功能代谢组学在中药抗抑郁机制研究中的策略及应用

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摘要: 抑郁症 (depression) 是一种常见的情感障碍类疾病, 在全世界范围内严重影响着人们的生命健康。抑郁症发病机制复杂, 抗抑郁中药因其多成分、多途径、多靶点的作用方式, 具有良好的治疗效果。目前, 中药抗抑郁机制尚未完全阐明, 但可以明确的是, 抑郁症与代谢健康有着十分紧密的联系。因此, 为深入挖掘中药抗抑郁机制, 本文从代谢角度出发, 提出了基于功能代谢组学策略的中药抗抑郁机制研究思路, 即借助多组学联合分析技术探析抑郁症潜在生物标志物, 同时开展抗抑郁中药功能性分子的研究, 利用分子生物学技术精确捕获抑郁症特征代谢分子和抗抑郁中药功能性分子之间的分子相互作用, 确定有效的药物靶点, 进一步阐明抑郁症代谢紊乱所涉及的生化功能和相关机制。本文系统综述了功能代谢组学在中药抗抑郁机制中的研究策略及应用, 阐述了功能代谢组学的核心价值, 整理了近几年抗抑郁中药的研究现状和热点问题, 以期借助功能代谢组学, 为中药抗抑郁机制研究提供新方法、新思路。

关键词: 抑郁症; 中药抗抑郁机制; 功能代谢组学; 研究策略

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Research strategies and applications of functional metabolomics in anti-depressive mechanisms of traditional Chinese medicine

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Abstract: Depression is a common emotional disorder that seriously affects people's life and health all over the world. The pathogenesis of depression is complex, and traditional Chinese medicine (TCM) for antidepressants has a good therapeutic effect because of its multi-component, multi-pathway, and multi-target action mode. At present, the anti-depressive mechanism of TCM has not been fully clarified, but it is clear that depression is closely related to metabolic health. Therefore, in order to further explore the anti-depressive mechanism of TCM, this paper proposes research strategies on the anti-depressive mechanism of TCM based on functional metabolomics from the perspective of metabolism, the potential biomarkers of depression are analyzed with the help of multi-omics combined analysis technology, and the functional molecules of TCM for antidepressant are studied. Molecular biology techniques are used to accurately capture the molecular interactions between biomarkers of depression and functional compounds, which identify effective drug targets and further elucidate the biochemical functions and related mechanisms involved in depression metabolic disorders. This paper systematically reviews the research strategies and applications of functional metabolomics in the anti-depressive mechanisms of TCM, expounds on the core value of functional metabolomics, and summarizes the current research status and hot issues of TCM for antidepressants in recent years, providing new methods and new ideas for the study of mechanisms of TCM with the help of functional metabolomics.

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Key words: depression; anti-depressive mechanisms of traditional Chinese medicine; functional metabolomics; research strategy

抑郁症 (depression) 是一种常见的情感障碍类疾病, 全世界有5%的成年人患有抑郁症。研究表明, 抑郁症与一系列躯体健康问题密切相关, 如心脑血管疾病、恶性肿瘤、代谢内分泌疾病、感染性疾病等[1]。抑郁症发病机制复杂且目前尚未完全阐明, 相应的治疗方法仅对部分人有效。值得一提的是, 国外一项长达27年的研究表明, 抑郁症与代谢健康有着十分紧密的联系[2]。中药作为中国的国粹和瑰宝, 其优良的治疗效果在长期的临床实践中得到了证明[3]。中医将抑郁症归入“郁证”的范畴, 包括肝气郁证、肝郁气滞证、肝郁脾虚证和心脾两虚证四种常见的中医证型。目前已有大量相关研究证实了治疗郁证的常用中药复方与代谢物的关系, 例如, 柴胡疏肝散能够部分调控平抑肝气郁证中发生异常的代谢产物, 对肝气郁证和肝郁气滞证大鼠代谢紊乱有一定的恢复作用[4]; 逍遥散干预慢性温和不可预知性应激 (chronic unpredictable mild stress, CUMS) 大鼠后, 其盲肠组织的代谢特征发生明显变化, 有效改善肝郁脾虚型大鼠抑郁样行为[5]; 归脾汤能够提高血清胃泌素, 有效改善睡眠障碍, 对心脾两虚证患者效果显著[6]。中药通过多成分的合理配伍, 多途径地协同作用于疾病各个靶点, 发挥整体调节的作用, 尽可能地规避了西药治疗效果差、耐受性不强等不良反应。疗效是中医生存和发展的关键, 难点在于如何建立一种生物学语言科学地解释其疗效[7]。此外, 中药抗抑郁机制研究目前尚未完善, 包括抗抑郁中药的组分配伍规律和药物作用机制, 有待发现新的研究策略进行生物学研究印证。

