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诊断治疗新视野

Frontiers in Autism Research

New Horizons for
Diagnosis and Treatment

主编 Valerie W Hu

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序

自闭症是一种复杂的神经发育疾患,近年发病率一路飙升,由于病因大多不清并缺乏特效治疗,该病症日益严重地困扰着迅速增多的患者及其家庭,已成为名副其实的公共健康危机。

自闭症的流行趋势、复杂的生物学机制及高度异质性,使其成为当今医学领域的难点和热点。近年来,自闭症研究方兴未艾,日新月异,知识爆炸之势令人目不暇接。Valerie Hu 教授主编的这部《自闭症研究前沿:诊断治疗新视野》,汇集了几十位世界顶级专家,参加撰写了 26 个章节,涵盖了自闭症领域最新的研究进展,从基因到表观遗传,从生理机制到靶向治疗,从生化代谢到诊断标记,从动物模型到临床实验,是当今内容全面、权威的自闭症专著之一。同时,本书布局完美,条理分明,每章前面有内容摘要,最后有“未来方向”和“本章要点”,使读者很容易掌握精髓;各章还有上百篇参考文献供有兴趣者深度钻研。我们认为,不论是对于自闭症专业人士还是自闭症患儿家长而言,本专著都是一部不可多得的教材。它不仅可以提高我们对自闭症的认识,开阔我们的眼界,而且可以使我们得到很多启迪。这也是我决定翻译此书的初衷,热切希望它在您的探索之路上助您一臂之力。

我要在此感谢所有参加本书翻译及校译的同仁们,感谢他们所付出的宝贵时间和精力,感谢他们奉献的才华和心血,特别感谢董存建、孔建、丁岩、陈一心、刘君在专业校对及组织上给予的大力协助,感谢王一迪、丁信嘉、潘娜、石寰、周洋、宋瑞、李莎莎、曹瑾、孙睿睿的辛勤付出,还要感谢尹跃平、肖密的校对帮助。我要感谢我的先生王晓春对书中插图翻译、编辑方面的帮助及其他方面的大力支持。翻译的过程是再创造的过程,虽然几经推敲,但由于中英文表达的差异,用词欠准之处在所难免,望读者见谅并指正。我也借此感谢 Valerie Hu 教授提供的指导和鼓励,感谢人民卫生出版社饶红梅编辑在翻译格式等方面的指导。最后但是最重要的,我要感谢我的儿子王睿萌,感谢他把我带入自闭症领域,成就了我对这个领域永恒的热情、执著和追求。从一个具有严重行为问题的自闭症患者到成绩优秀的大学二年级学生,儿子的成长道路见证了自闭症的希望。自闭症不是一成不变的,只要您站在科学巨人的肩膀上,就一定可以找到个体化的最佳治疗和康复方案。

——孔学君

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前言

自闭症谱系障碍(ASD)已迅速成为影响儿童和成人最常见的神经发育障碍之一。尽管 ASD 发病率迅速上升,具有相关的高遗传性,但人们对其病因学、病情发展,以及许多可能增加 ASD 的风险因素,不论是内在的还是环境的因素,仍知之甚少。目前,既没有经过验证的生物标志物用于诊断筛查,也没有针对 ASD 特效的药物治疗。因为大多数 ASD 个体的病因是未知的,所以诊断主要依据功能和行为异常的报告,大多数医疗也采用反复尝试的方法。这种不确定性的部分原因是 ASD 相关的临床和表型高度异质性。人们已在鉴定已明确的基因、代谢途径、细胞和组织功能方面的研究取得了进展,并且有证据表明,针对这些遗传缺陷或功能通路障碍的一些靶向治疗已使这个谱系中某些亚组患者的预后得到改观。

本书重点介绍了 ASD 研究的新兴领域,及其对开发更好的诊断方法和有效的治疗手段的潜能。这些以患者为主要考量的研究领域涉及创新和整合基因/基因组分析,以及表观遗传学影响的探讨,包括非编码 RNA、DNA 甲基化、选择性剪接、RNA 编辑的作用、基因调控和表达的错译、代谢和免疫功能失调、共病及激素和基因-环境间的相互作用可能造成的 ASD 致病风险增加。

本书还介绍了靶向或个性化治疗的进展及新型和替代性干预,例如经颅磁刺激、音乐和艺术治疗。此外涉及成人 ASD 患者这一在自闭症领域内被严重忽视的人群的研究,讨论了 ASD 患者在其人生不同阶段中改善病情和生活质量的目标。各章节中出现的共同主题包括:①应减少目前研究的 ASD 人群的异质性,以便更明确特定亚组的病理状况以进行靶向性治疗;②认识可被功能失调基因和环境影响的大规模基因调控的重要性;③需要采取全身系统方法治疗自闭症谱系上的患者,同时要考虑到个体差异和可行性。

