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Engineering
journal homepage: www.elsevier.com/locate/eng

Research
Food Safety and Health—Review

果蔬益生菌发酵技术及其产业化发展趋势

关倩倩 [a,b]，熊涛 [a,b]，谢明勇 [a,*]

[a] State Key Laboratory of Food Science and Technology, Nanchang 330047, China
[b] College of Food Science and Technology, Nanchang University, Nanchang 330031, China

ARTICLE INFO

Article history:
Received 27 September 2019
Revised 27 September 2019
Accepted 10 March 2020
Available online 9 September 2020

关键词
益生菌
发酵果蔬
人体健康
慢性疾病预防

摘要

本文简要介绍了现代人慢性疾病与肠道健康的关系，指出肠道菌群失调和膳食纤维摄入不足是慢性疾病发生的两大重要诱因。本文重点对益生菌发酵果蔬的研究现状、本团队在该领域取得的主要创新性成果以及相关产业未来发展趋势进行了综述。将益生菌发酵技术引入果蔬精深加工领域，开发益生菌发酵果蔬全新系列产品，不仅可以提高果蔬的附加值，还可将益生菌及其活性代谢产物与益生元（膳食纤维等）有机结合起来，对改善肠道健康、预防和缓解慢性疾病具有重要作用。果蔬益生菌发酵技术为益生菌影响人体健康的研究开辟了新思路，将为益生菌应用和果蔬加工新兴产业带来革命性影响，具有很大的市场潜力。

1. 引言

以心脑血管疾病、癌症、糖尿病和高血压等为代表的慢性疾病正严重威胁着人类健康。2015年1月19日世界卫生组织发布的最新报告[1]表明，2012年全球共有3800万人死于慢性疾病，其中40%以上（即近1600万人）的死亡属于原本可以避免的过早死亡，该数字远高于2000年的过早死亡人数（1460万人）。2018年中国国民健康与营养大数据报告[2]显示，中国慢性疾病患者已经超过2.6亿人，致死率占死亡人口总数的85%左右。此外，慢性疾病还呈现发病率持续上升、发病年龄日益年轻化的趋势。

早在20世纪初，诺贝尔奖获得者IIya Mechnikov在研究人体肠道菌群时就提出了“衰老源于人体和肠道菌群中某些细菌产生的毒素”的理论。该理论与我国传统医学中“粪毒入血，百病蜂起”的观念不谋而合。美国华盛顿大学的Turnbaugh等[3,4]和Ridaura等[5]通过对肠道菌群的长期研究，揭示了人体与肠道微生物之间的复杂关系，发现肠道菌群失调与营养不良、肥胖症、糖尿病等疾病密切相关。这些研究成果为人们理解肠道菌群与人体健康之间的微妙关系提供了全新的视角。肠道菌群失调可引起胰岛素抵抗和慢性炎症的发生，从而导致代谢综合征、肥胖症、糖尿病甚至癌症等慢性疾病[6–10]。除了肠道菌群失调，膳食纤维摄入不足是慢性疾病发生的另一大诱因。以美国为例，膳食纤维每日推荐摄入量为：成年男性38 g，女性25 g；而实际平均摄入

* Corresponding author.
E-mail address: xmync@163.com (M. Xie).

英文原文: Engineering 2021, 7(2): 212–218
引用本文: Qianqian Guan, Tao Xiong, Mingyong Xie. Influence of Probiotic Fermented Fruit and Vegetables on Human Health and the Related Industrial Development Trend. *Engineering*, https://doi.org/10.1016/j.eng.2020.03.018

量只有一半左右：男性18.7 g，女性15.6 g。我国居民日常膳食中每天仅摄入8~10g膳食纤维，远低于中国营养学会推荐的每日膳食纤维摄入量25~35g的标准。膳食纤维摄入不足会直接导致一些肠道微生物消失，进而引起各种慢性疾病[11]。更为严重的是，膳食纤维缺乏所引起的肠道菌群失调和健康问题，是有可能会遗传的；如果膳食纤维摄入持续不足，可能会导致肠道微生物不可逆转的消失[12]。

