Developing healthier food products through genome editing

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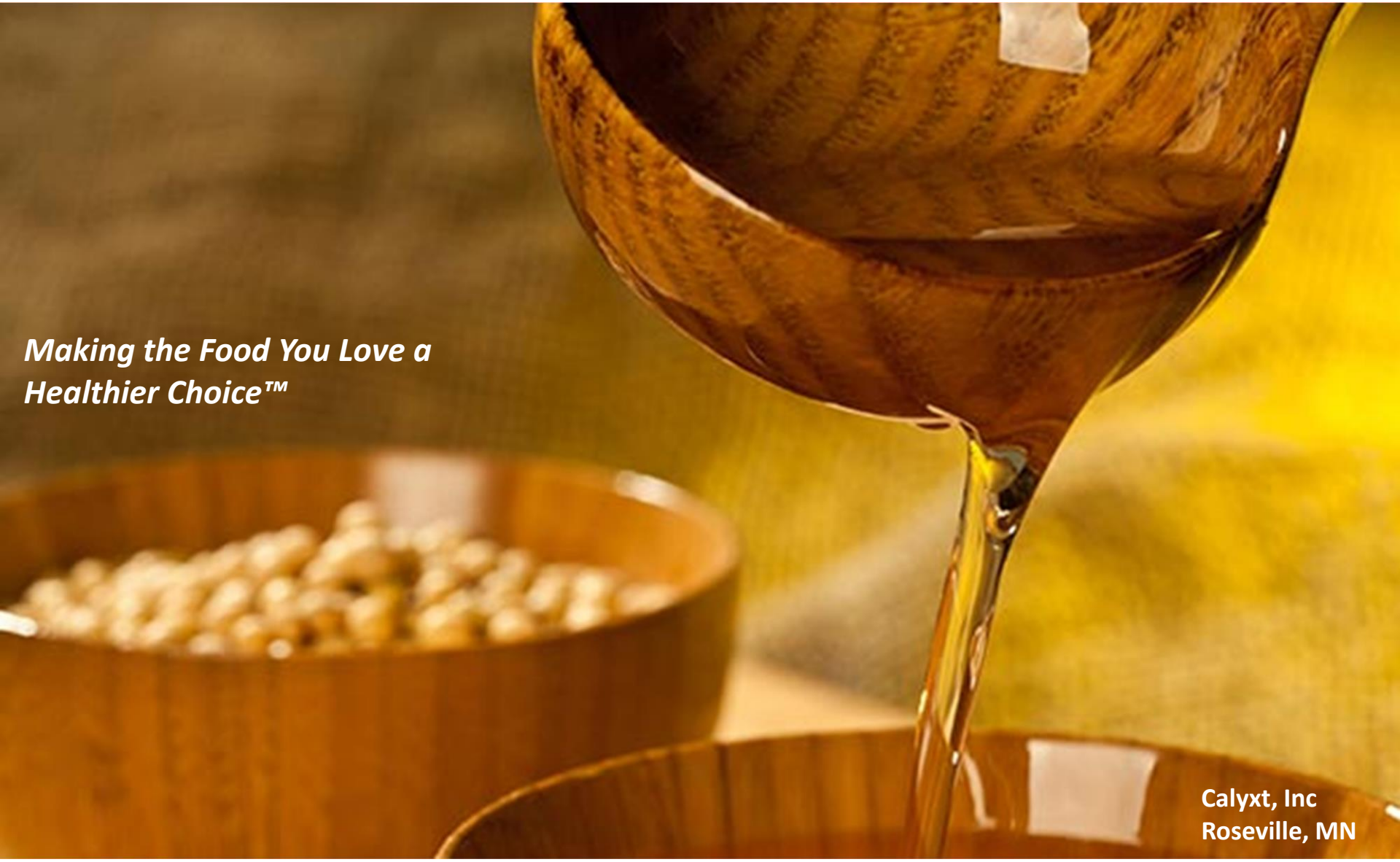

Calyxt, Inc
Roseville, MN

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Who is Calyxt?

Food ingredients for consumer health

We are…

a company developing healthier specialty food ingredients…

…by leveraging cutting edge science to develop food crops through gene editing technologies

Consumer Needs → *Healthier food ingredients*

Farmer Needs → *Agronomic Traits*

How we are building a path to market..

Best in Class	Best in Class	Best in Class	Best in Class
Gene Editing Technologies and Technical Expertise	***Product Development Capabilities***	***Identity Preserved Supply Chain***	***Specialty Food Ingredients***

Food Related Issues are Getting Worse

Legacy agriculture companies have overlooked society's food related issues

HEALTH CHALLENGES

- **100%** Increase in **Obesity** cases amongst adults in last 30 years
- **43%** Deaths caused by diseases linked to **Poor Diet** including **Diabetes** and **Heart Disease**
- **50%** Increase in **Food Allergies** in children between 1997 and 2011
- **48%** Increase in **medical care costs** from obesity ($315B in 2010)

Data Shown for United States of America

CURRENT INDUSTRY CHALLENGES

FOOD INDUSTRY:

- Processed foods with chemical additives
- Consumers want variety
- Provide 'clean labels'
- Provide health benefits and functionality

AG INDUSTRY:

- Commoditized supply chains
- Increase productivity
- Reduce cost/inputs
- Grow GMOs in main crops
- Limited consumer focused innovation

Source: Centers for Disease Control and Prevention, National Center for Health Statistics, and the Journal of Health Economics

Genome Editing is a Paradigm Shift

Our Technology Allows Us to Address Both Consumer and Farmer Needs

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LESS OF

- Saturated Fats Trans Fats
- Allergens
- Toxic Compounds

MORE OF

- Dietary Fibers
- Good Fats
- Nutrients
- Color, Flavor
- Plant Proteins
- Vitamins

- Reduce Waste
- Insect / Disease Resistance
- Increase Yield
- Reduce Inputs like nitrogen, phosphorus

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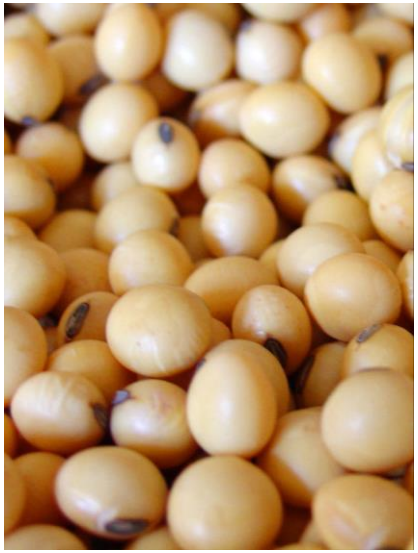
Gene editing opportunities in soybean

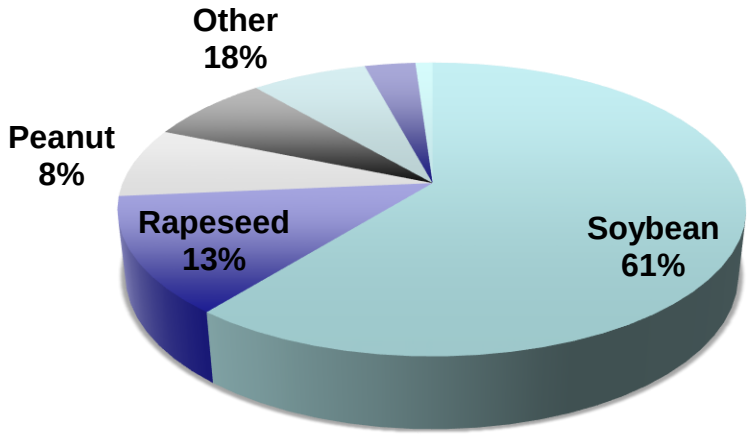
Glycine max (Soybean)



