Yield10 BIOSCIENCE

ASPB 2018

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Transporter manipulation in food crops for increased yield

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Yield10 company overview

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

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

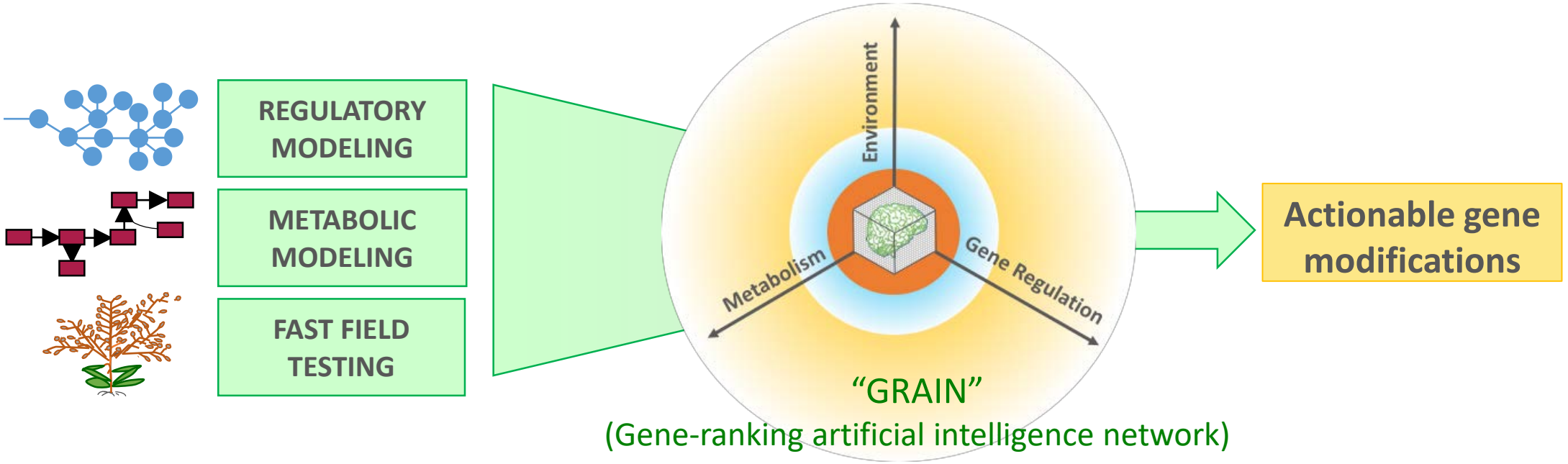
Yield10 brings extensive expertise and a track record in optimizing the flow of carbon in living systems to the agriculture sector to increase yield in key row crops

- Yield10 is targeting step-change (10-20%) increases in seed yield
- Technology based on 20 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

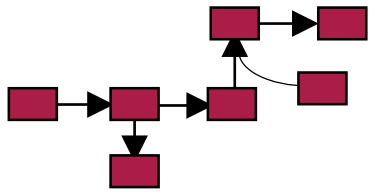
- Discover and de-risk yield technologies for major North American crops:
  corn and the two oilseed crops soybean and canola

The Yield10 platform



- Increasing crop yield is an extremely complex and challenging problem
- Screening thousands of individual plant genes has not delivered commercial yield traits
  - However, the sector has used this approach to generate billions of individual data points
- Modifying combinations of genes, metabolic and/or regulatory, will be necessary
- GRAIN's purpose is to be able to convert vast amounts of data into actionable gene modifications

Metabolic modeling



METABOLIC MODELING

FLUX-BALANCE ANALYSIS

- Purely stoichiometric
- Optimize production of biomass, oil, protein, etc.
- View optimal metabolism (vs. observed metabolism)
- Show effects of local metabolic changes on entire plant

KINETICS/THERMODYNAMICS

- Eliminate unrealistic reactions from flux-balance analysis
- Identify slow/difficult reactions within known metabolism
- Challenge conventional wisdom

