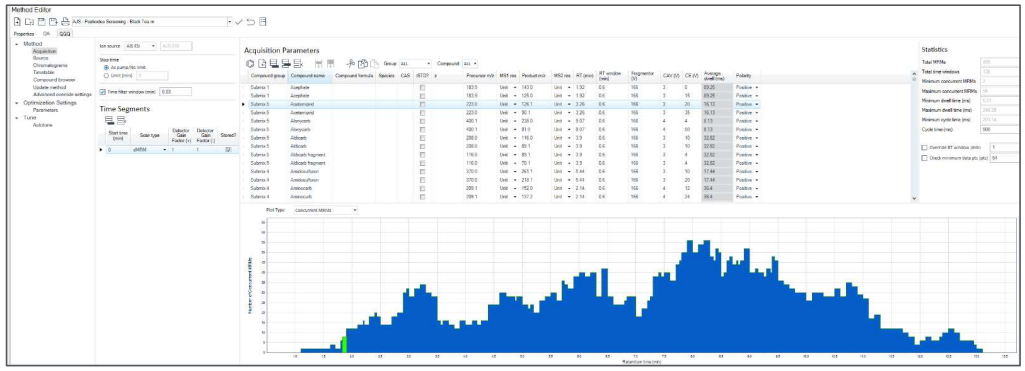
Automatically find MRMs

MRM1: 209.1 → 152.0
MRM2: 209.1 → 137.2



Automatically find Parameters

Collision Energies, Fragmentor



Consolidate Method

MRMs Defined
MRMs Optimized
Ion Source Optimized

安捷倫Masshunter TQ應用：流程化全功能軟體平台

單一平台支持 LCMS、GCMS、ICPMS 操作簡單、易用

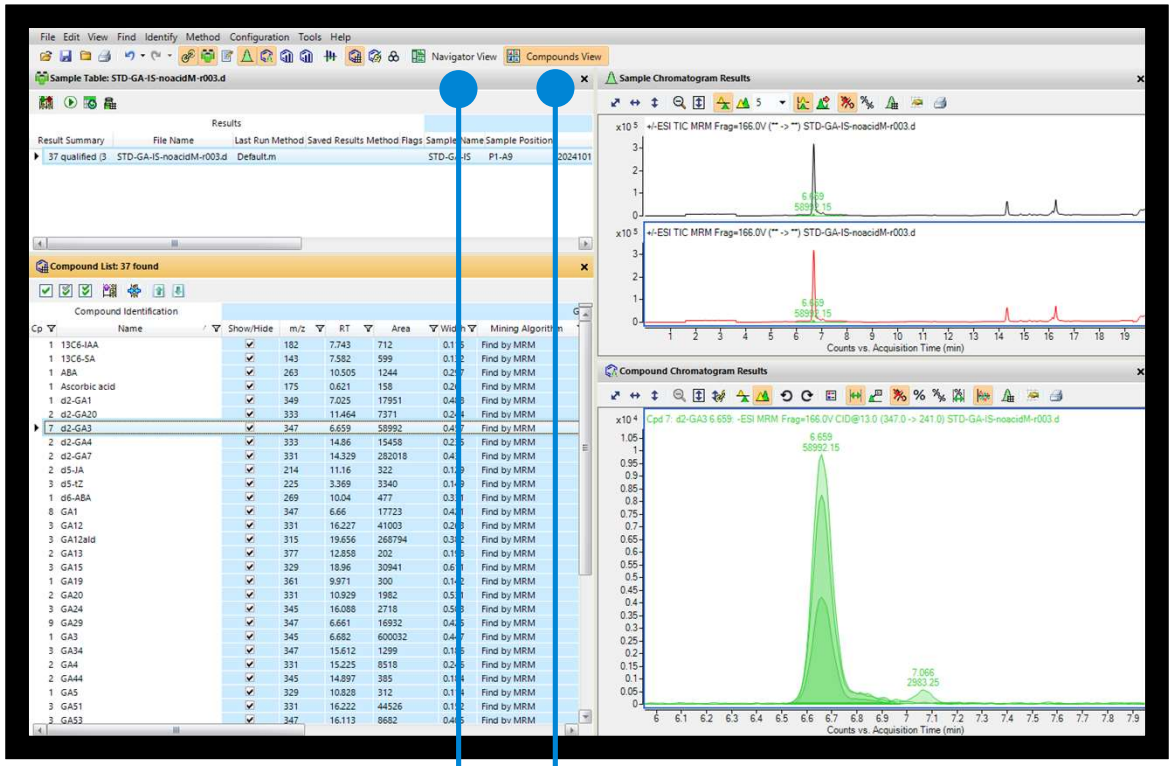
Qualitative 12.0 up
-Compound Extraction
(MRM 提取/確認)

Quantitative 12.0 up
- Targeted Quantitation
(目標定量分析)

MPP 15.1 Analysis
- Statistical Analysis
(代謝/蛋白統計分析)

Agilent MassHunter Workflow from Data to Statistical Analysis

安捷倫MassHunter Qualitative:自動/手動全功能智能定性軟體平台



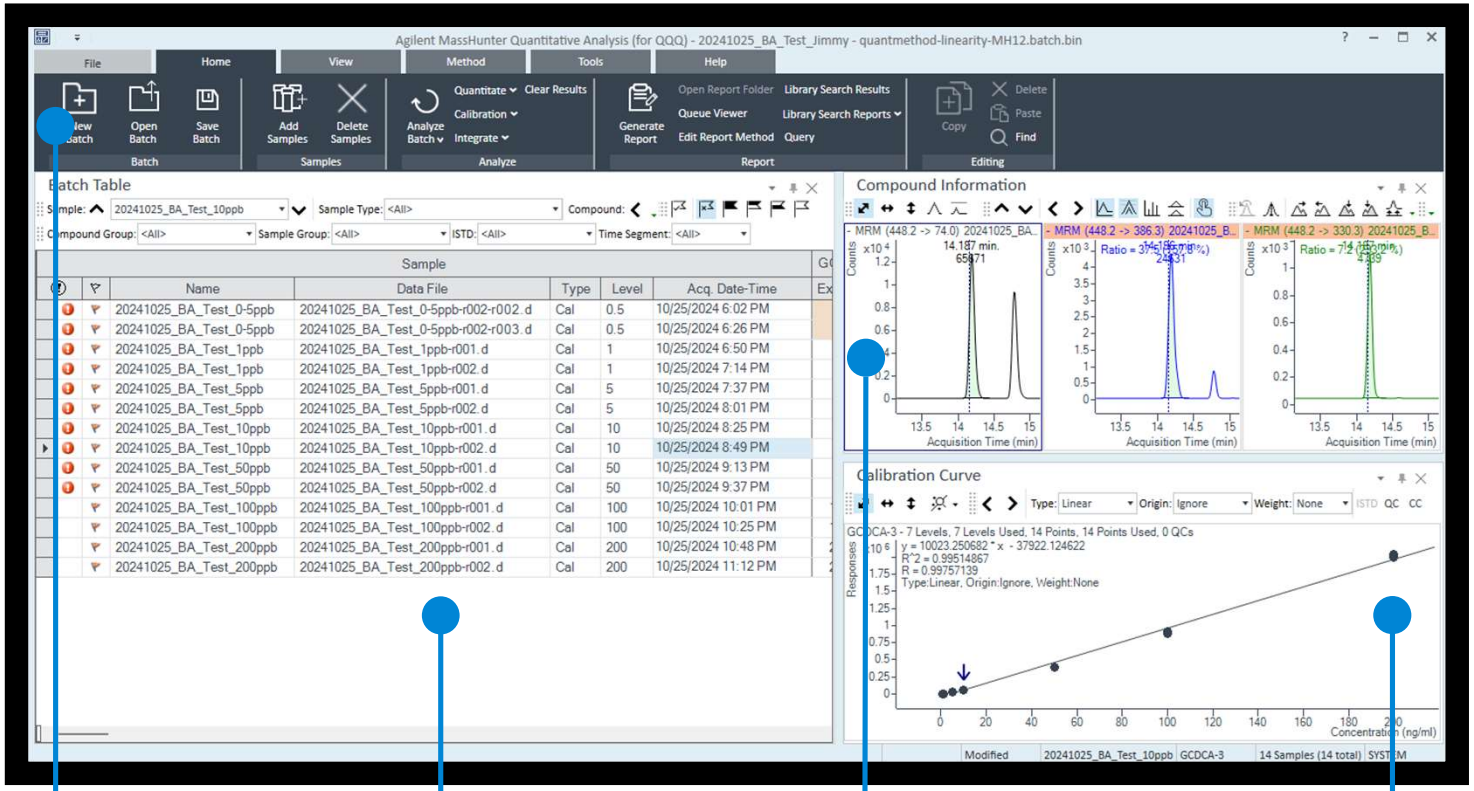
Navigator View

手動積分、計算S/N...等功能

Compound View

自動提取MRM數據、對比數據

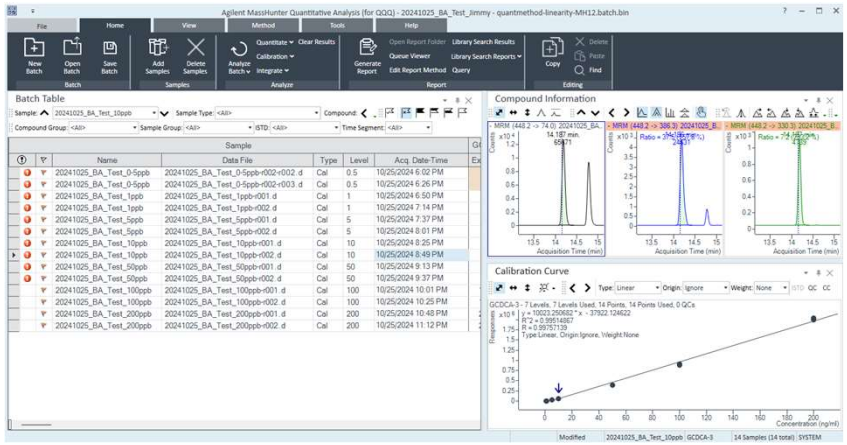
安捷倫MassHunter Quantitation:全功能智能定量軟體平台

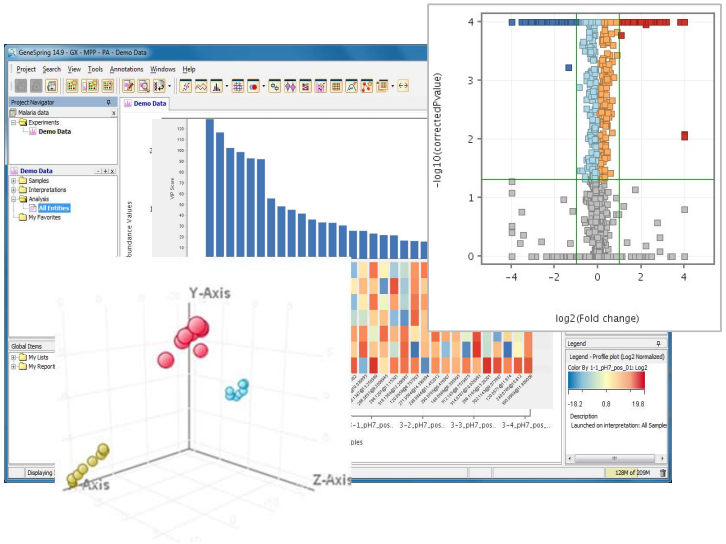


目標代謝體學流程二大重點: 數據提取和統計分析

Quantitation (定量數據提取)

Mass Profiler Professional (統計)





❖ 目標化合物提取:

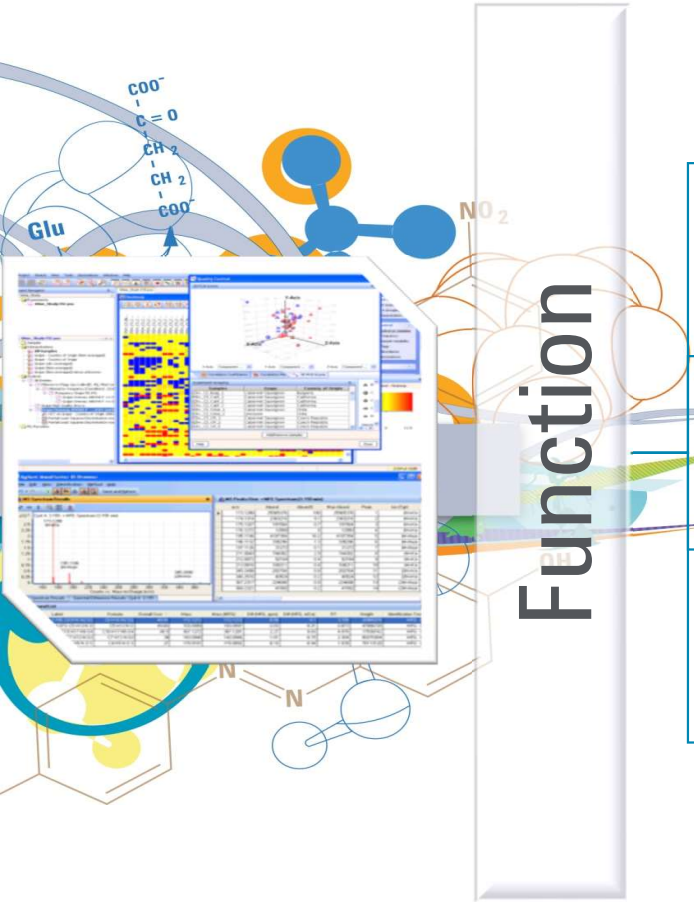
- 質量和保留時間的峰對齊、校正
- 可支持Excel特定格式導入MPP計算

❖ 統計和化學計量分析:

- 均一化， 火山圖， 主成分分析， 聚類分析.. etc. (Unsurpvised Analysis)
- 支持PLS-DA相關Supervised Analysis
- 可流程化功能編輯並自動運行

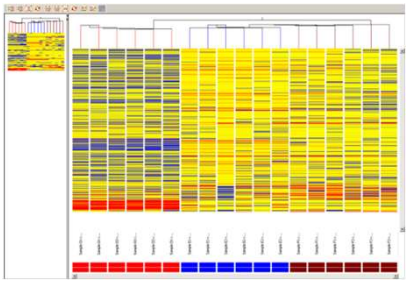
安捷倫Masshunter Mass Profiler Professional (MPP)

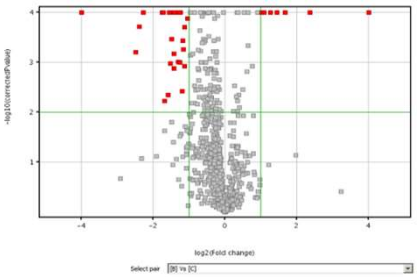
完整的統計學工具

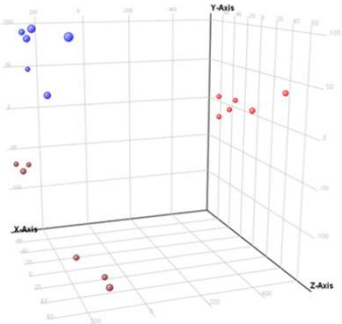


Function

- Alignment and Normalization
- Statistics
  - PCA and PLS-DA
  - ANOVA
  - Volcano Plot
  - Clustering
  - Correlation
- Identification (QTOF)
- Pathway Architect

