Genome Editing to Increase Seed Oil in Camelina

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CANOLA INNOVATION DAY

December 2021

Sustainable Growth Starts with a Seed

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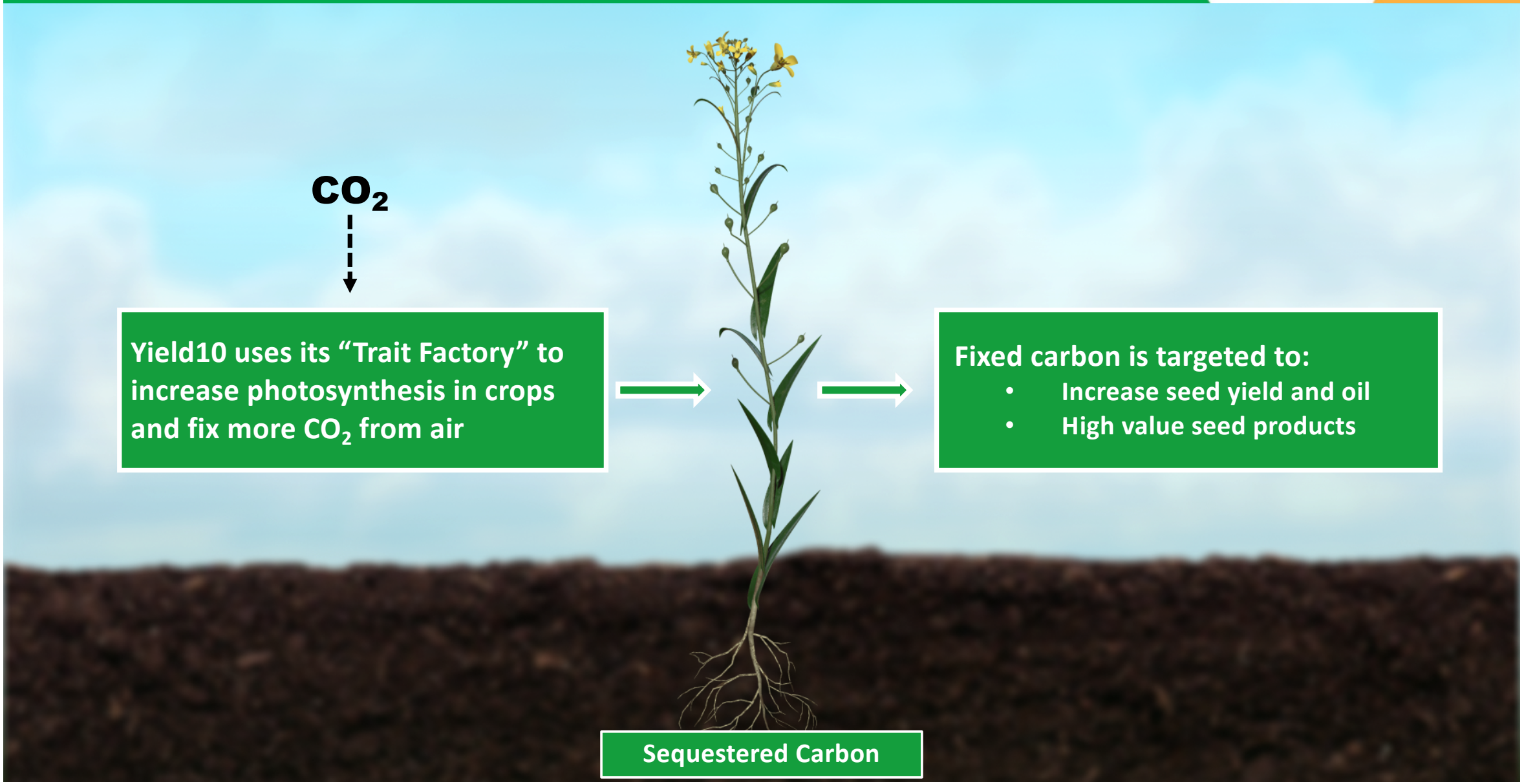
*Under the Private Securities Litigation Reform Act of 1995