CCP1 (C3003): Trait that increases seed yield

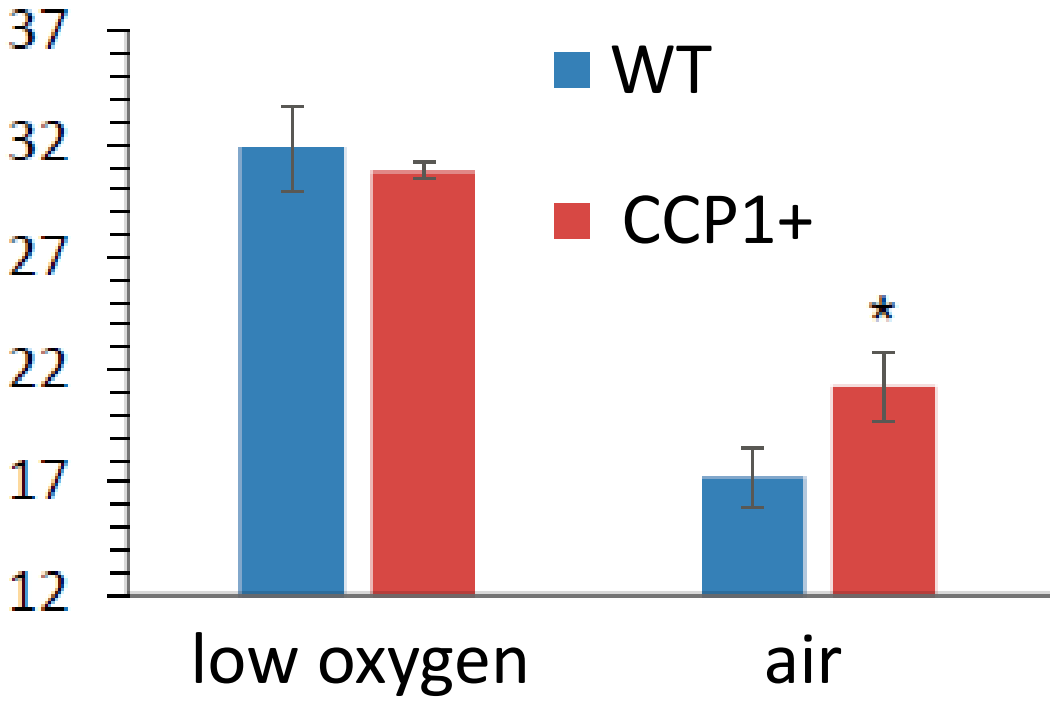
Crop	Expression	Trial	Group	Location	Best seed yield increase
Camelina	constitutive	field	Yield10	Canada	23%
Camelina	seed-specific	greenhouse	Yield10	Canada	24%
Camelina	seed-specific	field	Yield10	Canada	7%
Canola	constitutive	field	Yield10	Canada	13%
Camelina	constitutive	field	Schnell (Mich. St.)	U.S.	52%

What is CCP1?

- Transporter found in some algal species
- Induced at low CO_2
- Localizes to mitochondrial membrane

CCP1 is helpful in plants during photorespiration

Carbon assimilation in *Camelina* (mmol m^{-2} s^{-1})

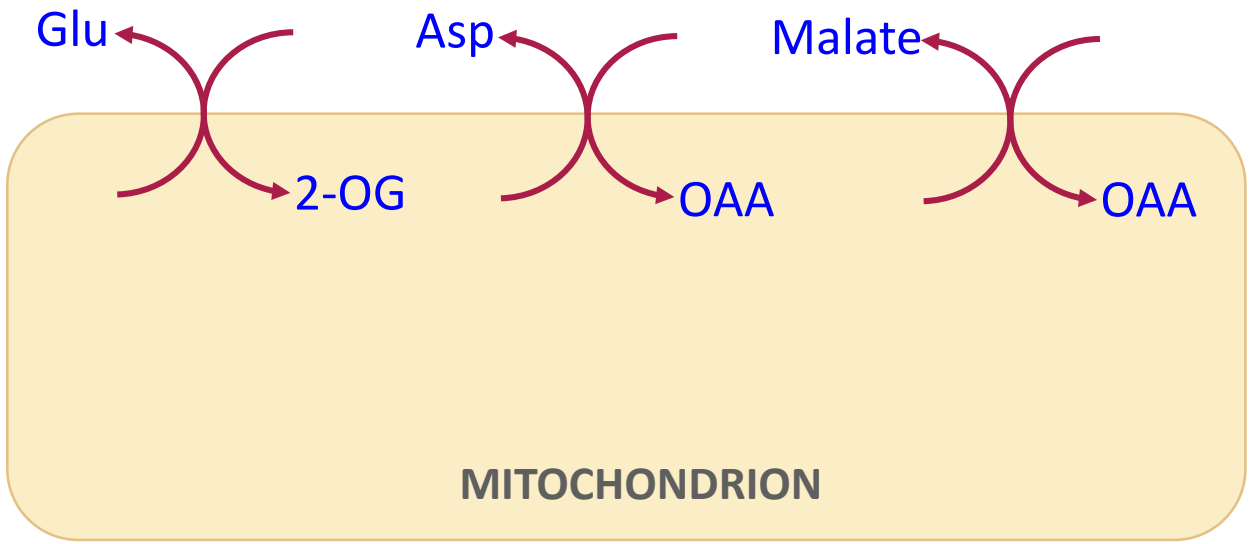


Data from laboratory of Prof. Danny Schnell (Michigan State Univ.)