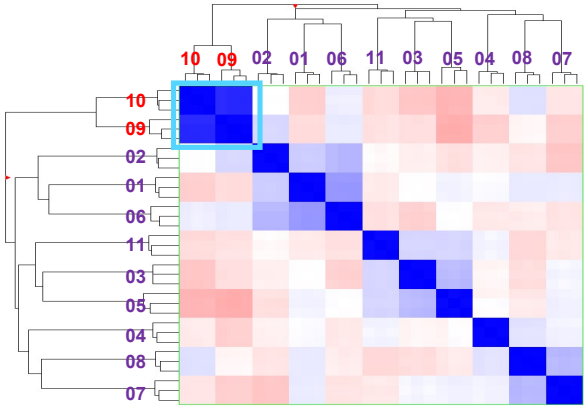




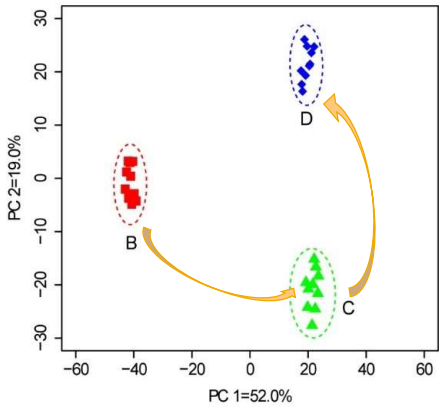


安捷倫MPP數據分析圖展示

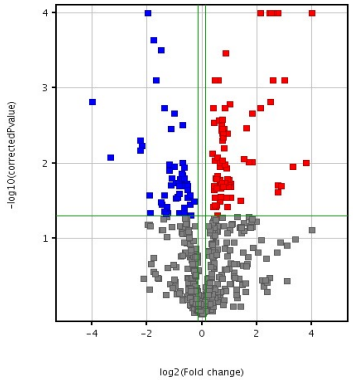
完整的統計學工具



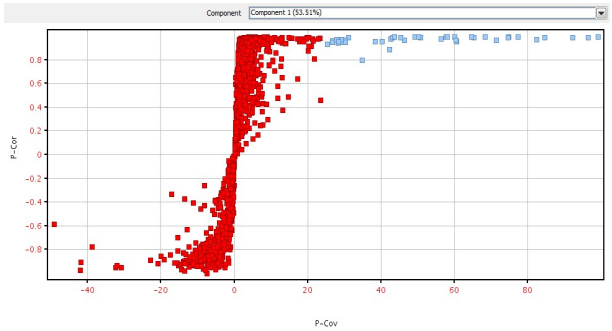
Sample-Sample Correlation



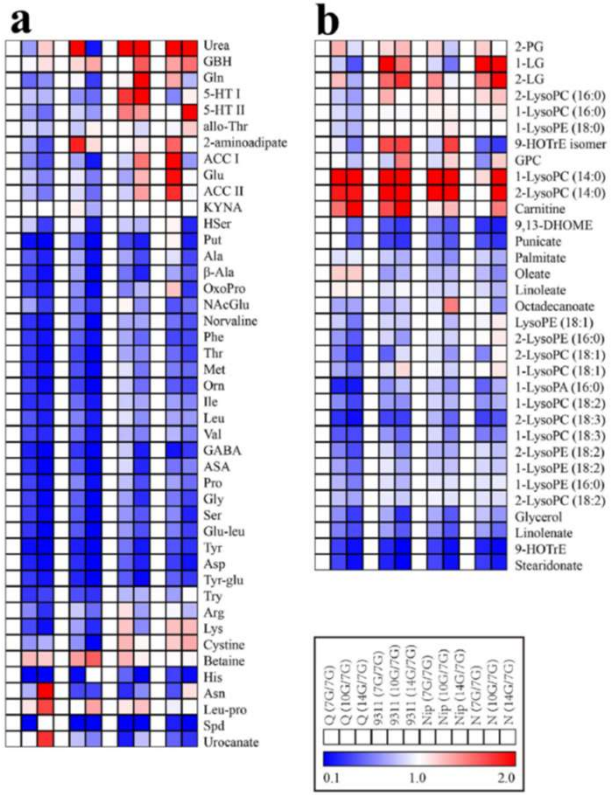
PCA Plot



Volcano Plot



S-S Plot (C-C Plot)



Heat map

6475A QQQ LC/MS – Key Applications

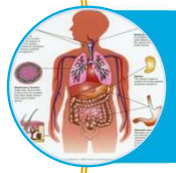
Validate Improved Performance, Robustness, and Demonstrate Enhanced Workflows

Food testing & Agriculture (食品安全)

Analysis of multi-residue pesticides in food matrix with higher degrees of sample dilution

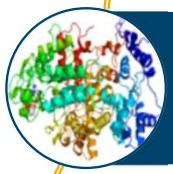
Environmental (環境暴露)

Determination of PPCPs in surface and waste water using direction injection



Clinical Research (臨床檢測)

Quantitation of immunosuppressants in whole blood with sample dilution



Targeted Metabolomics & Proteomics (代謝/蛋白體學應用)

Extended Mass Range Triple Quadrupole for Routine Analysis of High Mass-to-charge Peptide Ions

Pharmaceutical (製藥雜質或藥物動力研究)

Analysis of clozapine, alprazolam and metabolites in plasma; Extensive robustness test

TARGET

- ***Performance: Robustness / Reliability / Accuracy***
- ***Robustness / Longevity***

安捷倫分類最完整的目標代謝體解決方案 (持續合作擴建中)

代謝方案	目標代謝物數量	支持儀器	有沒有可採購混合標準品	靈敏度	狀態
目標功能性代謝體 (Glycolysis/PPP/TCA/NS/NTP/AA)	~140	QTOF & TQ	Parts of standards or mix standards	2-20pg	V
胺基酸 (Amino Acid)	~20	QTOF & TQ	Amino acid mix from vendors	1-5pg	
腸道菌應用(膽汁酸: Bile Acid)	~49	TQ	Caymen (21 mix)	10-50pg	
腸道菌應用 (短鍊脂肪酸:SCFA)	7	TQ (衍生)		<0.05pg	V

脂質代謝方案	目標代謝物數量	支持儀器	有沒有可採購混合標準品	靈敏度	狀態
目標通用脂質體(Phospholipids)	~800	轉移中	NIST1950 standard plasma	pg	
Oxylipins (氧化脂質)	~120	轉移中	Parts of standards from Caymen	pg	
脂肪酸氧化 (Acrylcarnitine, CAR)	~25	轉移中	Merck (4 mix standards)	pg	

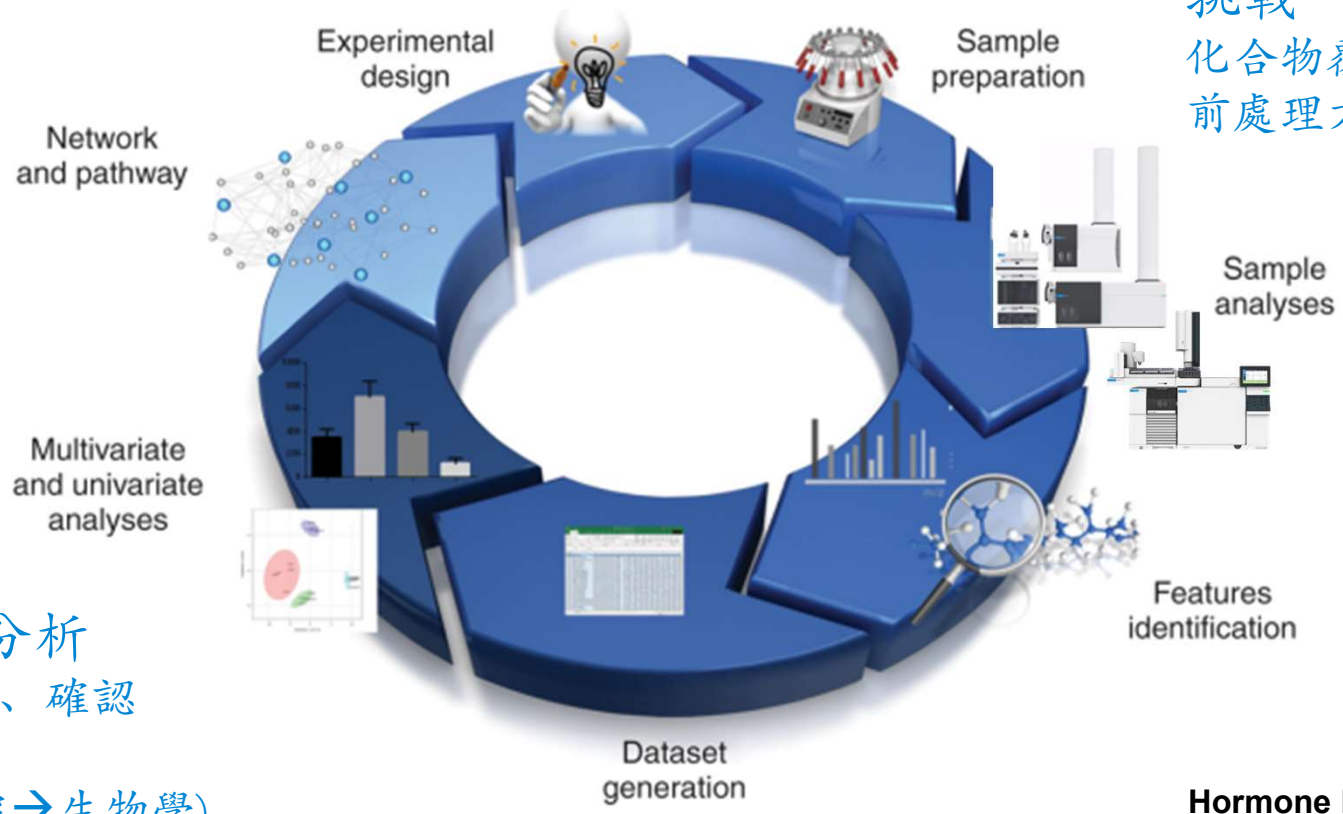
第三方代謝方案	目標代謝物數量	支持儀器	有沒有可採購混合標準品	狀態
Biocrates AbsoluteIDQ p180 kit	43 (小分子) 145 (脂質)	6470/6475	Kit+SW	

Agilent 6475 triple quadrupole LC/MS system –
the head and the heart of routine analysis

Thank You!

For more information, check out:
www.agilent.com/chem/6475

非目標代謝體流程讓研究處處是挑戰...



挑戰一: 樣品前處理
化合物覆蓋廣
前處理方法多

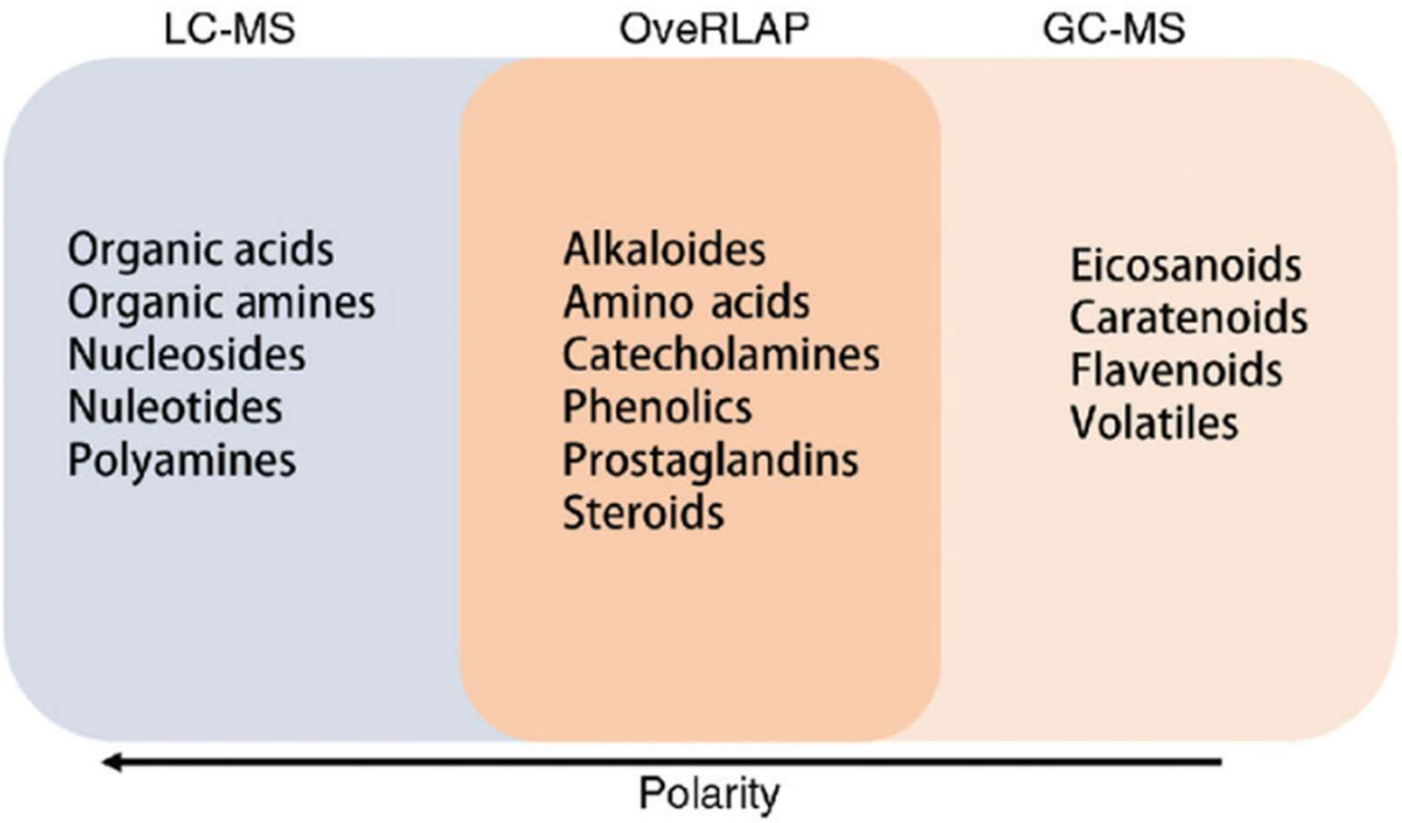
挑戰二: 儀器分析
儀器訊號複雜
- 化合物覆蓋廣
- 化合物同分異構多
- 方法種類多

挑戰三: 數據分析
未知化合物鑑定、確認
統計學分析
多體學分析(數據→生物學)

Hormone Molecular Biology and Clinical Investigation. 2019; 20180045 (Review Article)

非目標代謝體研究複雜的化合物覆蓋/樣品前處理、分析方法多的挑戰

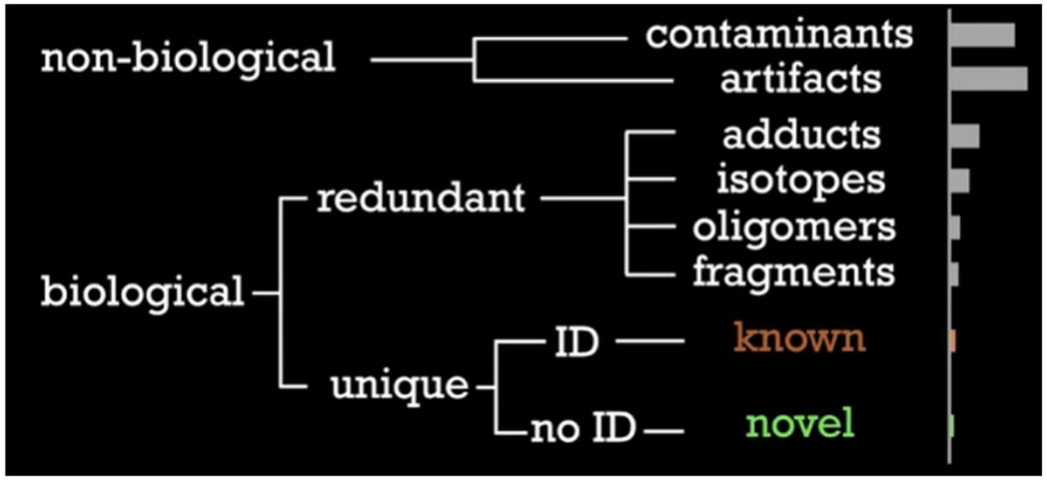
Metabolite classes identify by LC-MS, GCMS or Both



Hormone Molecular Biology and Clinical Investigation. 2019; 20180045 (Review Article)

非目標代謝體/複雜儀器訊號的挑戰...

