



# Technologies for Increasing Plant Yield and Oil Content: The Yield10 Bioscience Platform

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

**Yield10 Bioscience (NasdaqCM:YTEN) is developing technologies to enhance global food security**

- Headquartered in Woburn, MA USA
- Oilseeds center of excellence in Saskatoon, Canada

**Yield10 brings extensive expertise and a track record in optimizing the flow of carbon in living systems to the agriculture sector to increase yield in key row crops**

- Yield10 is targeting step-change (10-20%) increases in seed yield
- Technology based on >15 years of cutting edge crop metabolic engineering research
- 15 recent patent applications for increased crop yield
- Open innovation business model provides low hurdle for work with Ag majors

**Yield10 focuses on its core strengths of advanced bioscience and innovation**

- Discover and de-risk yield technologies for major North American crops: corn and the two oilseed crops soybean and canola

## Yield10 Technologies Enable Multiple Paths to Value Creation



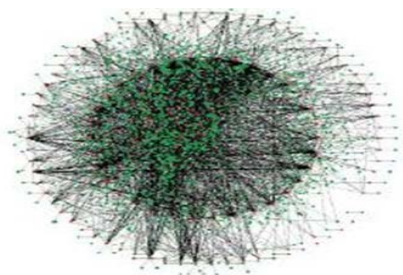
### Major North American Commodity Crops

- Accelerate deployment with Ag majors
- Provide low hurdle to deploy and test yield traits in elite germplasm
- License agreements with milestones and participation in downstream economics



### Specialty and Niche Crops including Nutritional Oils

- Form collaborations based on combining technologies to improve yield and/or improve nutritional value
- Focus on development of new products in food and animal feed
- Utilize technologies enabling a non-regulated path to market
- JV-type agreements with significant share of downstream economics



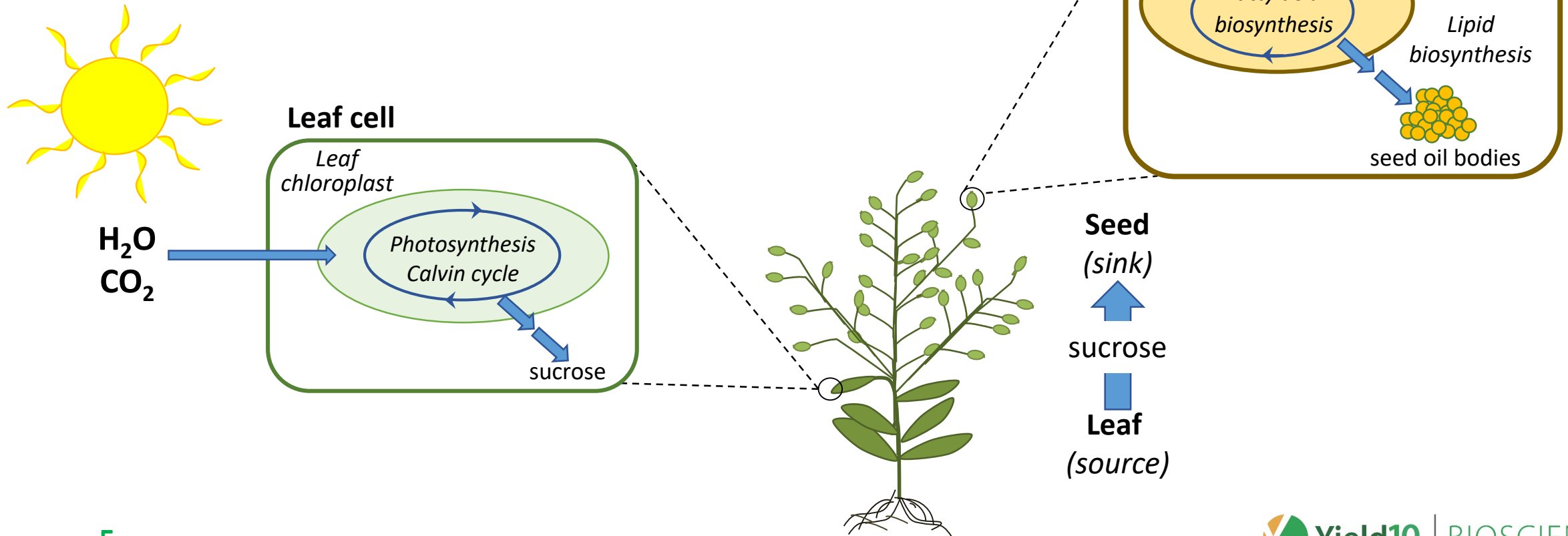
### Yield10 Technology Platforms

- Accelerate innovation based on unique approach to identifying gene combinations for editing
- Access government grants and relationships with leading plant scientists
- R&D support for partner funded programs

# Significantly Increasing Crop Yield Will Require Gene Combinations

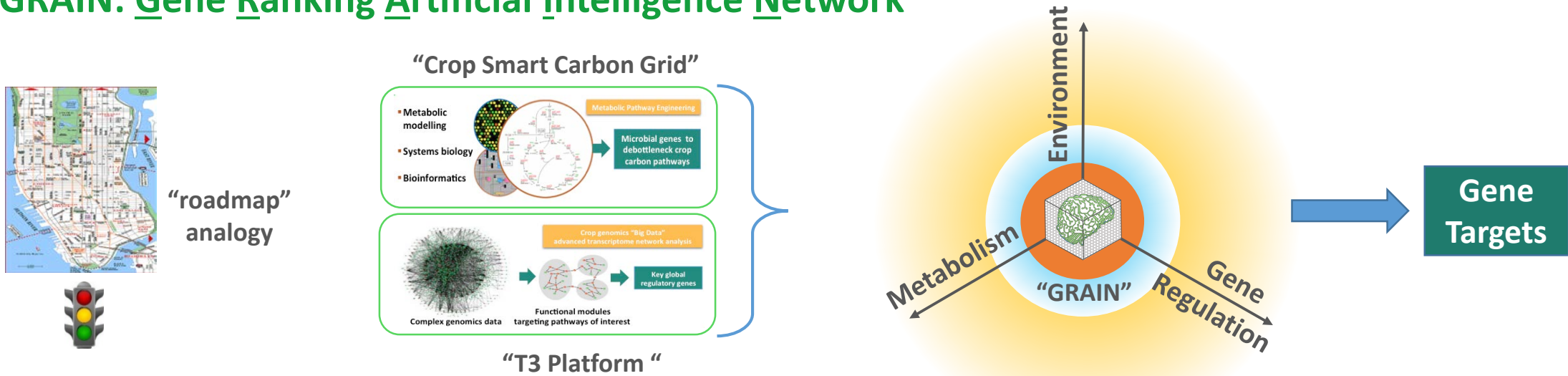
Step-change increases in seed yield will likely require increased photosynthetic carbon fixation and delivery of the increased fixed carbon to the seed