Photorespiration needs predicted by model

Flux-balance analysis, optimizing leaf biomass

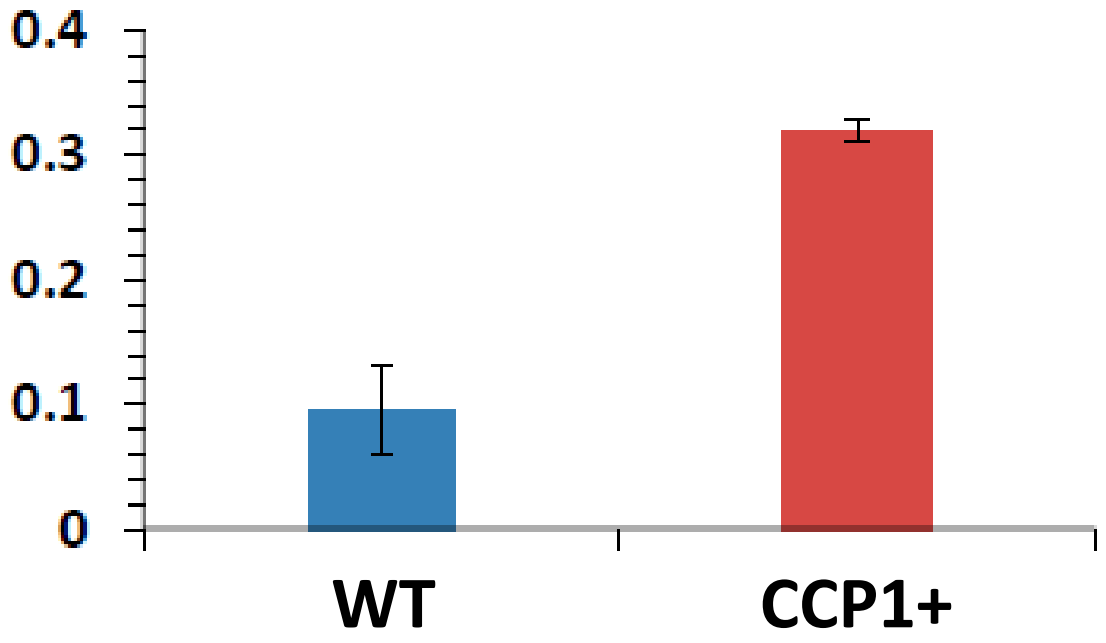
What mitochondrial factors should increase during photorespiration?

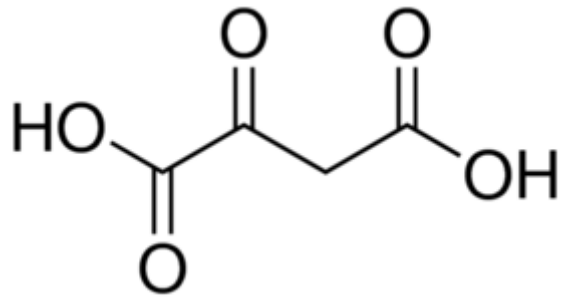


All of these remove electrons from the mitochondrion

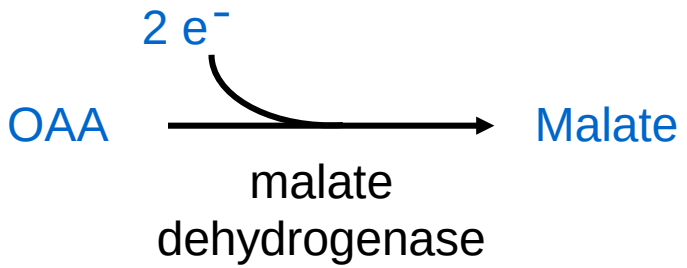
CCP1 facilitates OAA uptake into mitochondria

