岛津 SHIMADZU
Excellence in Science

代谢组学及新技术论文集
----许国旺研究员课题组专刊

序

岛津公司作为全球著名的分析仪器综合生产厂商，不但是世界上顶尖的液相色谱、气相色谱等分离仪器的生产厂商，也是质谱领域的领先者。中国科学院大连化学物理研究所“高分辨分离分析及代谢组学课题组”，已在色谱领域钻研探索多年。近年来以分离分析研究为立足点，生命科学、重大疾病、中医药现代化、公共安全等领域的复杂样品分析为切入点，正在开展极端复杂体系分析的方法学研究及其应用、代谢组学方法及其应用研究和转化医学等工作。岛津公司一直鼎力支持本课题组的科研工作，从早期的色谱光谱分析仪器、气质联用仪，再到高端质谱仪器如离子阱飞行时间质谱液质联用仪、三重四极杆液质联用仪、三重四极杆气质联用仪等。通过与岛津公司长期的密切合作，课题组的科研工作取得了一系列成果。

值此文集出版之际，我们衷心感谢岛津公司给予的支持和帮助。同时很高兴有此机会与同行分享我们的科研工作，希望得到大家的批评指正。

许国旺

中国科学院大连化学物理研究所

2019.12.19

前言

代谢组学(Metabonomics / Metabolomics) 是对生物体内所有小分子代谢物组成的时空变化进行研究的学科。代谢组学是继基因组学和蛋白质组学之后新近发展起来的一门学科，是系统生物学的重要组成部分。之后得到迅速发展并渗透到多项领域，比如疾病诊断、医药研制开发、营养食品科学、毒理学、环境学，植物学等与人类健康护理密切相关的领域。有学者总结，“基因组学和蛋白质组学告诉你什么可能会发生，而代谢组学则告诉你什么确实发生了。”

近年来，代谢组学受到研究者越来越多的关注，是当今分析化学和生命科学的一个前沿的交叉学科，有广阔的发展前景。代谢物种类众多，在体内的分布广泛，且不同代谢物的浓度范围相差极大，这对分析仪器及数据分析手段均提出了巨大的考验。岛津公司作为全球著名的分析仪器综合生产厂商，不但是世界上顶尖的液相色谱、气相色谱等分离仪器的生产厂商，也是质谱领域的领先者。岛津从上世纪七十年代开始进军质谱领域，2002 年岛津的员工田中耕一先生还因为基质辅助激光解吸电离源的发明获得了诺贝尔物理学奖，因此岛津拥有深厚的质谱研发基础和实力。目前岛津质谱的产品线齐全，有机质谱包括单四极杆质谱、三重四极杆质谱、高分辨质谱 LCMS-IT-TOF 和 Q-TOF；无机质谱有 ICP-MS；生命科学领域有 MALDI-TOF、质谱显微镜等。这些质谱仪器与分离技术联用，加上专业的数据库、方法包和丰富的数据处理软件，可以满足代谢组学研究的各种需求。

中国科学院大连化学物理研究所许国旺研究员课题组实验室配备了一系列岛津分析仪器，从早期的色谱光谱分析仪器 LC-10ATvp、GC-17A+QP-5000、 UV-2450，到气质联用仪 GCMS-QP 2010、GCMS-QP 2010 Plus，再到高端质谱仪器如离子阱飞行时间质谱液质联用仪 LCMS-IT-TOF，三重四极杆液质联用仪 LCMS-8050，三重四极杆气质联用仪 TQ-8050 等。2001 年大

连化物所高分辨分离分析及代谢组学组成立之后，截止 2019 年 10 月，该课题组利用岛津分析仪器已经在国内外各类期刊上发表了 77 篇文章。本论文集首先介绍了岛津在仪器硬件和配套软件方面在代谢组学领域的应对方案；第二章开始，基于许老师课题组发表的 77 篇文章，根据该课题组的研究方向进行分类，分别以代谢组学分析技术平台在疾病、中药、植物表型等方面的应用，复杂样品分离分析新方法、新技术等五个章节进行介绍，供相关领域用户和科研工作者参考。

在此谨代表岛津公司衷心感谢许国旺老师及其课题组成员杰出的工作和无私的分享。

岛津分析中心

2019-12-19

许国旺研究员及其课题组介绍

许国旺研究员于 1991 年在中国科学院大连化物所获得理学博士学位，97 年晋升为研究员，99 年聘为博士生导师，2005 年起担任代谢组学研究中心主任，2016 年起担任大连化物所生物技术部常务副主任， 2017 年起担任中国科学院分离分析化学重点实验室主任。现为中国化学会色谱专业委员会主任、中国抗癌协会肿瘤代谢委员会副主任、中国化学会理事、中国质谱学会常务理事。现担任 TrAC-Trends Anal. Chem.的特约编辑和 Anal. Chim. Acta, Metabolomics, Anal. Bioanal. Chem.，Metabolites, J. Pharm. Biomed. Anal.，J. Chromatogr. B, Chromatographia 等 10 多个国内外杂志编委，国际高效液相色谱会议（HPLC）科学委员会常委，以及多届国际毛细管色谱会议（ISCC）的科学委员会委员和国际代谢组学会议的组织者和科学委员会成员。至今为止，已发表 SCI 文章 410 多篇，包括 PNAS, Hepatology, Clin. Chem., Cancer Res., Diabetes Care, Diabetologia, Anal. Chem., TrAC, J. Chromatogr. A, J. Proteome Res., Mol. Cell Proteome 等国际著名杂志。H-指数: 57（Web of Science）、72 (Google)。申请发明专利超百件（其中 50 多项已授权）。一项成果获国家科技进步二等奖（第五名），一项获辽宁省科技发明二等奖（第一名），两项成果获中国分析测试协会科学技术成果一等奖。

许国旺研究员课题组是中科院大连化物所最具综合实力的课题组之一，前身是国家色谱研究分析中心气相色谱组，2001 年大连化物所成立生物技术部后，更名为高分辨分离分析及代谢组学组，也是我国最早进行代谢组学研究的课题组之一。该课题组多年来根据分析化学的特点和国际前沿研究领域的发展趋势，立足于中国现状，结合国家重大应用领域的需求与自身技术优势，以分离分析研究为立足点，生命科学、重大疾病、中医药现代化、公共安全等领域的

复杂样品分析为切入点，开展极端复杂体系分析的方法学研究及其应用、代谢组学方法及其应用研究和转化医学等工作。目前，课题组拥有以许国旺研究员为核心的固定职工 17 人，现有硕、博士研究生 20 多名，学科背景涵盖分析化学、生物化学、临床医学、药学和微生物学等领域。

许国旺老师近照

许国旺研究员及组员合影，摄于 2019 年 9 月

目录

第一部分：岛津代谢组学应对方案

组学是一门研究不同组别间复杂基质中存在的差异物的时空变化规律的科学。第一个提出来的组学（omics）概念是 1986 年由美国遗传学家 Thomas H. Roderick 提出的基因组学（genomics）。基因组学是对生物体所有基因进行系统表征、定量研究及不同基因组比较研究的一门交叉生物学学科。之后又基于差异组别整体分析对比的原理，产生了各种不同研究对象的组学，如转录组学（transcriptomics）是在整体水平上研究细胞中基因转录的情况及转录调控规律的学科；蛋白组学（proteomics）研究一种细胞乃至一种生物所表达的全部蛋白质的的数目、水平及其更新等；表型组学（phenomics）是研究某一生物或细胞在各种不同外部环境条件下所有表型的学科；代谢组学(metabonomics/metabolomics)则是对生物体内所有小分子代谢物组成的时空变化进行研究；研究对象小到一个细胞，大到一整个生命体。

具体地来讲，代谢组学是研究细胞、组织、器官在外部刺激或扰动后产生的内源性代谢物整体及其变化规律的学科。通过代谢组学的深入研究，最终发现疾病标志物及个体代谢表征，结合基因表达四号线疾病的诊断、病程监测，从而推动精准医学和个体化诊疗的发展。

那如何开展代谢组学研究呢？需要什么工具呢？

1．靶向、非靶向和拟靶向代谢组学

代谢组学按分析策略，传统上可分为非靶向和靶向，其分析检测技术主要包含基于质谱和基于核磁共振波谱的分析方法，尤其以色谱质谱联用技术在组学研究中使用更为广泛。

非靶向组学是使用高分辨质谱无偏向性地对所有代谢物进行检测分析，对不同组别样品中尽可能多的未知代谢物进行半定量对比，统计分析得到差异代谢物之后进行定性确认。

靶向组学主要针对在一定范围内已知代谢物的定性和定量，通过对比不同组别的样品中这些已知代谢物，筛选出具有统计学差异的特征代谢物。靶向组学可以应用于验证由非靶向组学实验提出的假说；或进行基于假说的探索性实验，针对特定化合物，研究代谢模型。

拟靶向代谢组学是许国旺课题组提出的一种新的组学策略，结合了非靶向和靶向的优点：在方法建立时，运用非靶向方法发现样品中存在的代谢物，并锁定其保留时间和检测的离子对，

在此基础上构建数据库；在实际代谢组学研究时，调用数据库的信息用三重四极杆质谱仪器的 MRM 模式对各个样品中的目标物进行半定量分析，统计分析得到差异代谢物之后进行定性确认。

这三种组学方式的优缺点对比如下表 1。

表 1. 三种组学策略对比

	非靶向组学	靶向组学	拟靶向组学
优点	无需标样，可发现未知化合物	定性、定量能力强，适合检测丰度低响应差的化合物	同时具有非靶向和靶向的优点
缺点	高分辨质谱价格更昂贵，灵敏度差，定量能力差，准确鉴定化合物的流程复杂，依赖公共数据库	需购买标准品（或预先建立靶向数据库），不能对未知化合物进行研究	灵敏度受限于高分辨质谱（未知物发现能力），高分辨离子对转移到三重四极杆质谱可能不是最优参数

2. 色谱仪器

岛津有非常广泛的前端分离或前处理仪器产品线，为组学研究提供全面的分离技术手段。对于常规分离需求，有普通气相色谱、液相色谱、快速液相色谱和超高效液相色谱等多种色谱产品；对于成分复杂或结构类似的样品，可以使用多款二维 LC 或二维 GC 系统以提高分离度；对于化合物极性分布范围广的样品，可以选择超临界流体色谱（SFC）或超临界流体萃取-超临界流体色谱（SFE-SFC）联用的 Nexera-UC 分析系统；对于一些痕量化合物或本身响应弱的目标物，可以采用 Micro-LC 或 Nano-LC 以大幅提高质谱响应信号，从而提高方法的灵敏度。另外，岛津还提供如 CLAM-2030 用于液体生物样品的全自动样品前处理-液质质联用分析，彻底解放实验人员的双手和时间，极大的提高方法的重现性。此外，岛津的 Nexera-MX 平行液相等可以显著提高分析通量，ATLAS-LEXT 可以提供自动化的液液萃取，这些仪器都能进一步提高样品前处理和分析的自动化和通量，为组学研究提供便利并提高数据质量。

图 1．岛津质谱前端产品线

3．质谱仪器

岛津从上世纪 70 年代开始研发扇形质谱，成功生产了世界上第一台商品化扇形磁场型质谱 GCMS-LKB9000；80 年代开发了 MALDI-TOF 和 ICP-MS，2002 年岛津科学家田中耕一先生更因为 MALDI 离子源的研发获得了诺贝尔物理学奖，因此岛津拥有深厚的质谱研发基础和实力。目前岛津质谱的产品线齐全，有机质谱包括单四极杆质谱、三重四极杆质谱、高分辨质谱 LCMS-IT-TOF 和 Q-TOF；无机质谱有 ICP-MS；生命科学领域还有 MALDI-TOF、质谱显微镜等。这些质谱仪器与分离技术联用，满足组学研究的各种需求。

图 2．岛津质谱仪器产品线

4. 组学软件分析工具介绍

组学研究广泛使用质谱相关的仪器，如 GC-MS、LC-MS/MS、LCMS-IT-TOF 或 Q-TOF 等。质谱仪器有较复杂的条件和参数设置，通过采集能得到大量的出峰时间和离子信息，因此有各种工具服务于组学研究的各个环节。

4.1 代谢组学相关方法包与数据库

4.1.1 初级代谢物方法包

本产品包括了两个方法文件即通过 LC-MS/MS 系统使用添加离子配对试剂的流动相的分析方法和使用 Pentafluorophenylpropyl （PFPP）柱的分析方法。采用使用离子配对试剂的分析方法时，可以对细胞内的中心代谢途径，如糖酵解系统、 TCA 循环、磷酸戊糖循环以及氨基酸 核苷酸等 生命科学专业的代谢组学分析 中 55 个重要代谢物组分进行同时分析。另外，采用使用 PFPP 柱的分析方法时，可以对使用离子配对试剂不能处理的若干种有机酸及 97 个其他代谢物组分进行同时分析（25 种成分与采用离子配对试剂的方法时相同）。由此就可以根据客户的目的装置的情况从本产品中选择对代谢物进行同时分析的方法。通过使用本产品，可以对正常 病态模型中的重要代谢物变化进行综合分析，还可以通过 LC/MS/MS 系统对转基因动物模型的组织在 代谢 途径中产生的影响进行评价。此外，本方法包还包括使用离子配对试剂和 PFPP 柱进行多组分同时分析的方法文件，该文件中登录有对应目标组分的分析条件和化合物信息，因此，减少了推测分离条件、各组分的 MS 参数最优化及登录化合物名称、保留时间等繁琐的操作。另外，为在多个样品间进行标准化，已最优化 2 种内标物质的分析条件。由此提供了从样品制备到同时分析多组分以及多个样品间的代谢物变化分析的一系列流程 整体解决方案 。

4.1.2 脂质介质方法包

脂质组学属于代谢组学的一个分支。为进行靶向脂质组学研究，岛津公司推出了第三版脂质介质方法包：包含了主要脂类化合物如类花生酸、二十二碳六烯酸（DHA）和二十碳五烯酸（EPA）等多价不饱和脂肪酸代谢物，花生四烯酸乙醇胺（AEA）、血小板活化因子（PAF）等 196 种主要脂质介质及其相关物质的色谱、质谱条件（MRM 通道）。该方法只需 20 分钟的色谱分析便能获得这 196 种化合物的脂质介质的分

析结果。此外，方法包中还根据出峰时间和结构特性，准备了 18 种氘代内标化合物的 MRM 通道。另外，该方法包可进行保留时间校正，可使用内标法进行半定量，所以可用于检索多变量解析时的标记物。

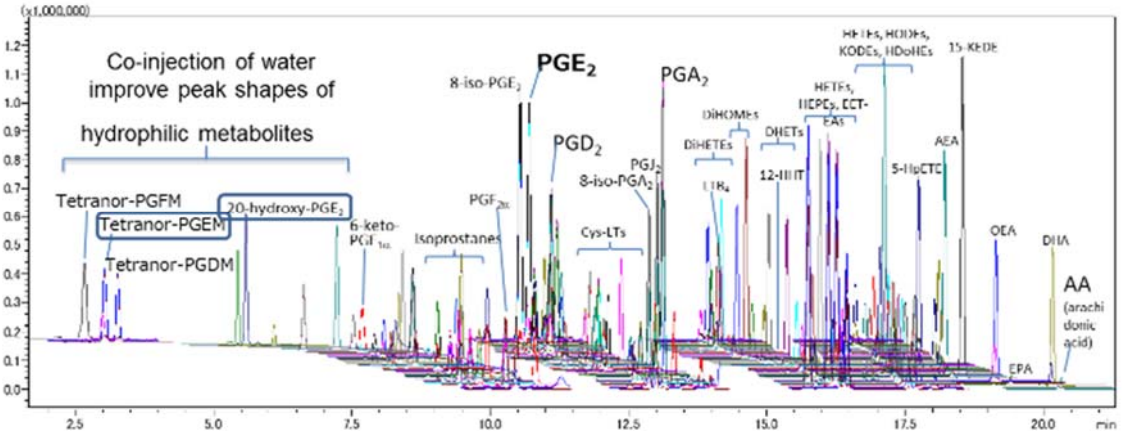
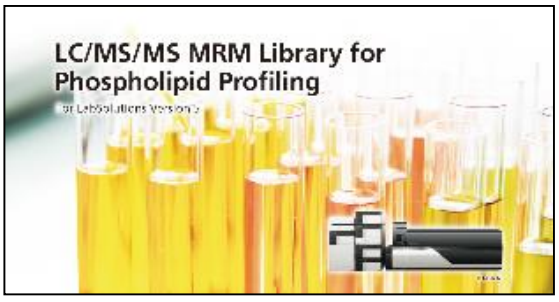


图 3. 脂质介质方法包用于 196 种脂质，18 种内标的分离

4.1.3 磷脂 MRM 质谱库

磷脂组成生物膜的主要成分，根据 LIPID MAPS 数据库显示，已确认的磷脂类化合物超过 8000 个。磷脂数据库提供了两个方法，第一个方法包含前处理条件，液相色谱条件，以及包含 422 个磷脂化合物的 MRM 通道用于 LC-MS/MS 检测。该方法能够通过出峰时间和 MRM 通道确定磷脂化合物的头基、碳原子个数以及双键个数。为了识别磷脂中脂肪酸结构，还需要推测其构成结构骨架中双键位置，方法 2 使用 MRM Event Link Finder 软件，通过 867 个 MRM 通道采集数据并进行数据库比对处理，最终确认双键位置。



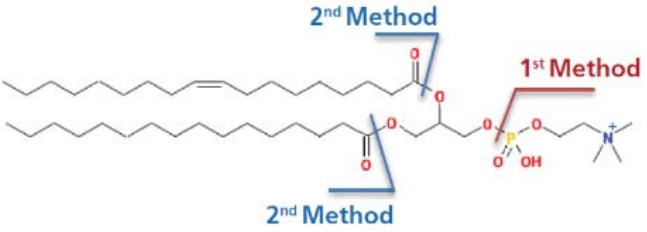


图 4. 磷脂数据库用于磷脂类化合物的检测

4.1.4 SimLipid 数据库

该软件是 PREMIER Biosoft 公司研发的用于脂质组分析的质谱数据解析软件，能够通过自带的强大数据库以及用户的自定义数据库对岛津质谱采集得到的脂质组数据进行高通量分析，并将结果整理成专业的报告文档。

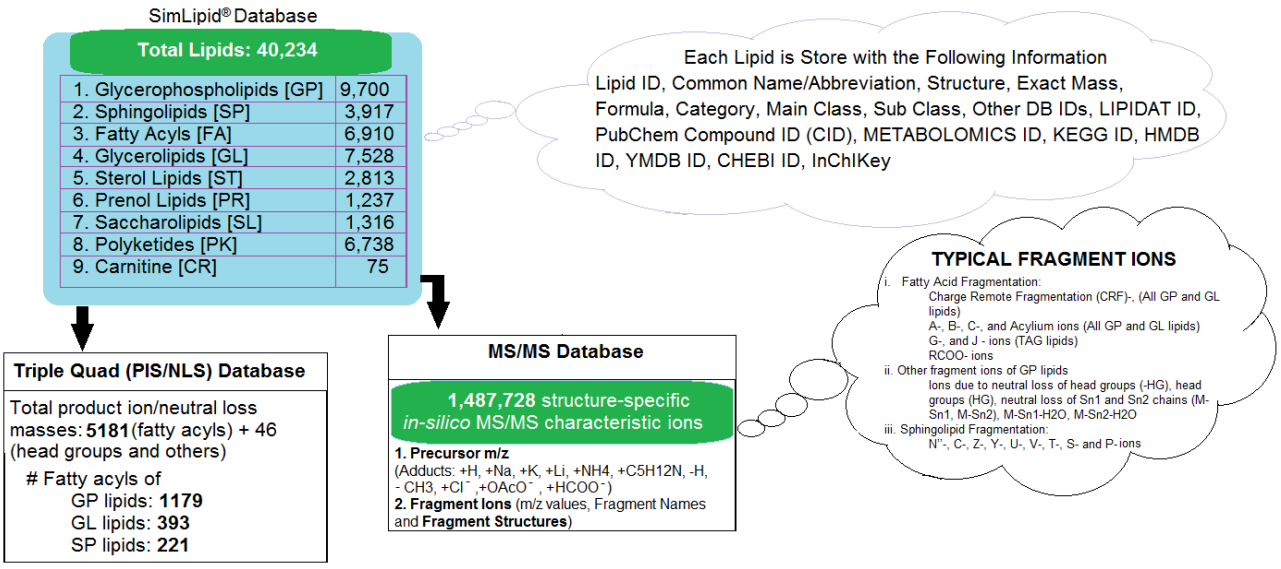


图 5. SimLipid 数据库

SimLipid 数据库是一个大型关系数据库，包含共计 40,298 种脂分子和 1,509,305 种结构特异性的 MS/MS 特征离子。该软件通过搜索 SimLipid 数据库中的已知脂质结构信息进行脂质鉴定和性能分析。同时还会给出一些相关参考信息，例如脂质 ID、缩写、系统名称、成份以及其他数据库链接。数据库会不断得以更新。用户也可以定制自己的数据库，并输入 retention time 和 drift time 用于今后的数据分析。

4.2 Traverse-MS 软件介绍

该软件由 Reifycs Inc 公司研发，用于岛津三重四极杆质谱仪采集的 MRM 数据的读取、查看、数据库建立、主成分分析和分层聚类分析，并以得分图、载荷图、柱状图和热图等形式展现结。此外，还可以绘制相关化合物的代谢通路，是组学分析的有力工具。其数据处理的顺序大致如下：

① 使用标准目标物在最优的 LC-MS/MS 方法下分析得到标准数据（方法中确立了化合物名称、离子对和出峰时间）；

② 导入标准数据，对各标准物进行筛选和编辑，建立数据库；

③ 以①中的同样的方法运行实际样品；

④ 导入取得的实际样品数据，得到 MRM Outlook 和 Data Matrix；

⑤ 基于 Data Matrix 创建各种可视化图形。

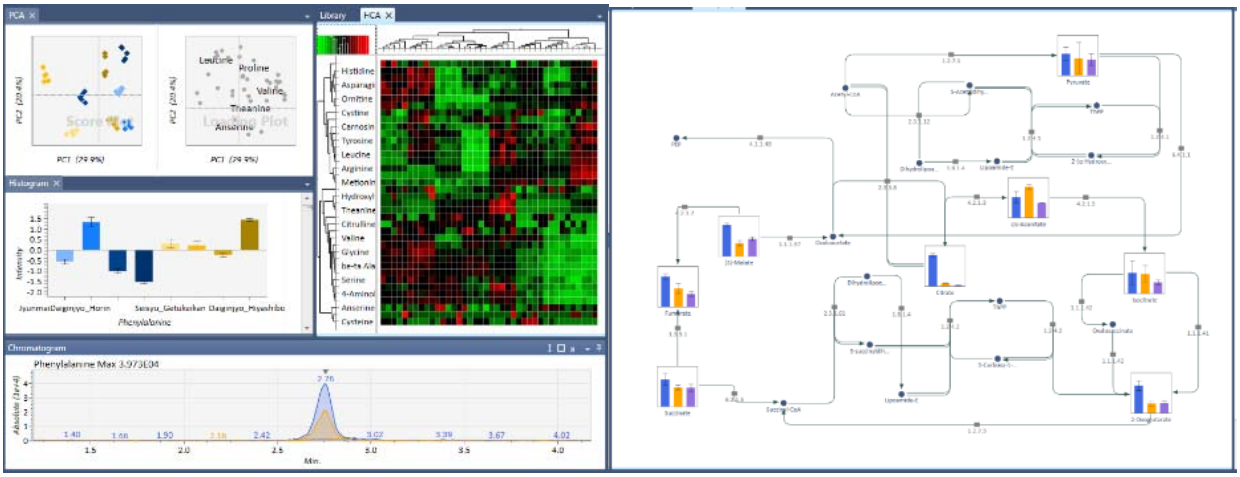


图 6. Traverse-MS 可视化结果

4.3 MS-Dial 分析平台

MS-Dial 作为支持多种仪器（GC/MS、GC/MS/MS、LC/MS 和 LC/MS/MS）的非靶向代谢组学的通用数据处理和分析平台，支持岛津数据的导入和处理。具有以下特点：（1）GC/MS 和独立于数据的 MS/MS 的光谱反卷积；（2）优化的峰值识别标准；（3）支持从原始数据导入到统计分析的所有数据处理步骤；（4）可实现未知物筛查；（5）用户友好的图形用户界面。

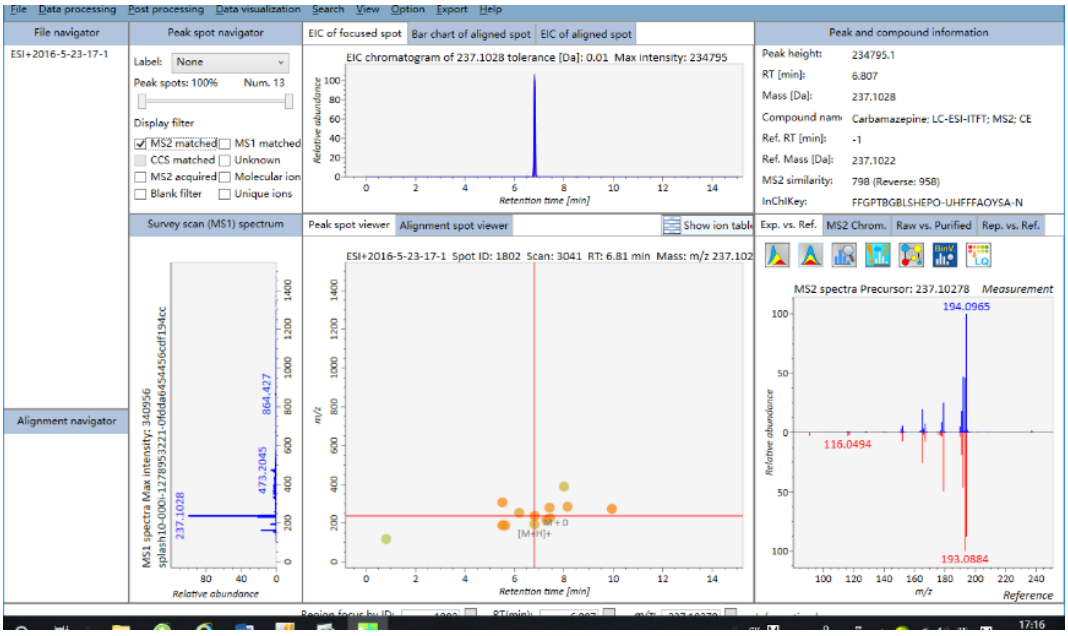


图 7. MS-Dial 的软件界面

4.4 Garuda 组学分析平台

Garuda 是一个开放、共同的生物分析平台，它提供了一个连接、发现和导航的框架，通过不同的应用

程序、数据库为生物学和医学研究提供数据分析和可视化输出。目前有 5 个插件是由岛津、日本系统生物学研究所和大阪大学信息科学与技术研究生院共同研发的，可以支持岛津的数据输入与处理，分别是 Shimadzu MSdata Import、Volcano Plot Generator、Blank GML Generator、Multiomics Data Mapper 和 Correlation coefficient Calculator。另外有三个公共软件 Cytoscape、iPath2 和 VANTED 可用于代谢分析结果的可视化输出。

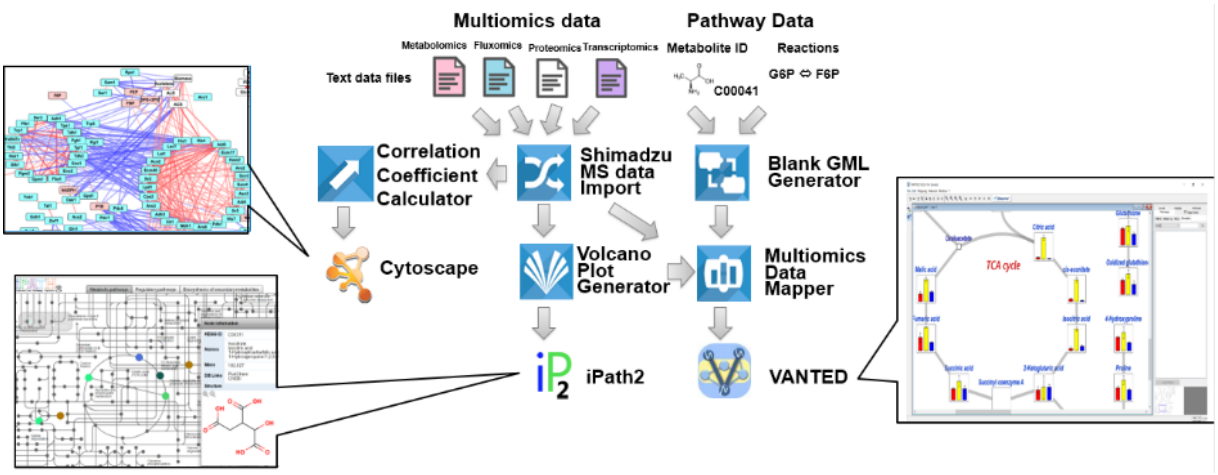


图 8. Garuda 组学分析平台

基于以上介绍的岛津分析仪器及配套软件、分析平台，助力国内外科学家完成了诸多优秀的代谢组学相关科研工作。从下一章开始，列出 2001 年至 2019 年 10 月，许国旺研究员课题组利用岛津分析仪器在国内外各类期刊上发表的 77 篇文章，分别以代谢组学分析技术平台在疾病、中药、植物表型等方面的应用，复杂样品分离分析新方法、新技术等五个章节进行介绍，供相关领域用户和科研工作者参考。

第二部分：代谢组学在疾病研究中的应用

Metabolism Clinical and Experimental 91 (2019) 18–29

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Metabolism Clinical and Experimental

journal homepage: www.metabolismjournal.com

Metabolomics profiling of metformin-mediated metabolic reprogramming bypassing AMPKα☆

Min Yan [a,b,1], Huan Qi [a,1], Tian Xia [a], Xinjie Zhao [a], Wen Wang [a,b], Zhichao Wang [a,b], Chang Lu [a,c], Zhen Ning [a,c], Huan Chen [a,b], Tongming Li [a], Dinesh Singh Tekcham [a], Xiumei Liu [a], Jing Liu [a], Di Chen [a], Xiaolong Liu [a], Guowang Xu [a,*], Hai-long Piao [a,b,*]

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利用代谢组学方法研究绕过 AMPKα 的二甲双胍介导代谢重编程机理

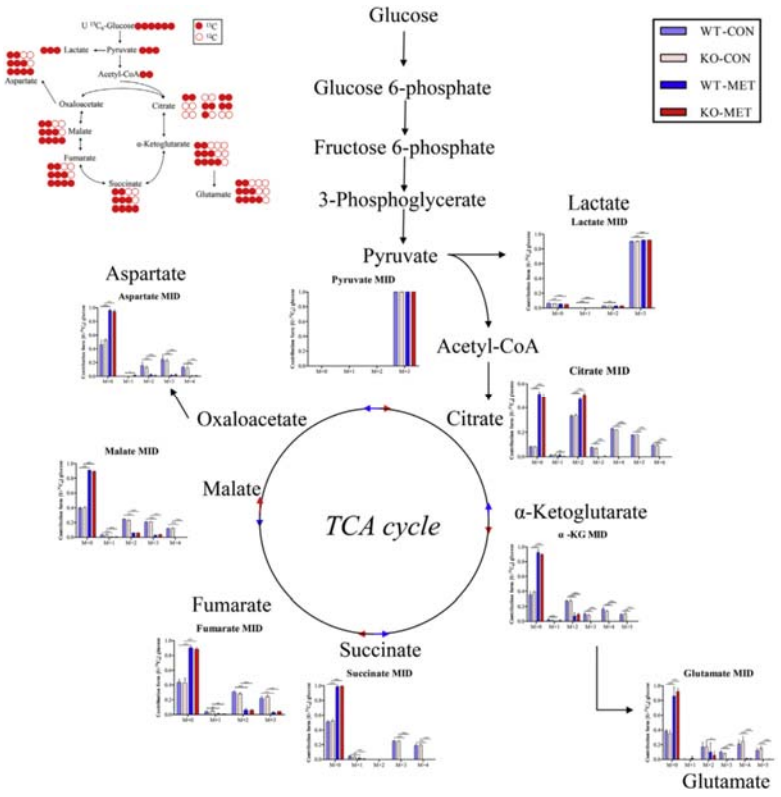
Background: Metformin is a fir**st-line drug for treating type 2 diabetes and has gained considerable interest as a potential anticancer agent. Increasing evidence suggests that metformin antagonizes diabetes and tumors through disrupting metabolic homeostasis and altering energy state. However, whether AMP activated protein kinase (AMPK) contributes to such effects of metformin remains controversial. Methods: We performed integrative metabolomics analyses to systematically examine the effects of metformin on metabolic pathways in Prkaa1 wild type (WT) and knock-out (KO) mouse embryonic fibroblast (MEF) cells as well as human cells based on gas chromatography–mass spectrometry and capillary electrophoresis–mass spectro**metry (CE–MS).

Results: Metformin treatment induced metabolic reprogramming and reduced the energy state of both Prkaa1 WT and KO MEF cells, as evidenced by suppressed tricarboxylic acid (TCA) cycle, elevated lactate production as well as decreased NAD+/NADH ratio. Additionally, metabolic flux analysis also showed that metformin Ampkα-independently increased metabolic flux from glucose to lactate and decreased metabolic flux from acetyl-CoA to TCA cycle as well as from pyruvate to malate.Moreover, metformin Ampkα-dependently upregulated P-Acc but Ampkα-independently inhibited the levels of P-mTor, P-S6,

Lc3, Atgl and P-Erk in MEF cells. Similarly, we demonstrated that a commonly used AMPK agonist 5-Aminoimidazole-4-carboxamide ribonucleotide (AICAR) and fetal bovine serum (FBS) starvation, as a common model for energy stress, both led to Ampkα-independent metabolism alterations in MEF cells. Furthermore, these effects of metformin were also confirmed in human hepatocellular carcinoma (HCC) cells aswell as inMCF10A shControl and shPRKAA1 cells. Importantly, we found that metformin could obviously inhibit colony conformation of HCC cells in an Ampkα-independent manner.

Conclusions: Our data highlight a comprehensive view of metabolic reprogramming mediated by metformin as well as AICAR. These observations suggest that metformin could affect cellular metabolism largely bypassing Ampkα, and may provide a new insight for its clinical usage.

使用的岛津仪器：GCMS-QP 2010



代表图片：以 U-^{13}C6-葡萄糖为示踪剂分析二甲双胍诱导代谢的变化

原文网址： https://doi.org/10.1016/j.metabol.2018.11.010

2019 年 8 月 August 2019 色 谱 Chinese Journal of Chromatography Vol.37 No.8 887～896

庆祝中国科学院大连化学物理研究所建所 70 周年专刊・研究论文 DOI：10.3724/SP.J.1123.2018.07008

细胞蛋白质组学和代谢组学整合策略表征散斑型 BTB/POZ 蛋白质突变调控的关键代谢通路

颜 敏[1,2]， 刘 静[1]， 夏 天[1]， 许国旺[1]， 朴海龙[1,2*]

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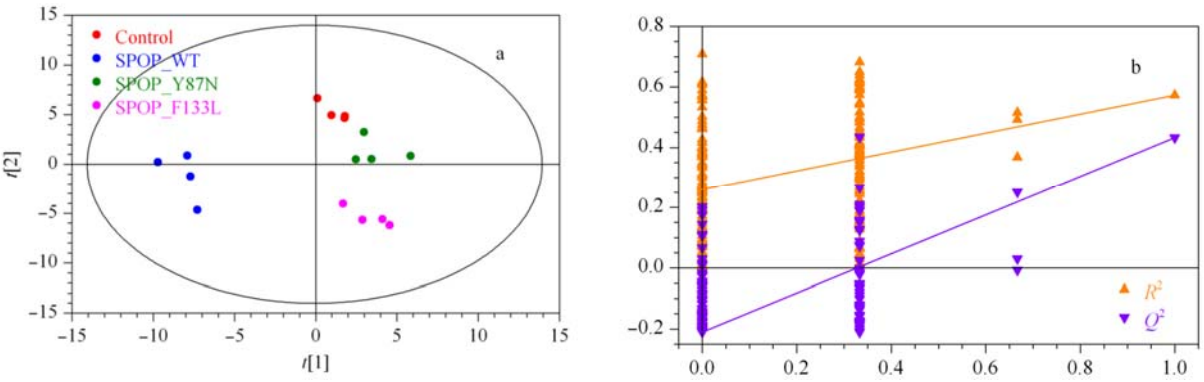
细胞蛋白质组学和代谢组学整合策略表型散斑型 BTB/POZ 蛋白质突变调控的关键代谢通路

摘要：散斑型 BTB/POZ 蛋白（SPOP）是前列腺癌中突变率最高的蛋白质之一。该研究通过整合细胞蛋白质组学和代谢组学的方法，揭示 SPOP 突变引起的代谢紊乱及其调控的代谢通路。首先，系统地研究了 LNCaP SPOP 野生型及突变型高表达细胞中的代谢变化。代谢组学结果显示，SPOP 野生型和突变型（SPOP_Y87N 和 SPOP_F133L）导入的 LNCaP 细胞在偏最小二乘法判别分析（PLS-DA）得分图上得到了很好的区分。进一步通过单因素方差分析发现，SPOP 突变引起富马酸、苹果酸、柠檬酸、天冬氨酸和天冬酰胺等代谢物含量的增加。蛋白质组学共发现 909 种蛋白质在两种 LNCap SPOP 突变体细胞中发生变化。分别对差异代谢物和差异蛋白质进行通路富集分析，发现三羧酸循环、氨酰基－转运核糖核酸生物合成在代谢组学和蛋白质组学分析中都发生了明显改变。最后，在 SPOP 敲除的 Du145 细胞中验证了上述研究结果。该研究证明 SPOP 突变可促进三羧酸循环。

使用的岛津仪器：GCMS-QP 2010



代表图片：偏最小二乘法判别分析（PLS-DA）LNCaP CON、SPOP_WT、SPOP_Y87N和SPOP_F133L细胞

原文链接：http://mall.cnki.net/magazine/Article/SPZZ201908014.htm

Journal of proteome research

Article

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pubs.acs.org/jpr

Serum Metabolomics Study of Nonsmoking Female Patients with Non-Small Cell Lung Cancer Using Gas Chromatography−Mass Spectrometry

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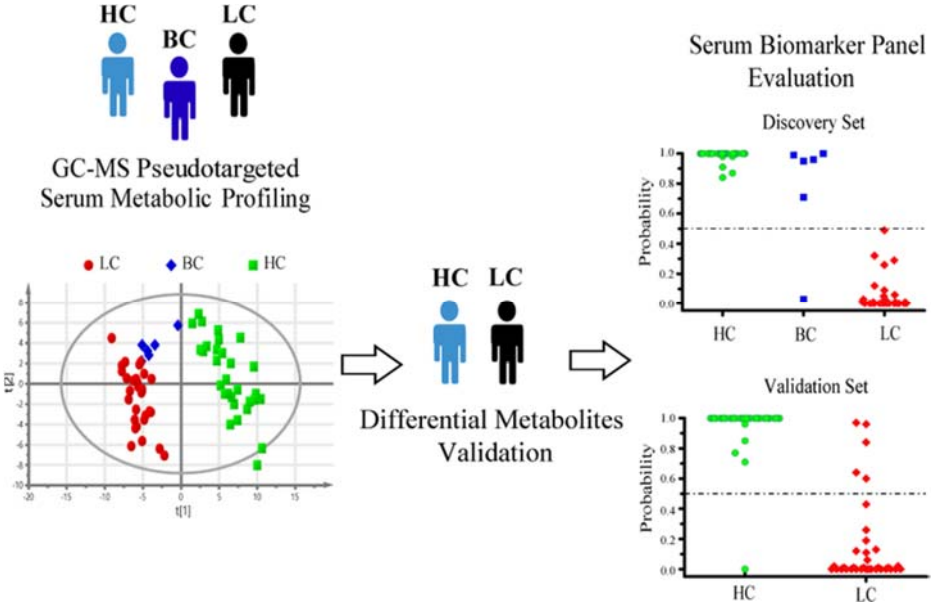
基于 GCMS 方法对患有非小细胞肺癌的不吸烟女性患者进行血清代谢组学研究

Abstract: The incidence of nonsmoking female patients with non-small cell lung cancer (NSCLC) has increased in recent decades; however, the pathogenesis of patients is unclear, and early diagnosis biomarkers are in urgent need. In this study, 136 nonsmoking female subjects (65 patients with NSCLC, 6 patients with benign lung tumors, and 65 healthy controls) were enrolled, and their metabolic profiling was investigated by using pseudo targeted gas chromatography−mass spectrometry. A total of 56 annotated metabolites were found and verified to be significantly different in nonsmoking females with NSCLC compared with the control. The metabolic profiling was featured by disturbed energy metabolism, amino acid metabolism, oxidative stress, lipid metabolism, and so on. Cysteine, serine, and 1-monooleoylglycerol were defined as the biomarker panel for the diagnosis of NSCLC patients. 98.5 and 91.4% of subjects were correctly distinguished in the discovery and validation sets, respectively. The biomarker panel was also useful for the diagnosis of in situ malignancy patients, with an accuracy of 97.7 and 97.8% in the discovery and validation sets, respectively. The study provides a biomarker panel for

the auxiliary diagnosis of nonsmoking females with NSCLC.