增强国民体质离不开健康食品产业的支撑。为推进健康中国建设，提高人民健康水平，2016年10月25日，中共中央、国务院印发并实施《"健康中国2030"规划纲要》（以下简称《纲要》），把国民身心健康提高到国家战略的高度。随着《纲要》的提出，大众也越来越关注食品营养与健康，尤其是食品对肠道健康的影响。肠道是人体最重要的器官之一，人体有70%以上的黏膜免疫发生在肠道，通过复杂的免疫机制，肠道与全身各部位器官发生紧密的联系。因此，要提升大众健康水平必须高度关注肠道健康问题。

目前，益生菌、益生元有益肠道健康的理念已深入人心，益生菌与益生元的研究已成为涉及食品科学、微生物学、医学、营养学、免疫学和肠道健康科学等多个领域的研究热点。研究食物对肠道健康的影响，重点应关注益生菌、益生元以及益生菌发酵食品对肠道健康的影响及其相互作用机制。近年来益生菌产品风靡全球，据统计，全球已有包括益生菌发酵酸奶、益生菌胶囊、益生菌粉剂等超过380种的益生菌产品，其中益生菌发酵乳制品的比例高达80%。但目前市场上鲜见益生菌发酵果蔬产品，其主要原因就在于果蔬发酵专用菌种缺乏、果蔬发酵专用复合菌剂规模化制备技术落后等突出问题尚待解决。

2. 益生菌及其发酵技术研究现状

自1899年法国Tissier博士发现第一株益生菌——双歧杆菌[13]以来，科学家们从未停止过对益生菌与人体健康关系的探索。大量科学研究证实，口服益生菌有助于预防或者治愈胃肠炎、抗生素引起的腹泻、旅行不适引起的腹泻、便秘及肠道感染，同时可抑制有害微生物在宿主肠道中定植，对肠易激综合征、炎症性肠炎及结肠癌等肠道相关疾病也具有良好的预防和治疗作用[14–17]。日本和欧美国家的大型乳业集团和乳酸菌（LAB）制剂公司都开发出自主菌株及产品品牌，并对菌株的益生功能进行了许多临床试验。如丹麦Chr. Hansen公司开发的动物双歧杆菌BB-12菌株是世界上临床研究最为充分的双歧杆菌菌株[18,19]。300多篇科学论文对该菌株进行过描述，其中的130多篇涉及人体临床试验。另一个例子是日本养乐多公司的干酪乳杆菌代田株[19]，在过去80多年中，日本对该菌株也开展了大量的科学研究与临床试验。截止到2015年5月，其在肠道内的存活性、有效性及安全性已经在英国、日本、泰国、中国等多个国家和地区得到科学验证[20–25]。

国内近年来在益生菌对肠道健康促进作用方面的研究也日渐深入。内蒙古农业大学的张和平团队[26]从内蒙古地区传统发酵的酸马奶中筛选到一株性能优异的菌株*Lactobacillus casei* Zhang，并对其益生功能进行了深入研究，结果表明：该菌株具有降血脂、免疫调节、抗氧化、拮抗肠道病原菌生长、抑制肿瘤细胞生长等优良的益生特性。江南大学的陈卫团队[27]构建了功能性益生乳酸菌筛选模型，在此基础上对筛选的植物乳杆菌ST-III的益生功能进行了深入研究，结果表明：该菌株可在肠道中有效定植并能调节肠道菌群，在降低胆固醇、调节血脂等方面也具有优良的益生特性。此外，关于益生菌发酵乳制品促进肠道健康的研究报道较多，包括《美国临床营养学杂志》在内的多种权威期刊都相继报道"每天喝发酵乳可提高人体免疫功能，减少过敏，降低炎症性肠炎、膀胱癌、结肠癌的发病率等"[28–32]。目前，养乐多乳酸菌饮料、味全乳酸菌饮料等多款市售益生菌发酵乳制品在促进人体肠道健康方面的功效已得到临床验证[33–36]。

相对益生菌发酵乳制品，目前国内外关于发酵果蔬制品对人体健康影响的研究较少。研究相对较多的是韩国泡菜，作为韩国"第一菜"，学者对其营养成分和保健功效研究较多。韩国学者报道了韩国泡菜在减肥、抗肿瘤、降胆固醇、降血脂等方面的健康功效[37]。此外，还有少数关于实验室自制益生菌发酵果蔬汁健康功效的研究报道。波兰罗兹工业大学（Technical University of Lodz）的Klewicka等[38,39]对实验室自制的乳酸菌发酵甜菜汁改善大鼠肠道菌群、抗氧化功效开展了研究。重庆医科大学的褚巧芳等[40]和管晓冉等[41,42]研究了实验室采用双歧杆菌发酵的自制混合果蔬汁对小鼠免疫调节及抗疲劳作用的影响，结果均证实发酵果蔬汁在促进大鼠、小鼠健康方面具有一定功效。