Yield10's Crop Innovation Platform



Yield10's Trait Factory and Business Models

From Crop Science to $200 Billion Total Addressable Market (TAM)

GRAIN 3.0

CRISPR editing

Camelina Genetic Engineering

GMO

Technology Platform - "Trait Factory"[1]

Camelina Seed Products

1. **Feedstock Oil (Biofuel)**
2. **Omega-3 Oil (EPA+DHA)**
3. **PHA Bioplastics**

+

Trait Licensing[2]

Bayer CropScience | GDM | Forage Genetics International | Simplot

[1]21 Patent Families Pending

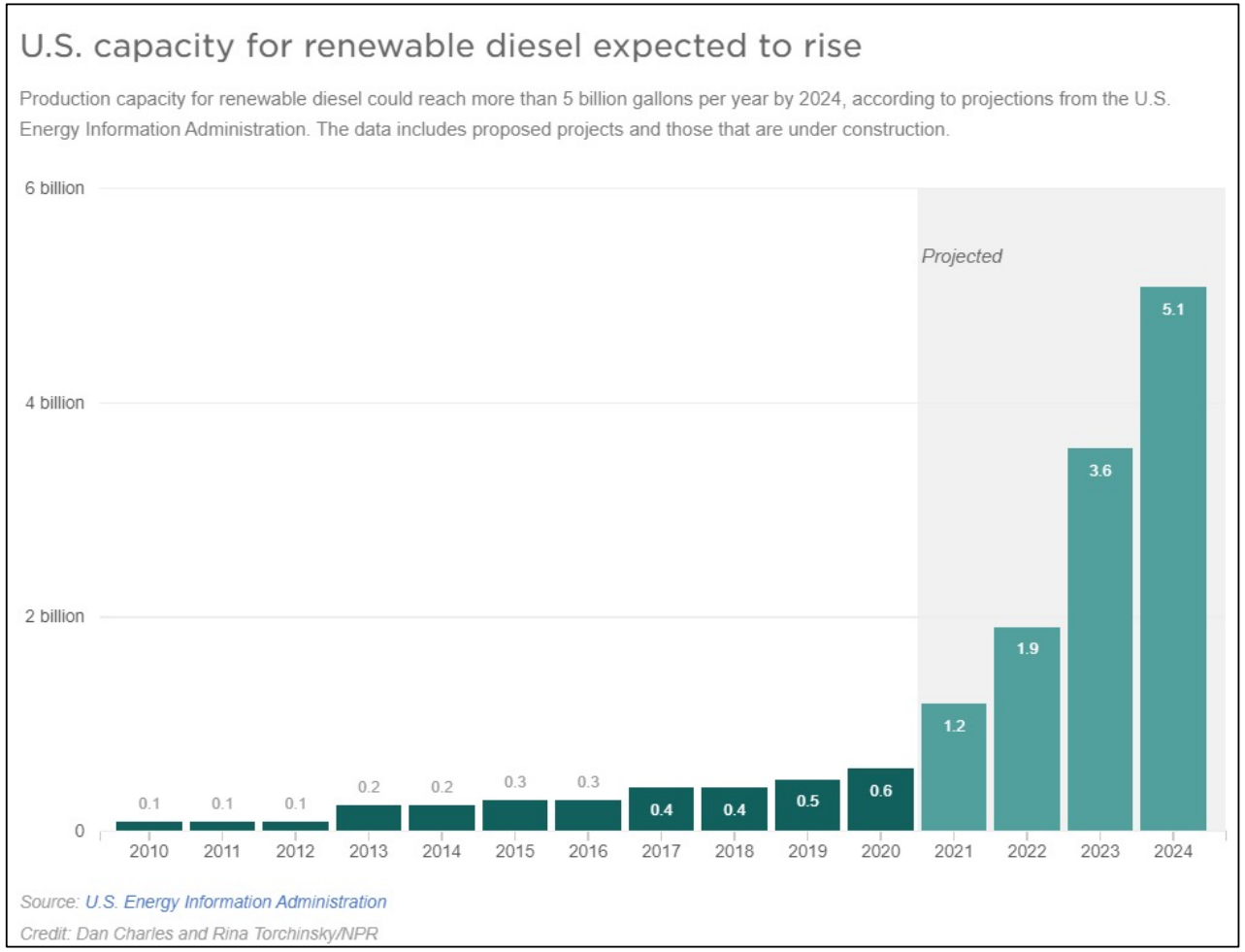
[2]Research License Agreements, 3rd party R&D to create option value for Yield10 gene traits on over 400 million acres of major crops (soybean, corn, canola, etc.)