Relative OAA uptake in mitochondria isolated from yeast cells





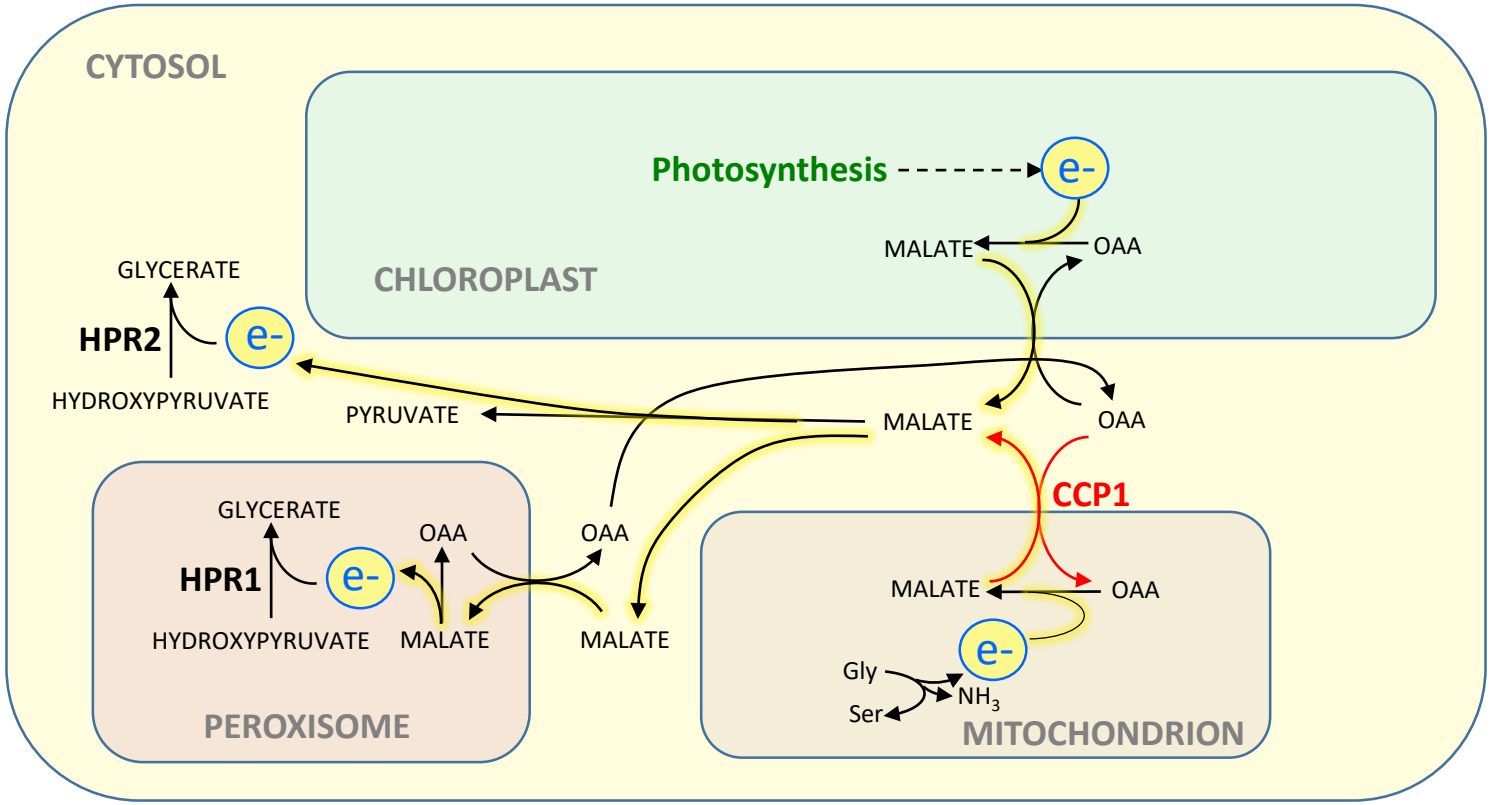
OAA (oxaloacetate) is an electron carrier



Data from laboratory of Prof. Danny Schnell (Michigan State Univ.)

Modeling suggests CCP1 role in optimum yield

- Collect electrons from mitochondrion and chloroplast
- Send to peroxisome or cytosol for hydroxypyruvate reductase (HPR)



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Role of CCP1 during photorespiration in the leaf