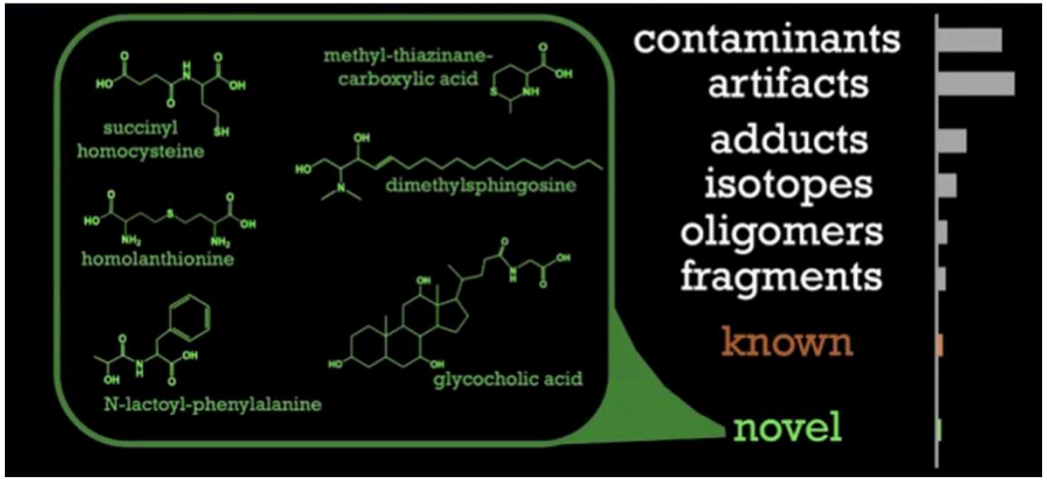
Prof. Gary Patti say…



SelectScience Agilent

Webinar: Population-scale metabolomics heralds new era in precision medicine

Available on demand

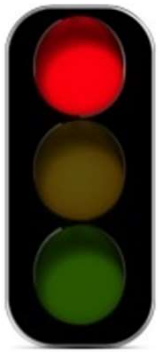


Population-scale metabolomics present by Gray Patti
https://view6.workcast.net/AuditoriumAuthenticator.aspx?cpak=6681367333436446&pak=7996754448866373

未知物結構鑑定/差異分析流程的挑戰...

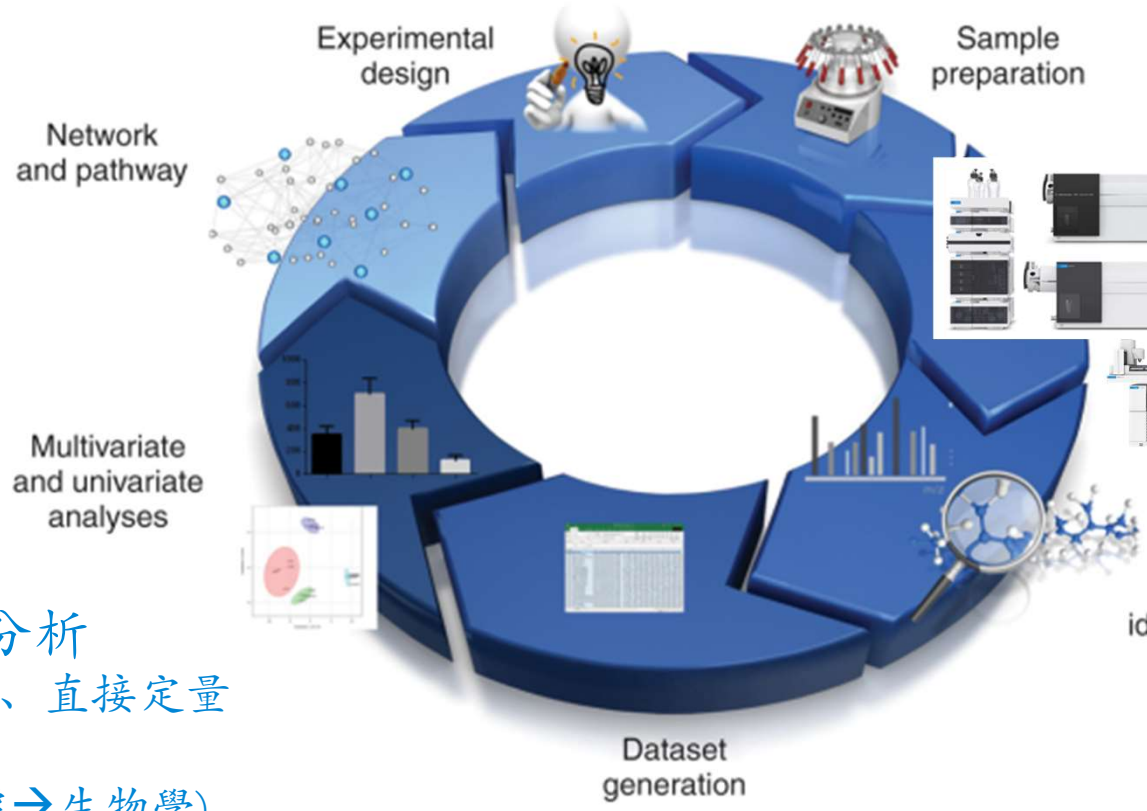
即使有數據庫/圖譜庫還是非常困難…

Sample prep. → LC/QTOF → Data Processing (based-on database/library) → Top-down Match:
ID: 僅確認有範圍的數據庫/圖譜庫
No ID: >~10K 訊號無法鑑定



Signals (DDA/DIA) → IDs → Bottom-up Match
- Special MS/MS fragment ions

目標代謝體流程讓目標和研究關聯性更明確



變化一: 樣品前處理
化合物專一
前處理方法可建立

變化二: 儀器分析
儀器訊號可追溯
- 化合物專一
- 化合物同分異構可分離
- 方法種類可控

變化三: 數據分析
目標化合物鑑定、直接定量
統計學分析
關聯性分析(數據→生物學)

全新「功能性」目標代謝體/代謝流解決方案
(標準化方案)

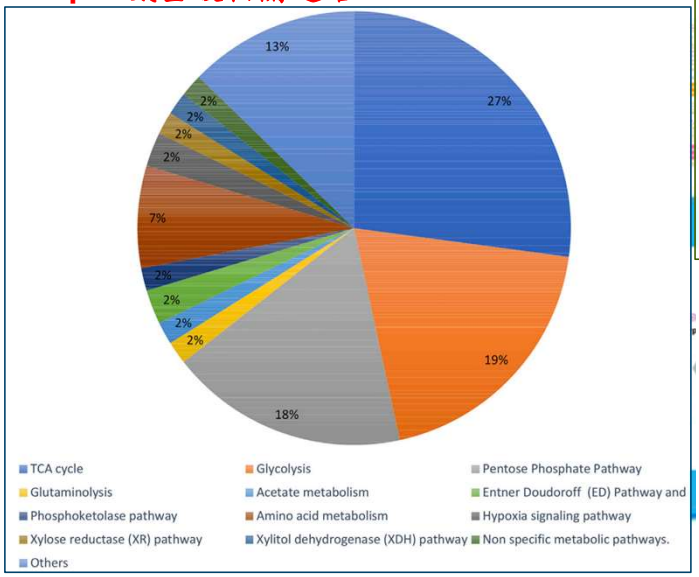
安捷倫「功能性」目標代謝體分析解決方案

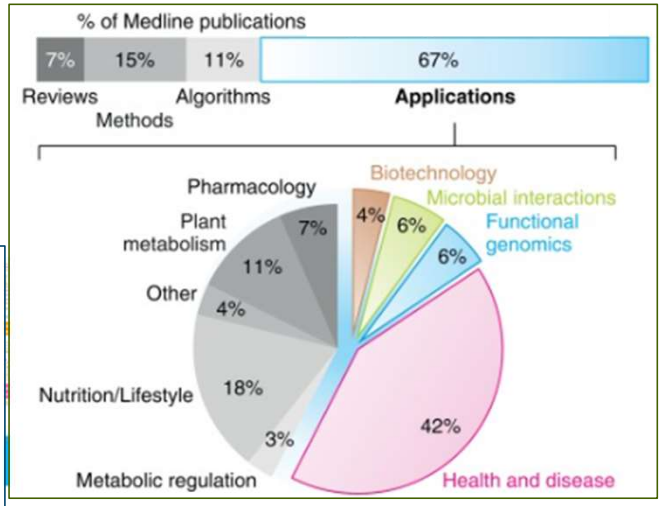
- 聚焦研究需求，加速平台建立，服務更多生物學研究人員

功能性代謝和代謝流通路研究:

Top 1: 三羧酸循環- 27%
Top 2: 醣解- 19%
Top 3: 磷酸戊糖途徑- 18%
Top 4: 其他- 13%
Top 5: 氨基酸相關通路- 7%

>70%





代謝應用方向分布:

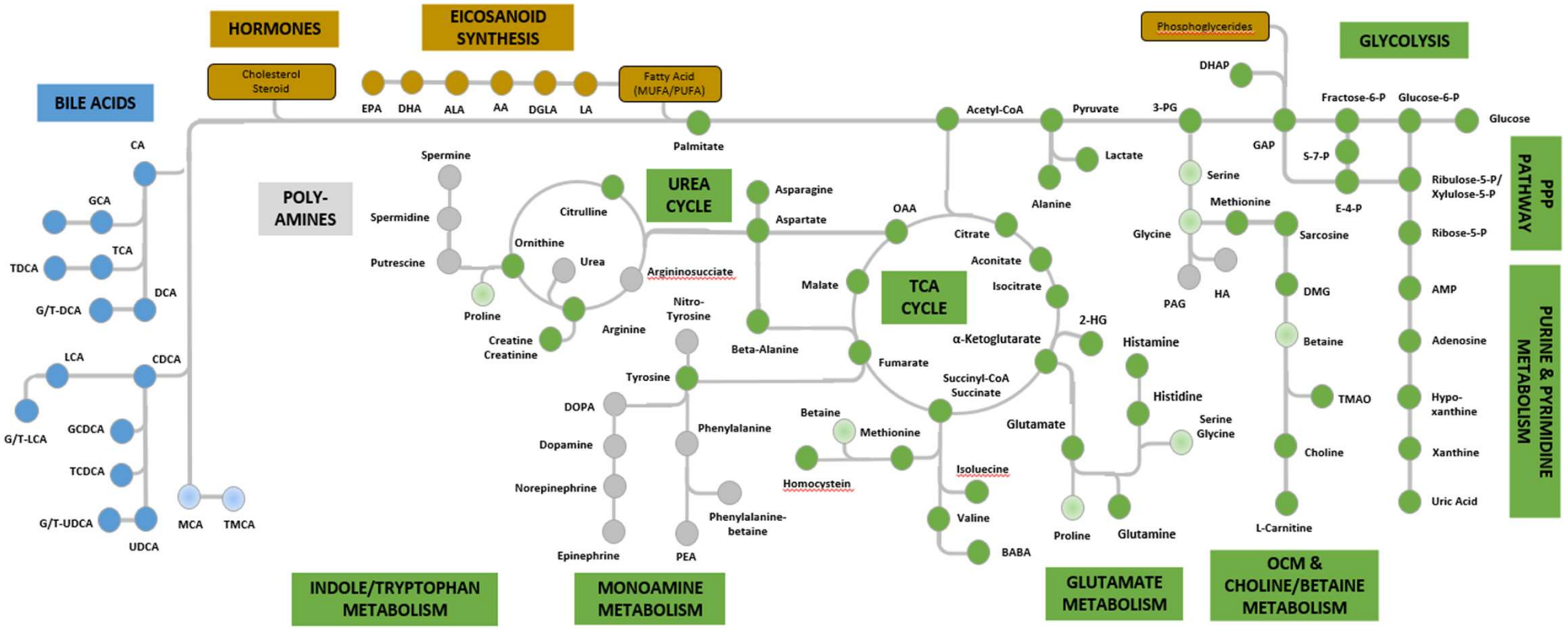
應用一: 健康/疾病(癌症)- 42%
應用二: 營養代謝/暴露组学- 18%
應用三: 微生物/基因/生物研究- 16%
應用四: 植物（代谢）研究- 11%
應用五: 藥物治療機制研究- 7%

>70%

Mass Spectrometry Reviews, 2020, Vol. 39, Issue 5-6, Haitao Lu
Frontiers in Pharmacology, Review Article, 21, March 2022, Abdul-Hamid Emwas
Current Opinion in Biotechnology, Vol. 34, Aug, 2015, Page 1-8, Uwe Sauer