代谢是指生物体通过一系列的生化反应维持机体正常运转的过程, 代谢异常则会引起内源小分子代谢物改变, 成为抑郁症、癌症、衰老等慢性病的重要原因[8,9]。代谢组学作为继基因组学和蛋白质组学后的一门新兴组学, 它在测量生物系统的化学变化方面具有一定的优势, 其中, 液质联用技术 (liquid chromatography-mass spectroscopy, LC-MS) 被认为是选择性、灵敏度和重复性最好的分析技术之一[10]。在以往的研究中, 中医的“方剂”理论早已与代谢组学有着密切的联系[11]。代谢组学利用质谱技术, 通过检测差异性内源小分子代谢物, 证明了在检测未来的疾病事件和干预结果方面的效用, 拓展了现代手段在中药安全性评价中的应用[12,13], 从“整体”的层次揭示了中药组分的配伍规律, 科学地解释了中药的药效物质基础和药效机制, 成为研究复杂系统理论和中药质量评价的利器[14-17]。迄今为止, 代谢组学在中药抗抑郁机制研究中的应用已经较为全面, 但仍面临着代谢物和代谢通路数量较少, 从而影响检测结果的情况。此外, 由于以代谢组学为基础的研究很大一部分仅停留于表型数据, 未能与其他功能基因组信息进行充分整合, 在定义代谢疾病检测策略和致病机制方面的全部潜力仍有待挖掘[18,19]。在描述生物学功能的基础上, 有必要寻求新的方法验证差异代谢物相关的蛋白、酶及基因, 自下而上地系统分析病理生理现象。

因此, 本文提出了功能代谢组学在中药抗抑郁机制中的研究新策略, 聚焦于功能性分子的精准定性和功能开发。通过早期分子诊断, 鉴定出抗抑郁中药的功能性分子, 深度解析中药抗抑郁机制, 从而发现新的靶点, 助力抗抑郁新药开发。综上所述, 应用功能代谢组学的方法研究中药抗抑郁机制, 并加强与其他组学的沟通, 有助于进一步探寻抑郁症的病理生理学靶点, 以及阐释和挖掘抗抑郁中药作用机制[20,21]。

1 功能代谢组学的基本内涵

随着人们对代谢物功能的认识不断提高, 以快速发展的代谢组学技术为基础, 结合分子生物学技术和临床试验, 发展了功能代谢组学[22]。在国外研究中, 功能代谢组学首次被定义为从生物标志物的发现到代谢的重编程[23], 在国内已被应用于生物医药领域研究[12]。如图1所示, 功能代谢组学基于代谢组学表型数据, 通过体内体外实验和关键差异性内源代谢物的验证, 采用单因素分析和多元数据建模进行综合分析和鉴别, 打破了代谢组学的困境, 克服了传统代谢组学主要依靠文献解释生化功能的局限性, 在定义疾病机制和研究生物学功能上有了新的突破[24]。为进一步探究致病靶点, 功能代谢组学通常借助流式细胞术 (flow cytometry, FCM)、蛋白质印迹法 (Western blotting, WB)、反转录聚合酶链反应 (reverse transcription-polymerase chain reaction, RT-PCR) 等分子生物学技术。功能代谢组学研究通过这些平台的结合, 经过临床验证, 有助于多角度了解代谢产物的关键功能。从发现差异代谢物到表征代谢物功能的跨越, 功能代谢组学将在尖端生化技术的帮助下书写代谢组学的新篇章, 揭示修饰代谢的详细分子功能和相关调节机制[23]。