Keywords: non-small cell lung cancer, metabolomics, nonsmoking female, gas chromatography–mass spectrometry, biomarker

使用的岛津仪器：GCMS-QP 2010



代表图片：分析流程图

原文网址：https://pubs.acs.org/doi/10.1021/acs.jproteome.9b00069

IJC
International Journal of Cancer

Metabolomics and transcriptomics profiles reveal the dysregulation of the tricarboxylic acid cycle and related mechanisms in prostate cancer

Yaping Shao [1,2], Guozhu Ye[1,2], Shancheng Ren[3], Hai-Long Piao[1,4], Xinjie Zhao[1], Xin Lu[1], Fubo Wang[3], Wang Ma[5], Jia Li[1,2], Peiyuan Yin[1], Tian Xia[4], Chuanliang Xu[3], Jane J. Yu[1,5,6], Yinghao Sun[3] and Guowang Xu[1]

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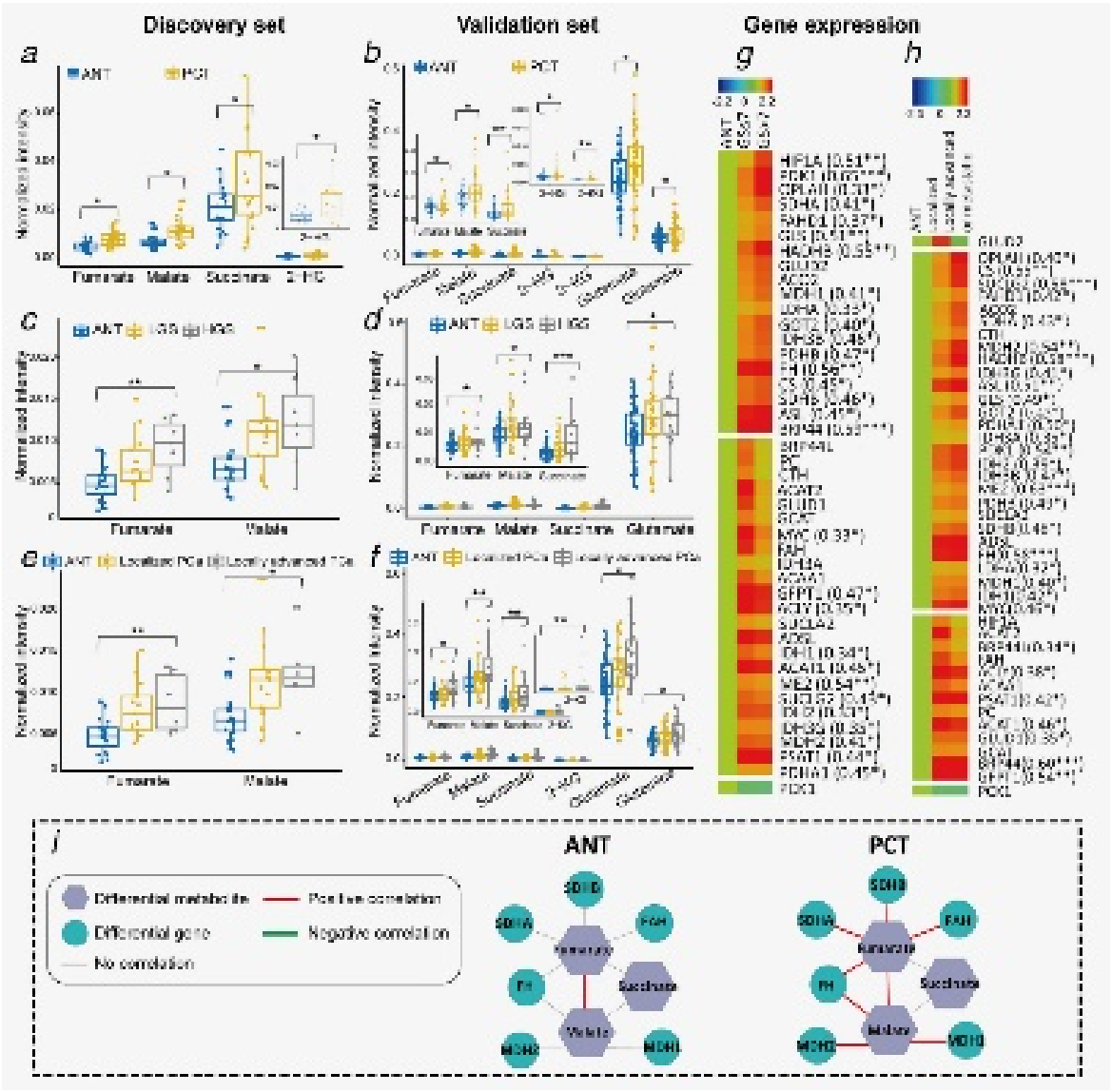
基于代谢组学和转录组学研究揭示前列腺癌中三羧酸循环的失调及其相关机制

Abstract: Genetic alterations drive metabolic reprograming to meet increased biosynthetic precursor and energy demands for cancer cell proliferation and survival in unfavorable environments. A systematic study of gene-metabolite regulatory networks and metabolic dysregulation should reveal the molecular mechanisms underlying prostate cancer (PCa) pathogenesis. Herein, we performed gas chromatography–mass spectrometry (GC–MS)-based metabolomics and RNA-seq analyses in prostate tumors and matched adjacent normal tissues (ANTs) to elucidate the molecular alterations and potential underlying regulatory mechanisms in PCa. Significant accumulation of metabolic intermediates and enrichment of genes in the tricarboxylic acid (TCA) cycle were observed in tumor tissues, indicating TCA cycle hyperactivation in PCa tissues. In addition, the levels of fumarate and malate were highly correlated with the Gleason score, tumor stage and expression of genes encoding related enzymes and were significantly related to the expression of genes involved in branched chain amino acid degradation. Using an integrated omics approach, we further revealed the potential anaplerotic routes from pyruvate, glutamine catabolism and branched chain amino acid (BCAA) degradation contributing to replenishing

metabolites for TCA cycle. Integrated omics techniques enable the performance of network-based analyses to gain a comprehensive and in-depth understanding of PCa pathophysiology and may facilitate the development of new and effective therapeutic strategies.

使用的岛津仪器：GCMS-QP 2010



代表图片：TCA循环中分子变化和GS与肿瘤进展的关系

原文网址：https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.31313

Journal of proteome research

Article

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pubs.acs.org/jpr

Serum Metabolomics Study of Gliclazide-Modified-Release-Treated Type 2 Diabetes Mellitus Patients Using a Gas Chromatography−Mass Spectrometry Method

Yang Zhou,[†,∥,⊥] Cheng Hu,[‡,§,⊥] Xinjie Zhao,[†,∥] Ping Luo,[†,∥] Jingyi Lu,[‡] Qing Li,[‡] Miao Chen,[‡] Dandan Yan,[‡] Xin Lu,[*,†,∥] Hongwei Kong,[†,∥] Weiping Jia,[*,‡] and Guowang Xu[*,†,∥]

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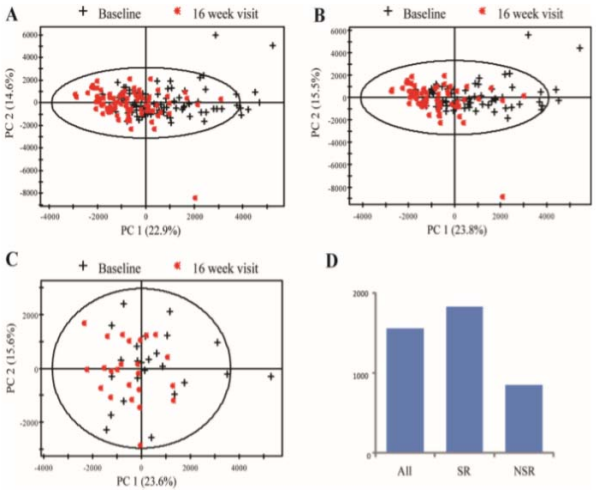
基于 GCMS 研究格列齐特缓释剂治疗 2 型糖尿病患者的血清代谢组学

Abstract: Sulfonylureas are one of the commonly used drugs in type 2 diabetes mellitus (T2DM) but with considerable incidence of monotherapy failure. However, the mechanism of patients' drug response is unclear, and suitability evaluation biomarkers are in urgent need for precision medicine. In this study, a pseudotargeted gas chromatography−mass spectrometry method was employed to investigate the serum metabolic profiling of 66 significant responders and 24 nonsignificant responders at baseline and 16 weeks after gliclazide modified-release (MR) monotherapy. Clinical improvements in blood glucose level and insulin sensitivity were closely associated with the alterations of TCA cycle, ketone body metabolism, lipid oxidation, branched-chain amino acid catabolism, and gut flora metabolism. The different baseline metabolic profiling observed in the two groups implied that patients with lower dyslipidemia level may be more suitable for sulfonylurea therapy. The biomarker panel consisting of HbA1c, 5,8,11,14,17eicosapentaenoic acid, methyl 8,11,14-eicosatrienoate, and methyl hexadecanoate shows a very good prediction ability for the suitability of gliclazide treatment, and it may be meaningful in personalized medicine of T2DM patients by sulfonylurea therapy.

使用的岛津仪器：GCMS-QP 2010



代表图片：(A)所有样本、(B)格列齐特反应样本和(C)格列齐特非反应样本的PCA分数分布图. 16周访视和基线检查之间代谢产物的欧几里德距离图

原文网址：https://pubs.acs.org/doi/10.1021/acs.jproteome.7b00866

www.impactjournals.com/oncotarget/ Oncotarget, 2018, Vol. 9, (No. 5), pp: 6245-6258

Research Paper

Determination of candidate metabolite biomarkers associated with recurrence of HCV-related hepatocellular carcinoma

Zhicheng Liu[1,2], Pierre Nahon[3,4,10], Zaifang Li[1], Peiyuan Yin[1], Yanli Li[1], Roland Amathieu[2,5], Nathalie Ganne-Carrié[3,10], Marianne Ziol[6,7], Nicolas Sellier[8], Olivier Seror[4,8], Laurence Le Moyec[9], Philippe Savarin[2,*] and Guowang Xu[1,*]

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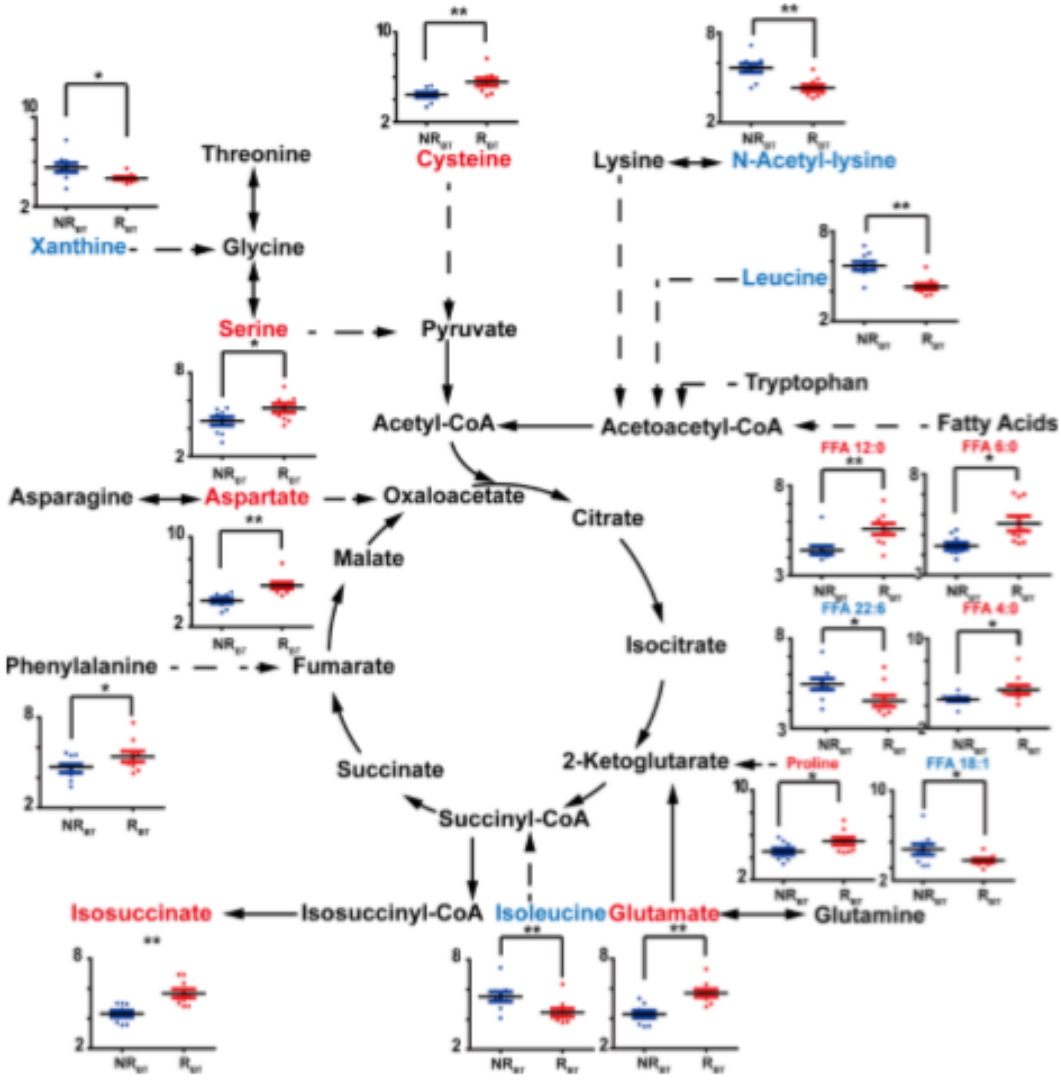
与 HCV 相关肝癌复发的候选代谢标志物的检测

Abstract: Hepatitis C virus (HCV) infection is associated with a high risk of developing hepatocellular carcinoma (HCC) and HCC recurrence remains the primary threat to outcomes after curative therapy. In this study, we compared recurrent and nonrecurrent HCC patients treated with radiofrequency ablation (RFA) in order to identify characteristic metabolic profile variations associated with HCC recurrence. Gas chromatography-mass spectrometry (GC-MS) -based metabolomic analyses were conducted on serum samples obtained before and after RFA therapy. Significant variations were observed in metabolites in the glycerolipid, tricarboxylic acid (TCA) cycle, fatty acid, and amino acid pathways between recurrent and non-recurrent patients. Observed differences in metabolites associated with recurrence did not coincide before and after treatment except for fatty acids. Based on the comparison of serum metabolomes between recurrent and non-recurrent patients, key discriminatory metabolites were defined by a random forest (RF) test. Two combinations of these metabolites before and after RFA

treatment showed outstanding performance in predicting HCV-related HCC recurrence, they were further confirmed by an external validation set. Our study showed that the determined combination of metabolites may be potential biomarkers for the prediction of HCC recurrence before and after RFA treatment.

使用的岛津仪器：GCMS-QP 2010



代表图片：(A)所有样NRBT(蓝色条形图)和RBT(红色条形图)的相对定量(y轴)和相关通路图

原文网址：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5814209/

frontiers in Endocrinology

ORIGINAL RESEARCH
published: 23 November 2018
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Integration of Proteomics and Metabolomics Revealed Metabolite–Protein Networks in ACTH-Secreting Pituitary Adenoma

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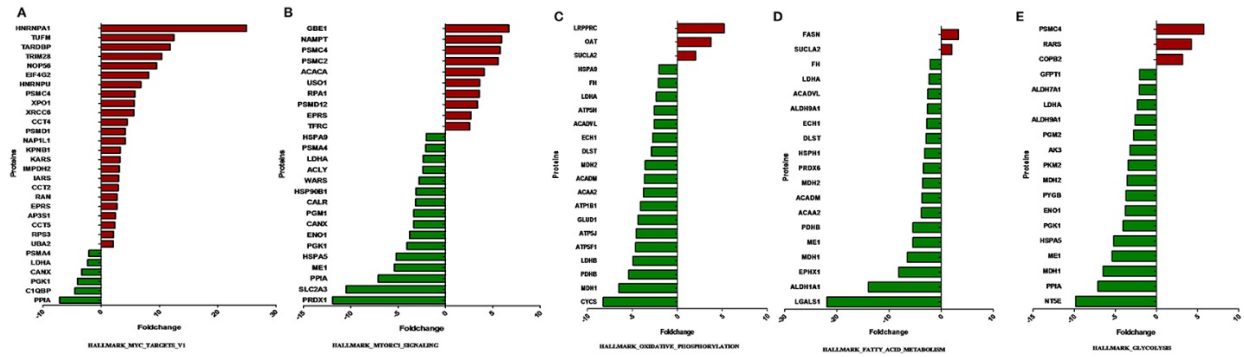
OPEN ACCESS

集成蛋白质组学和代谢组学揭示分泌 ACTH 的垂体瘤中的代谢-蛋白网络

Abstract: An effective treatment for the management of adrenocorticotropic hormone-secreting pituitary adenomas (ACTH-PA) is currently lacking, although surgery is a treatment option. We have integrated information obtained at the metabolomic and proteomic levels to identify critical networks and signaling pathways that may play important roles in the metabolic regulation of ACTH-PA and therefore hopefully represent potential therapeutic targets. Six ACTH-PAs and seven normal pituitary glands were investigated via gas chromatography-mass spectrometry (GC-MS) analysis for metabolomics. Five ACTH-PAs and five normal pituitary glands were subjected to proteomics analysis via nano liquid chromatography tandem-mass spectrometry (nanoLC-MS/MS). The joint pathway analysis and network analysis was performed using MetaboAnalyst 3.0. software. There were significant differences of metabolites and protein expression levels between the ACTH-PAs and normal pituitary glands. A proteomic analysis identified 417 differentially expressed proteins that were significantly enriched in the Myc signaling pathway. The protein–metabolite joint pathway analysis showed that differentially expressed proteins and metabolites were significantly enriched in glycolysis/gluconeogenesis, pyruvate metabolism, citrate cycle (TCA cycle), and the fatty acid metabolism pathway in ACTH-PA. The protein–

metabolite molecular interaction network identified from the metabolomics and proteomics investigation resulted in four subnetworks. Ten nodes in subnetwork 1 were the most significantly enriched in cell amino acid metabolism and pyrimidine nucleotide metabolism. Additionally, the metabolite–gene–disease interaction network established nine subnetworks. Ninety-two nodes in subnetwork 1 were the most significantly enriched in carboxylic acid metabolism and organic acid metabolism. The present study clarified the pathway networks that function in ACTH-PA. Our results demonstrated the presence of downregulated glycolysis and fatty acid synthesis in this tumor type. We also revealed that the Myc signaling pathway significantly participated in the metabolic changes and tumorigenesis of ACTH-PA. This data may provide biomarkers for ACTH-PA diagnosis and monitoring, and could also lead to the development of novel strategies for treating pituitary adenomas.

使用的岛津仪器：GCMS-QP 2010



代表图片：蛋白在代谢相关信号通路中的表达。ACTH-PAs与正常脑垂体间差异表达的蛋白沿x轴显示；y轴显示p值的-log。(A) HALLMARK_MYC_TARGETS_V1蛋白，(B) HALLMARK_MTORC1_SIGNALING蛋白，(C) hallmark_oxidative_磷酸化蛋白，(D) HALLMARK_FATTY_ACID_METABOLISM蛋白，(E) HALLMARK_GLYCOLYSIS蛋白。

原文网址：https://www.frontiersin.org/articles/10.3389/fendo.2018.00678/full

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 13), pp: 20719-20728

Research Paper

Discovery and validation of potential urinary biomarkers for bladder cancer diagnosis using a pseudotargeted GC-MS metabolomics method

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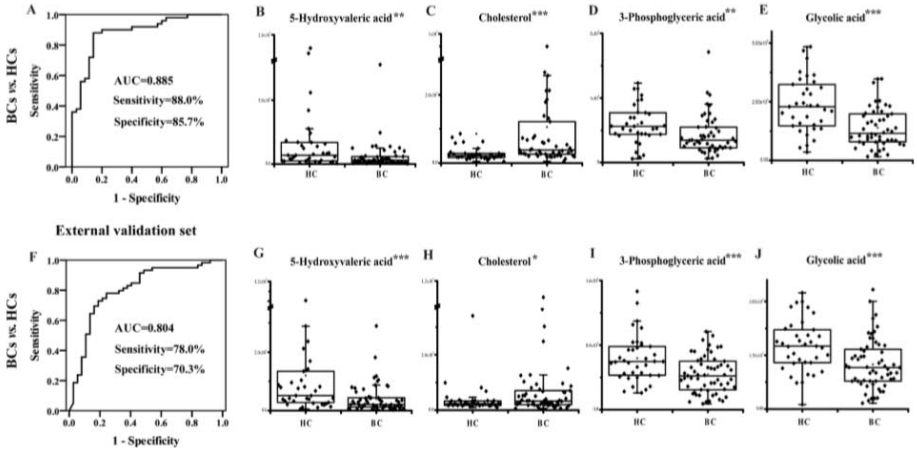
基于 GC-MS 拟靶向代谢组学方法发现和验证膀胱癌诊断中尿液里潜在的生物标志物

Abstract: Bladder cancer (BC) is the second most prevalent malignancy in the urinary system and is associated with significant mortality; thus, there is an urgent need for novel noninvasive diagnostic biomarkers. A urinary pseudotargeted method based on gas chromatography–mass spectrometry was developed and validated for a BC metabolomics study. The method exhibited good repeatability, intraday and interday precision, linearity and metabolome coverage. A total of 76 differential metabolites were defined in the discovery sample set, 58 of which were verified using an independent validation urine set. The verified differential metabolites revealed that energy metabolism, anabolic metabolism and cell redox states were disordered in BC. Based on a binary logistic regression analysis, a four-biomarker panel was defined for the diagnosis of BC. The area under the receiving operator characteristic curve was 0.885 with 88.0% sensitivity and 85.7% specificity in the discovery set and 0.804 with 78.0% sensitivity and 70.3% specificity in the validation set. The combinatorial biomarker panel was also useful for the early diagnosis of BC. This approach can be used to discriminate non-muscle invasive and low-grade BCs from healthy controls with satisfactory sensitivity and specificity. The results show that the developed urinary metabolomics method can be employed to effectively screen noninvasive biomarkers.

使用的岛津仪器： GCMS-QP 2010



代表图片：尿液中四种 BC 诊断标记物的性能

原文网址：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5400539/

SCIENTIFIC REPORTS

OPEN

Altered Lipid Metabolism in Recovered SARS Patients Twelve Years after Infection

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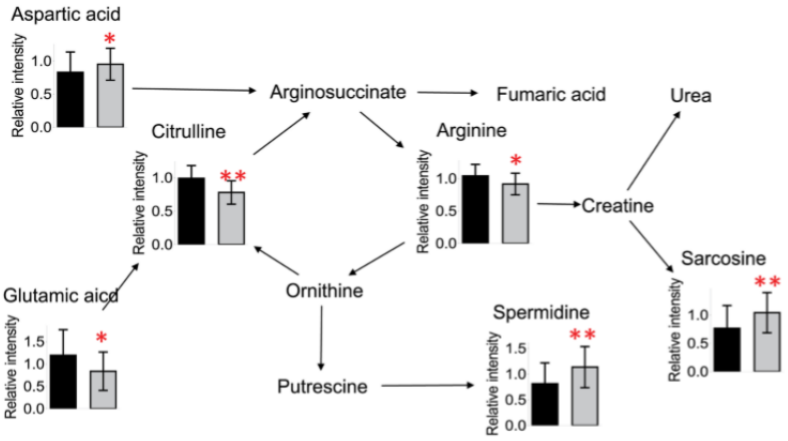
Qi Wu[1], Lina Zhou[2], Xin Sun[3], Zhongfang Yan[4], Chunxiu Hu[2], Junping Wu[3], Long Xu[3], Xue Li[5], Huiling Liu[6], Peiyuan Yin[2], Kuan Li[5], Jieyu Zhao[2], Yanli Li[2], Xiaolin Wang[2], Yu Li[5], Qiuyang Zhang[5], Guowang Xu[2] & Huaiyong Chen[1,5]

研究康复的非典型肺炎患者感染 12 年后脂质代谢的改变

Abstract: Severe acute respiratory syndrome-coronavirus (SARS-CoV) and SARS-like coronavirus are a potential threat to global health. However, reviews of the long-term effects of clinical treatments in SARS patients are lacking. Here a total of 25 recovered SARS patients were recruited 12 years after infection. Clinical questionnaire responses and examination findings indicated that the patients had experienced various diseases, including lung susceptibility to infections, tumors, cardiovascular disorders, and abnormal glucose metabolism. As compared to healthy controls, metabolomic analyses identified significant differences in the serum metabolomes of SARS survivors. The most significant metabolic disruptions were the comprehensive increase of phosphatidylinositol and lysophospha tidylinositol levels in recovered SARS patients, which coincided with the effect of methylprednisolone administration investigated further in the steroid treated non-SARS patients with severe pneumonia. These results suggested that high-dose pulses of methylprednisolone might cause long-term systemic damage associated with serum metabolic alterations. The present study provided information for an improved understanding of coronavirus-associated pathologies, which might permit further optimization of clinical treatments.

使用的岛津仪器：GCMS-QP2010



代表图片：与精氨酸和脯氨酸代谢相关的差异代谢物的通路图。数据以均数±SEM表示* < 0.05， ** < 0.01

原文网址：https://www.nature.com/articles/s41598-017-09536-z

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 61), pp: 103032-103046

Research Paper

Identification of *SPOP* related metabolic pathways in prostate cancer

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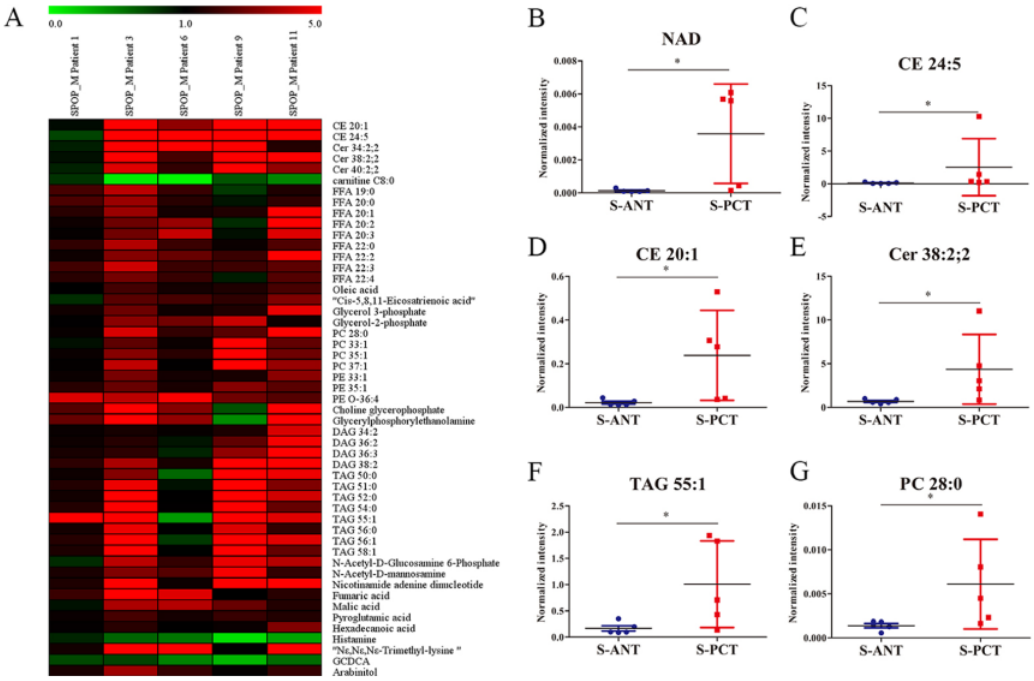
前列腺癌中 SPOP 相关代谢途径的识别

Abstract: Speckle-type POZ protein (SPOP), as a cullin-based E3 ubiquitin ligase, has been identified as one of the most frequently mutated genes in prostate cancer (PCa). However, whether *SPOP* mutations contribute to metabolic reprogramming in PCa remains unknown. Here, integrated studies of transcriptomics and metabolomics as well as lipidomics were performed in matched PCa tumor (PCT) and adjacent nontumor (ANT) tissues, followed by correlation analysis of *SPOP* mutations with altered metabolic pathways in *SPOP*-mutated PCa patients. Interestingly, transcriptomics profiling showed that all *SPOP* mutations (with 16.7% frequency, 11/66) occurred at the conserved residues in the substrate binding domain of meprin and TRAF homology (MATH). The results of integrated analysis indicated that three metabolic pathways, including tricarboxylic acid (TCA) cycle, fatty acid metabolism and glycerophospholipid metabolism, exhibited obvious upregulation in *SPOP*-mutated PCT tissues. Furthermore, both correlation analyses based on integrated data and cBioportal revealed that *FH, ELOVL2* and *ACADL* genes might be involved in *SPOP* mutation-related upregulation of these metabolic pathways. Taken together, our study provided new insights in understanding the relationship between metabolic pathways and *SPOP* mutations in PCa.

使用的岛津仪器：GCMS-QP 2010



代表图片： *SPOP* 突变的前列腺癌患者中肿瘤组织和癌旁非肿瘤组织的代谢物差异

原文网址： https://doi.org/10.18632/oncotarget.21460

Exhaled breath volatile biomarker analysis for thyroid cancer

LEI GUO, CHANGSONG WANG, CHUNJIE CHI, XIAOYANG WANG, SHANSHAN LIU, WEI ZHAO, CHAOFU KE, GUOWANG XU, and ENYOU LI

HARBIN AND DALIAN, CHINA

呼出气体中甲状腺癌的挥发性生物标志物分析

Abstract: Compared with other types of cancer, thyroid cancer incidence rates have increased rapidly worldwide in the past few decades. In recent years, potential thyroid cancer biomarkers have been studied, but these biomarkers have neither specificity nor good positive predictive value. Exhaled breath analysis is a recently developed convenient and noninvasive method for screening and diagnosing the disease. In this study, potential thyroid cancer biomarkers in volatile organic compounds (VOCs) were detected. Exhaled breath was collected from 64 patients with histologically confirmed cases of thyroid disease (including 39 individuals with papillary thyroid carcinoma and 25 individuals with nodular goiters) and 32 healthy volunteers. Solid-phase microextraction–gas chromatography and mass spectrometry was used to assess the exhaled VOCs of the study participants. The statistical methods of principal component analysis and partial leastsquares discriminant analysis were performed to process the final data. The VOCs exhibited significant differences between nodular goiter patients and normal controls, papillary thyroid carcinoma patients and normal controls, and papillary thyroid carcinoma patients and nodular goiter patients; 7, 7, and 3 characteristic metabolites played decisive roles in sample classification, respectively. Breath analysis may provide a new, noninvasive, and directly qualitative method for the clinical diagnosis of thyroid disease. (Translational Research 2015;166: 188–195)

使用的岛津仪器：GCMS-QP 2010

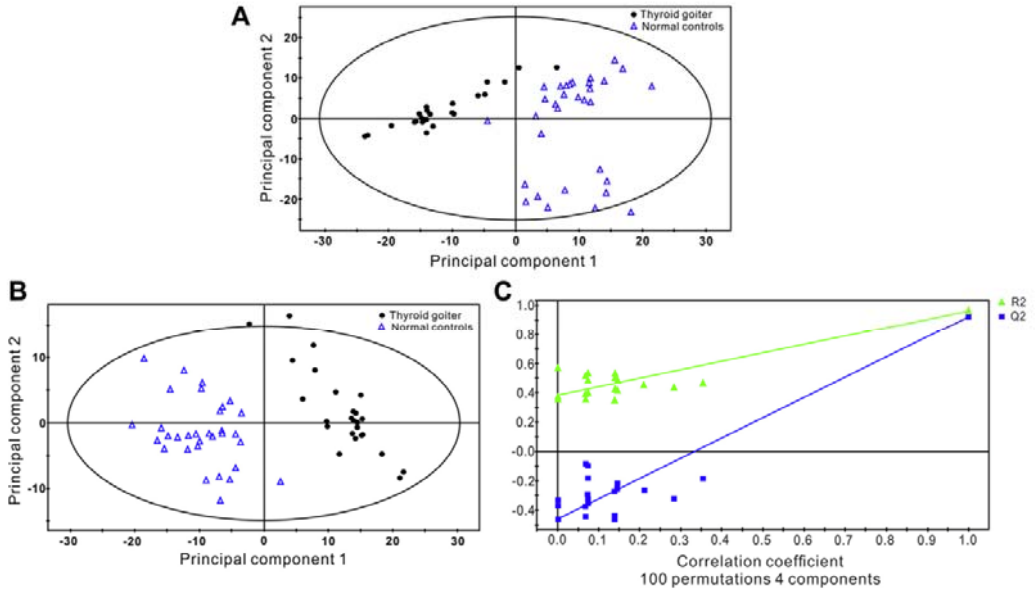


Fig 1. (**A**) PCA score plot (10 principal components, $R^2X = 0.878$, $Q^2 = 0.723$). (**B**) PLS-DA score plot (4 principal components, $R^2X = 0.656$, $R^2Y = 0.963$, $Q^2 = 0.92$). (**C**) PLS-DA validation plot intercepts: $R^2 = (0.0, 0.39)$, $Q^2 = (0.0, -0.43)$. PCA, principal component analysis; PLS-DA, partial least-squares discriminant analysis.

代表图片：甲状腺肿瘤患者和正常对照组的（A）主成分得分图；（B）PLS-DA 得份图；（C）PLS-DA 模型验证

原文网址：http://dx.doi.org/10.1016/j.trsl.2015.01.005

SCIENTIFIC REPORTS

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SUBJECT AREAS:
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Exhaled volatile organic compounds as lung cancer biomarkers during one-lung ventilation

Changsong Wang[1], Ran Dong[1], Xiaoyang Wang[1], Ailing Lian[1], Chunjie Chi[1], Chaofu Ke[2], Lei Guo[1], Shanshan Liu[1], Wei Zhao[1], Guowang Xu[3] & Enyou Li[1]

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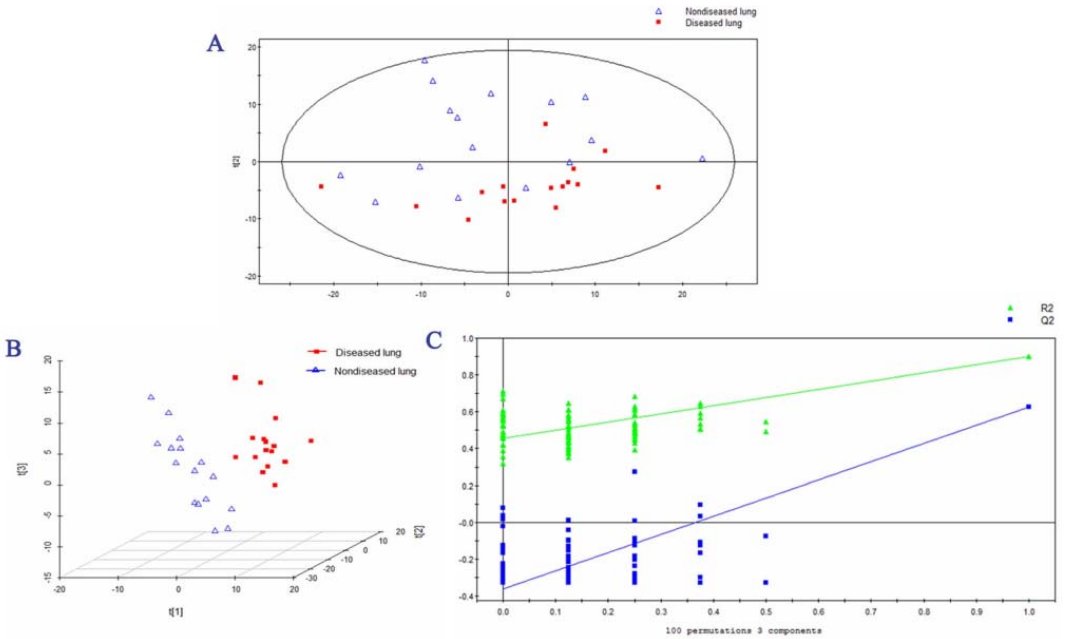
单一肺部呼出气体中挥发性有机物作为肺癌的生物标志物

Abstract: In this study, single-lung ventilation was used to detect differences in the volatile organic compound (VOCs) profiles between lung tissues in healthy and affected lungs. In addition, changes that occurred after lung cancer resection in both the VOCs profiles of exhaled breath from ipsilateral and contralateral lungs and the VOCs profiles of exhaled breath and blood sample headspaces were also determined. Eighteen patients with non-small cell carcinoma were enrolled. Alveolar breath samples were taken separately from healthy and diseased lungs before and after the tumor resection. Solid phase microextraction–gas chromatography/mass spectrometry was used to assess the exhaled VOCs of the study participants. The VOCs exhibited significant differences between the contralateral and ipsilateral lungs before surgery, the contralateral and ipsilateral lungs after surgery, the ipsilateral lungs before and after surgery, and the blood samples from before and after surgery; 12, 19, 12 and 5 characteristic metabolites played decisive roles in sample classification, respectively. 2,2-Dimethyldecane, tetradecane, 2,2,4,6,6-pentamethylheptane, 2,3,4-trimethyldecane, nonane, 3,4,5,6-tetramethyloctane, and hexadecane may be generated from lipid peroxidation during surgery. Caprolactam and propanoic acid may be more promising exhaled breath biomarkers for lung cancer.

使用的岛津仪器：GCMS-QP 2010



代表图片：疾病组和健康组的（A）PCA 得分图；（B）PLS-DA 得分图：（C）PLS-DA 模式有效性验证

原文网址：https://doi.org/10.1038/srep07312

Journal of proteome research

Article

pubs.acs.org/jpr

Study of Induction Chemotherapy Efficacy in Oral Squamous Cell Carcinoma Using Pseudotargeted Metabolomics

Guozhu Ye,[†,§] Ying Liu,[‡,§] Peiyuan Yin,[†] Zhongda Zeng,[†] Qiang Huang,[†] Hongwei Kong,[†] Xin Lu,[†] Laiping Zhong,[*,‡] Zhiyuan Zhang,[‡] and Guowang Xu[*,†]

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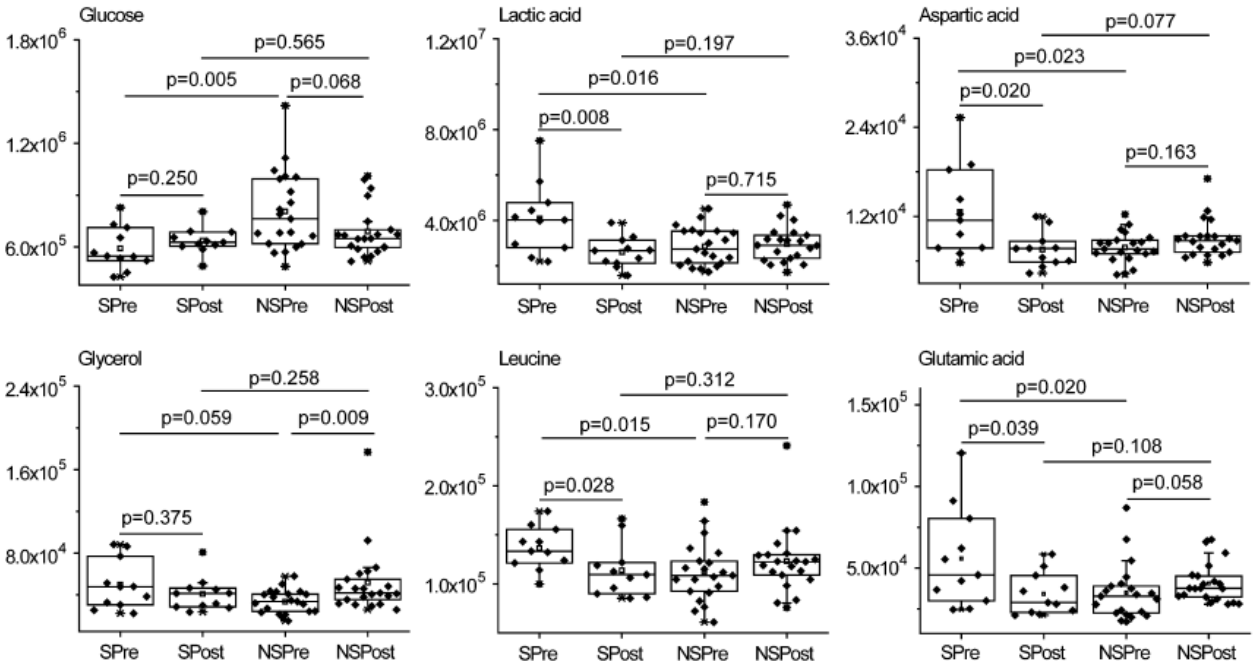
Supporting Information

基于拟靶向代谢组学的口腔鳞状细胞癌诱导化疗疗效的研究

ABSTRACT: The effect of induction chemotherapy on oral cancer is controversial owing to inconsistent results. However, the efficacy of induction chemotherapy is closely related to locoregional recurrence, distant metastasis, and overall survival after the treatment. A pseudotargeted metabolomics revealed that metabolites involved in glycolysis and amino acid metabolism were inversely regulated in patients with different chemotherapy responses, and most fatty acids, steroids, and antioxidant substances were up-regulated in all patients after the treatment. Among the metabolites, lactic acid, glucose, glutamic acid, aspartic acid, leucine, and glycerol were remarkably associated with induction chemotherapy efficacy. Subsequently, lactic acid, glutamic acid, and aspartic acid were defined as potential biomarkers of the suitability and efficacy of induction chemotherapy. Our results show that 100.0 and 84.37% of patients with different chemotherapy efficacy were correctly identified in the training and test sets, respectively. Moreover, patient suitability for treatment was correctly predicted for 100.0, 81.25, and 100.0% of patients in the training, test, and external validation sets, respectively. In conclusion, metabolites related to glycolysis, redox homeostasis, and anabolic progress were indicative of induction chemotherapy efficacy both pre- and postchemotherapy and beneficial for outcome evaluation and prediction. These results illustrate the potentials of metabolomics in personalized induction chemotherapy.