Oilseed Crop Choice: *Camelina sativa*

- Good platform for specialty/niche crops for high value products
  - Specialty oils, biopolymers, products in food and animal feed
- Seed oil levels typically 35-40% of seed weight
- Does not outcross with Canola
- Both spring and winter varieties of Camelina available
  - Winter varieties - possible cover crop to remove excess nitrogen from prior corn/soybean growth
- Camelina is currently planted on a very small acreage
  - Needs improvements

Yield10 Camelina Review: *Camelina sativa*, an oilseed at the nexus between model system and commercial crop. Malik et al., Plant Cell Rep., 2018

Opportunities and Challenges in Renewable Diesel



Improvements to Camelina

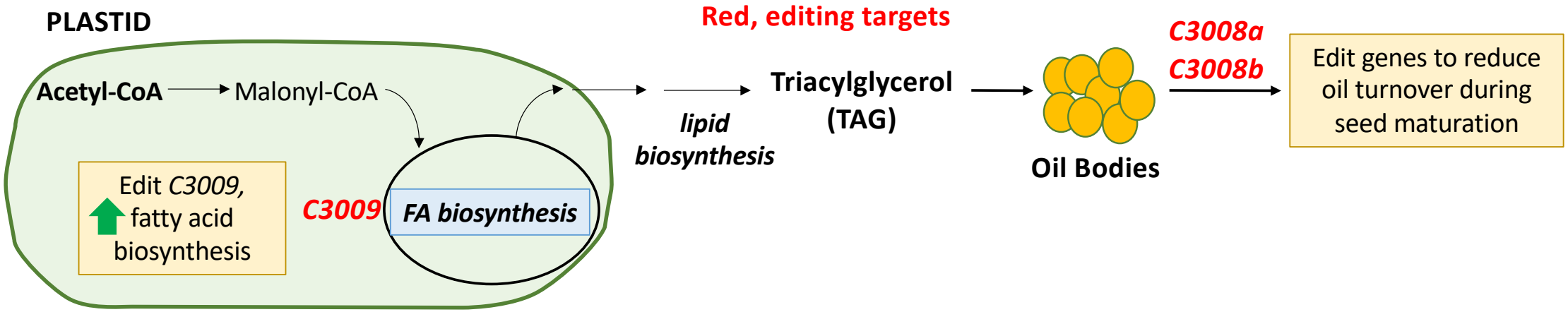
Transform into high revenue, high yield, low carbon-index crop, securing acreage for renewable diesel feedstock

Target:

- *High yield/oil spring & winter Camelina*
- *Herbicide tolerance*
- *Disease resistance*

Editing Combinations of Known Genes

Gene combinations to increase oil biosynthesis and prevent oil turnover[1]



1. C3009 - transcription factor target to upregulate fatty acid biosynthesis

— regulation of embryo fatty acid biosynthetic genes, + regulation of genes responsible for pigment in seed coat

2. C3008a and C3008b - gene targets to reduce oil turnover during seed maturation

C3008a and C3008b, oil body associated lipases

[1]Editing work supported in part by U.S. Department of Energy – BETO, Grant No. DE-EE0007003