3. 果蔬益生菌发酵技术发展现状

将益生菌与果蔬相结合，可同时提供人体所需要的益生菌及膳食纤维，是未来益生菌产业的重要发展方向。“益生菌+果蔬”形式多样，其中最简单的方式就是在现有的传统果蔬产品中直接添加益生菌。例如，将益生菌直接添加到冷藏果蔬汁饮料中，冷鲜保存。此外，还可以在果蔬汁中添加一定量的益生菌发酵乳，将其加工成活菌或非活菌饮品。然而，对于胡萝卜、苦瓜、芹菜等营养丰富但风味不佳的蔬菜类原料，简单添加益生菌并不能改善蔬菜产品本身欠佳的风味。因此，“益生菌+果蔬”最好的方式莫过于采用果蔬发酵专用益生菌种对其原料进行发酵。益生菌发酵可分解蔬菜原料中的大部分烯萜类物质，有效改善蔬菜产品欠佳的风味，同时还可产生大量的芳香醇、芳香酯等风味物质，使原料风味与发酵风味浑然一体，香味更加醇厚，口感更加柔和。另外，益生菌发酵还可产生大量短链脂肪酸、黏性多糖和多肽等活性物质，对改善便秘、缓解结肠炎、预防和治疗消化道炎症都有很好的作用。

尽管国内外学者在发酵果蔬领域做了不少研究，但迄今为止，关于果蔬益生菌发酵技术研究仍处于起步阶段，国内外市场尚没有品牌和质量过硬的益生菌发酵果蔬产品出现。究其原因，果蔬益生菌发酵相关核心技术仍需突破以下瓶颈：①果蔬发酵专用菌种缺乏。众所周知，保加利亚乳杆菌和嗜热酸链球菌是用于酸奶发酵的菌种，而用于果蔬发酵的菌种尚不明确；尽管目前有越来越多的报道将植物乳杆菌[43–45]、嗜酸乳杆菌[46–48]等植物源乳酸菌株用于果蔬汁的发酵，但由于果蔬原料的多样性，没有哪种菌种可用于所有果蔬原料的发酵。许多特殊的果蔬，如蓝莓的pH值低、花青素含量高，一般乳酸菌很难发酵。因此，非常有必要广泛筛选适合不同种类果蔬原料发酵的菌种，建立果蔬发酵专用菌种库。②适合工业化生产的菌种高密度培养技术缺乏。目前国内外对乳酸菌的高密度培养技术研究多集中在膜过滤透析培养[49,50]、离子交换[51]、细胞循环培养[52,53]等技术，尽管可以达到细胞的高密度富集，但此类高密度培养技术仅限于实验室水平，很难实现工业化大规模生产[54]。近年来，分批培养或补料分批培养与培养基成分优化相结合的方法越来越多地被用于乳酸菌的高密度培养，发酵液中乳酸菌的浓度一般可达到$1\times10^{9}\sim1\times10^{10}$ $CFU\cdot mL^{-1}$（CFU：菌落形成单位）[55,56]。③高活性工程菌剂规模化制备技术落后。目前国内外文献报道的菌剂制备技术多采用真空冷冻干燥法，制备的菌剂产品中活菌数基本为$1\times10^{10}\sim1\times10^{11}$ $CFU\cdot g^{-1}$ [57–59]。

4. 本团队在果蔬益生菌发酵关键技术与产业化应用方面的研究进展

本团队长期致力于果蔬益生菌发酵关键技术与产业化应用研究，从科学、技术、工程到产业化（STEI）全过程，突破了果蔬发酵菌种筛选、菌剂制备、新工艺产业化等技术瓶颈，创制了一个果蔬益生菌发酵上、中、下游全产业链的关键技术创新体系（图1），开发了具有“安全、营养、美味、方便”等鲜明特征的益生菌发酵果蔬全新系列产品，催生了一个全新的发酵果蔬绿色制造产业。在此基础上，初步研究了益生菌及其发酵果蔬产品对肠道健康的影响，取得了一定进展。

