ARTICLE IN PRESS

Plant Science xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Plant Science

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

Where are the drought tolerant crops? An assessment of more than two decades of plant biotechnology effort in crop improvement

Michael L. Nuccio[a,*], Matthew Paul[b], Nicholas J. Bate[a], Jonathan Cohn[a], Sean R. Cutler[c]

[a] Syngenta Crop Protection, LLC., 9 Davis Drive, Research Triangle Park, NC, 27709, USA
[b] Rothamsted Research, Harpenden, Hertfordshire, AL5 2JQ, UK
[c] Plant Cell Biology and Chemistry, Botany and Plant Sciences Chemistry Genomics Building, University of California Riverside, CA, 92521, USA

ARTICLE INFO

Keywords:
Drought tolerance
GMO
Crop genetic engineering
Agricultural biotechnology

ABSTRACT

Since the dawn of modern biotechnology public and private enterprise have pursued the development of a new breed of drought tolerant crop products. After more than 20 years of research and investment only a few such products have reached the market. This is due to several technical and market constraints. The technical challenges include the difficulty in defining tractable single-gene trait development strategies, the logistics of moving traits from initial to commercial genetic backgrounds, and the disconnect between conditions in farmer's fields and controlled environments. Market constraints include the significant difficulty, and associated costs, in obtaining access to markets around the world. Advances in the biology of plant water management, including response to water deficit reveal new opportunities to improve crop response to water deficit and new genome-based tools promise to usher in the next era of crop improvement. As biotechnology looks to improve crop productivity under drought conditions, the environmental and food security advantages will influence public perception and shift the debate toward benefits rather than risks.

1. Introduction

Drought and water use efficiency are important factors that contribute to agricultural productivity worldwide [1]. Most cropland is rain fed leaving overall productivity to less predictable weather patterns. Furthermore, increasing global temperatures introduce additional uncertainty [2]. In addition, there is a push to maintain or increase productivity in an environmentally sustainable way [3]. Finally, the rate of productivity improvement for many crops is also in decline [4]. All this is happening in a world that is projecting nearly 2 billion more mouths to feed in the next 30 years [5].

Researchers and growers around the world recognize that water is the single most important abiotic factor limiting crop productivity [6]. Biotechnology is considered one of the most promising ways to develop new cultivars with a substantially improved tolerance to water deficit [7,8]. In this context, biotechnology encompasses the introduction of transgenes that directly affect plant water use, much in the way transgenes were used to enable herbicide tolerance or insect resistance. This is also known as genetic engineering, genetic modification (GM) and the creation of genetically modified organisms (GMOs), one of many gene-based technologies being applied to crop improvement [9].

Industry research is not often published in peer-reviewed literature, but the few examples highlight research to develop drought tolerance traits for corn [10–15]. Despite significant effort, Monsanto's DroughtGard® is the only drought tolerant corn biotechnology product on the market [10,16]. DroughtGard® has not had a significant impact in the marketplace and does not appear to exhibit an advantage over non-GM efforts to improve drought tolerance [17] that would justify the cost of registration and research. Additional drought tolerance biotechnology products include Verdeca's HB4 soybean [18] which is in the regulatory approval process in the U.S. (https://www.aphis.usda.gov/brs/aphisdocs/17_22301p.pdf) and Argentina, and PT Perkebunan Nusantara XI's NXI-4T sugarcane which is approved for cultivation in Indonesia [19]. Other drought tolerance products developed using molecular marker assisted breeding include Dow-DuPont 's AQUAmax® [20] and Syngenta's Artesian® [21] product lines.

The lack of products does little to illustrate what has been accomplished. It is no small feat to develop a drought tolerant GM product with measurable performance in the field. The above results demonstrate that GM technology can contribute to improving crop response to water deficit [22]. It also indicates that metabolic processes that contribute to crop drought tolerance are not fully understood. New screens will be necessary to identify genes that significantly contribute to these important plant mechanisms.

* Corresponding author. Present address: 27 Bridge Street, Salem, NH, 03079, USA.
E-mail addresses: mlnuccio1065@gmail.com (M.L. Nuccio), matthew.paul@rothamsted.ac.uk (M. Paul), nic.bate@syngenta.com (N.J. Bate), josh.cohn@syngenta.com (J. Cohn), sean.cutler@ucr.edu (S.R. Cutler).

https://doi.org/10.1016/j.plantsci.2018.01.020
Received 15 December 2017; Received in revised form 29 January 2018; Accepted 31 January 2018
0168-9452/

Please cite this article as: Nuccio, M.L., Plant Science (2018), https://doi.org/10.1016/j.plantsci.2018.01.020

The lack of marketable products despite significant investment is not lost on the scientific community [23,24]. Many have openly questioned the way these products are developed [23], and recent presentations to investors suggests that some companies have shifted their research and development investments to other areas. This review examines the pursuit of drought tolerant or water use efficient crops through application of biotechnology. While there are significant technical hurdles, the global regulatory environment also imposes constraints that affect the way research is conducted. The presence of GMO products in the food supply chain remains a flash point in many countries [25–28]. This is well-understood by industry research teams. New plant breeding innovations, such as genome editing, offer promising opportunity to advance the development of drought tolerant products [29]. While some government agencies such as the United States Department of Agriculture have issued responses to letters of inquiry from developers seeking clarity on the regulated status of their products, the global regulatory landscape remains uncertain about genome-edited plants.

