

转基因作物和食品安全

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摘要 2050年全球人口将高达90亿,为了养活每一个人,就必须有效地运用每一项技术使粮食增产。毫无疑问,转基因作物很可能是可以达到全球粮食安全的技术之一,而且也会起到积极的作用。尽管目前针对转基因的虚假言论很多,但我们可以明确地表示,转基因作物对于人和动物来说是安全的。目前大规模种植的抗除草剂和抗虫的转基因作物,只要在合适的环境中进行,对小型或大型的农业发展都是有益的,同时也有助于粮食安全。如果将抗旱、氮高效利用、抗病以及改良营养成分的优质基因在原生质体中表达后再进行育种,将转基因技术与常规育种策略相结合,将会相互促进、相互发展。放眼未来,发展中国家需要制定出合理的监管制度来推动有益的转基因作物,而不是停留在无休止的田间试验阶段。基因组编辑等新技术能使我们对基因组特定区域进行精准、安全的改造,因此,这项技术应获得更为宽松的监管环境。

关键词 转基因作物; 食品安全; 基因组编辑; 发展中国家; 农业

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2050年全球人口达到90亿时,为了养活每一个人,就需要有效地运用能使粮食增产的每一项技术。当被问起转基因作物在实现全球食品安全过程中可能的作用时,我想说这个话题已经是老生常谈了。每当人们谈起转基因作物时,大部分的话题表达出的观点基本都是从“转基因作物对于实现食品安全是必须的”到“转基因作物是有害的,应该禁止”差异很大。通常在这两种极端的观点中没有严谨的求证和论据式的对话。因此,我强烈推荐几篇有深度的文章^[1-4],以科学为依据来讨论转基因作物。

1 关于转基因的一些虚假言论

妄言 1. 转基因技术与转基因作物不安全

任何以事实为依据的讨论必须首先澄清一个关键的问题:如今种植的转基因作物对于人类和动物来说是安全的。在转基因产品过去经历的30年中,没有人能给出合理的说法证明农作物中的转基因性状对人甚至动物造成了危害。只要农业政策方面出台了合理的监管制度,在将来我们就再也不用担心转基因作物的安全问题了。然而,反对转基因的激进分子已经花了上百万美元向百万民众反复宣传转基因作物有危害且不可食用。不幸的是民众相信了他

们的言论。科学团体和政府机构有责任去反对这样的言论,并且应该依据科学观点传达转基因作物的安全性。

Ottoline Leyser 近来写到^[5]:“……我们应该跳出这样的思维,转基因作为一种遗传改良技术,它和其他的作物改良技术包括传统的育种是一样的,我们不应该认为转基因技术有什么特殊之处。”就像Leyser说的,我一直认为,当我们评判一个新品种时,我们应该关注的是该品种中出现的新性状的价值和安全性,而不是它产生的方法和过程。例如,如果抗除草剂的作物是由于大量种子经过辐射引发突变的群体中筛选而来,即使这个种子也包含许多别的未被鉴定的突变表型,我们也无需特别的规范来批准它的使用。相反的,我们却需要用全套的规范流程来批准用转基因方法获得的同样抗除草剂作物的使用,即使插入的是我们已经鉴定过的基因。这样的做法有意义吗?

在美洲,人们都担心帝王蝶的严重减少。虽然草甘膦除草剂的广泛使用对帝王蝶并没有害,但是该除草剂的确能杀死帝王蝶主要的食物之一——马利筋,它一般生长在喷施了草甘膦的田地中^[6]。因此,我对反转人士的建议是,可以培育抗草甘膦的马

利筋,并让农民们将其种植在田边。当然到最后,这很可能是一个坏点子。但是,我觉得反转人士与其担心抗除草剂性状如何产生,不如把更多的注意力放在对抗除草剂性状或者某块地域的某种作物(或杂草)的利弊分析上。

妄言 2.转基因作物可能适合大规模的农业种植,不适合发展中国家的新农

1996 年世界粮食首脑会议对食品安全是这样定义的:当世界上所有的人随时都有充足、安全、营养的食物来维持健康有活力的生命时,才算达到了食品安全。世界卫生组织认为食品安全的含义有三个层次:

- 食品可供应性:有维持生存足量的食物;
- 食品来源的多样性:有满足各种营养需求的足够的食物来源;
- 食品可利用性:在维持基本营养和保健的基础上对食物合理的使用,就如同有充足的水和公共卫生设备一样。

显而易见,针对转基因作物能否改善食品安全中的任何讨论都必须集中在一点上,也是最重要的一点——食品的可得性,也就是要发展高产的作物。但是,另外几点也同样重要,那就是我们应当考虑作物的营养价值!因为许多人不仅缺少食物,还缺乏微量元素的摄入,最典型的是缺铁、锌和维生素 A。至于食物的来源,需要强调的是在发展中国家还要重视农业生产者的盈利与否。Bt 棉花就是一个很好的例子,它虽然未直接增加食物的供应量,但是能间接增加农民经济收入从而使他们获得更多的食物。Qaim 和 Kouser^[7]近期的研究证实,在印度,种植 Bt 棉花的小农户相比种植其他品种的农民收入有所增加,他们获得了更多的食物,间接地提高了食品安全性。使许多人吃惊的是,在 2013 年已有 1 800 万农民种植转基因作物,其中 90% 是贫穷的小农户,而且他们中很大一部分是在中国和印度种植 Bt 棉花^[8]。

然而,对于在偏远地区种植不到 1 hm² 田地的贫穷农民(他们得不到化肥和优良种子)来说,转基因作物很可能对他们的影响不大,因为缺少种子来源和许多别的农业生产的竞争需求。他们最可能做的是,自己留一些种子或者与邻居交易种子,然后祈祷好的天气和少一些害虫。但是,拉丁美洲和亚洲的许多小农户却可以轻易获得种子;在非洲,许多国家种子的质量正在提高,杂交玉米的种植也逐步增加^[9]。这说明种子可以买到,也说明农民收入超

过了成本,还说明不管种植面积有多少,农民们都愿意选择更好的种子,也愿意选择转基因种子。

最后,全球食品安全并非仅与贫穷的小农户相关。虽然 86% 的农田面积 < 2 hm²。但是,另外 14% 的 < 2 hm² 农田占据了世界总耕地面积的 88%,是可持续农业生产力的代表^[10]。历史告诉我们,城市化进程伴随着的是农场的集中化和规模化。当劳动力紧缺时,统一规模化生产的大型农场较零散的小农场的优势就会明显体现^[11]。正如下文将讨论的,虽然转基因作物对发达国家和发展中国家带来的好处或多或少,但无法忽视的是它对全球食品安全的贡献。

妄言 3.转基因作物是食品安全的唯一出路

当然不是!还有许多其他的好方法,比如:分子育种技术的应用,杂交作物的培育,土壤肥力的提高,灌溉管理的改善、农艺方式的改良,基础建设(如公路和电力设施建设)的加强,拉大市场需求,控制人口增长,建立更好的政策环境,消除贪污腐败。

2 哪些性状更能显著地提高食品安全性?