Multiplex Genome Editing of Three Genes in Camelina

Editing of lipase genes (*C3008a, C3008b*) and transcription factor gene (C*3009*)

- Identified best Camelina orthologs to Arabidopsis genes based on homology
- Simultaneous editing of 9 genes (3 target genes present in 3 copies each) using CRISPR
- Lines with different combinations of edits obtained and characterized
  - *Very difficult to get all 9 gene copies edited in same line, only one line obtained with all 9 genes edited*

- Fully edited *C3009* gene, loss of pigmentation in seed coat
  - ***Unique distinction to track edited seed***

Wild-type control

C3009 100% edited *(yellow seeded)*

Isolation of Line E3902 with Higher Oil Content

Trait performance in greenhouse

- E3902, **9% increase** in bulk seed oil content and **5% increase** in total oil produced per plant

	Gene Targets			% Increase, oil per individual seed (mgs)	% Increase, individual seed weight *(mgs)*	% Increase, seed oil content *(% of seed weight)*	% Increase, number of seeds per plant	% Increase, total oil produced per plant
	C3008b	*C3008a*	*C3009*					
E3902	X X _	X X X	X X X	+ 12	+ 1	+ 9	-5.2	+ 5
Line 2	X X X	X X _	X X X	**+ 38**	**+ 17**	**+ 5**	**- 19**	**- 15**
Line 3	X X X	X X X	X X X	**+ 34**	**+ 9**	+ 6	- 29	- 26

***X** = edited allele*

Patent pending

- Observed tradeoff between seed oil content with seed number
  - *Lines 2 and 3 have higher increases in "oil per individual seed" and "individual seed weight" and fewer seeds per plant*
  - *Suggests significant shift in carbon partitioning to oil*
- **Opportunity exists to further engineer edited lines to increase seed yield**

2019 Field Tests of Edited Lines

Received 2018 confirmation that USDA-APHIS does not consider lines to be regulated[1]

2019 field test of edited lines at site in US

(randomized complete block design, lines replicated 6 times)

- **E3902 oil trait stable in 2019 & 2020 field trials**
- **2021 field data becoming available and looking promising**
- **Scaling up E3902 in this year's contraseason to meet demand for renewable diesel**

2019 Field Data for E3902

% Increase, oil per individual seed (mgs)	% Increase, individual seed weight *(mgs)*	% Increase, seed yield *(kg seed per hectare)*	% Increase, seed oil content *(% of seed weight)*	% Increase, number of seeds harvested	% Increase, total oil produced per hectare
11.8*	8.7*	9.7	4.7*	- 3.7	15.0