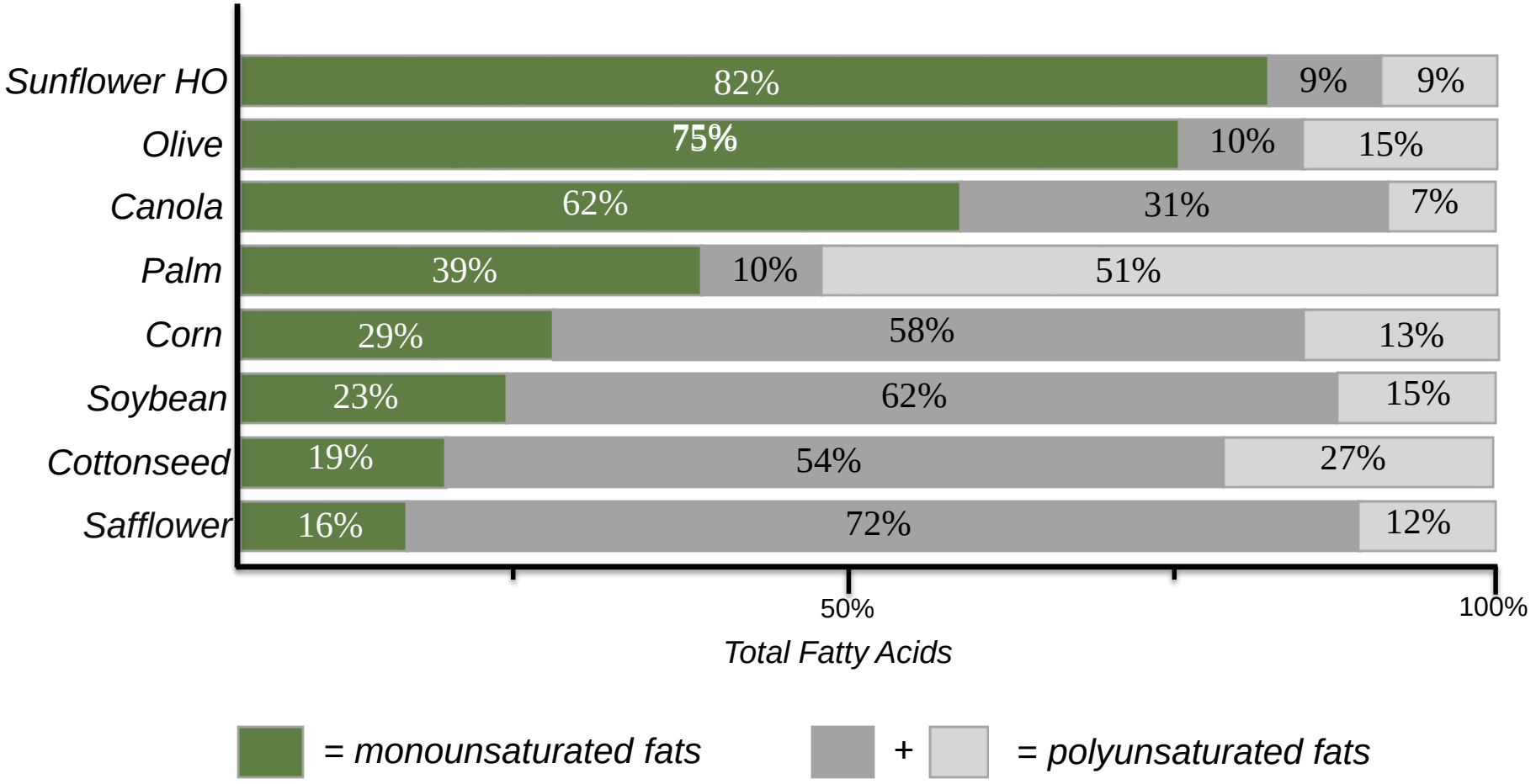
Soybean Production

- 320 million metric tons per year
- 297 million acres (~ area of South Africa)
- #1 source of protein for animal feed
- #2 source of oil for human consumption

Oilseed Production (World)



Fatty Acid Composition of Plant Oils



US Government Mandate and WHO Guidelines for Healthier Oil

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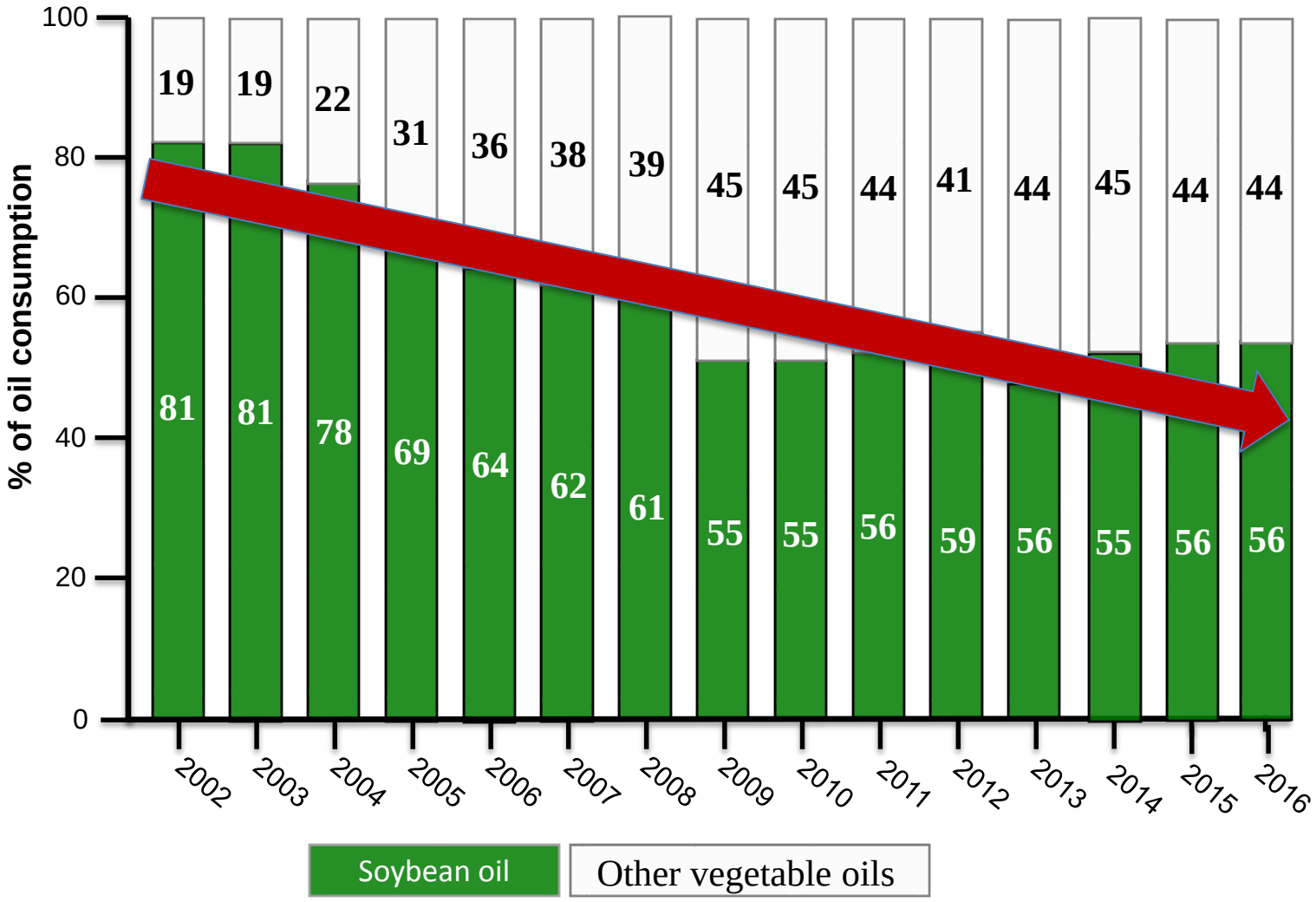
Hydrogenation Extends Shelf Life and Improves Heat Stability, But….. Hydrogenation >>>> Trans-fat