2.1 全球转基因作物中两个最主要性状

毋庸置疑,抗除草剂和抗虫(多是 Bt 基因)这 2 类转基因作物不管从哪个方面来说,在全球范围内都是应用最为广泛的。比如,在美国、巴西和阿根廷,抗除草剂和抗虫的转基因玉米和抗除草剂的转基因大豆已经大面积种植,主要用于动物饲料。我想,如果政府要求部分转基因玉米和豆类必须针对人类食用安全设计,且根据人们消费的直接需求而不是仅用于动物饲料来种植,那么这将有利于食品安全的实现。但是,不知是好还是坏,自从发展中国家(特别是中国)对肉类需求的急剧增长^[12],转基因玉米和大豆的高效、高产的规模化种植优势转换成了全球粮食价格的下降,因此,这也有助于实现食品安全。在中国,水稻是人们的主粮,而玉米则是主要的动物饲料。早在 2009 年,中国就已颁发了 Bt 抗虫水稻和植酸酶玉米的转基因生物安全证书,但是,迄今这两者都没有被允许商业化生产。与此同时,中国还是世界上最大的转基因玉米和大豆进口国(用于动物饲料)。

同样值得注意的是,尽管新的转基因作物品种和许多田间性状在很多国家不断地被研发,但是世界上还没有任何国家批准主要的粮食作物水稻和小麦转基因品种的合法种植。尽管水稻和小麦各含世

界粮食中 20% 的卡路里,但是可以明确的一点是,到目前为止,对于以水稻和小麦为主粮的上百万人民来说转基因作物对食品安全尚没有作出一丝贡献。

2.2 抗除草剂性状 (HT)

适合于大型农场种植方式的“免耕农业”的流行,绝大部分依赖于抗除草剂转基因作物的推广^[13]。近来,一篇报告^[14]分析了 11 种技术对水稻、玉米和小麦的产量和价格的影响,得出了这样的结论:提高氮的有效利用率、增强作物抗高温能力、免耕技术和精细农业最具应用前景。免耕技术可以减少劳动力和燃料的使用、保持土壤湿度、增强土壤肥力,但是对杂草的控制也同样关键。在美国,抗除草剂作物(特别是抗草甘膦作物)的推广明显增强了免耕技术在玉米、棉花和大豆中的应用^[13]。孟山都公司在多年前已研制出抗除草剂小麦,但迟迟未见推广,据称他们已重新开始考虑转基因小麦的市场化。毫无疑问,抗除草剂品种可以给越来越多采用免耕技术的小麦种植者们带来实实在在的好处。

劳动力成本增加和水资源紧缺导致直播水稻越来越受欢迎。水稻的生长一直伴随着杂草的危害,但是我从许多水稻种植者处了解到的是,除非有抗除草剂的水稻,否则直播水稻的方法还是会继续使用的。具有杂草特性的野生稻对多数除草剂有着和栽培稻相似的反应^[15]。尽管大家也在担心野生稻是否也会对除草剂产生抗性,但是,目前通过突变育种筛选方式已经获得了耐咪唑啉酮的抗除草剂水稻品种,已研发出多种抗除草剂(如抗草甘膦)水稻,但是还没有一个开始商业化应用。

目前人们讨论最多的还是抗除草剂杂草的出现,尤其是那些已经被广泛使用且常常被滥用的抗草甘膦作物。实际上,抗草甘膦基因的靶标是氨基酸生物合成途径中一个必需关键酶的活性位点,而且该抗性基因突变的概率远低于抗其他除草剂的基因^[16]。然而,大家必须接受一个事实:那就是草甘膦抗性的出现是必然的!这正如暴露在 Bt 蛋白作用下的害虫,或者任何通过常规育种获得的抗除草剂或抗虫或抗病的作物中也会出现抗性一样。那么,关键问题不是选择转基因或者非转基因作物,而是尽可能采用最佳的田间管理方案来尽可能地延误抗性的产生。应该再次强调的是,我们应该关注性状本身而不是产生性状的方法。

2.3 抗虫性状

正如前文所述,Bt 棉减少了杀虫剂的使用从而

带来了产量和经济上的收获。因此,即便 Bt 棉并不是人类的食物,但在印度^[7]、中国^[17]、布基纳法索^[18]和巴基斯坦^[19]等国,Bt 棉对食品安全确实作出了贡献。当然,还有 Bt 玉米,由于其被广泛接受,所以它对全球粮食生产进而对可持续的全球食品安全起到了关键作用。我已花了大量的篇幅讨论转基因作物发展的相关问题,但仅关注了棉花、玉米和大豆。所以,我准备将重点放在豆科植物抗虫的问题上,这对许多发展中国家的小农是十分重要的。

人们常说,如果大家少吃肉食、杜绝浪费,那么食品安全的问题很可能迎刃而解。通过调控我们已知的基因来调控作物生长,转基因技术在解决粮食浪费问题上可能起到一定作用^[20]。中国人擅长从豆类中提取植物蛋白,早在 2 000 年以前中国人已发明了豆腐。当今,随着肉类需求的不断增长,人们开始不断从豆类和麦麸中提取新的高蛋白食物(<http://www.peta.org/living/food/meat-replacements/>)。而且,据我所知,世界上再没有比豆类更好吃的素菜了。所以,印度贫困人群食谱中除了鹰嘴豆和木豆外,基本没有别的素菜。尽管这些豆科植物耐寒、耐旱且富有营养,但如果要大规模种植的话,就会面临诸如种子大、产量低、易感病、缺少杂种资源(特别是木豆)等挑战。也正因如此,它们对民间种子公司并没有很大的吸引力。

鹰嘴豆在豆类食物中的重要性排在第三。它十分耐寒、耐旱且具营养,在非洲、中东和亚洲广泛种植。在西非,豇豆既是人类主要的膳食蛋白来源,也是动物的饲料牧草,同时它还可以通过固氮作用改善土壤肥力。木豆作为印度 dal 菜中的主要配料被广泛应用,也是印度贫困人群膳食蛋白的主要来源。近年来,东非国家越来越多地种植木豆,它们不仅被用于本土消费,还被出口到印度。

鹰嘴豆、豇豆和木豆生产面对的最大挑战就是遭遇田间害虫的毁坏,尤其是棉铃虫 *Helicoverpa armigera* 和豆野螟 *Maruca vitrata* 这样的钻心虫,常常会导致急剧减产。据估计,直接经济损失每年超过 10 亿美元,而且还没算上每年超过 5 亿美元的杀虫成本(www.ICRISAT.org)。对于小农户们而言,并不总是能买到合适的杀虫剂,这样他们就经常使用安全性低的杀虫剂。钻心虫对多种不同的 Bt 蛋白是极度易感的。由于这些豆类中缺乏抗虫效果显著的种质资源,所以应对虫害带来的减产的唯一有效途径就是培育它们的转 Bt 基因材料。豇豆和鹰嘴豆都是自花授粉作物,几乎无法与其他物种或

其野生品种进行远缘杂交。因此,它们基本不存在基因漂流的问题,而且对于 3~4 年才购买一次种子的穷苦农民来说,留种亦不会丢失抗虫性状^[22]。相反,木豆是异花授粉作物,故存在基因漂流的问题,但另一方面有利于培育高产且抗虫的杂交种。该杂交种由民间公司提供,同时这些公司还能提供与抗性管理有关的专业知识或技能。的确,政府在从事转基因监管事务时遇到的最大挑战就是建立健康的种子管理系统,而这个问题对民间公司常常并不成为问题。吸引民间公司参加转基因产品的经营可能是解决该问题的最佳方案。转基因大豆的流行说明这样一个事实:民间公司已非常重视豆类转基因品种的培育。

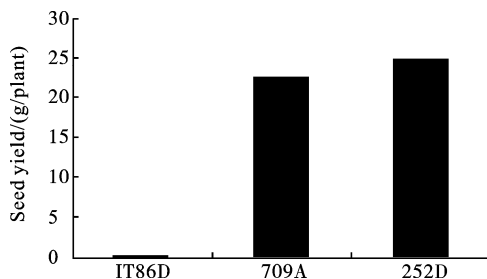
非洲发展转 Bt 豇豆这一项目已经非常全面和系统。在过去十多年中,已培育出超过 800 个转 Bt 基因豇豆品种 (www.aatf-africa.org; T J Higgins, 私人通讯)。通过该项目,我们可以认识到在非洲撒哈拉大沙漠以南(SSA)地区针对食品安全问题政府所面临的诸多挑战。首要的棘手问题就是开发一个程序将在澳大利亚 T J Higgins 实验室完成的高效豇豆转化体系在非洲撒哈拉大沙漠以南(SSA)完成^[22]。第 2 个问题就是怎样获得 *cry1AB* 基因的使用权。孟山都公司(该基因的拥有者,也是可能的捐献者)首先提出这个问题,随后非洲农业技术基金会(AATF)与孟山都达成协议使得问题得以解决。该协议规定,孟山都公司不会阻碍该项目利用 *cry1AB* 基因,但也不会提供含该基因的 DNA 载体;该项目的工作人员可以通过使用孟山都公司提供的 DNA 序列信息自己去合成目的基因。Higgins 实验室研制出的豇豆转化株在非洲温室中证实对豇豆荚螟(MPB)高抗,且没有明显异常表型。在西非经过若干年的田间试验后,该项目又在波多黎各进行了几次试验。由于缺少虫源,所以没法很好地测试抗虫效果,但是也出现了一些最好的转化植株在田间发育迟缓,这是在温室里没有观察到的表型。尼日利亚是西非国家中第 1 个有 4 年田间试验结果的国家。后来在布基纳法索也进行了几年试验,最近,加纳也完成了这些试验。