**statistically significant (t-test)*

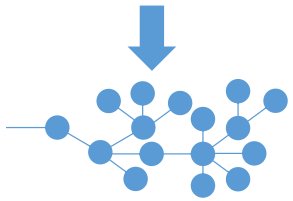
Patent pending

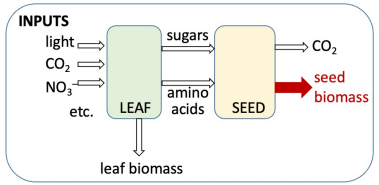
[1]pursuant to 7 CFR part 340*

GRAIN 3.0: Identify Unique Gene Combinations for a Trait

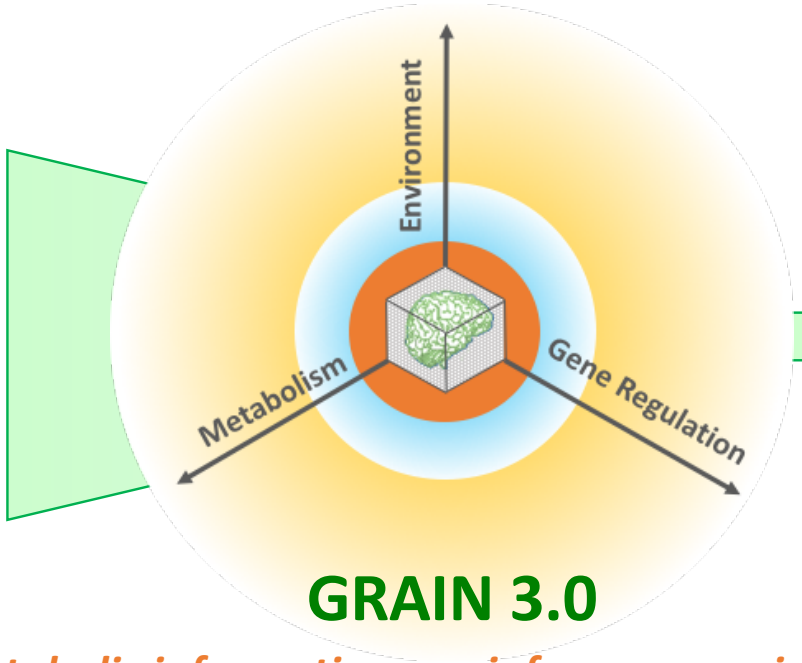
How do you move beyond known genes and identify new combinations?

CROP SPECIFIC GENOMICS DATA





- **REGULATORY MODELING**
- **METABOLIC MODELING**
- **FAST FIELD TESTING**



Actionable gene modifications leading to valuable, novel yield traits

Metabolic information can inform genomic decisions

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Yield10 Review Paper on Metabolic Engineering in Plants: Skraly et al., Metabolic engineering to increase crop yield: From concept to execution, 2018, Plant Science

GRAIN 3.0: Identification of High Oil C3020 Trait

Used GRAIN to search for transcription factors (TFs) to increase seed oil content in Camelina

Ranked List of Gene Targets

211 Identified TFs	
TF1 = WRI1	TF9
TF2 = WRI1	TF10
TF3 = WRI1	TF11
TF4 = MYB56	TF12
TF5	TF13
TF6	TF14
TF7	TF15 = MYB56
TF8	TF16 ….

Proprietary ranking procedures

25 TFs

Most relevant, least studied

4 TFs

Overexpression of TFs

Trait	Effect
C3020	**+10% oil**
C3019	Editing target
C3021	Editing target
C3022	Editing target

Editing of C3021 in progress

- Ranked list of TFs obtained
- Known TFs that impact oil and/or seed yield observed in top spots validating approach
- **Many uncharacterized genes identified, IP white space**
- **Overexpression of C3020 increases seed oil content by 10%**
- **Next steps: combinations of edits, combinations with E3902**

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Research supported in part by the Office of Science (BER),
U.S. Department of Energy, Grant No. DE-SC0018269

Why is a Prioritized Short-List of High-Value Targets Better?

Illustrative Example – Resources to test combinations of 3 gene changes for a trait

Test all 3 gene combinations with **1,000** interesting gene targets (from **genomics**)

166,167,000 combinations of 3 genes

Identifying successful gene combinations is impossible with many low-value targets

Test all 3 gene combinations with **10** interesting gene targets (from **GRAIN**)

➡ **120 combinations of 3 genes**

Summary

For oilseed crops: harvest value is driven by oil/acre = seed yield/acre x seed oil content

Need to increase Camelina seed yield and/or oil content to maximize oil yields per acre

Line E3902 with multiple genome edits has increased seed oil content in field

- 4.7% increase in seed oil content in 2019 field trials, 5.6% in 2020.
- 2021 trial under analysis and looking promising
- E3902 has a differentiated seed color
- Scaling up E3902 in 2021 contraseason to meet demand for renewable diesel

Yield10 using GRAIN to identify combinations of gene targets for increased oil/seed yield

- C3020 overexpression target increased oil by 10% (greenhouse)
- Editing C3021 target underway
- Plan to combine traits with E3902

Potential to combine E3902 edits with oil composition traits (high oleic, omega oil)

Have 5 to 6 additional disruptive trait targets that are in development

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