Yield10 BIOSCIENCE

Leveraging a novel carbon sink to investigate the potential and limitations of C4 photosynthesis in the C4 monocot warm season grass switchgrass

Kristi Snell, PhD
CSO and VP of Research

June 27, 2017

Safe Harbor Statement*

The statements made by Yield10 Bioscience, Inc. (the "Company," "we," "our" or "us") herein regarding the Company and its business may be forward-looking in nature and are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements describe the Company's future plans, projections, strategies and expectations, including statements regarding future results of operations and financial position, business strategy, prospective products and technologies, timing for receiving and reporting results of field tests and likelihood of success, and objectives of the Company for the future, and are based on certain assumptions and involve a number of risks and uncertainties, many of which are beyond the control of the Company, including, but not limited to, the risks detailed in the Company's Annual Report on Form 10-K for the year ended December 31, 2016 and other reports filed by the Company with the Securities and Exchange Commission (the "SEC"). Forward-looking statements include all statements which are not historical facts, and can generally be identified by terms such as anticipates, believes, could, estimates, intends, may, plans, projects, should, will, would, or the negative of those terms and similar expressions.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and may be beyond the Company's control, you should not rely on these statements as predictions of future events. Actual results could differ materially from those projected due to our history of losses, lack of market acceptance of our products and technologies, the complexity of technology development and relevant regulatory processes, market competition, changes in the local and national economies, and various other factors. All forward-looking statements contained herein speak only as of the date hereof, and the Company undertakes no obligation to update any forward-looking statements, whether to reflect new information, events or circumstances after the date hereof or otherwise, except as may be required by law.

***Under the Private Securities Litigation Reform Act of 1995**

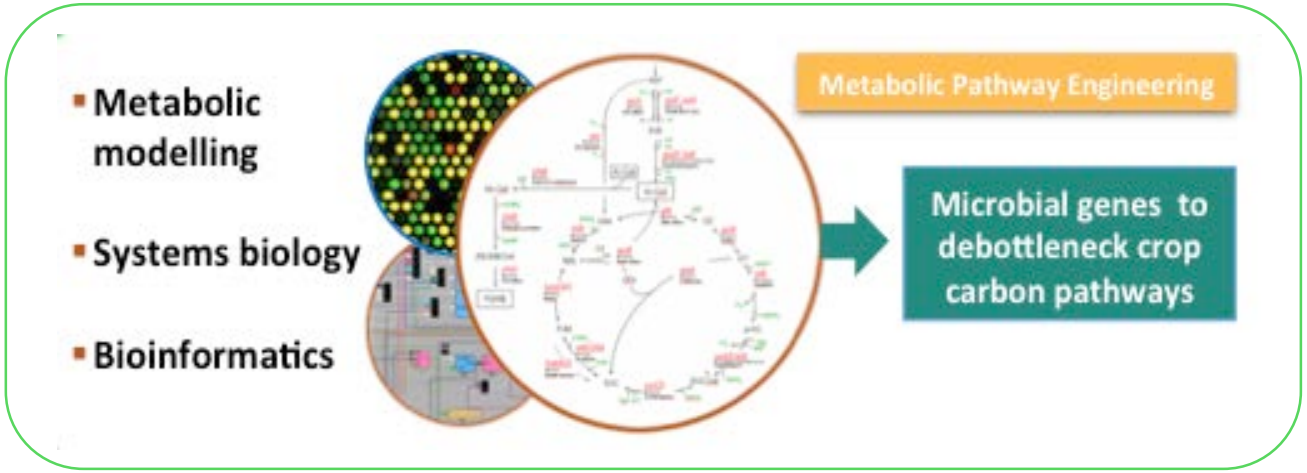
Company Overview and Objective

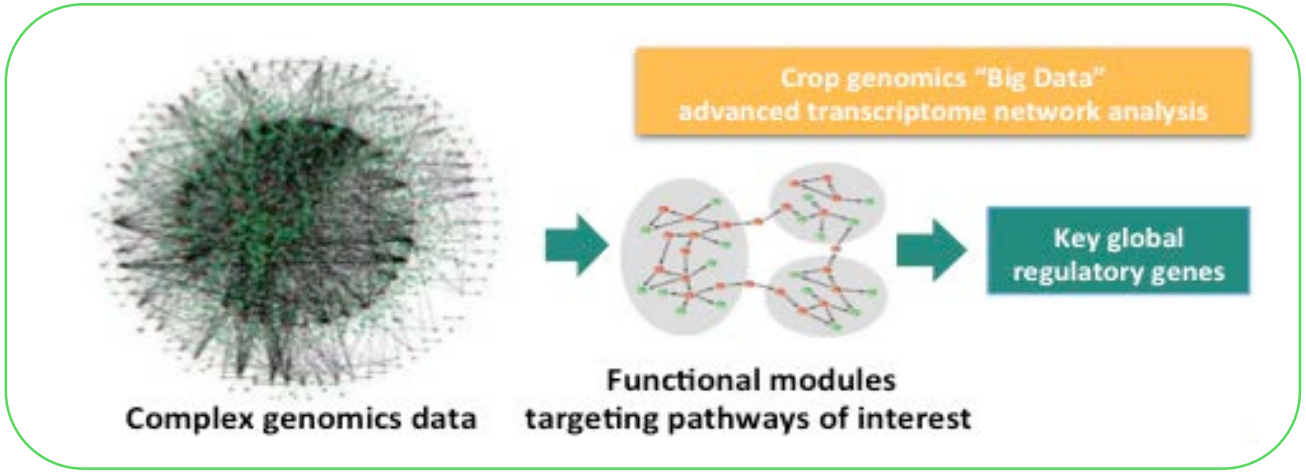
"Yield10 designs precise alterations to gene activity and the flow of carbon in food and feed crops to produce higher yields with lower inputs of land, water, or fertilizer"