2 中药抗抑郁机制

2.1 中药抗抑郁机制的研究现状

抑郁症在临床上是比较常见的一组综合症状, 存

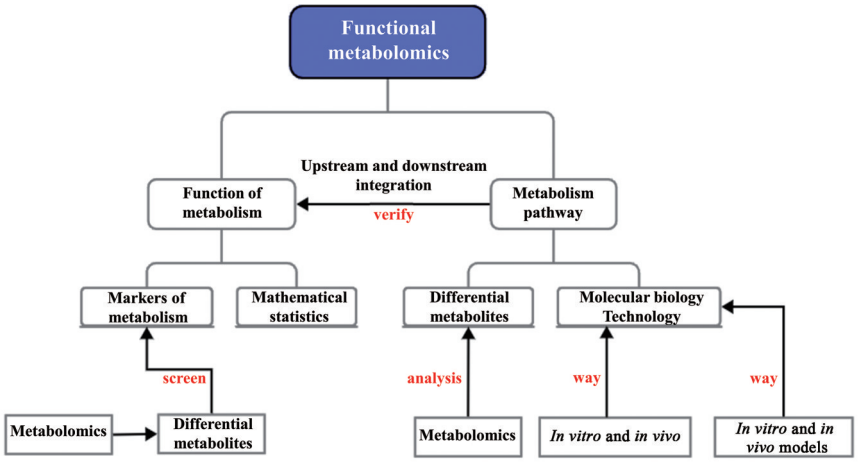

Figure 1 The basic framework for the study of functional metabolomics

在多种潜在的机制, 不可能在所有患者中确定导致或阻止抑郁的特定因素。因此, 更好的治疗方法是应用个性化的诊疗, 有利于减轻抑郁症状, 纠正引发抑郁症状的身体功能障碍[25]。中药不仅能显著地重新平衡代谢通量的动态, 而且能通过恢复关键代谢产物和代谢途径的功能, 引发代谢网络的重组, 安全性和耐受性得到了有效的保障[26,27]。如图2所示, 近几年中药抗抑郁机制的研究主要集中于: ① 调节单胺类神经递质: 如增加多巴胺、5-羟色胺、去甲肾上腺素等神经递质的分泌[28,29]; ② 调节炎性因子: 通过降低促炎性细胞因子如肿瘤坏死因子α和白细胞介素1的活性, 从而抑制吲哚胺2,3-双加氧酶过度表达, 以及抑制NLRP3炎症小体的活化, 降低炎性因子的水平[30]; ③ 调节神经营养因子: 如促进脑源性神经营养因子 (BDNF) 的表达[31]; ④ 调节肠道菌群微环境[32]; ⑤ 调节下丘脑−垂体−肾上腺轴; ⑥ 改善能量代谢障碍等。在这些研究中, 各种机制彼此作用、相互联系。例如, 炎症介质水平升高可降低BDNF的表达[33]。

2.2 中药抗抑郁机制的研究瓶颈与对策

目前, 中药由于不良反应较小, 被推荐用于轻度至中度抑郁症的专科治疗[34]。但是, 中药功能性生物标志化合物却难以表征, 多组分的配伍规律复杂。中药抗抑郁机制研究大多集中在已确定抑郁症致病因子的描述, 如单胺类神经递质的分泌或BDNF等蛋白表达情况, 未能深层次探寻抑郁症潜在病理生理学靶点, 以及阐明抑郁症复杂的发病机制和如何定性分析中药功能组分的药理作用。代谢组学在中药抗抑郁机制方面的已有研究多停留于表型数据, 没有深度解析代谢物分子的功能和相关机制。有研究表明, 通过功能代谢组学的方法, 更有利于确定中药关键组分, 捕获中药衍生功能化合物与疾病失调的生化反应之间复杂的分子相互作用, 从而确定疾病的系统代谢靶点, 诠释治疗机制[35]。例如, 采用转录组学技术、蛋白组学技术、多组学数据整合分析方法, 明确逍遥散在“代谢物−基因−蛋白−酶”多层次抗抑郁的分子机制, 通过调节CUMS大鼠谷氨酸能突触通路和氧化磷酸化通路发挥抗抑郁作用[36]。依此可以看出, 功能代谢组学方法在中药抗抑郁机制研究中具有重要价值, 它科学地阐释了中医药“辨证论治”的理论基础和对抗代谢类疾病的“系统”作用, 为揭示抗抑郁中药的不同方面, 如识别功能性化合物、药理作用和治疗机制上作出了卓越贡献。