4.1. 果蔬发酵过程中多菌种协同发酵代谢调控机制

我们研究了我国各类传统发酵果蔬在自然发酵过程中的菌系结构及其消长规律，揭示了果蔬发酵过程中各主要发酵菌株及其代谢产物与发酵底物间的互作关系，阐明了果蔬发酵过程中多菌种协同发酵代谢调控机制，为优良菌种的高通量筛选、复合菌剂制备和果蔬发酵生产工艺奠定了坚实的理论基础[60–67]。

4.2. 果蔬发酵优良益生菌种高通量筛选体系

基于上述理论基础，本团队海量收集国内外传统发酵果蔬样本近千份，并对传统工艺及其微生物资源进行了充分挖掘及标准化整理，分离、鉴定和保藏了56种6000多株乳酸菌（表1），建立了我国首个具有自主知识产权的果蔬发酵专用菌库，其中发酵性能优良并具有多种功能特性的果蔬发酵专用益生菌有335株，这些菌株的胃酸和胆盐耐受性强，肠道黏附性好，具有调节肠道微生态平衡、缓解便秘、调节免疫等益生功能[68–78]。

同时，选择一株从我国传统泡菜中筛选出的具有多种益生功能（耐胃肠道环境、降糖、降脂、降胆固醇、缓解便秘等）的果蔬发酵专用菌株——植物乳杆菌NCU116作为代表，采用第三代测序技术对其进行全基因组测序，分析相关基因功能，并与植物乳杆菌WCFS1和植物乳杆菌JDM1作比较基因组分析。结果表明，植物乳杆菌NCU116和几株已完成测序的植物乳杆菌有很大的相似性，但相比之下，植