何謂「功能性」目標代謝體

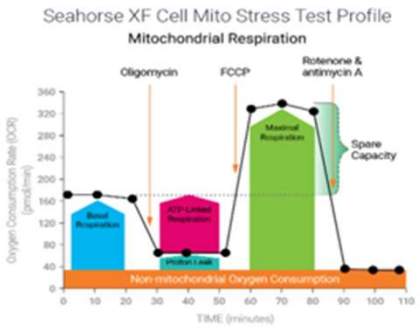
實現加速代謝體平台建立過程, 快速提供服務, 產出結果



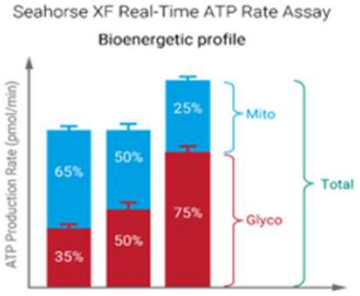
不僅僅提供分析方法, 分析方法與生物學功能性通路關聯

Seahorse豐富的試劑套組: 粒腺體功能代謝、能量代謝

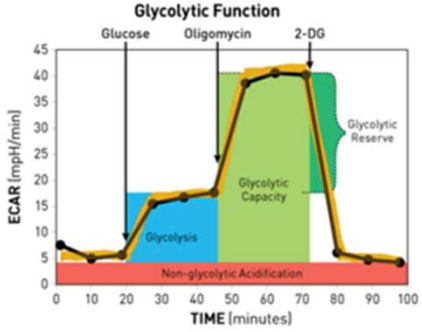
Seahorse



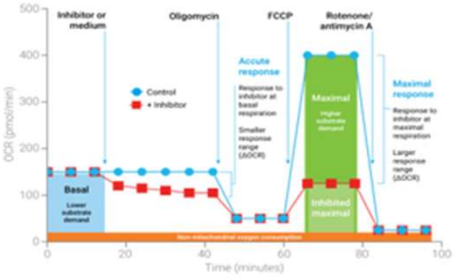
Cell Mito Stress Test
粒線體氧化壓力實驗



Real-Time ATP Rate Assay
實時ATP速率測定實驗



Glycolytic Stress Test
糖解壓力實驗



Substrate Oxidation Stress Test
檢測細胞對Substrate的依賴性

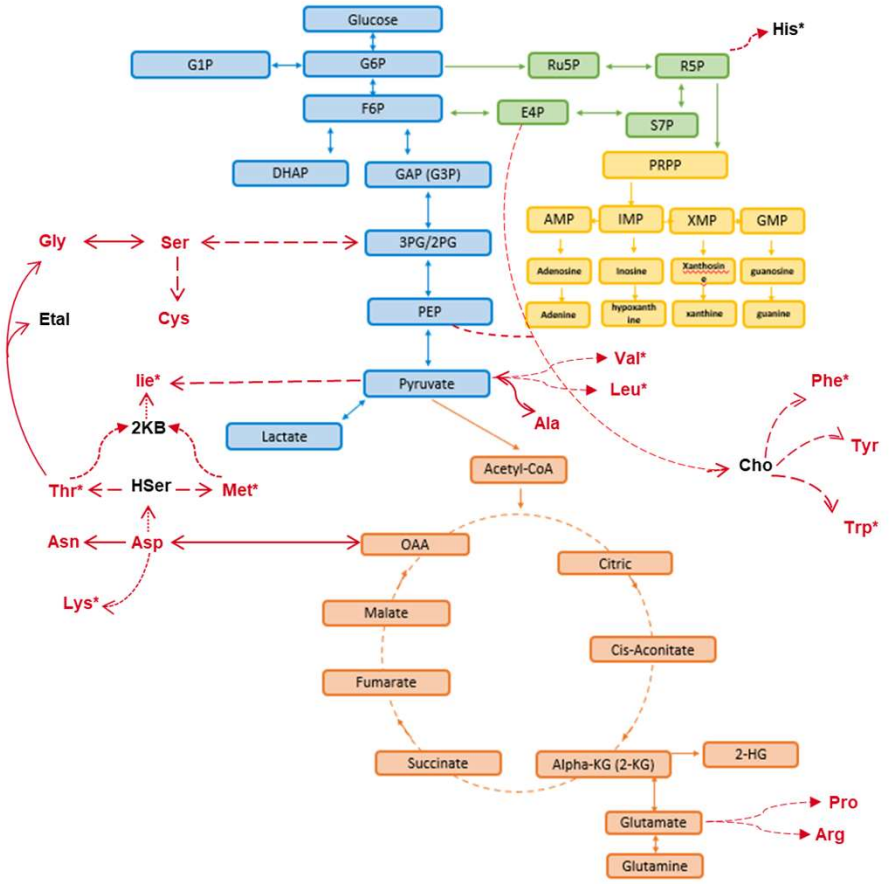
陽明交通大學(台北榮總)
高雄榮總
高醫、台大、中研院

生物功能性目標代謝體標準化方案
- 中心碳代謝、粒線體(自由基)、能量代謝研究

LCTQ & LCQTOF

- 140+功能性代謝物,含中心碳、氨基酸和能量代謝標準化方案(無須標準品)
- 提供500+功能性代謝物質譜庫(儀器條件)

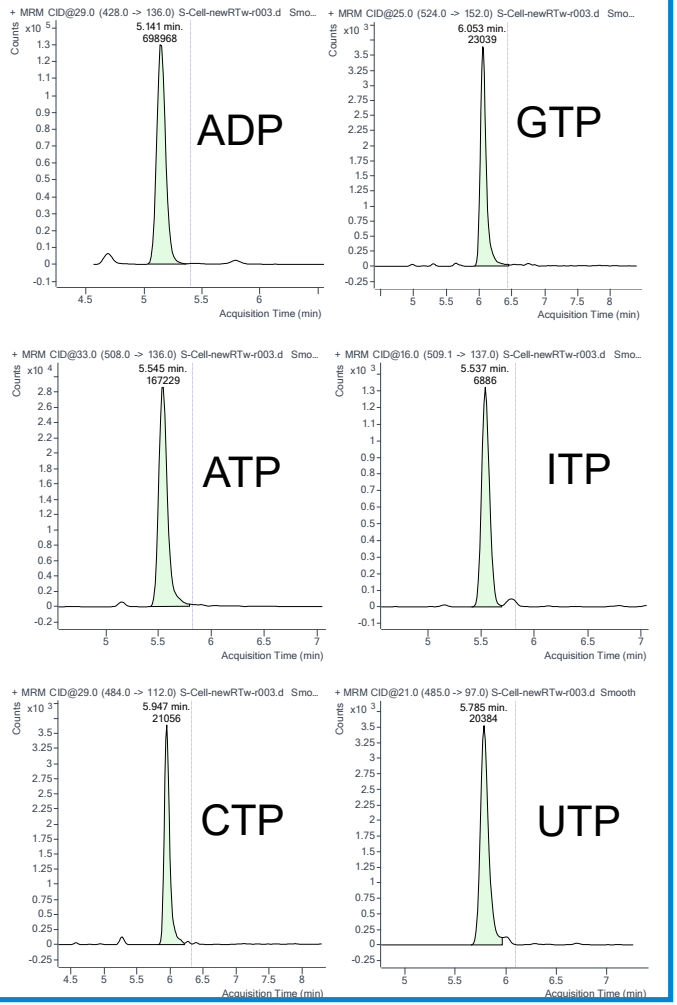
通路名稱	代謝物数量	通路覆蓋度
糖解 (Glycolysis, EMP/ED)	17	100%
戊糖磷酸途径 (PPP)	12	100%
三羧酸循環 (TCA)	20	100%
氨基酸代謝 (AA)	40	>90%
能量代謝/合成 (Nucleotide/Nucleoside)	39	>90%
其他	17	>90%

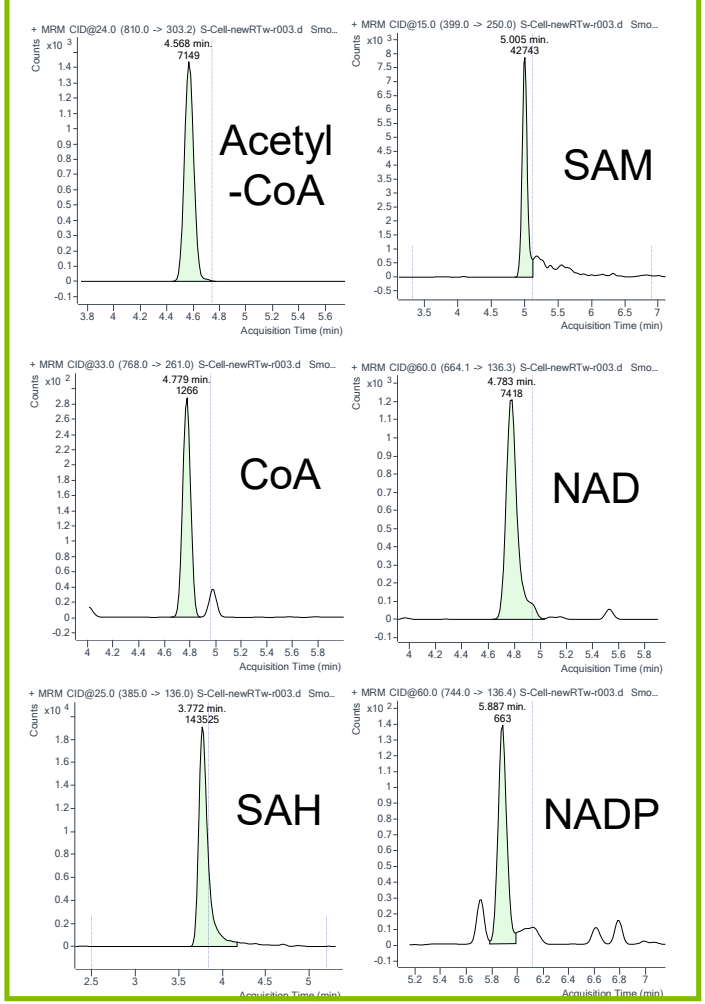


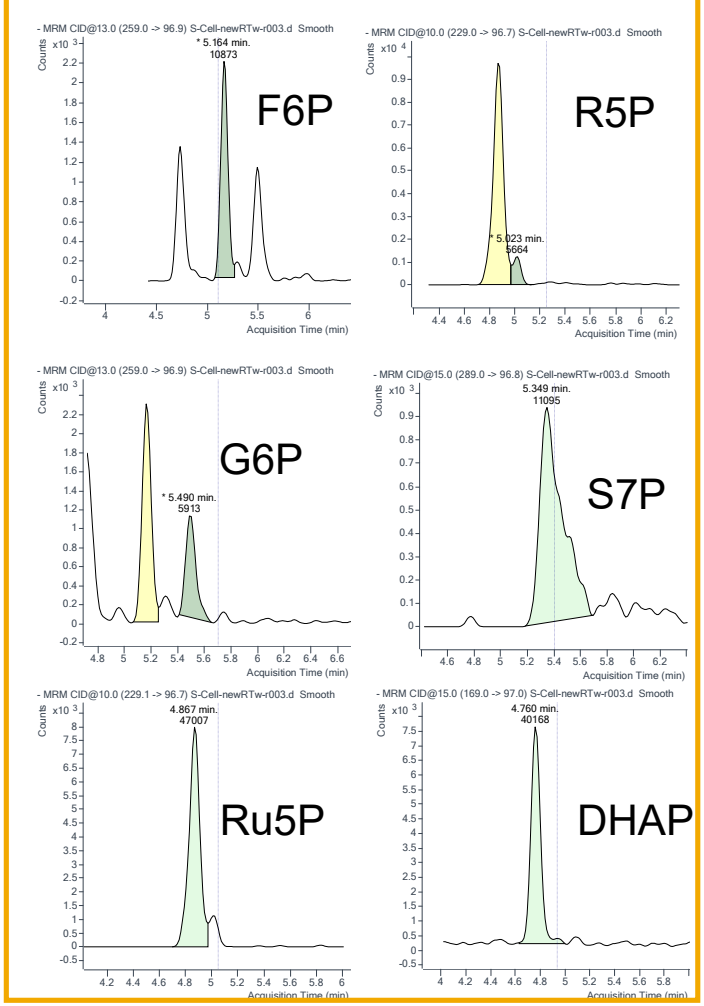
生物功能性目標代謝體標準化方案培訓流程

Pathway name	metabolites
Glycolysis (12)	1,3-BPG、2,3-BPG、2-PG、3-PG、DHAP、F6P、FBP、G1P、GAP、Glc(Glucose)、Lactate、PEP & Pyruvate
Glycolysis-TCA (2)	NAD、NADH
Glycolysis-NTP (2)	ADP、ATP
Pentose phosphate pathway (PPP, 9)	6-PG、E4P、FMN、G6P、NADP、NADPH、R5P、Ru5P、S7P
TCA cycle (11)	2-HG、Acetyl-CoA、alpha-KG、cis-Aconitate、Citric/Isocitric、CoA、Fumarate、Malate、OAA、Succinate、Succinate-CoA
TCA-AA (2)	Gln(Glutamine)、Glu(Glutamic acid)*
TCA-NTP (2)	GDP、GTP
Amino acids (AA, 40)	3-AIBA、5-Oxoproline、Adenylosuccinic acid、Ala(Alanine)*、Arg(Arginine)*、Argininosuccinic acid、Asn(Asparagine)*、Asp(Aspartic acid)*、Betaine、Cit(Citrulline)、Creatine、(Cysthi)Cystathiononine、Cys(Cysteine)、Cystine*、、、Gly(Glycine)*、His(Histidine)*、Hyp(Hydroxyproline)、H-Ser(Ser衍生物)、Ile(Isoleucine)*、Kynurenate、Leu(Leucine)*、L-Kynunrenine、Lys(Lysine)*、Met(Methionine)*、N-Acetyl-Asp、N-Carbamoyl-Asp、O-Acetyl-Serine、Orn(Ornithinr)*、Phe(Pheny;alanine)*、Pro(Proline)*、P-Ser(Ser 衍 生 物)、Ser(Serine)*、Taurine、Thr(Threonine)*、Trp(Tryptophan)*、Tryptamine、 Tyr(Tyrosine)*、Uracil、Urate & Val(Valine)*
Nucleotides (NTP,23)	AMP、cAMP、CDP、CDP-choline、cGMP、CMP、CTP、dAMP、dCDP、dCMP、dCTP、dGMP、dGTP、dTTP、dUTP、GMP、IDP、IMP、ITP、TMP、UDP、UMP & UTP
Nucleosides (NS,18)	Adenine、Adenosine、Cytidine、Cytosine、dA、dC、Deoxyribose、dG、dU、Guanine、Guanosine、Hypoxanthin、Inosine、Ribose、Thymidine、Thymine、Uridine & Xanthine
Others (15)	Dimethylglycine、GABA、GSH、GSSG、Inositol、Itaconic acid、Malonyl-CoA、O-Phosphorylethanolamine、Oroate、Retinol Acetate、SAH、SAM、Sarcosine、Urea & Xanthosine

高醫測試樣品- 肺癌細胞 (展示代表性圖譜:能量代謝/氧化還原/特殊分離)



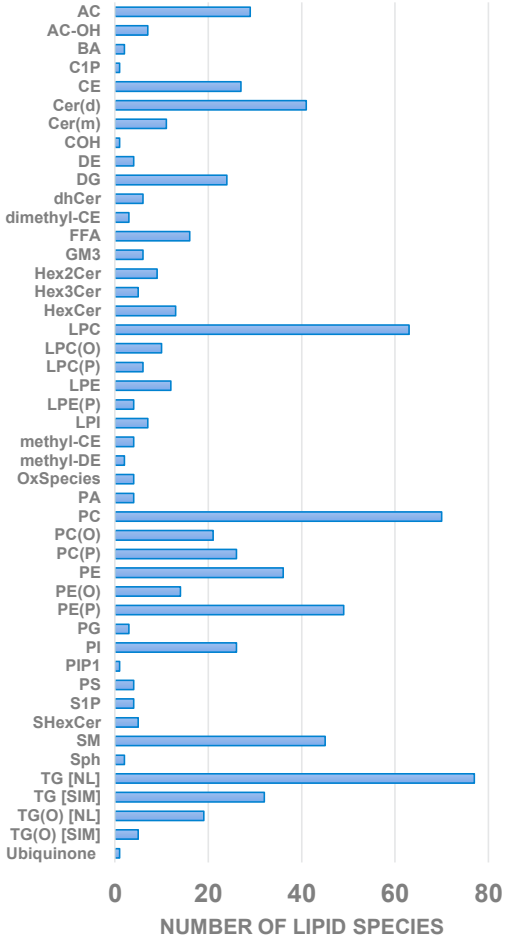


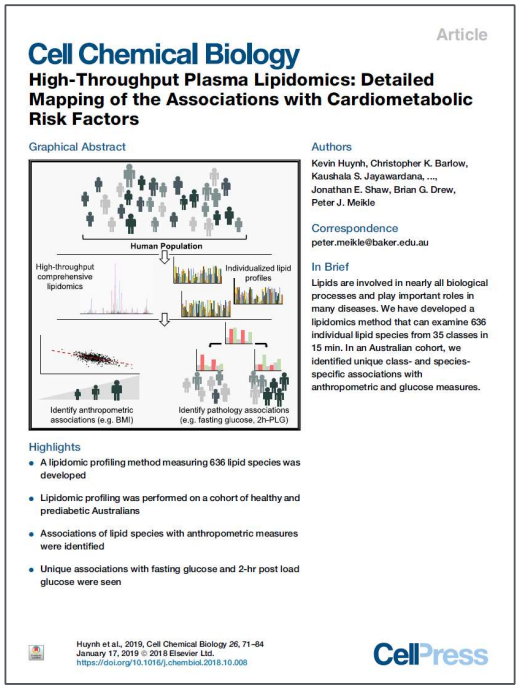


安捷倫目標脂質體學標準化方案: 常規脂質輪廓分析

LCTQ

763 Lipids Measured across 44 Lipid Classes





Article

Cell Chemical Biology

High-Throughput Plasma Lipidomics: Detailed Mapping of the Associations with Cardiometabolic Risk Factors

Graphical Abstract

Authors
Kevin Huynh, Christopher K. Barlow, Kaushala S. Jayawardana, ..., Jonathan E. Shaw, Brian G. Drew, Peter J. Meikle

Correspondence
peter.meikle@baker.edu.au

In Brief
Lipids are involved in nearly all biological processes and play important roles in many diseases. We have developed a lipidomics method that can examine 636 individual lipid species from 35 classes in 15 min. In an Australian cohort, we identified unique class- and species-specific associations with anthropometric and glucose measures.