- Identifying the right combination of genes is a key task



# “GRAIN” Trait Gene Discovery Platform

## GRAIN: Gene Ranking Artificial Intelligence Network



- We are developing “GRAIN”, a “Waze” or “Google Earth”-like system for identifying gene targets
- Integrating three key technology elements:
  - Metabolic engineering or synthetic biology, the “Crop Smart Carbon Grid” (carbon capture/conversion infrastructure)
  - Transcriptome network analysis, the “T3 Platform “ (gene regulators or traffic lights) – C4001-C4003 traits
  - Powerful feedback loops incorporating data from high yield lines
- We are progressing gene targets from elements of the GRAIN platform (C4004-C4026: C3011 and C3012)

# Rich Pipeline of Trait Genes in Development

CROP TRAITS IN DEVELOPMENT	
Business Area	Current Status
<b>Seed Yield Traits-Regulated</b>	
C3003	Camelina 1 <sup>st</sup> and 2 <sup>nd</sup> generation in field testing
	Canola 1 <sup>st</sup> generation in field testing
	Soybean and rice in development
<b>Seed/Oil Enhancing Traits-Non-Regulated</b>	
C3004	Camelina testing underway
C3007	Camelina, canola editing underway
C3008a	Camelina non-regulated <sup>1</sup> status achieved
C3008a, C3008b and C3009 combinations	Camelina, editing of all 3 gene targets underway
Additional oil trait combinations	Research in progress
<b>Yield Improvement Discovery Platform (“GRAIN”)</b>	
C4001 and C4003	Wheat program underway
	Rice transformation underway
	Corn transformation next step
C4002	Corn transformation next step
C4004	Editing in rice underway
C4004 plus 23 additional gene editing targets	Research with rice and wheat next step

**Many opportunities exist for licensing and/or partnerships**

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<sup>1</sup> not regulated by USDA-APHIS in US, could be regulated by EPA and/or FDA



## C3003 is a component of an algal system for increasing photosynthesis in low CO<sub>2</sub> conditions

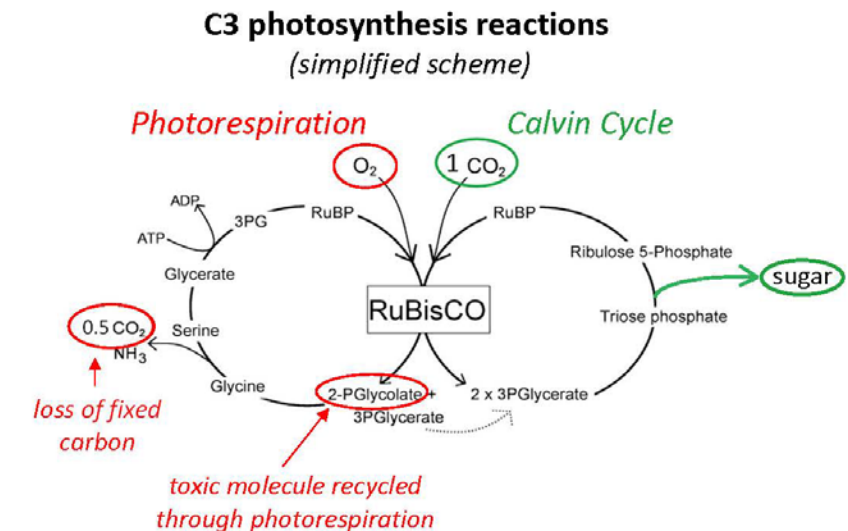
- A scientific discovery from University of Massachusetts with a unique biological mechanism
- C3003 improves the metabolic infrastructure of the plants, believed to impact photorespiration
- Potential to be useful in a wide range of C3 crops: Camelina, canola, soybean, corn, wheat, rice and others

## Scientific progress provides new insights on mechanism

- Four additional patent applications filed in 2017
- Recent DOE grant sub-awardee (Michigan State prime awardee)
- Modeling suggests testing in combination with C3004

## Development program for C3003

- Leverage the development speed of Camelina to optimize the impact of C3003 in major crops
- Demonstrate Camelina results translate into canola, soybean and rice
- Execute 2018 Field Tests in oilseed crops to optimize constructs
- Monsanto license provides a path to test C3003 in elite soybean germplasm and in combination with C3004



A 5% reduction of photorespiration in soybean and wheat would add ~\$500 million/year of economic value in the US (Walker et al., 2016, Ann. Rev. Plant Biol. 67:17.1 – 17.23)



# C3003: Trait that Increases Seed Yield Likely by Impacting Photorespiration

- Yield10 and Metabolix Oilseeds have engineered Camelina and canola to express C3003 from constitutive (Gen 1) or seed specific (Gen2) promoters

Crop/Trait	Year		
	2017	2018	2019
<b>Camelina</b> Gen 1 C3003	▪ 2016 field test data reported ( <i>up to 23% seed yield increase</i> )		
<b>Camelina</b> Gen 2 C3003	▪ Greenhouse ( <i>up to 24% seed yield increase</i> ) ▪ 2017 field test ( <i>up to 7% seed yield increase</i> )	▪ Field tests	
<b>Canola</b> Gen 1 C3003	▪ 2017 field test ( <i>up to 13% seed yield increase</i> )	▪ Field tests	
<b>Canola</b> Gen 2 C3003		▪ Greenhouse data ▪ Field tests	▪ Field tests
<b>Soybean</b> Gen 1 & Gen 2	▪ Greenhouse data from early generations	▪ Small scale field plots	▪ Field tests
<b>Rice</b> Gen 1 & Gen 2		▪ Greenhouse data	