- Leveraging a large historical investment in advanced metabolic engineering into a new arena
- Technology platforms and unique knowledge base span over 30 years of advanced metabolic engineering research experience and major accomplishments, including 19 years in crops
- Targeting over $15 billion of incremental value creation in North American crops
  - *Canola, soybean and corn*
- Headquartered in Woburn, MA USA, with an Oilseeds center in Saskatoon, Canada

Yield10 Technology Platform Overview

Discovery paradigm based on metabolic pathway engineering expertise, enables the intelligent targeted manipulation of specific gene combinations





The "Smart Carbon Grid for Crops"

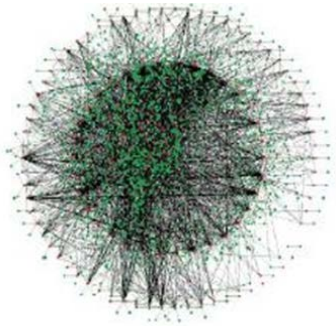
- Metabolic engineering platform to improve carbon capture and conversion efficiency to seed
- Leverages microbial diversity to eliminate bottlenecks in plant carbon metabolism

The "T3 Platform"

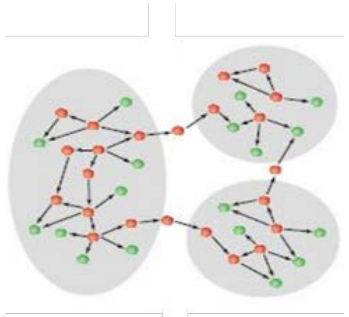
- Advanced transcriptome network analysis
- identify global regulator genes to control complex global regulatory networks and gene cascades and achieve step change improvements in crop yield

Global Regulatory Genes to Increase Biomass Yield

Used transcriptome-based regulatory association networks to identify candidate regulatory genes predicted to increase photosynthesis and biomass yield



Complex transcriptomics data



Gene interaction network

Functional modules target pathways of interest – increased photosynthesis and biomass production

Global regulatory gene candidates identified

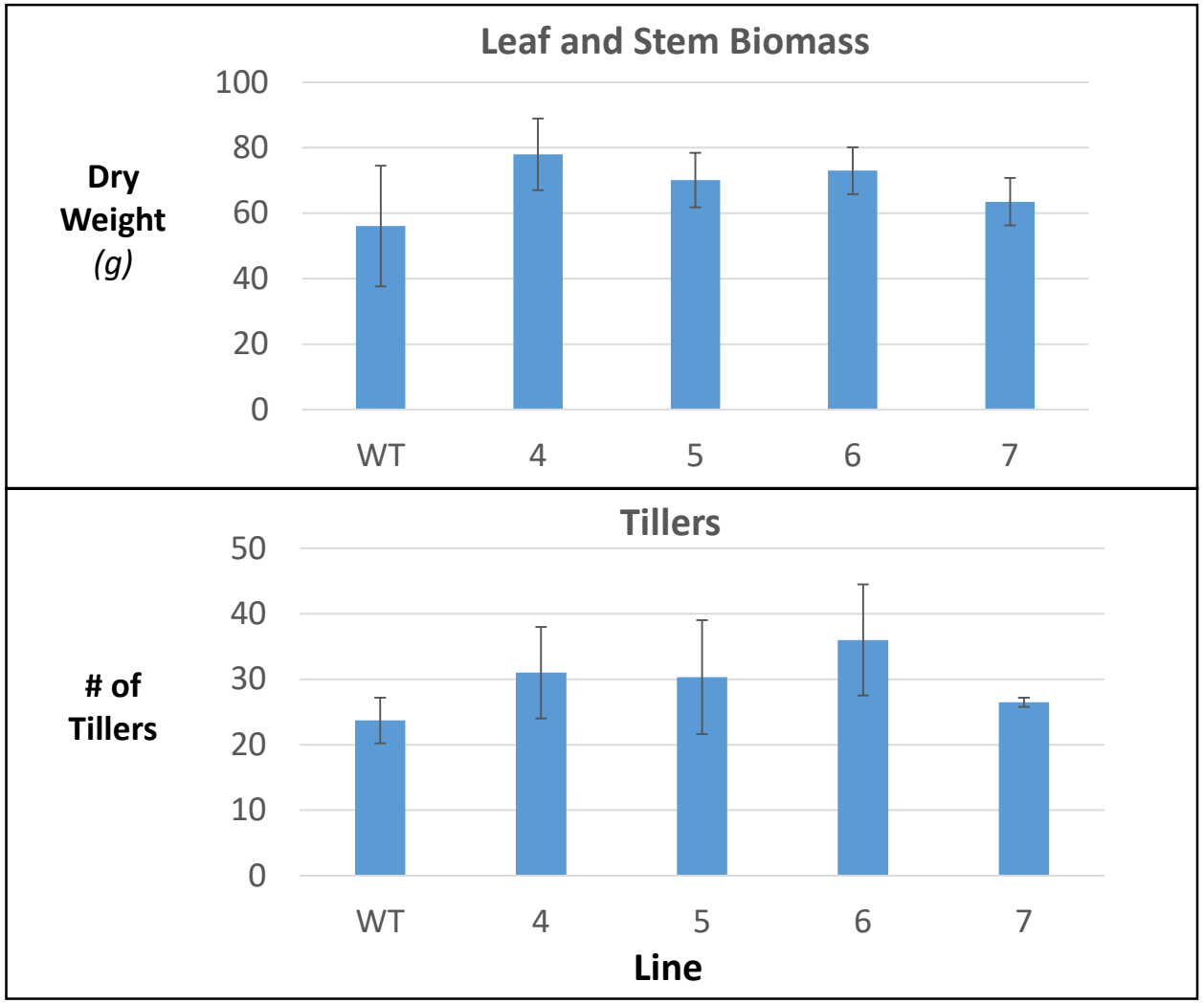
(C4001, C4002, C4003)