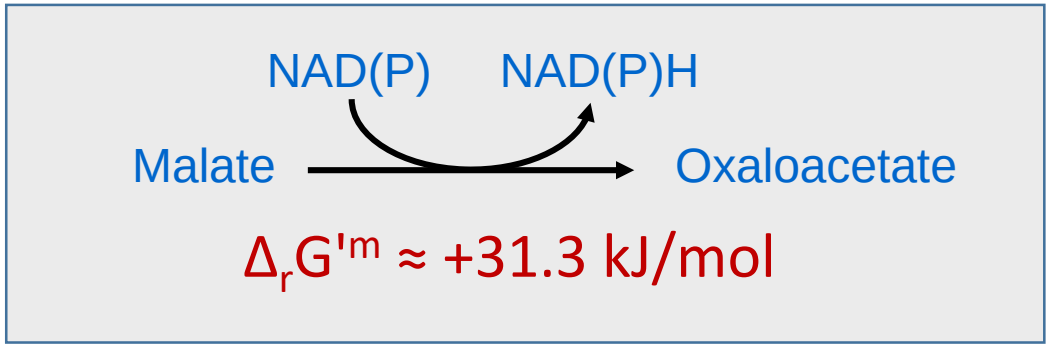
CCP1 may facilitate photorespiration

- HPR flux must be very high at times during photorespiration
- Modeling shows that lack of electron shuttling to HPR means >20% yield loss
- Accumulation of photorespiratory intermediates could also be a problem

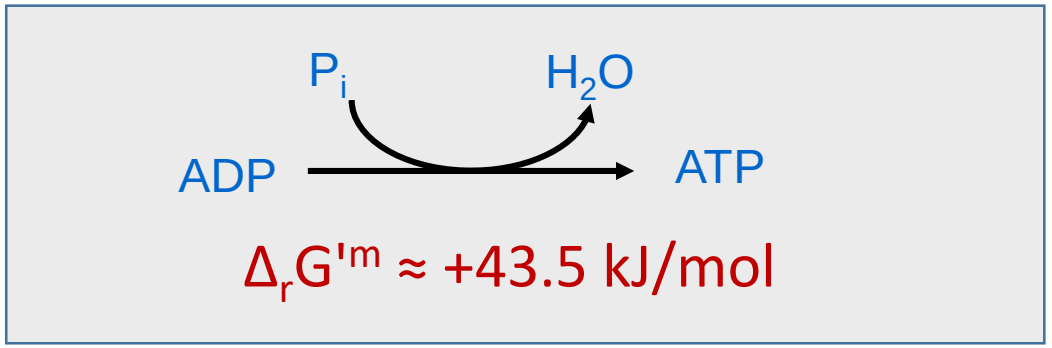
Can CCP1 benefit seed metabolism?

The TCA cycle must run during sugar metabolism in the seed, but one of its steps is very unfavorable:

malate dehydrogenase (MDH)