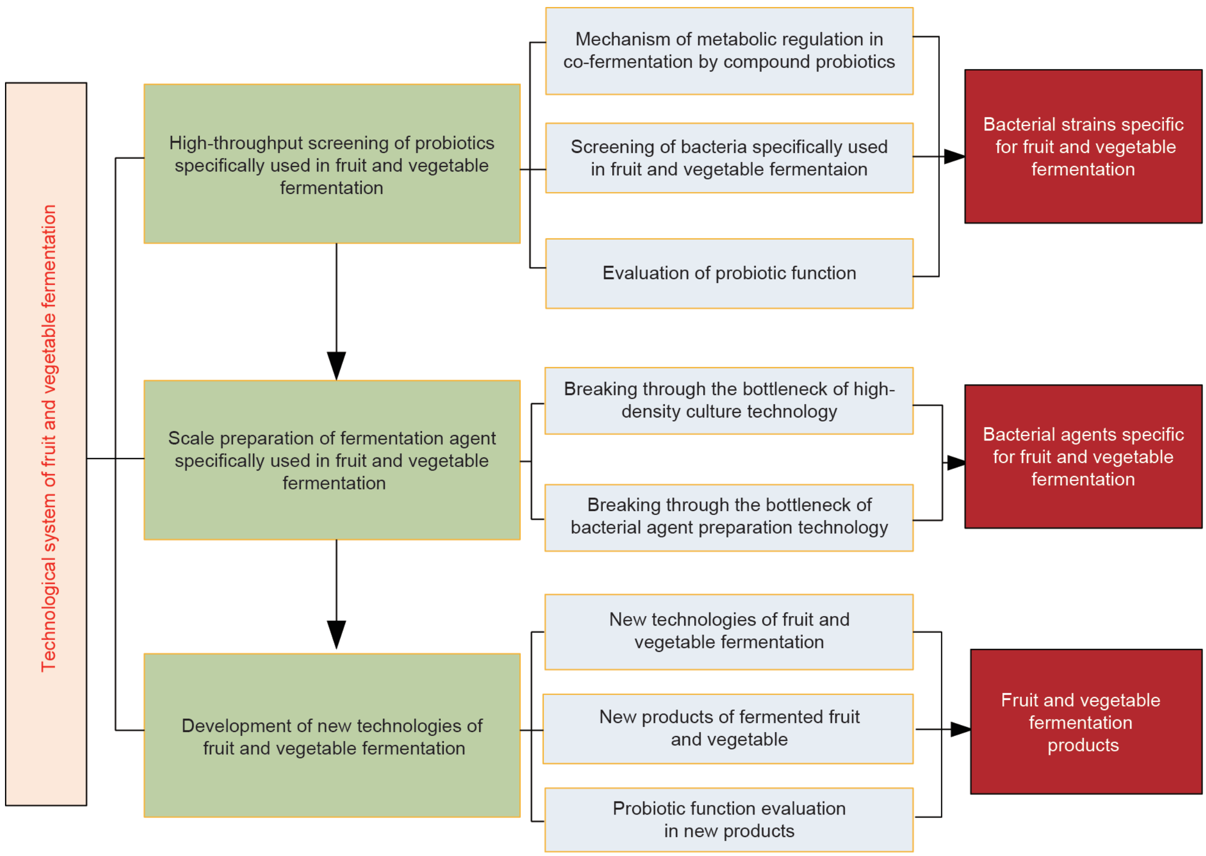

图1. 果蔬益生菌发酵上、中、下游全产业链的关键技术创新体系。

表1 分离和保藏的56种乳酸菌

No.	LAB	No.	LAB
1	*Lactobacillus plantarum*	29	*Lactobacillus nodensis*
2	*Lactobacillus brevis*	30	*Lactobacillus silagei*
3	*Lactobacillus fermentum*	31	*Lactobacillus oligofermentans*
4	*Lactobacillus coryniformis*	32	*Lactobacillus diolivorans*
5	*Lactobacillus curvatus*	33	*Lactobacillus harbinensis*
6	*Lactobacillus sakei*	34	*Lactobacillus rapi*
7	*Lactobacillus buchneri*	35	*Lactobacillus versmoldensis*
8	*Lactobacillus alimentarius*	36	*Lactobacillus tucceti*
9	*Lactobacillus parabrevis*	37	*Lactobacillus rossiae*
10	*Lactobacillus koreensis*	38	*Lactobacillus acidipiscis*
11	*Lactobacillus delbrueckii*	39	*Lactobacillus fabifermentans*
12	*Lactobacillus yonginensis*	40	*Weissella hellenica strain*
13	*Lactobacillus parabuchneri*	41	*Weissella paramesenteroides*
14	*Lactobacillus parafarraginis*	42	*Weissella viridescens partial*
15	*Lactobacillus paracasei*	43	*Weissella confusa*
16	*Lactobacillus xiangfangensis*	44	*Weissella cibaria*
17	*Lactobacillus casei*	45	*Weissella koreensis*
18	*Lactobacillus paralimentarius*	46	*Leuconostoc mesenteroides*
19	*Lactobacillus nagelii*	47	*Leuconostoc pseudomesenteroides*
20	*Lactobacillus amylolyticus*	48	*Leuconostoc citreum*

（续表）

No.	LAB	No.	LAB
21	*Lactobacillus heilongjiangensis*	49	*Leuconostoc fallax*
22	*Lactobacillus sunkii*	50	*Pediococcus parvulus*
23	*Lactobacillus paraplantarum*	51	*Pediococcus ethanolidurans*
24	*Lactobacillus pentosus*	52	*Pediococcus pentosaceus*
25	*Lactobacillus hammesii*	53	*Lactococcus lactis*
26	*Lactobacillus namurensis*	54	*Pediococcus inopinatus*
27	*Lactobacillus senmaizukei*	55	*Enterococcus durans*
28	*Lactobacillus fuchuensis*	56	*Pediococcus damnosus*

物乳杆菌NCU116基因组编码大量糖酵解相关基因簇（NCU116GM001792、NCU116GM002858等）、PTS相关基因簇（NCU116GM003248、NCU116GM000887等）以及丙酸酮盐相关及调控基因，使得植物乳杆菌NCU116既可以转运又能代谢单糖、二糖、低聚糖类和糖醇类碳源[79]；同时编码ABC超家族转运系统的相关基因簇，这与植物乳杆菌NCU116表现出的耐酸、耐渗透压等生理功能一致。NCU116基因组中未发现任何致病基因，与动物实验结果契合，证明该菌株是一株安全可靠的益生菌株。

4.3. 高活性工程菌剂规模化制备技术体系

采用指数流加、模糊逻辑控制、反馈控制及提升式菌体悬浮培养等技术集成，大幅提升工厂发酵液中的活菌浓度[80–82]；发明了两步干燥法生产高活性乳酸菌剂的规模化制备技术，开发出高活性果蔬发酵专用益生菌剂产品，其活菌数高达1×10^{12} CFU·g^{-1}[83]。该技术填补了果蔬发酵专用菌剂的生产空白。