这些结果相当地鼓舞人心,因为从中我们可以了解到在特定国家进行田间试验的重要性。图 1 所示的是,2012 年在尼日利亚进行的特定田间试验的早期情况。在对照无害虫的条件下,最好的 2 个转基因事件与对照比起来并无产量损失。图 2 所示的是,2012 年在布基纳法索得到的试验数据,在害虫



图 1 2012 年在尼日利亚进行的田间试验

Fig.1 Confined field trial (CFT) in Nigeria in 2012



该试验于 2012 年在布基纳法索进行。IT86D 为受体非转基因对照材料;转基因事件 709A 和 252D 中均带有 *cry1AB* 基因。其中 709A 事件已经被选为供体亲本用以将 Bt 基因导入的农民喜爱的品种中(T J Higgins 馈赠)。Trial was held in Burkina Faso in 2012. IT86D represents the control non-transgenic parent line used for transformation; transgenic events 709A and 252D contain the *cry1AB* (Bt) gene. Event 709A has been chosen as the key event that is being introgressed now into farmer-preferred varieties (Courtesy of T J Higgins).

图 2 转 Bt 豇豆田间接虫后的试验数据

Fig.2 Results of a CFT of transgenic Bt cowpea in a field heavily infested by pod borer *Maruca vitrata*

存在的条件下,对照几乎绝产;其中转基因事件 709A 作为供体亲本,用来将抗 MPB 性状导入到农民喜爱的抗独脚金、蚜虫和蓟马的品种中去。

Huesing 等^[21]已经考察了该项目中遇到的许多问题。他们除了观察到豇豆自花授粉的特性减缓了远缘杂交的发生,还指出有效地抗豇豆荚螟(MPB)的 Bt 基因已广泛地应用于其他作物上了,而且 Bt 基因对非靶标害虫无明显毒害作用。导入不会使昆虫产生交叉抗性的第 2 个 Bt 基因到已有抗豇豆荚螟(MPB)事件中,或 MPB 由南至北迁徙的习性,均可以起到延缓昆虫对 Bt 蛋白抗性作用的产生。虽然并未采用很高级的技术,但通过转基因豇豆的成功我们可以推测转基因鹰嘴豆和木豆(目前这 2 个物种都能够作为转基因的受体^[23-24])也是可能实现的(与 K. Sharma 和 T J Higgins 的私人

通讯)。再加上近期转 Bt 茄子已在孟加拉国上市(印度正在等待上市^[25])。这些项目使我们清楚地认识到,利用政府和民间合作项目在食物缺乏的地域推广转基因作物是可能的。

2.4 抗病性状

发达国家的规模化农业生产可以通过常规育种、喷洒杀虫剂、杀真菌剂以及高效田间管理等方式有效地控制植物病害。第1个(也是唯一一个)通过政府的努力成功商业化的转基因抗病作物是抗环斑病毒木瓜。它实际上拯救了夏威夷的番木瓜产业^[26]。同样,在中国转基因木瓜也上市了^[8]。另一个正在发展的转基因抗病作物是抗细菌性萎凋病香蕉,近期已在乌干达进行了首次田间试验^[27]。

危害许多蔬菜的双生病毒是发展中国家遇到的特殊问题,其中玉米条纹病和木薯花叶病毒绝非是非洲特有的。褐条纹病毒是一类 RNA 病毒,它会导致东非木薯的大量减产。虽然有一些抗性位点和对部分病毒耐受的位点可用于育种,但是,这类数目十分有限。那么转基因策略应视为一个重要的候补,特别是考虑到一些病毒能够产生大量的突变^[28]。一些研究团队正在着手应对玉米和木薯上的非洲病毒,而且不少抗病材料已在非洲不同国家的温室或田间进行试验^[1]。现今,由巴西农牧研究院(EMBRAPA)培育出的转基因抗金色花叶病毒豆已成功的在巴西上市^[29]。黄龙病正成为影响全球柑橘类水果产量的主要病害,现在就应该考虑转基因策略是否是唯一能对抗黄龙病的方案^[30]。

2.5 抗旱性状

全球气候变化和城市生活用水与农村灌溉用水间的竞争带来的不确定因素,对全球农业而言,必须促使我们找到增强作物抗旱能力的方法^[31]。从以往经验来看,多数育种者认为干旱耐受能力是由植物从各个方面调控的一个复杂性状。然而,许许多多已发表论文显示许多单个基因的超表达可以产生与干旱耐受相关的表型^[32]。但是,这类研究的大多数仅针对模式植物而言,也没有涉及在相应水分控制条件下的田间试验结果。

在过去2年里,2个跨国公司都在美国发布了新的玉米品种,这使得我们可以在分子标记辅助选择育种和转基因之间做一个非常有趣的比较。第1个是 Optimum[®] AQUAmax[®] (杜邦先锋旗下的品牌),它有一系列能适应美国不同气候区域的抗旱杂交品种,这些品种是通过经典的分子标记辅助选择育种手段获得的(<https://www.pioneer.com/>

<http://www.monsanto.com/products/pages/droughtgard-hybrids.aspx>),它通过在亲本中表达一个编码伴侣蛋白的基因来提供抗旱能力^[33]。有趣的是,2013年是这2个品种在美国商业化的第1个年头。但通过进口到中国,它们的抗旱性能已得到证实,这似乎可以间接证实转基因 DT 杂交玉米品种具有巨大的经济效益。

尽管现在来判断这2种手段培育出的抗旱品种是否成功为时尚早,但通过早期的结果可以看到这2种手段得到的抗旱品种在干旱条件下产量适中,正常条件下不会减产。AquaMax 品种经历了更长的田间试验,在过去的3个种植季已比较了42 000株。Optimum[®] AQUAmax[®] 的产品在干旱环境下有着6.9蒲式耳的优势,在正常环境下有着3.6蒲式耳的优势(https://www.pioneer.com/cmroot/pioneer/us/products/seed_trait_technology/optimum_aquamax/Infographic_AQUAmax_2014.pdf)。对 DroughtGard 品种,很早就有报告指出干旱条件下其每英亩可增产5蒲式耳。通过多年在多种环境下对其产量稳定性的考察,这些增产数据可能看上去很一般^[31],但是以往商业化的杂交玉米并没有特意针对抗旱性状作选择。而且这些数据亦可以解除这样的一类误解:通过单个或多个基因的导入可以得到既抗旱又有着奇迹般的产量增加的品种。很明显,这2个公司都青睐于将分子育种和转基因育种相结合来培育更好的抗旱品种。杜邦先锋现今正在评估多个抗旱基因,很可能准备将其导入到通过分子育种获得的抗旱玉米中。同时孟山都也正努力将它们的单个抗旱基因导入到已报道的具抗旱能力的种质资源中。

孟山都公司正与 CIMMYT 和 NARS(东非多个国家)合作一个 WEMA (Water Efficient Maize for Africa)项目,该项目将测试 DroughtGard 品种在非洲的性状(<http://wema.aatf-africa.org/>)。协议规定,获得成功的品种将在这些国家免收专利费。正如以上所述,结合分子育种和转基因的优势,在非洲培育具有高产、抗旱性状的品种毫无疑问是极为重要的。

不管用哪种技术来获得抗旱性状,我们能够明白的一点就是,抗旱性状是所有性状中最具挑战的。

因为,在高度严格的条件下设计可重复的试验是非常困难的。这方面不仅需要民间企业付出不同往常的努力,也需要政府与民间企业建立更富有创造力的合作关系来推动发展中国家的农业生产。

2.6 氮高效利用性状

不管是在发达国家还是发展中国家,土壤中氮的天然含量都是作物产量的主要限制因素^[34]。氮使用的最优化是所有农民都想达到的目标,这样既省钱又能避免过度施肥影响环境。对于很多农村的贫困人群而言,授权和成本也是一个关键因素。研究者们现已把更多的注意力放在氮高效作物的培育上,但是要面对的挑战有:氮高效可以从不同的角度定义且难量化;再加上氮高效涉及许多复杂的代谢途径。然而,氮高效已是作物遗传改良中不可忽略的一部分,并已通过传统育种和转基因方法的改良取得了一些进展^[34]。

