

Trends in AgBiotech

4th International Conference on Agriculture and Horticulture
Beijing, July 13, 2015

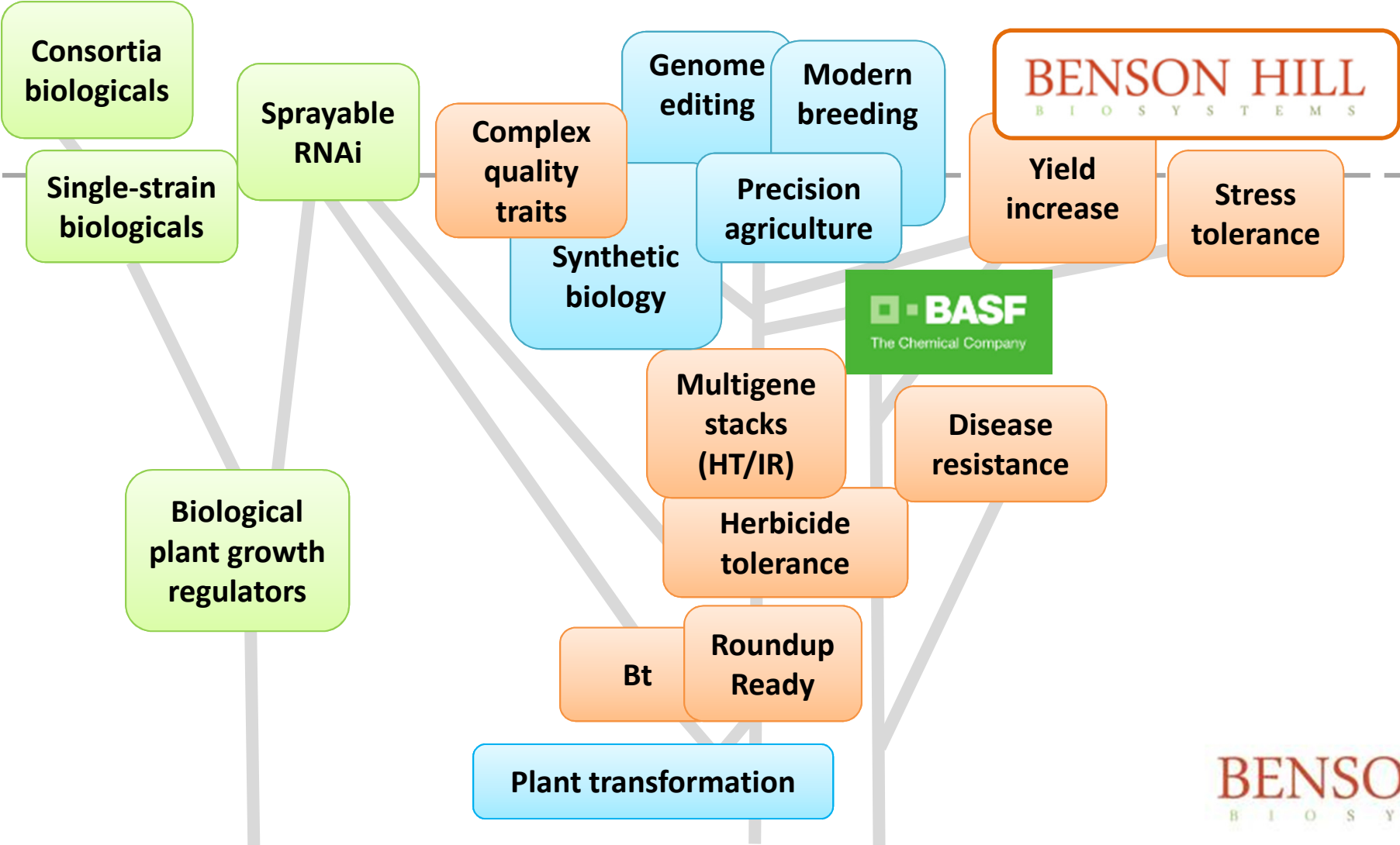
Andy Renz, Vice President Business Development

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Overview

- Scope
- 1st Generation ag biotech – Bt & HT
- The Challenge: feed the world
- 2nd Generation ag biotech – complex traits
 - Disease resistance
 - Complex quality traits
 - Abiotic stress tolerance and yield improvement
- Biologicals – rise from a niche product to a key market
- Breakthrough technologies
 - The sequencing revolution
 - Molecular breeding
 - Phenotyping and big data integration
 - Genome editing
- Future Trends
 - Precision Crops
 - Plant-microbiome interactions