Demand for Soybean oil has decreased because of *trans*-fats



High-Oleic Soybean Variety Development

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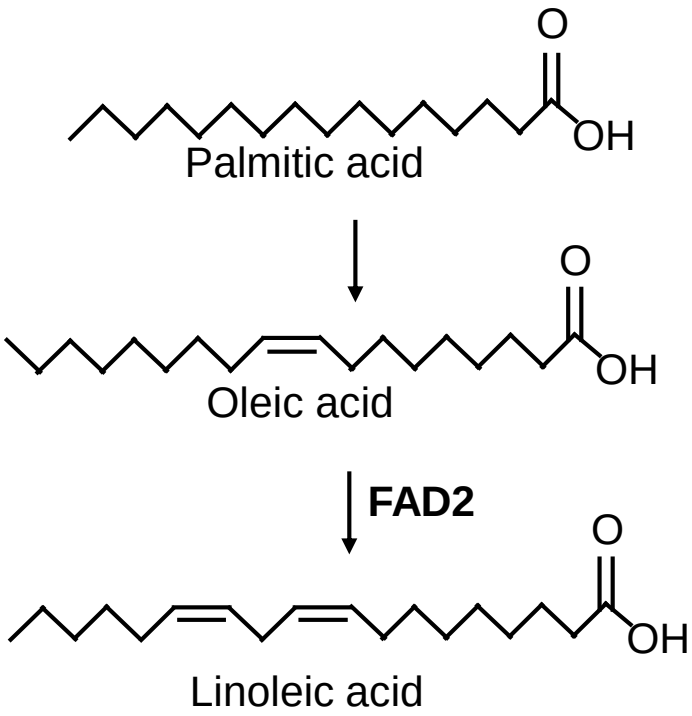
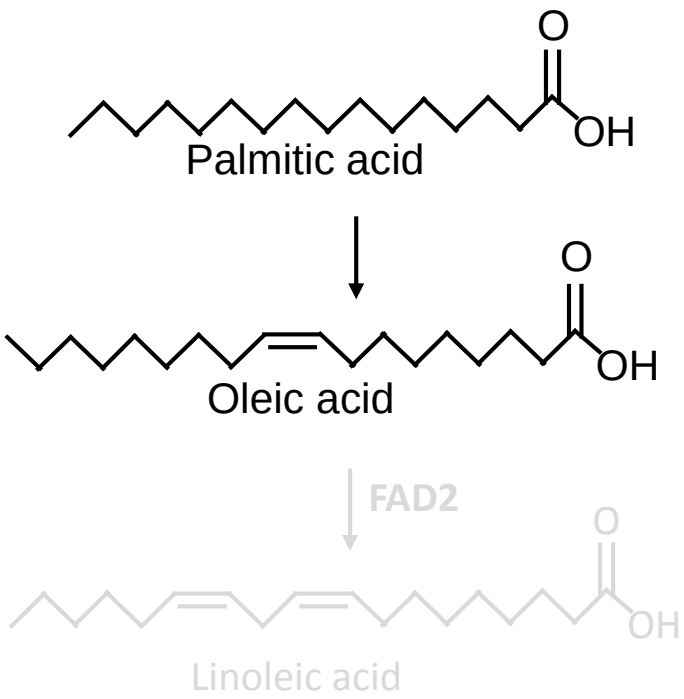
Natural pathway