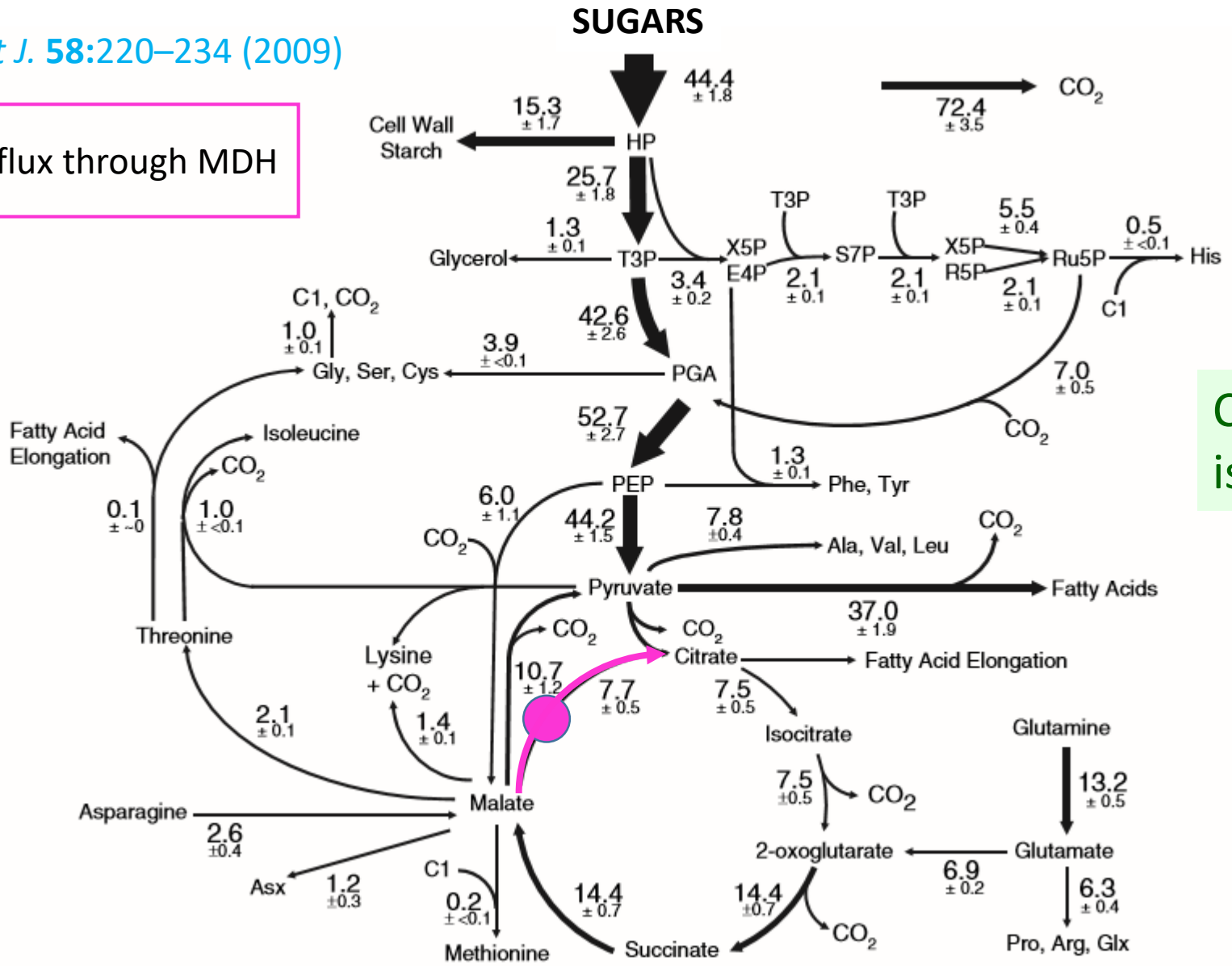
compare with spontaneous ATP formation



Cultured soybean embryo flux data

Allen et al., *Plant J.* **58:**220–234 (2009)