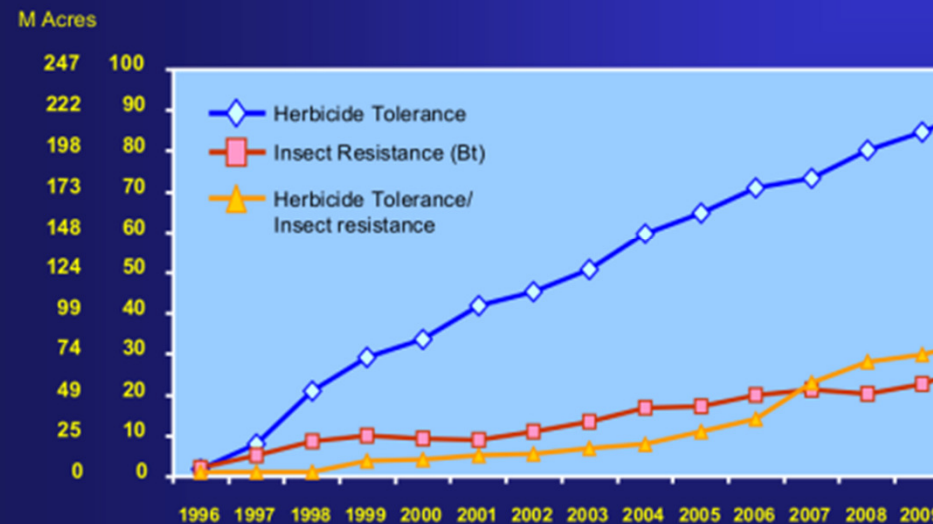
Scope – Ag Biotech in the Past and Today



1st Generation Ag Biotech – Bt and Herbicide Tolerance (HT)

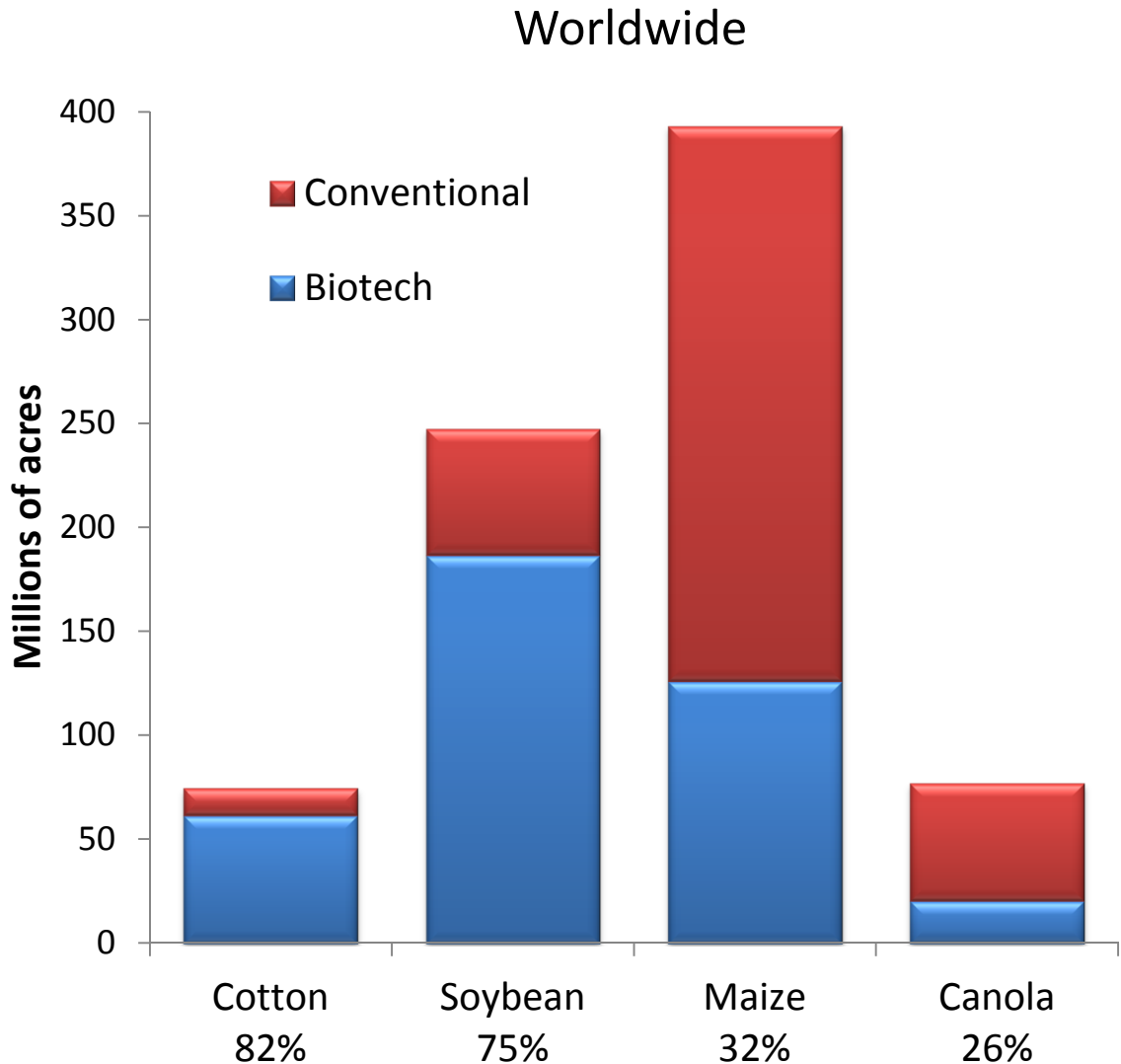
- 1994: Calgene's FlavrSavr™ tomato received FDA approval
- 1996-2013:
from 1.7 to 175 million hectares
GM crops world wide;
all Bt and HT
- Single-gene traits;
no or not much interference with crop
metabolism
- Today: Multi-gene stacks of Bt and HT