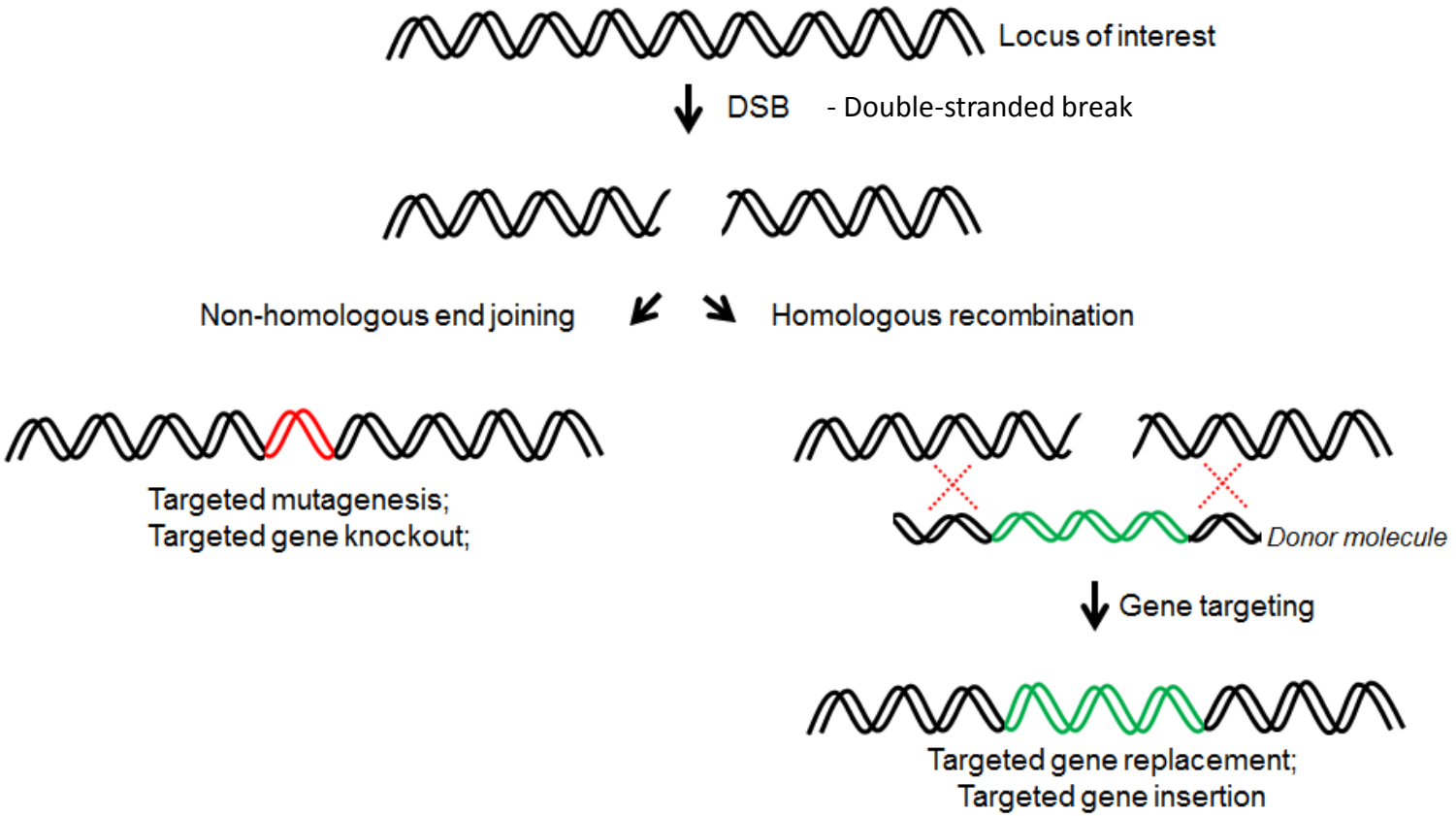
Modified pathway



Use of TALEN® Technology in Agriculture

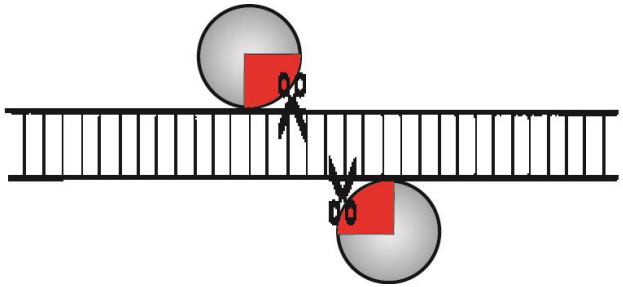
TALEN® is a registered trademark owned by the Cellectis Group

Genome Editing: Harnessing DNA Double Strand Break Repair Pathways

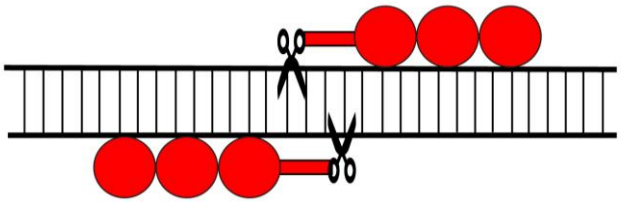


Sequence-specific nucleases enable efficient genome editing

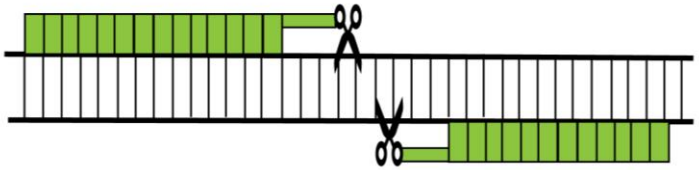
Meganucleases (homing endonucleases)



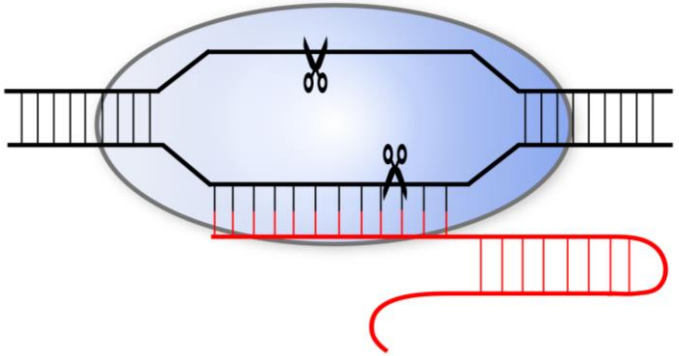
Zinc-Finger Nucleases



TALEN® (Transcription activator-like effector nucleases)



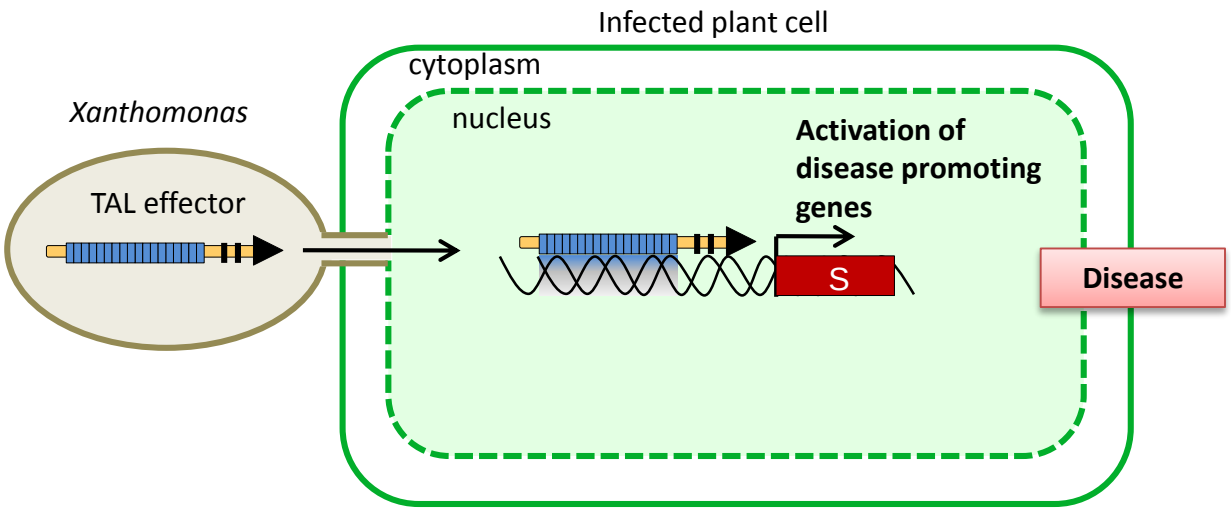
CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)

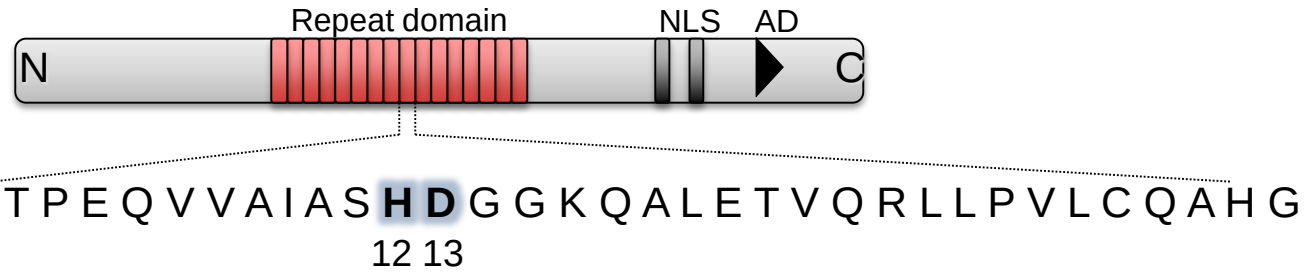


The Discovery of TAL effectors

- The TAL effectors were found to promote disease by altering plant gene expression