使用的岛津仪器：GCMS-QP 2010



代表图片：与化疗疗效相关的主要代谢产物的代谢差异。主要代谢产物通过相关性分析发现。

原文网址：http:// dx.doi.org/10.1021/pr4011298

Cancer Biology & Therapy 15:2, 200–206; February 2014; © 2014 Landes Bioscience

Blood volatile compounds as biomarkers for colorectal cancer

Changsong Wang[1], Peng Li[1], Ailing Lian[1], Bo Sun[1], Xiaoyang Wang[1], Lei Guo[1], Chunjie Chi[1], Shanshan Liu[1], Wei Zhao[1], Suqi Luo[1], Zhigang Guo[1], Yang Zhang[1], Chaofu Ke[2], Guozhu Ye[3], Guowang Xu[3], Fengmin Zhang[4,5], and Enyou Li[1]*

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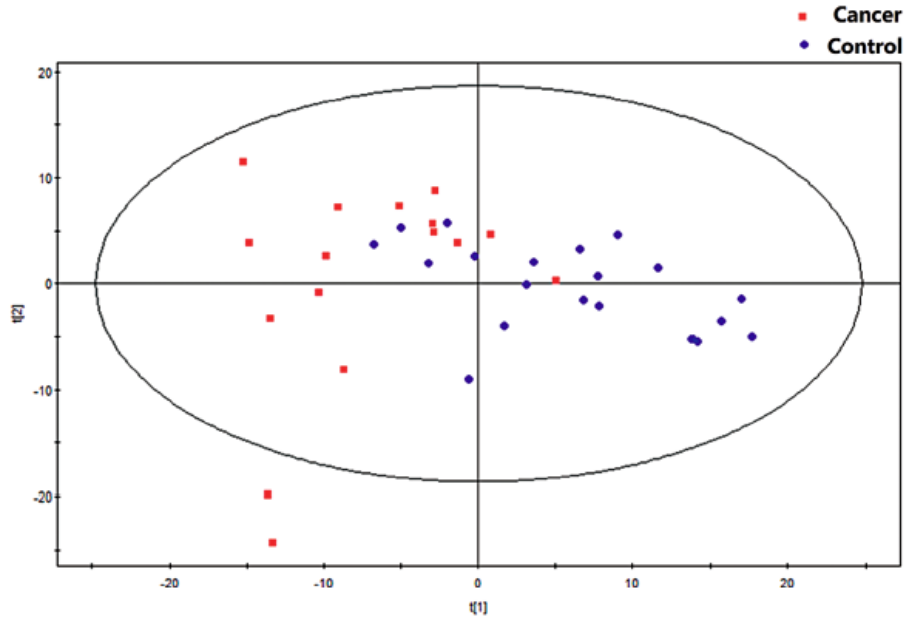
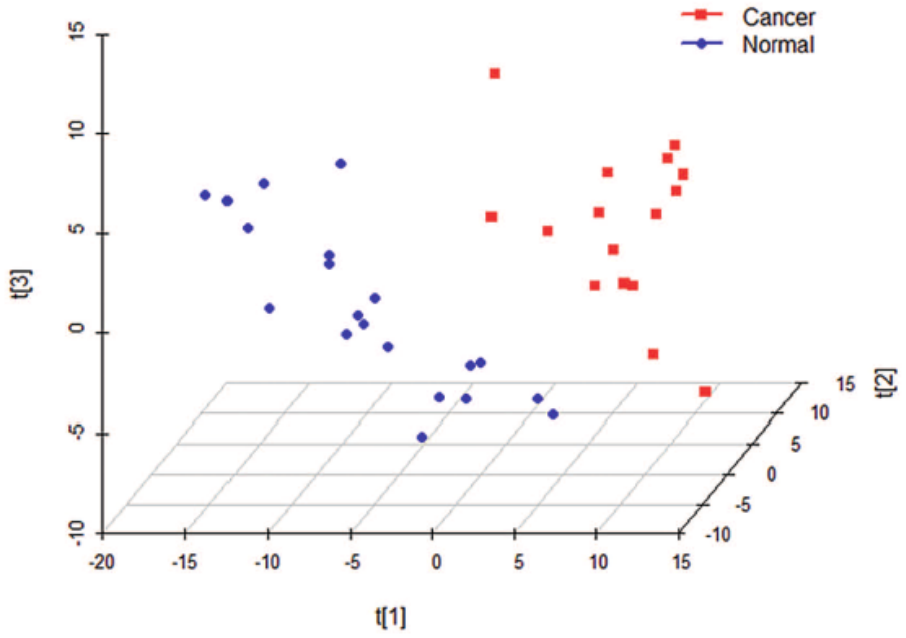
血液挥发性化合物作为结直肠癌的生物标记物

Abstract： Many recent studies have focused on the connection between the composition of specific volatile organic compounds (VOCs) in exhaled breath and various forms of cancer. However, the composition of exhaled breath is affected by many factors, such as lung disease, smoking, and diet. VOCs are released into the bloodstream before they are exhaled; therefore, the analysis of VOCs in blood will provide more accurate results than the analysis of VOCs in exhaled breath. Blood were collected from 16 colorectal cancer patients and 20 healthy controls, then solid phase microextraction–chromatography–mass spectrometry (SPME-GC-MS) was used to analysis the exhaled volatile organic compounds (VOCs). The statistical methods principal component analysis (PCA) and partial least-squares discriminant analysis (PLSDA) were performed to deal with the final dates. Three metabolic biomarkers were found at significantly lower levels in the group of CRC patients than in the normal control group ($P < 0.01$): phenyl methylcarbamate, ethylhexanol, and 6-t-butyl-2,2,9,9-tetramethyl-3,5-decadien-7-yne. In addition, significantly higher levels of 1,1,4,4-tetramethyl-2,5-dimethylene-cyclohexane were found in the group of CRC patients than in the normal control group ($P < 0.05$). Compared with healthy individuals, patients with colorectal adenocarcinoma exhibited a distinct blood metabolic profile with respect to VOCs. The analysis of blood VOCs appears to have potential clinical applications for CRC screening.

使用的岛津仪器： GCMS-QP 2010



代表图片：主成分分析（PCA）模型



代表图片：PLS-DA得分图

原文网址：http://dx.doi.org/10.4161/cbt.26723

Electrophoresis 2013, *34*, 2848–2856

Shili Chen[1]
Peiyuan Yin[1]
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Research Article

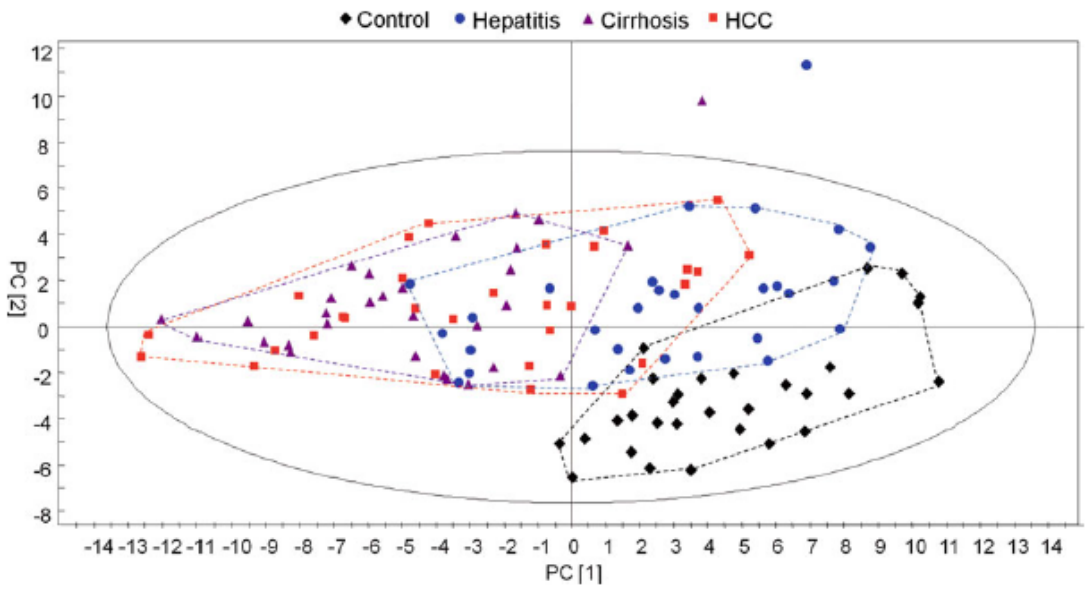
Serum lipid profiling of patients with chronic hepatitis B, cirrhosis, and hepatocellular carcinoma by ultra fast LC/IT-TOF MS

In this study, an ultra fast LC/IT-TOF MS (UFLC/IT-TOF MS)-based serum lipidomics method was employed to characterize the serum lipid profile of patients with chronic hepatitis B, cirrhosis, and hepatocellular carcinoma (HCC). After data collection and processing, 96 lipids including lysophosphatidylcholines, phosphatidylcholines, sphingomyelins, triacylglycerides, and cholesterol esters were identified and used for subsequent data analysis. Partial least squares-discriminant analysis revealed that patients with liver diseases had distinctly different serum lipid profile from that of healthy controls; while cirrhosis and HCC patients had a similar serum lipid profile, but different from that of hepatitis patients. The ANOVA analysis found 75 of the 96 identified lipids to be abnormally regulated, among which most of these lipids were downregulated in cirrhosis and HCC patients compared with those of healthy controls and hepatitis patients, while hepatitis patients induced several lipids downregulated and others upregulated compared with those of healthy controls, indicating the aberrant lipid metabolism in patients with liver diseases. This work demonstrated the utility of UFLC/IT-TOF MS-based serum lipidomics as a powerful tool to investigate the lipid metabolism of liver diseases.

基于超快速 LC/IT-TOF-MS 分析慢性乙型肝炎、肝硬化、肝癌患者的血脂组成

Abstract: In this study, an ultra fast LC/IT-TOF MS (UFLC/IT-TOF MS)-based serum lipidomics method was employed to characterize the serum lipid profile of patients with chronic hepatitis B, cirrhosis, and hepatocellular carcinoma (HCC). After data collection and processing, 96 lipids including lysophosphatidylcholines, phosphatidylcholines, sphingomyelins, triacylglycerides, and cholesterol esters were identified and used for subsequent data analysis. Partial least squares-discriminant analysis revealed that patients with liver diseases had distinctly different serum lipid profile from that of healthy controls; while cirrhosis and HCC patients had a similar serum lipid profile, but different from that of hepatitis patients. The ANOVA analysis found 75 of the 96 identified lipids to be abnormally regulated, among which most of these lipids were downregulated in cirrhosis and HCC patients compared with those of healthy controls and hepatitis patients, while hepatitis patients induced several lipids downregulated and others upregulated compared with those of healthy controls, indicating the aberrant lipid metabolism in patients with liver diseases. This work demonstrated the utility of UFLC/IT-TOF MS-based serum lipidomics as a powerful tool to investigate the lipid metabolism of liver diseases.

使用的岛津仪器：LCMS -IT-TOF



代表图片：PLS-DA评分图

原文网址：http://doi.10.1002/elps.201200629

OPEN ACCESS Freely available online

PLOS ONE

Breath Pentane as a Potential Biomarker for Survival in Hepatic Ischemia and Reperfusion Injury—A Pilot Study

Changsong Wang[1☯], Jinghui Shi[2☯], Bo Sun[1], Desheng Liu[1], Peng Li[1], Yulei Gong[1], Ying He[1], Shujuan Liu[1], Guowang Xu[3], Jianyi Li[4], Ailin Luo[2], Enyou Li[1]*

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呼出气戊烷作为肝缺血再灌注损伤生物标志物的初步研究

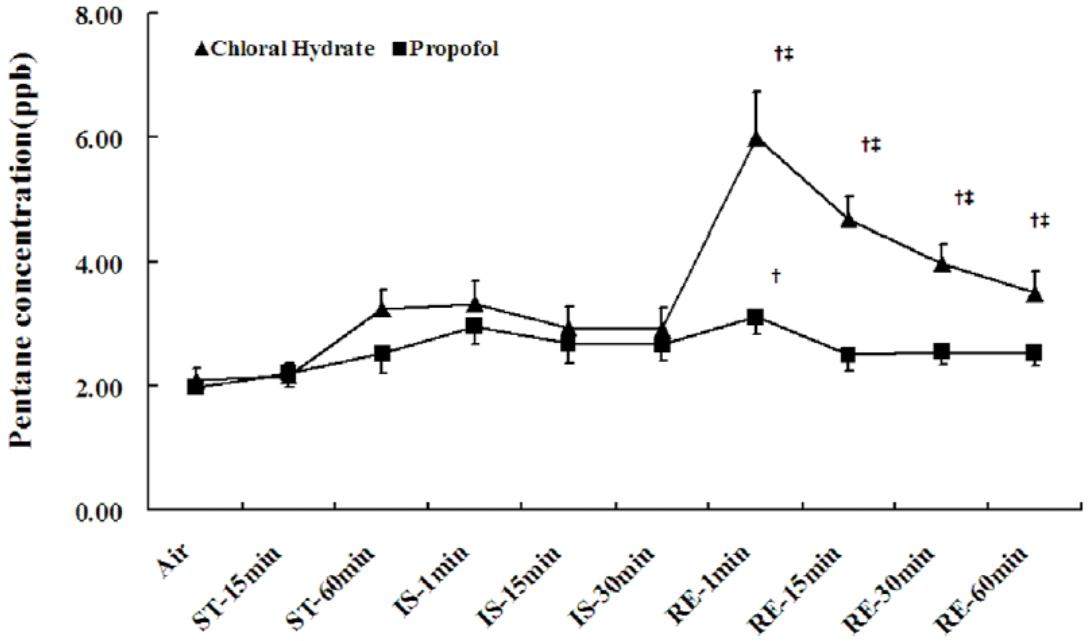
Background: Exhaled pentane, which is produced as a consequence of reactive oxygen species-mediated lipid peroxidation, is a marker of oxidative stress. Propofol is widely used as a hypnotic agent in intensive care units and the operating room. Moreover, this agent has been reported to inhibit lipid peroxidation by directly scavenging reactive oxygen species. In this study, using a porcine liver ischemia-reperfusion injury model, we have evaluated the hypothesis that high concentrations of breath pentane are related to adverse outcome and that propofol could reduce breath pentane and improve liver injury and outcome in swine in this situation.

Methodology/Principal Findings: Twenty male swine were assigned to two groups: propofol (n = 10) and chloral hydrate groups (n = 10). Hepatic ischemia was induced by occluding the portal inflow vessels. Ischemia lasted for 30 min, followed by reperfusion for 360 min. Exhaled and blood pentane concentrations in the chloral hydrate group markedly increased 1 min after reperfusion and then decreased to baseline. Breath and blood pentane concentrations in the propofol group increased 1 min after reperfusion but were significantly lower than in the chloral hydrate group. A negative correlation was found

between breath pentane levels and survival in the chloral hydrate group. The median overall survival was 251 min after reperfusion (range 150–360 min) in the chloral hydrate group. All of the swine were alive in the propofol group.

Conclusions: Monitoring of exhaled pentane may be useful for evaluating the severity of hepatic ischemia-reperfusion injury and aid in predicting the outcome; propofol may improve the outcome in this situation.

使用的岛津仪器：GCMS-QP 2010



代表图片：呼出气戊烷浓度的变化

原文网址：http://doi.10.1371/journal.pone.0044940

2012 年 3 月 March 2012 色 谱 Chinese Journal of Chromatography Vol. 30 No. 3 245 ~ 251

研究论文 DOI: 10.3724/SP.J.1123.2011.12037

气相色谱-质谱和液相色谱-质谱联用方法用于口腔癌代谢组学分析

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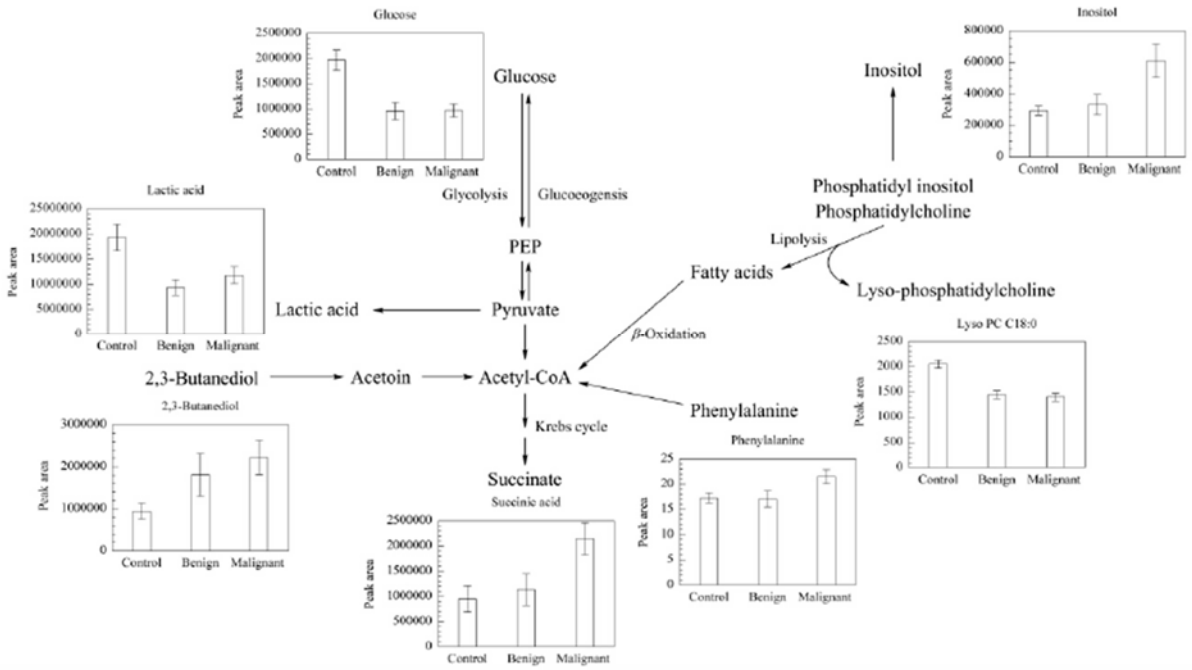
气相色谱-质谱和液相色谱-质谱联用方法用于口腔癌代谢组学分析

摘要: 口腔癌的发病率占全身恶性肿瘤的第6 位，正确区分正常状态与良性和恶性口腔肿瘤，是恰当选择治疗方案的关键所在。本研究中，首先利用液相色谱-质谱和气相色谱-质谱联用方法分别得到健康人、良性口腔肿瘤患者和恶性口腔肿瘤患者血浆、尿液和唾液的代谢轮廓，然后应用正交信号校正的偏最小二乘法进行多变量统计分析。结果表明健康人、良性肿瘤患者和恶性肿瘤患者在血浆、尿液和唾液等3 种体液代谢中都可以被区分开，而且找到和鉴定出19个重要差异代谢物。相关代谢通路分析显示，与健康人相比，良性和恶性口腔肿瘤患者都存在能量代谢紊乱和脂类代谢失衡的现象，但恶性口腔肿瘤患者还表现出三羧酸循环和肌醇代谢异常，这为临床诊断及治疗提供了重要信息。

使用的岛津仪器：GCMS-QP 2010



代表图片：重要差异代谢物在相关代谢通路中的代谢变化

原文网址： https://DOI: 10．3724 /SP．J．1123．2011．12037

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Effect of the traditional Chinese medicine tongxinluo on endothelial dysfunction rats studied by using urinary metabonomics based on liquid chromatography–mass spectrometry

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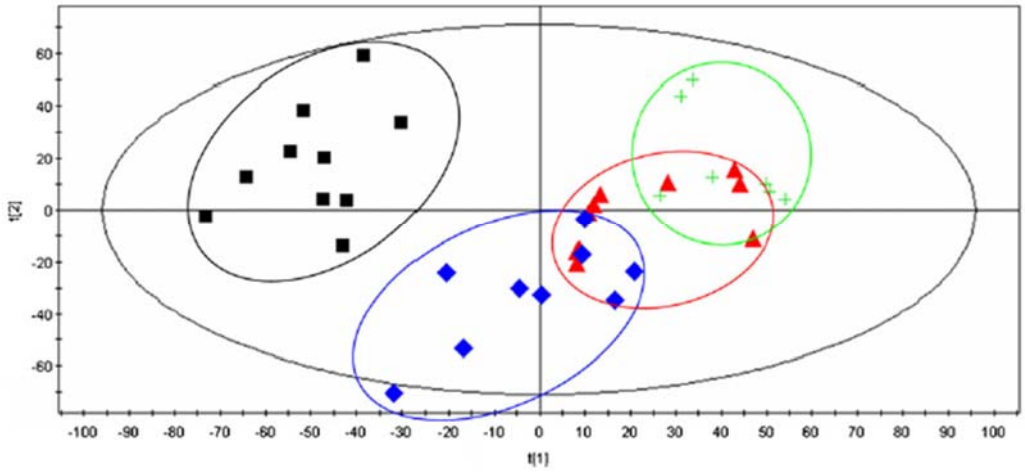
应用液相色谱-质谱的尿液代谢组学研究通心络对大鼠血管内皮功能障碍的影响

Abstract： A urinary metabonomic method based on ultra-fast liquid chromatography coupled with ion trap-time of flight mass spectrometry (UFLC/MS-IT-TOF) was employed to study the preventive efficacy and the gmetabolic changes caused by simavastatin and the traditional Chinese medicine tongxinluo in endothelial dysfunction rats. Principal component analysis (PCA) was applied to study metabolic patterns of endothelial dysfunction rats and healthy control rats. 1-Methyladenosine, indoxyl sulfate, hippuric acid, riboflavin, coproporphyrin, and p-cresol glucuronide were identified as potential biomarkers, indicating that pathways of adenine, tryptophan, phenylalanine, riboflavin and porphyrin metabolism were disturbed in endothelial dysfunction rats. Applications of simvastatin and tongxinluo to endothelial dysfunction rats improved endothelial function according to the results of histopathology and measurements of endothelin-1 and nitric oxide. Metabonomic studies suggested that tongxinluo prevents endothelial dysfunction by

regulating multiple metabolic pathways to their normal state, whereas simvastatin only altered selected metabolic pathways. This research demonstrated that metabonomics is a powerful and promising tool for disease investigation and the efficacy evaluation of complex traditional Chinese medicines.

使用的岛津仪器：LCMS-IT-TOF



代表图片：对4组样本进行主成分分析的得分图

原文网址： https://doi:10.1016/j.jpba.2011.04.020

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Molecular BioSystems

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www.rsc.org/molecularbiosystems

PAPER

Application of plasma lipidomics in studying the response of patients with essential hypertension to antihypertensive drug therapy†

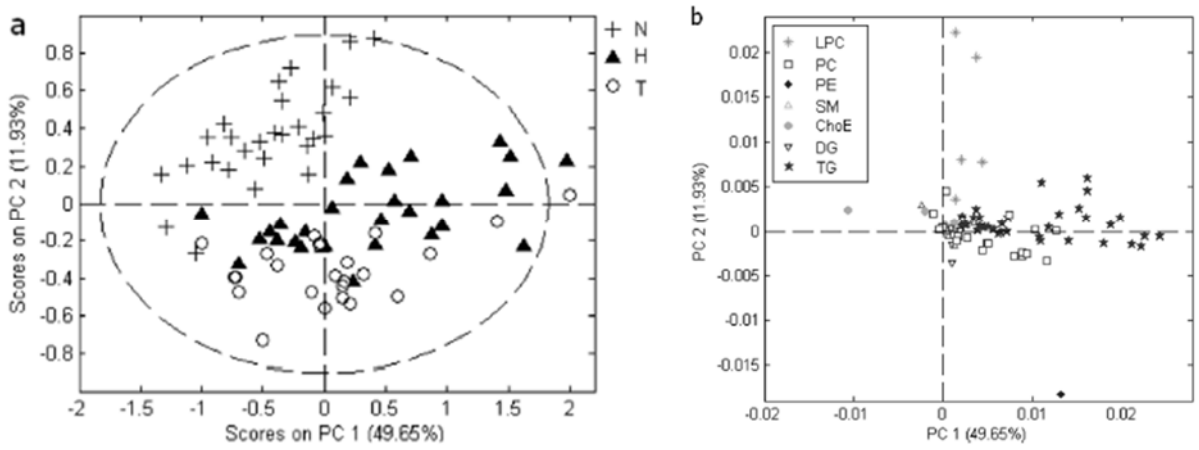
Chunxiu Hu,[a] Hongwei Kong,[a] Fengxue Qu,[b] Yong Li,[a] Zhenqiu Yu,[b] Peng Gao,[a] Shuangqing Peng*[c] and Guowang Xu*[a]

血浆脂质组学在原发性高血压患者抗高血压药物疗效研究中的应用

Abstract：Hypertension is a key risk factor in the progression of cardiovascular disease (CVD). Dyslipidemia, a strong predictor of CVD, frequently coexists with hypertension. Therefore, the control of hypertension and dyslipidemia may help reduce CVD morbidity and mortality. In the present study, the therapeutic effects of antihypertensive agents on blood pressure control and plasma lipid metabolism were evaluated. The plasma lipid profiles of patients with treated (n = 25) or untreated (n = 30) essential hypertension as well as of subjects with normotension (n = 28) were analyzed using liquid chromatography mass spectrometry. Principal component analysis of the lipidomics data revealed distinct clusters among studied subjects across three human populations. Phosphatidylcholines and triacylglycerols (TG) dominated the pattern of hypertension-influenced plasma lipid metabolism. Discriminatory lipid metabolites were analyzed using one-way analysis of variance followed by a post hoc multiple comparison correction. TG lipid class was significantly increased by 49.0% (p o 0.001) in hypertensive vs. normotensive groups while

tended to decrease (_21.2%, p = 0.054) in hypertensive patients after treatment. Total cholesteryl esters were significantly decreased by _16.9% (p o 0.001) in hypertensive patients after treatment. In particular, a large number of individual neutral lipid species were significantly elevated in hypertensive subjects but significantly decreased after treatment with antihypertensive agents. The present study applied, for the first time, a systems biology based lipidomics approach to investigate differentiation among plasma lipid metabolism of patients with treated/untreated essential hypertension and subjects with normotension. Our results demonstrate that antihypertensive medications to lower blood pressure of hypertensive patients to target levels produced moderate plasma lipid metabolism improvement of patients with hypertension.

使用的岛津仪器：LCMS-IT-TOF



代表图片：三个研究组血浆脂质组学数据的主成分分析（a）和负荷（b）图。N：血压正常者；H：高血压患者；T：治疗高血压患者。

原文网址： https://DOI: 10.1039/c1mb05342f

PAPER www.rsc.org/molecularbiosystems | Molecular BioSystems

Metabonomics study of urine and plasma in depression and excess fatigue rats by ultra fast liquid chromatography coupled with ion trap-time of flight mass spectrometry†

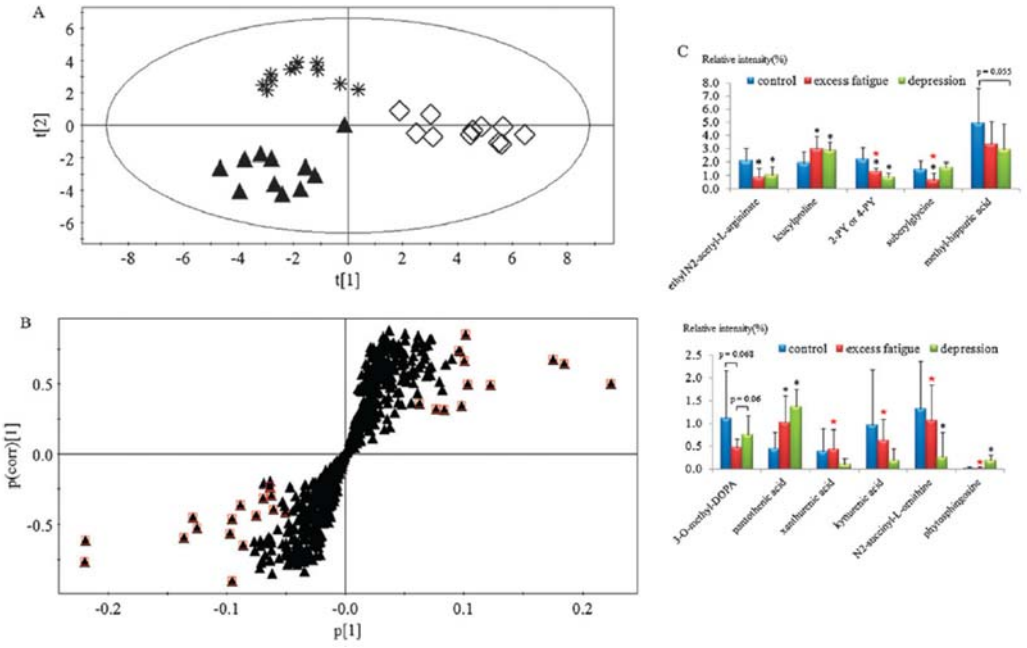
Fengxia Zhang,‡[ab] Zhenhua Jia,‡[c] Peng Gao,[a] Hongwei Kong,[a] Xiang Li,[a] Xin Lu,[a] Yiling Wu*[c] and Guowang Xu*[a]

超快速液相色谱-离子阱飞行时间质谱联用研究抑郁症和过度疲劳大鼠的尿和血浆代谢组学

ABSTRACT：A novel metabonomic method based on fast liquid chromatography coupled with ion trap-time of flight mass spectrometry (UFLC/MS-IT-TOF) was applied to study the metabolic changes of plasma and urine in depression and excess fatigue rats. Principal component analysis (PCA) and partial least squares-discriminant analysis (PLS-DA) were applied for classifying the depression, excess fatigue and the control rats. Metabolites which were important for the classification in the three groups of rats were selected as potential biomarkers and identified by MSn information achieved from UFLC/MS-IT-TOF analysis. Spermine, propionylcarnitine, butyrylcarnitine, phenylalanine, lysophosphatidylcholine (LPC) C14:0 and LPC C18:2 were down-regulated, methyl-hippuric acid and chenodeoxycholic acid (CDCA) were up-regulated significantly in plasma of the excess fatigue rats. Spermine, leucine, propionylcarnitine, and butyrylcarnitine decreased, hippuric acid, methyl-hippuric acid, cholic acid, CDCA and LPC C16:0 increased markedly in plasma of the depression rats. Ethyl N2-acetyl-L-argininate and N-methyl-2-pyridone-5-carboxamide (2-PY) (or N-methyl-4-pyridone-3-carboxamide (4-PY)) were down-regulated, leucylproline and pantothenic acid were up-regulated remarkably both in urine of

depression and excess fatigue rats. The concentration of kynurenic acid and N2-succinyl-L-ornithine was low in urine of depression rats compared with control rats. Based on the data, correlation networks for depression and excess fatigue rats revealed the abnormality of nicotinate and nicotinamide metabolism, arginine metabolism, cholesterol metabolism, tryptophan metabolism and kynurenine metabolism in depression rats, and in excess fatigue rat alterations of energy metabolism, nicotinate and nicotinamide metabolism and lecithin metabolism. Our results provide novel insights in the complex metabolic mechanisms occurring in depression and excess fatigue rats.

使用的岛津仪器：LCMS-IT-TOF



代表图片：基于尿液分析的PLS-DA模型结果。A:对照组、抑郁大鼠、过度疲劳大鼠PLS-DA评分图，R2Y=0.869，Q2=0.787。B：选择潜在生物标志物的PLS-DA模型的S图。C：对照组和模型组大鼠尿液中潜在生物标志物的比较。

原文网址： https://DOI: 10.1039/b914751a

OPEN ACCESS Freely available online PLoS one

Lipidomics Analysis Reveals Efficient Storage of Hepatic Triacylglycerides Enriched in Unsaturated Fatty Acids after One Bout of Exercise in Mice

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脂质组学分析显示小鼠一次运动后富含不饱和脂肪酸的肝三酰甘油酯的高效储存

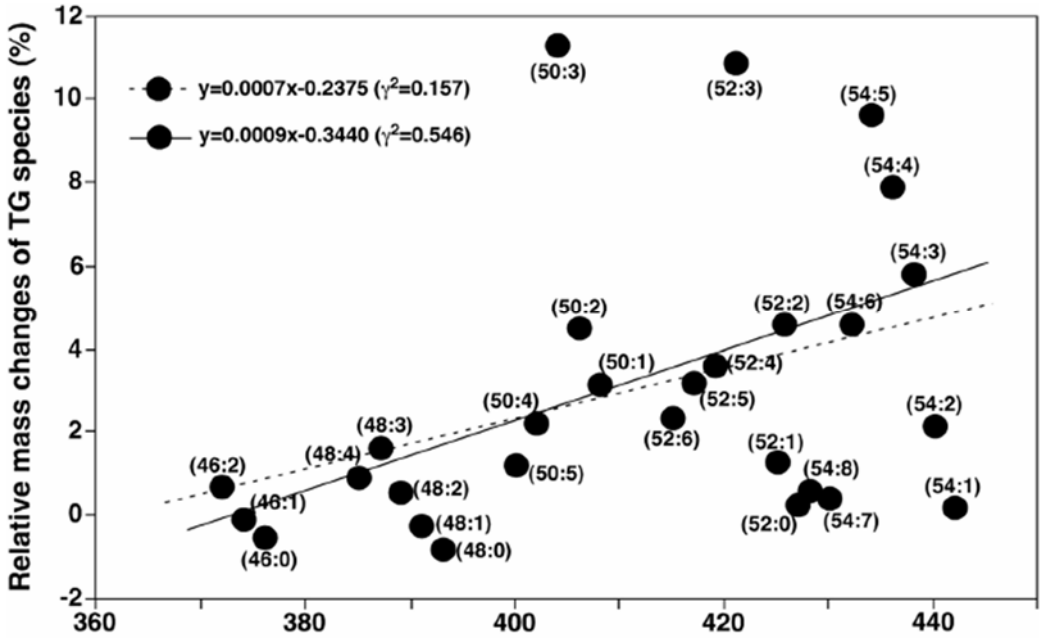
Background: Endurance exercise induces lipolysis, increases circulating concentrations of free fatty acids (FFA) and the uptake and oxidation of fatty acids in the working muscle. Less is known about the regulation of lipid metabolism in the liver during and post-exercise.

Methodology/Principal Findings: We performed an ultra fast liquid chromatography-mass spectrometry (UFLC-MS) based lipidomics analysis of liver tissue samples obtained from C57Bl/6J mice immediately after a 60 min treadmill run of moderate intensity, and after 3 h of recovery. The PLS-DA scores plot for 115 quantified lipid molecular species revealed a clear separation of the hepatic lipid profile of sedentary from recovering mice, but not from mice immediately after running. 21 lipid species were considered to be most responsible for the difference in the hepatic lipid profiles, including 17 triacylglycerides (TG), one lysophosphatidylcholine (LPC) and three phosphatidylcholines (PC). TG species were found to be more abundant in the recovery phase, while PC species were decreased. The degree of accumulation of individual TG species correlated well with the amount of theoretical energy stored whereas no increase was found for TG species containing only saturated or

one monounsaturated fatty acid. Total liver TG content as assayed by an enzymatic method was increased to 163% in the recovery phase, while it was significantly decreased in skeletal muscle by the exercise bout and remained less in the recovery phase. Results from fasted and refed mice indicate that fasting-induced lipolysis was associated with a pronounced accumulation of hepatic TG, which is reversed by refeeding for 5 h. Thus food intake per se did not elevate hepatic TG.

Conclusion: These data indicate that high availability of FFA induced by endurance exercise or fasting resulted in a transient hepatic TG accumulation, while muscle TG content was decreased during exercise presumably due to increased muscle fatty acid oxidation.

使用的岛津仪器：LCMS-IT-TOF



代表图片：甘油三酯中包含的三磷酸腺苷理论数量

原文网址： https://doi:10.1371/journal.pone.0013318

络气郁滞型血管内皮功能障碍病症大鼠的 LC/MS 代谢轮廓分析

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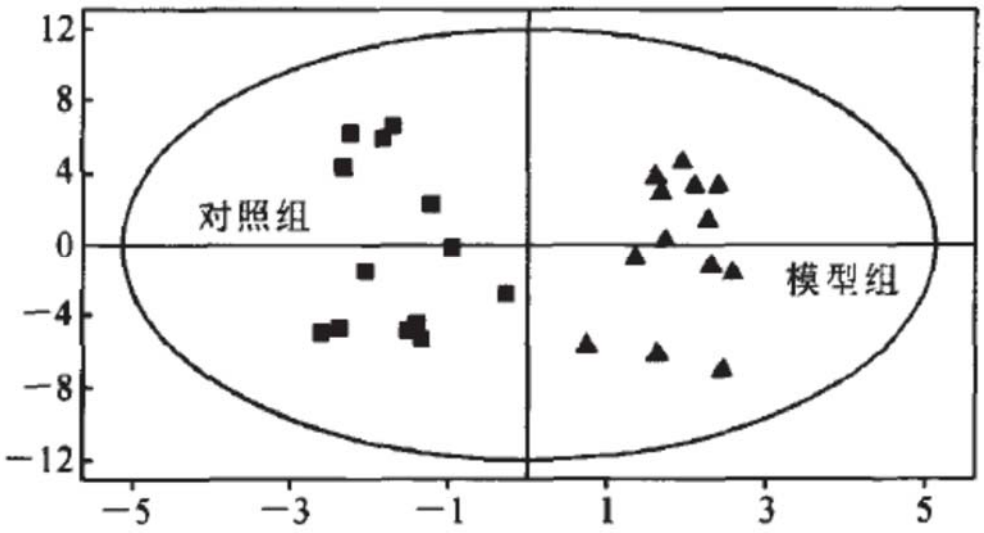
络气郁滞型血管内皮功能障碍病症大鼠的 LC/MS 代谢轮廓分析

摘要： 血管内皮在调节血管张力、抗血栓、内分泌方面具有重要的作用，当血管内皮发生障碍时，可引起一系列的心血管的疾病，如动脉粥样硬化、冠心病、高血压等。运用代谢组学技术可以较全面地研究机体代谢轮廓，从而探究“脉络-血管病变”对机体的影响。本实验采用液相色谱-离子阱/飞行时间质谱（LCMS-IT-TOF）研究络气郁滞型血管内皮功能障碍症大鼠的代谢轮廓变化。

使用的岛津仪器：LCMS-IT-TOF



代表图片： 对照组与络气郁滞型内皮功能障碍模型大鼠的OPLS分类结果

原文网址：http://www.wanfangdata.com.cn/details/detail.do?_type=conference&id=7335982

·重症医学·

兔肝缺血再灌注时呼出气戊烷浓度的变化

刘淑娟 李恩有 许国旺 李鹏 赫颖

兔肝缺血再灌注时呼出气戊烷浓度的变化

摘要： 目的 探讨兔肝缺血再灌注（IR）时呼出气戊烷浓度的变化。方法 健康雄性日本大耳白兔30只，体重2.4~3.0 kg，随机分为2组（n=15）：假手术组（S组）和IR组。分别于缺血前（基础状态，T_0）、缺血1、10、25 min、再灌注1、10、25、60、120、180 min（T_{1-9}）时采集呼出气，采用气相色谱-质谱法测定戊烷浓度，并采集动脉血样，测定血清ALT、AST和SOD活性及MDA浓度。于再灌注180 min时处死动物，观察肝组织病理学结果。结果 S组各时点呼出气戊烷浓度及血清ALT、AST、SOD活性、MDA浓度差异无统计学意义(P>0.05)。与基础值及S组比较，IR组$T_{4,5}$时呼出气戊烷浓度升高，T_{7-9}时血清ALT、AST活性和MDA浓度升高，SOD活性降低(P<0.05或0.01)。结论 兔肝脏缺血再灌注时呼出气戊烷浓度升高，可反映缺血再灌注期间脂质过氧化反应的程度，且比血液酶学指标更敏感。

使用的岛津仪器：GCMS QP-2010

指标	组别	T_0	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8	T_9
ALT	S 组	38 ± 4	39 ± 4	38 ± 5	38 ± 3	41 ± 6	45 ± 4	39 ± 4	39 ± 4	41 ± 4	39 ± 4
(U/L)	IR 组	39 ± 5	40 ± 3	37 ± 3	43 ± 6	43 ± 4	46 ± 4	47 ± 5	71 ± 5[ac]	114 ± 24[bd]	138 ± 31[bd]
AST	S 组	37 ± 3	43 ± 6	45 ± 3	35 ± 5	39 ± 3	41 ± 3	38 ± 5	42 ± 7	41 ± 5	47 ± 5
(U/L)	IR 组	39 ± 4	43 ± 6	42 ± 3	36 ± 5	46 ± 6	48 ± 7	49 ± 6	235 ± 23[bd]	259 ± 27[bd]	338 ± 39[bd]
SOD	S 组	344 ± 21	353 ± 28	359 ± 47	327 ± 31	349 ± 23	351 ± 26	339 ± 34	334 ± 31	338 ± 35	357 ± 35
(U/ml)	IR 组	344 ± 21	356 ± 23	361 ± 39	359 ± 45	354 ± 19	334 ± 28	354 ± 35	271 ± 31[bd]	287 ± 31[bd]	245 ± 39[bd]
MDA	S 组	5.6 ± 0.6	6.8 ± 0.7	6.6 ± 1.1	6.0 ± 0.4	6.2 ± 0.9	6.5 ± 0.6	5.7 ± 0.4	6.5 ± 1.3	5.9 ± 0.6	6.4 ± 1.4
(nmol/ml)	IR 组	6.3 ± 0.8	6.9 ± 1.2	6.7 ± 1.3	6.5 ± 0.9	5.9 ± 0.5	5.8 ± 0.6	6.0 ± 1.1	9.7 ± 1.3[ad]	12.1 ± 1.8[bd]	18.4 ± 2.3[bd]
戊烷	S 组	9.7 ± 1.9	9.5 ± 1.3	9.7 ± 1.8	11.0 ± 1.9	10.3 ± 1.4	10.5 ± 1.1	10.2 ± 1.3	10.3 ± 1.8	10.8 ± 2.1	10.2 ± 1.7
(ppb)	IR 组	9.4 ± 1.8	9.4 ± 1.5	9.6 ± 2.1	9.5 ± 1.9	16.3 ± 0.8[bd]	13.5 ± 1.2[ac]	9.9 ± 1.1	11.2 ± 2.3	9.7 ± 1.7	9.6 ± 1.4

注：与 T_0 时比较，[a]$P<0.05$ [b]$P<0.01$ 与 S 组比较，[c]$P<0.05$ [d]$P<0.01$

代表表格： 两组兔血清ALT、AST、SOD活性和MDA浓度及呼出气戊烷浓度的比较（n=15，$\tilde{x}$+s）

原文网址：http://lib.cqvip.com/Qikan/Article/Detail?id=34468162

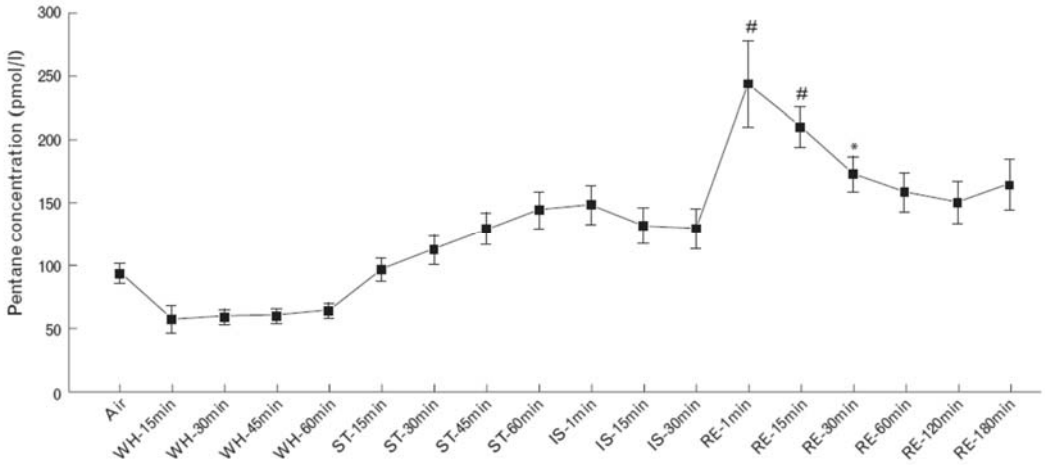
Breath pentane: an indicator for early and continuous monitoring of lipid peroxidation in hepatic ischaemia–reperfusion injury

Peng Li[a], Enyou Li[a], Guowang Xu[b], Changsong Wang[a], Yulei Gong[a] and Ying He[a]

呼出气戊烷：肝脏缺血再灌注损伤中脂质过氧化的早期和持续性指标

Background and objective Lipid peroxidation plays an important role during liver ischaemia–reperfusion injury. Pentane in breath is often used as an index of lipid peroxidation. We observed the changes in levels of breath pentane during the lipid peroxidation process caused by liver ischaemia–reperfusion injury. Methods Ten male swine were anaesthetized with chloral hydrate 0.3–0.5 g kg^{-1} min^{-1}. Total hepatic ischaemia was induced by occluding the portal inflow vessels. Ischaemia lasted 30 min followed by reperfusion for 180 min. Breath samples were sampled from the anaesthesia circuit and blood samples were collected from the inferior vena cava. Pentane concentrations in breath and blood were quantified by means of solid phase microextraction and gas chromatography-mass spectrography technique. Results Exhaled pentane concentrations (means+SE) increased markedly after reperfusion for 1 min (244.13+33.3 pmol l^{-1}) and decreased gradually to initial levels after reperfusion for 60 min. Blood pentane concentrations (means+SE) increased significantly after reperfusion for 1 min (333.46+63.05 pmol l^{-1}) and then decreased to basal level. Breath pentane concentrations showed a correlation with blood ($r=0.709$, $P<0.05$). Conclusion Breath pentane analysis could provide early, rapid, noninvasive and continuous assessment of lipid peroxidation during hepatic ischaemia–reperfusion injury.