3 功能代谢组学在中药抗抑郁机制中的研究策略

功能代谢组学的研究策略是基于功能性分子的研究, 或基于差异性代谢物所在代谢途径的研究。功能代谢组学通过精确捕获抑郁症特征代谢分子和抗抑郁中药功能性分子之间的分子相互作用, 具有表征抗抑郁中药“系统”治疗作用的能力, 高效地识别并阐明了抗抑郁中药功能化合物的药理作用以及相关机制[37]。本文基于功能代谢组学研究策略, 通过对抗抑郁中药功能性分子的系统性研究, 构建出一套“抗抑郁中药−生物标志物−功能性成分−抑郁症新靶点及潜在代谢通路-抗抑郁中药作用新机制”的研究框架。

3.1 抗抑郁中药功能性分子的定义

功能代谢组学策略在中药抗抑郁机制研究中最重要的价值即是精准发现抗抑郁中药的功能性分子。功能性分子可分为三类: 第一类分子是表型分子 (phenotypic metabolites), 用于抑郁症的分子诊断或分型; 第二类分子是机制分子 (mechanistic metabolites), 用于理解代谢产物的生物合成与代谢调控, 以及理解抑郁症的发病机制; 第三类分子则是治疗分子 (drug molecules), 可以用于研发抗抑郁新药的分子。

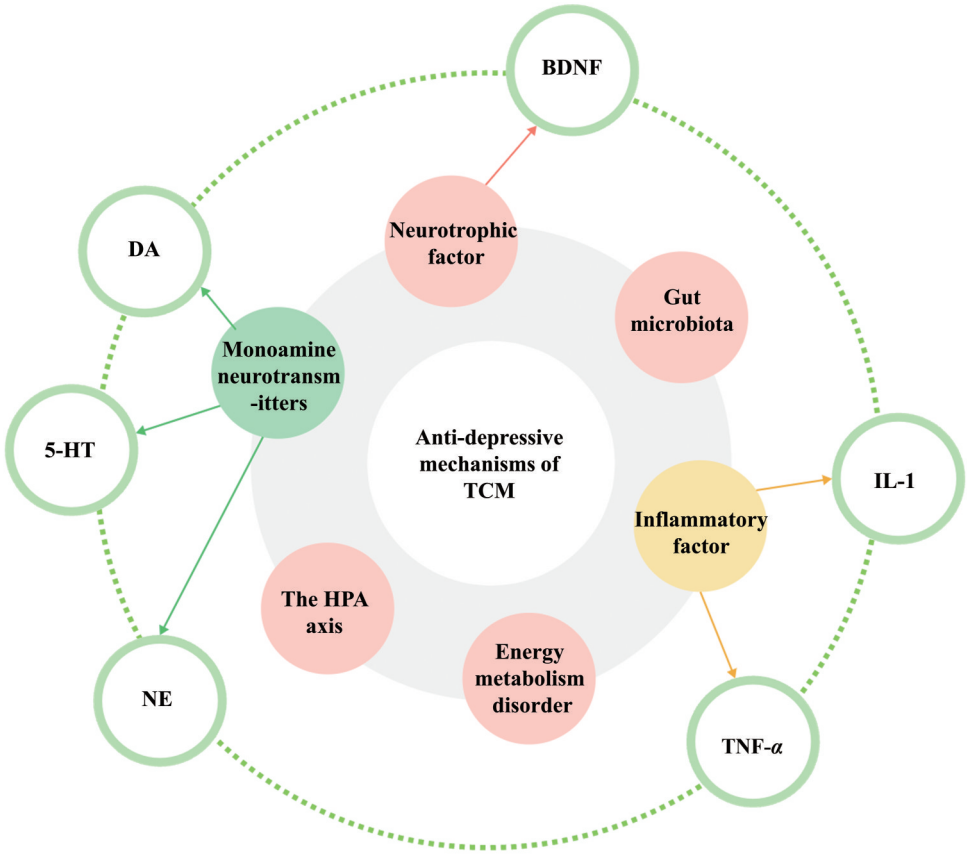

Figure 2 Anti-depressive mechanisms of traditional Chinese medicine. DA: Dopamine; 5-HT: 5-Hydroxytryptamine; NE: Norepinephrine; TNF-*α*: Tumor necrosis factor-*α*; IL-1: Interleukin-1; BDNF: Brain-derived neurotrophic factor