IMAS 项目 (Improved Maize for African Soils; http://www.pioneer.com/CMRoot/Pioneer/About_Global/news_media/pannar/IMAS_fact_sheet_061813.pdf) 类似于上文提及的 WEMA 项目。该项目由 CIMMYT、非洲 NARD 和大型跨国公司杜邦先锋之间合作完成。对于 WEMA 项目来说,由 IMAS 项目生产出的种子对于 SSA 国家将免除专利费。但不同的是,该项目更强调氮高效杂交玉米的改良。该项目将结合常规育种与分子育种方法来导入和评估多个可能提高氮吸收效率的基因。考虑到这些国家和地区土地贫瘠、化肥价高且难买,实现氮高效无疑类似于一项免费^[14]的技术。所以,这将是一项有前景的政府与民间企业的合作项目,而且还有利于 SSA 国家的食品安全。还有另一项政府民间合作项目, Arcadia 生物科技公司已经捐献出它的氮高效和水利用高效基因技术。这个项目由 Africa Rice 和 CIAT 执行、AATF 协调(<http://aatf-africa.org/files/files/publications/Rice-Progress-Report-2012.pdf>),已在加纳和乌干达开始早期田间试验。

2.7 营养强化

食品安全不仅仅只是满足卡路里的需求。导致营养不良的一个主要因素是缺乏铁、锌和维生素 A 中之一或更多。很多研究者正尝试用生物强化的方法来应对营养不良——增加可吸收微量元素在作物中的积累。Harvest Plus (www.harvestplus.org) 是一个全球化的项目,旨在通过深度挖掘已有育种材料和收集高铁、高锌和高维生素 A 原的种质资源

来创造生物强化型作物。已有许多应用此方法的成功案例,如高铁含量的豆和狼尾草、高维生素 A 原含量的木薯、玉米和甘薯。但该方法的缺点之一是提高这些微量元素的水平不及通过转基因方法达到的,二是性状的遗传很复杂且易发生对当地品种的基因渗入。应用转基因策略的经典案例就是黄金大米^[35]。类似的黄金香蕉^[36]和黄金木薯也正在非洲进行田间试验^[1]。

已证实最具挑战的微量元素是铁。铁很活跃,但是植物中有着一套十分复杂的机制来维持其动态平衡以避免铁的过剩积累。最近的一项研究工作表明,超表达一个编码铁离子螯合酶(烟酰胺合酶)基因能够将水稻中铁离子和锌离子的含量提高到常规手段难以达到的水平^[37]。这项十分具有前景的发现也可能应用到其他作物上。

3 展 望

3.1 永无止境的田间试验

在很长的一段时间里,仅少数国家允许转基因作物的田间试验。这一点是最不幸的,因为没法在当地的条件下考察这些作物的性状,或是让农户有机会亲自观察这些结果。然而,现在非洲至少有 8 个国家和亚洲有如中国、越南、缅甸、印尼、菲律宾、孟加拉国、巴基斯坦等多个国家已允许转基因作物的田间试验,再加上时而允许时而禁止的印度。但正如 Bailey 等^[1]指出的那样,在许多国家,永无止境的田间试验好像没有违反规定,也好像永不会将转基因作物释放给农户。不幸的是,政治家们现在已经意识到允许田间试验是安全的,并可以借此展示他们的开明,而且,他们也意识到更安全的策略一是要求更多的田间试验,而不是批准悬而未决的生物安全法案(即使该法案已在当地立定);二是找到更多借口延迟转基因作物的推广(尽管其已经在田间试验中进行过无数次测试)。布基纳法索作为一个小国家批准了 Bt 棉的上市,受到了许多人的赞赏,而且已得到许多可喜的回报。批准的第 1 年,棉花产量增加 18%,在杀虫剂上节省的开支弥补了在种子上的花费^[18]。批准 6 年后,Bt 棉种植的比例已达到 70%。Bt 茄子近期在孟加拉国的上市也将是一个进步^[25]。

3.2 协调监管制度

众所周知,绝大多数食品紧缺国家缺少官方的转基因监管制度,或是监督制度不合理,这是阻碍转基因作物发展的绊脚石之一。发达国家花费了高额

的成本去迎合所有生物安全的要求。这个先例表明,对于缺乏资金的发展中国家来说,这些花费应该被禁止。建立全球认同的单一监督制度当然有助于转基因作物的发展,也有助于确认已有转基因作物的安全性。有一些例子是可以借鉴的,如加拿大就有一套合理的程序来考察作物新品种的性状而不是创造新品种的技术手段;巴西所有的制度都由一个机构制定;美国在这方面有着最丰富的经验,但有趣的是,在2010年由19个成员国组成的COMESA机构颁发了一项草案用于协调监督转基因作物,并帮助所有成员国科学地评估转基因作物,不过成员国是否接受转基因作物却是自愿的^[38]。这项草案在2013年被批准,其中还包括建立一个专门的COMESA生物技术和生物安全部门,来合理地确定生物评估的耗费,以保证它可能被所有成员国接受。可以预见到,反转基因的激进分子正在四处游说以期废除该政策^[39]。但不管怎样,如果非洲能在协调监管制度上建立一个模板,这将是转基因作物全球化进程中很重要的一步。

3.3 转基因作物该怎样定义?

生物技术发展如此迅速致使转基因作物的定义很容易就过时。在文章结束之际,我将举3个生物技术的实例来介绍。这3个实例都是利用转基因手段改造植物,但是最终获得的转化植物并不能称之为转基因的。第1例由已故的Simon Chan发明的“基因组介导消除”工作的一部分,提供了创造双单倍体的一种新手段。双单倍体中的每个基因位点都是纯合的,因此,它广受植物育种家的喜爱并被广泛应用于玉米育种工作中。但是另一些对贫困人群重要的作物如木薯和香蕉已被证实很难获得双单倍体。通过该方法,使用*cenH3-1 GFP-tailswap*转基因材料(含着丝粒改造后组蛋白GENH3)来诱导单倍体。当它与其他育种材料杂交后,从转基因亲本中得到的那条染色体发生丢失。因此,可以得到育种材料的单倍体胚随后再获得种子,那么从这些种子中就可以获得可育的双单倍体,它是非转基因的^[40]。一个由IITA、CIAT和UC Davis参加的项目正在尝试该技术在木薯和香蕉中是否可行。

第2例技术由杜邦先锋公司发明的,叫种子生产技术(SPT),该技术是可以产生杂交植物的新方法(http://www.pioneer.com/CMRoot/Pioneer/About_Global/our_research/enabling_technologies/enabling_technologies_sheets/Tech_SPT_2014.pdf)。它使用了一个转基因保持系,但是后代

和获得的杂交种中都不含转基因。在美国,该技术已成功在玉米中应用。在水稻中的应用还在进一步研发之中,同时对于在非洲种植的高粱和黍等作物中也有成功的希望。

由于育种过程会不断地改变植物的基因组信息,在我看来,第3项新技术极具希望,它可以实现对靶基因的定点改造,通过靶基因部分或完全失活来改良相应性状。锌指核酸酶技术可通过定点的核酸酶切割(SSN)对基因组精确编辑。定点核酸酶切割涉及到核酸内切酶对特定基因序列的识别以及切割。该技术是通过改造核酸酶,让其识别特定DNA序列(TALEN技术^[41])或是改造核酸酶上引导识别的RNA序列(CRISPR/Cas9技术)来实现的^[42-43]。核酸酶一旦靶到DNA上,就会切割DNA链,随后细胞中DNA自我修复,目标区段或是发生缺失或是发生少量序列改变,导致蛋白产物表达变化或是根本不表达。TALEN技术已经被用于获得具有白叶枯抗性的水稻突变体,并且带有TALEN骨架结构的载体序列在后期的育种中会自动消除,使转基因植物中没有外源DNA残留,并且除了目的基因的特定定位点修饰之外,植物基因组没有任何改变^[44]。

这些基因组编辑技术还可以用在包括哺乳动物在内的许多物种中^[43],其中CRISPR/Cas9技术因其仅靠与靶基因DNA序列同源的RNA序列识别而操作起来最为容易。有人预测,该技术将成为人类基因治疗和作物准确育种的有力工具。还有一点并没有被提及,那就是转基因和基因组编辑技术都能使育种家快速鉴定一个影响重要表型的大效应QTL位点中是否存在特异的位点。不幸的是,从事转基因的公司(也是基因的捐献者)阻碍发展中国家的研究团队做以上的尝试,即便是仅出于研究目的需要。

综上所述,转基因作物既可以给富有农民、还可以给贫穷农民带来好处,而且已证实它的安全性。加之已经有了很多不同于常规转基因手段的新技术。至少这些新技术在早期发展中应得到宽松的环境,通过它们创造的新品种不应该被视为转基因,也不应该以转基因作物的方式监管。看到这些具有前景的科学技术,特别是基因组编辑技术,我们应该对作物改良的前景更加乐观。但是,可以举这么一个小例子来说明我们将面临的挑战依然挥之不去。当我和我熟悉的一个反转人士谈论一项新技术——它的实现可以引起人类重大疾病基因突变的修正时,

他是相当兴奋,而且很赞同这项技术。但是当我又问到,如果将这项技术用来创造抗病的水稻品种呢,他犹豫一下,然后问道:“那它不就是转基因的吗?因为它是转基因,所以当然不可以!”