Generated transgenic plants to characterize candidate genes

- Transformed switchgrass with genes expressed from strong promoter active in green tissue
- Initial transgenic line analysis to pick best candidate lines for further characterization
  - Expression analysis (eg. RT-PCR and qRT-PCR)
  - Leaf starch and chlorophyll content
- Will present data for C4001

Biomass Yield of Switchgrass C4001 lines

Increase in total biomass observed in C4001 transgenic lines



Plants grown in a greenhouse for 5 months

WT 4 6 7

Picture taken 2 months after transfer to soil

Yield10 | BIOSCIENCE

Regrowth of C4001 Lines

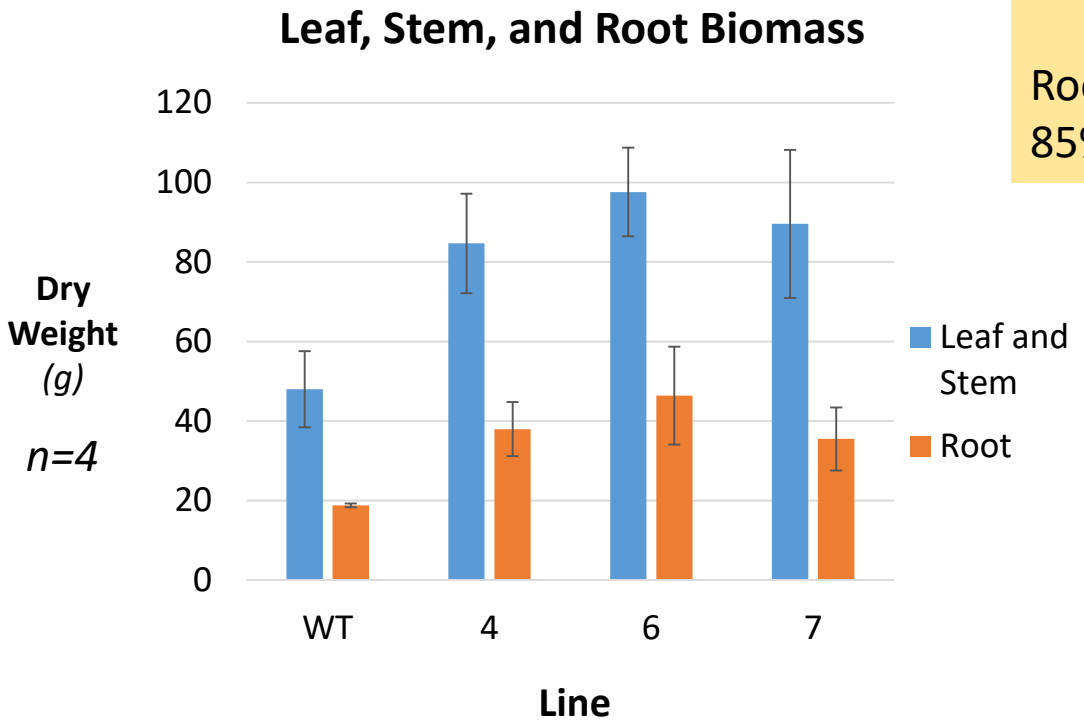
- Immature inflorescence derived cultures obtained from best primary transformants
- Plants regenerated from cultures and 4 plants from each line were grown in greenhouse
- Panicles cut during growth (*requirement of greenhouse used*)