3.2 抗抑郁中药功能性分子的精准发现

为了精准发现抗抑郁中药的功能性分子, 通常有两个标准: ① 精准定性。对抗抑郁中药的功能分子精准鉴定; ② 功能开发。利用分子生物学技术理解和开发代谢物的功能。如图 3 所示, 通过对功能性分子的精准发现, 该研究策略实现了抑郁症的早期诊断, 以及鉴定有效的药物靶点和理解抑郁症的发病机制, 最终促进了有效的抗抑郁新药研发。

3.2.1 抗抑郁中药功能性分子的精准鉴定 功能代谢组学在中药抗抑郁机制中的研究策略如图 3 所示, 首先, 由靶向代谢组学方法对抗抑郁中药主要化学成分进行首次表征, 用于精确识别疾病生物标志物及其相关的修饰代谢通路[38]。然后, 利用靶标发现技术, 如蛋白质组学, 确定抑郁症的潜在蛋白质靶点。之后, 采用高通量筛选技术, 捕获可能具有抗抑郁作用的候选化合物。最后, 通过体内体外实验和 RT-PCR 等分子生物学技术, 进一步识别具有功能蛋白质和基因的系统代谢靶点, 以及验证抗抑郁中药的功能性分子[19]。

3.2.2 抗抑郁中药功能性分子的功能开发 将功能代谢组学的方法应用于中药抗抑郁机制研究中, 即靶向代谢组学与蛋白质组学和功能基因组学相结合, 发展明确的功能代谢组学方法, 进一步识别具有功能蛋白质和基因的系统代谢靶标, 从原因、结果两个层次揭示生物“系统”的变化, 把握由代谢紊乱或失调导致的发病规律, 阐明上下游关联的生物机制, 从而可以精确识别功能性分子和系统代谢靶点, 形成一套“抗抑郁中药-生物标志物-功能性成分-抑郁症新靶点及潜在代谢通路-抗抑郁中药作用新机制”的研究新策略, 进一步发掘出抗抑郁中药的治疗潜力[37]。总之, 通过功能代谢组学的研究, 有助于揭示抗抑郁中药功能性成分的药理作用和治疗机制, 实现组织精度的功能代谢物的精准动态捕获、可视化表征和有效分子合成调控操纵, 从而为抗抑郁新药的发现和开发提供了重要参考[39]。

4 功能代谢组学在中药抗抑郁机制中的应用

由于中医诊断的复杂性, 强调机体的整体性和环境对机体内部动态平衡的影响, 抗抑郁中药组合种类繁多, 配伍规律难以阐明, 难以对不同方剂和单味中药的优劣下定论。应用功能代谢组学, 通过研究功能性分子以及借助分子生物学技术验证, 能够优化抗抑郁中药配伍机制。中药的长期安全性、用药过量的影响