使用的岛津仪器：GCMS QP-2010



代表图片：呼出气中戊烷浓度变化。IS—缺血期，RE—再灌注期，ST—稳定期，WH—高速冲洗期；ST 60 min 作为基线，*P<0.05，#P<0.01

原文网址：https://doi.org/ 10.1097/eja.0b013e328326f7b7

Anal Bioanal Chem (2014) 406:4757–4763
DOI 10.1007/s00216-014-7865-x

RESEARCH PAPER

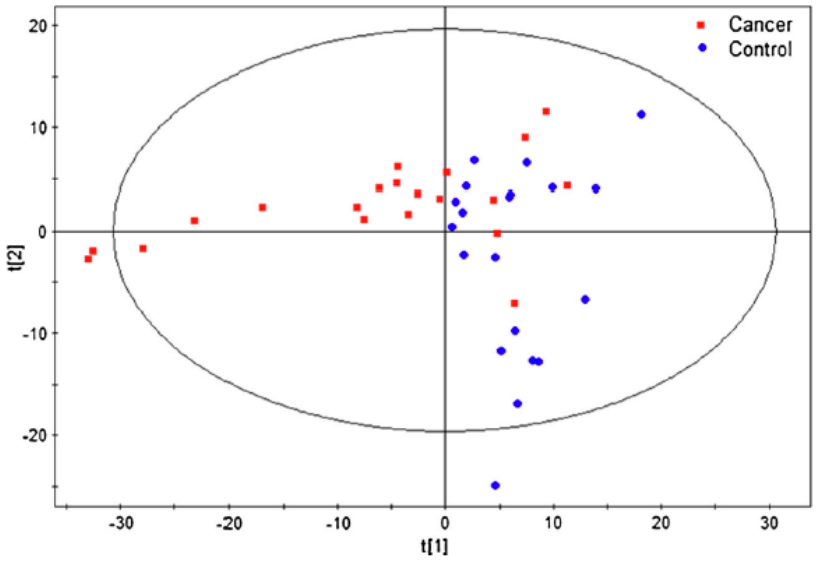
Noninvasive detection of colorectal cancer by analysis of exhaled breath

Changsong Wang · Chaofu Ke · Xiaoyang Wang · Chunjie Chi · Lei Guo · Suqi Luo · Zhigang Guo · Guowang Xu · Fengmin Zhang · Enyou Li

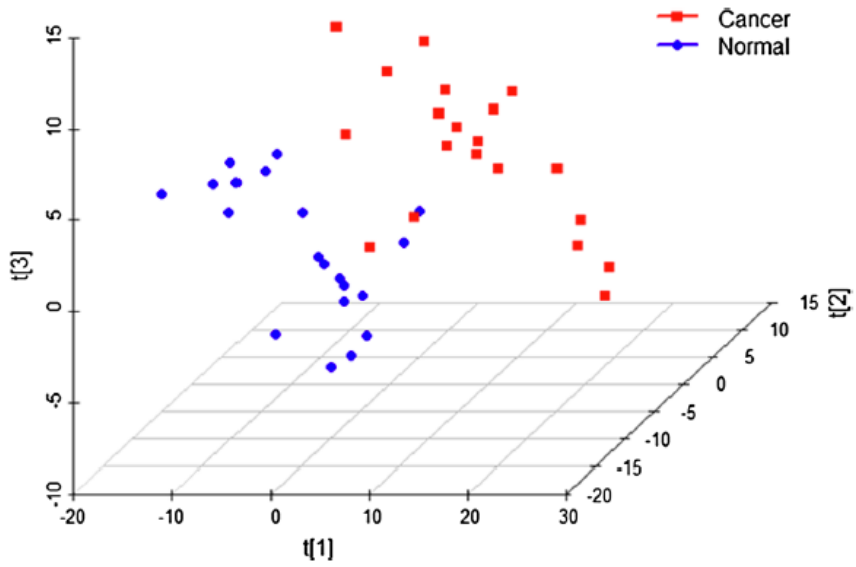
使用呼出气分析无创检测结直肠癌

Abstract: There has been growing interest in exhaled breath analysis for cancer screening and disease monitoring; however, limited breath biomarker information exists regarding colorectal cancer (CRC). The objective of this study was to screen for breath biomarkers of CRC. Exhaled breath was collected from 20 CRC patients and 20 healthy controls; subsequently, solid-phase microextraction–gas chromatography/mass spectrometry (SPME-GC/MS) was used to assess the exhaled volatile organic compounds (VOCs) of the study participants. The statistical methods of principal component analysis (PCA) and partial least squares discriminant analysis (PLS-DA) were performed to process the final data. The VOCs in the exhalations of CRC patients exhibited significant differences from the VOCs in the exhalations of healthy controls; in particular, relative to the latter exhalations, the former exhalations contain significantly higher levels of cyclohexanone, 2,2-dimethyldecane, dodecane, 4-ethyl-1-octyn - 3 - o l , ethylan i l i n e , cyclooctylmethanol, trans-2-dodecen-1-ol, and 3-hydroxy-2,4,4-trimethylpentyl 2-methylpropanoate but significantly lower levels of 6-t-butyl-2,2,9,9-tetramethyl-3,5-decadien-7-yne ($P<0.05$). Analyses of breath VOCs provide a related model of CRC exhalation that could represent an effective and convenient screening method for this disease.

使用的岛津仪器：GCMS-QP 2010



代表图片：主成分分析（PCA）模型



代表图片：PLS-DA得分图

原文网址：http://doi.10.1007/s00216-014-7865-x

IOP PUBLISHING JOURNAL OF BREATH RESEARCH
J. Breath Res. 6 (2012) 026003 (6pp) doi:10.1088/1752-7155/6/2/026003

Measurement of pentane in expiratory gas during rabbit hepatic ischemia/ reperfusion by solid-phase microextraction and gas chromatography–mass spectrometry (SPME GC/MS)

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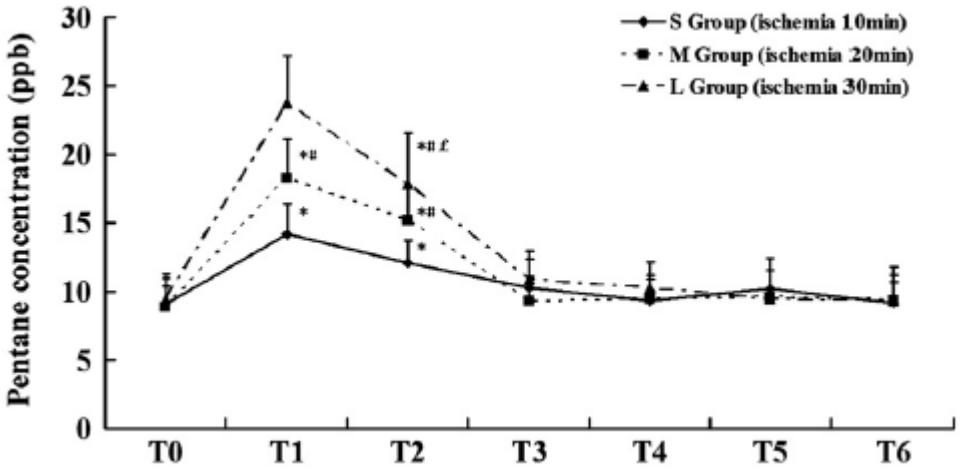
固相微萃取结合气相色谱质谱技术测定兔肝缺血再灌注时呼出气戊烷浓度的变化

Abstract: The aim of this study was to determine the changes in the pentane concentration of expiratory gas as well as the relationship between this pentane concentration and hepatic oxidative stress during rabbit hepatic ischemia/reperfusion using solid-phase microextraction (SPME) and gas chromatography–mass spectrometry (GC/MS). 45 white male rabbits with body weights between 2.5 and 3.0 kg were randomly assigned to the following three groups: the 10 min ischemia group (group S); the 20 min ischemia group (group M); or the 30 min ischemia group (group L). Expiratory gases were collected prior to ischemia (T0) and for 1, 10, 20, 30, 60 and

120 min (T1–T6) following reperfusion. Pentane concentrations were determined using SPME and GC/MS. In addition, arterial blood samples were collected, and serum aminotransferase (AST) and malondialdehyde (MDA) concentrations were measured. In the three groups, the pentane concentrations of the expiratory gases at points T1 and T2 were significantly increased ($P < 0.05$) compared with those at point T0, and the serum AST and MDA concentrations at points T5 and T6 were

also significantly increased ($P < 0.05$) compared with those at point T0. Therefore, the use of SPME in combination with GC/MS represents an improved anesthesia system that can be used to continuously measure the concentration of pentane in expiratory gases, which can reflect the degree of oxidative stress during hepatic ischemia/reperfusion.

使用的岛津仪器：GCMS-QP 2010



代表图片：手术过程中不同时间呼出气戊烷浓度的变化

原文网址：http://doi.10.1088/1752-7155/6/2/026003

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journal homepage: www.elsevier.com/locate/talanta

Metabonomics study of atherosclerosis rats by ultra fast liquid chromatography coupled with ion trap-time of flight mass spectrometry

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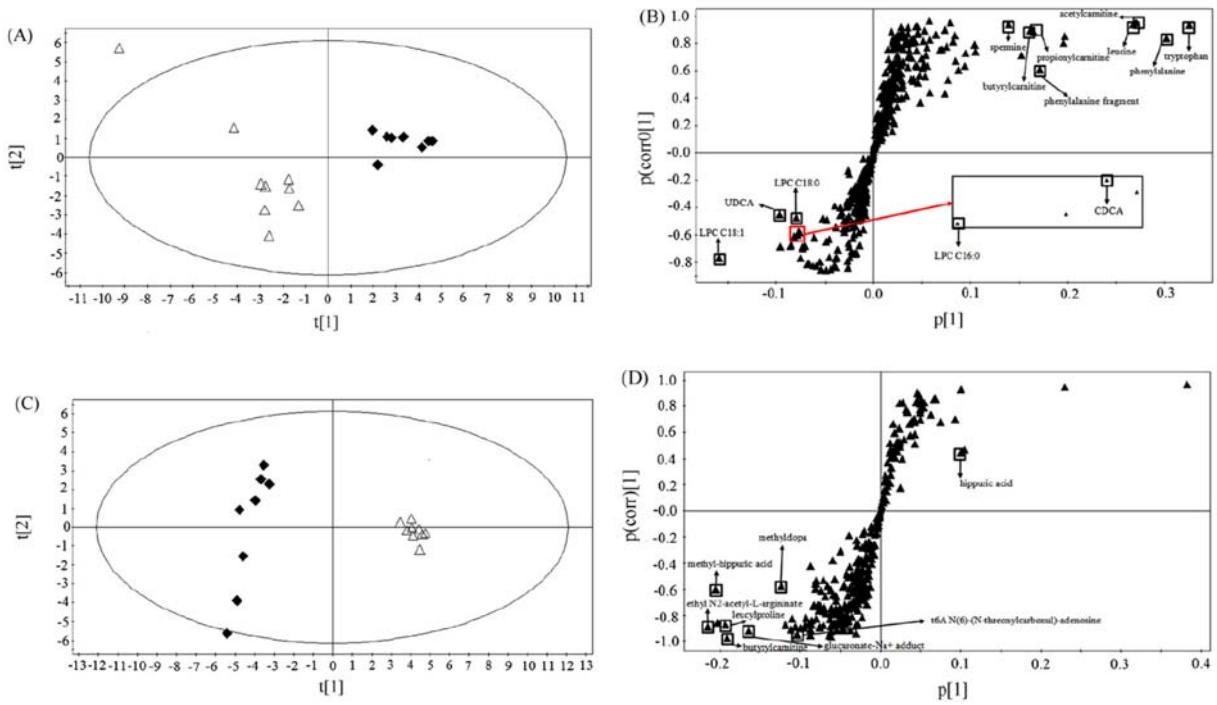
利用超快速液相色谱离子阱飞行时间质谱法进行动脉粥样硬化大鼠的代谢组学研究

Abstract: An ultra fast liquid chromatography coupled with IT-TOF mass spectrometry (UFLC/MS-IT-TOF) metabonomic approach was employed to study the plasma and urine metabolic profiling of atherosclerosis rats. Acquired data were subjected to principal component analysis (PCA) for differentiating the atherosclerosis and the control groups. Potential biomarkers were screened by using S-plot and were identified by the accurate mass and MS^n fragments information obtained from UFLC/MS-IT-TOF analysis. 12 metabolites in rat plasma and 8 metabolites in urine were identified as potential biomarkers. Concentrations of leucine, phenylalanine, tryptophan, acetylcarnitine, butyrylcarnitine, propionylcarnitine and spermine in plasma and 3-O-methyl-dopa, ethyl N2-acetyl-l-argininate, leucylproline, glucuronate, t6A N(6)-(N-threonylcarbonyl)-adenosine and methyl-hippuric acid in urine decreased in atherosclerosis rats. Ursodeoxycholic acid, chenodeoxycholic acid, LPC (C16:0), LPC (C18:0) and LPC (C18:1) in plasma and hippuric acid in urine were in higher levels in atherosclerosis rats. The alterated metabolites demonstrated abnormal metabolism of phenylalanine, tryptophan, bile acids and amino acids. This research proved that metabonomics is a promising tool for disease research.

使用的岛津仪器：LCMS-IT-TOF



代表图片：（A）基于动脉粥样硬化组大鼠（△）和对照组（◆）的血浆代谢物轮廓图的PCA得分图；（B）基于血浆轮廓图的S-plot图；（C）基于动脉粥样硬化组大鼠（△）和对照组（◆）的尿液代谢物轮廓图的PCA得分图；（D）基于尿液轮廓图的S-plot图。S-plot图中方框标记为通过标准样品和文献验证的潜在生物标记物。

原文网址：https://doi.org/ 10.1016/j.talanta.2009.05.010

PAPER www.rsc.org/analyst | The Analyst

Integrated GC–MS and LC–MS plasma metabonomics analysis of ankylosing spondylitis†

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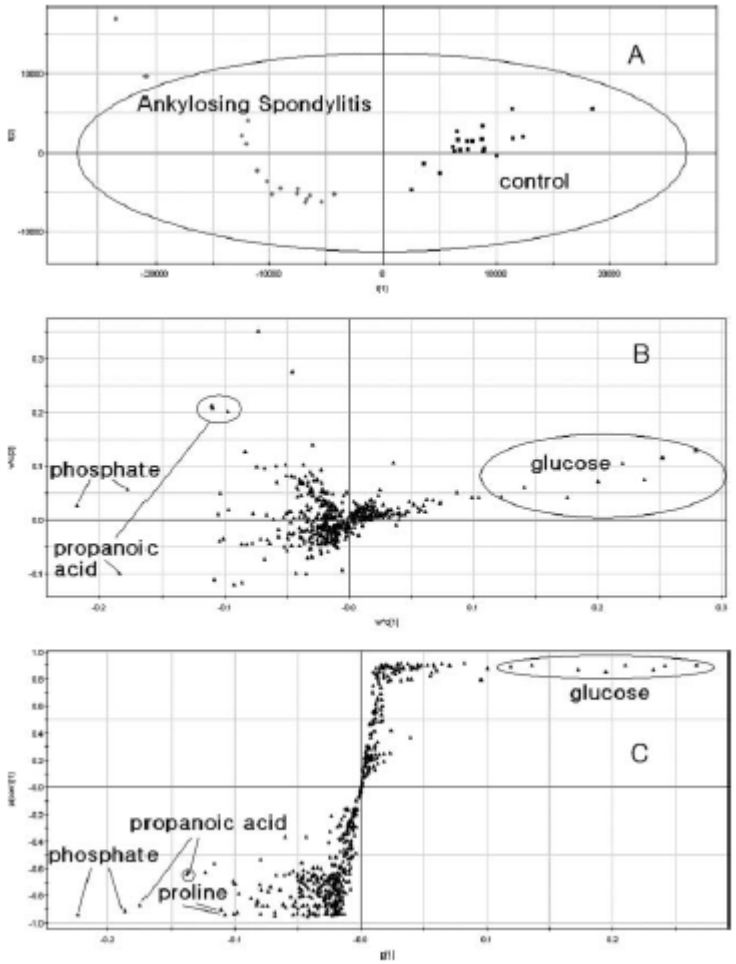
强直性脊柱炎的 GC-MS 和 LC-MS 血浆代谢组学分析

Abstract： Ankylosing spondylitis (AS) is a chronic inflammatory arthritis that predominantly affects the axial skeleton in adolescent patients. The natural history of the disease remains poorly characterized. In this study, we combined GC–MS and LC–MS techniques to evaluate the major metabolic changes in the plasma of AS patients in view of metabonomics. Univariate and multivariate analysis were employed for altered metabolite comparison and pattern recognition. Application of supervised partial least-squares discrminant analysis to either GC–MS or LC–MS data allowed accurate discrimination of AS patients from normal controls, demonstrating its potential diagnostic utilization. In addition, AS patients presented elevated plasma concentrations of proline, glucose, phosphate, urea, glycerol, phenylalanine and homocysteine but reduced levels of phosphocholines, tryptophan and a bipeptide – phenylalanyl-phenylalanine. In the context of their involved metabolic pathways, the identified metabolites were discussed accordingly. This investigation primarily proved that integrated chromatography–mass spectrometry and integrated uni- and multi-variate statistical analysis facilitated metabonomics to be a more promising tool in disease research.

使用的岛津仪器： GCMS-QP2010，LC-20AD，LCMS-IT-TOF



代表图片： （A）PLS-DA得分图；（B）载荷图；（C）相关载荷图；

原文网址 ： https://doi.org/ 10.1039/b807369d

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Journal of Chromatography B, 827 (2005) 83–87
JOURNAL OF CHROMATOGRAPHY B
www.elsevier.com/locate/chromb

Determination of urinary 8-hydroxy-2′-deoxyguanosine by two approaches—capillary electrophoresis and GC/MS: An assay for in vivo oxidative DNA damage in cancer patients

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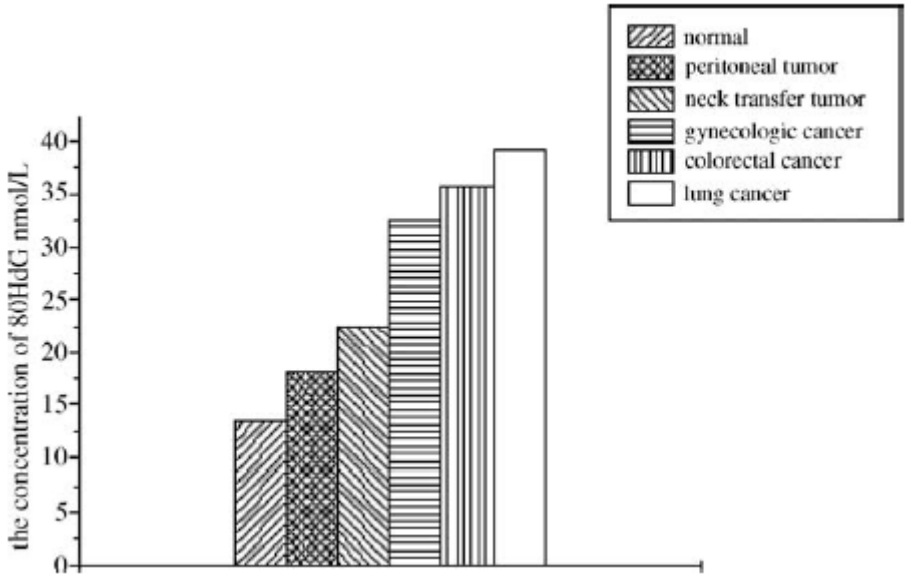
[b] Department of Chemistry, Wuhan University, Wuhan 430072, PR China

用毛细管电泳和 GC/MS 两种方法测定尿中 8-羟基-2′-脱氧鸟苷：一种癌症患者体内氧化性 DNA 损伤的检定

Abstract: 8-Hydroxy-2′-deoxyguanosine (8OHdG) has been considered as an excellent marker of oxidative DNA damage associated with age-related diseases such as cancer. In this paper, two sensitive methods—capillary electrophoresis with electrochemical detection (CE-ECD) and gas chromatography/mass spectrometry (GC/MS) were developed for urinary 8OHdG analysis. The R.S.D. of the spiked recovery of the two methods for determining urinary 8OHdG was 4.03% and 8.25%, respectively, and the results from the two methods have a good consistency ($r = 0.999$, $P < 0.01$). The developed CE-ECD method was applied to investigate the urinary 8OHdG levels in different cancer patients and follow up the response of therapy. It was found that the excretion levels of urinary 8OHdG in cancer patients were significantly higher than those in healthy persons (35.26±27.96nM versus 13.51±5.08 nM, $P < 0.05$), and cancer patients receiving surgical therapy and chemotherapy showed a significant decrease in urinary 8OHdG.

使用的岛津仪器：GC-17A+QP-5000



代表图片：不同癌症患者组尿8OHdG浓度的测定图；

原文网址 ： https://doi.org/ 10.1016/j.jchromb.2005.04.001

·临床研究·

尿中核苷检测在胃癌诊断中的意义

陈英杰[1]， 郑育芳[2]， 王凝芳[3]， 吕 申[4]， 逄 涛[2]，
杨 青[2]， 许国旺[2]

Significance of Urinary Nucleosides in Diagnosis of Gastric Carcinoma

Chen Ying-Jie[1], Zheng Yu-Fang[2], Wang Ning-Fang[1], Lu Shen[3],
Pang Tao[2], Yang Qing[2], Xu Guo-Wang[2]

尿中核苷检测在胃癌诊断中的意义

背景与目的：有研究表明，尿中修饰核苷的含量在多数恶性肿瘤患者中

有明显升高。本研究拟探讨检测尿中核苷在胃癌诊断中的意义。方法：应用高效液相色谱法分别检测 50 名正常人与 48 例胃癌患者尿中 15 种核苷的水平，48 例胃癌患者中有 25 例同时接受了血清 CEA 检测。结果：50 名正常人和 48 例胃癌患者尿中 15 种核苷的平均值分别依次为：Pseu 22.91±4.90，34.78±21.41；U0.34±0.32,0.62±0.82；A 0.58±0.16,0.96±0.75；C 0.17±0.15,0.24±0.19；m5U 0.03±0.07，0.07±0.06；I 0.26±0.10,0.43±0.36；m1I 1.34±0.34,2.44±1.39；ac4C 0.75±0.24,1.08±0.72；G 0.09±0.04,0.14±0.10；X 1.20±0.42,1.90±1.09；m2G 0.61±0.16,1.00±0.69；m6A 0.04±1.13,0.07±0.08；m1A 2.26±0.56,3.71±2.21；m22G 1.34±0.27,2.25±1.39；m1G 0.80±0.25,1.41±0.86。胃癌患者尿中除 m5U 外，其余 14 种核苷的平均值明显高于正常人（P<0.05）；次黄嘌呤与肿瘤大小，淋巴结转移正相关（P<0.05）；黄嘌呤核苷与肿瘤淋巴结转移正相关（P<0.05）。以其中 15 种核苷浓度作为数据矢量，结合主成分分析-投影判别法区分正常人和胃癌患者，63%的胃癌患者被识别，识别率大大高于 CAE 检测（12%）。结论：胃癌患者尿中修饰核苷水平升高，检测尿中修饰核苷对胃癌的初筛有一定的参考意义。

使用的岛津仪器：LC-10ATvp

原文网址 ： https://doi.org/ 10.3969/j.issn.1000-467X.2003.05.022

第 20 卷第 6 期
2002 年 11 月
色 谱
CHINESE JOURNAL OF CHROMATOGRAPHY
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November 2002

肠癌患者尿中核苷排放的高效液相色谱法研究

郑育芳[1]， 陈英杰[2]， 逄 涛[1]， 石先哲[1]， 孔宏伟[1]，
吕 申[1,2]， 杨 青[1]， 许国旺[1]
（1. 中国科学院大连化学物理研究所国家色谱研究分析中心，辽宁 大连 116011；
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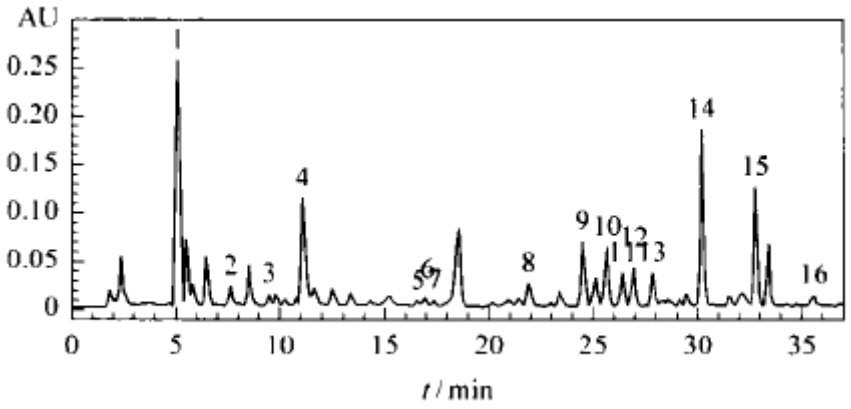
肠癌患者尿中核苷排放的高效液相色谱法研究

摘要：用反相高效液相色谱法测定尿中核苷。通过苯基硼酸亲和色谱法提取尿中核苷，在色谱柱(4.6 mm i.d.×250 mm , 5 μm)上以 25 mmol/L 磷酸二氢钾溶液(pH4.55)和 60%的甲醇水溶液作为流动相进行二元梯度淋洗，于 22 ℃下进行反相色谱分离，260 nm 处紫外检测。用该法测定了 41 例肠癌患者和 52 例正常人尿中 15 种核苷的含量(用核苷与肌酐的摩尔比表示，下同)，结果表明肠癌患者中有 12 种核苷的含量比正常人显著性增高(P <0.001)。以 15 种核苷的含量作为参量，结合主成分分析区分正常人和肠癌患者，对癌症病人的识别率达 76%(31/41)。该方法灵敏、可靠，适合恶性肿瘤防治的基础研究和临床应用。

使用的岛津仪器：LC-10ATvp



代表图片：肠癌患者尿中核苷的RP-HPLC分离谱图

原文网址 ： https://doi.org/ 10.3321/j.issn:1000-8713.2002.06.004

第三部分：代谢组学在中药研究中的应用

第 39 卷第 3 期
2014 年 2 月

中国中药杂志
China Journal of Chinese Materia Medica

Vol. 39, Issue 3
February, 2014

基于 GC-MS 代谢组学法研究黄连、生地黄治疗Ⅱ型糖尿病的配伍机制

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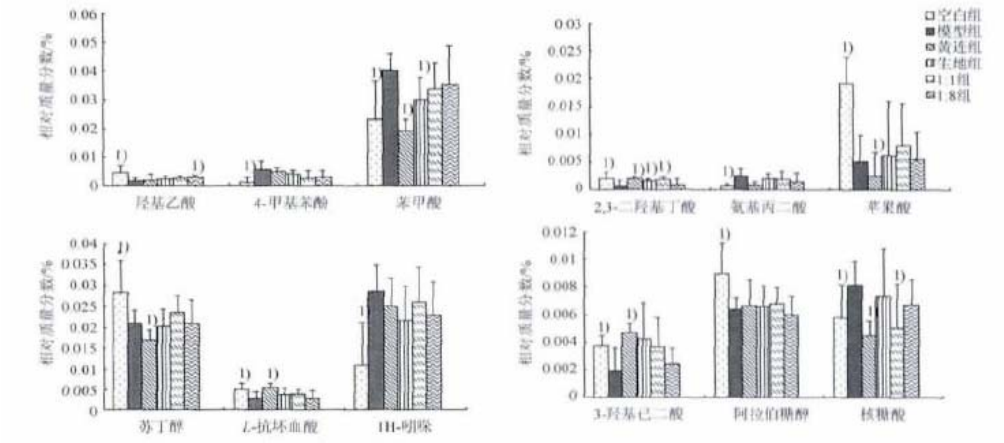
2. 中国科学院 大连化学物理研究所 生物技术部，辽宁 大连 116023）

摘要：该研究采用代谢组学方法对黄连、生地黄配伍前后用于Ⅱ型糖尿病治疗的配伍机制进行初步阐明。建立脂肪乳伴腹腔注射链脲佐菌素致大鼠Ⅱ型糖尿病动物模型，比较黄连、生地黄及其不同比例配伍药对的降血糖、降血脂作用。基于气相色谱-质谱联用技术分析黄连、生地黄配伍前后大鼠尿样代谢轨迹，采用主成分分析法(PCA) 研究各组间的代谢物组差异。生化指标结果表明，黄连、生地黄配伍前后均能降低高血糖、高甘油三酯、高胆固醇。尿样代谢组的 PCA 分析结果表明，黄连组最接近于正常组，不同配伍比例黄连、生地黄组没有明显区分。确定 12 个差异代谢物与Ⅱ型糖尿病相关，与模型组相比较，黄连给药后对其中 7 个差异代谢物有显著的回调作用。黄连、生地黄及其不同配伍比例药对在治疗Ⅱ型糖尿病时，黄连起到主要作用，是君药。生地黄是臣药，辅助黄连药材发挥药效作用，本研究为阐明中药配伍机制奠定基础。

使用的岛津仪器：GCMS-QP 2010



代表图片：各组差异代谢物的相对含量

原文网址：http://doi.10.4268/cjcmm20140332

Journal of Pharmaceutical and Biomedical Analysis 83 (2013) 57–64

Contents lists available at SciVerse ScienceDirect

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journal homepage: www.elsevier.com/locate/jpba

A novel strategy to evaluate the quality of traditional Chinese medicine based on the correlation analysis of chemical fingerprint and biological effect

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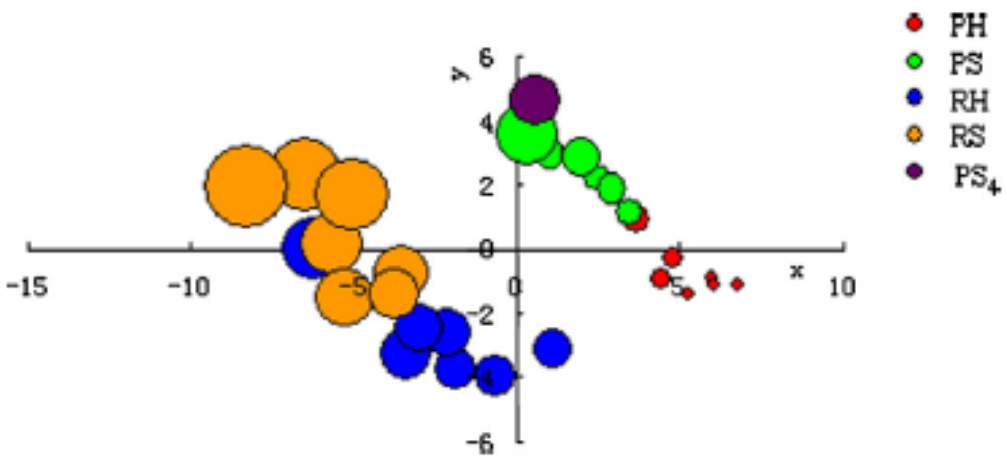
[b] College of Pharmacy, Liaoning University of Traditional Chinese Medicine, Dalian 116600, China

基于化学指纹图谱与生物效应相关性分析的中药质量评价新策略

Abstract： A novel strategy was developed to assess the quality of TCM (traditional Chinese medicine) based onthe correlation analysis of the chemical fingerprint and biological effect. Using Rehmanniae glutinosa(RG) to treat the kidney yin deficiency as an example, chemical fingerprints of 27 RG samples wereanalyzed by liquid chromatography–mass spectrometry (LC–MS), and urinary metabolic profiling of RGtreatment of kidney yin deficiency in rats was explored by using LC–MS. A correlation analysis betweenthe chemical fingerprints and efficacy evaluation was developed to identify quality marker componentsto assess TCM quality. Thirty-four variables in chemical fingerprints were successfully defined to have aclose relationship with the efficacy of RG. The validation test with a new RG sample indicated that theseefficacy-related components could be used to evaluate the integral quality of RG accurately. Comparedwith conventional chemical fingerprint methodology, not only is the proposed approach a powerful toolto identify efficacy-related components for the quality evaluation of TCM, but the approach can also beused to predict the therapeutic efficacy of TCMs.

使用的岛津仪器： LCMS-IT-TOF



代表图片：不同产地地黄治疗肾阴虚效果的气泡图。采用主成分分析法对地黄样品的化学指纹图谱数据进行分析。将地黄样品的主成分1和主成分2分别设为x和y变量。治疗效果的平均值y0设定为气泡的直径。气泡直径越大，地黄样品的治疗效果越差。PH：河南省地黄加工品。PS：山西省地黄加工品。RH：河南省地黄原料。RS：山西省地黄原料。PS4：山西省地黄加工品，不同于PS，用于质量验证试验。

原文网址：http://dx.doi.org/10.1016/j.jpba.2013.04.035

2012 年 1 月 色 谱 Vol. 30 No. 1
January 2012 Chinese Journal of Chromatography 8 ~ 13

研究论文 DOI: 10.3724/SP. J. 1123. 2011. 08039

基于气相色谱-质谱联用的代谢组学用于黄连治疗Ⅱ型糖尿病的机理探索

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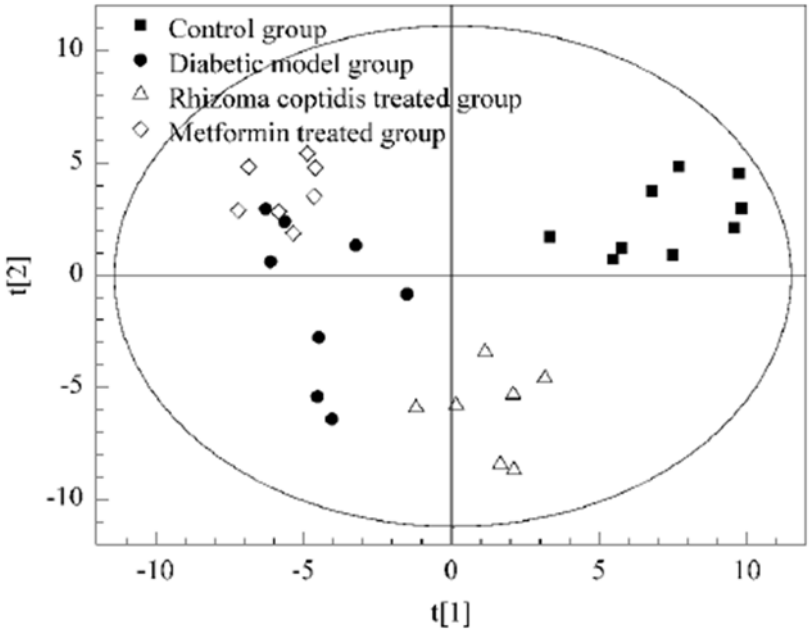
（1. 中国科学院分离分析化学重点实验室，中国科学院大连化学物理研究所，辽宁 大连 116023；
2. 辽宁中医药大学，辽宁 大连 116600）

基于气相色谱-质谱联用的代谢组学用于黄连治疗Ⅱ型糖尿病的机理探索

摘要： 将代谢组学的方法用于研究黄连治疗 II 型糖尿病的机理。II 型糖尿病造模采用对大鼠灌胃脂肪乳并腹腔注射40 mg/kg 链脲佐菌素的方法，大鼠分为正常组、模型组、黄连给药治疗组(10 g/kg) 、二甲双胍给药治疗组(0.08g/kg) 。大鼠给药30 天后，采集血样用于生化指标的检测，采集24 h 尿样用于代谢组学的分析。与模型组相比，糖尿病大鼠给药黄连30 天后，空腹血糖值(FBG) 显著降低了59.26%，总胆固醇(TC)降低了58.66%，甘油三酯(TG)降低了42.18%。采用气相色谱-质谱联用技术(GC-MS) 对大鼠尿样中的内源性物质进行了相对含量测定，主成分分析结果表明，正常组与模型组显著分离，黄连组处于正常组与模型组之间，更接近于正常组。发现12 个代谢物与糖尿病有关，包括4-甲基苯酚、苯甲酸、氨基丙二酸等。给药黄连后，其中的7 个代谢物发生显著性回调，与氧化应激状态相关的氨基丙二酸和L-抗坏血酸出现向正常组显著性调节的趋势。这些结果表明，黄连不仅具有降糖和降血脂的作用，而且具有抗氧化作用，在一定程度上可能会抑制糖尿病合并症的发生和发展。

使用的岛津仪器： GCMS-QP 2010



代表图片：各组大鼠尿样的主成分分析结果

原文网址： https://DOI: 10．3724 /SP．J．1123．2011．08039

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www.rsc.org/molecularbiosystems

PAPER

Linking biological activity with herbal constituents by systems biology-based approaches: effects of *Panax ginseng* in type 2 diabetic Goto-Kakizaki rats†

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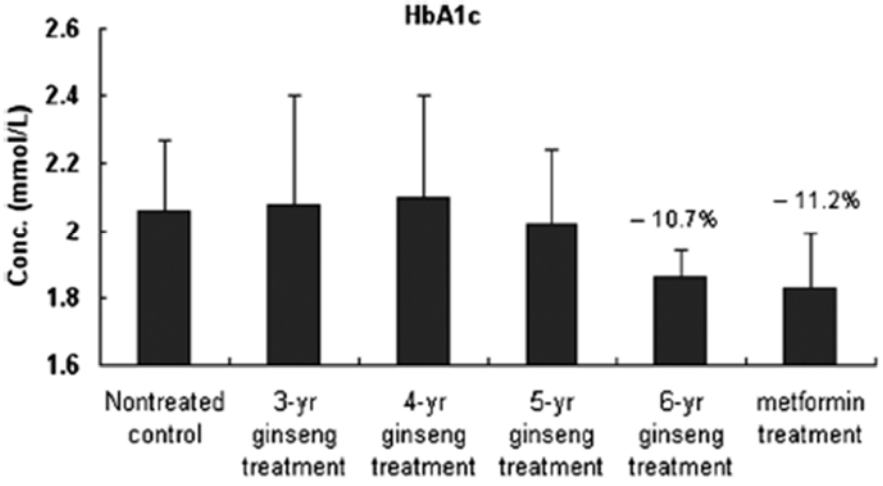
系统生物学方法将生物活性与草药成分联系起来：人参对 2 型糖尿病大鼠的作用

Abstract：Although a number of animal experiments and clinical trials have investigated the effects of ginseng roots on diabetes, the relationship between their therapeutic effects on diabetes and the quality and the growth age of this herb have not yet been reported. This study systematically investigated the effects of 3- to 6-year-old ginseng roots on glycemic and plasma lipid control in a rat model of type 2 diabetes. Six groups of male Goto-Kakizaki (GK) rats received either metformin, 3- to 6-year-old ginseng roots, or no treatment. The treatments were administered twice daily for 9 weeks. A combined approach was used that involved applying liquid chromatography–mass spectrometry-based lipidomics, measuring biochemical parameters and profiling the components of ginseng roots of different ages. Compared to the untreated controls, treatment with 4- and 6-year-old ginseng roots significantly improved glucose disposal, and 5-year-old ginseng treatment significantly increased high density lipoprotein cholesterol. Treatment with 6-year-old ginseng significantly decreased total plasma triacylglyceride (TG) and very-low-density lipoprotein cholesterol and improved plasma glycated hemoglobin (HbA1c).In addition, treatment with 4- to 6-year-old ginseng influenced plasma lipidomics in diabetic GK rats by reducing TG lipid species. Metformin significantly reduced fasting blood glucose by 41% and reduced HbA1c by 11%, but showed no effects on the plasma lipid parameters. The present

study demonstrates that ginseng roots show growth age-dependent therapeutic effects on hyperlipidemia and hyperglycemia in diabetic GK rats. These age-dependent effects may be linked with the variation in both the ratios and concentrations of specific bioactive ginsenosides in ginseng roots of different growth ages. This study introduced novel systems biology-based approaches for linking biological activities with potential active components in herbal mixtures.