Translation

Value Demonstration

# Novel Traits for Boosting Seed Oil Content

## Yield10 is uniquely positioned to re-engineer the oil biosynthesis pathway in oilseed crops

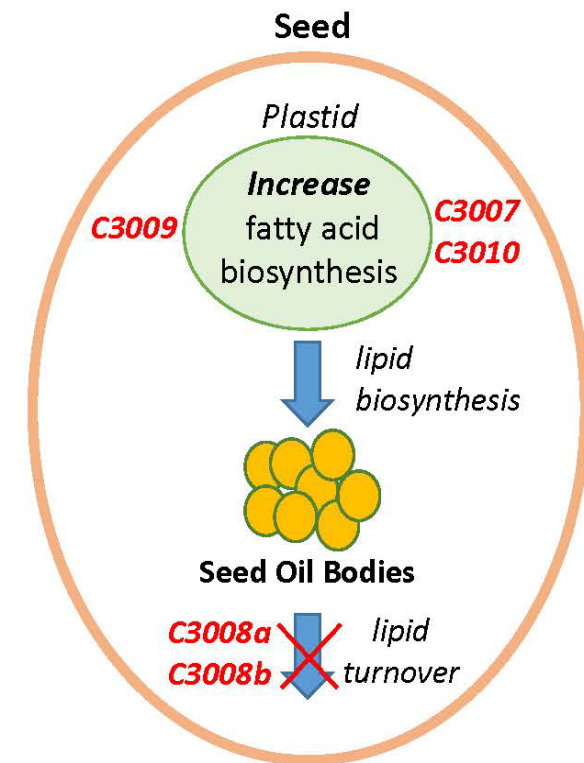
*Seed oil content is a key value driver in oilseed crops*

### Current Status

- Progressing gene targets involved in oil biosynthesis pathway
- Building the IP position
- Potential to combine (stack) with oil composition traits (e.g. high oleic, omega fatty acids)
- Obtained first non-regulated<sup>1</sup> Camelina line (C3008a) via a submission to USDA-APHIS in 2017
- Multi-gene edited oilseed lines developed (eg. C3008a, C3008b, C3009)

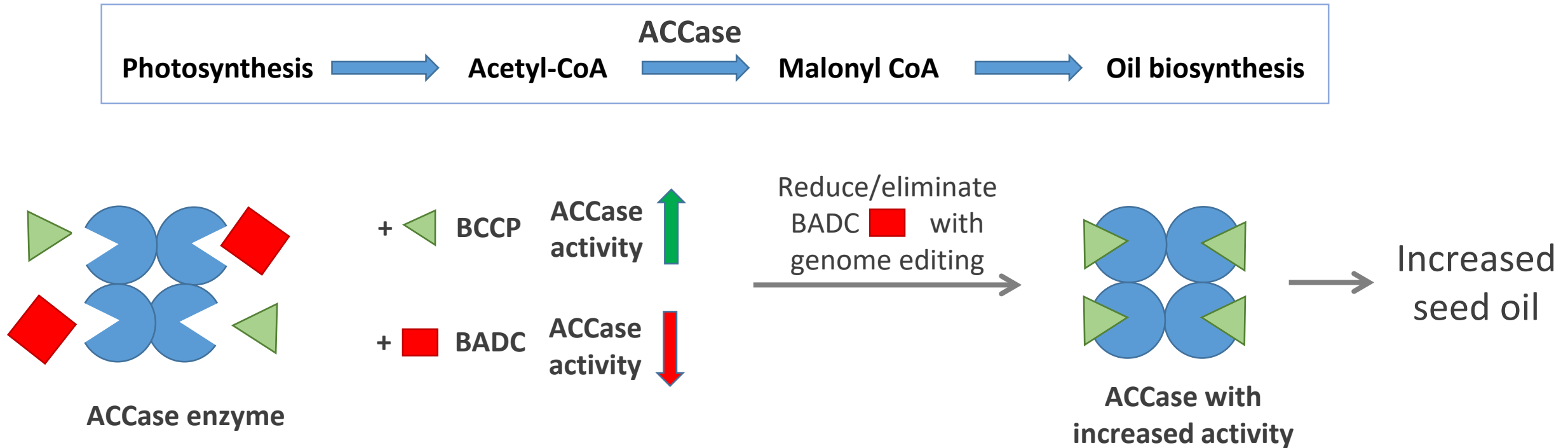
### Next Steps

- Integrating C3007/C3010 to further boost oil content
- Make submissions of traits/plants to USDA-APHIS to enable non-regulated US field tests
- Conduct field tests to generate data
- Identify opportunities for licenses and collaborations for nutritional oils



# Editing of C3007 Trait: A Negative Regulator of a Key Enzyme in Oil Biosynthesis

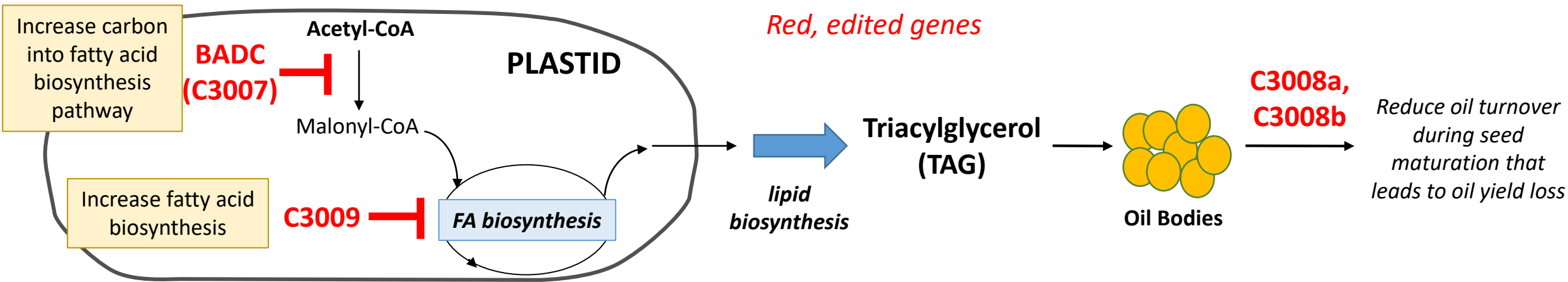
- Acetyl-CoA carboxylase (ACCase) - a key enzyme in oil biosynthesis with a complex, multi-subunit enzyme structure
- BADC (C3007), a key negative regulator of ACCase (*Salie, M. et al., 2016, Plant Cell*)
- Use genome editing to reduce/eliminate availability of BADC (*red squares*) to increase the activity of the key ACCase enzyme to increase carbon for fatty acid biosynthetic pathway