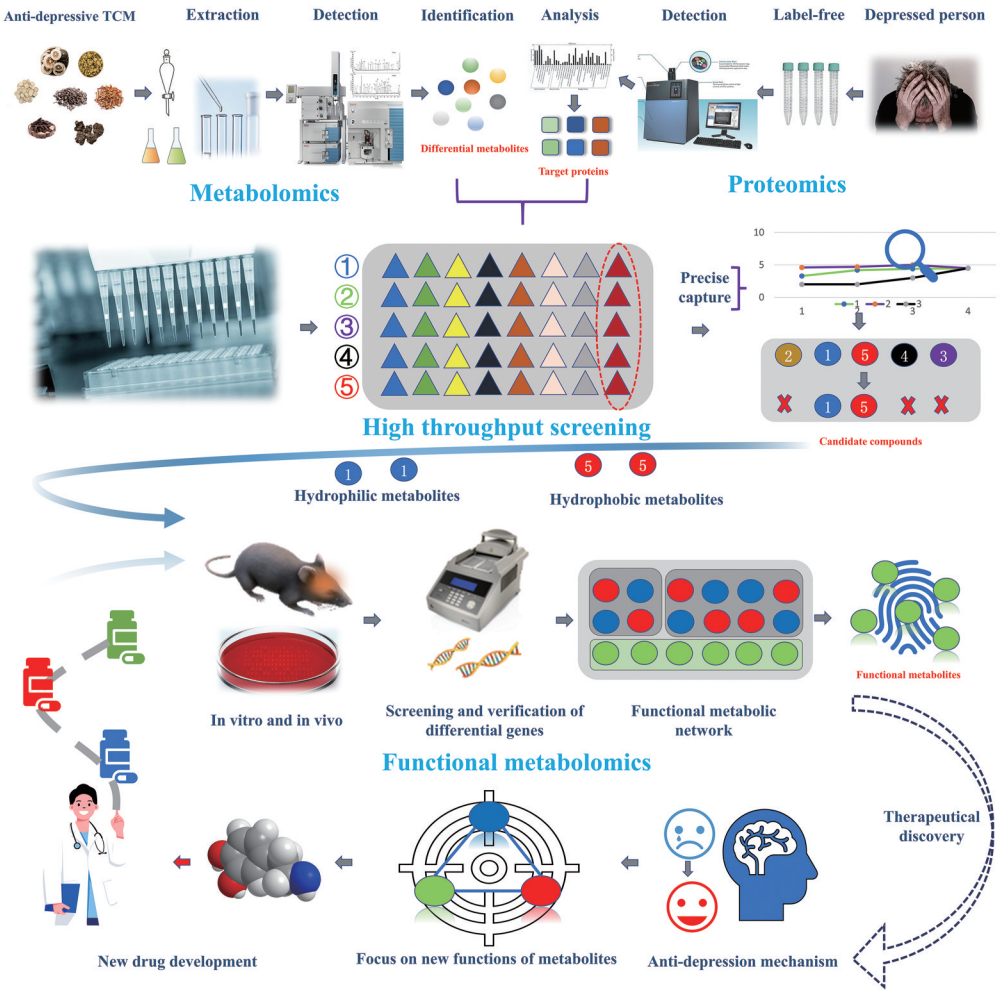

Figure 3 Research strategies of functional metabolomics in the anti-depressive mechanisms of traditional Chinese medicine

还有待考证。功能代谢组学是一种有效的评价方法，能够为中药抗抑郁机制的有效性和安全性提供重要依据。

4.1 功能代谢组学在抗抑郁中药有效性评价中的应用

本文检索出十种抗抑郁高频中药复方，见表1[40-68]，总结了抗抑郁中药成分配伍规律和中药复方多靶点多途径的抗抑郁机制。运用功能代谢组学的方法，通过检测差异性代谢物进一步找到生物标志物和潜在治疗靶点，突破了代谢组学停留于表型数据和功能性描述的困境，对抗抑郁中药多靶点多途径的治疗机制有了更深层次的理解，且具有高预测性，高整体性，实现了代谢物到关联基因/蛋白/酶的有机整合。由该种方法产出结论，多个方面地阐明了代谢类疾病背后的生化意义：① 应用功能代谢组学优化抗抑郁中药配伍机制。例如，越鞠丸全方都有一定的抗抑郁活性，但抗抑郁活性成分可能主要存在于苍术、川芎2味药材之中[69]。此外，从表1[40-68]可以看出，白芍和柴胡在不同的中药方剂中均有广泛的应用[70]。采用基于LC-MS的代谢组学方法结合16S rRNA基因测序技术，研究柴胡单方对CUMS大鼠肠道微生物群和代谢产物的影响，证实了柴胡可显著增加海马BDNF的含量。② 应用功能代谢组学发现抑郁症代谢通路，挖掘抗抑郁作用的潜在靶点。例如，基于肠道代谢组学研究，筛选出16个与柴胡抗抑郁作用相关的生物标志物，发现涉及初级胆汁酸生物合成、牛磺酸代谢、乙醛酸和二羧酸代谢3个代谢途径[71]。③ 应用功能代谢组学精准辨识功能性分子表型，筛选潜在生物标志物。例如，在抗抑郁中药复方逍遥散的研究中，发现草酸和硬脂酸的结合有望作为诊断生物标志物[72]。通过接受者操作特性曲线分析和Pearson相关分析，进一步筛选出*L*-异亮氨酸、癸二酸和尿囊素作为与传统中药美丽崖豆藤疗效相关的潜在药效学生物标志物[73]。④ 应用功能代谢组学识别功能蛋白质和基因的系统代谢靶点，实现功能代谢物的精准调控。例如，对养心氏片进行蛋白组学-代谢组学整合分析后，通过荧光定量PCR验证蛋白质组学结果，发现了养心氏片显著纠正神经肽Y的含量，起到与