apparent flux through MDH



Carbon efficiency is already >90%

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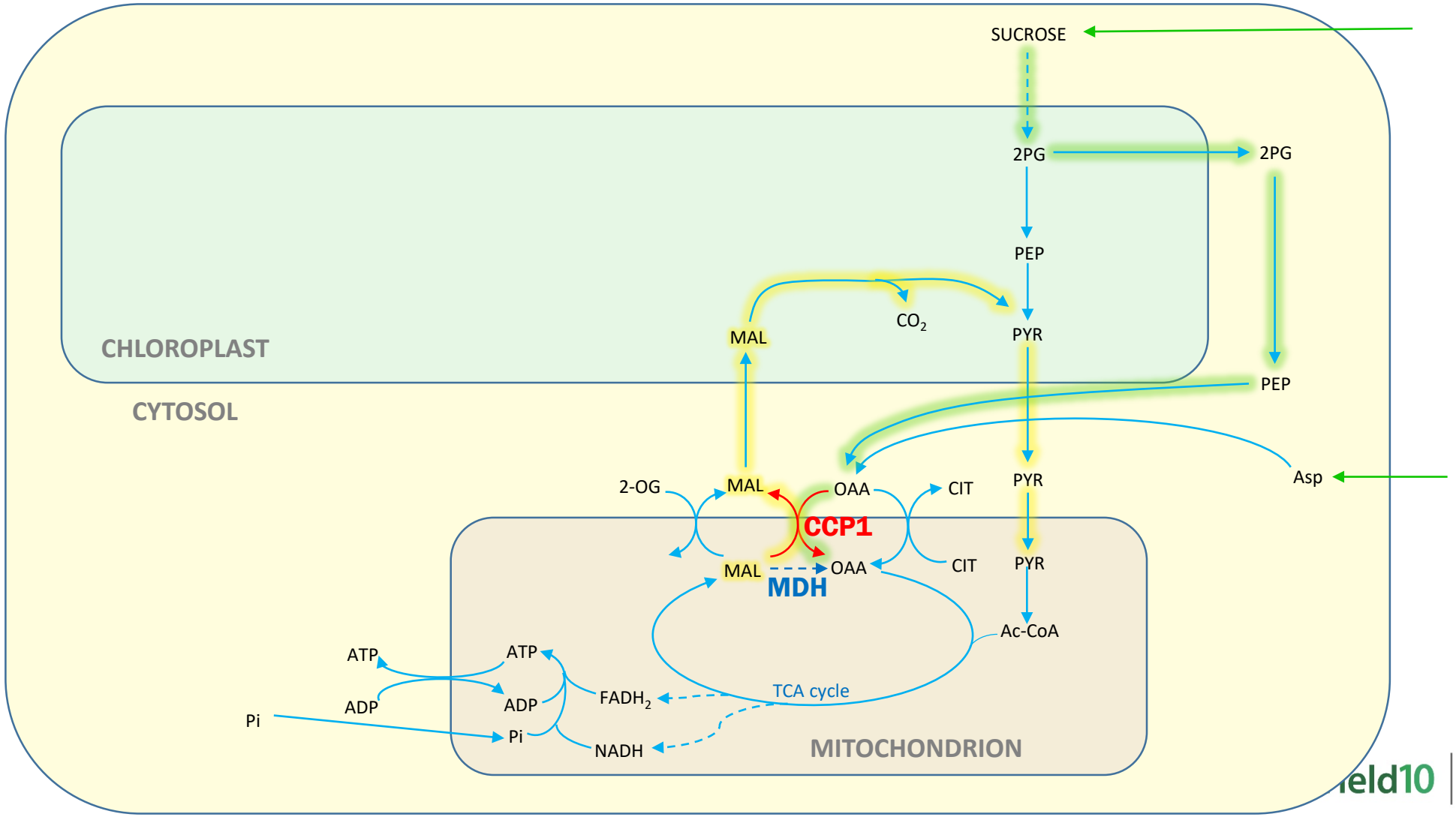
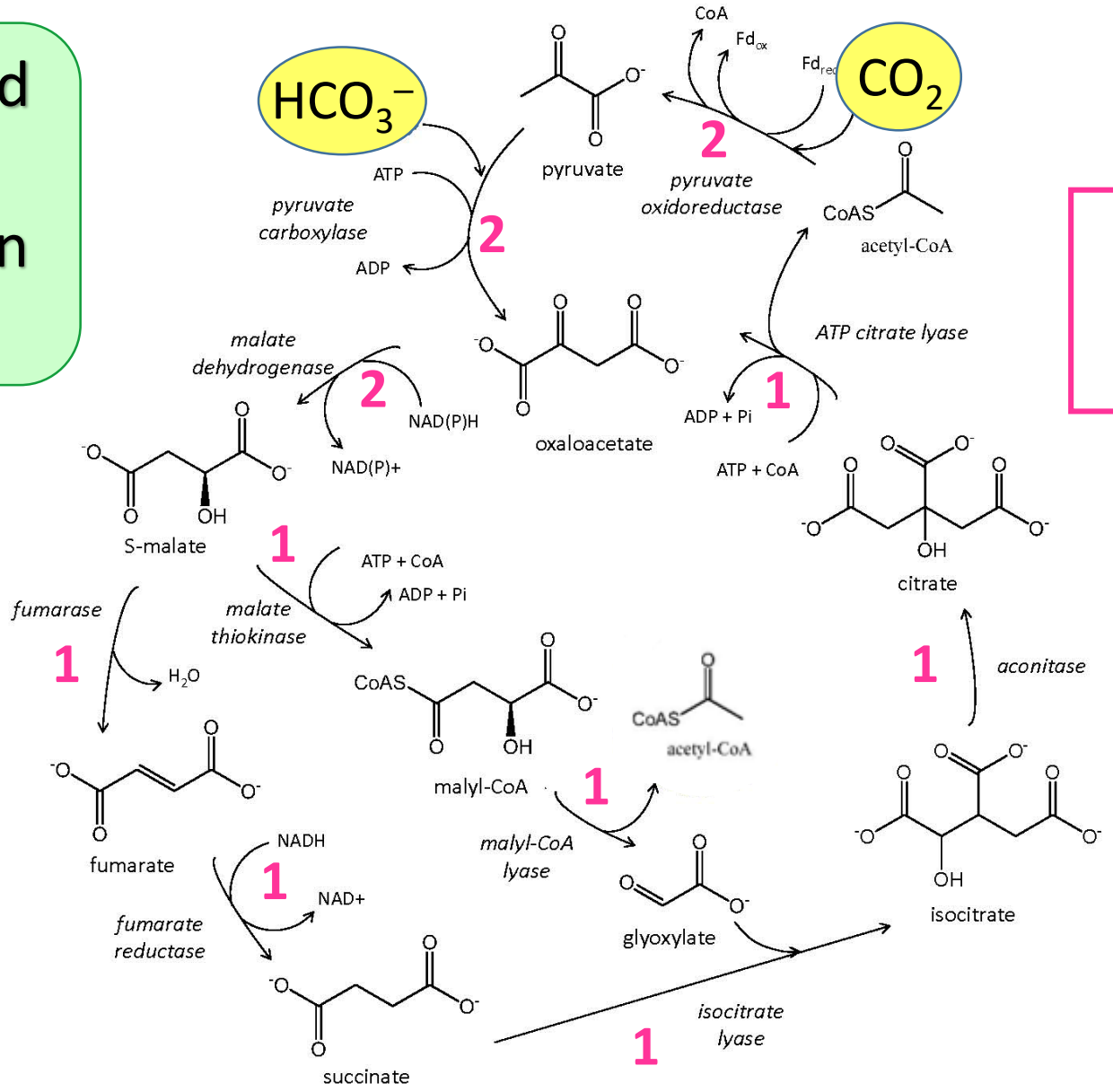
Can CCP1 benefit seed metabolism?