在每一章里,专家们回顾了在他们相关领域里的最新研究,同时展望了这些领域的发展方向,其中包括会遇到的挑战、需要何种类型的研究或进展以推动该领域的发展进而达到预期的目标。这些独特的前瞻性论点为将来的自闭症研究提供了聚焦点并发人深省,而各章末的“每章要点”提纲挈领地突出了每章的主要内容。在我们探索自闭症研究的前沿时,谨记 William Bragg 爵士(诺贝尔物理学奖,1915 年)的睿智建议也是很重要的:“科学中最重要的事情不在于获得新的事实,而在于发现新的思维方式”。

由于许多章节都展现了新的治疗策略和其他可行的干预方法的研究,我

们预期本书不仅对从事自闭症研究的学生和资深科研人员具有参考价值,而且还会使社会大众,尤其是那些 ASD 患者的亲属和照顾病患的专业护理人员从中受益。

最后,我要感谢所有作者为撰写本书所付出的宝贵时间、专长和精力,以及所有世界顶级科学家帮助我使本书的问世成为现实。最后但同样重要的是,我要感谢我的儿子 Matthew Hu-Smith,为我的自闭症研究不断提供了灵感和动力。

Valerie W. Hu

(王一迪 译,刘君 孔学君 校)

主 译



孔学君,哈佛大学医学院附属贝斯以色列医院主治医师,哈佛大学医学院附属麻省总医院课题负责人(PI),美中医学交流协会会长,治愈自闭症研究所所长,机体-大脑康复中心共同创始人。孔医师本科及研究生毕业于北京医科大学医学系(现为北京大学医学部),先后在北京大学第一医院及美国马萨诸塞大学医学院的教学医院完成内科住院医师训练,并在美国塔芙兹(Tufts)医学院新英伦医学中心完成博士后研究,1997年后一直在哈佛大学医学院附属医院从事临床、教学及科研工作。2000

年儿子被诊断为自闭症后专注于自闭症研究并建立了自闭症专业门诊,多年来致力于循证医学、系统生物学、中西医结合为基础的自闭症诊疗及康复,并开创了自闭症全科诊疗模式及医学评估套餐,取得可靠的临床疗效。孔医师的研究兴趣主要在自闭症早期诊断方法、病因探讨及分型,涉及肠道和口腔微生物及基因研究、生物标记物、电生理、影像及新兴疗法的临床试验,寻找早期诊断指标及靶向治疗。2008年创立《北美医学与健康》与《北美医学与科学》杂志并任主编。组织出版自闭症学术专刊6期,发表数十篇论文。2015年主译其哈佛同事 Martha Herbert 的自闭症畅销书《自闭症革命》,人民卫生出版社出版。多年来组织自闭症国际论坛,并经常回国讲学,开展国际合作,2014年向深圳引进哈佛自闭症专家组成的团队并担任主任,作为主要申请人获批深圳市“三名工程”基金,并同深圳妇幼保健院共建深圳自闭症中心开展医教研合作。孔医师的初衷是把哈佛的经验和知识带给国内的自闭症患者及其家庭,从深圳到全国,更好地服务自闭症社区。

主 编

Valerie W. Hu 博士是美国华盛顿特区乔治华盛顿大学医学和健康科学学院的生物化学和分子医学教授,也是一名自闭症谱系障碍(ASD)患者的母亲。Hu 博士作为一位化学家,拥有加州理工学院化学博士学位和夏威夷大学化学学士学位。她在跨学科研究方面有着长期的研究历程,专注于蛋白质结构-功能关系和细胞膜-蛋白质相互作用。2004 年底,由于对 ASD 的个人兴趣,她将她的研究重点转向自闭症。Hu 博士自此成为将多学科综合基因组学方法应用于 ASD 的领军人物,专注于整合来自基因表达、行为、遗传和表观遗传学分析的大规模数据资料。她研究的主要目标是基于生物标志物诊断和对于自闭症患者的个性化治疗,实现这些目标需要更好地理解导致自闭症不同表现的潜在的病理生物学机制。揭示这些病理生物学机制,一部分通过识别 ASD 的不同亚型中改变的基因、功能失调的通路和异常的基因调节机制,同时需要识别 ASD 的环境风险因素。Hu 博士希望本书中体现的自闭症研究及其展望有助于阐明这些过程,引出更早期和更明确的诊断、基于证据的治疗选择,最终使所有 ASD 患者的人生更加丰富充实。



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