Highlights

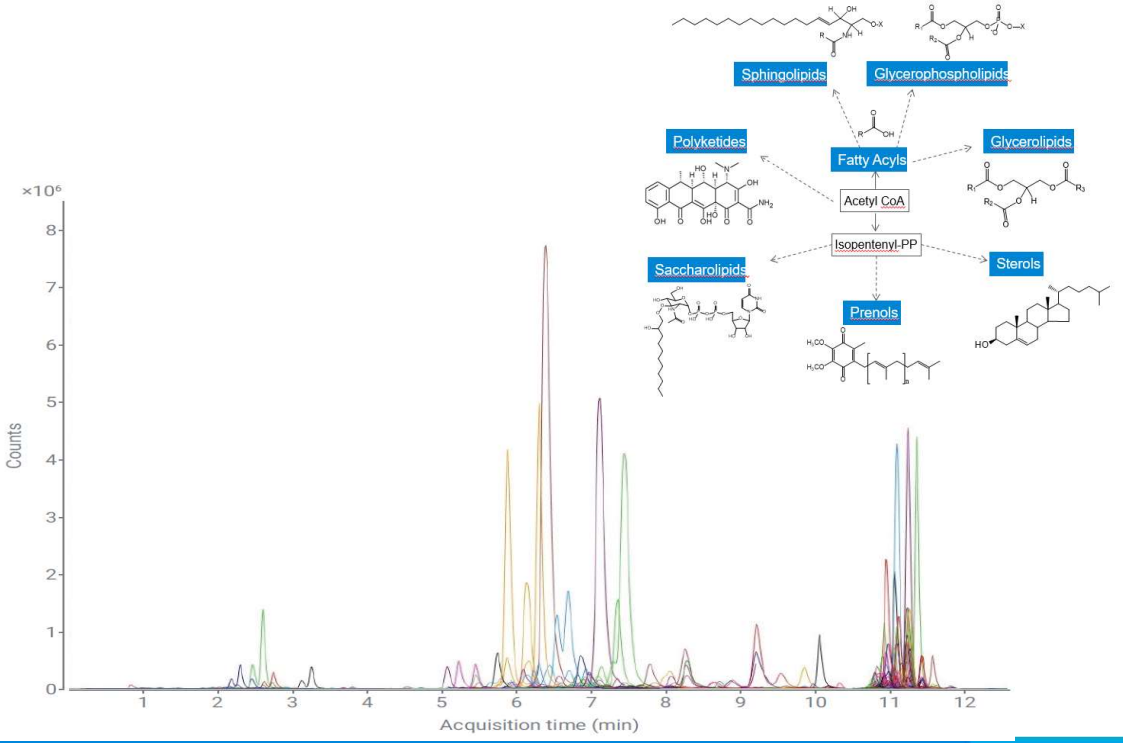
- A lipidomic profiling method measuring 636 lipid species was developed
- Lipidomic profiling was performed on a cohort of healthy and prediabetic Australians
- Associations of lipid species with anthropometric measures were identified
- Unique associations with fasting glucose and 2-hr post load glucose were seen

Huynh et al., 2019, Cell Chemical Biology 26, 71–84
January 17, 2019 © 2018 Elsevier Ltd.
https://doi.org/10.1016/j.chembiol.2018.10.008

CellPress

❖ Targeted Lipidomics Method

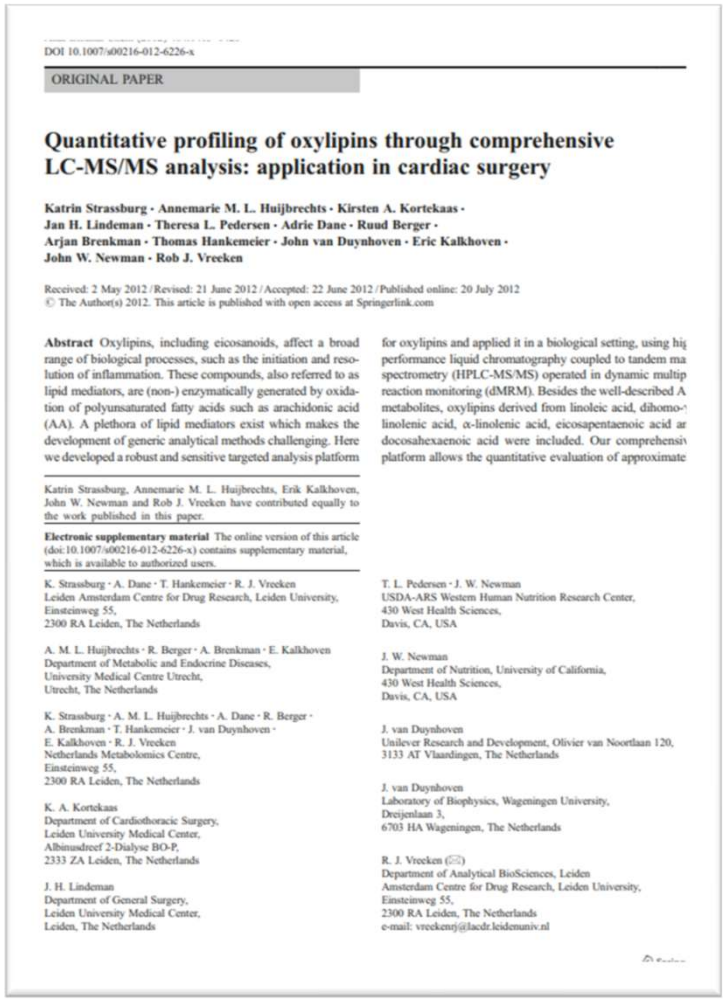
- Developed for plasma samples
- Covers 44 lipid classes, 763 lipids covered
- Sample preparation of 10 µL plasma



Agilent

安捷倫目標脂質體標準化方案:氧化脂質輪廓分析(炎症相關)

LCTQ (6475/6495)



DOI 10.1007/s00216-012-6226-x

ORIGINAL PAPER

Quantitative profiling of oxylipins through comprehensive LC-MS/MS analysis: application in cardiac surgery

Katrin Strassburg · Annemarie M. L. Huijbrechts · Kirsten A. Kortekaas · Jan H. Lindeman · Theresa L. Pedersen · Adrie Dane · Ruud Berger · Arjan Brenkman · Thomas Hankemeier · John van Duynhoven · Eric Kalkhoven · John W. Newman · Rob J. Vreeken

Received: 2 May 2012 / Revised: 21 June 2012 / Accepted: 22 June 2012 / Published online: 20 July 2012

Abstract Oxylipins, including eicosanoids, affect a broad range of biological processes, such as the initiation and resolution of inflammation. These compounds, also referred to as lipid mediators, are (non-) enzymatically generated by oxidation of polyunsaturated fatty acids such as arachidonic acid (AA). A plethora of lipid mediators exist which makes the development of generic analytical methods challenging. Here we developed a robust and sensitive targeted analysis platform for oxylipins and applied it in a biological setting, using hig performance liquid chromatography coupled to tandem ma spectrometry (HPLC-MS/MS) operated in dynamic multip reaction monitoring (dMRM). Besides the well-described A metabolites, oxylipins derived from linoleic acid, dihomo- linolenic acid, α-linolenic acid, eicosapentaenoic acid ar docosahexaenoic acid were included. Our comprehensi platform allows the quantitative evaluation of approximate

Katrin Strassburg, Annemarie M. L. Huijbrechts, Erik Kalkhoven, John W. Newman and Rob J. Vreeken have contributed equally to the work published in this paper.

Electronic supplementary material The online version of this article (doi:10.1007/s00216-012-6226-x) contains supplementary material, which is available to authorized users.

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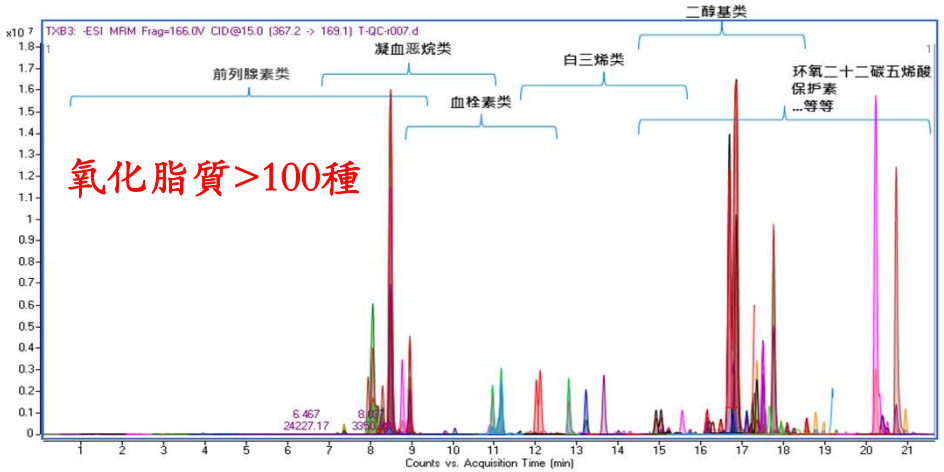
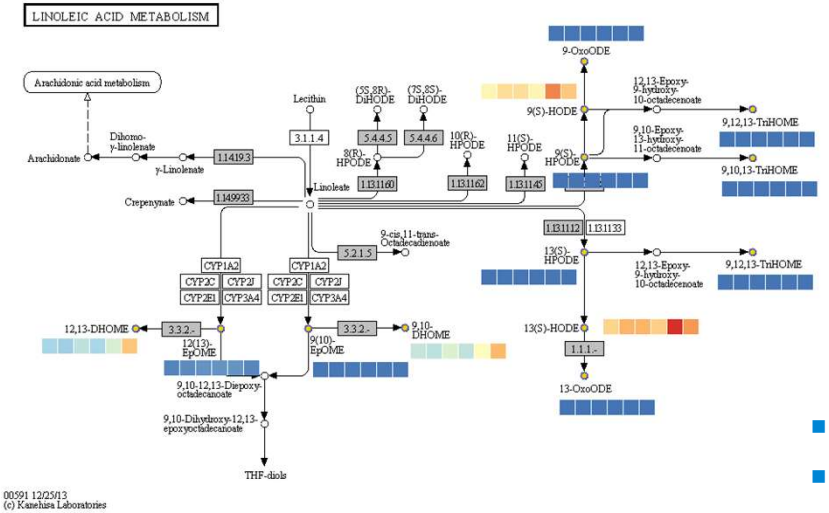




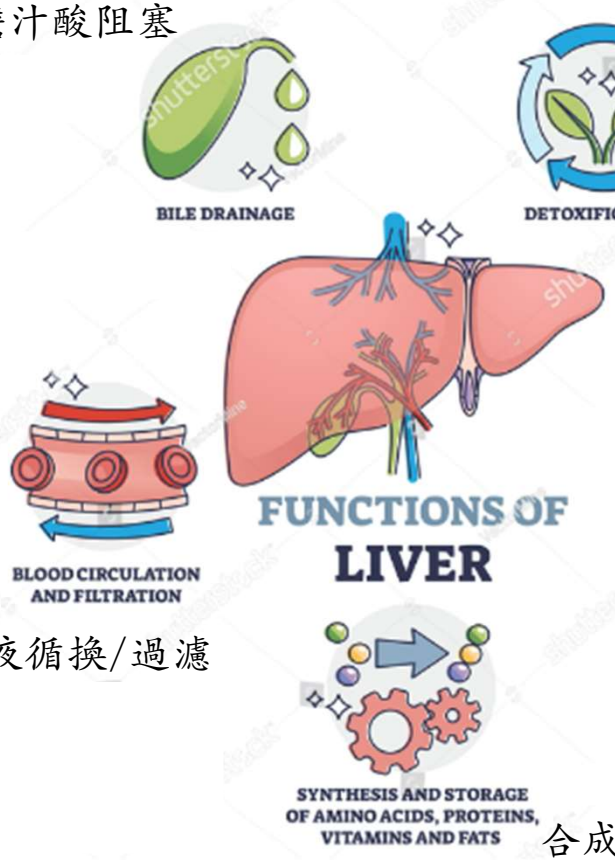
- 同分異構體分離
- 標準品非常貴

肝膽相照: 膽汁酸的重要性

LCTQ (6475/6495)