C4001

WT **4d** **6e** **7e**

Roots

WT **4d** **6e** **7e**



Leaf and stem biomass
75%-100% increase

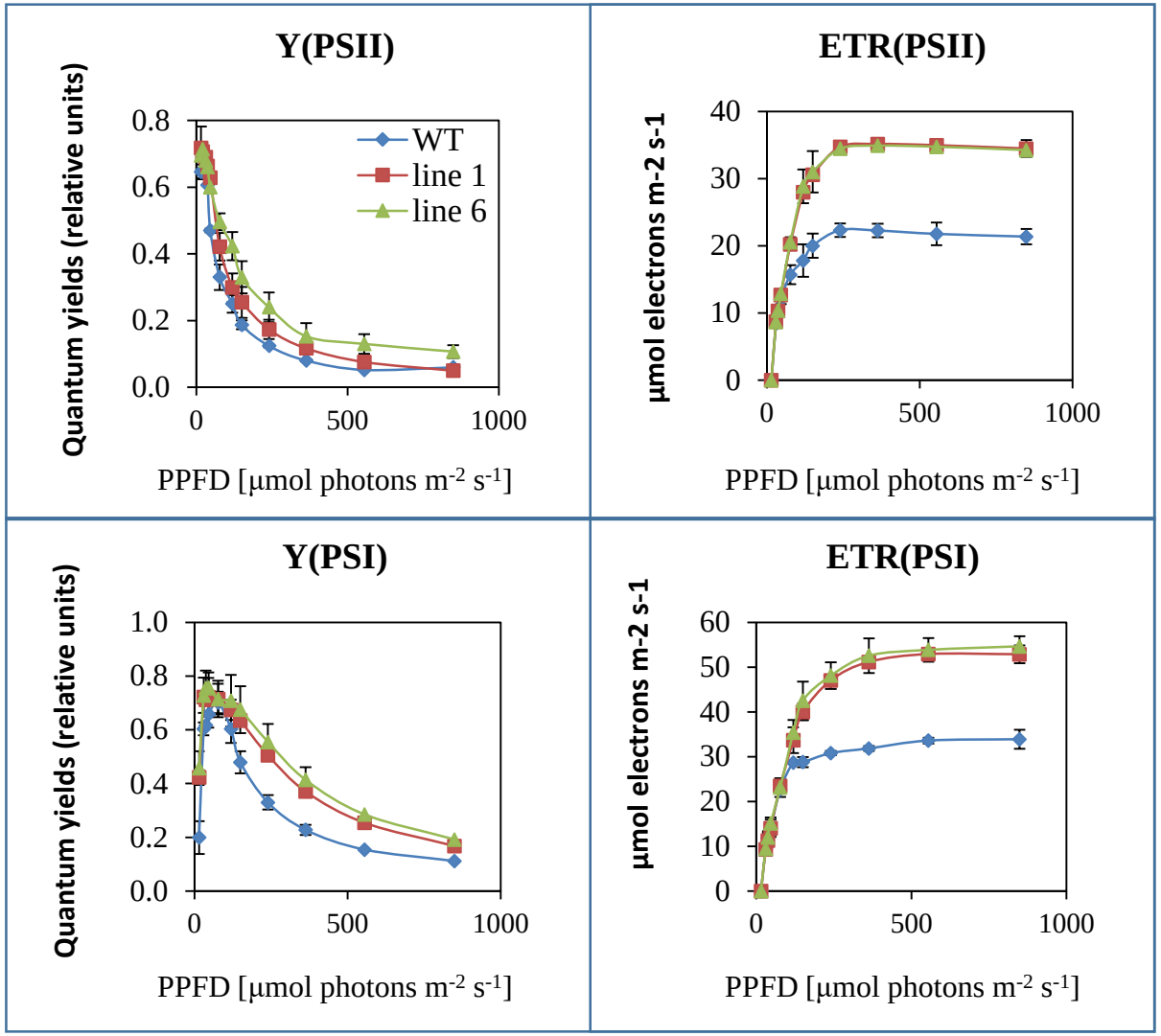
Root biomass
85%-145% increase

Plants grown in a greenhouse for 5 months

Yield10 | BIOSCIENCE

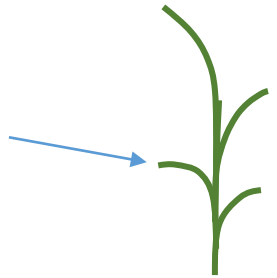
Measurement of Photosynthetic Parameters for C4001

Effect of photosystem I (PSI) and photosystem II (PSII) studied by measuring photochemical quantum yield (Y) and electron transport rate (ETR)



Primary difference observed in electron transport rate around photosystem I and II

- Photosynthesis rate measurements using Dual-PAM-100 (Heinz Walz GmbH) in 2 month old plants with light adapted leaves on a sunny morning