使用的岛津仪器：LCMS-IT-TOF



代表图片：接受3-6岁人参根或二甲双胍治疗或不治疗的GK大鼠HbA1c水平。6岁的人参根和二甲双胍治疗组的HbA1c水平与未治疗对照组相比有下降趋势（两者均为P0.1）。

原文网址： https://DOI: 10.1039/c1mb05254c

2011 年 11 月 November 2011 色 谱 Chinese Journal of Chromatography Vol. 29 No. 11 1049 ~ 1054

研究论文 DOI: 10.3724/SP.J.1123.2011.01049

基于液相色谱–质谱联用技术的代谢组学方法用于中药通心络和人参对过度疲劳大鼠干预作用的评价

戴伟东[1]， 张凤霞[1]， 贾振华[2]， 魏 聪[2]， 高 鹏[1]，
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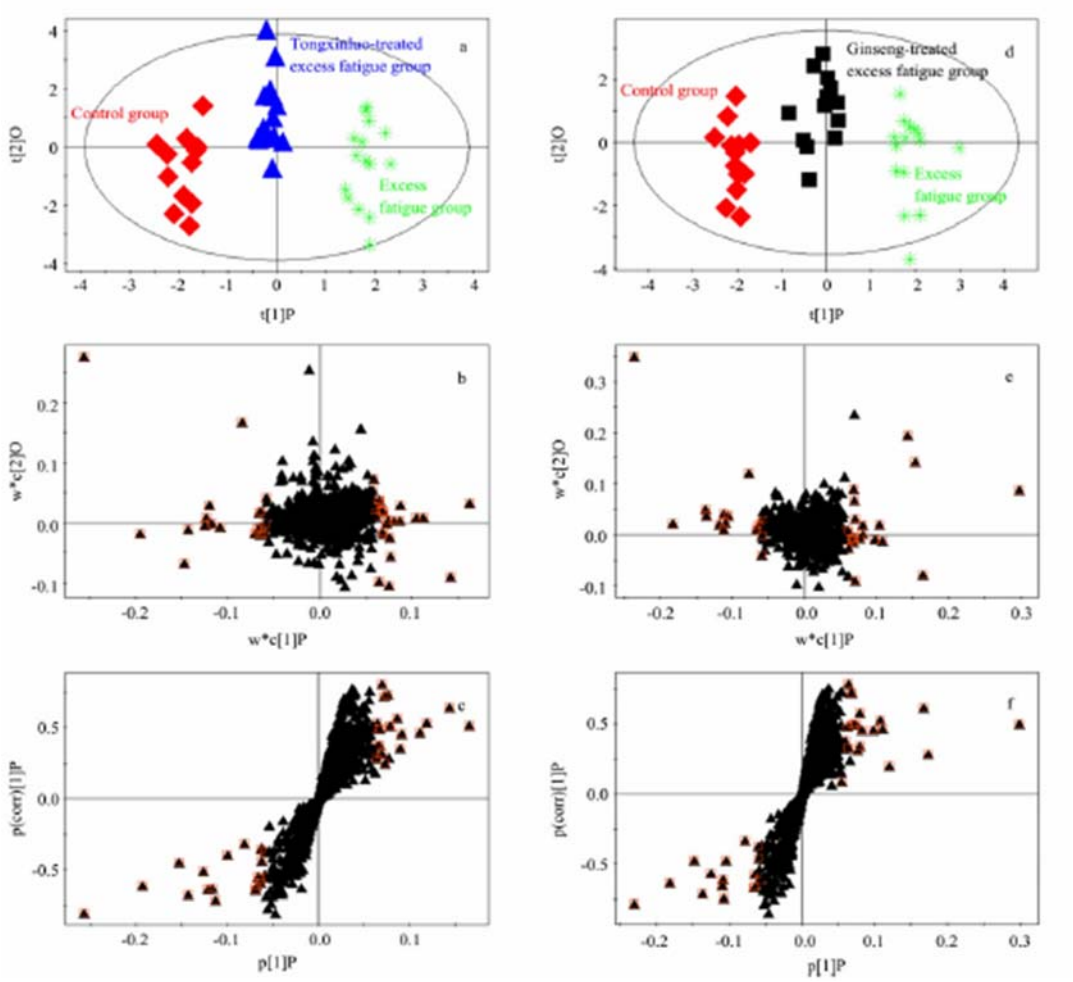
基于液相色谱-质谱联用技术的代谢组学方法用于中药通心络和人参对过度疲劳大鼠干预作用的评价

Abstract: Excess fatigue is a pathological state of continuing accumulation of fatigue, which may cause the deterioration of body health,occurrence of diseases,and even lead to death. A metabonomics study was performed on the excess fatigue rats treated with traditional Chinese medicine Tongxinluo or ginseng based on ultra fast liquid chromatography coupled with ion trap-time of flight mass spectrometry (UFLC-IT-TOF-MS).The plasma metabolic profiling data of the control rats,excess fatigue rats,and excess fatigue rats treated with Tongxinluo or ginseng were acquired. The orthogonal partial least squares analysis (OPLS) was applied for the multivariate statistics and the discovery of important differential metabolites distinguishing the excess fatigue rats treated with Tongxinluo or ginseng from the control rats and excess

fatigue rats. The results showed tryptophan,bile acid,lysophosphatidylcholine metabolism were disturbed in the excess fatigue rats.The metabolic pattern including the related metabolic pathways of the rats,being treated with Tongxinluo or ginseng, was adjusted towards the normal state.

使用的岛津仪器：LCMS-IT-TOF



代表图片：通心络和人参干预的大鼠血浆OPLS 分析结果

原文网址： https://DOI: 10．3724 /SP．J．1123．2011．01049

Industrial Crops and Products 31 (2010) 214–218

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journal homepage: www.elsevier.com/locate/indcrop

Effects of exogenous methyl jasmonate on artemisinin biosynthesis and secondary metabolites in *Artemisia annua* L.

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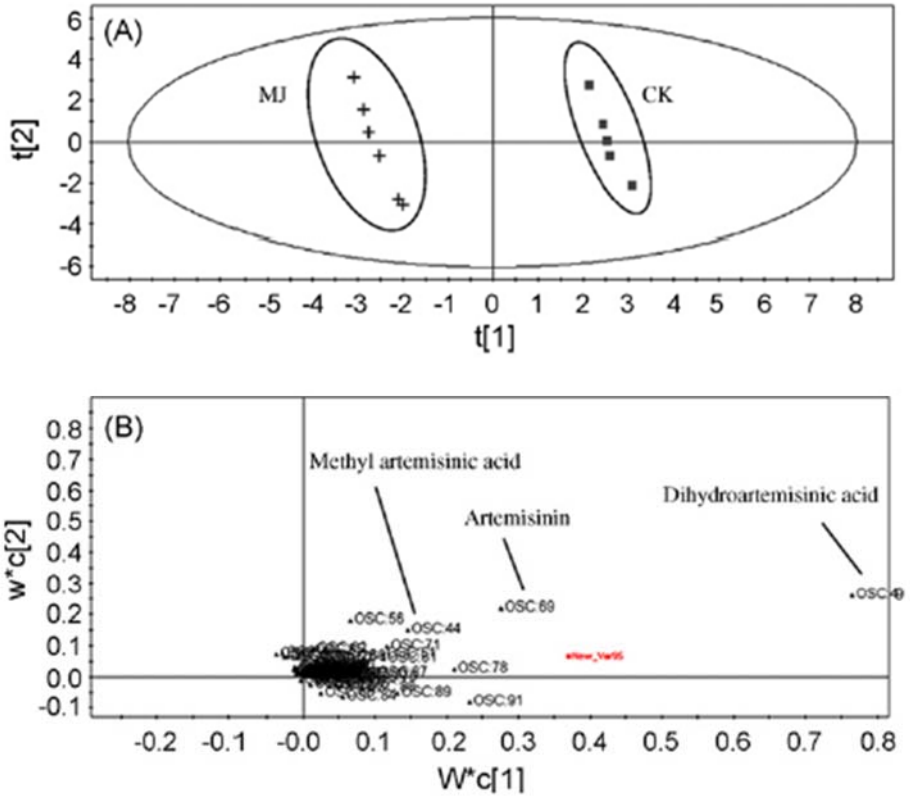
外源茉莉酸甲酯对青蒿青蒿素生物合成及次生代谢产物的影响。

Abstract: Artemisin is a sesquiterpene lactone with an endoperoxide bridge first isolated from the aerial parts of Artemisia annua L. (Compositae). It is an important antimalarial component, but as of present remains quite expensive due to its low content in the plant, the only commercial source of the compound. In this study, we found a 49% increase of the artemisinin content in A. annua SP18 on day 8 after treatment with methyl jasmonate (MeJA), together with an80%increase in artemisinic acid and 28% in dihydroartemisinic acid, the two potential precursors of artemisinin. In addition, the effects of exogenous MeJA on other secondary metabolites were evaluated by metabolite profiling using orthogonal signal correction partial least square discriminant analysis (OSC-PLS). Six sesquiterpenoids and three triterpenoids were selected as marker compounds in OSC-PLS. Their content also changed significantly after MeJA treatment, including a 50% increase in methyl artemisinic acid, a 67% increase in squalene and a 60% increase in peak 51 (an unidentified sesquiterpenoid). These compounds are promising targets for further studies on artemisinin biosynthesis and metabolic engineering.

使用的岛津仪器： GC–MS QP 2010



代表图片：MeJA治疗组与对照组之间的OSC-PLS评分（A）和负荷（B）曲线图。

原文网址： https://doi:10.1016/j.indcrop.2009.10.008

中国科学: 化学 2010 年 第 40 卷 第 6 期: 725 ~ 732
SCIENTIA SINICA Chimica www.scichina.com chem.scichina.com
《中国科学》杂志社 SCIENCE CHINA PRESS
论 文

中药通心络对抑郁-动脉粥样硬化大鼠干预作用的血浆代谢组学研究

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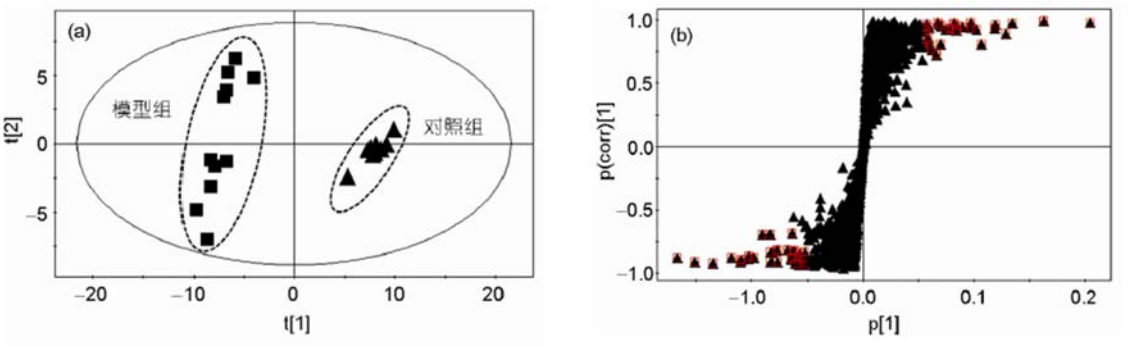
③ 河北省中西医结合医药研究院, 石家庄 050035
*通讯作者, E-mail: xugw@dicp.ac.cn; jiatcm@163.com
†作者对本研究具同等贡献

中药通心络对抑郁-动脉粥样硬化大鼠干预作用的血浆代谢组学研究

摘要：采用快速液相色谱串联离子阱飞行时间质谱(UFLC/MS-IT-TOF)技术对通心络干预下的抑郁-动脉粥样硬化大鼠的血浆代谢谱进行研究. 结果表明, 抑郁-动脉粥样硬化模型大鼠体内的氨基酸代谢、脂肪酸的β-氧化、胆固醇代谢及磷脂代谢发生了异常. 中药通心络通过调节模型大鼠体内的色氨酸、苯丙氨酸代谢及某些胆汁酸的代谢, 抑制大鼠抑郁-动脉粥样硬化的形成. 该研究结果表明代谢组学在中药整体性药效评价、作用机理的阐明等方面具有很好的应用前景.

使用的岛津仪器：LCMS-IT-TOF



代表图片：基于正、负离子模式下血浆代谢谱的对照组(▲)与抑郁-动脉粥样硬化模型(■)大鼠的PCA 分类结果. 进行PCA 模式识别前, 数据采用Pareto 方法进行预处理. (a) PCA 的得分图;(b) PCA 的S-plot，标红色方框的是对分类起重要作用的变量

原文网址：无

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June 2010 Chinese Journal of Chromatography 566 ~ 571
研究论文 DOI: 10.3724/SP.J.1123.2010.00566

不同石斛枫斗中酚酸类活性成分的比较及杓唇石斛素和石斛酚含量的测定

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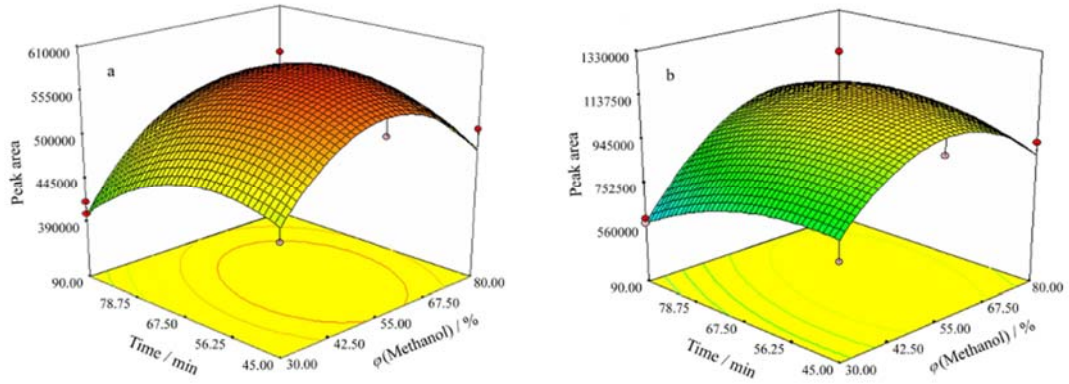
不同石斛枫斗中酚酸类活性成分的比较及杓唇石斛素和石斛酚含量的测定

摘要:建立了基于液相色谱-离子阱飞行时间串联质谱(LC-IT-TOF MS/ MS)的酚酸类分析方法，对6 种共18 批次的石斛枫斗药材中的酚类化合物进行了研究，其中18 种酚酸类化合物得到初步定性。在共有化合物中选择杓唇石斛素和石斛酚作为质量控制的目标化合物。在此基础上，采用响应面法(RSM)确定了提取溶剂为60%甲醇、提取时间为65 min 的超声提取杓唇石斛素和石斛酚的最佳条件，建立了石斛枫斗中杓唇石斛素、石斛酚的高效液相色谱(HPLC)含量测定方法。定量线性优于0.999 8，检出限(LOD)分别为0.18 mg/ L 和0.09 mg/ L，重复性的相对标准偏差(RSD)小于3 %，加标回收率均值分别为97.1%和101.4 %。这些结果表明本研究建立的方法可用于石斛枫斗药材中酚酸类化学成分研究及质量控制。

使用的岛津仪器：LCMS-IT-TOF



代表图片：分别以(a)杓唇石斛素和(b)石斛酚为响应值，在超声提取条件下提取时间-甲醇浓度的交互作用响应曲面图及等高图

原文网址： https://DOI :10 .3724/SP.J.1123 .2010 .00566

2010 年 8 月 色 谱 Vol. 28 No. 8
August 2010 Chinese Journal of Chromatography 765 ~ 768

研究论文 DOI: 10.3724/SP.J.1123.2010.00765

基于液相色谱–质谱联用技术的代谢组学方法研究薄荷烟对大鼠代谢的影响

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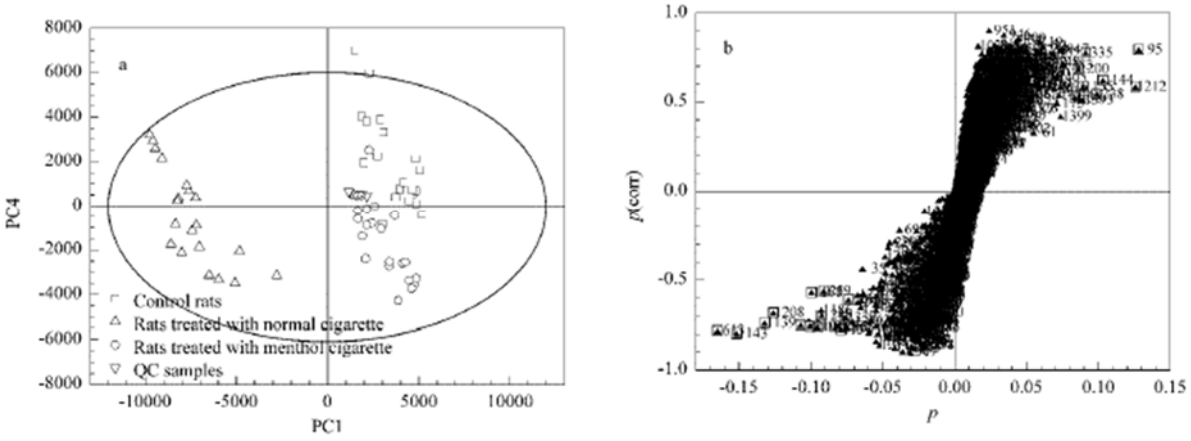
2. 湖南中烟工业有限责任公司技术中心，湖南 长沙 410007）

基于液相色谱-质谱联用技术的代谢组学方法研究薄荷烟对大鼠代谢的影响

摘要: 将基于液相色谱-质谱联用(LC-MS) 技术的代谢组学分析平台用于薄荷烟对大鼠代谢影响的研究。分析了3组大鼠的尿样，包括对照大鼠、吸食普通烟大鼠和吸食薄荷烟大鼠，并采用主成分分析(PCA) 方法对数据进行模式识别。PCA 得分图表明吸食薄荷烟大鼠与对照组大鼠尿样的代谢差异要小于吸食普通烟大鼠。从PCA 载荷图中找到并鉴定了犬尿喹啉酸等8 种重要代谢物。通过考察代谢物在对照大鼠、吸食薄荷烟大鼠和吸食普通烟大鼠尿样中的相对含量变化，进一步说明了烟草中添加薄荷醇可减少烟草对大鼠代谢的影响。

使用的岛津仪器： LCMS-IT-TOF



代表图片： 3组大鼠的PCA分析结果

原文网址： https://DOI: 10．3724 /SP．J．1123．2010．00765

Secondary Metabolic Profiling and Artemisinin Biosynthesis of Two Genotypes of *Artemisia annua*

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Affiliations:
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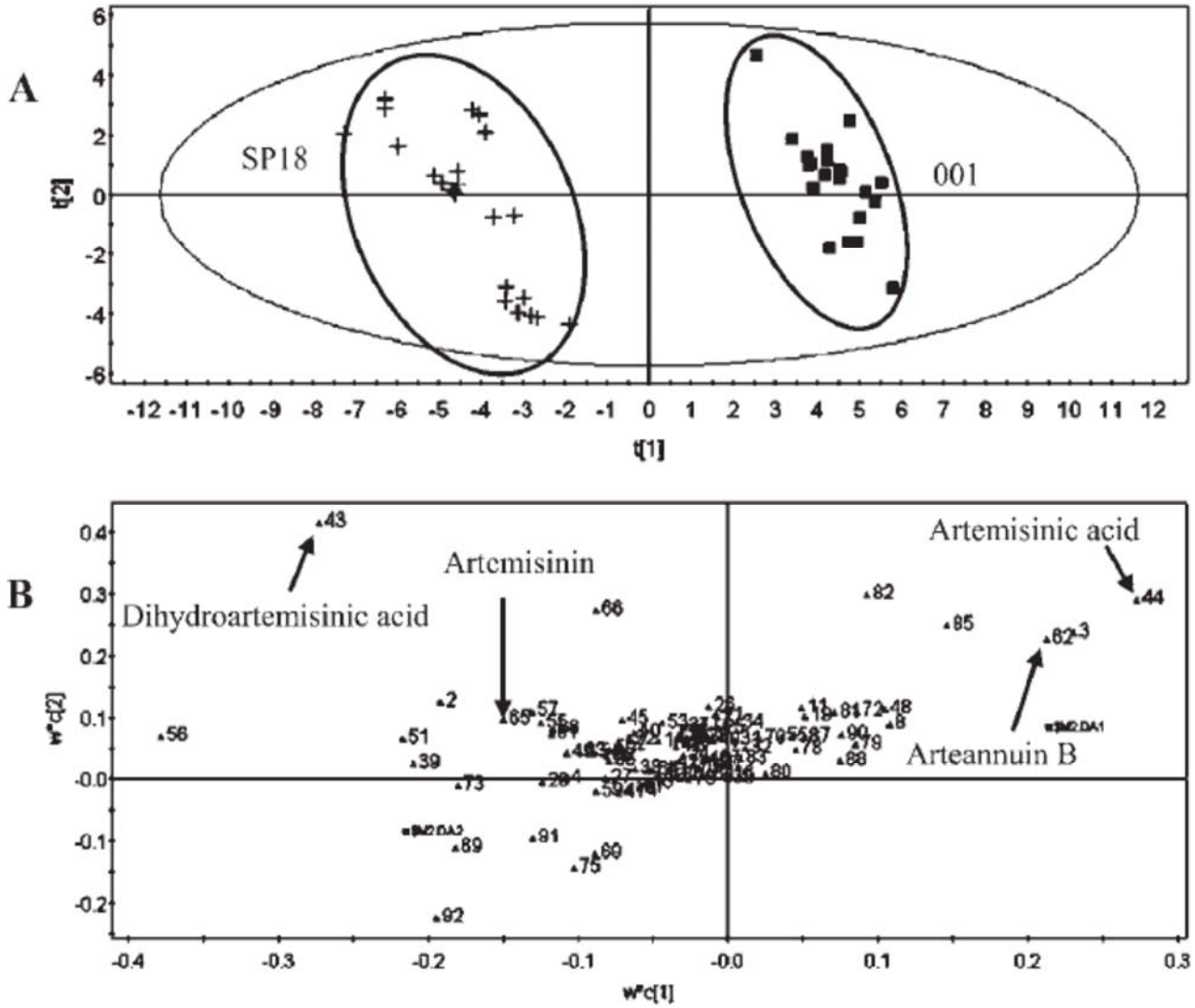
两种基因型黄花蒿的次级代谢产物谱和青蒿素生物合成

Antimalarial compound, especially for chloroquine-resistant and cerebral malaria. However, its biosynthesis pathway is still not completely clear. In order to get new clues about artemisinin biosynthesis, metabolic profiling by gas chromatography (GC) and gas chromatography-mass spectrometry (GC-MS) was applied to compare the secondary metabolites of two Artemisia annua L., genotype SP18 and 001, for some phenotypic and agricultural trait differences, including artemisinin content, existed between the two genotypes. Samples at 7 time points of three growth stages were studied. The data of profiles were subjected to multivariate analysis with partial least squares discriminant analysis (PLS-DA). The results indicated that there were clear differences in terpenoids and artemisinin metabolism between different growth stages and genotypes. Twenty-one compounds, including artemisinin and its related precursors, were selected as the marker compounds of the PLS-DA between the two genotypes. Among them, artemisinic acid, arteannuin B, borneol, β-farnesene and an unidentified sesquiterpenoid (peak 48) were abundant in 001, while camphor, methyl artemisinic acid and lanceol accumulated mainly in SP18. The relationship between these differences and artemisinin biosynthesis in the two genotypes of A. annua were discussed.

使用的岛津仪器：GCMS QP-2010



代表图片：黄花蒿 SP18和001的次级代谢产物轮廓分析的PLS-DA结果。A. PLS-DA得分图，R^2X=0.68，R^2Y=0.98，Q^2=0.97，t为评分向量。B. PLS-DA变量载荷图，通过峰数已标记变异量；w*c为权重向量。

原文网址：Planta medica (2009), 75, 1625-1633. https://doi.org/ 10.1055/s-0029-1185814

Systems Biology Guided by Chinese Medicine Reveals New Markers for Sub-Typing Rheumatoid Arthritis Patients

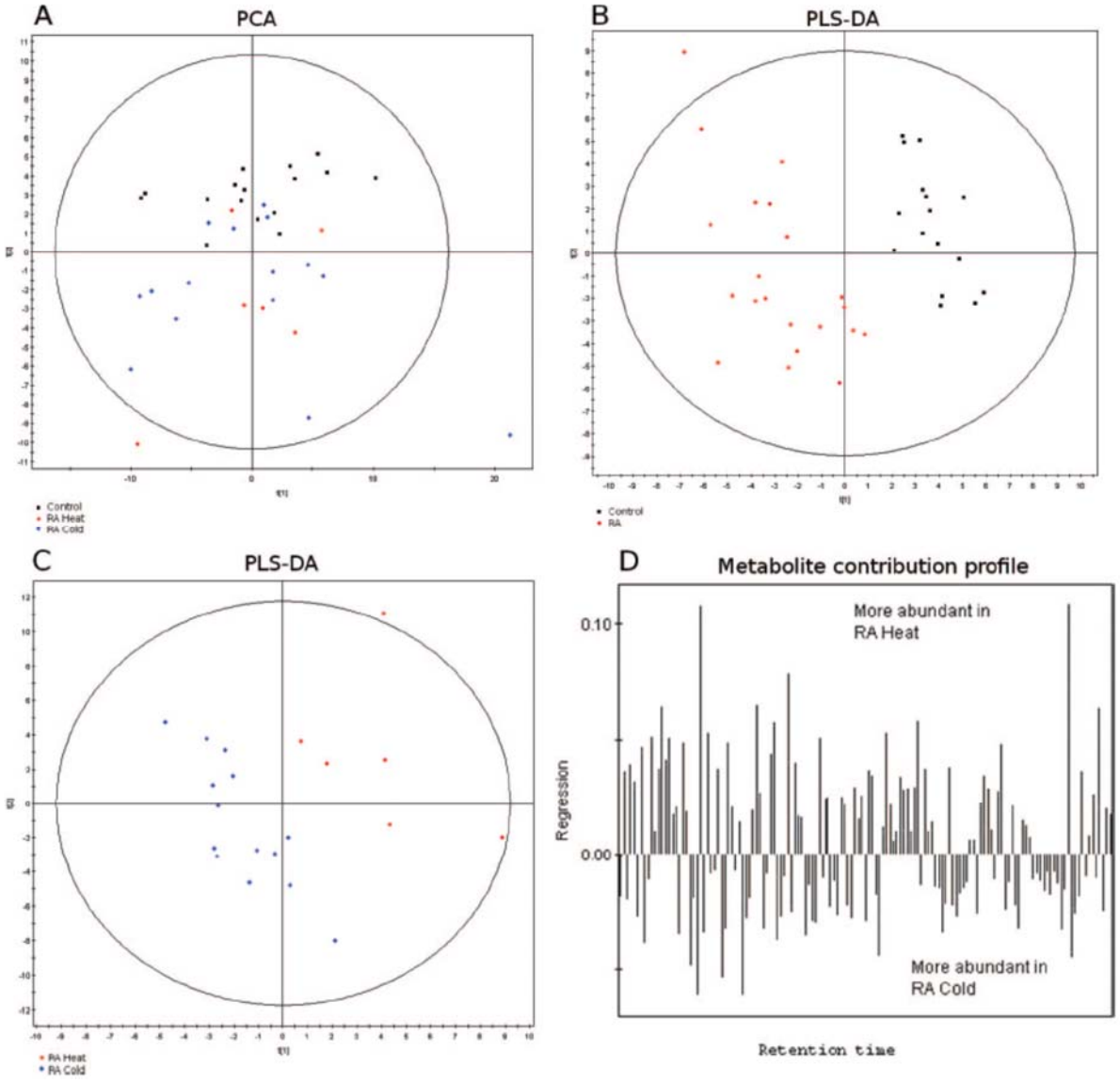
Herman van Wietmarschen, Drs, Kailong Yuan, PhD,† Cheng Lu,‡ Peng Gao,† Jiangshan Wang,† Cheng Xiao, PhD,‡ Xiaoping Yan,‡ Mei Wang, PhD,§ Jan Schroën,¶ Aiping Lu, PhD,‡ Guowang Xu, PhD,† and Jan van der Greef, PhD*§‖*

中医指导下的系统生物学揭示类风湿关节炎亚型患者的新标志物

Background: Complex chronic diseases such as rheumatoid arthritis have become a major challenge in medicine and for the pharmaceutical industry. New impulses for drug development are needed. Objective: A systems biology approach is explored to find subtypes of rheumatoid arthritis patients enabling a development towards more personalized medicine. Methods: Blood samples of 33 rheumatoid arthritis (RA) patients and 16 healthy volunteers were collected. The RA patients were diagnosed according to Chinese medicine (CM) theory and divided into 2 groups, the RA Heat and RA Cold group. CD4_ T-cells were used for a total gene expression analysis. Metabolite profiles were measured in plasma using gas chromatography/mass spectrometry. Multivariate statistics was employed to find potential biomarkers for the RA Heat and RA Cold phenotype. A comprehensive biologic interpretation of the results is discussed. Results: The genomics and metabolomics analysis showed statistically relevant different gene expression and metabolite profiles between healthy controls and RA patients as well as between the RA Heat and RA Cold group. Differences were found in the regulation of apoptosis. In the RA Heat group caspase 8 activated apoptosis seems to be stimulated while in the RA Cold group apoptosis seems to be suppressed through the Nrf2 pathway. Conclusions: RA patients could be divided in 2 groups according to CM theory. Molecular differences between the RA Cold and RA Heat groups were found which suggest differences in apoptotic activity. Subgrouping of patients according to CM diagnosis has the potential to provide opportunities for better treatment outcomes by

targeting Western or CM treatment to specific groups of patients.

使用的岛津仪器：GCMS QP-2010



代表图片：A. RA和对照病人的PCA得分图； B. 2个主要因素的PLS-DA得分图； C. PLS-DA得分图中RA静止和活跃期的区分； D. 影响RA的静止和活跃期组分类的代谢物

原文网址：https://doi.org/ 10.1097/rhu.0b013e3181ba3926

UFLC–ESI–IT–TOF 鉴定六味地黄丸中的化学成分和代谢成分*

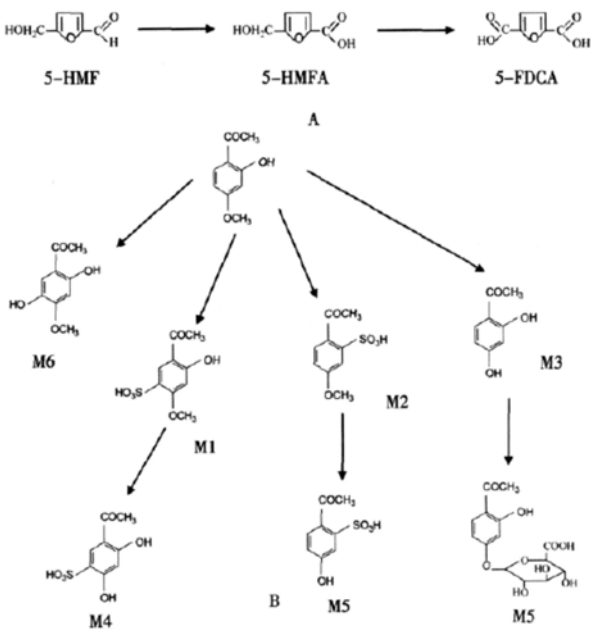
□赵新峰　孔宏伟　汪江山　许国旺**

（中国科学院大连化学物理研究所代谢组学研究中心　大连　116023）

UFLC-ESI-IT-TOF 鉴定六味地黄丸中的化学成分和代谢成分

摘要： 目的：鉴定六味地黄丸中的化学成分和代谢成分。方法：采用超快液相色谱梯度洗脱，飞行时间质谱正负离子同时检测。结果：在六味地黄提取物中鉴定了40 种化学成分，在大鼠血中鉴定了6 种原型药物和9 种代谢产物，并推断了以上产物的代谢途径。结论：UFLC-ESI-IT-TOF 方法适合于复杂中成药样品的分析，有助于全面了解六味地黄丸中的化学成分和代谢成分。

使用的岛津仪器：LCMS-IT-TOF



代表图片：5-HMF（A）和丹皮酚（B）的代谢途径

原文网址： https://doi.org/ 10.11842/wst.2009.1.

Available online at www.sciencedirect.com
ScienceDirect
Journal of Chromatography A, 1150 (2007) 50–53
JOURNAL OF CHROMATOGRAPHY A
www.elsevier.com/locate/chroma

Short communication

Analysis of *Artemisia annua* L. volatile oil by comprehensive two-dimensional gas chromatography time-of-flight mass spectrometry

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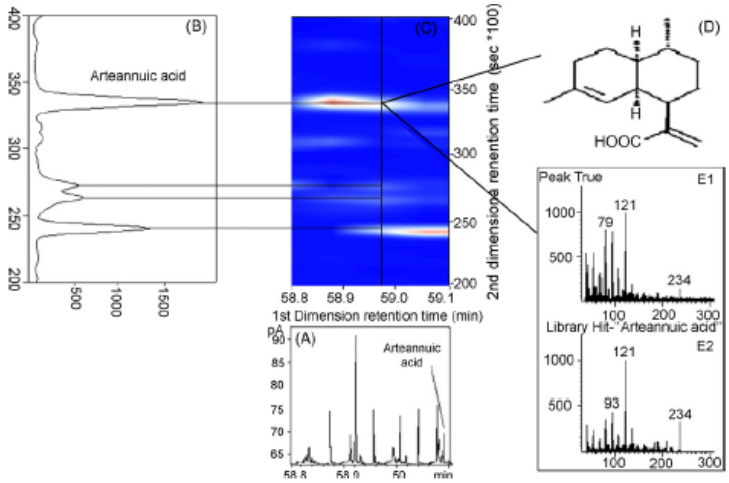
Available online 12 October 2006

青蒿挥发油的全二维气相色谱-飞行时间质谱分析

Abstract: Artemisia annua L. is an annual herb native of Asia, it has been used for many centuries for the treatment of fever and malaria. In this paper, analysis of the volatile oil of Artemisia annua L. was performed by comprehensive two-dimensional gas chromatography time-of-flight mass spectrometry (GC×GC–TOF MS). Three hundred and three components were tentatively identified and terpene compounds are the main components of Artemisia annua L. volatile oil. Artemisinic acid is tentatively qualified.

使用的岛津仪器：GCMS-QP2010



代表图片：青蒿素酸的详细信息；

原文网址 ： https://doi.org/ 10.1016/j.chroma.2006.08.080

第四部分：代谢组学在植物表型研究中的应用

Anal Bioanal Chem (2018) 410:839–851
DOI 10.1007/s00216-017-0596-z

PAPER IN FOREFRONT

Metabolic changes in primary, secondary, and lipid metabolism in tobacco leaf in response to topping

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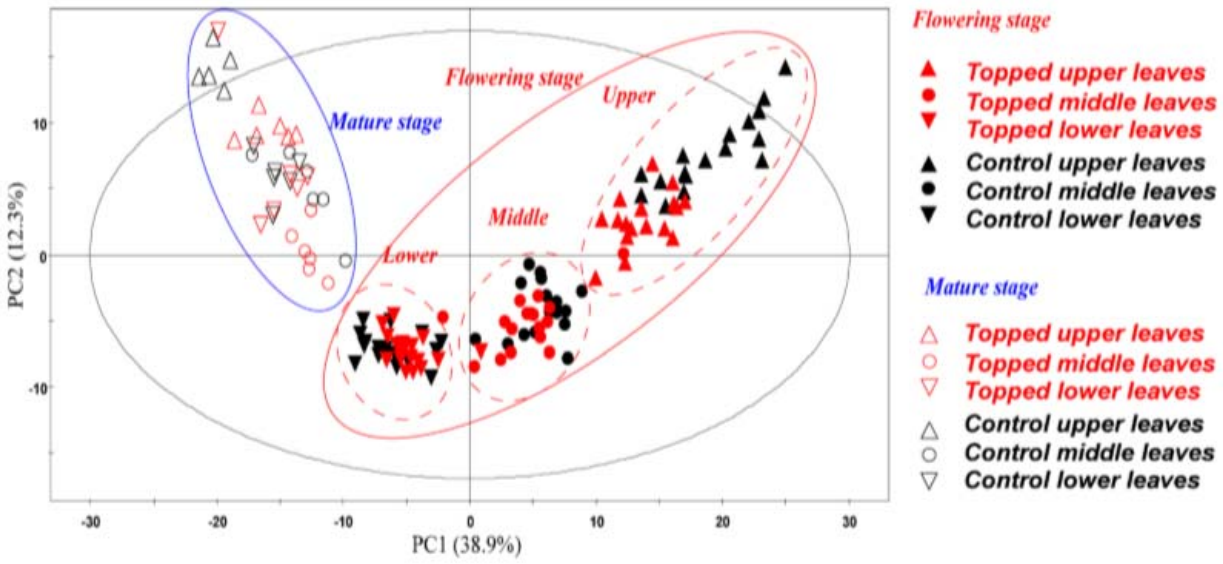
研究打顶对烟叶中初级、次级代谢物和脂质代谢物的影响

Abstract: As an important cultivation practice used for fluecured tobacco, topping affects diverse biological processes in the later stages of development and growth. Some studies have focused on using tobacco genes to reflect the physiological changes caused by topping. However, the complex metabolic shifts in the leaf resulting from topping have not yet been investigated in detail. In this study, a comprehensive metabolic profile of primary, secondary, and lipid metabolism in fluecured tobacco leaf was generated with use of a multiple platform consisting of gas chromatography–mass spectrometry, capillary electrophoresis–mass spectrometry, and liquid chromatography–mass spectrometry/ultraviolet spectroscopy. A total of 367 metabolites were identified and determined. Both principal component analysis and the number of significantly different metabolites indicated that topping had the greatest influence on the upper leaves. During the early stage of topping, great lipid level variations in the upper leaves were observed, and antioxidant defense metabolites were accumulated. This indicated that the topping activated lipid turnover and the antioxidant defense system. At the mature stage, lower levels of senescence-related metabolites and higher levels of secondary metabolites were found in the topped mature leaves. This implied that topping delayed leaf senescence and promoted secondary metabolite accumulation. This study provides a global view of the metabolic perturbation in response to topping.