膽汁酸阻塞

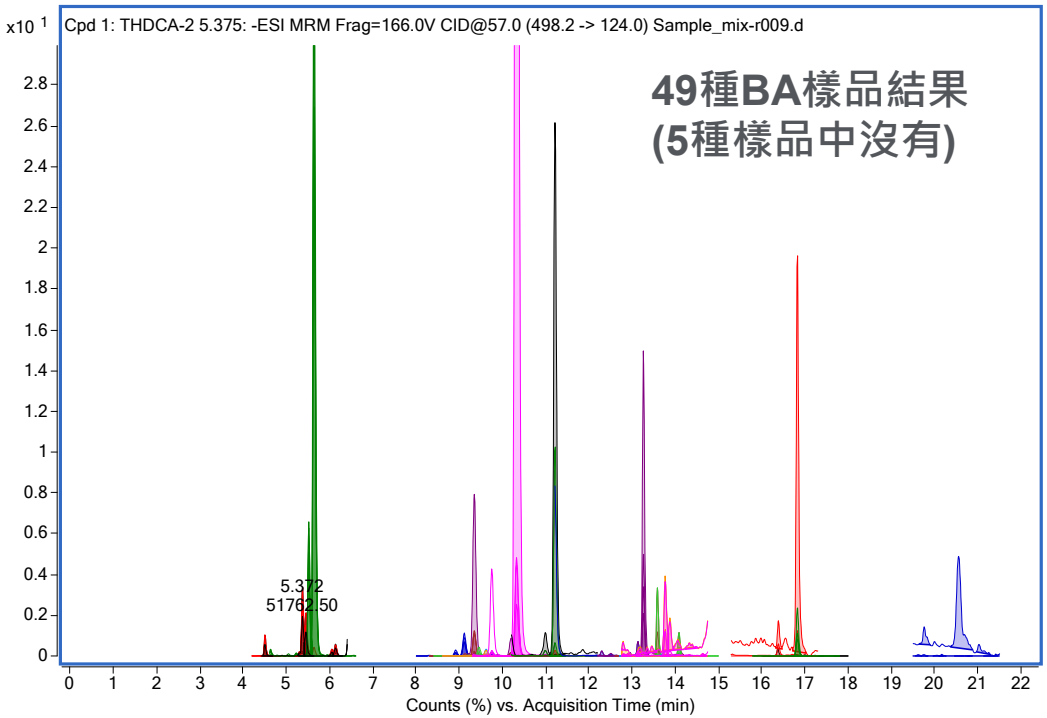
排毒功能



血液循換/過濾

血液糖分調節

合成、保存胺基酸、
蛋白、維生素或脂質

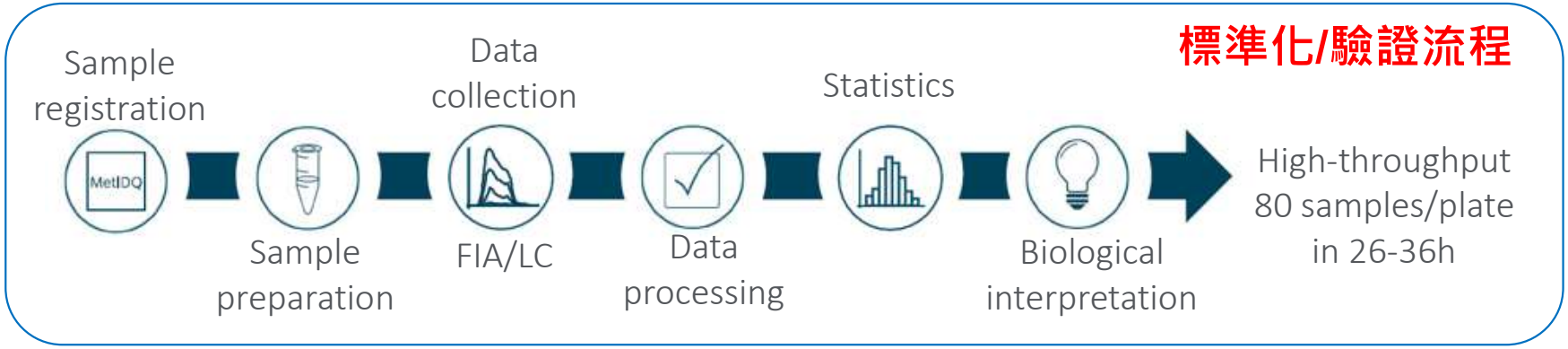


- 同分異構體分離
- 標準品非常貴
- 人體常檢18-20種; 老鼠會增加3種MCA

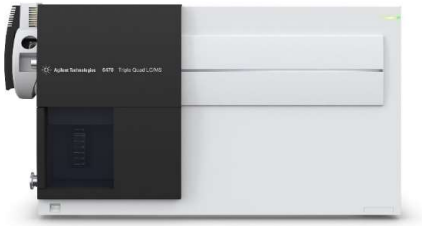
Biocrates Kits Available on Agilent LC/TQ Systems (第三方試劑套組)

LCTQ

Targeted Metabolomics analysis for central carbon metabolism and downstream products



biocrates AbsoluteIDQ p180 kit
1290 Infinity II LC – 6470或6475 LC/TQ



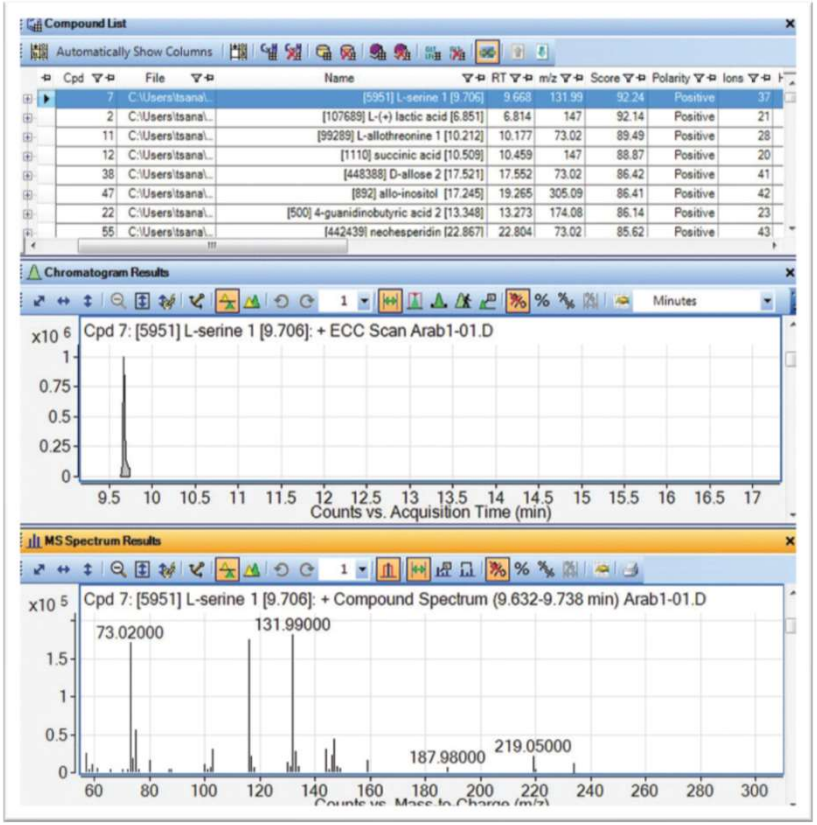
- Up to 188 metabolites across 6 biochemical classes (lipids, biogenic amines, amino acids, acylcarnitines…)

安捷倫目標代謝體標準化方案-氣相質譜

GCMS

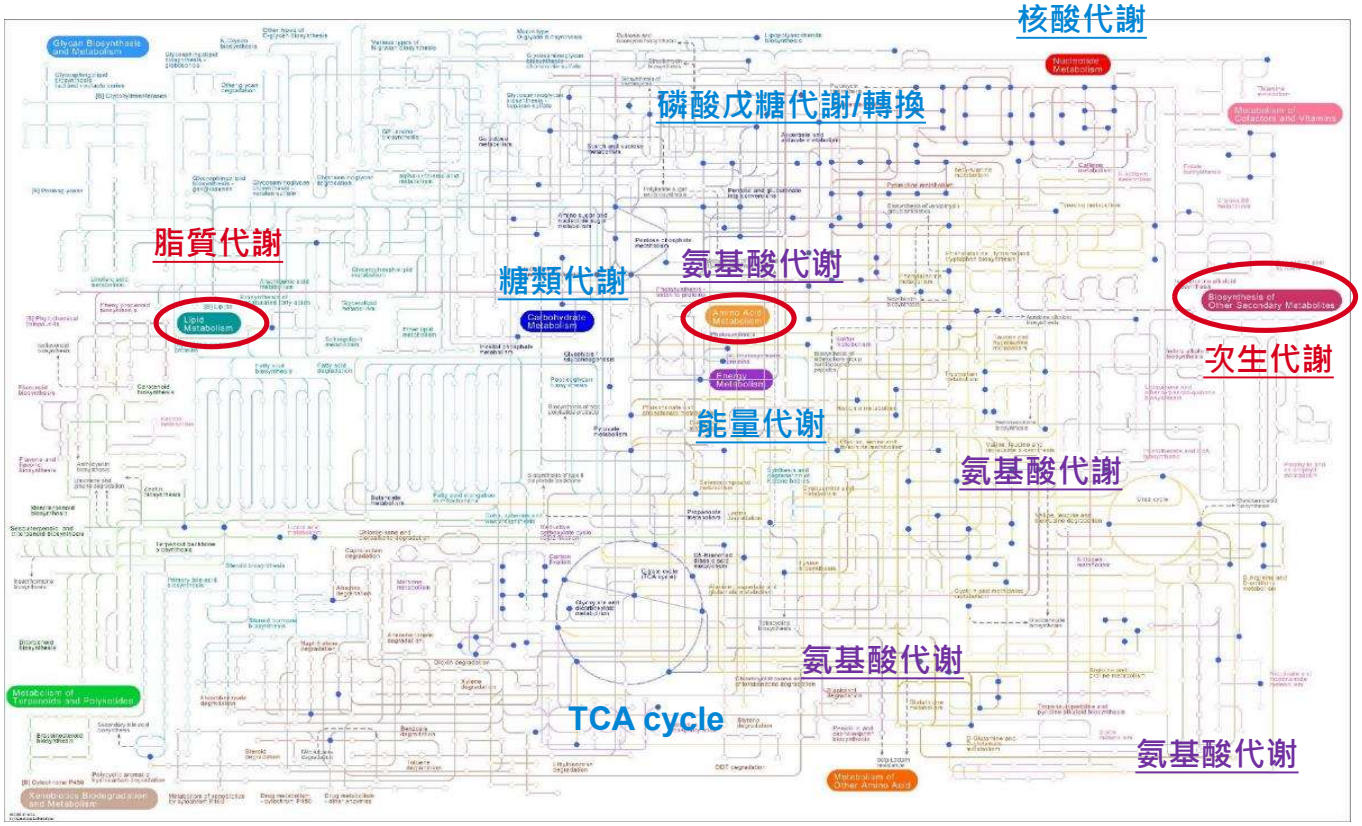
- Agilent Fiehn GC/MS RTL Metabolomics Library Complete Workflow (全球目前代謝體Top實驗室之一)

- Complete, preprogrammed GC/MS methods with a retention time locked method
- EI spectra library with retention indexing (RI) for around 1,400 compounds



安捷倫「功能性」目標代謝(脂質)體生物醫學研究策略

安捷倫標準化方案+第三方試劑套組



There is little overlap between these targeted solutions!

Agilent focuses on central carbon metabolites (blue dots)

Biocrates kit focuses on downstream products of central carbon metabolism such as lipids, biogenic amines, and acylcarnitines (red circles)

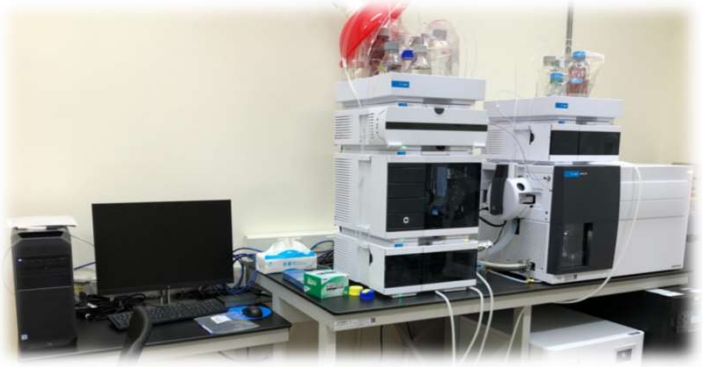
Only overlap is amino acids

(purple circles)

安捷倫聚焦打造生物功能性代謝通路研究, 不僅僅是目標化合物分析

安捷倫台灣多體學合作網路

建構多維深度代謝體平台、打造創新方案、保證領先技術同步



代謝體學/脂質體學

台大基因體、中研院、中研院基因體研究中心、台北醫學大學生物化學細胞分子生物學科、國衛院LCMSMS共儀、陽明交通大免疫所、中興環農所、中興食品應用生物科技、中國醫醫學院癌症生物研究所…

跨領域、新方向客戶群：

細胞治療/幹細胞代謝流

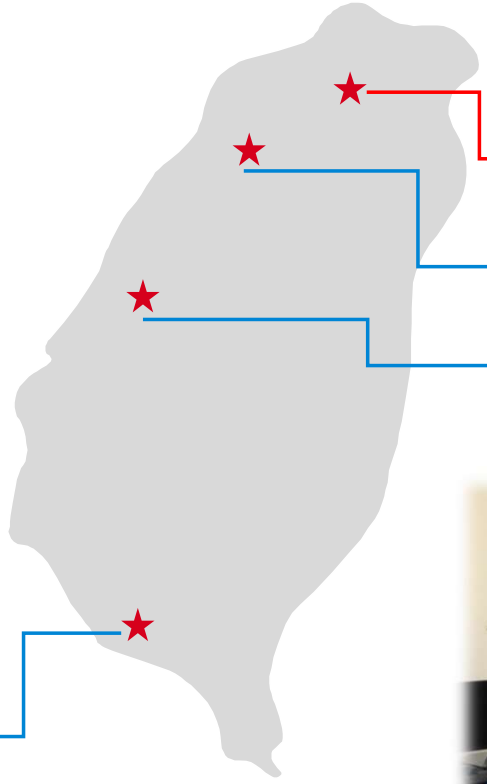
陽明交大口生所、台大生命科學、台大醫學院…

合成生物學

中研院生化所、中興化工所…

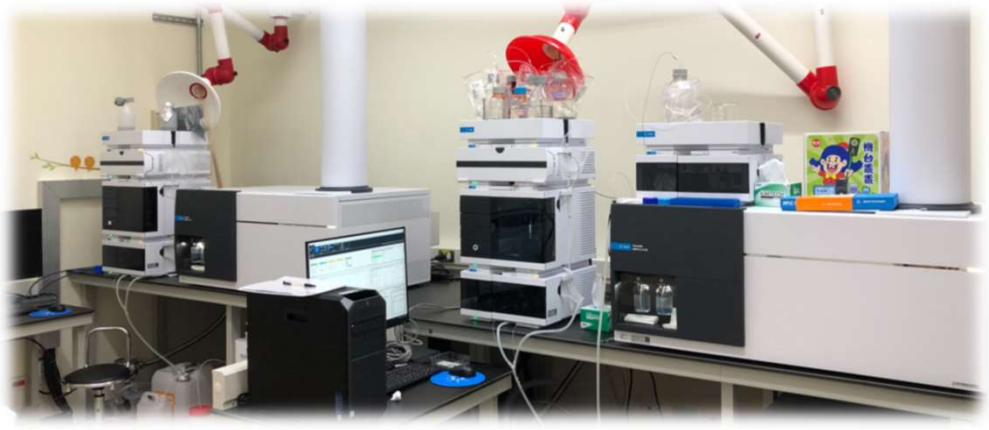
天然物(植物)、中草藥代謝研究

中研院南院、高醫天然藥物所…



- 中央研究院農生共儀(6545XT/6495D)-FY18 & 24
- 台大基因體代謝核心 (6540/6460/6495)-FY23
- 台大醫學院共儀代謝核心 (6545XT/6470)-FY23
- 台大醫學院尖端計畫 (6545XT)-FY23
- 國衛院LCMSMS共儀 (6495)-FY22