CCP1 may increase sink strength, NOT carbon efficiency



The reverse glyoxylate shunt (rGS)

What if we could eliminate photorespiration altogether?



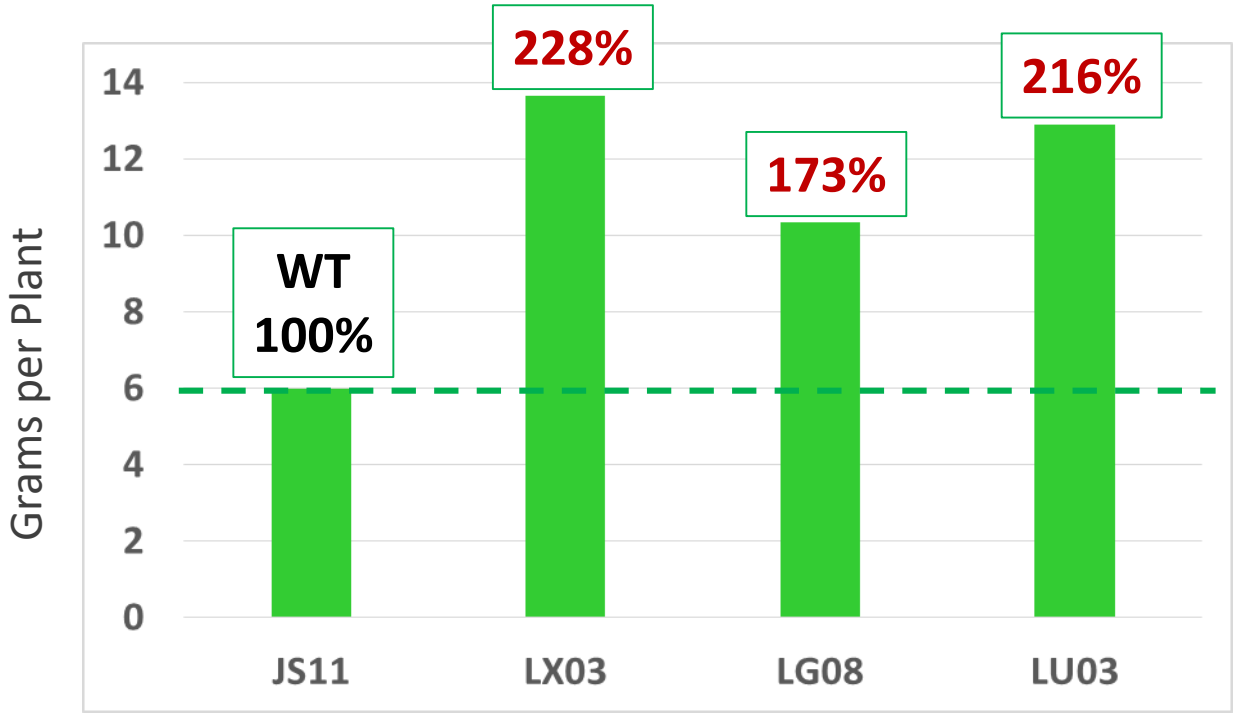
RELATIVE FLUXES

NET

$2\ CO_2 + 2\ HCO_3^- \rightarrow OAA$

Maximum relative theoretical yield with rGS under photorespiratory conditions = 212%

Camelina greenhouse study: Best plants



Malik, M.R., Tang, J., Sharma, N. et al. *Plant Cell Rep.* (2018). https://doi.org/10.1007/s00299-018-2308-3

Summary

- Yield10 uses modeling and experimentation to identify and de-risk yield gene traits
- Metabolic modeling is a key part of this – but needs to be validated with results
- C3003 (CCP1) has shown significant oilseed yield increases in field trials
- Modeling has helped to explain its role and to suggest further targets
- The reverse glyoxylate shunt (rGS) pathway doubles seed yield in greenhouse studies, demonstrating that improving carbon conversion efficiency has high yield potential
- Top rGS yield increases agree with model's predictions

Thank you

Questions?

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