2nd leaf of a 2 month old plant

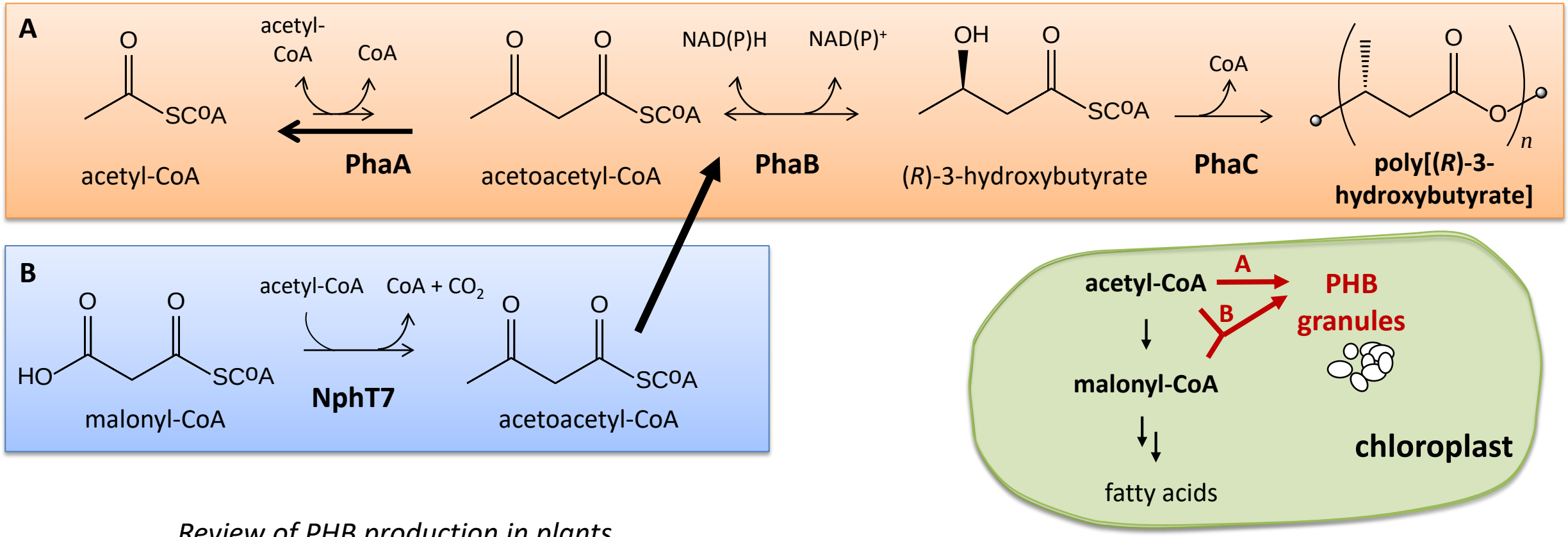
- PPFD = photosynthetic flux density

Yield10 | BIOSCIENCE

Novel Insoluble Carbon Sink to Challenge System

PHB is an insoluble polymer that can be used as a novel carbon sink to capture carbon

- High levels of PHB production produces a stunted phenotype in most plants
- Targeted PHB production in chloroplasts of switchgrass transgenic C4001 lines and controls



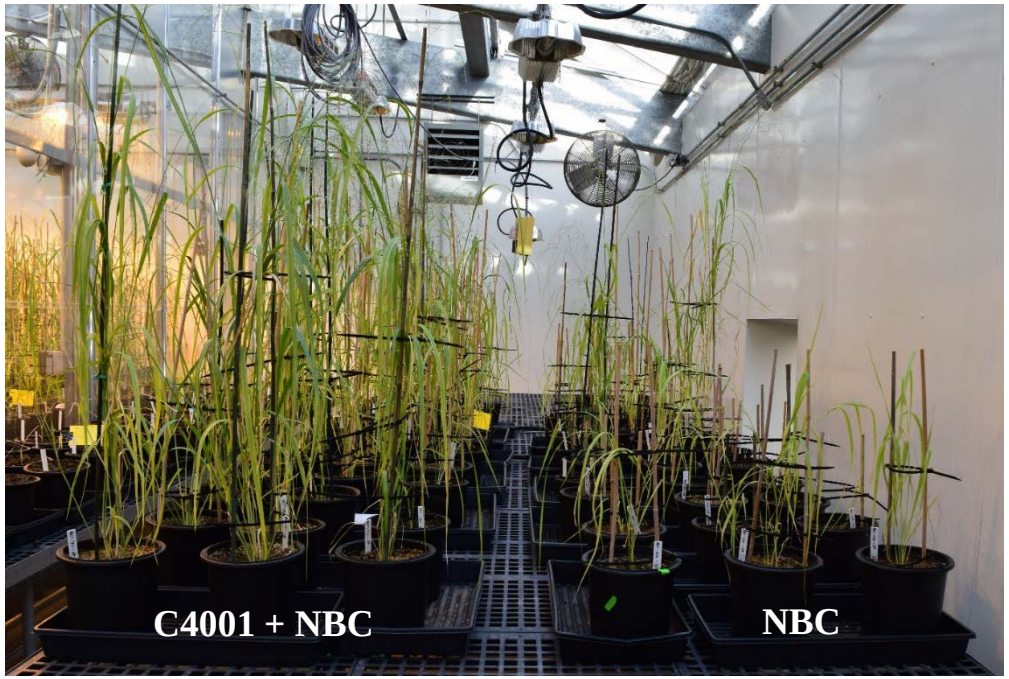
Review of PHB production in plants
Snell, Singh, & Brumbley, Current Opinion in Biotechnology, 2015, 32, 68