Keywords: Topping. Tobacco leaf. Metabolomics. Liquid chromatography–mass spectrometry. Gas chromatography –mass spectrometry .Capillary electrophoresis–mass spectrometry

使用的岛津仪器：GCMS-QP 2010



代表图片：顶叶和对照叶上、中、下叶主成分分析评分图. PC1为主成分1，PC2为主成分2

原文网址：https://link.springer.com/article/10.1007%2Fs00216-017-0596-z

Plant Biotechnology Journal

Plant Biotechnology Journal (2017) **15**, pp. 1204–1213 doi: 10.1111/pbi.12709

Next-generation transgenic cotton: pyramiding RNAi and Bt counters insect resistance

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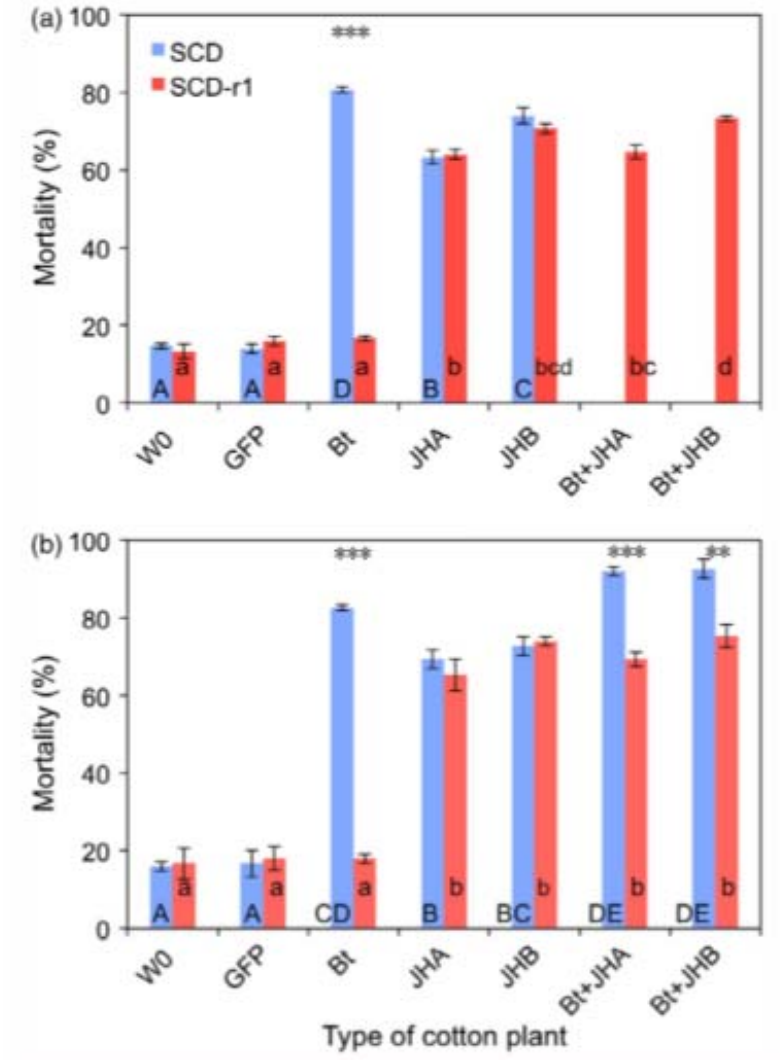
新一代转基因棉花:金字塔化 RNAi 和 Bt 抗虫

Abstract: Transgenic crops producing insecticidal proteins from the bacterium Bacillus thuringiensis (Bt) are extensively cultivated worldwide. To counter rapidly increasing pest resistance to crops that produce single Bt toxins, transgenic plant ‘pyramids’ producing two or more Bt toxins that kill the same pest have been widely adopted. However, cross-resistance and antagonism between Bt toxins limit the sustainability of this approach. Here we describe development and testing of the first pyramids of cotton combining protection from a Bt toxin and RNA interference (RNAi). We developed two types of transgenic cotton plants producing double-stranded RNA (dsRNA) from the global lepidopteran pest Helicoverpa armigera designed to interfere with its metabolism of juvenile hormone (JH). We focused on suppression of JH acid methyltransferase (JHAMT), which is crucial for JH synthesis, and JH-binding protein (JHBP), which transports JH to organs. In 2015 and 2016, we tested larvae from a Bt-resistant strain and a related susceptible strain of H. armigera on seven types of cotton: two controls, Bt cotton, two types of RNAi cotton (targeting JHAMT or JHBP) and two pyramids (Bt cotton plus each type of RNAi). Both types of RNAi cotton were effective against Bt-resistant insects. Bt cotton and RNAi acted independently against the susceptible strain. In computer simulations of conditions in northern China, where millions of farmers

grow Bt cotton as well as abundant non-transgenic host plants of H. armigera, pyramided cotton combining a Bt toxin and RNAi substantially delayed resistance relative to using Bt cotton alone.

Keywords: genetic engineering, RNA interference, Bacillus thuringiensis, juvenile hormone, Helicoverpa armigera, sustainability.

使用的岛津仪器：LCMS-8050



代表图片：棉铃虫敏感幼虫(SCD-r1)和抗性幼虫(SCD-r1)分别以非转基因亲本(W0)、转基因对照(GFP)、苏云金芽孢杆菌(Bt)、RNAi (JHA和JHB)和锥状体(Bt + JHA和Bt + JHB)叶片为食.

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SCIENTIFIC REPORTS

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Comprehensive investigation of tobacco leaves during natural early senescence via multi-platform metabolomics analyses

Lili Li[1,2,*], Jieyu Zhao[1,2,*], Yanni Zhao[1,2], Xin Lu[1,2], Zhihui Zhou[1,2], Chunxia Zhao[1,2] & Guowang Xu[1,2]

利用多平台代谢组学分析对自然早期老化的烟叶进行综合的研究

Abstract: Senescence is the final stage of leaf growth and development. Many different physiological activities occur during this process. A comprehensive metabolomics analysis of tobacco middle leaves at 5 different developmental stages was implemented through multi-platform methods based on liquid chromatography, capillary electrophoresis and gas chromatography coupled with mass spectrometry. In total, 412 metabolites were identified, including pigments, sterols, lipids, amino acids, polyamines, sugars and secondary metabolites. Dramatic metabolic changes were observed. Firstly, membrane degradation and chlorophyll down-regulation occurred after the 50% flower bud stage. Levels of major membrane lipids decreased, including those of the glycolipids in chloroplast thylakoids and phospholipids in membrane envelopes. Clear decreases in free sterols and acylated sterol glucosides were detected along with the accumulation of sterol esters. The accumulation of alkaloids was found. The amino acid levels were significantly decreased, particularly those of N-rich amino acids (glutamine and asparagine), thus reflecting N translocation. Subsequently, the antioxidant system was activated. Sugar alcohols and polyphenols accumulated when the lower leaves turned yellow. These results comprehensively revealed the metabolic changes that occur during tobacco leaf development and

senescence under natural conditions.

使用的岛津仪器：GCMS-QP 2010

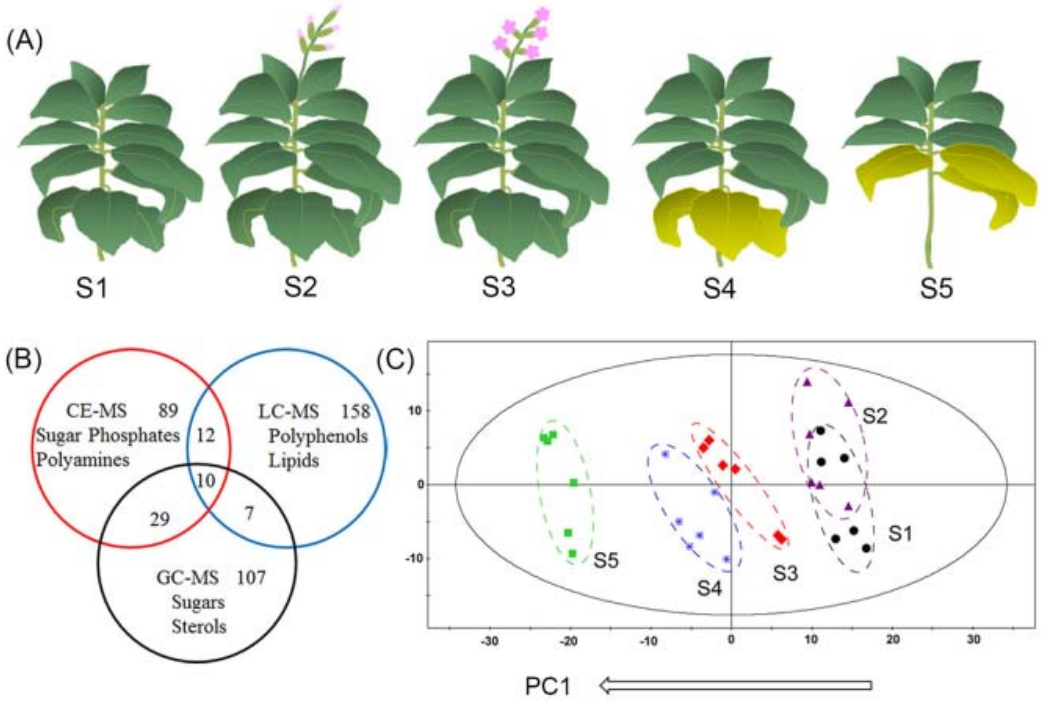

Figure 1. (**A**) Experimental design of tobacco leaves at 5 stages. (**B**) The metabolites detected by CE-MS, GC-MS and LC-MS. The labeled metabolites were specifically detected by each analytical platform. (**C**) PCA score plot of the tobacco leaves at 5 stages. S1, vigorous growth stage. S2, 50% flower bud stage. S3, full-bloom stage. S4, lower leaf ripening stage. S5, middle leaf ripening stage.

代表图片：（A）实验用烟叶的 5 个生长阶段；（B）分别用 CE-MS、GC-MS 和 LC-MS 检测到的代谢物及数量；（C）5 个生长阶段的烟叶主成分得分图

原文网址：https://doi.org/10.1038/srep37976

Algal Research 13 (2016) 207–217

Contents lists available at ScienceDirect

Algal Research

journal homepage: www.elsevier.com/locate/algal

Free amino acids and small molecular acids profiling of marine microalga *Isochrysis zhangjiangensis* under nitrogen deficiency

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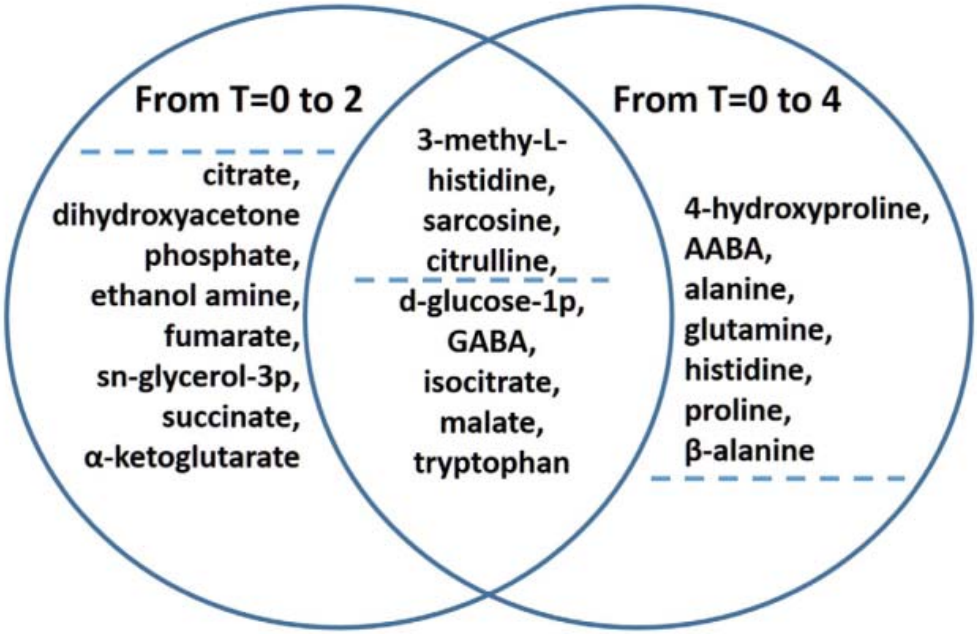
氮缺乏条件下海洋微藻湛江等鞭金藻（Isochrysis zhangjiangensis）体内游离氨基酸及小分子酸的组成

Abstract: *Isochrysis zhangjiangensis* is a marine microalga with potential usage in biofuel production. The alga is known to exhibit enhanced lipid and polysaccharide storage under nitrogen deficiency conditions, though the regulatory mechanism has not been elucidated.

In this study, to monitor the metabolic transition in response to nitrogen starvation, the intracellular metabolite fluctuation within 32 h was profiled by gas chromatography–mass spectrometry and liquid chromatography– mass spectrometry scanned in selected ion monitoring mode for the first time. These techniques identified and quantified the levels of 14 SMAs, 2 carbohydrates involved in the TCA cycle and glycolysis, and 28 free amino acids (AAs). The pulsed increase of pyruvate, which is the precursor of acetyl-CoA and fatty acids (FAs), indicated a potential to produce more FAs. Surprisingly, although overall AAs showed a decreasing trend under the experimental conditions, Ala and Phe showed increased levels initially. It has been postulated that a carbon flux switch between lipids and polysaccharides exists in *I. zhangjiangensis.* To be feasible for biofuel production, enhancement of carbon flux to lipids is expected. Facilitating the intracellular lipid storage, together with nitrogen deficiency, a β-1,3-glucanase inhibitor

(Micafungin) was introduced to block the formation of chrysolaminarin, the major polysaccharide in *I. zhangjiangensis*. The treatment resulted in 10% reduction of polysaccharides and 50% transient increase of total lipids. AAs and other metabolites involved in the TCA cycle and glycolysis, were also perturbed by the treatment with Micafungin, among which gamma-aminobutyric acid (GABA) was profoundly affected although the effects of Micafungin were only transient. This study indicates that β-1,3-glucanase could be a good candidate for further genetic manipulation and that the possibility of regulating GABA for high oil yield warrants detailed study.

使用的岛津仪器：GCMS-QP 2010



代表图片：M+和 M-组别中有明显变化的代谢物种类

原文网址：http://dx.doi.org/10.1016/j.algal.2015.12.001

Journal of proteome research

Article

pubs.acs.org/jpr

Metabolic Profiling with Gas Chromatography–Mass Spectrometry and Capillary Electrophoresis–Mass Spectrometry Reveals the Carbon–Nitrogen Status of Tobacco Leaves Across Different Planting Areas

Jieyu Zhao,[†,‡] Yanni Zhao,[‡] Chunxiu Hu,[‡] Chunxia Zhao,[‡] Junjie Zhang,[‡] Lili Li,[‡] Jun Zeng,[‡] Xiaojun Peng,[†] Xin Lu,[*,‡] and Guowang Xu[‡]

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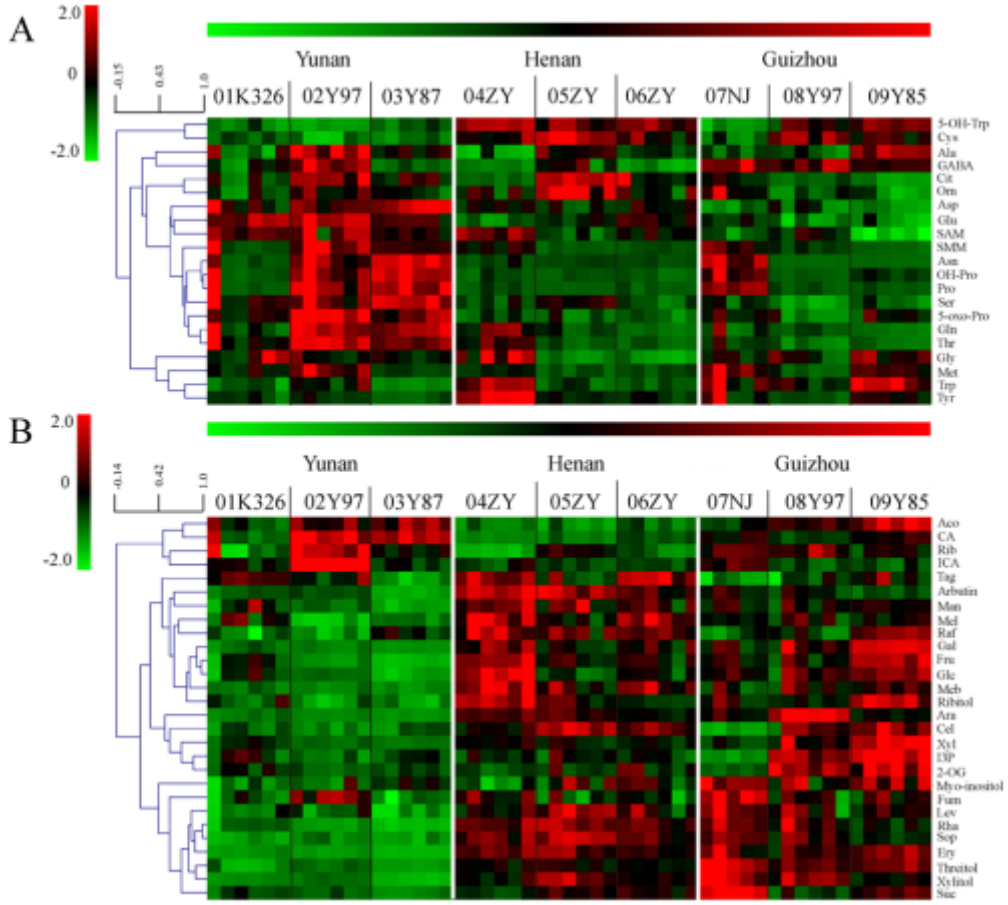
Supporting Information

基于气相色谱-质谱和毛细管电泳-质谱的代谢组学研究揭示不同种植区域烟草的碳-氮代谢状态

ABSTRACT: The interaction between carbon (C) and nitrogen (N) metabolism can reflect plant growth status and environmental factors. Little is known regarding the connections between C-N metabolism and growing regions under field conditions. To comprehensively investigate the relationship in mature tobacco leaves, we established metabolomics approaches based on gas chromatography-mass spectrometry (GC- MS) and capillary electrophoresis-time-of-flight-mass spectrometry (CE-TOF-MS). Approximately 240 polar metabolites were determined. Multivariate statistical analysis revealed that the growing region greatly influenced the metabolic profiles of tobacco leaves. A metabolic correlation network and related pathway maps were used to reveal the global overview of the alteration of C-N metabolism across three typical regions. In Yunnan, sugars and tricarboxylic acid (TCA) cycle intermediates were closely correlated with amino acid pools. Henan tobacco leaves showed positive correlation between the pentose phosphate pathway (PPP) intermediates and C-rich secondary metabolism. In Guizhou, the proline and asparagine had significant links with TCA cycle intermediates and urea cycle, and antioxidant accumulation was observed in response to drought. These results

demonstrate that combined analytical approaches have great potential to detect polar metabolites and provide information on C-N metabolism related to planting regional characteristics.

使用的岛津仪器：GCMS-QP 2010



代表图片：氨基酸代谢（A）和糖代谢（B）中显著差异性代谢物热图

原文网址：https://doi.org/10.1021/acs.jproteome.5b00807

Metabolomics (2015) 11:1802–1814
DOI 10.1007/s11306-015-0834-3

ORIGINAL ARTICLE

Metabolic responses of rice leaves and seeds under transgenic backcross breeding and pesticide stress by pseudotargeted metabolomics

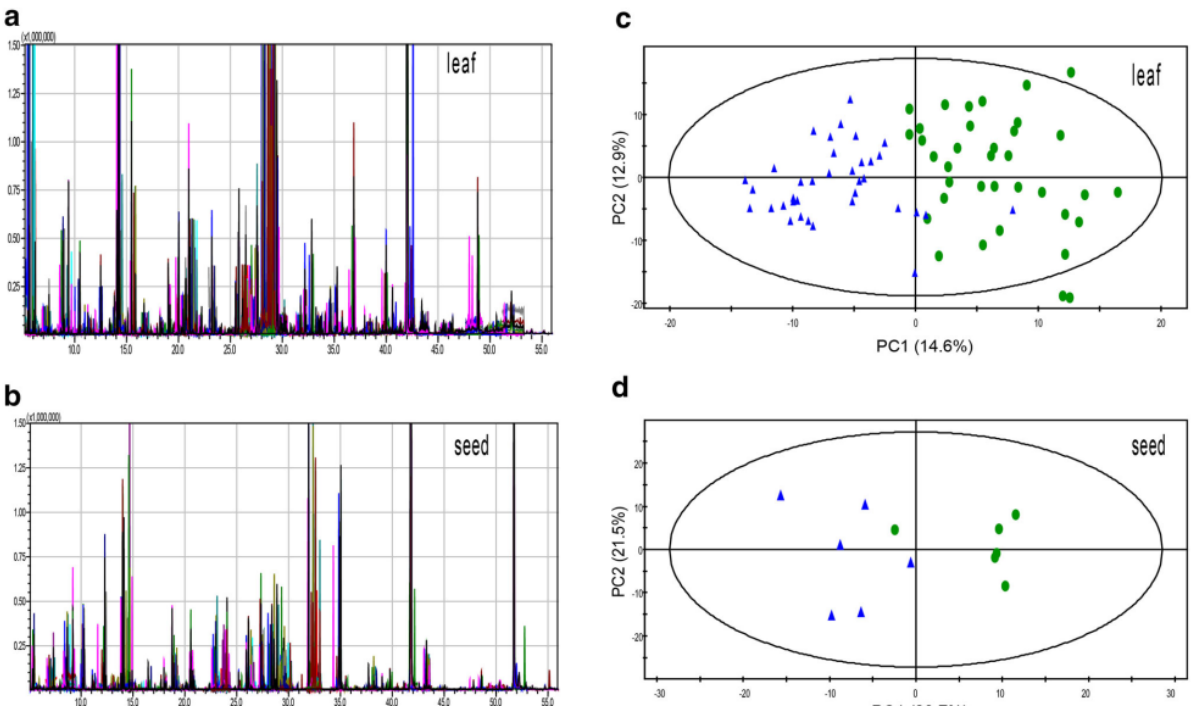
Yanni Zhao[1] · Lei Zhang[2] · Chunxia Zhao[1] · Chunxiu Hu[1] · Yanli Li[1] · Jieyu Zhao[1] · Junjie Zhang[1] · Lili Li[1] · Yuwei Chang[1] · Feng Wang[3] · Xin Lu[1] · Zhen Zhu[2] · Guowang Xu[1]

Received: 25 November 2014 / Accepted: 27 July 2015 / Published online: 2 August 2015

转基因杂交育种和虫害胁迫下水稻叶片和种子的拟靶向代谢组学研究

Abstract: Pesticide and anti-insect gene are two effective strategies to prevent insects from seriously influencing the growth and production of crops in agroecosystem. Few investigators have yet concerned the metabolic responses of different plant tissues to pesticide treatment and transgene with backcross breeding. In this study, the metabolic variations in samples of rice leaf and seed induced by transgenic backcross breeding and pesticide stress were investigated by a pseudotargeted metabolomics method based on gas chromatography–mass spectrometry. The results showed transgenic backcross breeding caused diverse metabolic changes for rice leaf and seed. Higher abundances of a wide range of carbohydrates, antioxidants and phenols were observed in transgenic backcross breeding leaves, while some amino acids and carbohydrates in rice seeds were down-regulated after transgenic backcross breeding. Moreover, the defense responses of rice leaves to pesticide stress were tightly associated with transgenic backcross breeding. Defense system accompanied with the accumulations of phenols and antioxidants was rapidly activated in non-transgenic parent compared to transgenic backcross breeding leaves under pesticide stress.

使用的岛津仪器：GCMS-QP 2010



代表图片：叶片（a）和种子（b）样品总离子流图；叶片（c）和种子（d）样品主成分得分图

原文网址：https://doi.org/10.1007/s11306-015-0834-3

J. Sep. Sci. 2014, 37, 2177–2184

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Key Laboratory of Separation Science for Analytical Chemistry, Dalian Institute of Chemical

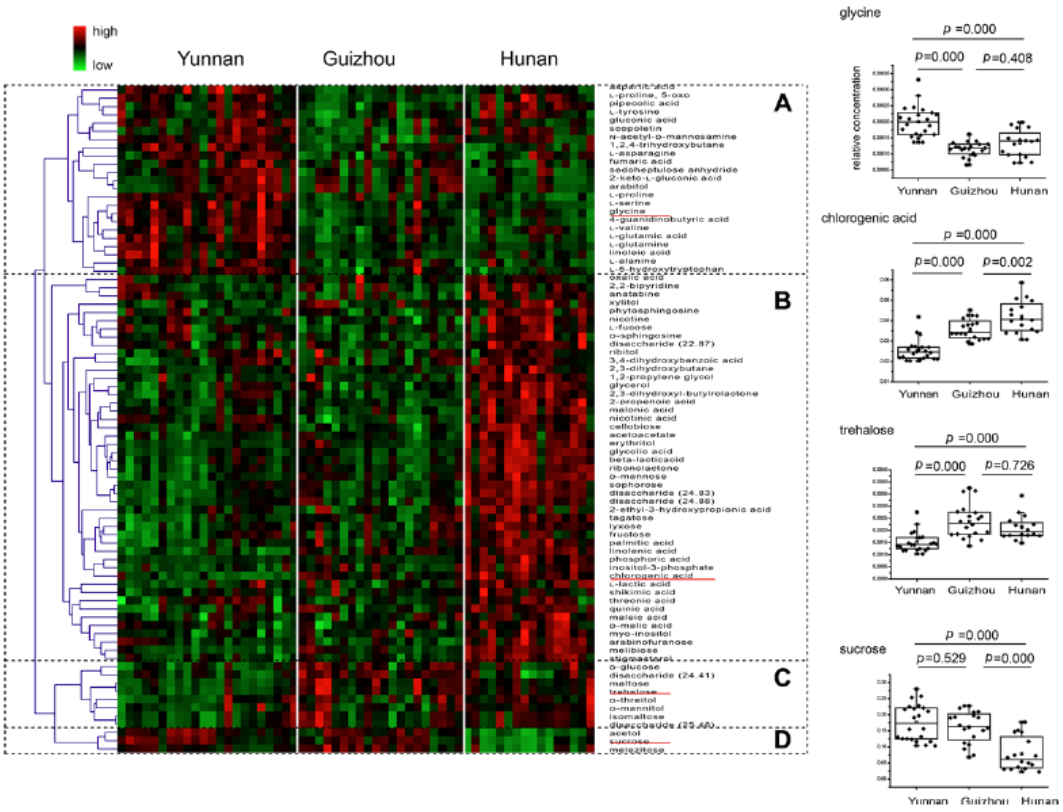
Research Article

Study of metabolite differences of flue-cured tobacco from different regions using a pseudotargeted gas chromatography with mass spectrometry selected-ion monitoring method

基于拟靶向气相色谱质谱选择离子检测法研究不同产地烟草代谢物的差异

A pseudotargeted method based on gas chromatography and mass spectrometry with selected-ion monitoring was established to investigate the metabolite differences of fluecured tobacco from three different growing regions. The mixed solvent of acetonitrile/isopropanol/water (3:3:2, v/v/v) was chosen as the optimal extraction system based on the good repeatability and extraction efficiency. A self-developed software coupled with commercial software was used to establish the pseudotargeted method including 289 peaks and 47 groups. Multivariable statistical analysis indicated that tobacco samples can be obviously separated based on the geographical origins. On the basis of a Mann–Whitney U test, organic acids, phenols, and alkaloids had higher levels in Hunan province. In contrast, a large proportion of amino acids (including L-tyrosine, L-proline, and serine), sucrose, and linoleic acid were the highest in Yunnan province. Meanwhile, multiple metabolic pathways (including carbohydrate metabolism, tricarboxylic acid cycle, and nitrogenmetabolism) were influenced by growing regions. Twenty-eight differential metabolites, which had great contributions to the classification of tobacco samples of three growing regions, were further defined. The results demonstrated that the developed pseudotargeted method was a powerful tool to investigate the metabolic profiling of tobacco leaves and discriminate tobacco leaves of different growing regions.

使用的岛津仪器：GCMS-QP 2010



代表图片：不同产地烟草差异代谢物热图和代表性代谢物箱线图。代谢物的p值采用非参数检验计算。A、B两组代谢产物含量以云南、湖南最高，C、D两组代谢产物含量以云南、湖南最低。

原文网址：http://doi.10.1002/jssc.201400097

Journal of proteome research

Article

pubs.acs.org/jpr

Investigation of the Relationship between the Metabolic Profile of Tobacco Leaves in Different Planting Regions and Climate Factors Using a Pseudotargeted Method Based on Gas Chromatography/ Mass Spectrometry

Yanni Zhao,[†] Chunxia Zhao,[†] Xin Lu,*[†] Huina Zhou,[‡] Yanli Li,[†] Jia Zhou,[†] Yuwei Chang,[†] Junjie Zhang,[†] Lifeng Jin,[‡] Fucheng Lin,[‡] and Guowang Xu*[†]

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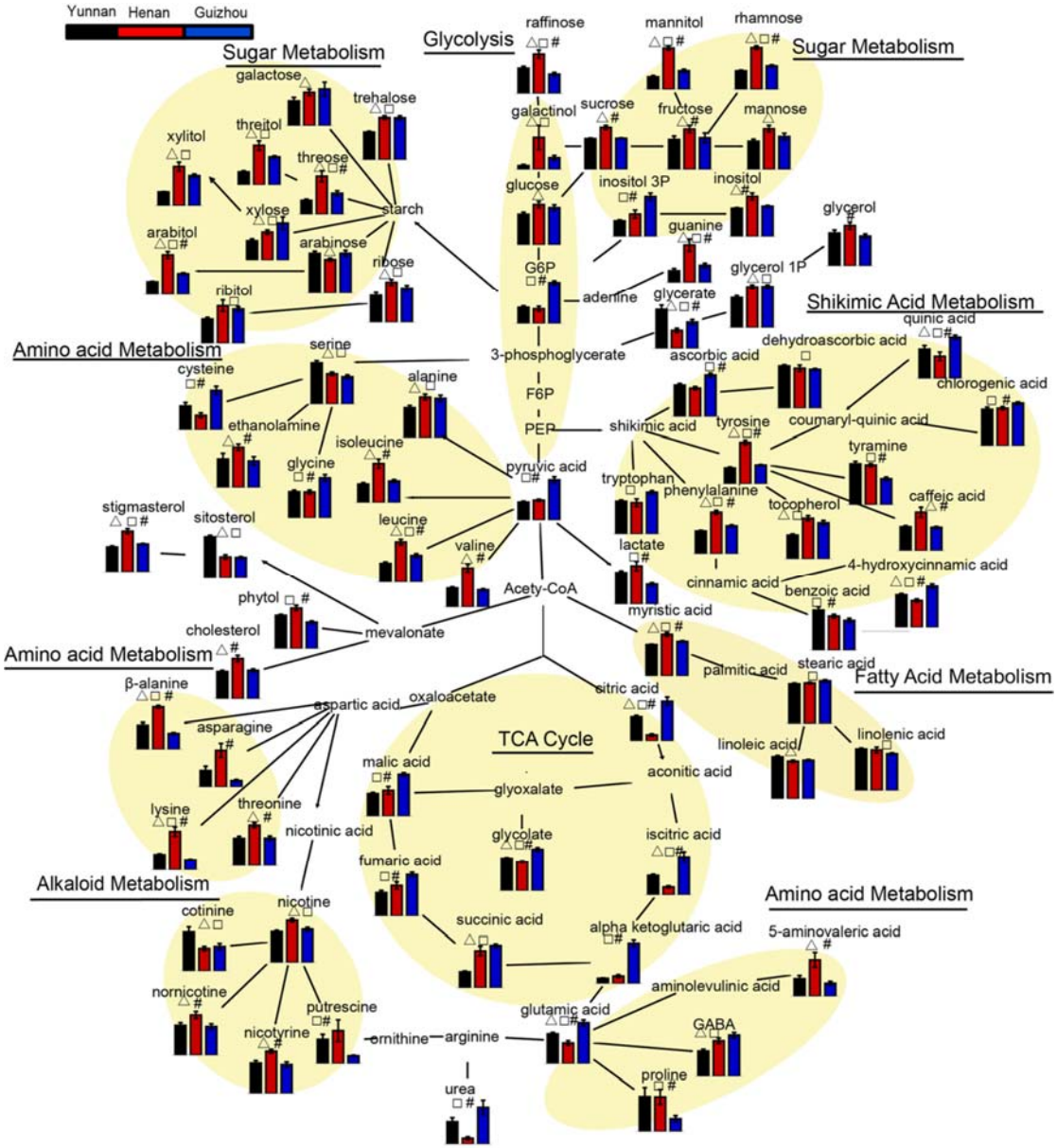
基于拟靶向气相色谱-质谱法研究不同种植区烟叶代谢谱与气候因素的关系

Abstract: An improved pseudotargeted method using gas chromatography/mass spectrometry (GC/MS) was developed to investigate the metabolic profile of tobacco leaves from three planting regions (Yunnan, Guizhou, and Henan provinces). The analytical characteristics of the method with regard to reproducibility, precision, linearity, and stability were satisfactory for metabolic profiling study. Partial least-squares-discriminant analysis and hierarchical cluster analysis demonstrated that the metabolic profiles of tobacco from the Yunnan and Guizhou regions were different from that from the Henan province. The amino acid (e.g., phenylalanine, leucine, and tyrosine) and carbohydrate (e.g., fructose, trehalose, and sucrose) contents were the highest in Henan tobacco. The highest contents of organic acids (e.g., isocitrate, citrate, and fumarate) of the TCA cycle and antioxidants (e.g., quinate, chlorogenic acid, and ascorbate) were found in Guizhou tobacco. The correlation coefficients between metabolite content and climate factors (rainfall, sunshine, and temperature) demonstrated that drought facilitated the accumulation of sugars and amino acids. The content of TCA cycle intermediates could be influenced by multiple climate factors. This study demonstrates that the pseudotargeted method with GC/MS is suitable for the investigation of the metabolic profiling of tobacco leaves and the assessment of differential metabolite levels related to the growing regions.

使用的岛津仪器：GCMS-QP 2010



代表图片：3个不同种植区烟叶的代谢路径。黑色、红色和蓝色分别表示云南、河南和贵州烟草代谢物的相对浓度。采用非参数检验计算代谢物的*p*值，#、△和□分别表示河南vs贵州、云南vs河南、云南vs贵州*p*值小于0.05。

原文网址：http://dx.doi.org/10.1021/pr400799a

Metabolomics (2012) 8:529–539
DOI 10.1007/s11306-011-0338-8

ORIGINAL ARTICLE

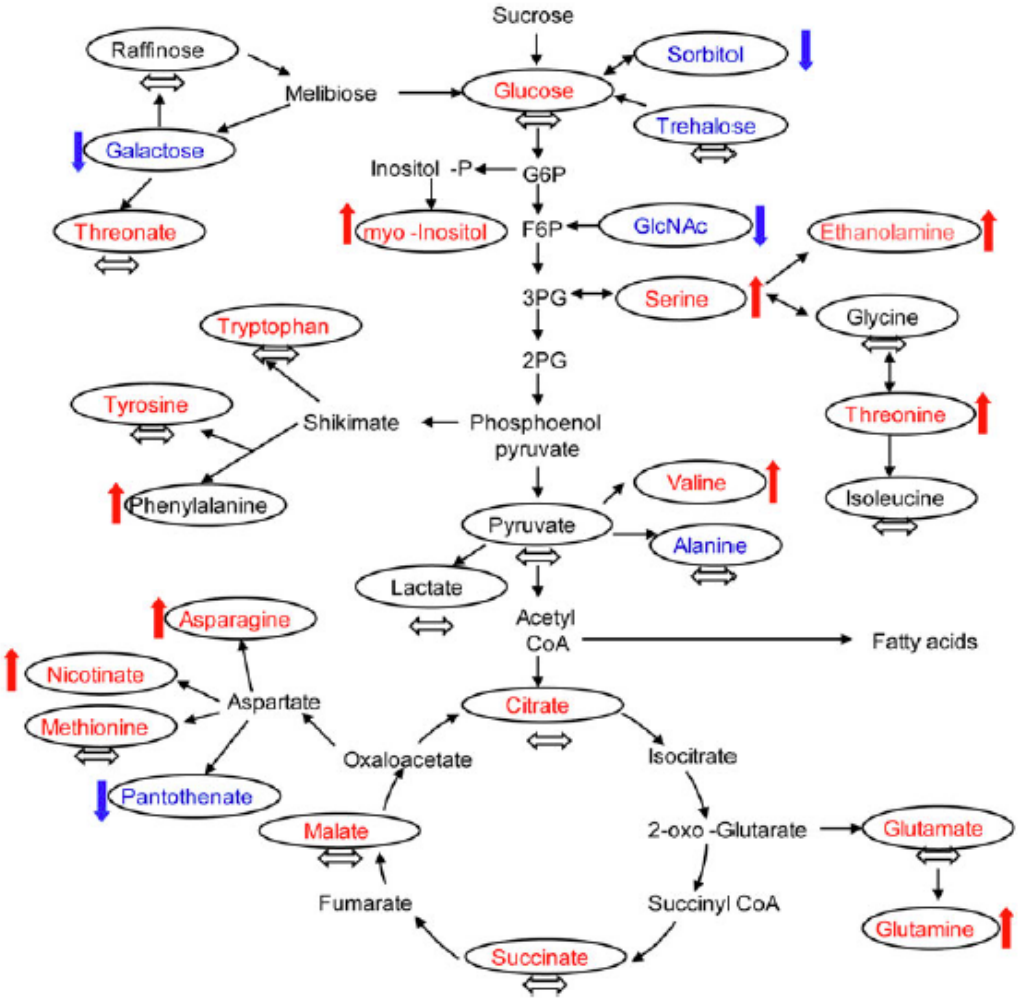
Metabolic profiling of transgenic rice progeny using gas chromatography–mass spectrometry: the effects of gene insertion, tissue culture and breeding

Jia Zhou · Lei Zhang · Xiang Li · Yuwei Chang · Qun Gu · Xin Lu · Zhen Zhu · Guowang Xu

气相色谱-质谱法分析基因插入、组织培养与育种对转基因水稻后代代谢的影响

Abstract: The Bacillus thuringiensis d-endotoxin and cowpea trypsin inhibitor genes have been introduced into the rice genome to improve its pest resistance via Agrobacterium-mediated transformation. A gas chromatography-mass spectrometry (GC–MS) based metabolic profiling method was employed to determine the unpredictable metabolic changes resulting from the gene insertion and tissue culture separately. Descendants of the same transformant were obtained from different breeding programs, including both the transgenic and null-segregant progeny. The comparison of the transgenic and respective null-segregant plants enabled the evaluation of variations caused by transgenes; also the null-segregant plants were compared with the wild-type control to identify the influence of tissue culture. Based on the GC–MS metabolic profiles, the principal component analysis and significant differences determined by Student’s t-test suggested that there were more metabolic changes from the tissue culture than those from the insertion of the transgenes. By comparing different breeding programs, it was clear that the progeny which was developed after several generations of backcross with the non-transformed rice as the recurrent parent, displayed fewer metabolic differences from the non-transformed parent. A GC–MS based metabolic profiling study confirmed that backcrossing can help to reduce unwanted variations that occur during transformation processes.