告诉那些谨小慎微的公众们如何合理评估任何新的科学技术(包括转基因和基因组编辑)的好坏以及这些技术在实现全球食品安全过程中是怎样帮助我们解决遇到的问题将是我们面临的严峻挑战。

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GM crops and food security

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Abstract If the world is to feed 9 billion people by 2050,it will need to use every technology available. Needless to say,GM crops are only one of many approaches needed to achieve global food security, but they certainly can play a positive role. Counteracting some of the current myths about GM crops,one can state unequivocally that current GM crops are safe for both humans and animals. Current GM crops that are herbicide tolerant or insect resistant can,under the right circumstances,benefit either small- or large-scale agriculture,both of which contribute to food security. Breeding and GM technology can synergize when genes for traits such as drought tolerance,improved nitrogen use efficiency,disease resistance, and/or improved nutritional content are expressed in superior germplasm developed through breeding. Looking to the future,the developing world needs to move beyond the stage of endless field trials and to develop harmonized regulatory regimes that will facilitate deregulation of events that have shown proven benefits in trials. New technologies such as genome editing offer great promise to carry out safe and precise changes to specific regions of the genome and should require much less regulatory oversight.

Key words GM crops; food security; genome editing; developing world; agriculture

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1 Introduction

If the world is to feed 9 billion people by 2050, it will need to use every technology available. When asked to address the potential role for GM crops in achieving global food security, I wondered if there is any more one can say about this topic that hasn't already been said. As with most issues surrounding GM crops, expressed sentiments can vary widely ranging from "GM crops are essential for achieving food security" to "GM crops are dangerous and should be banned". Often there is little serious dialog in between these two extremes, but I highly recommend some recent very thoughtful articles that provide a science-based discussion of GM crops^[1-4].

2 Addressing some common myths about GM crops

Myth 1. GM technology and the resulting GM crops are not safe

Any fact-based discussion must begin by clarifying one key issue: GM crops, as produced today are safe for consumption by animals and humans. In all the 30 years of production, one cannot cite even one legitimate argument that harm came to an individual or even an

animal that can be attributed to a GM trait in any crop. And, as long as reasonable regulatory systems are in place for agriculture, the safety of future GM crops should be assured. Yet millions of dollars have been spent by anti-GM activists and, as a result, millions of people have been told repeatedly that GM crops are not safe to eat and unfortunately, millions of people believe it. This is a case where the scientific community, serious voices in the press, and government officials are obliged to counter this argument and speak with one voice using science-based arguments for the safety of GM crops.

Ottoline Leyser^[5] recently wrote: "...we need to get beyond the idea that GM, as a technique for genetic improvement, is specifically and generically different from other crop improvement techniques, including conventional breeding." Like Leyser, I have long believed that, when judging a newly improved crop, we need to focus on the value and safety of any new trait and not on the way it was introduced. For example, no special regulation is required to approve use of an herbicide tolerant (HT) crop when it was created by selection of a mutant generated through irradiation of the seeds of a large parent population even though the selected seed may also contain many other uncharacterized mutations. By contrast, a full regulatory process is necessary to approve an analogous

HT crop generated through a transgenic approach involving insertion of one very well characterized gene. Does this make sense?

In the Americas we all worry about the serious decline in monarch butterflies. Although the widely used herbicide glyphosate does not harm butterflies, it does kill milkweed that is the major source of food for them—and milkweed often grows beside fields sprayed with glyphosate^[6]. I suggested to some anti-GM acquaintances that one solution might be to create a glyphosate-resistant milkweed and to ask farmers to grow it at the edges of their fields. Of course this could in the end be a bad idea—but wouldn't it be better to focus instead on a risk-benefit analysis of having HT or not in a particular crop (or weed) in a particular location rather than worrying so much about how the trait was produced?

Myth 2. GM crops may be suitable for large-scale agriculture but not for smallholder farmers in the developing world

The World Food Summit of 1996 defined food security as existing “when all people at all times have access to sufficient, safe, nutritious food to maintain a healthy and active life”. And the World Health Organization states that food security is built on three pillars

- Food availability: sufficient quantities of food available on a consistent basis.
- Food access: having sufficient resources to obtain appropriate foods for a nutritious diet.
- Food use: appropriate use based on knowledge of basic nutrition and care, as well as adequate water and sanitation.

It is obvious that any discussion of the suitability of GM crops to promote food security must focus first and foremost on the first pillar—food availability—in the form of higher-yielding crops. But the other pillars are also important—such crops should also address issues of nutritional value as we increasingly realize that many populations suffer not just from a deficit of calories but also from a lack of key micronutrients—the most critical of which are identified as deficits in iron, zinc and vitamin A. As for food access—there is a new emphasis in the developing world on promoting the profitability of agricultural endeavors. Bt cotton is a good example of a crop that has not directly enhanced food availability but certainly has enhanced economic access to food. A recent study by Qaim and Kouser^[7] provides evidence of improved food security for smallholder farmers in India who adopted Bt cotton when compared with non-adopters as a result of increased income that led to improved economic access

to food. And it may be surprising to many that, in 2013, of the 18 million farmers growing GM crops, 90% were resource-poor smallholder farmers, a large percentage of whom were growing Bt cotton in China and India^[8].

However, for a very poor person farming less than one hectare of land in a remote region with no access to fertilizer or improved seed, the very existence of GM crops is not likely to affect her prospects because of lack of seed access and so many other competing needs. She will have to save seed and/or trade it with neighbors, and hope for good weather and few pests. But moving up one level, many smallholder farmers in Latin America and Asia do have access to seed, and the quality of seed systems and penetration of crops like hybrid maize is increasing in many countries in Africa^[9]. Thus, provided that the seed is available and shown to provide benefits that outweigh the costs, evidence indicates that farmers, regardless of farm size, opt to buy improved seed and are also willing to consider a GM option.

Finally, global food security is not all about poor smallholder farmers. Although 86% of the world's farms are <2 hectares, the other 14% of the farms >2 hectares represent 88% of the world's farmland and account for a substantial proportion of agricultural production^[10]. History indicates that increasing urbanization is usually accompanied by consolidation of small farms, and when one considers the benefits that come from mechanization and uniform crop production on large farms when labor is limiting, the benefits of small farms diminish^[11]. But, as discussed later, large or small, the positive effects of the phenomenal uptake of GM crops in both the developed and developing world and their contribution to global food security cannot be minimized.

Myth 3. GM crops provide the only real solution for achieving food security

Of course not. Just consider some of these other good approaches that are also needed: increasing use of molecular approaches to breeding, development of more hybrid crops, enhancing soil fertility, improving water management, promoting better agronomic practices, building more and better roads, improving access to local power, developing stronger markets, slowing population growth, and promoting better government policies while getting rid of corruption.