- Yield10 has exclusive option to license BADC technology from University of Missouri
- There are multiple types of BADC genes in plants (*Salie, M. et al., 2016, Plant Cell*)
- Yield10 has identified
  - *3 different BADC genes (9 homologs) in Camelina*
  - *3 different BADC genes (6 homologs) in canola*
- Yield10 working to edit combinations of BADC homologs in Camelina and canola to increase oil yield
  - *Target editing of all homologs*
  - *Target editing of only some homologs*

# Multiplex Editing to Increase Seed Oil Content

- Combine BADC edits with edits to other genes in oil biosynthesis pathway
- Funded by US Department of Energy – BETO to Yield10 Bioscience with Metabolix Oilseeds as subawardee



## Progress with multiplex editing in allohexaploid Camelina

Nature of edits obtained	Gene Targets, Plant 1		
	C3008a	C3008b	C3009
Line type 1	X X _	X X X	X X X
Line type 2	X X X	X X _	X X X
Line type 3	X X X	X X X	X X X

X = mutation that leads to inactive protein  
\_ = homolog that is difficult to mutate

## Progressing genome editing of BADC in Camelina

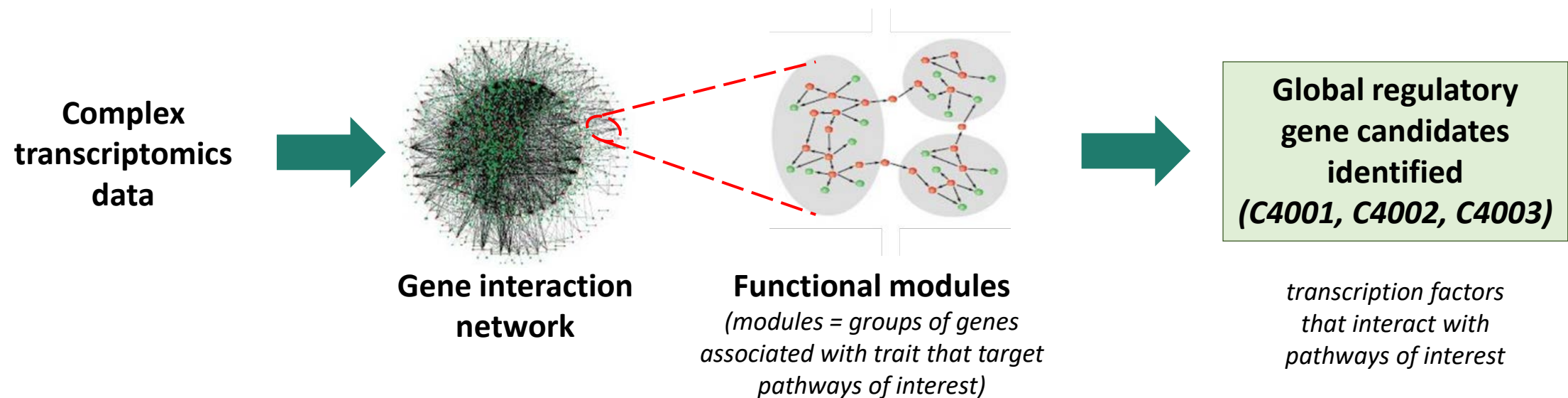
Gene Targets, Plant 2		
C3007a	C3007b	C3007c
In progress	In progress	In progress

# GRAIN platform: Identify Global Regulatory Genes

- Transcriptome-based regulatory association networks to identify candidate global regulatory genes
- These transcription factors or “gene switches” allow manipulation of multiple genes that can modify a trait

## Work with switchgrass

*Identify candidate global regulatory genes to increase photosynthesis and biomass yield*



Functional modules used for switchgrass

- *Increased photosynthesis, biomass, and central carbon metabolism*



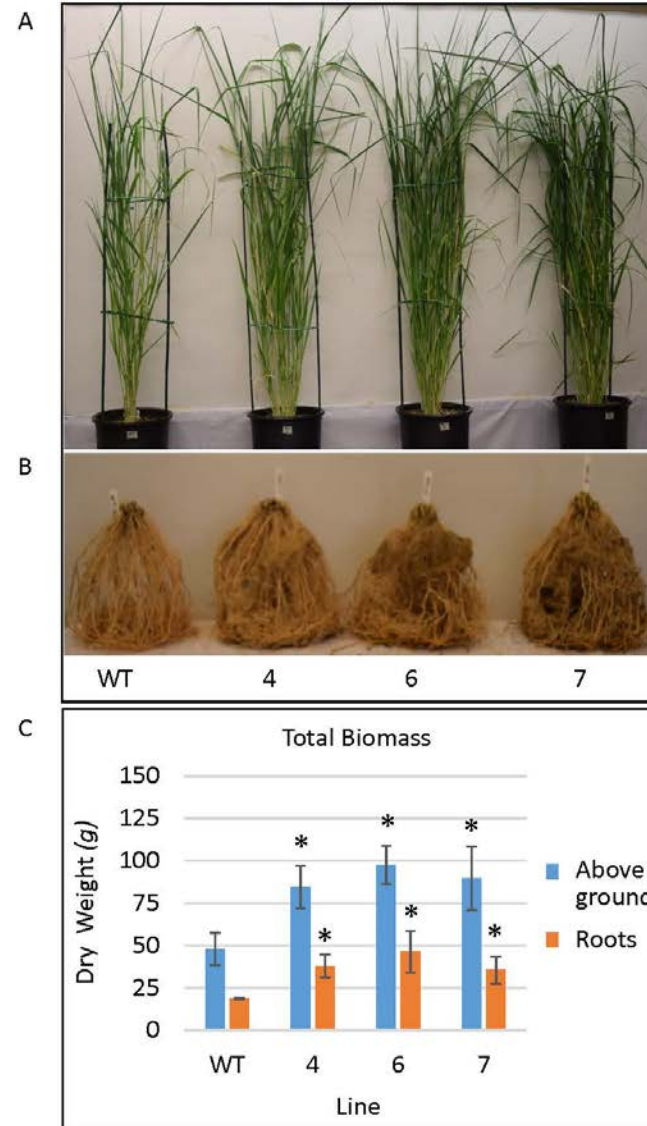
# Global Regulatory Genes in Switchgrass

- Transgenic plants produced
  - genes expressed from strong promoter active in green tissue*
- Increases in aboveground and root biomass observed