Modification of Source/Sink with C4001

C4001 Partially Restores Plant Growth in Plants Engineered with a Novel Carbon Sink

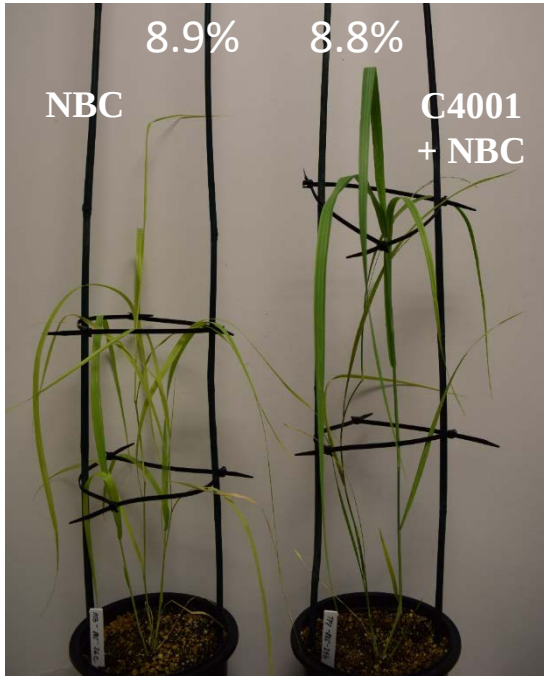
- PHB biopolymer pathway transformed into immature inflorescence derived cultures of C4001 lines
- PHB pathway alone produces high levels of polymer at expense of plant growth
- Co-expression of C4001 with the PHB pathway partially restores biomass
- Suggests step change performance requires multi-gene modifications

Greenhouse view of plants



Plants grown in greenhouse for 6 months

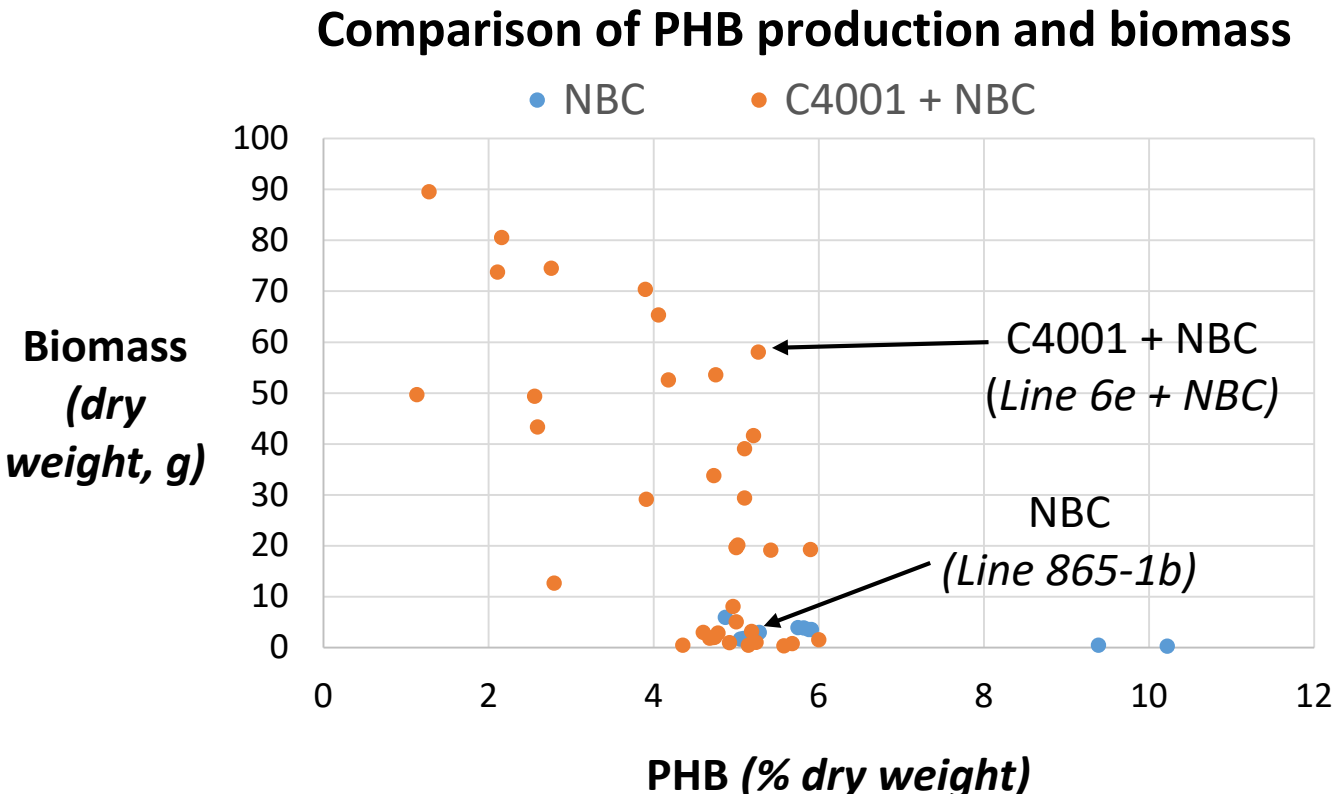
Comparison of plant size with similar polymer levels