3 What traits might contribute most to enhancement of food security?

3.1 Two traits dominate in GM crops globally

Overwhelmingly, the two most important traits today

in GM crops, singly or stacked together, are tolerance to herbicides (HT) and insect resistance (IR) as conferred by one of a number of Bt genes. Globally, a very high percentage of two major GM crops, maize (HT/IR) and soybean (HT), is grown in the U.S., Brazil and Argentina and used mostly for animal feed. I have thought to myself that, if governments mandated that a certain percentage of maize and a legume must be designed and grown only for direct human consumption instead of for animal feed, it could be a great help for achieving food security. But, for better or worse, since demand for meat is increasing dramatically in the developing world, and particularly in China^[12], the benefits of these highly-efficient, highly-productive large-scale production systems for maize and soybean translate to lower food prices globally and thus contributes to food security. In China, rice is the major food for human consumption while maize is the major crop used for animal feed. Bt rice (for control of a major pest the stem borer) was approved in 2009 as was low phytate maize, but neither has, as yet, been released to farmers, and China continues to be the biggest importer of GM maize and soybean for animal feed.

It is also important to note that nowhere in the world are GM versions of two major food crops, rice and wheat, grown legally by farmers, although development of new GM varieties and numerous field trials continue in a number of countries. Since 20% of the world's calories come from rice and a similar amount from wheat, at present, it is clear that GM currently plays no role in food security for the millions of people who rely upon one of these two crops as their major source of calories.

3.2 Herbicide tolerance (HT)

The increased prevalence of no-till agriculture, thought to be more suitable to larger farm sizes, relies heavily upon the availability of GM HT crops^[13]. A recent report^[14] that analyzes the impact that 11 selected technologies could have on the global yields and prices of rice, maize, and wheat and concluded that improvement in nitrogen use efficiency and heat tolerance of crops and use of no-till and precision agriculture offered the most promise. The benefits of no-till include use of less labor and fuel, preservation of soil moisture, and enhancement of soil fertility. But control of weeds is also critical, and, in the U. S. , the development of HT crops (predominantly glyphosate-tolerant) has clearly promoted the use of no-till for maize, cotton and soybean^[13]. HT wheat was developed

years ago by Monsanto but never released; the company is now saying that they are again considering marketing GM wheat, and HT varieties could certainly be a real benefit to wheat growers who are moving more and more to no-till.

Issues of labor costs and water availability are driving increasing interest in direct-seeded rice. Growing rice in paddies has built-in weed control, but I have been told by many rice growers that direct-seeded rice will never really take off unless they also can get HT varieties. Weedy, wild rices are a particular problem as they have similar responses as cultivated rice to most herbicides^[15]. One HT rice with tolerance to imidazolinone type of herbicides was selected through mutation breeding and is available, although there are worries about development of resistant wild rices. Other GM HT rices (e.g. to glyphosate) have been developed but are not commercially available.

There is much discussion now about the emergence of HT weeds, particularly those resistant to glyphosate that has been so widely used and not always managed well. Actually, the gene employed for resistance targets the active site of a key enzyme required in amino acid biosynthesis, and the rate of mutation to resistance is much lower than that for many other resistance genes targeting other herbicides^[16]. Yet, it is accepted that resistance to glyphosate was inevitable just as it can and does emerge in insects with respect to Bt toxins or in any crop plant bred through traditional means for resistance to any herbicide or pest or disease. The key issue is not GM vs. non-GM but rather promotion of the best possible management scenarios that can delay emergence as long as possible. Again—it is the trait that is relevant and not the way the trait was created in the crop.

3.3 Insect resistance (IR)

As mentioned previously, Bt cotton, through economic benefits from reduced pesticide costs and/or yield benefits, certainly contributes to food security in countries such as India^[7], China^[17], Burkina Faso^[18] and Pakistan^[19] even though it is not directly consumed by humans. Certainly Bt maize, because of its widespread adoption, plays a significant role in global food production and contributes substantially to global food security. However, I'd like to focus more on the issue of IR in some legumes important to smallholder farmers in a number of developing countries because I think this story covers a lot of issues relevant to development of transgenic crops that extend beyond just cotton, maize, and soybean.

It is often pointed out that the food security issue might be effectively solved if humans would stop the growing trend toward eating more meat and solved the problem of wasted food. GM approaches might play a role in the food waste problem through manipulation of the many genes we know regulate the process^[20]. And the Chinese were the leaders in creation of a plant-based protein product from legumes with the invention more than 2 000 ago of Tofu. Today, with rising meat demand, use of legumes and wheat gluten to create new protein-rich products from plants is gaining ever more attention (<http://www.peta.org/living/food/meat-replacements/>). And, to my mind, there are no more interesting vegetarian dishes in the world than those eaten regularly by the poor of India that rely heavily on chickpea and pigeon pea. But, even though hardy and nutritious, these legumes present many challenges such as large seed size, low yields, diseases, and lack of hybrids (except for pigeon pea) that make them less attractive to private sector seed companies.

Chickpea is the third most important food legume and is very hardy and nutritious and widely grown in Africa, the Middle East, and Asia. In West Africa, cowpea provides a major source of dietary protein for humans and fodder for animals, and, through fixation of nitrogen, also contributes to soil fertility. Pigeon pea is widely used as the major ingredient in dal and, as such, a major source of dietary protein for the poor of India; in recent years, it has become more widely grown in East Africa where it is consumed locally but also serves as an important export crop to India.

One major challenge is that chickpea, cowpea, and pigeon pea are devastated on farmers' fields by insect pests, particularly the pod borers (PBs), *Helicoverpa armigera* and *Maruca vitrata*. They cause an estimated loss of over USD 1 billion annually, despite application of insecticides costing over \$500 million annually (www.ICRISAT.org). Appropriate insecticides are not always available to smallholder farmers and less safe ones are often substituted. PBs are quite susceptible to several different Bt proteins, and, due to lack of significant resistance in available germplasm, creation of Bt versions for each of these legumes represents essentially the only guaranteed path for addressing yield losses due to PBs. Both cowpea and chickpea are self-pollinating, and outcrossing to other varieties or wild relatives is limited; this makes gene flow much less of a problem and maintenance of the trait more assured when seed is saved by poor farmers who tend to purchase seed only every 3-4 years^[22]. Pigeon pea by contrast, is an outcrossing species, which could be

a disadvantage for gene flow, but an advantage in that it has allowed development of hybrids that are higher yielding and could be offered by the private sector that might also be able to contribute expertise with respect to resistance management. Indeed, I think the greatest challenge for public sector efforts aimed at crops not commonly targeted by the private sector is to develop robust seed systems that can also contribute to resistance management. Attracting the private sector is probably the best solution; certainly the popularity of GM soybean represents a case where the private sector has been heavily engaged with one legume.

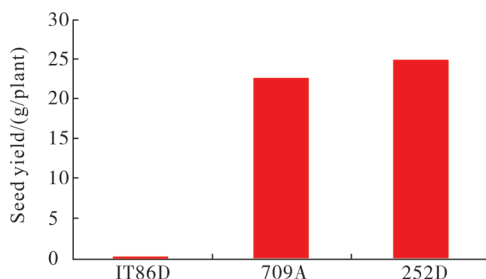
A very comprehensive project to develop Bt cowpea for Africa has produced over 800 transgenic Bt cowpea events over more than a decade of work (www.aatf-africa.org; T J Higgins, personal communication). This project has provided many insights into the many challenges faced by a public sector project that targets food-insecure areas of sub-Saharan Africa (SSA). The first hurdle was to develop a procedure for efficient transformation of cowpea that was accomplished in the lab of T J Higgins in Australia^[22]. The second hurdle of obtaining rights to use of the *cry1AB* gene was surmounted by AATF when it was recognized that liability issues were the primary concern of Monsanto, the potential donor. This concern was dealt with by an agreement that Monsanto would not interfere with use of the gene for this project, but it would not provide tangible DNA constructs containing the gene; the project itself would be responsible for production of the genes using critical DNA sequence information provided by Monsanto. Produced by the Higgins laboratory, the transgenics when tested locally in greenhouses proved to be highly resistant to applied Maruca pod borer (MPB) and showed no obvious phenotypic abnormalities. While waiting a number of years for approval to carry out confined field trials (CFTs) in West Africa, the project carried out a few trials in Puerto Rico; lack of good infestation prevented testing efficacy, but these trials did provide some evidence that some of the best events did show stunting that had not been observed in the greenhouse. Nigeria proved to be the first country in West Africa where CFTs have been carried out now for 4 years; this has been accompanied later by several years of trials in Burkina Faso and more recently in Ghana.