Work funded by DOE-EERE

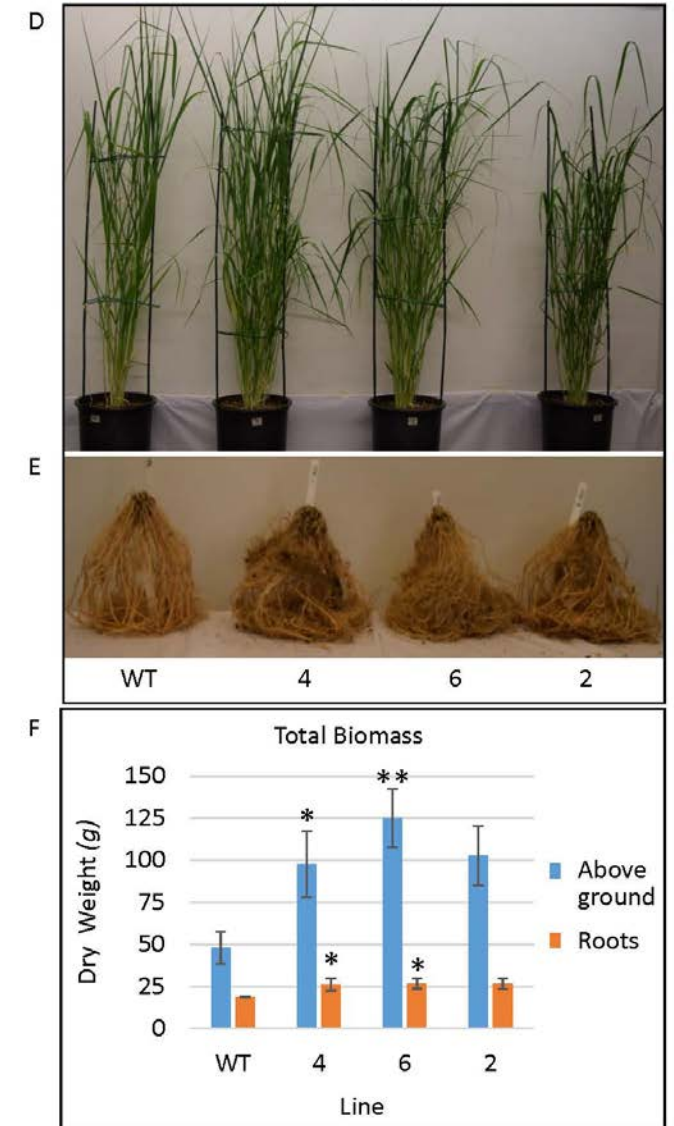
For more data, see: Ambavaram et al., *Novel transcription factors PvBMY1 and PvBMY3 increase biomass yield in greenhouse-grown switchgrass (Panicum virgatum L.)*, 2018, *Plant Science*, in press

C4001 (PvBMY1)



Leaves & stems, 75%-100% increase  
Roots, 85-140% increase

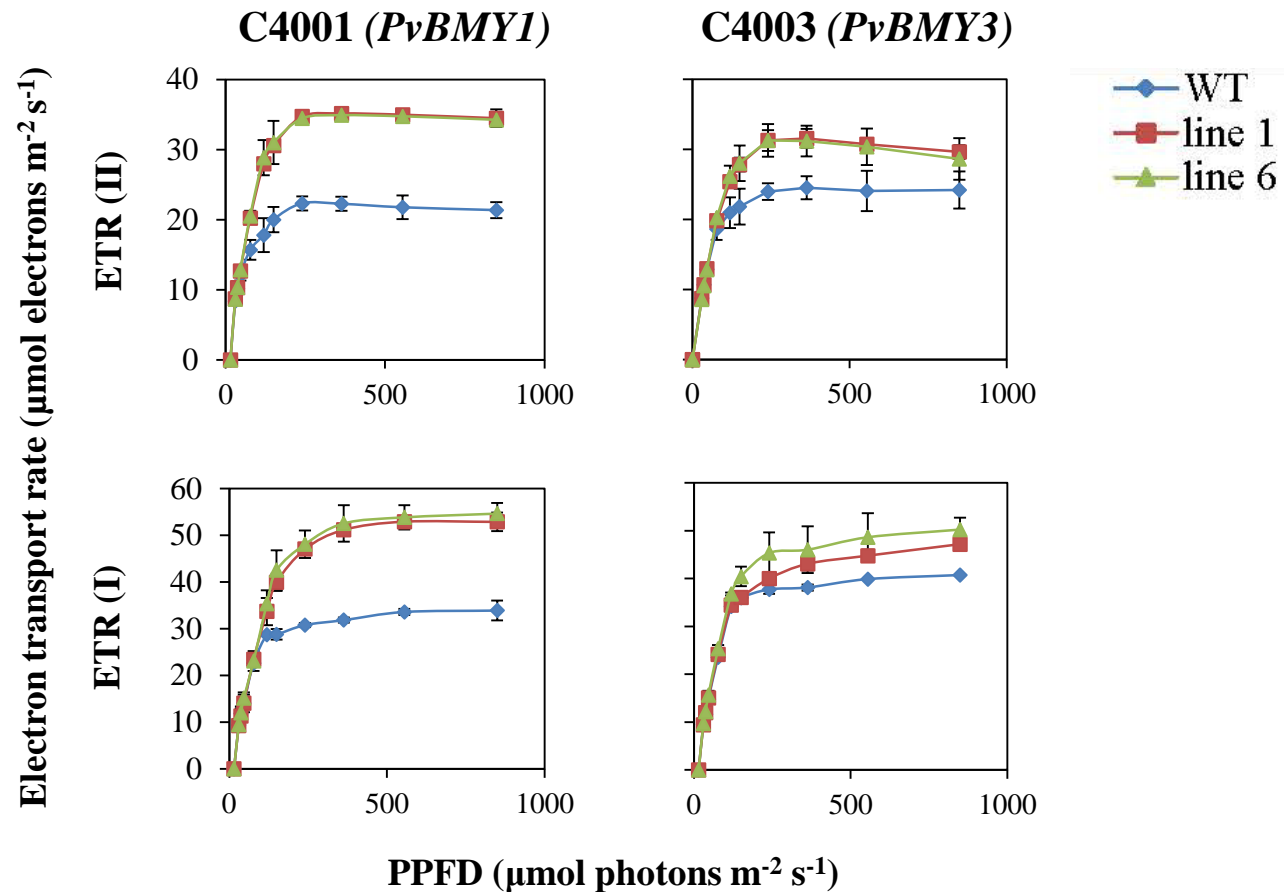
C4003 (PvBMY3)