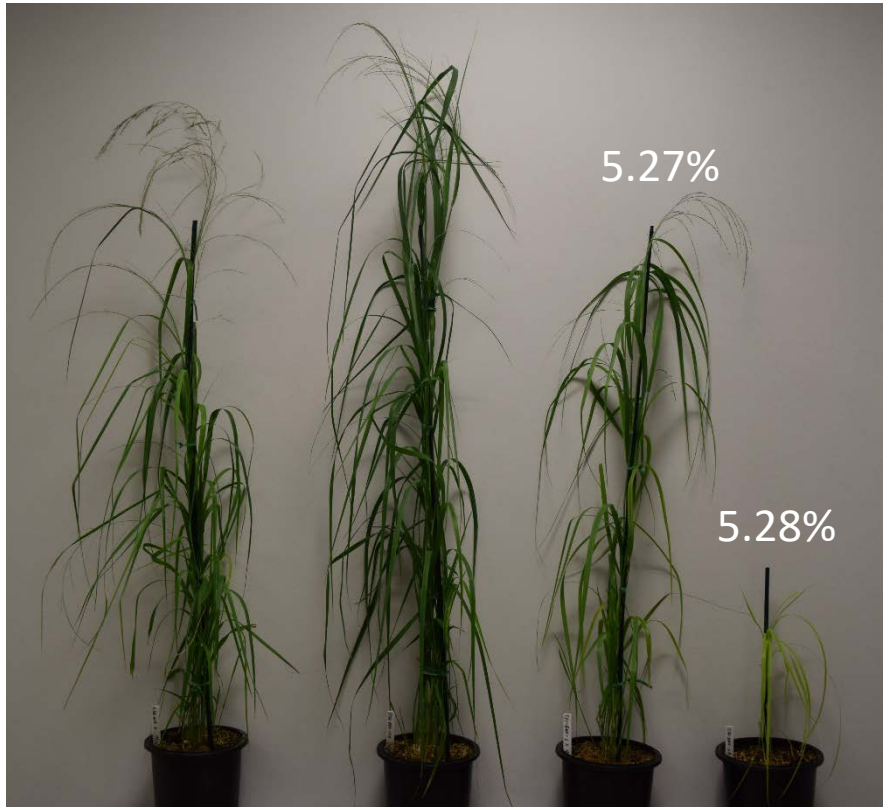


**PHB content is from tip of 2nd leaf of plant; plants grown in greenhouse for 6 months*

Yield10 BIOSCIENCE

PHB Production in Repotted Plants





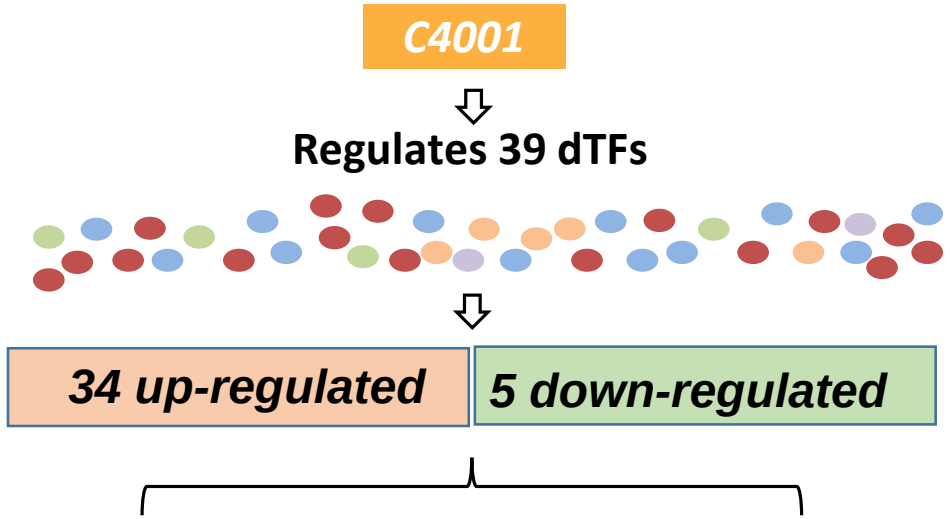
WT | C4001 *(Line 6e)* | C4001 + NBC *(Line 6e + NBC)* | NBC *(Line 865-1b)*

PHB measurement is from a leaf sample at 2 months
Biomass data is after 6 months growth in greenhouse

Yield10 BIOSCIENCE

Microarray Analysis of C4001 Transgenic Lines

Multiple downstream transcription factors and key pathways are regulated in C4001 lines