The results are certainly impressive and point out how important it is to be able to carry out CFTs in the target countries. Fig.1 shows an early stage in a large CFT in Nigeria in 2012 where final results showed that there was no yield drag in the best two events

compared to the control in the absence of insects. Fig.2 shows the results of a trial in 2012 in Burkina Faso in which infestation of controls was particularly severe. Event 709A is now being used as a donor parent to introgress the MPB resistance trait into farmer-preferred varieties that have resistance to Striga, aphids and thrips. Huesing et al^[21] have examined a number of regulatory issues facing this project. In addition to the self-pollinating behavior of cowpea that mitigates extensive outcrossing, they have also pointed out that the Bt genes that are effective against the MPB have been extensively characterized for other crops, and are not expected to have significant effects on non-target insects. Development of resistance to the Bt proteins may also be delayed due to a pattern of south to north migration of the MPB and through current efforts to introgress of a second Bt gene with a different mode of action. Although not so advanced, efforts to develop Bt chickpea and pigeon pea, both of which can now also be transformed^[23-24] are underway with indications that success similar to that obtained with cowpea should be possible (K. Sharma and T J Higgins, personal communications). Together with the recent release of Bt brinjal (eggplant) in Bangladesh (and pending still in



Fig.1 Confined field trial (CFT) in Nigeria in 2012



Trial was held in Burkina Faso in 2012. IT86D represents the control non-transgenic parent line used for transformation; transgenic events 709A and 252D contain the *cryIAB* (Bt) gene. Event 709A has been chosen as the key event that is being introgressed now into farmer-preferred varieties (Courtesy of TJ Higgins).

Fig.2 Results of a CFT of transgenic Bt cowpea in a field heavily infested by pod borer *Maruca vitrata*

India, see Barwale-Zehr^[25]), these projects demonstrate that public-private efforts to develop transgenic crops targeted for food-insecure consumers are clearly possible.

3.4 Disease resistance

Large-scale agriculture in the developed world effectively controls plant diseases through conventional breeding, use of pesticides and fungicides, and very effective management strategies. The first (and only) public sector effort to succeed to develop a GM crop that has been released to farmers was a papaya resistant to ring-spot virus—an effort that virtually saved the papaya industry in Hawaii^[26], and GM papaya has now also been released to farmers in China^[8]. Another encouraging development is that the first successful public sector CFT for resistance to *Xanthomonas* wilt disease in banana has recently been carried out in Uganda^[27].

Geminiviruses are a particular problem in the developing world, affecting many vegetables, and, unique to Africa, maize streak and cassava mosaic viruses. Cassava in East Africa is also suffering large yield losses due to a an RNA virus called Brown Streak. While a few loci conferring resistance or tolerance to some of these viruses are used in breeding programs, the numbers are limited, and a GM approach is considered important as a backup, especially as some of the viruses can undergo extensive mutations^[28]. A number of groups are working to develop resistance to the African viruses of maize and cassava and many of these are now in greenhouse or confined field trials (CFTs) in various African countries (see Bailey et al.^[1] for an up-to-date list of current efforts on GM crops in Africa). A public sector effort by EMBRAPA in Brazil has now succeeded to obtain commercial release of a GM bean resistant to golden mosaic virus^[29]. It is beginning to look as if a transgenic approach may be the only solution to citrus-greening disease that is fast becoming a global crisis for the citrus industry^[30].

3.5 Drought tolerance (DT)

With all the uncertainties imposed by climate change and the rising competition between urban versus rural water use, finding ways to enhance the tolerance of crops to drought has emerged as a high priority for agriculture around the world^[31]. From long experience, most breeders have concluded that drought tolerance is a complex trait that is controlled by plants in a wide variety of ways. Nevertheless, there are countless numbers of publications showing that over-expression of a variety of single genes leads to some sort of

phenotype relating to drought tolerance^[32]. But many of these studies have been done in model plants or did not involve extensive field trials under well-controlled conditions.

In the past two years, two multi-national companies have released new maize varieties in the U. S. that offer a very interesting comparison between use of genomics and molecular breeding versus transgenic approaches. The first example is that of Optimum[®] AQUAmax[®], a brand name of Dupont-Pioneer for a series of drought-tolerant hybrids adapted to various climatic zones in the U.S., and produced through state-of-the-art molecular breeding approaches (see <https://www.pioneer.com/home/site/us/products/corn/seed-traits-technologies-corn/optimum-aquamax-hybrids>). By contrast, Monsanto has recently released to farmers its first line of GM DT hybrid maize, called Ingenuity[®] DroughtGard[™] Hybrids (see <http://www.monsanto.com/products/pages/droughtgard-hybrids.aspx>). In this case, tolerance is conferred by expression in inbred lines of a single gene encoding a chaperonin^[33]. Interestingly, in 2013, even though these hybrids were only in their first year of release in the U. S., the trait was approved for import by China which seems to indicate great interest in DT maize varieties.

While it is still premature to judge the relative success of these two approaches to achieving drought tolerance, early results do indicate that both approaches can lead to modest yield gains under stress with no reduction in yield without stress. Aquamax has been in the field longer, and across the past three growing seasons among 42 000 comparisons, Optimum[®] AQUAmax[®] products have shown a 6.9 bushel yield advantage in water-limited environments and a 3.6 bushel yield advantage in normal growing conditions. (https://www.pioneer.com/cmroot/pioneer/us/products/seed_trait_technology/optimum_aquamax/Infographic_AQUAmax_2014.pdf). Very early reports on Drought Gard indicated about a 5 bushel/acre increase under stress. These gains for the two different approaches may seem modest, but development of commercial hybrid maize has already inadvertently selected for DT through its many years of selecting for yield stability in multiple environments^[31]. These results also dispel a common misunderstanding that there could be miracle gains in DT obtained by manipulating either a single gene or large numbers of genes. Indeed, both companies apparently believe in promoting a strong synergy between molecular breeding and GM; Pioneer-Dupont is currently assessing several genes that they may want to introgress into their DT maize that was

developed by molecular breeding; and Monsanto is making an effort to introgress their single gene into germplasm that already has some documented DT.

Monsanto is currently collaborating with CIMMYT and NARS from a number of countries of East Africa in a project called WEMA (Water Efficient Maize for Africa) in which the DroughtGard trait is being tested in African maize (<http://wema.aatf-africa.org/>). Under an agreement, any successful hybrids will be released royalty-free in these countries. Again emphasizing the synergy between breeding and GM, the concomitant promotion of high-yielding hybrids adapted for Africa will undoubtedly be as important as the deployment of the DT trait.

Regardless of the technology used to deliver the DT trait, one thing has clearly emerged—DT is one of the most challenging of all traits because of the extreme difficulty of designing trials under highly controlled conditions that are reproducible. This is one area where the private sector has extraordinary expertise that one would hope could be shared in further imaginative public-private partnerships for the benefit of developing world agriculture.

3.6 Nitrogen use efficiency (NUE)

In most agricultural situations both in the developed and developing world, the natural supply of N in the soil is a major limiting factor for yield^[34]. Optimizing N fertilizer application is a goal for all farmers in order to save money and minimize effects of overuse on the environment. Access and cost are obviously also critical factors for many of the rural poor. Much attention now is given to development of crops with enhanced NUE, but this is proving challenging since NUE can be defined in many ways, is difficult to measure, and can involve many complex metabolic pathways. Nevertheless, NUE has emerged as a serious topic for crop improvement, and some progress is being made both with breeding and transgenic approaches^[34].

Similar to the WEMA project mentioned above, another project called IMAS (Improved Maize for African Soils; http://www.pioneer.com/CMRoot/Pioneer/About_Global/news_media/pannar/IMAS_fact_sheet_061813.pdf), a collaboration between CIMMYT, African NARS and another large multi-national Dupont Pioneer. As for WEMA, seed produced by IMAS will be available royalty-free to farmers in SSA, but, in this case, the target is improved hybrid maize with emphasis on NUE. Employing both classical and molecular breeding, the project will also introgress and assess several genes identified as possibly conferring increased NUE. Given that NUE

was targeted as a technology with high likelihood of pay off^[14] because of poor soil quality and the high cost and poor access for fertilizer in SSA, this is another promising public-private partnership with real potential to enhance food security in SSA. In another interesting public-private partnership, Arcadia Biosciences has donated its gene technologies for NUE and water use efficiency in rice for use in a project carried out by Africa Rice and CIAT and coordinated by AATF (<http://aatf-africa.org/files/files/publications/Rice-Progress-Report-2012.pdf>). CFTs are in early stages in Ghana and Uganda.