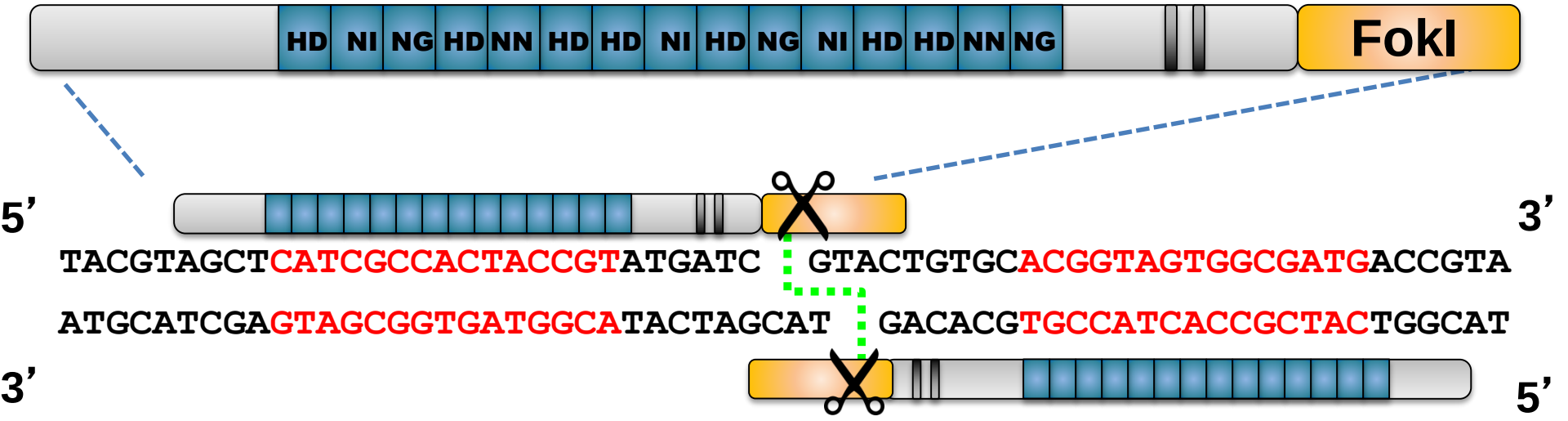
Plant species infected by *Xanthomonas*





Römer et al 2010

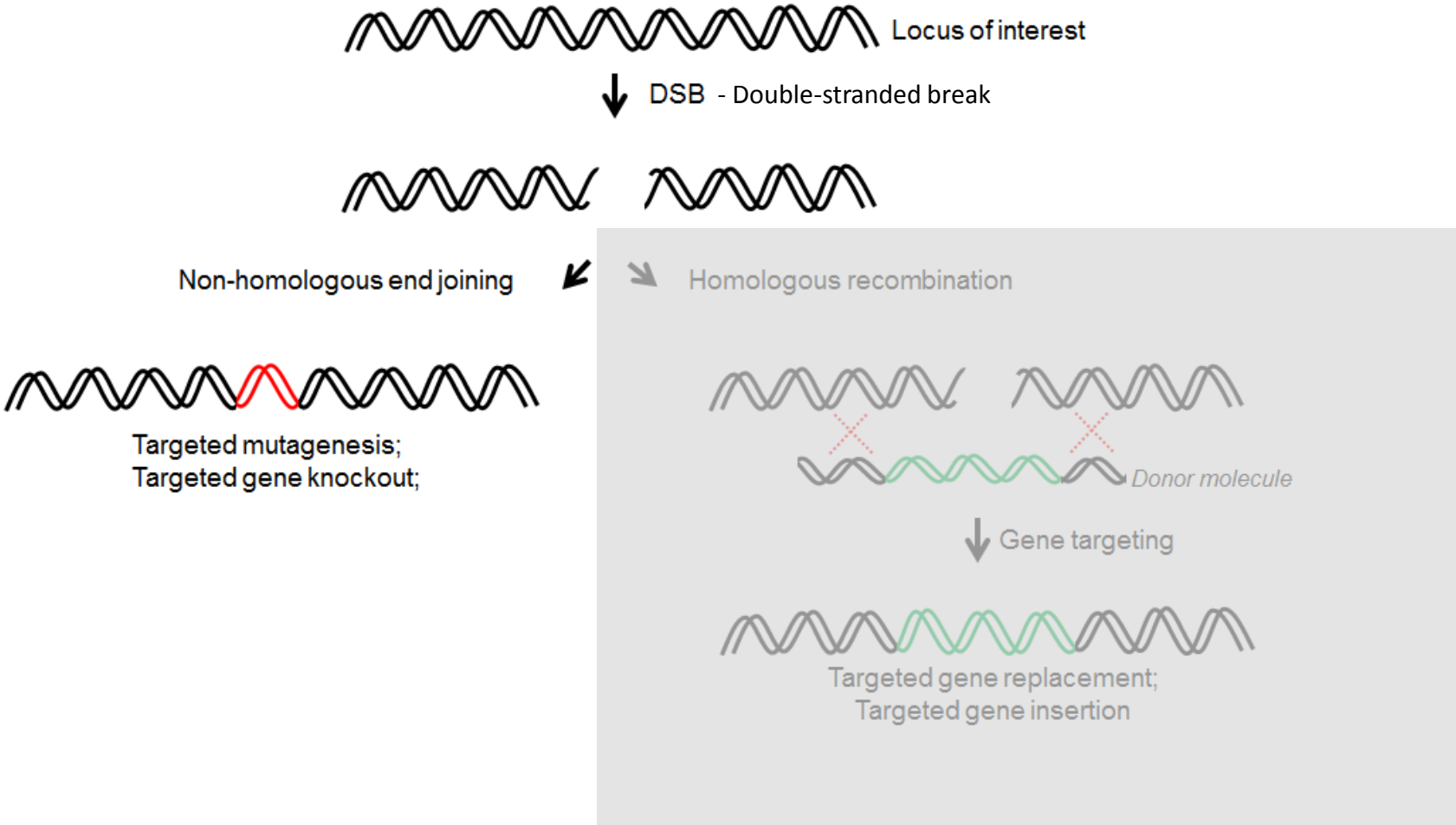
TAL effectors can be modified to create site-specific nucleases



First TALEN® were created using naturally occurring TAL effector proteins

Christian et al. 2010

Genome Editing: Harnessing DNA Double Strand Break Repair Pathways



Strategies for making targeted gene knockouts

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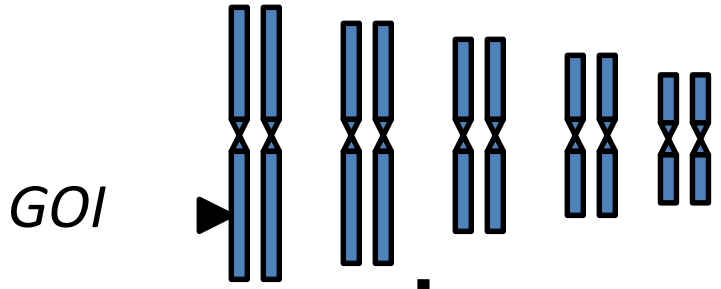
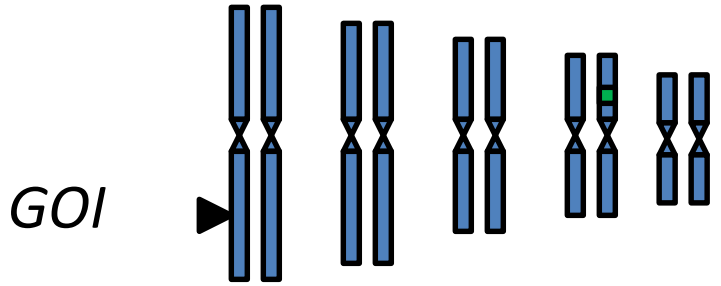
Wild type plant