Leaves & stems, 100-160% increase  
Roots, ~40% increase

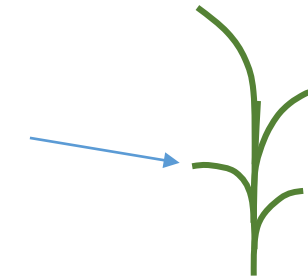
# Measurement of Photosynthetic Parameters for C4001, C4003

Various photosynthetic parameters measured. Primary difference observed in electron transport rate around photosystem I and II [ETR(I) and ETR(II)]



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

Leaf used

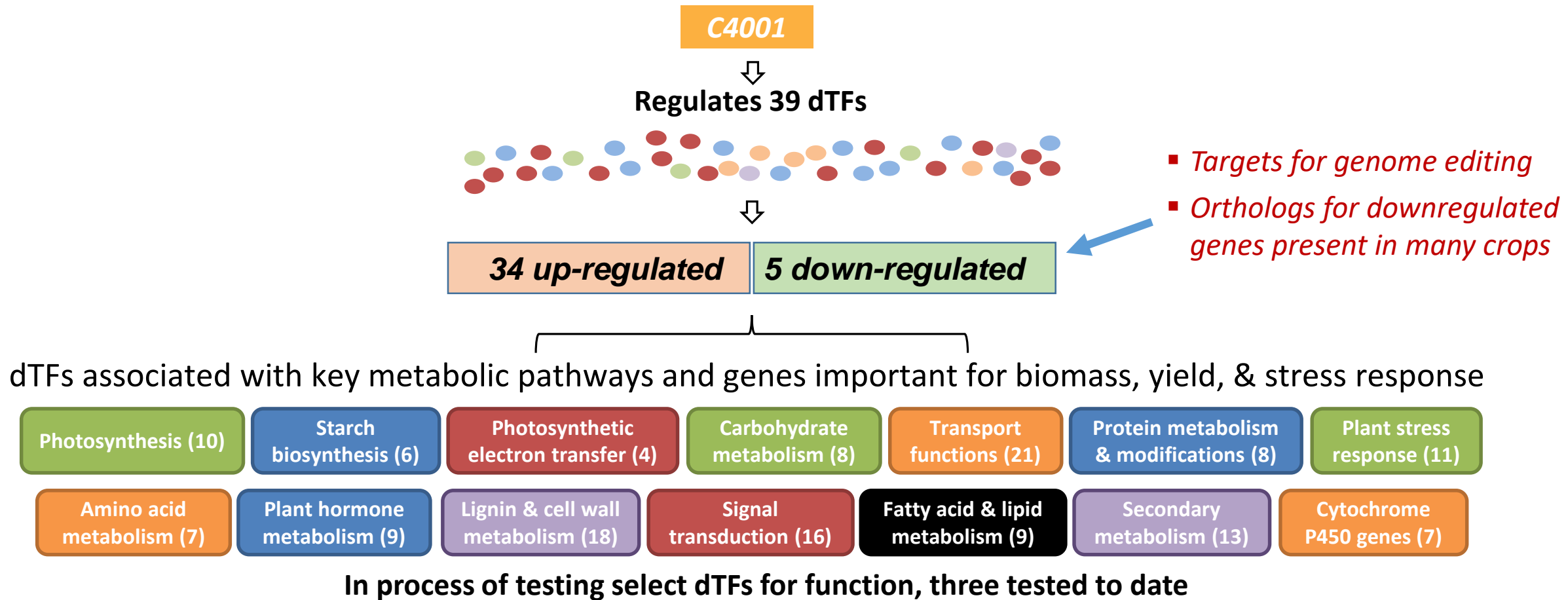


2<sup>nd</sup> leaf of a 2 month old plant

- PPFD = photosynthetic photon flux density

# Microarray Analysis of C4001 Transgenic Switchgrass Lines

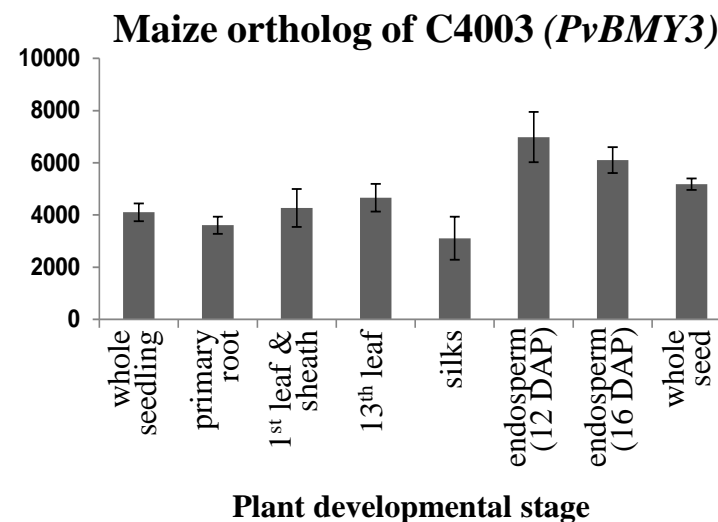
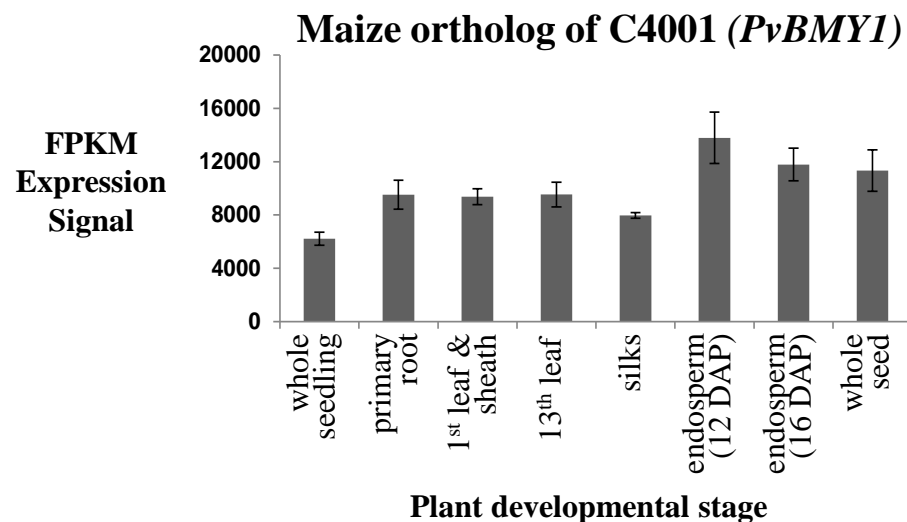
- High yielding lines useful for identifying pathways controlled by TFs and genome editing targets
- Multiple downstream transcription factors (dTFs) and key pathways are regulated in C4001 lines