Targets for genome editing

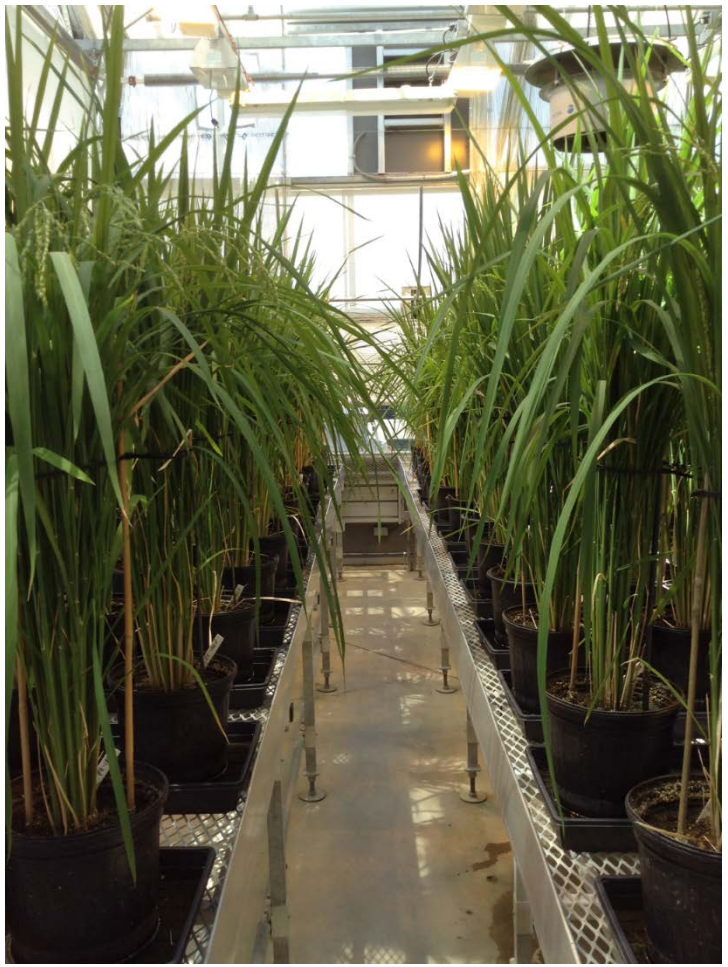
dTFs associated with key metabolic pathways and genes important for biomass, yield, & stress response

- Photosynthesis (10)
- Starch biosynthesis (6)
- Photosynthetic electron transfer (4)
- Carbohydrate metabolism (8)
- Transport functions (21)
- Protein metabolism & modifications (8)
- Plant stress response (11)
- Amino acid metabolism (7)
- Plant hormone metabolism (9)
- Lignin & cell wall metabolism (18)
- Signal transduction (16)
- Fatty acid & lipid metabolism (9)
- Secondary metabolism (13)
- Cytochrome P450 genes (7)

In process of testing select dTFs for function, three tested to date

Next Steps: Evaluation of C4001 in Crops

- Orthologs of the switchgrass C4001 gene are in major crops (corn, rice, wheat, etc.)
- Both the switchgrass C4001 gene and the rice ortholog of C4001 have been transformed into rice at Yield10
- T_0 plants are growing in greenhouse



Switchgrass C4001 in rice

Rice ortholog of switchgrass C4001 in rice

Yield10 Trait Genes in Development

Yield10 has a rich pipeline of crop traits, including C4001 and its dTFs, and many opportunities exist for licensing and/or partnerships

	Trait	Value Driver	Genetic Engineering	Genome Editing	Current Activity Next Steps	Licensing/Partnering Opportunities
	C3003 (1st & 2nd Gen)	Seed yield Water use	+	-	Camelina field testing Canola, soybean and rice in development	alfalfa, cotton, potato, rice, wheat, sugar beet and potentially corn
	C3004	Seed yield	+	+	Camelina editing underway	cotton, potato, rice, wheat, sugar beet and potentially corn
	C3007	Oil content	+	+	Camelina, canola editing underway	Camelina, canola, soybean
Global regulatory genes	C4001	Yield	+	+/-	Rice transformation Corn transformation next step	Forage, all major crops
	C4002	Yield	+	+/-	Corn transformation next step	Forage, all major crops
	C4003	Yield	+	+/-	Rice transformation Corn transformation next step	All major crops
dTFS up or down-regulated by C4001, C4002, or C4003	C4004	Yield	+	+	Corn transformation next step	All major crops
	C4005	Drought	+	+/-	Corn transformation next step	All major crops
	C4006	Drought	+	+/-	Corn transformation next step	All major crops
	22 additional targets for genome editing have been identified and will undergo validation					

Conclusions

- T3 Platform is a powerful tool for gene discovery
- Heterologous expression of global regulatory gene C4001 increases photosynthesis, green biomass production by 75-100%, and root biomass by 85-145%
- C4001 regulates 39 dTFs and 428 other genes
  - *Downregulated genes (5 dTFs and 115 other genes) are good targets for genome editing*
- Heterologous expression of C4001 has a positive impact on plants challenged with a novel carbon sink, production of the biopolymer PHB
  - *High level PHB production impacts plant health and size in wild-type plants*
  - *C4001 co-expression with PHB pathway partially restores biomass production and increases plant health*

Acknowledgments

Madana M.R. Ambavaram

Aminat Ali

Kieran P. Ryan

Renate Ruszczyk

Oliver Peoples

Kristi Snell* (snell@yield10bio.com)

Maria N. Somleva

Work supported by an award from The Department of Energy,

Bioenergy Technologies Office (BETO)