Plant expressing TALEN® Technology



***GOI* = gene of interest**

Strategies for making targeted gene knockouts

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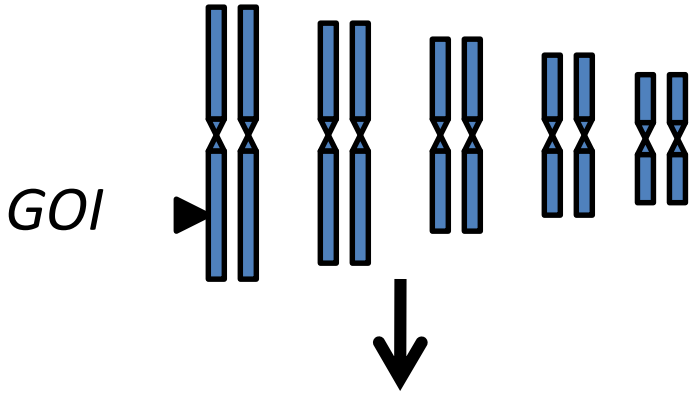
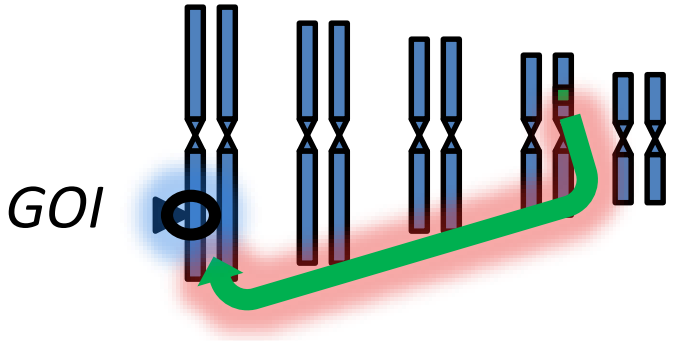
Wild type plant



Plant expressing TALEN® Technology



Strategies for making targeted gene knockouts

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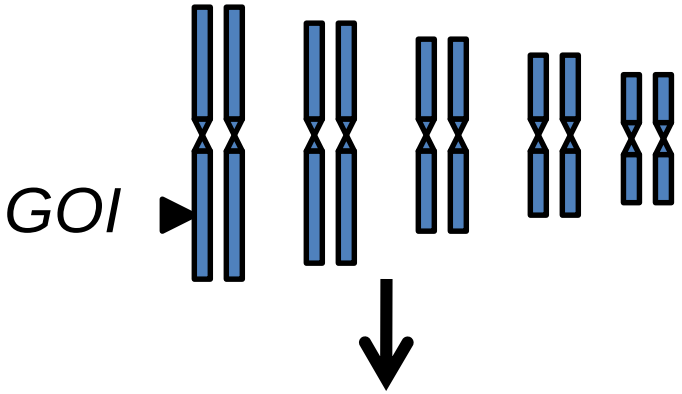
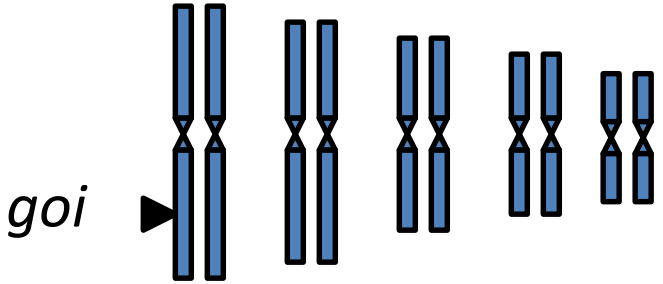
Wild type plant



Removal of TALEN® Technology



No foreign DNA remains in mutant plant

Work flow for making soybean knockout lines

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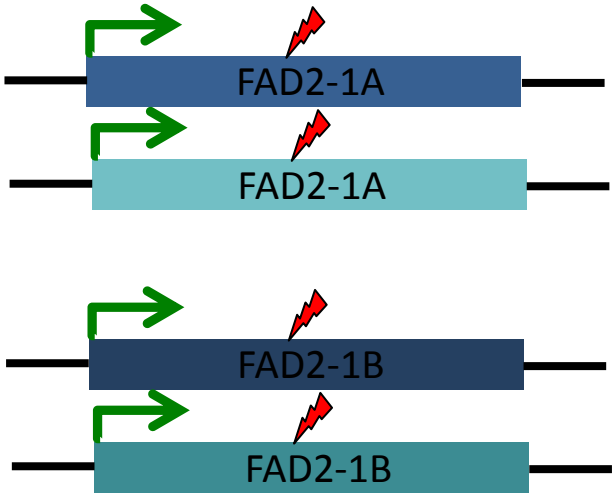
Soybean

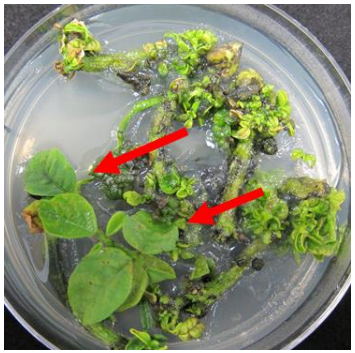
Transformation

FAD2 Nuclease



Callus Formation

Plant Regeneration



PCR Screening for FAD2-1 KOs

Self plants

Make KOs homozygous

T_0 Plant

T_1 Plant

Screen for high oleic acid oil phenotype:

AAbb
aaBB
Aabb
aaBb
aabb
Wild-type

Backcross to relevant maturity groups

Field selections, phenotyping, field trials, seed bulking

Sequence-specific nucleases typically make small deletions at the cleavage site that can disrupt gene function

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Examples of targeted mutations made by TALEN®

ccctt**ATTTCTCATGGAAAATAAGCCAT**cgccgccatcactccaacacaggttcccttg**ACCGTGATGAAGTGTTTGTCCC**aaaac
ccctt**ATTTCTCATGGAAAATAAGCCAT**cgccgccatcactccaacac--------ttg**ACCGTGATGAAGTGTTTGTCCC**aaaac
ccctt**ATTTCTCATGGAAAATAAGCCAT**cgccgc----------**GATGAAGTGTTTGTCCC**aaaac
ccctt**ATTTCTCATGGAAAATAAGCCAT**cgcc----------ttg**ACCGTGATGAAGTGTTTGTCCC**aaaac
ccctt**ATTTCTCATGGAAAATAAGCCAT**ccc----------ttg**ACCGTGATGAAGTGTTTGTCCC**aaaac
c----------tcccttg**ACCGTGATGAAGTGTTTGTCCC**aaaac
ccctt**ATTTCTCATGGAAAATAAGCCA**----------**CCGTGATGAAGTGTTTGTCCC**aaaac

How will plants with targeted mutations be regulated?