使用的岛津仪器：GCMS-QP 2010



代表图片：野生水稻MH86后代（MF2036a）与转基因后代（MF6000a）代谢途径的差异。椭圆标注的代谢物是所有QCs中检测到高于定量限（LOQ）的代谢物。采用T检验抗性后代（MF2036a或MF6000a）与MH86的差异显著性，并特别指出具有统计学显著性差异（P<0.05）或高度显著性差异（P<0.01）的代谢物。MF6000a中含量明显高于MH86的代谢物以红色字体显示，含量较低的代谢物以蓝色字体显示，代谢物没有显著变化的以黑色字体显示。与MH86相比，MF2036a中显著升高或降低的代谢物，分别用上箭头或下箭头标记，双向箭头表示代谢物水平无明显差异。

原文网址：http://doi.10.1007/s11306-011-0338-8)

化 学 学 报
ACTA CHIMICA SINICA
研究论文
Article
DOI: 10.6023/A12110883

代谢指纹分析筛选调节金橙黄微小杆菌 ATCC49676 乳酸产量的代谢物

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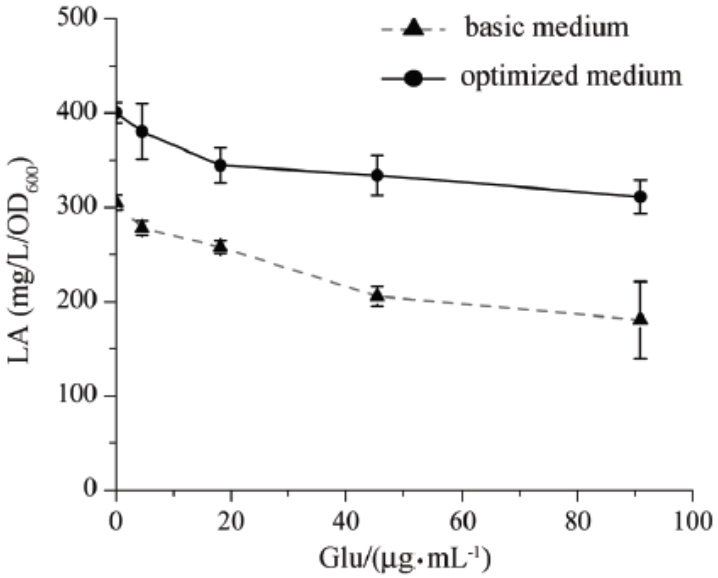
代谢指纹分析筛选调节金橙黄微小杆菌 ATCC49676 乳酸产量的代谢物

摘要：金橙黄微小杆菌ATCC49676 具有巨大的产乳酸潜力. 为筛查可能影响或调节乳酸产量的代谢物，研究首先通过全因子实验设计优化并确定了最大乳酸产量的培养基组成. 然后，通过气相色谱质谱联用技术对在基础培养基和优化培养基培养条件下的培养物进行代谢指纹分析. 显著性分析发现，两种培养条件下胞内的谷氨酸变化最为显著. 当ATCC49676 在外加谷氨酸培养时，乳酸的产量随着谷氨酸浓度的增加而下降. 相对酶定量证实了谷氨酸可降低胞内乳酸脱氢酶含量. 研究证实了代谢指纹分析在探究表型特异性胞内代谢物上的价值以及它在改进工业发酵效率上的潜在作用。

使用的岛津仪器：GCMS-QP 2010



代表图片：谷氨酸对乳酸产量的影响

原文网址：http://doi.10.6023/A12110883

Journal of Chromatography B, 877 (2009) 725–732

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Metabolic profiling of transgenic rice with *cryIAc* and *sck* genes: An evaluation of unintended effects at metabolic level by using GC-FID and GC–MS

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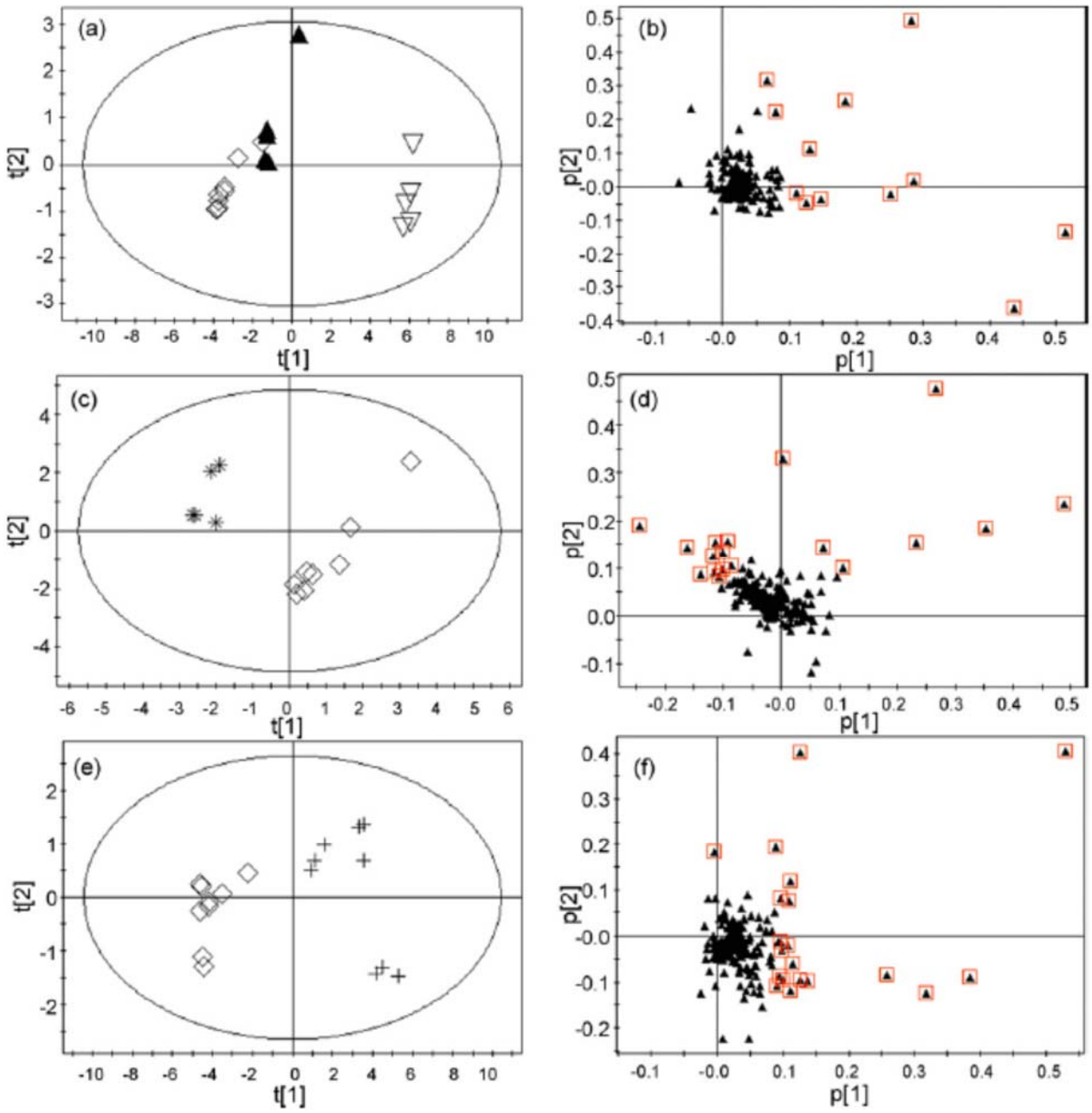
转 crylAC 和 sck 基因大米代谢谱研究：用 GC-FID 和 GC-MS 评估代谢水平的非预期效应

The crylAc and sck genes were introduced to the rice for the purpose of improving the insect resistance. Metabolic profiles of wild and transgenic rice were compared to assess the unintended effects related to gene modification. Wild samples with different sowing dates or sites were also examined to determine the environmental effects on metabolites. The polar compounds of grains were extracted, trimethylsilylated and analyzed by gas chromatography-flame ionization detection (GC-FID). Partial leastsquares-discriminant analysis (PLS-DA) and principal component analysis (PCA) were applied to differentiate transgenic and wild rice grains. The significantly distinguishable metabolites were picked out, and then identified by gas chromatography–mass spectrometry (GC–MS). It was found that both the environment and gene manipulation had remarkable impacts on the contents of glycerol-3-phosphate, citric acid, linoleic acid, oleic acid, hexadecanoic acid, 2,3-dihydroxypropyl ester, sucrose, 9-octadecenoic acid (Z)-, 2,3-dihydroxypropyl ester and so on. Sucrose, mannitol and glutamic acid had a significant increase in transgenic grains in contrast to those in non-genetically modified (GM) rice.

使用的岛津仪器：GCMS QP-2010



代表图片： M86-C, M86-D1和M86-D2 (R2X = 0.875)（a）PCA得分图（b）载荷图；M86-C和M86-F（R2X = 0.775）（c）PCA得分图（d）载荷图；M86-C和N6（R2X = 0.89）（e）PCA得分图（f）载荷图。符号意义：◇M86-C，+N6，▲M86-D1，▽M86-D2，*M86-F；红框标记代表所选变量组间有显著差异。

原文网址：https://doi.org/10.1016/j.jchromb.2009.01.040

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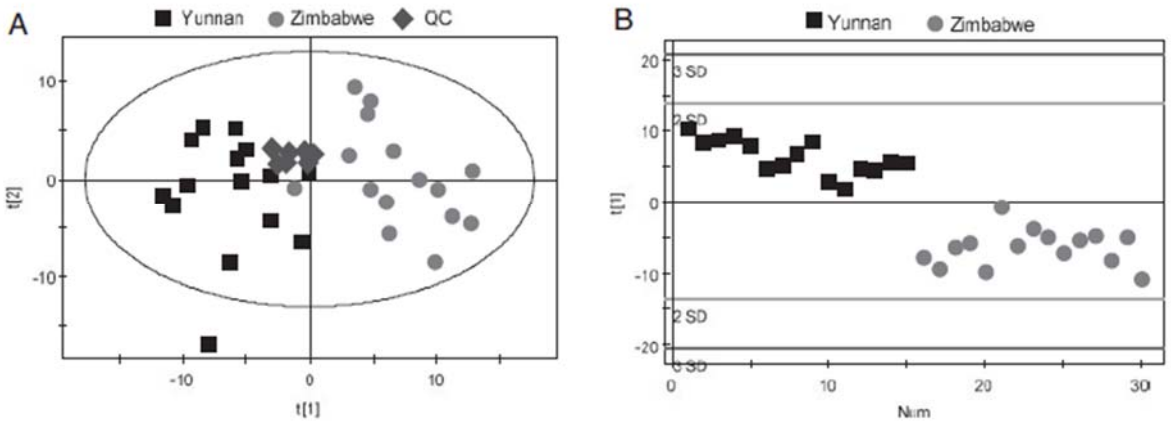
Research Article

Gas chromatography-mass spectrometric method for metabolic profiling of tobacco leaves

烟叶代谢图谱的气相色谱-质谱分析方法

Abstract：A gas chromatography-mass spectrometric method was developed for profiling of tobacco leaves. The differentiation among tobacco leaves planted in two different regions was investigated. Prior to analysis, the extraction solvent formulation was optimized and a combination of water, methanol and acetonitrile with a volume ratio of 3:1:1 was found to be optimal. The reproducibility of the method was satisfactory. Kendall tau-b rank correlation coefficients were equal to 1 (po0.05) for 82% of the resolved peaks (up to 95% of the overall peak areas), indicating the good response correlation. Forty-four compounds including 9 saccharides, 9 alcohols, 9 amino acids, 16 organic acids and phosphoric acid were identified based on standard compounds. The method was successfully applied for profiling of tobacco leaves from Zimbabwe and Yunnan of China. Our result revealed that levels of saccharides and their derivatives including xylose, ribose, fructose, glucose, turanose, xylitol and glyceric acid were more abundant while sucrose, glucitol and Dgluconic acid were less abundant in tobacco leaves from Yunnan as compared to those from Zimbabwe. Amino acids such as L-alanine, L-tyrosine and L-threonine were found to be richer in Zimbabwe tobacco than in Yunnan tobacco.

使用的岛津仪器：GCMS-QP 2010



代表图片：烟草样品PCA（A）和PLS-DA（B）评分图。

原文网址： https://DOI 10.1002/jssc.201100106

第 34卷 分析化学（FENXI HUAXUE） 研究简报 第 3期
2006年 3月 Chinese Journal of Analytical Chemistry 382～384

气相色谱 质谱分析烟草中的主要生物碱

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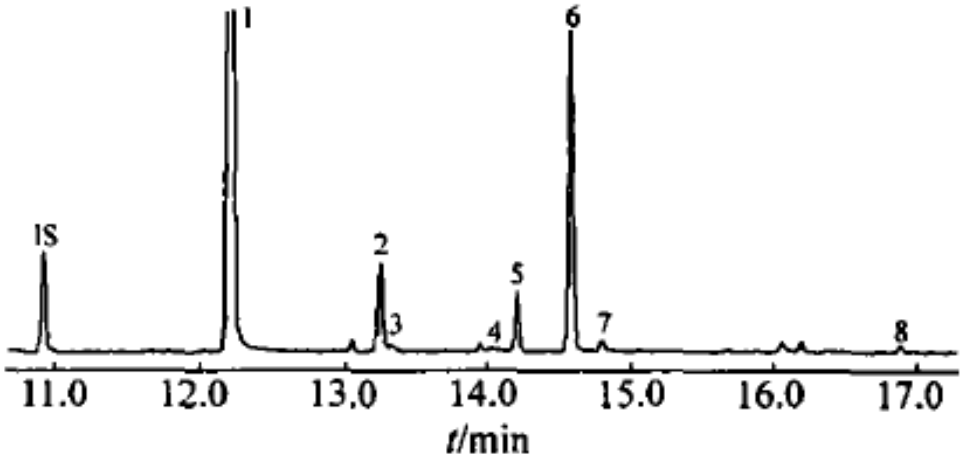
气相色谱/质谱分析烟草中的主要生物碱

摘要：用毛细管气相色谱法测定烟草中烟碱、降烟碱、麦斯明、二烯烟碱、新烟碱、去氢新烟碱、2,3′-联二吡啶、可替宁 8 种主要生物碱的方法。烟草样品经二氯甲烷/甲醇(V/V，3：1)萃取，过一次性滤膜，进样，经 DB-5MS 毛细管柱分离，由气相色谱-氢火焰离子化检测器(F ID)检测定量，质谱定性。该方法操作简单，重现性好，回收率较高。8 种生物碱相对标准偏差为 2.59%～7.07%;回收率为 89.4%～98.7%。

使用的岛津仪器：GCMS-QP2010



代表图片：烟样总离子流图。

原文网址 ： https://doi.org/ 10.3321/j.issn:0253-3820.2006.03.025

2006年 5月 色 谱 Vol 24 No 3
May 2006 Chinese Journal of Chromatography 315~316

溶剂萃取-气相色谱/质谱法分析烟草中的主要甾醇

许燕娟[1,3]，钟科军[2]，白长敏[1]，黄建国[2]，唐婉莹[3]，
路 鑫[1]，卢 果[1]，许国旺[1]
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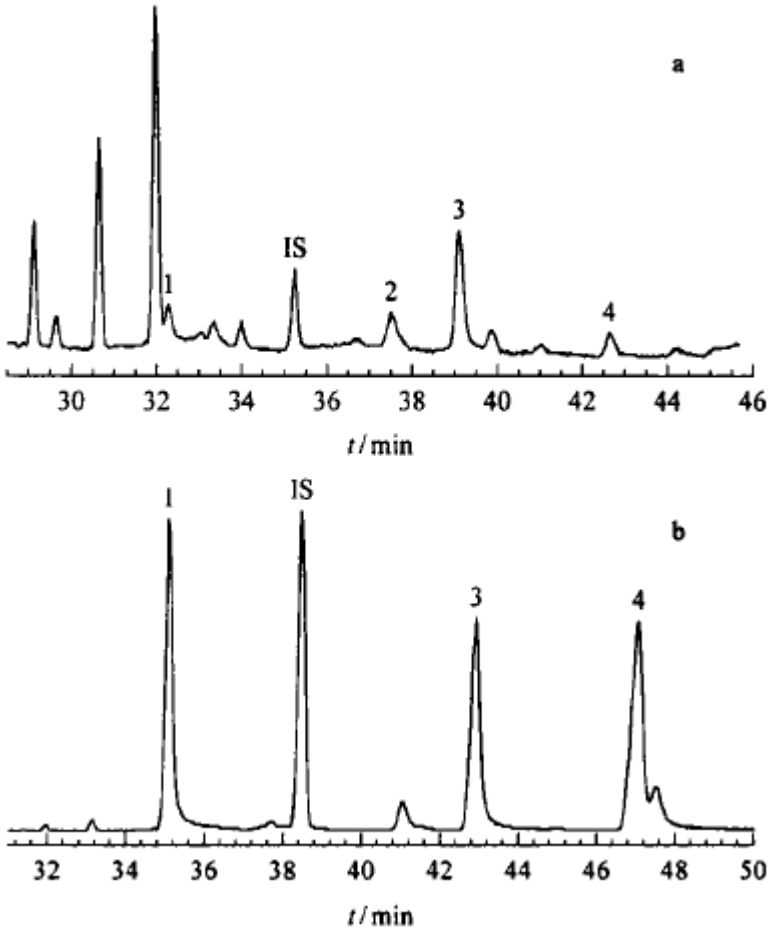
溶剂萃取-气相色谱/质谱法分析烟草中的主要甾醇

摘要：烟草中的甾醇类物质主要有胆甾醇、菜油甾醇、豆甾醇和β-谷甾醇等，这些甾醇的结构中都含有羟基，热解时其母体的多环结构可形成稠环芳烃[1]，因此烟草中的甾醇是一种潜在的影响人体健康的物质，故对甾醇种类和含量进行分析对卷烟的配方研究具有参考价值。常用的甾醇分析方法有衍生化气相色谱法[2-4]、高效液相色谱法[5-7]、毛细管电泳法[8-9]和超临界流体色谱法[10-11]。由于衍生化气相色谱法前处理操作复杂，因而在一定程度上降低了被测组分的回收率。考虑到甾醇在三氯甲烷中的溶解性很好，本文采用三氯甲烷直接萃取烟样中的甾醇，萃取液经过滤后进行气相色谱/质谱(GC/MS)分析。结果表明所建立的方法前处理十分简单，回收率高，适合大量样品的定量分析。

使用的岛津仪器：GCMS-QP2010



代表图片：（a）烟样中甾醇总离子流图；（b）甾醇混合标准液总离子流图；

原文网址 ： http://cpfd.cnki.com.cn/Article/CPFDTOTAL-ZGHY200504002141.htm

第五部分：复杂样品分离分析新方法、新技术

Analytical and Bioanalytical Chemistry (2019) 411:6377–6386
https://doi.org/10.1007/s00216-019-02011-w

RESEARCH PAPER

A novel analysis method for biomarker identification based on horizontal relationship: identifying potential biomarkers from large-scale hepatocellular carcinoma metabolomics data

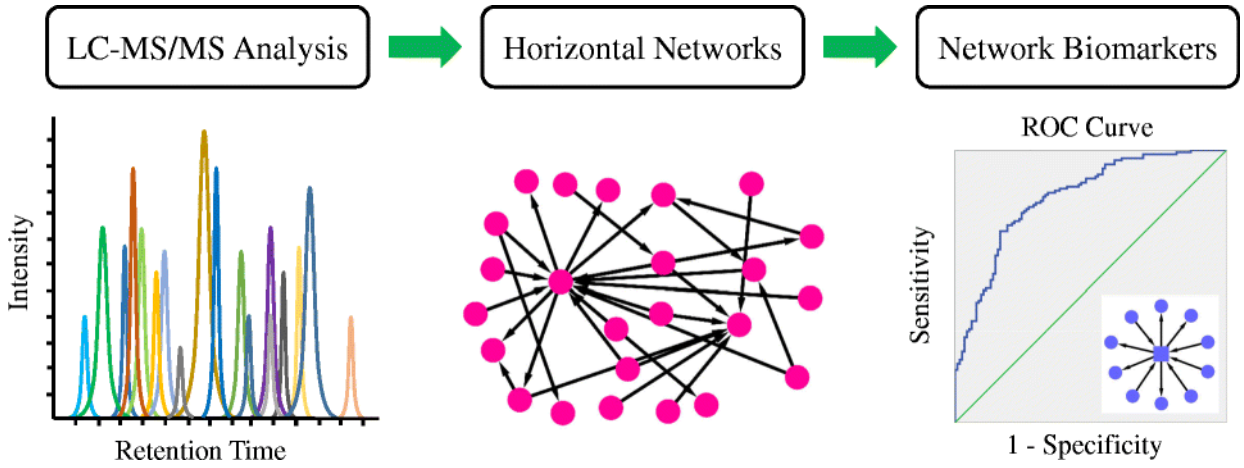
Benzhe Su[1] · Ping Luo[2] · Zhao Yang[3] · Pei Yu[3] · Zaifang Li[2] · Peiyuan Yin[2] · Lina Zhou[2] · Jinhu Fan[3] · Xin Huang[1] · Xiaohui Lin[1] · Youlin Qiao[3] · Guowang Xu[2]

基于横向比较识别生物标志物的新方法：从大规模肝癌代谢组学数据中识别潜在生物标志物

Abstract: Omics techniques develop quickly and have made a great contribution to disease study. Omics data are usually complex. How to analyze the data and mine important information has been a key part in omics research. To study the nature of disease mechanisms systematically, we propose a new data analysis method to define the network biomarkers based on horizontal comparison (DNB-HC). DNB-HC performs molecule horizontal relationships to characterize the physiological status and differential network analysis to screen the biomarkers. We applied DNB-HC to analyze a large-scale metabolomics data, which contained 550 samples from a nested case-control hepatocellular carcinoma (HCC) study. A network biomarker was defined, and its areas under curves (AUC) in the receiver-operating characteristic (ROC) analysis for HCC discrimination were larger than those defined by six efficient feature selection methods in most cases. The effectiveness was further corroborated by another nested HCC dataset. Besides, the performance of the defined biomarkers was better than that of α-fetoprotein (AFP), a commonly used clinical biomarker for distinguishing HCC from high-risk population of liver cirrhosis in other two independent metabolomics validation sets. All and 90.3% of the AFP false-negative patients with HCC were correctly diagnosed in these two sets, respectively. The experimental results illustrate that DNB-HC can mine more important information reflecting the nature of the research problems by studying the feature horizontal relationship systematically and identifying effective disease biomarkers

in clinical practice.

使用的岛津仪器：LCMS-8050



代表图片：DNB-HC的工作流程

原文网址：https://link.springer.com/article/10.1007%2Fs00216-019-02011-w

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Contents lists available at ScienceDirect

Analytica Chimica Acta

journal homepage: www.elsevier.com/locate/aca

Serum or plasma, what is the difference? Investigations to facilitate the sample material selection decision making process for metabolomics studies and beyond

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[d] German Center for Diabetes Research (DZD), Germany

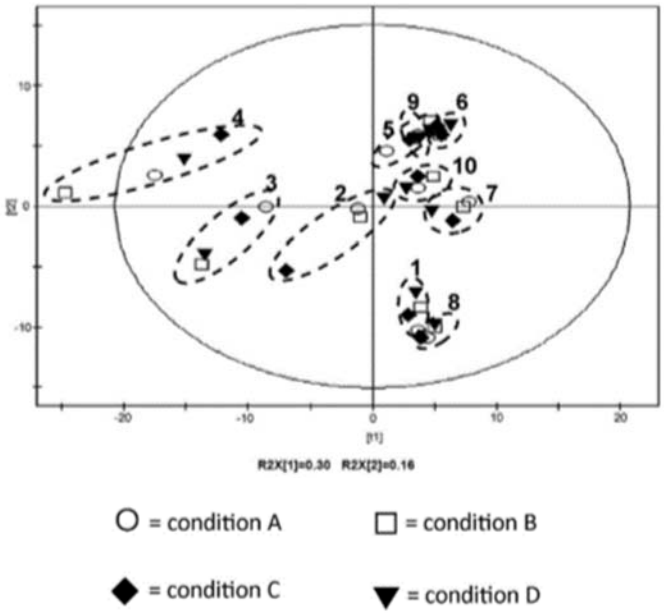
调研血清与血浆的区别促进代谢组学研究时样本材料的选择

Abstract：In analytical chemistry serum as well as plasma are recommended as sample material of choice. However, blood processing for the generation of serum or plasma is rather different. Whether plasma or serum is the preferable sample material is still controversial discussed. We performed in paired samples three UHPLC-mass spectrometry-driven metabolomics studies. In study 1 metabolite profiles of serum vs plasma were compared. 46% out of 216 identified metabolites showed significant different levels (paired Wilcoxon signed-rank test, $p < 0.05$, FDR <0.01) with only three metabolites (methionine, C2:0- and C3:0-carnitine) showing lower levels in serum. In study 2 comparison of three different serum blood collection tubes revealed that coagulation and associated processes distinctly alter metabolite levels depending on the tube-specific clotting process. Most pronounced differences were found for the dipeptide phenylalanine-phenylalanine (highest levels in silicate containing serum blood collection tubes). In study 3 possible adverse effects of platelets, which still remain in standard plasma even after correct processing, were investigated. No differences in a pattern of 216 metabolites were detected in the comparison of standard and platelet-free plasma (PFP). Our results give novel insights in fundamental

differences between serum and plasma, thereby providing valuable information for analytical chemists for decision making to either use serum or plasma before starting complex and time-consuming analytical investigations.

Keywords：Plasma，Serum，Metabolic profiling，Sample material selection，Metabolomics

使用的岛津仪器：LCMS-8050



代表图片：来自10个个体的配对标准血浆和无血小板血浆的比较。主成分分析(PCA)对标准血浆(条件A)和三种不同制备的无血小板血浆样品(条件B-D)进行评分。

原文网址：https://www.sciencedirect.com/science/article/pii/S000326701830374X?via%3Dihub

analytical chemistry

Technical Note

pubs.acs.org/ac

Online Three Dimensional Liquid Chromatography/Mass Spectrometry Method for the Separation of Complex Samples

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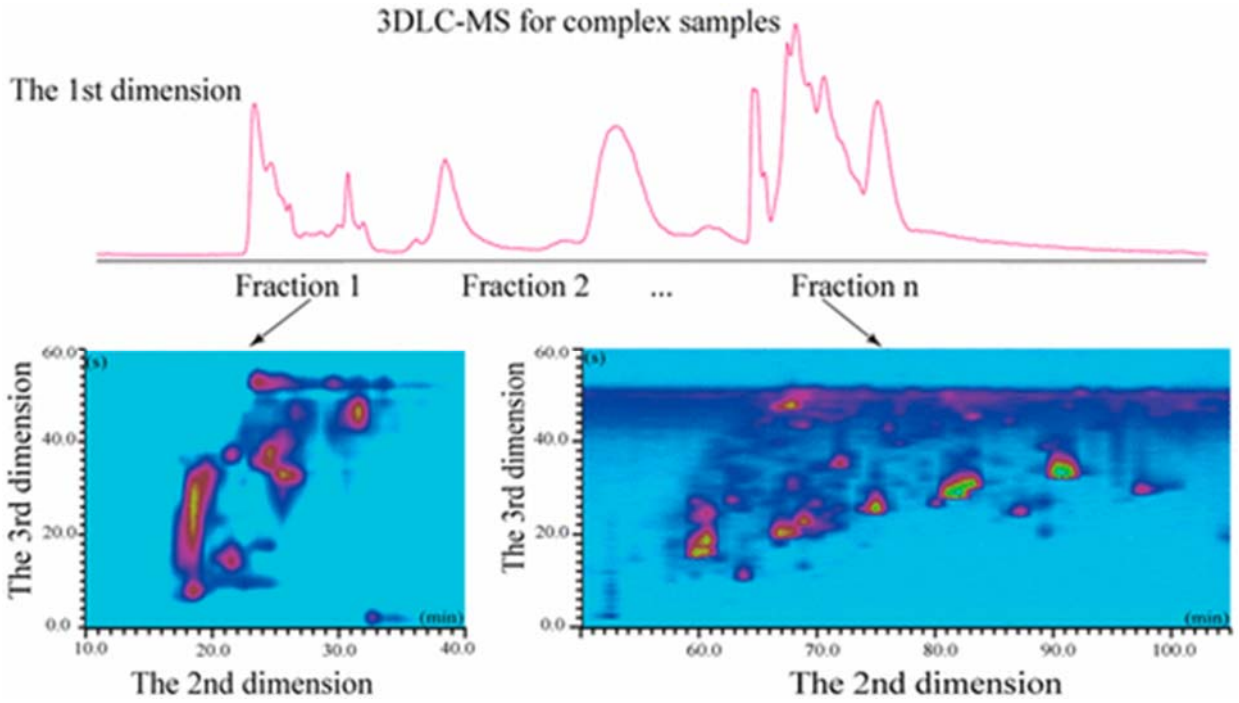
在线三维液相色谱/质谱法分离复杂样品

Abstract: In this work, a novel online three dimensional liquid chromatography (3D-LC) system was first developed by effectively coupling of preseparation and comprehensive 2DLC using a stop-flow interface, aiming at improving the separation of complex samples. The sample was separated into two or several fractions through the first dimensional separation, and then each fraction was transferred in an orderly way into the following comprehensive 2D-LC part for further analysis. More optimal conditions could be operated in the second and third dimensions according to the properties of each fraction. Thus, the resolution of the 3D-LC system was substantially improved. Analysis of soybean extract was taken as a proof-of-principle to demonstrate the powerful separation of the established 3D-LC system. The amide column was selected as the first dimension column. Weakly polar metabolites (such as lipids, aglycones, etc.) and polar metabolites (such as glycosides, etc.) were separated into different fractions. Fluorophenyl and C18 columns were used in the second and third dimensions of the 3D-LC system for further separation, respectively. There were 83 flavonoids characterized in the soybean extract, including many difficult to separate isomers and low-abundance flavonoids; in total, they were nearly 30% more than those identified in the comparative comprehensive 2D-LC approach. In conclusion, this 3D-LC system is flexible in construction and applicable to complex sample analysis.

使用的岛津仪器：LCMS-IT-TOF



代表图片：采用3D-LC法对大豆提取液进行了色谱分析。A和B分别显示了第1和第2部分的TIC色谱图

原文网址：https://pubs.acs.org/doi/10.1021/acs.analchem.6b04401

2017 年 1 月 January 2017
色 谱 Chinese Journal of Chromatography
Vol.35 No.1 75~79
邹汉法研究员纪念专辑（下）· 研究论文
DOI：10.3724/SP.J.1123.2016.10004

基于气相色谱-质谱联用技术的高通量细胞表型分析方法

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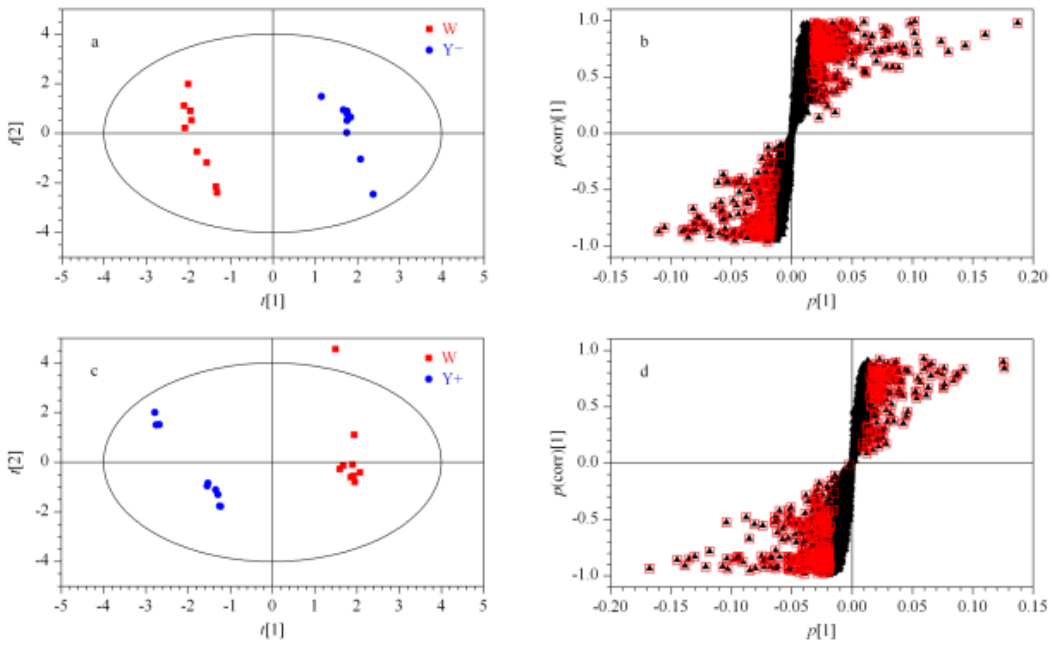
（1. 吉林化工学院，吉林 吉林 132022；2. 中国科学院大连化学物理研究所，辽宁 大连 116023；3. 大连医科大学附属大连市第六人民医院，辽宁 大连 116021）

基于气相色谱-质谱联用技术的高通量细胞表型分析方法

摘要：研究开发了一种基于 96 孔板培养和气相色谱－质谱联用（GC-MS）技术的高通量细胞表型分析方法。该方法分别以 48 种物质作为唯一能源对大肠杆菌进行培养， 利用 GC-MS 研究野生型和 *yfcC* 基因改造大肠杆菌对各物质的分解代谢情况，实现高通量的细胞表型分析。结果显示，野生型和 *yfcC* 基因过表达大肠杆菌对 14 种物质的代谢能力有显著差异，*yfcC* 基因过表达大肠杆菌对甘氨酸和柠檬酸的代谢能力明显强于野生型大肠杆菌，而对其他物质的代谢能力较弱，我们推测可能是由于 *yfcC* 基因促进乙醛酸代谢，导致 *yfcC* 过表达菌株对甘氨酸的代谢能力较强；野生型和 *yfcC* 基因敲除大肠杆菌间分解有显著差异的共 16 种物质，其中 *yfcC* 基因敲除大肠杆菌对丙氨酸、乳糖、肌醇和柠檬酸的代谢能力较强。该方法简单、高效，可以为未知基因功能研究提供更多代谢功能相关的参考数据。

使用的岛津仪器：GCMS-QP 2010



代表图片：W 与 *yfcC* 基因敲除菌（Y-） 的（a） PLS-DA 得分图及（b）相应的 S-Plot 图和 W 与 *yfcC* 基因过表达菌（Y+）的（c）PLS-DA 得分图及（d）相应的 S-Plot 图

原文网址：https://doi.org/10.3724/sp.j.1123.2016.10004

analytical chemistry

Article

pubs.acs.org/ac

A Novel Strategy for Large-Scale Metabolomics Study by Calibrating Gross and Systematic Errors in Gas Chromatography−Mass Spectrometry

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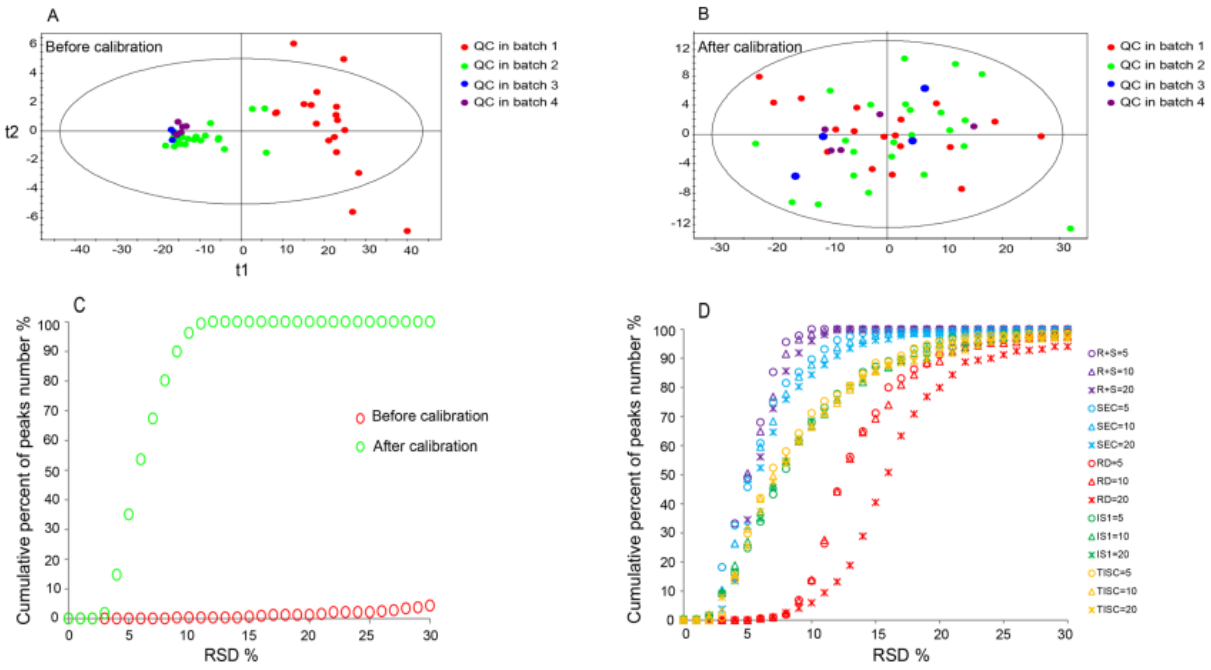
通过校正 GC-MS 的过失误差和系统误差的大规模代谢组学研究新策略

ABSTRACT: Metabolomics is increasingly applied to discover and validate metabolite biomarkers and illuminate biological variations. Combination of multiple analytical batches in large-scale and long-term metabolomics is commonly utilized to generate robust metabolomics data, but gross and systematic errors are often observed. The appropriate calibration methods are required before statistical analyses. Here, we develop a novel correction strategy for large-scale and long-term metabolomics study, which could integrate metabolomics data from multiple batches and different instruments by calibrating gross and systematic errors. The gross error calibration method applied various statistical and fitting models of the feature ratios between two adjacent quality control (QC) samples to screen and calibrate outlier variables. Virtual QC of each sample was produced by a linear fitting model of the feature intensities between two neighboring QCs to obtain a correction factor and remove the systematic bias. The suggested method was applied to handle metabolic profiling data of 1197 plant samples in nine batches analyzed by two gas chromatography-mass spectrometry instruments. The method was evaluated by the relative standard deviations of all the detected peaks, the average Pearson correlation coefficients, and Euclidean distance of QCs and non-QC replicates. The results showed the established approach outperforms the commonly used internal standard correction and total intensity signal correction

methods, it could be used to integrate the metabolomics data from multiple analytical batches and instruments, and it allows the frequency of QC to one injection of every 20 real samples. The suggested method makes a large amount of metabolomics analysis practicable.

使用的岛津仪器：GCMS-QP 2010 和 GCMS-QP 2010 Plus



代表图片：4 个批次中 50 个 QC 样品的校正前（A）和校正后（B）的主成分得分图；G+S 校正前和校正后的 QC 样品累积 RSD 曲线（C）；不同校正方法下的 QC 样品 RSD 累积曲线（D）。

原文网址：https://doi.org/10.1021/acs.analchem.5b03912

Journal of Chromatography A, 1465 (2016) 30–37

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journal homepage: www.elsevier.com/locate/chroma

High-sensitivity detection of biogenic amines with multiple reaction monitoring in fish based on benzoyl chloride derivatization

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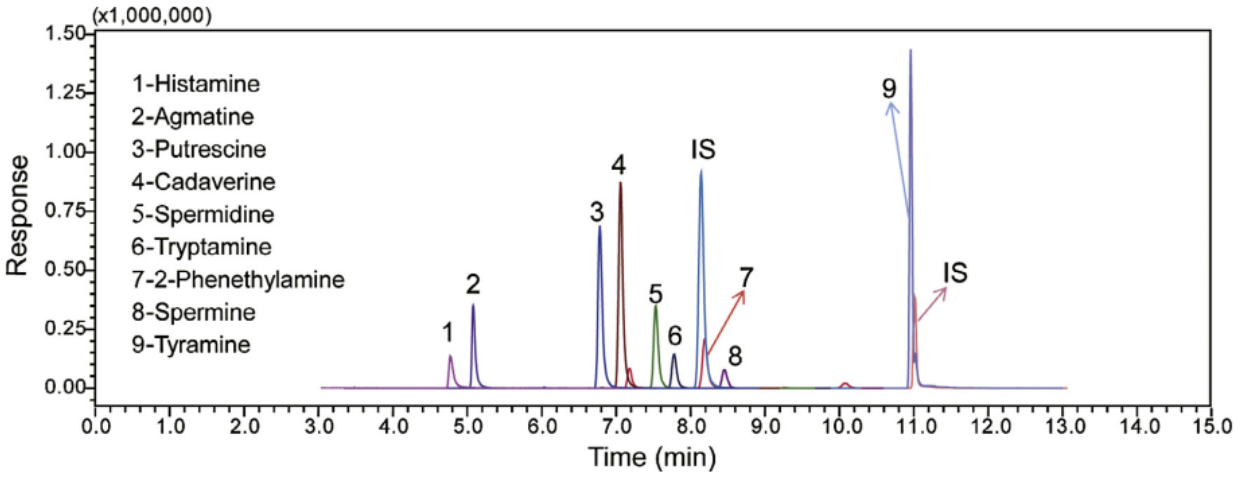
基于苯甲酰氯衍生的多反应监测用于高灵敏度测定鱼体内的生物胺

Abstract: In this study an efficient and sensitive method for biogenic amines detection was established by combining rapid extraction and derivatization with multiple reaction monitoring (MRM) based on ultra high performance liquid chromatography-triple quadrupole mass spectrometry. Bead-beating disruption and extraction using 5-sulfosalicylic acid not only improved the extraction efficiency but also was environmentally friendly. Benzoyl chloride derivatization could obtain stable biogenic amine derivatives with a shorter reaction time. By combining with MRM detection mode, higher detection sensitivity for biogenic amines could be achieved. The method showed a good linearity with linear range of 3–4 orders of magnitude and regression coefficients ranging from 0.9966 to 0.9999. The limit of detection and limit of quantitation could even reach lower pg/mL level. Satisfactory recovery was obtained from 74.9% to 119.3%. And the derivatives were stable within 48 h at 4 ◦C. The method established was used to determine content of biogenic amines in different fishes at different storage conditions. The results indicated that this method was suitable for analysis of biogenic amines.

使用的岛津仪器：LCMS-8050



代表图片：9 种苯甲酰氯衍生的生物胺和 2 种内标的提取离子流图（1 ng/mL 混标）

原文网址：http://dx.doi.org/10.1016/j.chroma.2016.08.067

Anal Bioanal Chem (2016) 408:6741–6749
DOI 10.1007/s00216-016-9797-0

RESEARCH PAPER

The development of plasma pseudotargeted GC-MS metabolic profiling and its application in bladder cancer

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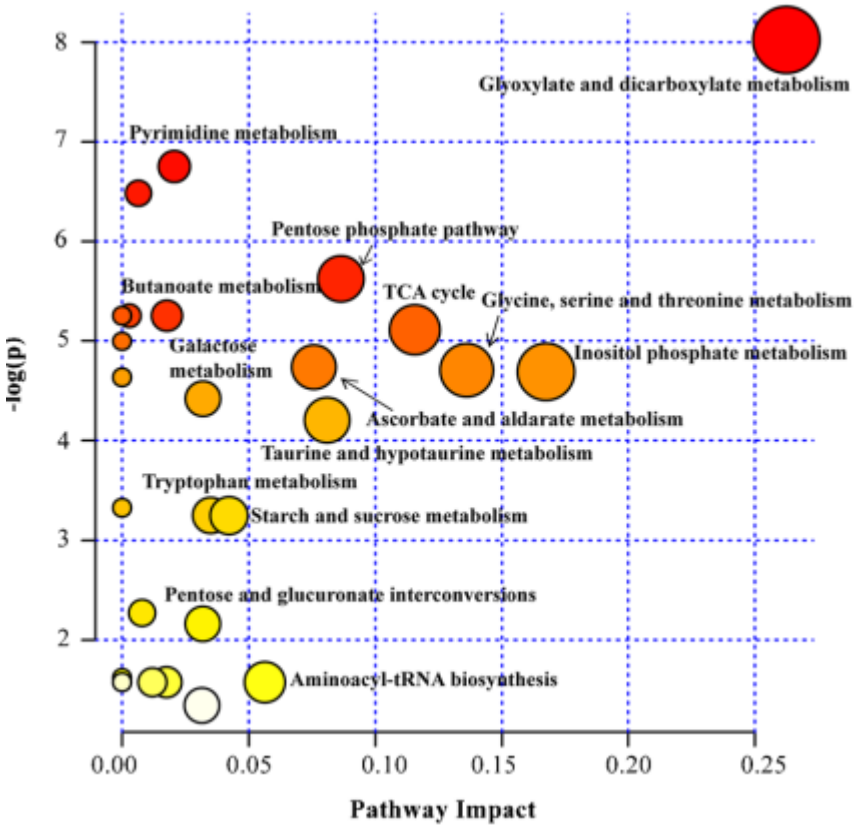
发展基于 GC-MS 的血浆拟靶向代谢组学分析方法及其在膀胱癌研究中的应用

Abstract: Bladder cancer (BC) is a fatal malignancy with considerable mortality. BC urinary metabolomics has been extensively investigated for biomarker discovery, but few BC blood metabolomic studies have been performed. Hence, a plasma pseudotargeted metabolomic method based on gas chromatography–mass spectrometry with selected ion monitoring (GC-MSSIM) was developed to study metabolic alterations in BC. The analytical performance of the developed method was compared with that of a nontargeted method. The relative standard deviation (RSD) values of 89 and 70.7 % of the peaks obtained using the pseudotargeted and nontargeted methods, respectively, were less than 20 %. The Pearson correlations of 90.7 and 78.3 % of the peaks obtained using the pseudotargeted and nontargeted methods, respectively, exceeded 0.90 in the linearity evaluation. Compared with the nontargeted method, the signal-to-noise ratios (S/N) of 97.9 and 69.3 % of the peaks increased two- and fivefold, respectively. The developed method was fully validated, with good precision, recovery, and stability of the trimethylsilyl (TMS) derivatives. The method was applied to investigate BC. Significant increases in the contents of metabolites involved in, for example, the pentose phosphate pathway (PPP) and nucleotide and fatty acid synthesis were found in the high-grade (HG) BC group compared to the healthy control (HC) group. These differences imply that the activated PPP may regulate BC cell proliferation by promoting lipid and nucleotide biosynthesis and the detoxification of reactive oxygen species (ROS). These results

illustrate that the plasma pseudotargeted method is a powerful tool for metabolic profiling.