3.7 Enhanced nutrition

Food security is more than just calories; indeed, a major factor in malnutrition is a deficiency of one or more of the micronutrients iron, zinc, and vitamin A, and there are a number of efforts underway to approach the problem of malnutrition through biofortification—the development of crops richer in available micronutrients. Harvest Plus (www.harvestplus.org) is a global project that is primarily aimed at developing biofortified crops through extensive mining of breeding lines and germplasm collections for accessions showing elevated levels of iron, zinc or pro-vitamin A. Some successes from this approach are emerging such as high iron beans and pearl millet, and high pro-vitamin A cassava, maize and sweet potato. But often the enhanced levels are not as high as might be obtained through transgenic approaches, and heritability of the trait can sometimes be complex making introgression into local varieties challenging. The classic transgenic approach is that of “Golden Rice” that is discussed elsewhere in this proceedings^[35]. Similar efforts to create “golden” banana^[36] and cassava are in CFTs in Africa^[1].

The micronutrient that has proven most challenging is iron. Iron is highly reactive, and plants have devised a very complex mechanism of homeostasis that prevents elevation of excess iron. But recent work has shown that over-expression of a gene encoding an enzyme catalyzing synthesis of a chelator of iron, nicotianamine synthase, can lead to levels of both iron and zinc in rice that exceed any found through conventional approaches^[37]. This very promising finding may also be applicable for a wide variety of other crops.

4 Looking to the future

4.1 The endless game of CFTs

For many years, very few countries would even allow CFTs of newly developed GM crops. This was most

unfortunate as there was really no opportunity to test the efficacy of these crops in local environments or to give farmers a chance to view results themselves. However, CFTs are permitted now in at least 8 countries in Africa and many important ones in Asia (e.g., China, Vietnam, Myanmar, Indonesia, Philippines, Bangladesh, Pakistan, and “on and off” also India). But as Bailey et al. point out^[1], in many of these countries there is a pattern of never-ending field trials that seem never to lead to deregulation and release to farmers. Unfortunately politicians have now learned that it is safe to allow field trials showing they are open-minded, and safer still to keep demanding more trials instead of making the harder decision to approve pending biosafety bills or, even where such bills are in place, to find more and more reasons to delay deployment of crops that have been endlessly tested in CFTs. Much praise goes to Burkina Faso as an example of a small country that took the leap and allowed release of Bt cotton, and the results have been very rewarding; in the first year of release, yields were increased by 18% and the extra cost of the seed was offset by the savings in use of pesticides^[18]. After 6 years in the field, the percent of cotton that is Bt has risen to almost 70%, and the benefits continue. Recent release of Bt brinjal in Bangladesh is also a positive development^[25].

4.2 Harmonizing regulatory regimes

There is widespread recognition that the lack of, or inadequacy of, national regulatory regimes in most of the food-insecure countries is one of the serious roadblocks to deployment of GM crops. The high cost of meeting all the biosafety requirements in the developed world has also set a precedent that costs could be prohibitive for poorly funded efforts in the developing world. Creating a globally recognized single regulatory regime that any country could opt to adopt could certainly contribute to GM crop development and also assure safety of approved crops. Drawing from some good examples, the Canadians use a procedure that looks at the trait rather than the method used to produce it; Brazil has all of its regime within one agency; the U. S. has by far the most experience. But perhaps most interesting is the effort of regional organization COMESA (Common Market for Eastern and Southern Africa) that produced in 2010 a draft policy on a harmonized regulation of GM technology proposing that COMESA itself would scientifically assess GM crops for all its 19 member countries, although acceptance by each country was proposed to be voluntary^[38]. This draft was approved in

2013 by the Council of Ministers of COMESA, and the policy includes creation of a COMESA biotechnology and biosafety unit that should allow for biosafety assessments at a reasonable price that could potentially be accepted by all countries in the region. Predictably, anti-GMO activists are lobbying to have the policy scrapped^[39], but it would be an amazing step forward for GM crops globally if Africa could lead the way in development of a model for harmonized regulation.

4.3 What defines a GM crop?

Biotechnology advances so rapidly that definitions can easily become outdated. In closing, I will cite three cases where plants have been altered using techniques related to transgene technology but where the final product in no way can be defined as transgenic. The first is a lovely piece of work that came from a discovery by the laboratory of the late Simon Chan called “genome mediated elimination” that offered a new approach to creating doubled haploids (DHs). Being homozygous at each allele, DHs are of huge value to plant breeders and are widely used in maize breeding, but some crops, including cassava and banana so important to the poor, have proven difficult to convert to DHs. To induce haploidy, this method relies on a transgenic line, *cenH3-1 GFP-tailswap*, which contains a modified version of the centromere-specific histone protein CENH3. When crossed with any desirable breeding line, the chromosomes of the transgenic line are lost, producing haploid embryos of the breeding line that can spontaneously produce seed, some of which are fertile doubled haploids that are NOT transgenic^[40]. A project involving IITA, CIAT and UC Davis are now testing the feasibility of this technology for both cassava and banana.

A second technology is from Dupont Pioneer and involves an innovative approach to making hybrid plants called SPT (Seed Production Technology) (http://www.pioneer.com/CMRoot/Pioneer/About_Global/our_research/enabling_technologies/enabling_technologies_sheets/Tech_SPT_2014.pdf...). In this case a transgenic maintainer line is used, but the progeny and resulting hybrid seed contain no transgenes. Approved now for maize in the U. S. , it is also under development for rice and might show real promise for other crops such as sorghum and millets in Africa.

Just as genomics has changed the face of breeding forever, the third new technology, in my opinion, offers the most precise way possible to carry out editing of a targeted gene to create a more or less active or null form that leads to trait improvement. Extending earlier work

with zinc-finger nucleases, the technology is a form of precise genome editing referred to as Site Specific Nuclease Fusion (SSN). SSN involves the targeting of an endonuclease to a specific gene sequence wherein the specificity of targeting is directed by the recognition of a specific DNA sequence by engineered proteins (TALEN SSN technology)^[41] or by an engineered guide RNA (CRISPR/Cas9 SSN technology) that is fused to the nuclease^[42-43]. Once targeted, the nuclease cleaves the DNA and attempts by the cell to repair the DNA can result in a deletion or minor sequence changes that can lead to altered expression of the protein product or a knock-out with no gene product. The TALEN approach has been used as proof of concept to generate a mutant of rice resistant to bacterial blight, and the vector containing the TALEN construct was eliminated through subsequent breeding leaving a plant with no foreign DNA or genome changes beyond the very specific editing of the targeted rice gene^[44].

These systems work in many different organisms including mammals^[43]; the CRISPR/Cas9 system is the easiest to design since its specificity is based upon RNA sequence homology with the targeted DNA sequence, and one predicts it will become a powerful tool for gene therapy in humans and for precision breeding of crops. One point not often discussed is that both GM and SSN are also powerful research tools that can allow breeders to rapidly check whether a specific allele within a larger QTL is responsible for the sought-after phenotype. Unfortunately, pressure from donors wary of GM has discouraged many groups in the developing world to minimize all such efforts, even for research purposes.

In sum, GM has demonstrated its promise to provide benefits to both rich and poor farmers and has proven itself safe. In addition, there are powerful new technologies that are fundamentally different from classic GM approaches, and the resulting products, while needing some form of oversight at least in the early stages development, they should not be viewed nor regulated as GM organisms. The great promise of these technologies, particular genome editing using SSN, offers great cause for optimism. However, the challenges ahead can be exemplified by this little story: I asked an anti-GM acquaintance of mine how he would feel about a new technology that could correct the genetic mutations responsible for serious human diseases. He was incredibly excited and positive. Then I asked him how he would feel about using it to create resistance to a disease in rice, and he hesitated and then asked, “But is it GM? Because if it

is, then certainly not!”

It is indeed our challenge to continue to help a wary public to learn how to logically assess the risks and benefits of any and all new technologies—including GM and SSN—that can certainly contribute, along with many other technologies, to our quest for global food security.

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