Regulatory status of crop varieties developed through targeted gene knockouts:

TALEN:
Nutritionally-Enhanced Wheat Developed, Calyxt, March 20, 2018
Improved alfalfa – Calyxt, September 25,2017
Browning resistant potato – Simplot, December 2, 2016
Browning resistant potato – Calyxt, September 15, 2016
Fungal resistant wheat – Calyxt, February 11, 2016
Disease resistant rice – Iowa State University, May 22, 2015
Low linoleic soybean – Calyxt, May 20, 2015
High oleic soybean – Calyxt, May 5, 2015
Low acrylamide potato – Calyxt, August 28, 2014

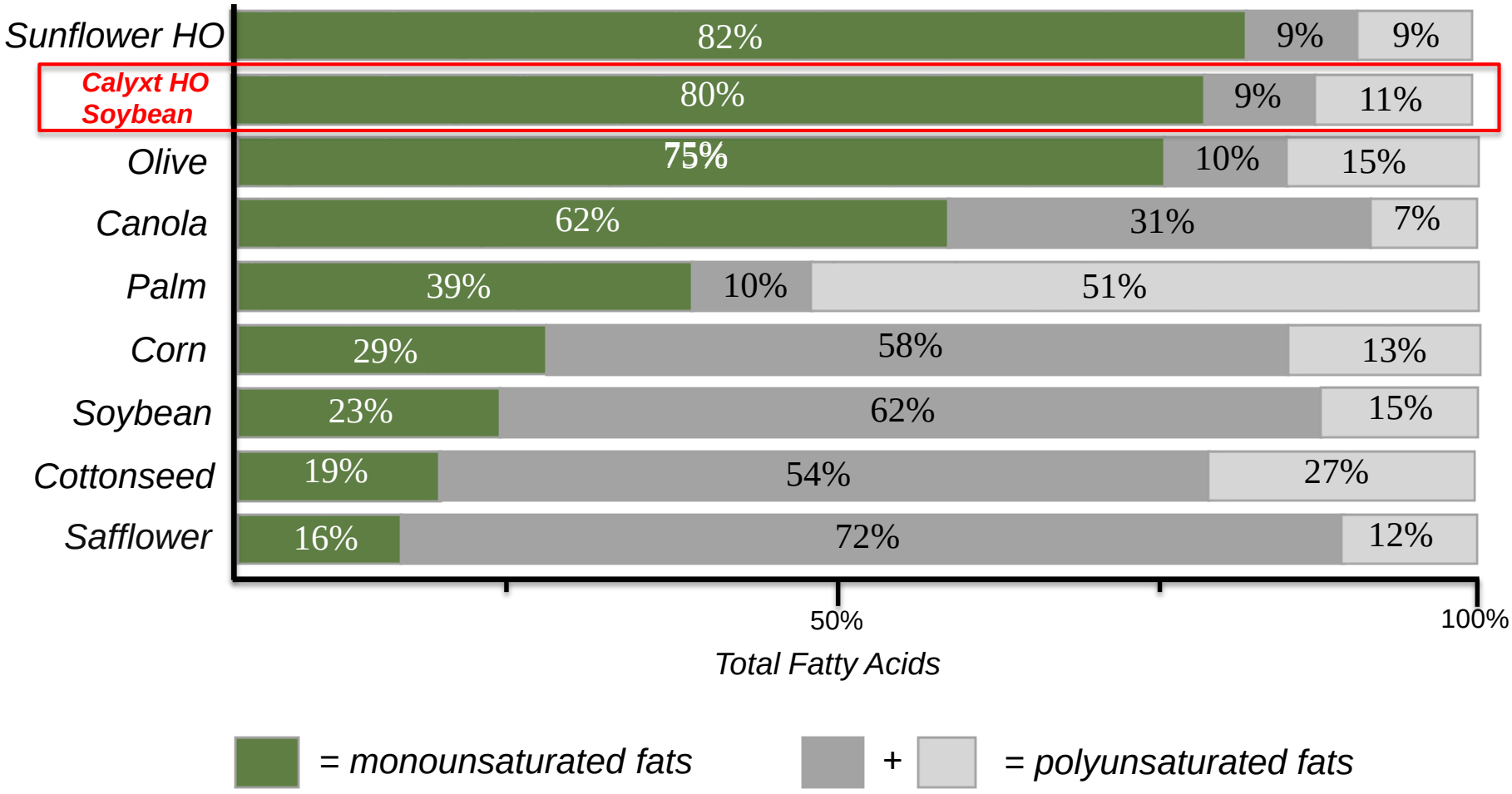
Meganucleases
Maize trait -- Agrivida, November 30, 2015
Use of meganucleases for plant trait development – Calyxt, January 16, 2011

Zinc Finger Nucleases:
Low phytate corn -- Dow AgroScience, March 8, 2012

CRISPR/Cas:
Genome Edited Maize – Iowa State University, July 12, 2018
Genome Edited Tomato – University of Florida, May 14, 2018
Soybean with Drought and Salt Tolerance – USDA, October 16, 2017
Altered Camelina – Yield10 Bioscience, August 29, 2017
Altered flowering millet – Danforth Center, April 7, 2017
Waxy corn – Dupont/Pioneer, April 18, 2016
Anti-browning mushroom – Penn State University, April 13, 2016

Source: USDA website

Fatty Acid Composition of Plant Oils



Calyxt HO Soy Business Model

High Oleic Soybean Value Chain has Three Revenue Opportunities

Seed Production

- Calyxt utilizes existing seed producers to produce high oleic soybeans

Grain Production

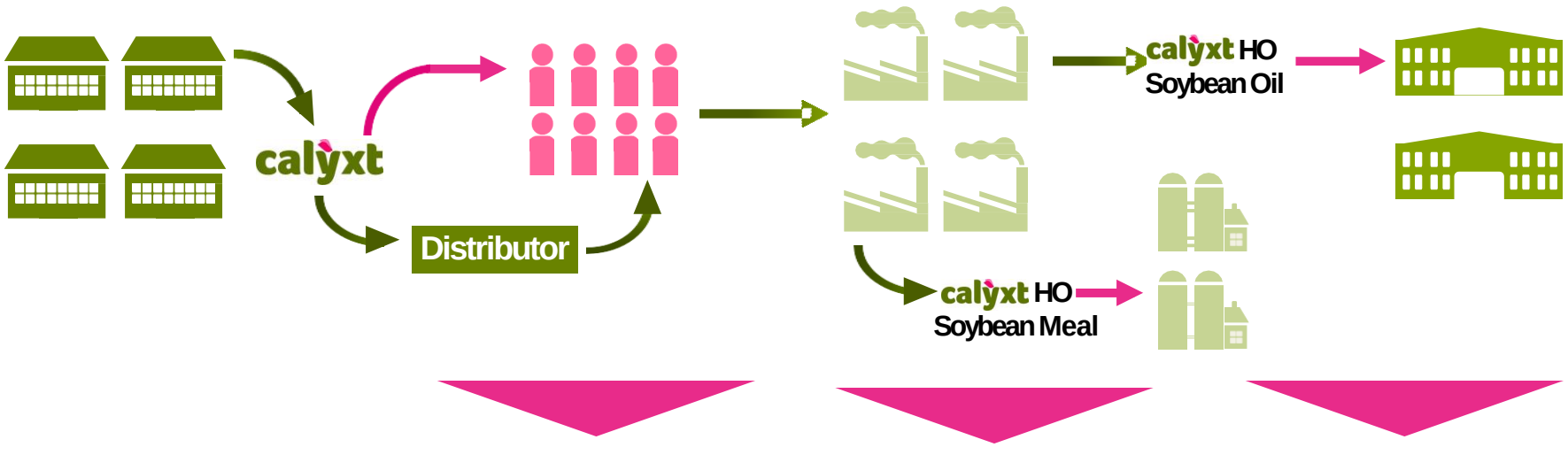
- Calyxt contracts farmers to grow high oleic soybeans under identity-preserved contracts

Processing

- Calyxt contracts crushers to process high oleic soybeans to meal and oil under toll processing agreement