# Orthologs of C4001 and 4003 are Widespread in Terrestrial Plants

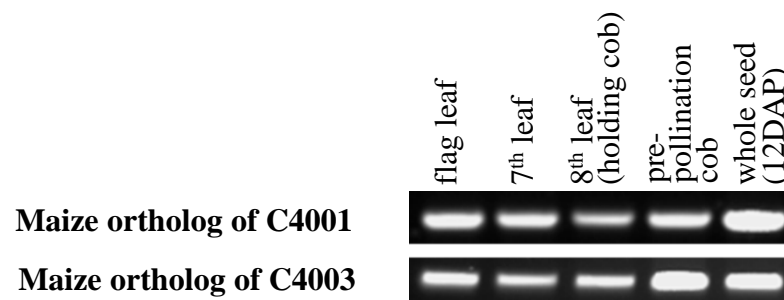
## Analyzed expression profiles of maize orthologs to determine if they are expressed in seed tissues

- *In silico* analysis of gene expression from maize Electronic Fluorescent Pictograph browser<sup>1</sup>



<sup>1</sup>[http://bar.utoronto.ca/efp\\_maize/cgi-bin/efpWeb.cgi](http://bar.utoronto.ca/efp_maize/cgi-bin/efpWeb.cgi). Levels of expression signals are in FPKM units (Fragment Per Kilobase of exon per Million fragments mapped). FPKM estimates the relative transcript abundance of each gene by combining the expression of all the transcripts of a gene.

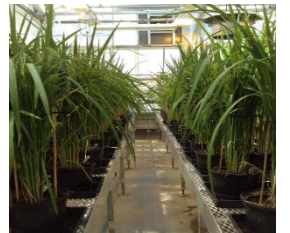
- Measurements of expression levels in greenhouse grown maize (inbred line B73) by RT-PCR



**Yield10 is uniquely positioned to identify valuable targets based on global transcription factors**

## Current Status

- Reported data showing that global regulatory genes C4001 and C4003 boost key parameters of photosynthesis and improve plant biomass in switchgrass
- Conducting studies of C4001 and C4003 in rice
- Signed collaboration with National Research Council (NRC), Canada in wheat for C4001, C4003 and a downstream transcription factor C4004 - research advancing
- Foundation IP filed on C4004-C4024 genes (downstream transcription factors) and combinations as editing targets
- Editing of C4004 underway in rice

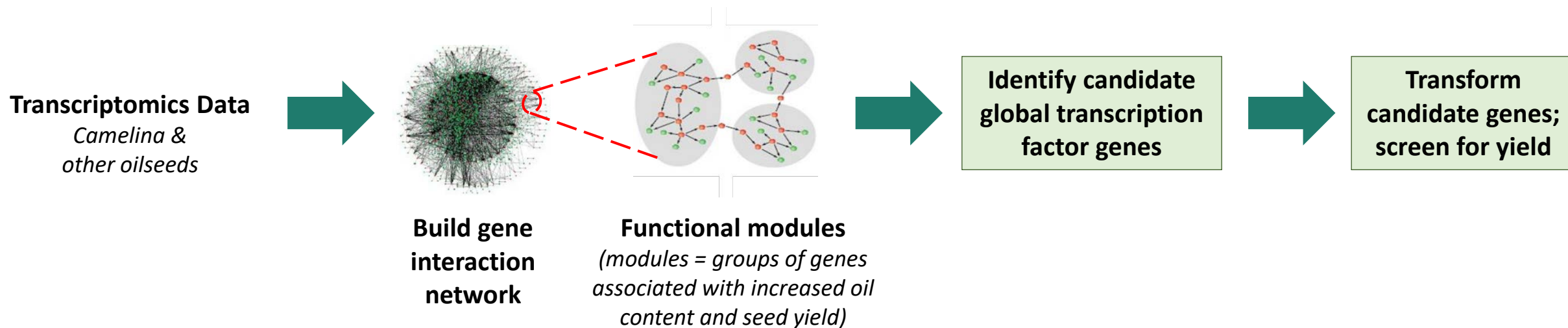


## Next Steps

- Generate data in rice and wheat with C4001 and C4003 traits
- Begin corn transformations to enable greenhouse and field tests
- Identify additional targets from “GRAIN” platform accessible with genome editing

# Program to Increase Seed Yield and Oil Content in Camelina

- Funded by US Department of Energy
- Michigan State University lead (Danny Schnell, PI)
- Yield10 Bioscience and Metabolix Oilseeds are subawardees
- **Goal Yield10 and Metabolix Oilseeds:**
  - Use GRAIN platform (*transcriptome-based regulatory association networks*) to identify global regulatory genes that increase seed yield and oil content
  - Similar approach to previous work with switchgrass but with modules of increased oil content and seed yield