Table 1 Application of functional metabolomics in the evaluation of the effectiveness of anti-depressive traditional Chinese medicine (TCM). Glu: Glutamic acid; AVP: Arginine vasopressin; TRH: Thyrotropin-releasing hormone; GABA: Gamma amino butyric acid; Il-6: Interleukin-6; Il-18: Interleukin-18

TCM compound	Key component	Detection strategy	Biomarker	Antidepressant mechanism	Ref.
Xiaoyao San	Bupleurum, atractylodes, white peony, *etc*.	Based on stable isotope-resolved metabolomics, cell metabolomics, brain tissue metabolomics technology strategy.	Oxalic acid and stearic acid.	Play an antidepressant role through related metabolites that regulate the energy metabolism, the synthesis of neurotransmitters, and the metabolism of the intestinal flora.	[40-42]
ChaihuShugan Powder	Bupleurum, peony, orange peel, *etc*.	Based on molecular biological techniques, such as metabolomics, ELISA and western blotting.	5-HT, DA and NE.	Play an antidepressant role by regulating the secretion of neurotransmitters and neurotrophic factors in the brain.	[43-45]
ZuoguiJiang-tangJieyu For-mulation	Astragalus, wolfberry, cooked rehmannia, *etc*.	Based on western blotting and other molecular biological techniques.	Glu, 5-HT, DA.	Play an antidepressant role by improving energy metabolism disorders and regulating the secretion of monoamine neurotransmitters.	[46-48]
Kaixin San	Ginseng, longzhi, calamus, poria.	Based on metabolomics, bioinformatics, target “hooking” strategies.	AVP, TRH.	Play an antidepressant role by regulating the HPA axis, regulating inflammatory factors, regulating energy metabolism, *etc*.	[49-51]
Yueju Pill	Cyperusrotundus, Fructus Gardeniae, *Ligusticum chuanxionghort*, *etc*.	Based on sequencing technology, bioinformatics, molecular biology technology strategies.	TNF-*α*.	Play an antidepressant role by regulating the expression of CREB target genes in the hippocampus of mice and regulating neurotrophic factors in the brain.	[52, 53]
Chaihujia-Longgumuli Decoction	Chaihu, keel, oyster, *etc*.	Based on metabolomics, and molecular biology technology strategies.	IL-18, IL-6, and TNF-*α*.	Play an antidepressant role by regulating monoamine neurotransmitters, neurotrophic factors.	[54-56]
Guipi Decoction	Astragalus, fried sour jujube kernel, ginseng, *etc*.	Based on network pharmacology and molecular biological technology strategies.	Glu, GABA.	Play an antidepressant role by regulating neurotransmi-tter level and brain neuro-trophic factor.	[57-59]
Sini San	Radix Bupleuri, Radix Paeoniae Alba, Fructus Aurantii Immaturus, and liquorice.	Based on the systems biology, multidirectional pharmacology, network pharmacology, and the systemic approach to the entity grammar of TCM.	IL-6, TNF-*α*.	Play an antidepressant role by regulating neurotrophic factors and inflammatory factors.	[60-62]
Banxia Houpu Soup	*Pinellia ternate*, *Magnolia officinalis*, *Poria cocos*, *etc*.	Based on metabolomics and molecular biology technology strategies.	Phenylalanine, leucine, tryptophan, choline.	Play an antidepressant role by improving energy metabolism disorder and regulating the secretion of neurotransmitters.	[63-65]
Yinao Jieyu Recipe	Chaihu, *Acanthopanax senticosus*, gardenia, *etc*.	Based on metabolomics and molecular biology technology strategies.	TNF-*α*, IL-6, NE, DA, 5-HT.	Play an antidepressant role by inhibiting p38-MAPK phosphorylation in hypothalamus and regulating inflammatory factors.	[66-68]

目前已知抗抑郁药物帕罗西汀、氟西汀相类似的效果[74]。此外, 运用测序技术, PCR技术等验证差异表达基因, 找到潜在抑郁症治疗靶点, 为寻找抗抑郁中药关键分子提供了重要参考[75,76]。