Sale to Food Industry Customers

- Calyxt sells high oleic soybean oil

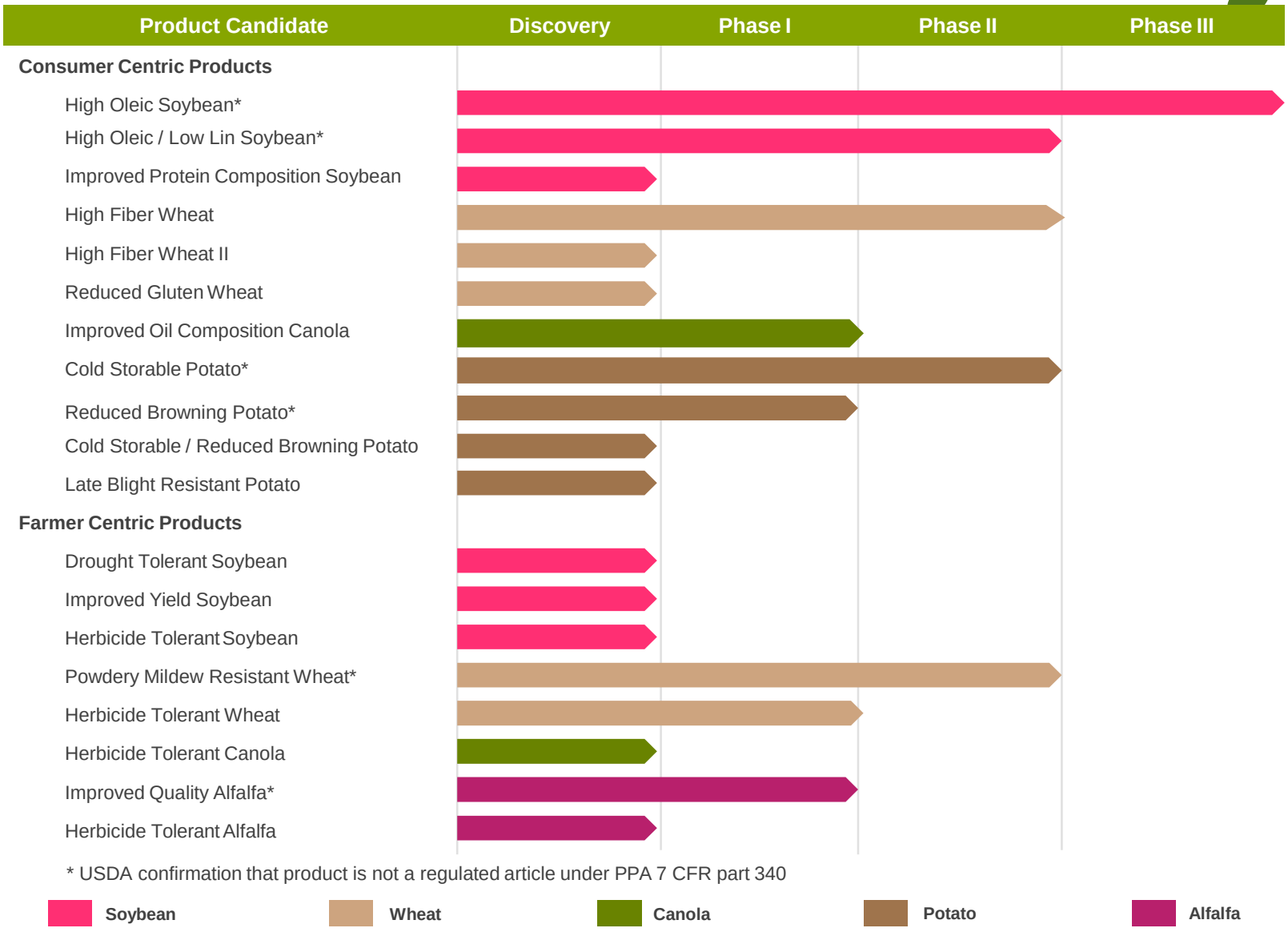


calyxt HO Soybean Seed Sold to Growers

calyxt HO Soybean Meal Sold as Protein for Animal Nutriton

calyxt HO Soybean Oil Sold as Premium Veg. Oil to Food Companies as a Specialty Ingredient

Rich Product Pipeline



High Fiber Wheat - White Wheat Flour with Up to 3 Times More Fiber

Status / Timing

- Currently in *Phase 2*
- 2018: Functionality testing of Calyxt Wheat Flour, *Phase 2*
- 2019: Development of supply chain (e.g., seed producers, grain producers, millers, food industry customers), *Phase 3*
- 2020-2021: Anticipated commercial launch

Potetial Features and Benefits for Consumers:

- "High in fiber" content claim[1]
- "May reduce risk of some types of cancer" labeling claim[2]
- "May reduce risk of coronary heart disease" labeling claim[3]

Calyxt's High Fiber Wheat Composition [5]

Whole Wheat Flour

Nutrition Facts

Serving Size 100g

Total Carbohydrate 73 g	**24%**
Dietary Fiber 12 g	49%
Sugars 0 g	

Whole Wheat Calyxt Flour

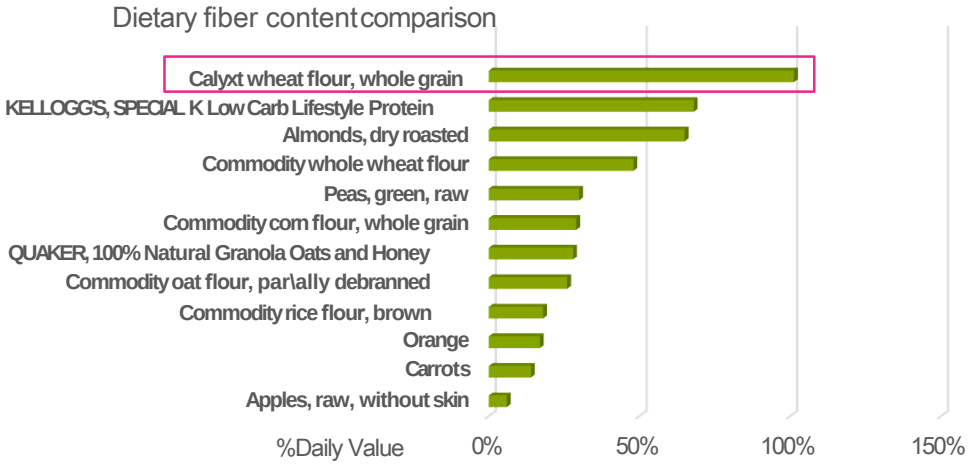
Nutrition Facts

Serving Size 100g

Total Carbohydrate 73 g	**24%**
Dietary Fiber 25 g	100%
Sugars 0 g	

A single serving of Calyxt high fiber flour may provide up to 100% of the recommended daily value

Calyxt High Fiber Wheat Comparison[4,5]



1.Code of Federal Regula.ons (2012). Title 21, Sec.on 101.54 - Nutrient content claims for "good source," "high," "more," and "high potency."
2.Code of Federal Regula.ons (2012). Title 21, Sec.on 101.76 - Health claims: fiber-containing grain products, fruits, and vegetables and cancer.
3.Code of Federal Regula.ons (2012). Title 21, Sec.on 101.77 - Health claims: fruits, vegetables, and grain products that contain fiber, par.cularly soluble fiber, and risk of coronary heart disease.
4.Calyxt internal calcula.on
5.hip://nutri.ondata.self.com/

Conclusions

- Calyxt is a consumer-centric food and agriculture company that is pioneering a paradigm shift to deliver healthier food and ingredients.
- Calyxt's proprietary TALEN® technology is a precise gene editing tool that has led to an innovative product pipeline.
- Our first product is a High Oleic Soybean and is expected to be launched later this year.
- High Fiber Wheat product is also in the pipeline and will deliver white wheat flour with up to 3 times more fiber.