**Global Area of Biotech Crops, 1996 to 2011:
By Trait (Million Hectares, Million Acres)**



Source: Clive James, 2012

High Penetration Rate of GM Traits for Major Crops

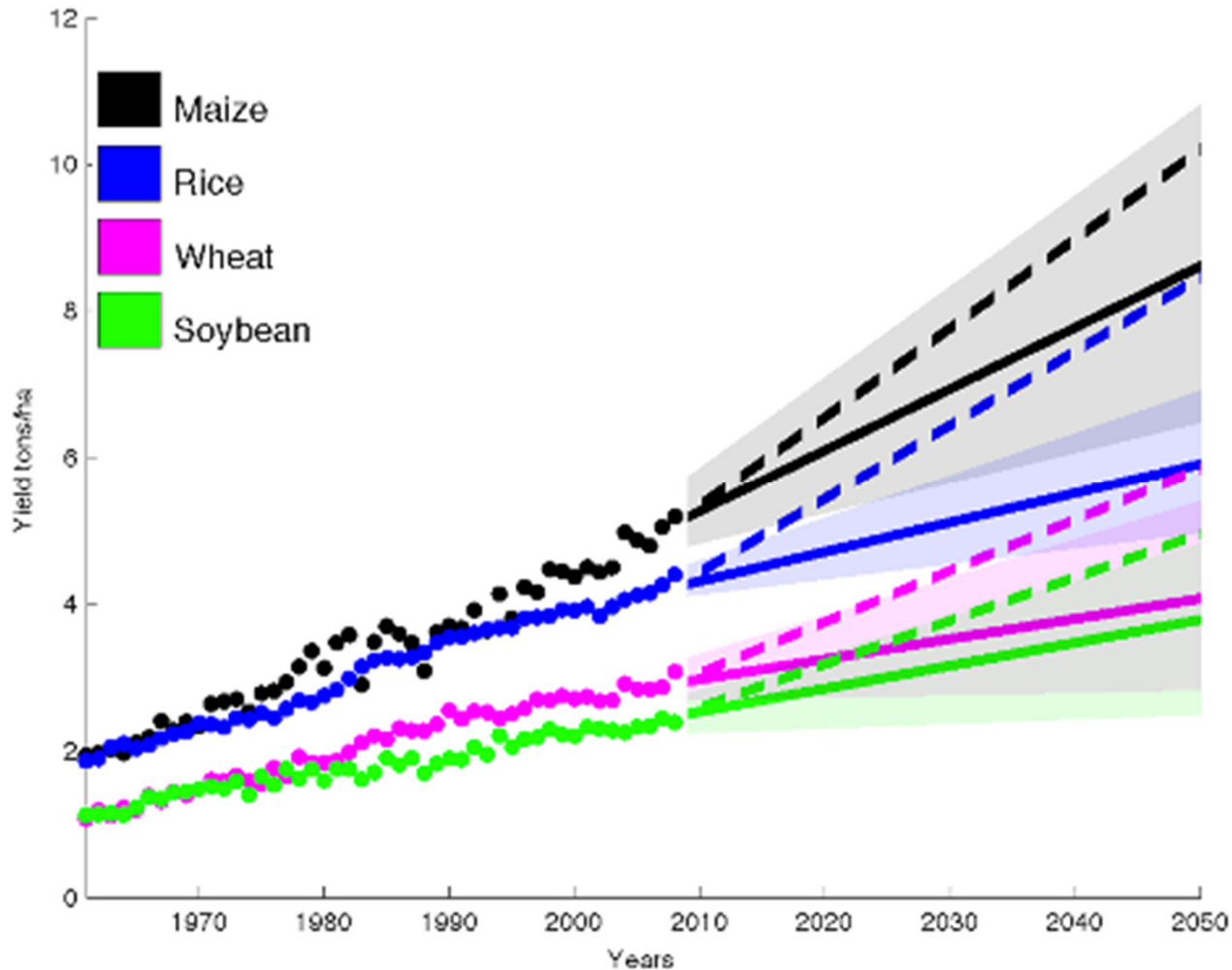


- Projected future biotech crops:
(millions of acres annually)
- Wheat (544)
 - Rice (406)
 - Sugarcane (63)
 - Potato (48)
 - Eucalyptus (47)
 - Tomato (12)