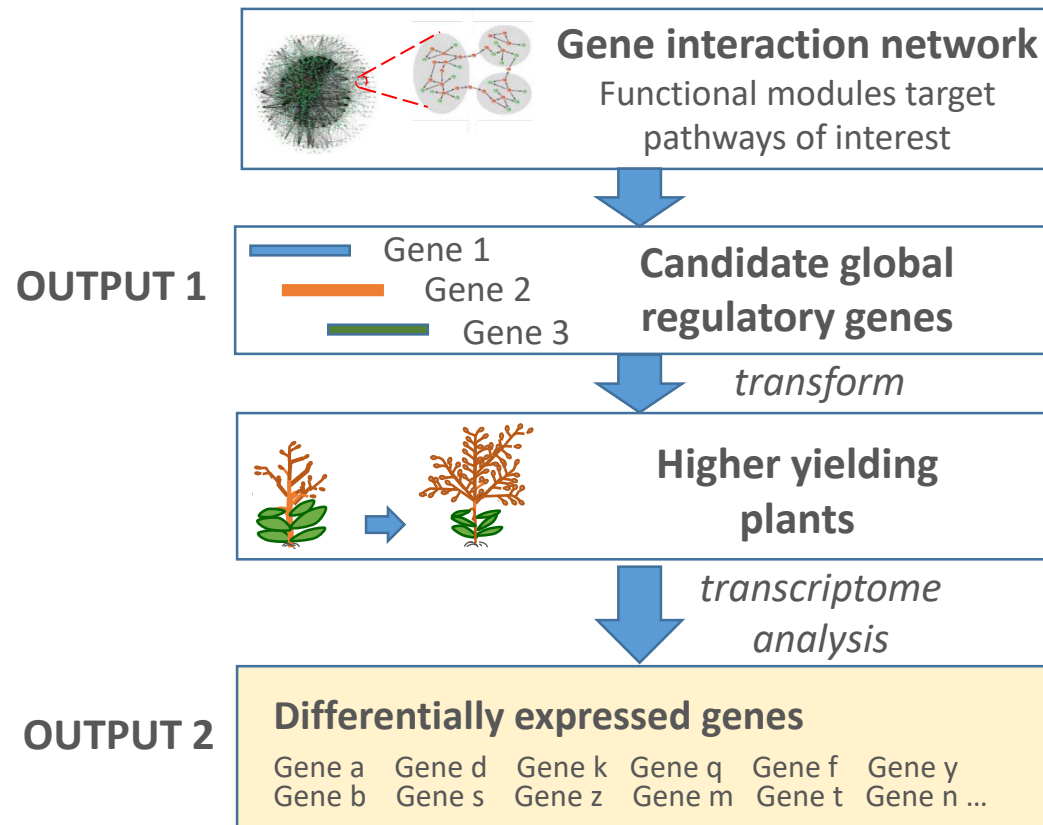




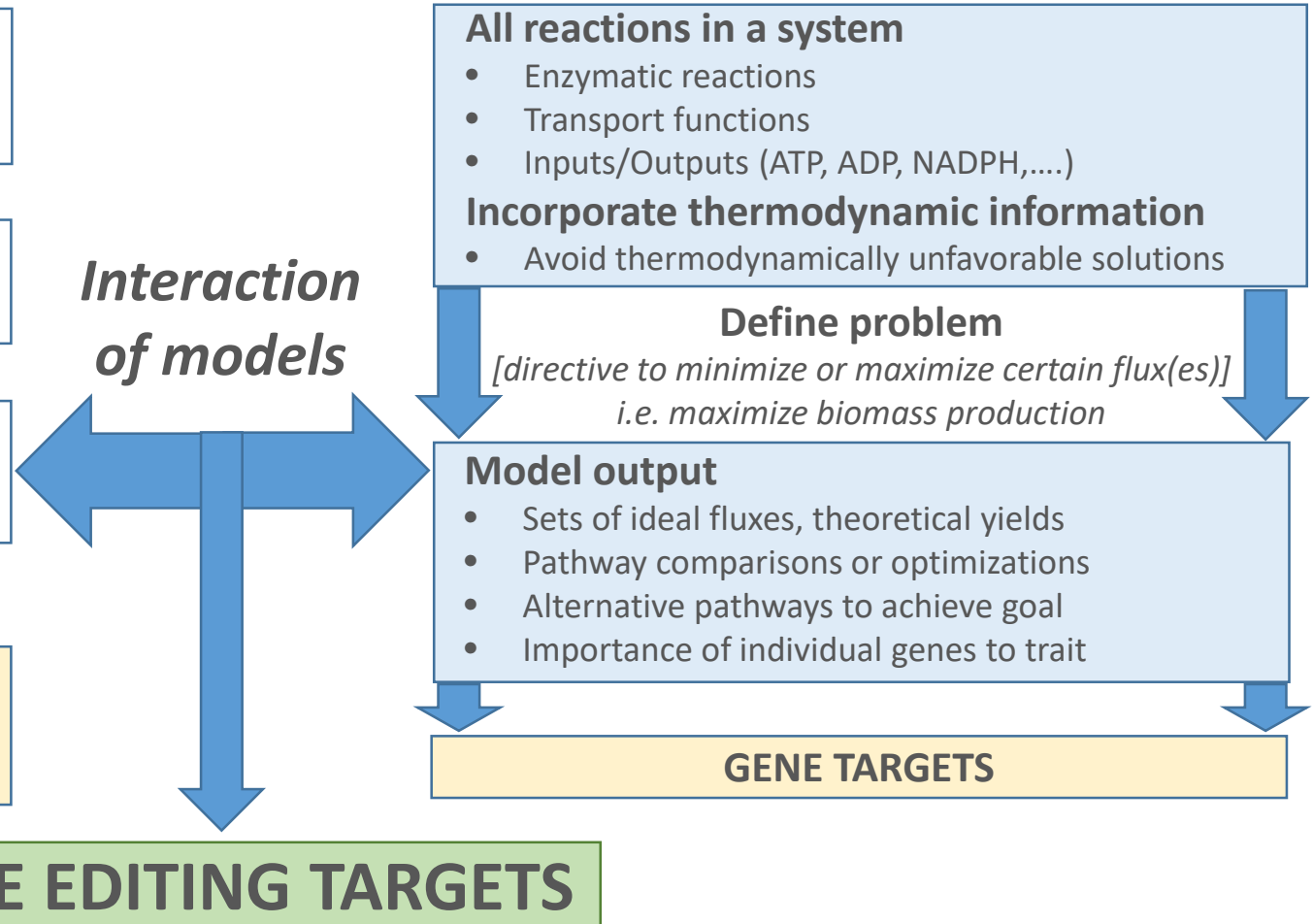
# GRAIN Platform: Next Generation Gene Discovery Approach

Yield10 is developing and validating predictive models to guide efforts in gene discovery

## Transcriptome-based regulatory association networks



## Flux Balance Analysis



- Yield10 GRAIN platform: a unique approach for identifying gene combinations to increase yield
  - *Building and validating predictive models to discover and prioritize traits*
- Strong collaborations with multiple academic groups to enhance trait pipeline
- Yield10 is progressing traits to increase oil content and seed yield in canola and camelina
  - *Traits are also being progressed in other commodity crops such as soybean and rice*
- Employing both GMO and genome editing approaches to achieve goals
- Many opportunities exist for licensing, partnerships, and/or collaborations

# Thank you

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