- 中興大學土壤調查環農所 (6545/6530)-FY21



- 高雄醫學大學 (6475)-FY24

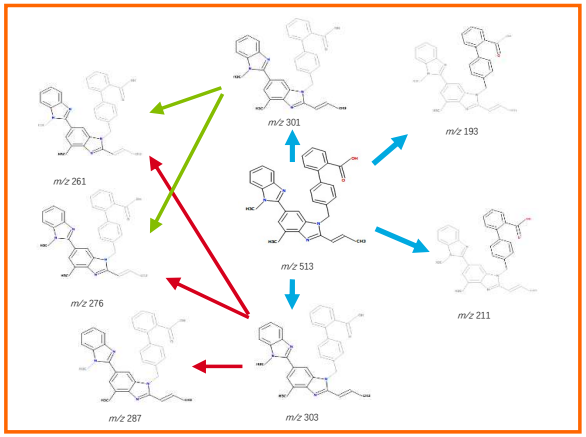
安捷倫6475A在藥物領域應用

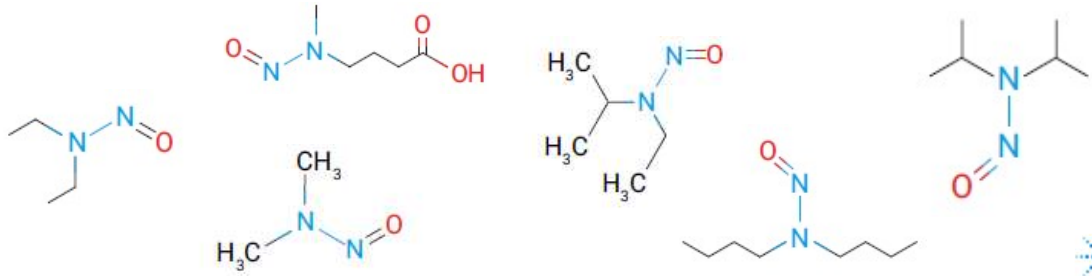
Jimmy Chan (詹舜安)

LC/MS Sr. Application Scientist (Application Development /Project Cooperation)

Agilent Technologies

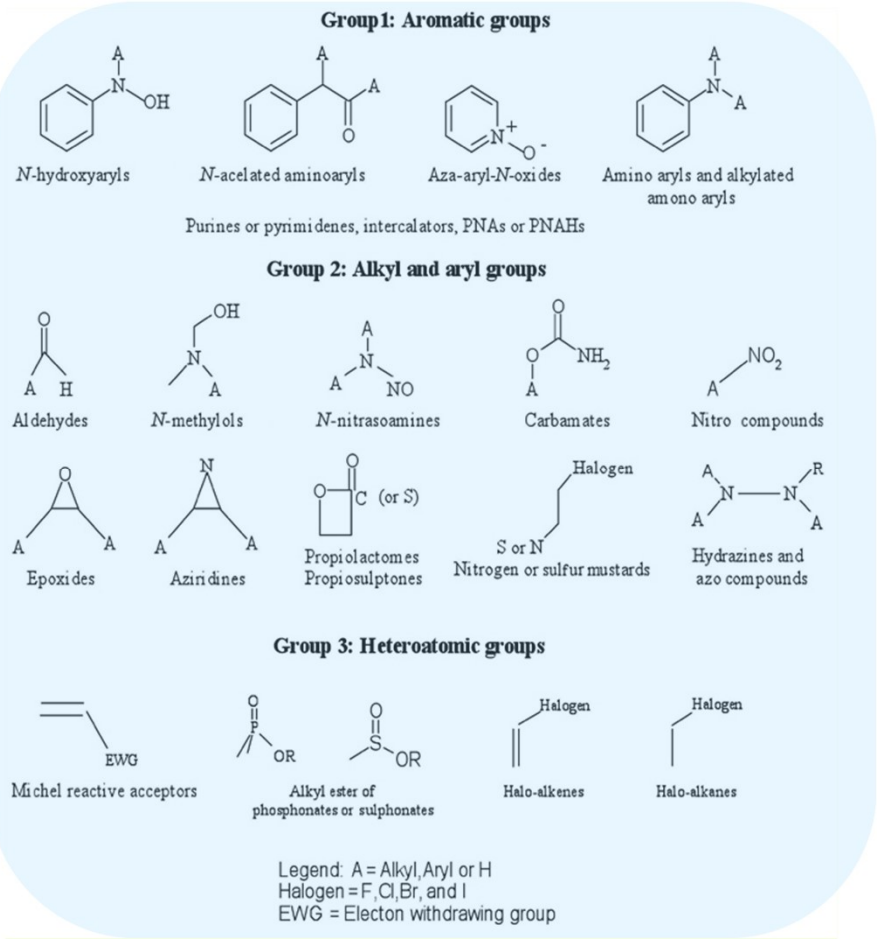
2024-11





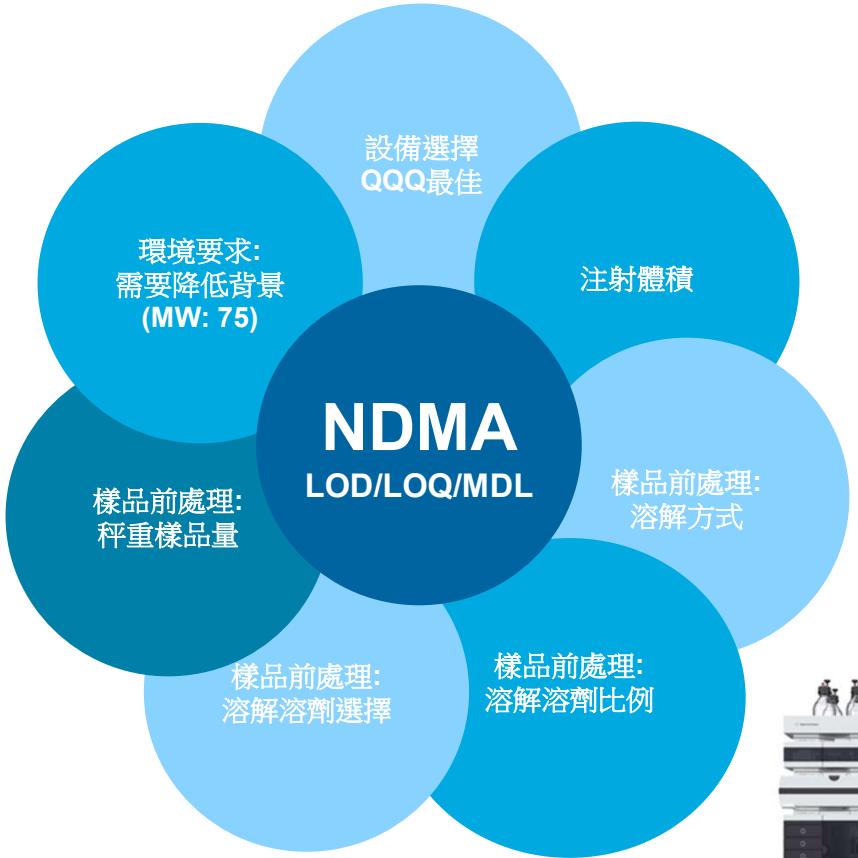
Agilent

NDMA: Structural Alerts (Mutagenicity) in Pharmaceuticals

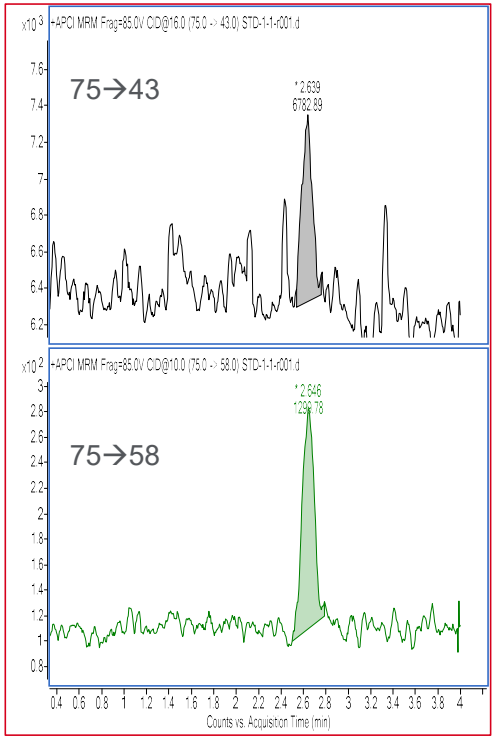


突變性不純物又可稱為基毒性或遺毒性雜質(Genotoxicity Impurity), 這類不純物是指能直接或間接損傷細胞 DNA, 產生致突變和致癌作用的物質。全球各大藥品監督官方, 如歐洲藥品管理局(European Medicines Agency,EMA) 和美國食品藥物管理局 (U.S.FDA) 為這類毒性不純物控制方法提供了初步的框架, 基於現行國際醫藥法規協合組織 (International Conference on Harmonization, ICH) 法規中的ICH M7 對於毒性不純物的識別、 鑑定和控制提供相關的參考指南。法規中建議經過查閱相關文獻數據、利用基因毒性測試結果或原料藥與預期不純物中鑑定是否有警示結構(Alerting structure)存在,同時評估結構與毒性測間的關聯性 (Structure-Activity Relationship, SAR)。

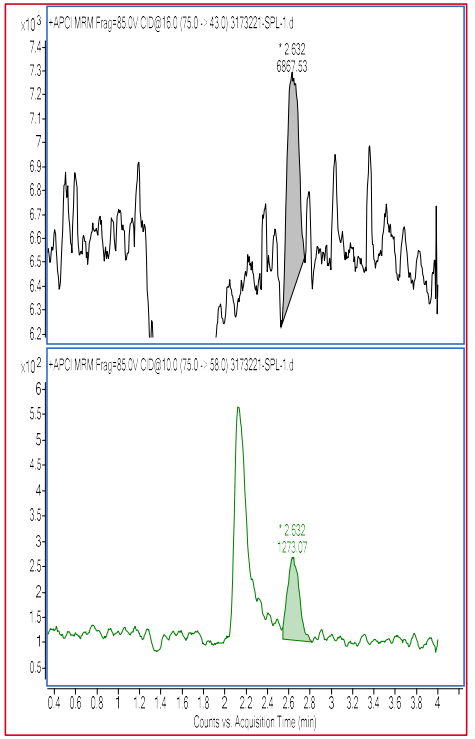
NDMA檢測的關鍵



STD(0.12ng/ml in 85%H2O)



API spike (0.12ng/ml in 85%H2O)



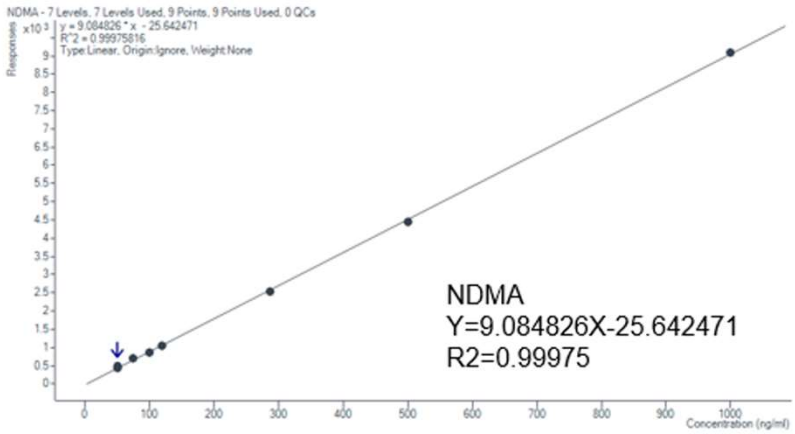
Agilent 6475 QQQ 使用二級定量/定性, 完全符合且優於目前全球法規需求(2-6pg)

6475 QQQ Technologies - Continued Development

1
- New Enhanced Q1 Ion Optics
- Improved ion transmission

2
- New Tapered Hexapole Collision Cell
- Effective ion collection and transmission

3
- New Detector with High Energy Conversion Dynode
- Improved NEG ion detection with low noise



低噪音 & 高靈敏度 (完美詮釋S/N)

The importance of clinical mass spectrometry - Clinical Laboratory & Clinical Research

The application of mass spectrometry (MS) to clinical analysis has evolved considerably since it was first used, both in research facilities and for routine analysis in clinical laboratories.

Mass spectrometry has long been recognized as the gold standard for validation of quantitative analytical assays.

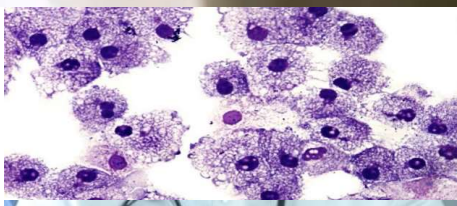
Applied for medicine departments

- Internal medicine (內科學)
- Surgery (外科學)
- Obstetrics & Gynecology (婦產科學)
- Pediatrics (小兒科學)
- Psychology (精神醫學)
- Neuroscience (神經科學)
- Urology (泌尿科學)
- Opthalmology (眼科學)

……..

Advantages

- Understand the relationship of “Biomarkers” & “Disease”
- Diagnostic & Therapeutic
- Communication between medical workers & patients
- Precision Medicine from “Health Examination”



The Routine Applications with Clinical Mass Spectrometry

Endocrinology/Estrogen/Vitamin

內分泌系統分析
情緒賀爾蒙
雌激素
腫瘤標誌物監控

- Cortisol
- Epinepherine
- Nor-Epinepherine
- Dopamine

Newborn Screening (NBS)

- Amino Acid
- Carnitine
- Acrylcarnitine
- Homocystein

代謝系統分析
有機酸代謝
胺基酸代謝
環境賀爾蒙分析

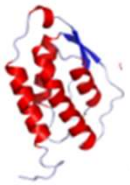
TDM/Clinical Toxicology

藥(毒)物濫用分析
止痛藥濫用
抗癲癇藥物
免疫抑制劑藥物

Proteomic/Peptide/Nucleotide Biomarkers Monitoring (*New Area!!*)

- Apolipoprotein E (E2 E3 E4
- Insulin-like Growth Factor-1 (IGF-1)
- Insulin-like Growth factor-binding prote
  globulin (SHBG)

腦部老化
孕前標誌物監控(早產兒)
阿茲海默症標誌物監控
HIV 治療藥物監控



安捷倫台灣重點臨床/臨床研究用戶:

- ❑ 台北榮總-胺基酸、有機酸、藥(毒)物監控
- ❑ 台大基因體(醫院合作)-藥(毒)物監控、代謝監控、蛋白藥物監控(癌症疾病)
- ❑ 台北醫學大學-藥物監控、蛋白藥監控(癌症疾病)

A Five Minute 1D/2D LCMS/MS Analysis of Vitamin D2 & D3 from Serum

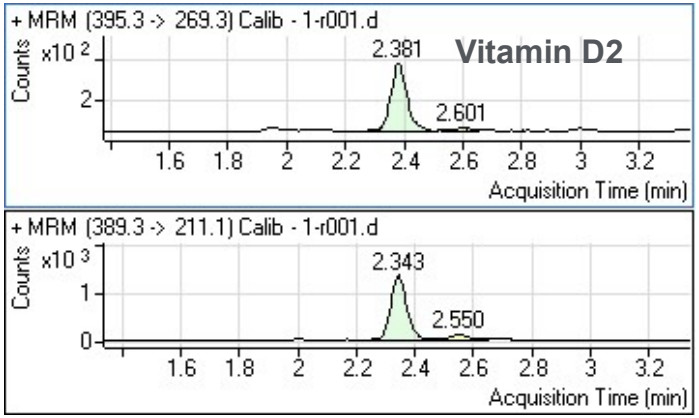
利用一維/二維液相串聯質譜檢測血清中維生素D2和D3

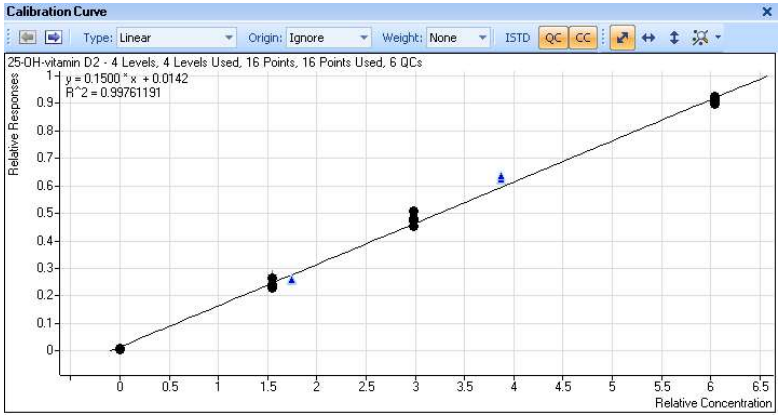
維生素D測定和方法說明

- 維生素D是骨骼健康的重要指標
- 最近的研究表明維生素D缺乏可能和其他一些身體狀況相關：
  - 骨質疏鬆
  - 幾種類型的癌症
  - 自身免疫性疾病
  - 心臟病
  - 糖尿病
  - and more…
- 由於公眾增加關注維生素D缺乏對於身體健康的影響，在過去幾年內，樣品數量檢測大大增加。
- 目標分析物通常 是25-OH-VD2 和 25-OH-VD3