使用的岛津仪器：GCMS-QP 2010



代表图片：代谢通路分析

原文网址：https://doi.org/10.1007/s00216-016-9797-0

J. Sep. Sci. 2009, 32, 2281 – 2288

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Peng Gao[2]
Ruiyan Fu[3]
Dawei Yang[1,2]
Lei Zhang[2]
Jing Zhou[2]
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Original Paper

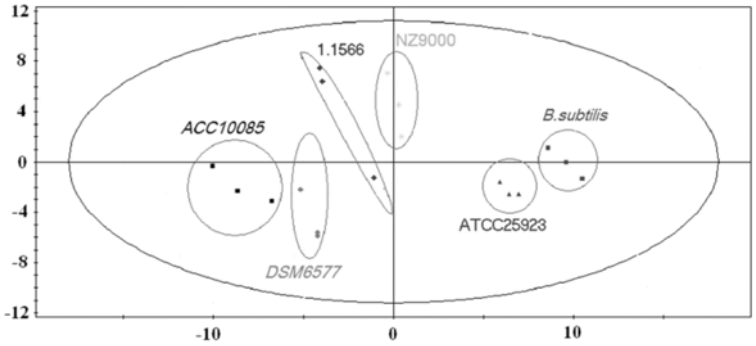
Optimization of a GC–MS metabolic fingerprint method and its application in characterizing engineered bacterial metabolic shift

Metabolomics influences many aspects of life sciences including microbiology. Here, we describe the systematic optimization of metabolic quenching and a sample derivatization method for GC–MS metabolic fingerprint analysis. Methanol, etha-

GC-MS 代谢指纹图谱方法优化及其在表征工程菌代谢迁移中的应用

Metabolomics influences many aspects of life sciences including microbiology. Here, we describe the systematic optimization of metabolic quenching and a sample derivatization method for GC–MS metabolic fingerprint analysis. Methanol, ethanol, acetone, and acetonitrile were selected to evaluate their metabolic quenching ability, and acetonitrile was regarded as the most efficient agent. The optimized derivatization conditions were determined by full factorial design considering temperature, solvent, and time as parameters. The best conditions were attained with N,O-bis(trimethylsiyl) trifluoroacetamide as derivatization agent and pyridine as solvent at 758C for 45 min. Method validation ascertained the optimized method to be robust. The above method was applied to metabolomic analysis of six different strains and it is proved that the metabolic trait of an engineered strain can be easily deduced by clustering analysis of metabolic fingerprints.

使用的岛津仪器：GCMS QP-2010



代表图片：分化的6株菌OSC-PLS得分图（n=3）（R^2=0.405，Q^2=-0.352）

原文网址：https://doi.org/ 10.1002/jssc. 200800727

The Journal of International Medical Research
2009; 37: 1465 – 1471

Investigation of Propofol Concentrations in Human Breath by Solid-phase Microextraction Gas Chromatography–Mass Spectrometry

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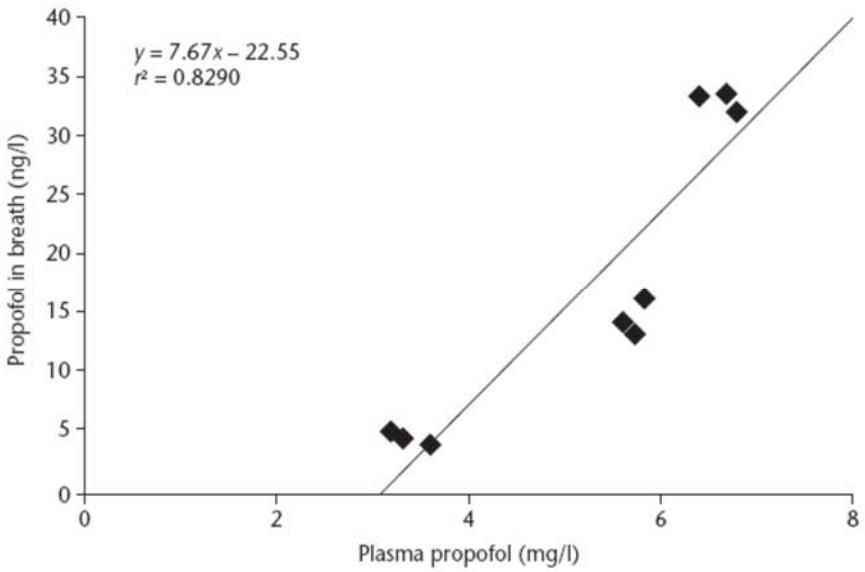
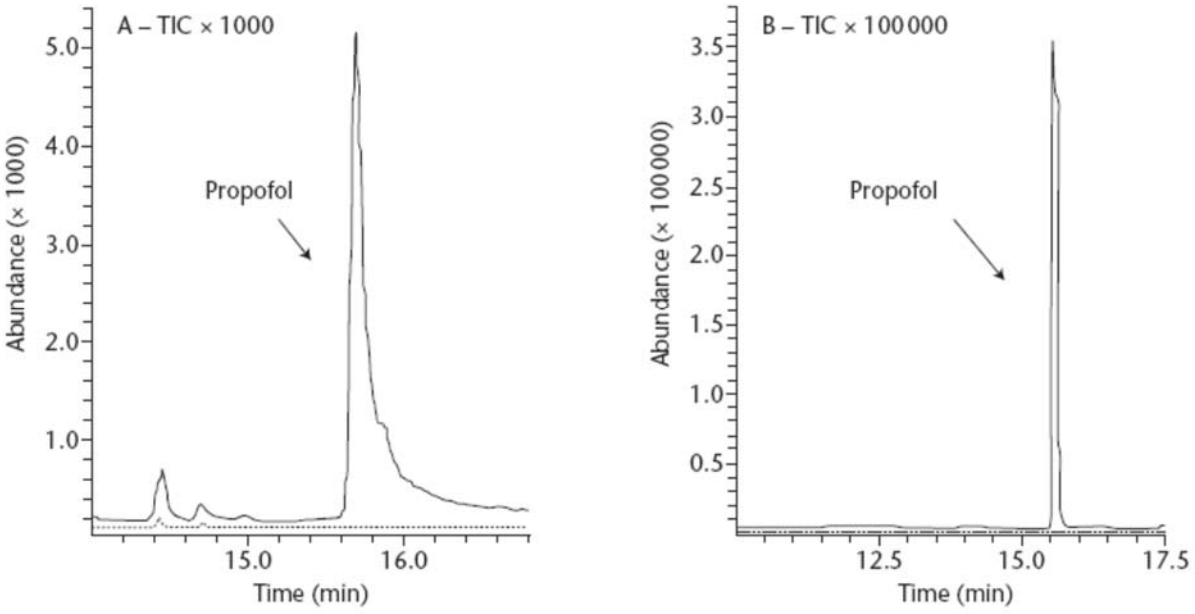
固相微萃取-气相色谱-质谱法测定人呼出气中异丙酚浓度

Propofol has been detected in human breath after being used as an intravenous anaesthetic, and this could provide a noninvasive method for monitoring propofol anaesthesia. The physicochemical properties of propofol allow it to diffuse across the alveolocapillary membrane and to be prepared as a calibration gas. In this study, headspace solid-phase microextraction gas chromatography-mass spectrometry (HS-SPME-GC–MS), coupled with an external standard, was applied to assess propofol levels in the breath and plasma from three subjects under intravenous anaesthesia. Lower quantitation limits were 3.6 ng/l and 0.2 mg/l for propofol analysis in breath and arterial plasma, respectively. Intraday precision and recovery percentages for propofol detection in breath were 4.3-6.7% and 98-108%, respectively, and in plasma they were 3.8-6.1% and 90.1-125.1%, respectively. Propofol concentrations were 4.3-33.5 ng/l in breath and 3.2 – 6.8 mg/l in arterial plasma. A correlation was shown between propofol concentration in breath and plasma. Thus, HS-SPME-GC–MS, coupled with an external standard, could be a reliable and sensitive analytical technique for detecting propofol in breath during anaesthesia.

使用的岛津仪器：GCMS QP-2010



代表图片： 3位病人血浆和呼气中异丙酚浓度。病人呼气和血浆中异丙酚浓度的相关性分析，依据y=Bx+A方程回归计算，r^2=0.8290。



代表图片： 异丙酚（实线）和不给药样品（虚线）的总离子流图（A）呼气（B）病人血浆

原文网址：The Journal of International Medical Research (2009), 37, 1465-1471. https://doi.org/10.1177/147323000903700522

2003 年 1 月 January 2003 | 色 谱 Chinese Journal of Chromatography | Vol. 21 No. 1 76～80

固相微萃取-气相色谱/质谱测定工业废水中痕量有机物的研究

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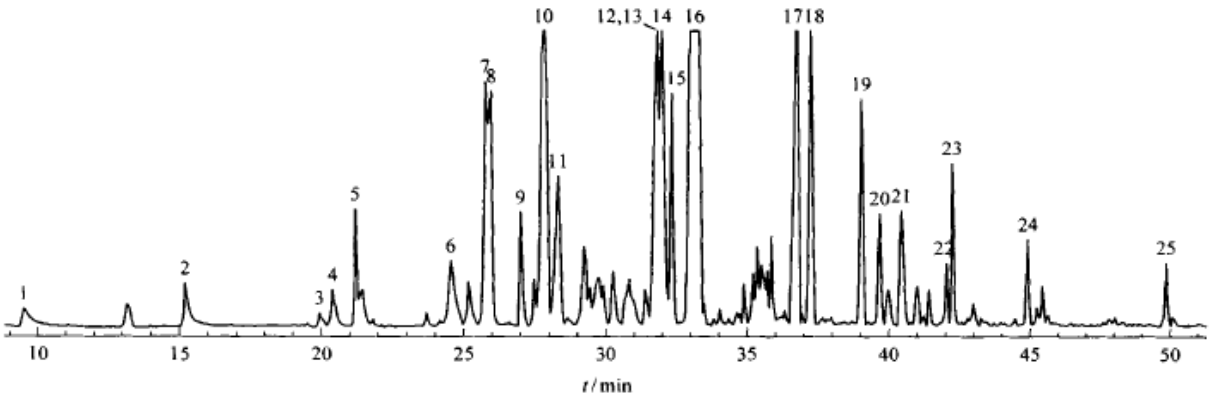
2. 茂名石化乙烯工业公司，广东 茂名 525021）

固相微萃取-气相色谱/质谱测定工业废水中痕量有机物的研究

摘要:采用固相微萃取(SPM E)技术结合气相色谱-质谱(GC/MS)法对石化工业废水中的痕量有机物进行检测和分析。针对废水中存在的几种主要有机物，对影响 SPME 的参数进行了优化。建立的方法在所测的范围内具有良好的线性(相关系数:0.98～1.00)，检测限达 0.3～29.1 μg/L，重复测定的相对标准偏差小于 7%，回收率为 78.6%～125.1 %。采用该方法对某石化工业废水样品中主要存在的 25 种痕量有机物进行测定，结果表明这是一种简便、准确的分析方法，所测得的结果可为废水的治理提供科学依据。

使用的岛津仪器：GC-17A+QP-5000



代表图片：SPME-GC/MS 测定废水样品的总离子流色谱图；

原文网址 ：

https://kns.cnki.net/KCMS/detail/detail.aspx?dbcode=CJFQ&dbname=CJFD2003&filename=SPZZ20030

1019&v=MzA0NzN5L2hVNzNMTmozUmRMRzRIdExNcm85RWJZUjhlWDFMdXhZUzdEaDFUM3FUcldNMU

ZyQ1VSTE9lWnVSdkY=

2003 年 11 月 November 2003 | 色 谱 Chinese Journal of Chromatography | Vol. 21 No. 6 590～592

反相高效液相色谱法测定血浆中的辅酶 Q_{10}

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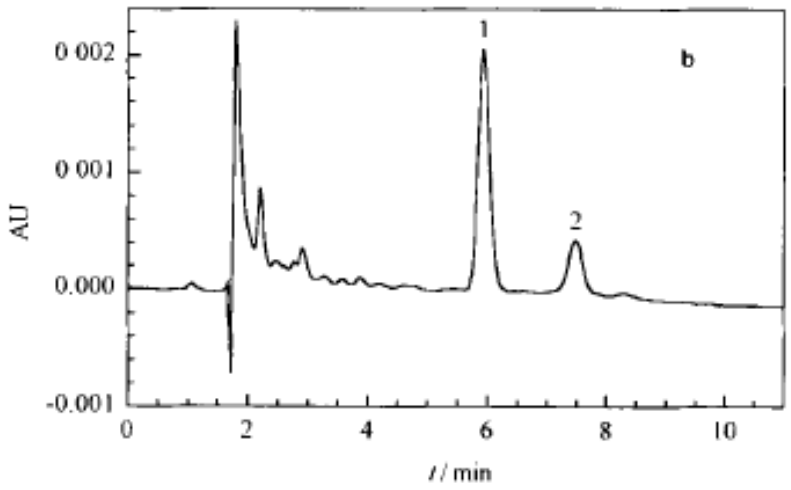
（1. 大连理工大学化工学院，辽宁 大连 116023；2. 中国科学院大连化学物理研究所 国家色谱研究分析中心，辽宁 大连 116011；3. 大连市中心医院，辽宁 大连 116033）

反相高效液相色谱法测定血浆中的辅酶 Q10

摘要：建立了一种检测血浆中辅酶 Q10 含量的高效液相色谱法。血浆经甲醇脱脂蛋白后，以正己烷萃取，萃取液依次经硅胶柱净化、C18 柱固相萃取，再进行高效液相色谱分析。色谱柱为 Hypersil ODS_2 柱(5 μm；150 mm×4.6 mm i.d.)，以异丙醇-甲醇(体积比为 45∶55)溶液作流动相，辅酶 Q9 作内标，检测波长为 275 nm。在 0.1～50.0 mg/L 质量浓度范围内，辅酶 Q10 与辅酶 Q9 的峰面积比与相应 CoQ10 的质量浓度呈良好的线性关系(r2=0.999)，血浆中辅酶 Q10 的检测限为 0.03 mg/L(S/N=3)，加标回收率为 96%～98%，方法重现性好(RSD<3 %)。用此法测定正常人血浆中辅酶 Q10 的含量水平，结果令人满意。

使用的岛津仪器：LC-10ATvp



代表图片：血浆样品的色谱图；

原文网址 ： https://doi.org/10.3321/j.issn:1000-8713.2003.06.014

ANALYTICAL SCIENCES JUNE 2001, VOL. 17

Notes

Method for the Analysis of 8-Hydroxy-2′-deoxyguanosine in Urine by Gas Chromatography

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**National Chromatographic Research and Analysis Center, Dalian Institute of Chemical Physics, Chinese Academy of Science, Dalian 116011, China

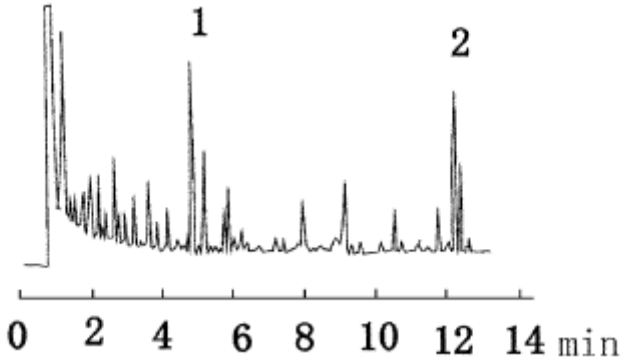
尿液中 8-羟基-2′-脱氧鸟苷的气相色谱分析方法

Oxidative damage to DNA is considered to be important in mutagenesis, carcinogenesis and the ageing process. Of about 20 major oxidative DNA adducts that have been characterized, 8-hydroxy-2′-deoxyguanosine (8OHdG) has received considerable attention due to its demonstrated mutagenic potential, which has been shown to cause the GC→TA transversion. It is worth mentioning that many GC→TA transversions have been detected in p53 genes (an important carcinogenic gene) isolated from human lung and liver cancers. This result suggests that 8OHdG may be a good marker or carcinogenesis. Since oxidative damage to DNA is a continuous process, intracellular repair mechanisms have evolved to avoid the rapid and lethal accumulation of oxidative NDA damages. In the case of 8OHdG, the experimental evidence indicates that mammalian cells possess nonspecific (excinucleases) and specific (glycosylases) DNA repair enzymes that can excise this modification, which is subsequently excreted in urine as nucleoside or free base without any further metabolism. The determination of urinary 8OHdG had thus been proposed as a noninvasive assay of in vivo oxidative DNA lesions. Loft *et al.* have reported that smokers excrete 50% more urinary 8OHdG than nonsmokers. This indicates a 50% increased rate of oxidative DNA damage from smoking. The urinary 8OHdG levels in patients with gynecologic cancer and non-insulin-dependent diabetes mellitus are also significantly higher than that in control subjects.

At present, several methodologies for measuring 8ODhG have been developed, including high-

performance liquid chromatography (HPLC) with electrochemical (EC) detection and gas chromatography/mass spectrometry (GC/MS). Although HPLE-EC is a highly sensitive method for the analysis of 8OHdG, the applicability of this method is not as general as that expected from a suitable and sensitive GC/MS method. To the best of our knowledge, here have been a few reports concerning the analysis of urinary 8OHdG by GC/MS. However, for a method before GC analysis of the products of oxidative DNA damage can be accomplished, these compounds must first be converted to volatile derivatives with suitable chromatographic properties. Among various derivatives of nucleoside, the trimethylsilyl (TMS) derivative is the most suitable to work for the derivatization of nucleosides when compared to other derivatives. Although there are a few reports of studied concerning the best reaction condition for the derivatization of normal nucleosides with TMS reagents, these investigations were carried out at the milligram level. Here we report on an optimization of the derivatization procedure while focusing on sub-microgram levels of 8OHdG with TMS reagents, bis(trimethylsilyl)trifluoroacetamide(BATFA). An optimal method is established to analyze urinary 8OHdG by GC and a single-step solid-phase extraction. This method had been successfully applied to the detection of 8OHdG in spike urine. In general, the results show that it is possible to provide a noninvasive assay for an indirect measurement of oxidative DNA damage.

使用的岛津仪器：GC-17A+QP-5000



代表图片：尿液加标的气相色谱图

原文网址 ： https://doi.org/ 10.2116/analsci.17.779

第 29 卷　　分析化学（FENXI HUAXUE）　研究简报　　第 12 期
2001 年 12 月　　Chinese Journal of Analytical Chemistry　　1394～1397

研 究 简 报

人尿中 8-羟基脱氧鸟苷的气相色谱分析方法

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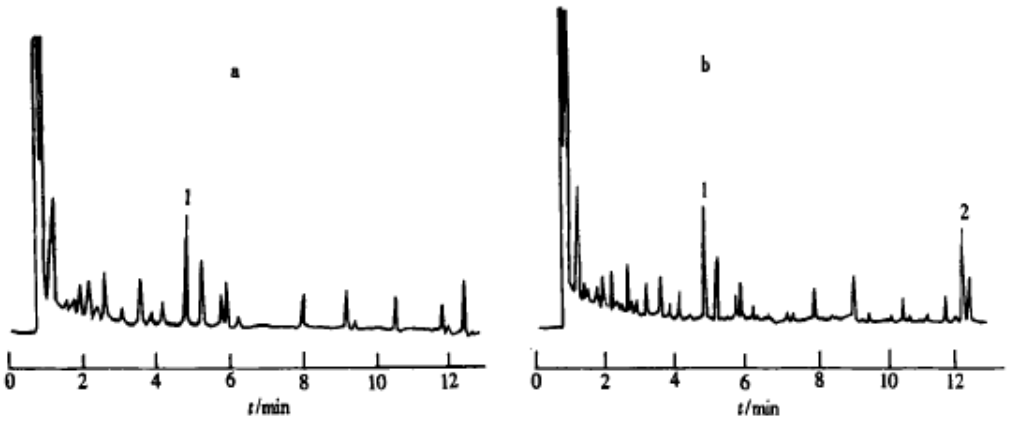
人尿中 8-羟基脱氧鸟苷的气相色谱分析方法

摘要：报道了人尿中脱氧核糖核酸(DNA)氧化损伤产物8-羟基脱氧鸟苷的气相色谱分析方法。采用固相萃取和衍生化前处理步骤，用色谱保留值及气相色谱/质谱进行定性鉴定，在给定的色谱条件下，尿中的8-羟基脱氧鸟苷能与其他杂质很好地分离，内标法定量。方法的线性范围为0.2～100 μg，FID的检测限为4.56pg/s。分析尿样的相对标准偏差小于8.0%。

使用的岛津仪器：GC-17A+QP-5000



代表图片：空白尿样及加标尿样的气相色谱图

原文网址：　https://doi.org/ 10.3321/j.issn:0253-3820.2001.12.007

第六部分：其他

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journal homepage: www.elsevier.com/locate/ibmb

GC/MS-based metabolomic studies reveal key roles of glycine in regulating silk synthesis in silkworm, *Bombyx mori*

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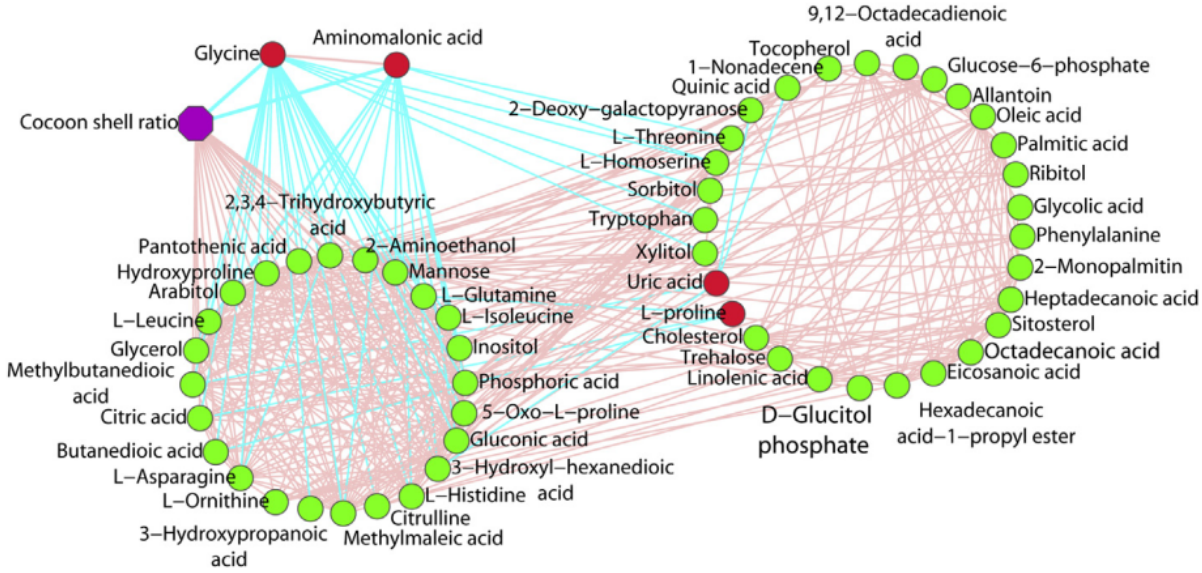
基于 GC-MS 的代谢组学研究显示甘氨酸在调节家蚕（Bombyx Mori）体内蚕丝合成过程中起重要作用

Abstract: Metabolic profiling of silkworm, especially the factors that affect silk synthesis at the metabolic level, is little known. Herein, metabolomic method based on gas chromatography-mass spectrometry was applied to identify key metabolic changes in silk synthesis deficient silkworms. Forty-six differential metabolites were identified in *Nd* group with the defect of silk synthesis. Significant changes in the levels of glycine and uric acid (up-regulation), carbohydrates a *Nd* free fatty acids (down-regulation) were observed. The further metabolomics of silk synthesis deficient silkworms by decreasing silk proteins synthesis using knocking out fibroin heavy chain gene or extirpating silk glands operation showed that the changes of the metabolites were almost consistent with those of the *Nd* group. Furthermore, the increased silk yields by supplying more glycine or its related metabolite confirmed that glycine is a key metabolite to regulate silk synthesis. These findings provide important insights into the regulation between metabolic profiling and silk synthesis.

使用的岛津仪器：GCMS-QP 2010



代表图片：与结茧率相关的代谢物网络图

原文网址：http://dx.doi.org/10.1016/j.ibmb.2014.12.007

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液质联用代谢组学研究多氯联苯和二噁英对大鼠毒性作用*

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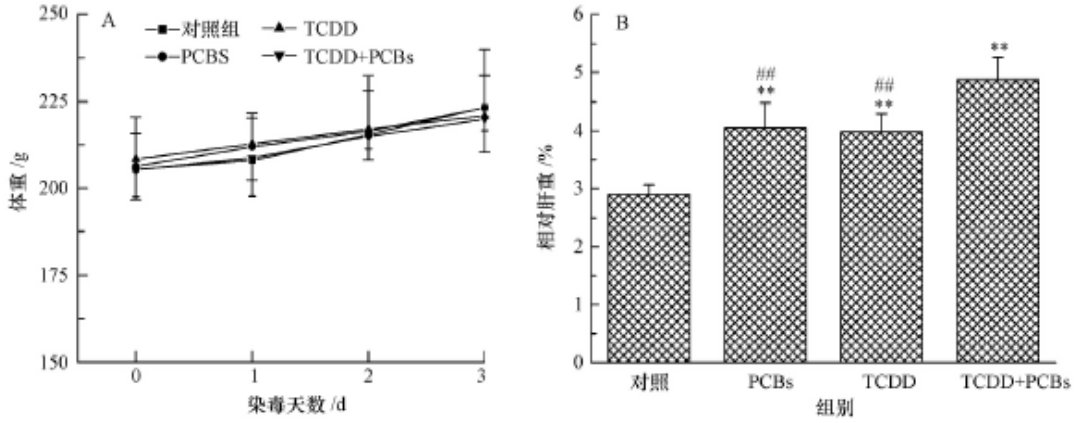
液质联用代谢组学研究多氯联苯和二噁英对大鼠毒性作用

摘要：采用基于液质联用(LC-MS) 的代谢组学方法研究多氯联苯(PCBs) 和2，3，7，8-四氯二苯并-p-二噁英(TCDD) 及联合染毒对大鼠生化代谢的影响。对雄性Sprague-Dawley 大鼠连续3 d 分别灌胃TCDD (10 μg·kg-1) 、PCBs(Aroclor 1254，10 mg·kg-1) 及其混合溶液(10 μg·kg-1TCDD 和10 mg·kg-1 Aroclor 1254) ，采用液质联用法在尿液和血浆样本中分别检测出749 个和343 个色谱峰。PCBs、TCDD 及其联合染毒后引起大鼠生化代谢的显著变化。多变量分析结果表明，毒性的大小是：联合染毒＞ TCDD ＞ PCBs。采用标准物对照、准确质量数、多级质谱碎片离子图和数据库检索的方法，分别在尿液和血浆样本中鉴定出8 个和20 个生物标记物，表明PCBs 和TCDD 能导致免疫系统、肝脏和神经系统障碍、干扰脂代谢。

使用的岛津仪器：LC(UFLC)MS-IT-TOF



代表图片：PCBs、TCDD以及联合染毒后雄性大鼠连续3d的体重（A）和相对肝重（B）变化

原文网址：http://doi.CNKI:SUN:HJHX.0.2013-07-017

The Journal of International Medical Research
2009; 37: 1158 – 1166 [first published online as 37(4) 8]

Intravenous Fentanyl is Exhaled and the Concentration Fluctuates with Time

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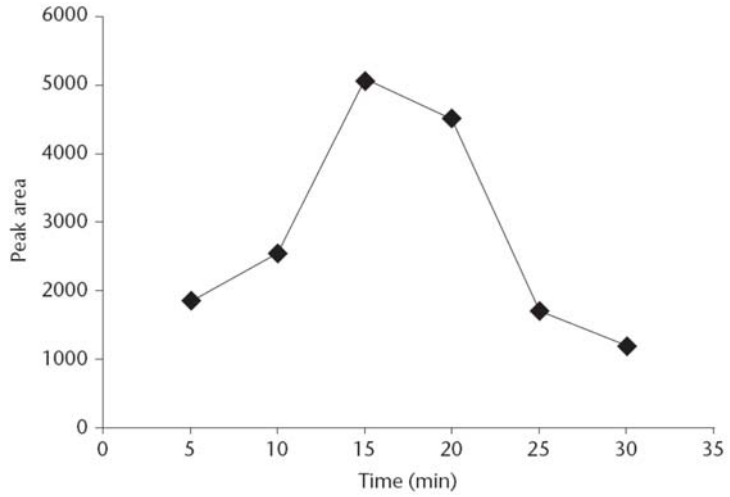
呼气中静脉芬太尼及其浓度随时间的变化

Previous studies have reported that fentanyl is eliminated predominantly by hepatic biotransformation, and that some is eliminated unchanged in urine and stools. No reports have described the elimination of fentanyl via the lungs. In this study, exhaled gas samples from eight anaesthetized patients undergoing cardiac surgery were analysed using solidphase microextraction (SPME) coupled with gas chromatography–mass spectrometry (GC–MS). Results confirmed that fentanyl was exhaled by patients after intravenous administration, that the concentration of exhaled fentanyl fluctuated with time and peak concentrations were reached approximately 15 -20 min after intravenous fentanyl administration. Thus, in addition to hepatic biotrans formation and elimination via urine and faeces, fentanyl is also eliminated unchanged by the lungs. The potential risk to operating theatre personnel from long-term exposure to low levels of exhaled anaesthetic agents following intravenous administration to patients during surgery warrants further research.

使用的岛津仪器：GCMS QP-2010



代表图片：静脉麻醉病人（30 μg/kg 芬太尼）呼出芬太尼的浓度-时间曲线

原文网址： https://doi.org/10.1177/147323000903700421

Microchemical Journal 91 (2009) 149–152

Contents lists available at ScienceDirect

Microchemical Journal

journal homepage: www.elsevier.com/locate/microc

Determination of fentanyl in human breath by solid-phase microextraction and gas chromatography–mass spectrometry

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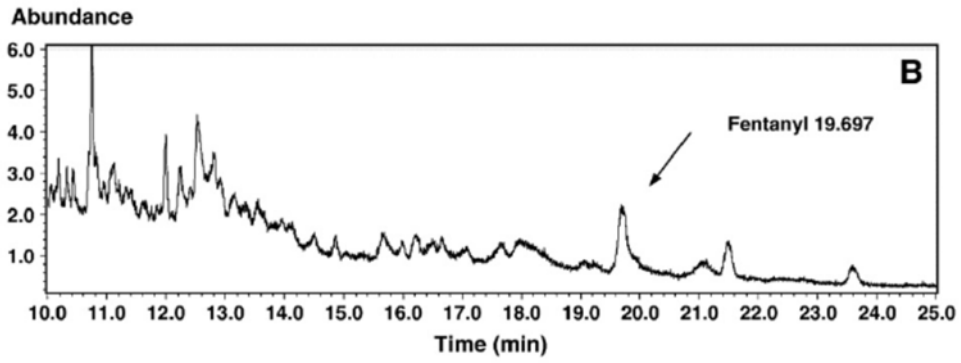
固相微萃取结合气相色谱质谱技术测定人呼出气中的芬太尼

Fentanyl, a kind of intravenous narcotic analgesic, is widely used in clinical anesthesia. As a potential pollution, it was detected in both the air of the cardiothoracic operating room and patients' expiratory circuit. However, whether the fentanyl in patients' expiratory circuit is exhaled by patients is unknown. In this study, breath samples were taken from the expiratory circuits of anesthetic machine linked to the patients who received intravenous fentanyl, a solid-phase microextraction (SPME) coupled with gas chromatography–mass spectrometry (GC–MS) method was developed to detect and quantify fentanyl in breath samples. The parameters influencing adsorption (extraction time, temperature,) and desorption (desorption time) of the analyte on the fiber were investigated and validated for method development. The developed method was proved to be simple, easy, and inexpensive and offer high sensitivity and reproducibility. Linear range was obtained from 0.05 ng/mL to 0.8 ng/mL. The limit of detection was 0.01 ng/mL while an interday precision of less than 12.13% (n=5) could be achieved. Six patients were involved in this study; results showed presence of fentanyl in the breath of patients who received intravenous fentanyl, and fentanyl concentrations in breath varied from 6.00 to 20.89 pg/mL. In conclusion, fentanyl can be exhaled by patients who received intravenous fentanyl.

使用的岛津仪器：GCMS QP-2010



代表图片：选择离子流模式下 0.2 ng/mL 芬太尼典型色谱图

原文网址： https://doi.org/10.1016/j.microc.2008.09.002

Journal of Chromatography B, 871 (2008) 220–226

Contents lists available at ScienceDirect

Journal of Chromatography B

journal homepage: www.elsevier.com/locate/chromb

Phenotype differentiation of three *E. coli* strains by GC-FID and GC–MS based metabolomics☆

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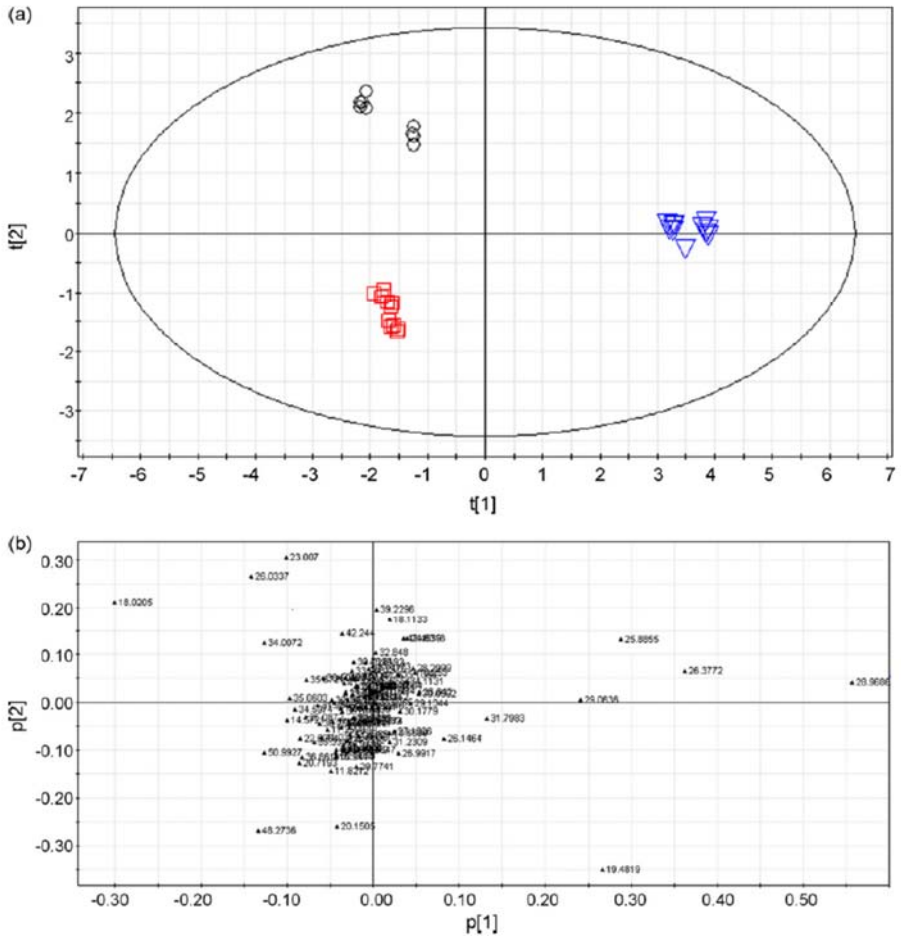
基于 GC-FID 和 GC-MS 的代谢组学区分 3 株大肠杆菌的表型分化

Two mutants of *E. coli* with deletion of *sdhAB* and *ackA-pta* genes respectively and their wild-type strains were subjected to gas chromatography-flame-ionization detection (GC-FID) and gas chromatographymass spectrometry (GC–MS) metabolomics analysis. Intracellular metabolites of the three strains were profiled by GC-FID firstly. Methodological evaluation of the employed platform indicated that the limit of detection ranges were from 0.2 to 12.5 ng for some representative metabolites and the corresponding recoveries were varied from 68.7 to 122.7%. Secondly, multivariable data analysis was applied to the acquired data sets. As expected, the three phenotypes could be easily differentiated, and the perturbed metabolite pools in the genetically modified strains were screened. Lastly, the metabolites playing key roles in the differentiation were further identified by GC–MS. It was confirmed that succinic acid and aspartic acid were similarly affected in the modified strains. But proline content was altered contrarily. Additionally, deletion of *sdhAB* gene also affected the growth property of relevant mutant greatly. The potential mechanism was postulated accordingly.

使用的岛津仪器：GCMS QP-2010



代表图片：基于GC-FID数据的菌株wild-type（○）, ackA-pta （□）和sdhAB（▽）的PCA得分图（a）和载荷图（b）

原文网址：https://doi.org/ 10.1016/j.jchromb.2008.06.031

第 36卷 分析化学 (FENXI HUAXUE) 研究报告 第 8期
2008年 8月 Chinese Journal of Analytical Chemistry 1024 ~ 1028

生物催化生成对苯二甲酸微生物协同作用的代谢途径分析

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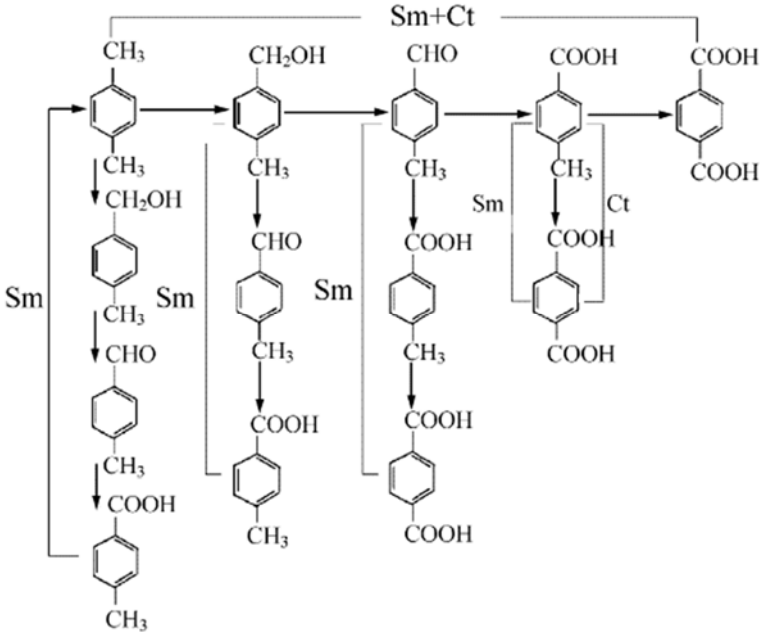
[1](大连工业大学, 大连 116034)
[2](中国科学院大连化学物理研究所国家色谱研究分析中心, 大连 116023)

生物催化生成对苯二甲酸微生物协同作用的代谢途径分析

摘要:建立了对苯二甲酸、对甲基苯甲醛、对甲基苯甲醇、对甲基苯甲酸的高效液相色谱分析方法。采用 Hypersil SAX 阴离子交换柱，流动相为 2.5 mol/L$NH_4H_2PO_4$(含 10%乙腈)，pH4.32，流速 0.8 mL/min，柱温 30 ℃，紫外检测波长为 254 nm。在此色谱条件下，各组分在 7 min 内得到很好地分离，回收率符合测定要求。运用本方法测定了睾丸酮丛毛单胞菌和嗜麦芽窄食单胞菌生物催化生成对苯二甲酸不同发酵时间发酵液中主要代谢物含量。同时，采用 GC-MS 方法检测了有机酸、氨基酸、糖及长链脂肪酸等胞内代谢物，结合 HPLC 和 GC-MS 检测结果，分析了嗜麦芽窄食单胞菌和睾丸酮丛毛单胞菌协同作用催化对二甲苯生成对苯二甲酸的代谢途径。

使用的岛津仪器：GCMS-QP2010，UV-2450



代表图片： 两株菌协同作用由PX生成PTA的代谢途径；

原文网址:

https://kns.cnki.net/KCMS/detail/detail.aspx?dbcode=CJFQ&dbname=CJFD2008&filename=FXHX20080

8005&v=MTExMTFNcDQ5RllZUjhlWDFMdXhZUzdEaDFUM3FUcldNMUZyQ1VSTE9lWnVSdkZ5L2xXcnJLSX

pYRGRyRzRIdG4=

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