2. The Drought Tolerance Product Concept

2.1. Research to improve crop drought tolerance

Both public and private investment in drought tolerant crops saw a steady increase through the 1990′s and early 2000′s. Fig. 1 is an examination of PUBMED for articles with the terms ‘drought’ and ‘plant’ in the Abstract/Title since 1990. There is a rapid increase in publications starting in the early 2000′s which continues to this day. This broadly captures the field of drought research. The term ‘gene’ was added to the search to narrow focus toward biotechnology research which is often gene centric. These publications rose from less than 1% in the early 1990s to 46% in 2005–2010. The results indicate that while drought research continues to increase, the share of published research attributed to biotechnology has fallen to just over 36%.

The level of commercial drought research can be estimated in a similar way. A search of U.S. Patent Applications, in Fig. 2, with the same terms in the Claims section indicates a sharp rise in applications from 2001 to 2003 which remains steady then rises in 2009 and again in 2013. The share attributed to biotechnology rose to nearly 45% in 2009 and has since declined to 25% today. Granted U.S. Patents, in Fig. 3, follow a similar trend. This rather crude assessment of drought research is meant to reveal trends. A fair question is why hasn’t biotechnology research resulted in more drought tolerant products? To address this, we examined the research produced by industry and academic groups and discuss the similarities and differences.

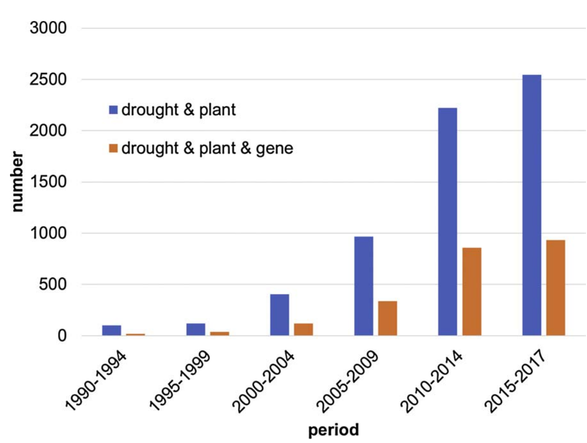

Fig. 1. Growth of peer-reviewed literature in PubMed focused on drought tolerance. PubMed was surveyed for articles with ‘drought’ and ‘plant’ in the title/abstract. ‘Gene’ was added to identify articles informing biotechnology applications.

2.2. Defining drought

Drought or water deficit means many things to growers [30]. It is a consequence of the environment which varies with place and time. No two environments are exactly alike and weather conditions on a farm change throughout and across growing seasons. The impact of water deficit on crop productivity varies with respect to crop, when it occurs in the crop cycle and its duration/intensity. Genetics that provide durable resistance to periods of water deficit are likely already fixed in commercial germplasm or are the subject of on-going breeding programs [31–33]. Molecular biologists and biotechnologists initially sought to apply the basic strategy that drove the development of commercial insect control and herbicide tolerance traits. This often began with proxy or surrogate assays, such as withholding water from potted plants, often conducted in controlled environments [22,34].

Many approaches were developed to simulate water deficit. They ranged from imposing osmotic stress with chemicals like sodium chloride or polyethylene glycol (PEG) or withholding water for a period of time or until differences between experimental and control groups where obvious. The latter evolved into the common practice of applying a lethal drought, where most control plants die and most traited or transgenic plants survive the treatment. Many studies identified genes with activity in these assays and several papers discuss the relevance of this research to water deficit in a production environment (reviewed in [23]). But the discovery process begins with 100′s to 1000′s of genes to test and surrogate assays are the most efficient way to conduct an initial evaluation [22]. This is of particular importance if drought tolerance is one of many traits in a biotechnology program [35]. Industry groups often employ research strategies to control costs and maximize throughput/efficiency which are often referred to as platforms. The investment in platforms typically makes it necessary for the research to fit the platform. The limitations of a discovery pipeline approach do not only apply to agriculture, similar issues affected success in pharmaceutical discovery [36], particularly in translation from early discovery to clinical trials (the so-called Valley of Death) [37].

The challenge is defining a practical water deficit problem that is compelling enough to initiate a product development project. This informs all the downstream work, including the crop to focus on, what genes to work on, how to express candidate genes and how to evaluate their effect. The initial hypothesis needs to be granular enough to connect metabolism to the desired phenotype, and many drought researchers know that this is non-trivial. One approach hypothesizes that there is a class of genes that confer drought tolerance when expressed using the CaMV 35 promoter [38] in plants exposed to water deficit but, do not impact productivity in well-watered environments. The bacterial cold shock protein [10] in Monsanto’s DroughtGard® trait is an example, and given the breadth and depth of their drought research program the evidence suggests these genes are extremely rare. Another approach only considers the impact of water deficit during early reproductive development [14]. Most crop production incorporates a package of technologies to make it as efficient and profitable as possible. Many modern traits are based on single genes, but it might be possible to extend this to a few genes per trait. Ideally a drought tolerance trait complements other technologies and focuses on problems not easily addressed by other approaches. The obvious advantage of biotechnology is its ability to introduce novel genetic information. Another advantage is its modularity, for example the ability to create novel combinations of regulatory sequence and protein coding sequence.

2.3. Crop choice for drought tolerance traits

Biotechnology trait development is an expensive enterprise [35]. It is not cheap or easy to produce transgenic crops, and many crops cannot be easily transformed. A recent assessment estimates, based on successful trait development, that more than 19 cumulative years are