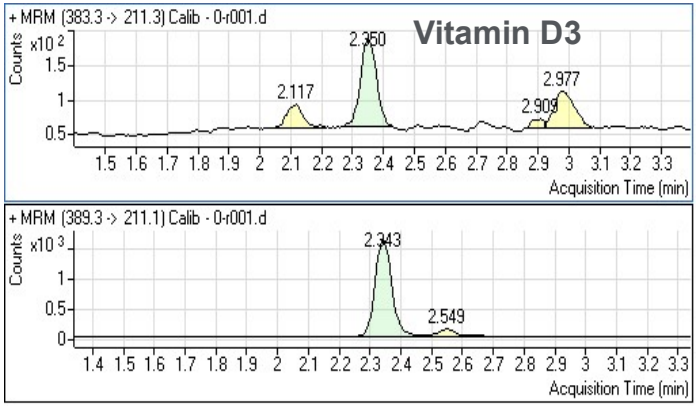
- 方法成熟
- 一般檢測單位使用免疫法試劑盒,但只能針對總量進行檢測,且存在干擾
- 過往液質檢測主要使用一維液相串聯質譜,需搭配人工樣品處理步驟 (LLE+LCMS)
- 使用二維液相串聯質譜,可在蛋白沉澱後實現從樣品前處理到儀器檢測自動化
- 整個分析時間約5分鐘, 可得優異線性與定量結果

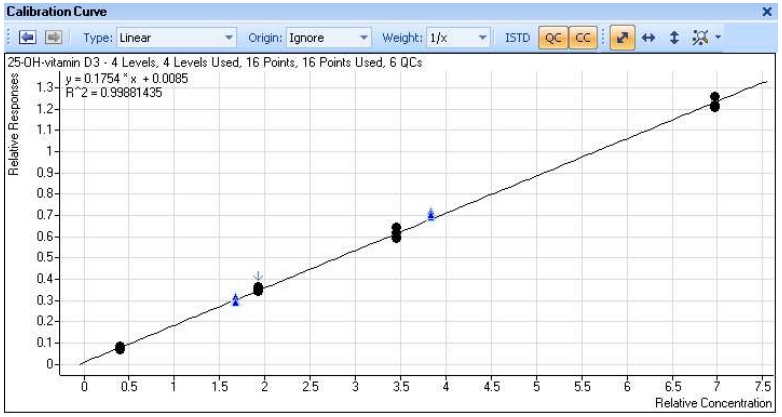
25-OH-Vitamin D2/D3
- Lowest Calibrant, IS and Calibration plot and RSD





R^2 – 0.9976
RSD at lowest Calibrator – 6.1%





R^2 – 0.9988
RSD at lowest Calibrator – 7.8%

Rapid Quantitative Analysis of Immunosuppressant Drugs in Blood & Plasma

利用安捷倫液相串聯質譜進行治療藥物監控檢測(免疫抑制劑)

治療藥物監控檢測
- Therapeutic Drug Monitoring (TDM)

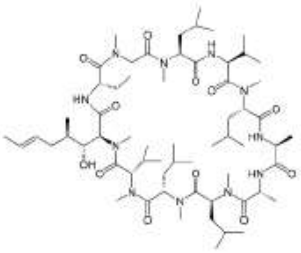
通過測定血液中或其它體液中藥物的濃度並利用藥代動力學的原理和公式使給藥方案個體化，以提高藥物的療效，避免或減少毒副反應；同時也為藥物過量中毒的診斷和處理提供有價值的實驗室依據

- 是近代藥物治療學劃時代的重大進展之一，將臨床用藥從傳統的經驗模式提高到比較科學的水準
- 是臨床藥學工作的一個重要方面，也是藥物治療學的重要內容
- 是提高醫療服務品質、進行科研與臨床相結合的有效途徑

臨床藥代動力學監測

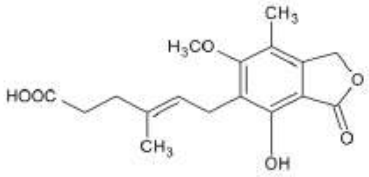
- （Clinical Pharmacokinetic Monitoring, CPM）

治療藥物監控檢測 - 常見免疫抑制劑



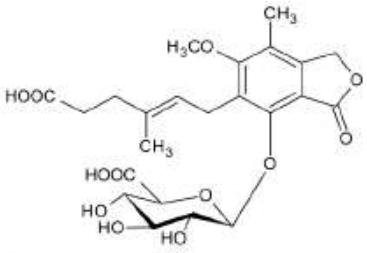
Cyclosporin A (Cs A)

環孢菌素A

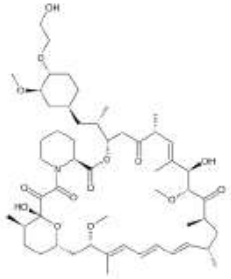


Mycophenolic Acid (MPA)

黴酚酸

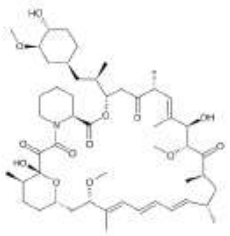


Mycophenolic Acid – Gluc (MPA-G)



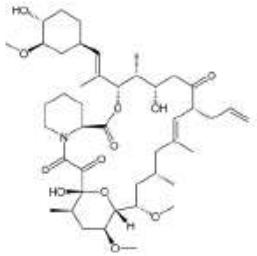
Everolimus (Eve)

依維莫司



Sirolimus (Sir)

西羅莫司



Tacrolimus (Tac)

他克莫司

抗癲癇藥物

- 苯妥英鈉*，卡馬西平*…

抗心律失常藥物

- 地高辛*、利多卡因…

抗生素藥物

- 萬古黴素…

抗抑鬱藥物

- 丙咪嗪 …

治療哮喘藥物

- 氨茶鹼*…

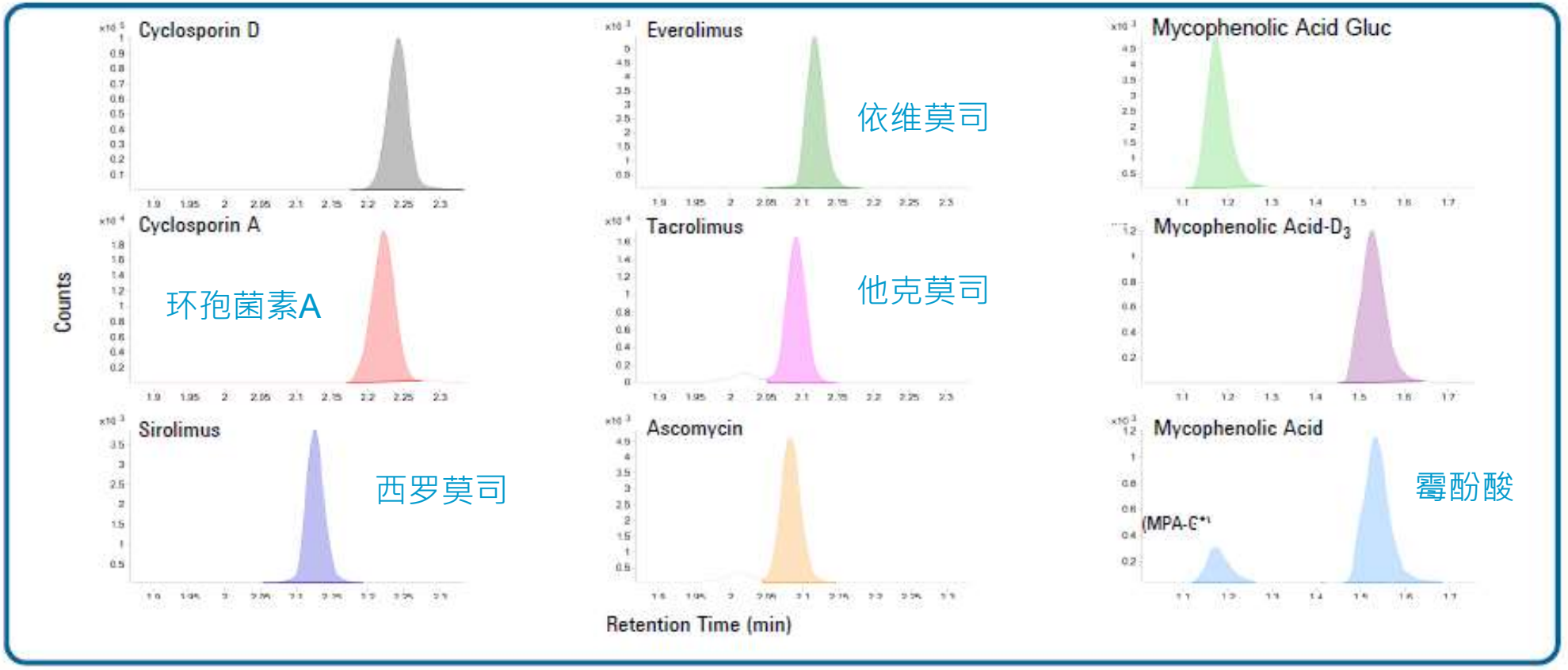
抗腫瘤藥物

- 甲氨蝶呤*…

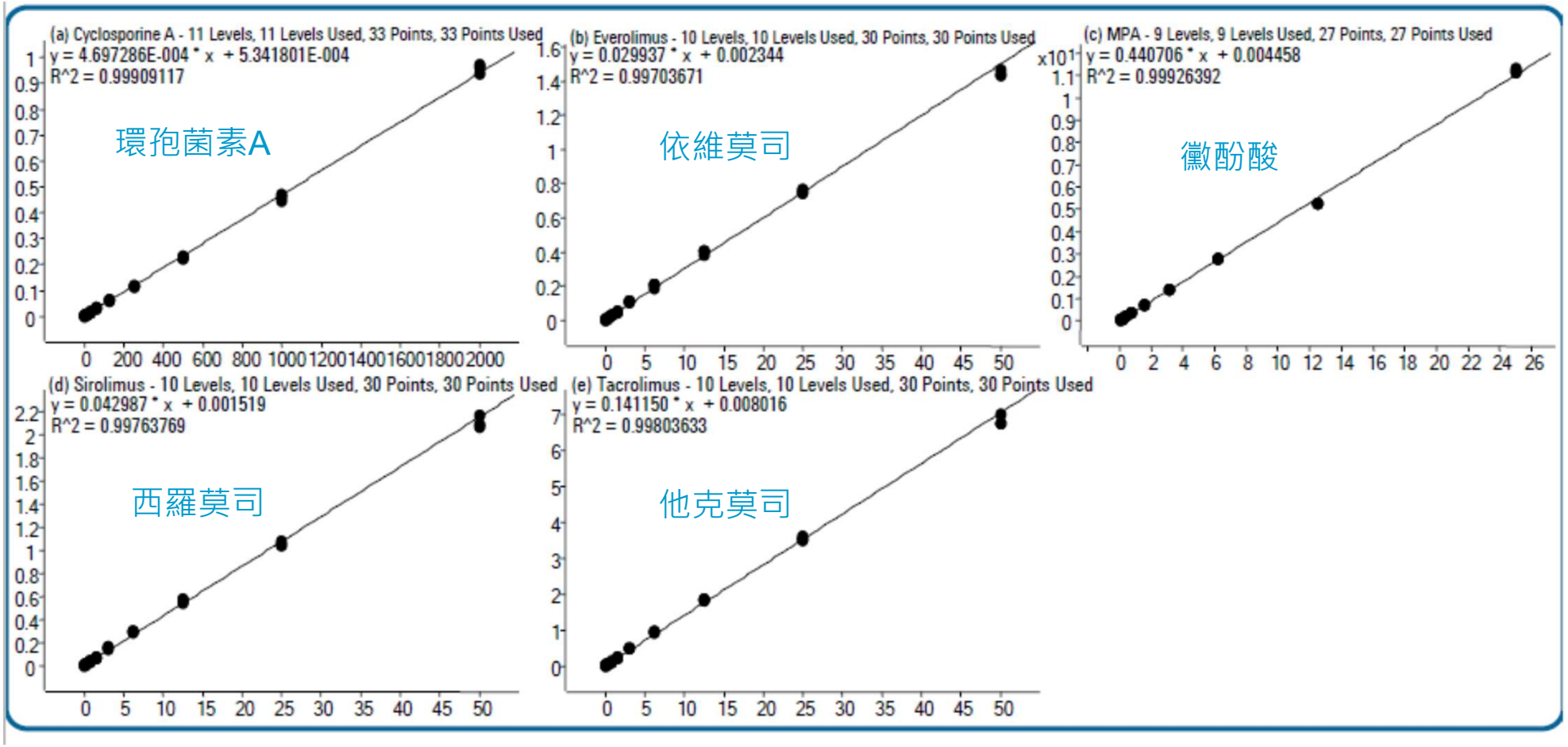
抗愛滋病藥物

- 疊氮胸苷…

免疫抑制劑分析結果 (1)
- 分析時間<2 min



免疫抑制劑分析結果 (2)


(a) Cyclosporine A - 11 Levels, 11 Levels Used, 33 Points, 33 Points Used
y = 4.697286E-004 * x + 5.341801E-004
R^2 = 0.99909117
環孢菌素A
(b) Everolimus - 10 Levels, 10 Levels Used, 30 Points, 30 Points Used
y = 0.029937 * x + 0.002344
R^2 = 0.99703671
依維莫司
(c) MPA - 9 Levels, 9 Levels Used, 27 Points, 27 Points Used
y = 0.440706 * x + 0.004458
R^2 = 0.99926392
黴酚酸
(d) Sirolimus - 10 Levels, 10 Levels Used, 30 Points, 30 Points Used
y = 0.042987 * x + 0.001519
R^2 = 0.99763769
西羅莫司
(e) Tacrolimus - 10 Levels, 10 Levels Used, 30 Points, 30 Points Used
y = 0.141150 * x + 0.008016
R^2 = 0.99803633
他克莫司

Intelligence That Inspires

New Agilent LC/MS Solutions

As the world trends towards more self-aware, smart solutions to make life easier, lab solutions are no different. Innovative, intelligent LC/MS systems together with complete end-to-end workflows enable time-saving efficiencies, advances to meet future challenges and the ability to analyze your most complex samples. Giving you the peace-of-mind to focus on what inspires you and meet every challenge that comes your way.