4.2 功能代谢组学在抗抑郁中药安全性评价中的应用

功能代谢组学是为解决临床问题和干预疾病发病机制而设计的研究。要实现科研成果的转化, 还需要临床试验平台进行验证。目前大多数研究结果都是基于细胞和动物实验。然而, 这些机制对人类是否起作用还有待考证。为了提高抗抑郁中药安全性和可靠性, 从细胞或动物中获得的研究结果应该在人类中得到验证, 在功能代谢组学研究中, 与疾病相关的生物标志物包括人体组织、血浆和尿液等[22]。在抗抑郁中药治疗抑郁症的临床试验中, 通常采用汉密尔顿抑郁量表 (Hamilton depression scale, HAMD)、临床疗效总评量表 (clinical global impression, CGI) 及中医证候量表进行疗效评价。如果临床数据与实验室实验结果相一致, 科学研究的价值将会得到很大的提升。

例如, Feng等[77]前期通过大量动物实验对逍遥散剂量进行了筛选比较, 推荐逍遥散临床用药剂量约为原方剂量的两倍, 同时结合临床用药报道, 确定采用逍遥散剂量为370 g生药/天治疗抑郁症,为中药大剂量临床用药提供了临床依据。此外, Xu[78]在研究逍遥散治疗抑郁症的临床研究中, 发现抑郁症患者血浆甘丙肽水平与抑郁症呈显著相关, 与HAMD量表呈正相关, 提示血浆甘丙肽对抑郁症临床药效评价具有一定价值。Ding等[79]采用Meta分析, 显示柴胡疏肝散治疗组在CGI量表总有效率、HAMD量表抑郁评分降低等方面均优于对照组 (帕罗西汀、氟西汀等), 且不良反应较少, 安全性风险低, 得出柴胡疏肝散对原发性抑郁症的疗效确切。需要强调的是, 临床样本的质量直接决定了功能代谢组学工作的可靠性。因此, 一个好的临床检验平台可以帮助科学家获得可靠的临床样本和样本信息, 实现科研成果的有效转化。

5 结语及展望

抑郁症被认为是由基因脆弱性和不利环境事件的复杂相互作用引起的[80], 近年来, COVID-19大流行严重威胁着全世界人民的身心健康。抑郁症的发病机制复杂, 甚至与机体持续的免疫与代谢反应有关[81]。例如, 有报道称抑郁症不完全与炎性因子关联, 很多老年人的抑郁症或许是独立于炎症发生, 而受自身免疫性疾病影响[82]。抑郁症在中医被称为“郁证, 郁病”, 含义是气郁不畅, 是一种严重的心理障碍, 属于情志类疾病。中药抗抑郁机制具有多靶点多途径的特点, 找到关键靶点和主要抗抑郁信号通路显得尤为重要。功能代谢组学技术与中药抗抑郁机制都具有“系统”的特点, 通过关键差异性代谢物的分析, 有助于分析出精准的治疗机制。

在中药抗抑郁机制研究中, 本文综述了基于功能代谢组学方法的“抗抑郁中药-生物标志物-功能性成分-抑郁症新靶点及潜在代谢通路-抗抑郁中药作用新机制”研究策略及应用。首先, 借助质谱和核磁共振技术, 找到差异性内源代谢物, 干预疾病; 然后, 借助网络药理学[83]、生物信息学等分析技术, 筛选出治疗抑郁症的生物标志物; 之后, 借助FCM、WB等分子生物学技术, 捕获抗抑郁中药功能化合物与疾病失调的生化反应之间复杂的分子相互作用, 从而确定抗抑郁中药功能性成分; 最后, 通过对功能性分子的精准辨识, 发现抑郁症新靶点及其潜在代谢通路, 实现抗抑郁中药作用新机制的精准注释和解析。后基因组时代, 功能代谢组学随着代谢组学分析技术和分子生物学技术的发展, 促进了中药的研究和中药的现代化, 发现了新的分子靶点和信号通路[84,85], 为解决抑郁症及其他疾病问题提供了新方法、新思路。同时, 功能代谢组学技术的发展还有很多提升空间, 尤其是对差异代谢物进行功能验证后, 新靶点的产出仍需更多的分子生物学技术和临床验证进行补充[20]。此外, 面对抑郁症发病机制的特殊性和中药化学特征的分子复杂性, 要发现中药衍生的功能性化合物, 还需要更多先进的技术才能够精准辨识功能性分子表型。但随着更多科技成果的转化, 功能代谢组学将成为研究不同生物系统中存在的小分子代谢功能紊乱及其相关机制的新策略, 并有望解决生命科学中不同生态位的关键问题, 促进复杂疾病的新药开发。

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