4.4. 益生菌发酵果蔬生产新工艺

构建直投式益生菌发酵果蔬新技术，开发益生菌发酵果蔬原浆、发酵果蔬饮料、发酵泡菜、发酵果蔬粉、发酵果冻等益生菌发酵果蔬全新产品系列。这些产品不仅具有良好的口感和风味[84]，且含有大量对人体健康有益的短链脂肪酸、黏性多糖和多肽等活性物质[85]。

4.5. 益生菌及其发酵果蔬产品的功能评价体系

构建有关便秘、免疫抑制、高脂血症、脂肪肝、结肠炎和糖尿病等疾病的动物模型，用于评价果蔬发酵专用益生菌株及其发酵果蔬产品的功能特性。以植物乳杆菌NCU116为例，对该菌株及其发酵胡萝卜产品的益生功能评价结果表明：植物乳杆菌NCU116及其发酵胡萝卜产品在提高小鼠免疫能力、改善肠道黏膜损伤、缓解便秘、缓解糖尿病和结肠炎、缓解高脂血症、调节肠道菌群等方面具有很好的益生特性[85–96]。

5. 益生菌发酵果蔬产业未来发展趋势及挑战

尽管果蔬益生菌发酵技术目前取得了阶段性突破，但该产业的发展依然面临一系列关键科学技术问题。首先，由于我们前期的菌种筛选工作主要集中在大宗果蔬发酵专用优良菌株的选育方面，使得目前开发的益生菌发酵果蔬系列产品仅涉及胡萝卜、芒果、雪梨、南瓜以及其他常见的大宗水果和蔬菜。然而，果蔬种类众多，每种水果和蔬菜都有其独特的性质，因此，要开发更多种类的益生菌发酵果蔬产品，就必然要针对不同果蔬原料筛选具有优良发酵性能的不同种类益生菌株。尤其是对于某些特殊的果蔬原料，筛选适合其发酵的优良菌株具有很大的挑战。以山楂为例，由于原料本身酸度很高，一般的菌种很难耐受如此高的酸度，因此要筛选适合其发酵的专用菌种具有一定的困难。其次，关于益生菌发酵果蔬产品的安全性和功能性评价，目前仅开展了体外和动物实验，尚未进行系统的临床研究。为明确益生菌种及其发酵果蔬产品的益生功能，就要构建更加全面的果蔬发酵益生菌种及其发酵产品的营养功能和安全性评价体系。此外，还需开展更加先进的高活性低成本果蔬发酵专用益生菌剂的规模化制备技术研究。最后，益生元、益生菌和益生菌发酵果蔬产品对人体健康的影响及其作用机制尚需进一步阐明。有效解决上述关键问题，可为益生菌发酵果蔬领域的研究及其产业化发展带来更大的契机。

6. 结论

近年来传统饮料业的业绩下滑已呈现出不可逆转的趋势，益生菌发酵果蔬产品迎合了消费者对“安全、营养、美味、健康”产品的需求，符合大健康产业发展趋势。因此，以益生菌发酵果蔬为代表的健康产品必将为果蔬与发酵食品行业带来重要影响。本文提出了“肠道菌群失调和膳食纤维摄入不足是慢性疾病发生的两大重要诱因”这一观点，然后对果蔬发酵专用益生菌种的筛选、高活性工程菌剂的规模化制备以及益生菌发酵果蔬系列新产品的开发等果蔬益生菌发酵关键技术的研究现状进行了综述。同时，还从多个角度对果蔬益生菌发酵技术发展趋势及面临的挑战进行了探讨。未来，我们将开发出越来越多具有“安全、营养、美味、健康”等鲜明特征的益生菌发酵果蔬产品，以期为消费者提供更多优质的果蔬制品。

致谢

本研究获得了“十三五”国家重点研发计划（2017YFD0400705-2、2017YFD0400503-3）、国家自然科学基金项目（31560449、31760457）和江西省重点研发计划项目（20165ABC28004）的支持。

Compliance with ethics guidelines

Qianqian Guan, Tao Xiong and Mingyong Xie declare that they have no conflict of interest or financial conflicts to disclose.

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