Note: Sugarbeet and alfalfa hold >90% of worldwide production, respectively, but each constitute <1% of worldwide production. Small acreages of papaya, squash, and poplar are also grown.

Source: Clive James, 2012

The Challenge and Innovation Driver: 100% Increase in Productivity Required by 2050



- Rapidly growing world population
- Growing middle class
- Higher meat consumption
- Biofuels production
- Limited arable land

Ray et al, 2013, PLoS ONE

Required yield increases are significantly higher than historical yield increases

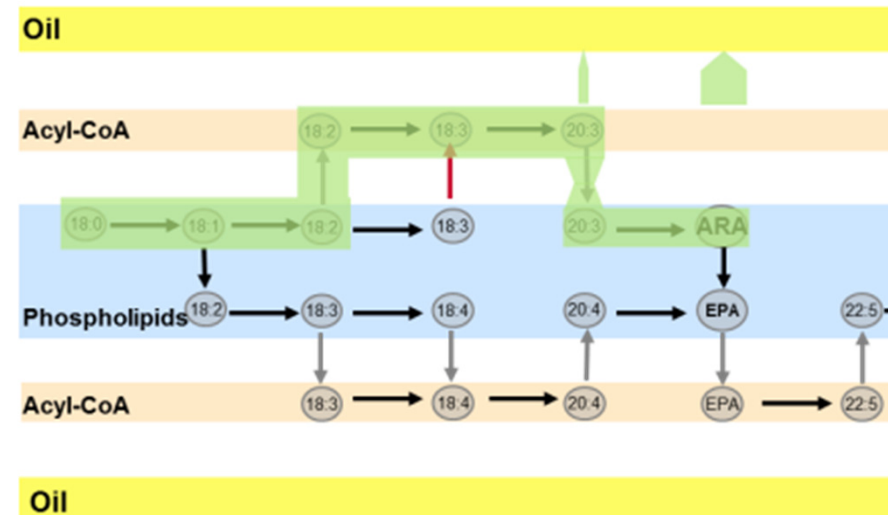
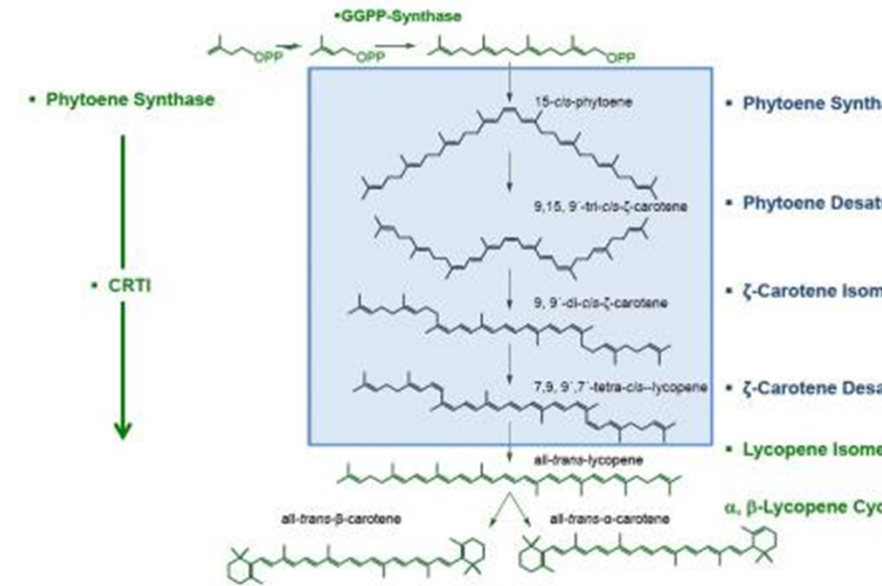
2nd Generation Ag Biotech – Disease Resistance

- Syngenta & Monsanto: GM wheat programs in late 90's
- BASF's Phytophthora resistant potato Fortuna™ approved, but finally shelved
 - 2 resistance genes from a wild potato variety introduced via GM-technology
 - Strong resistance & good agronomic performance
- So far most fungal disease resistance programs are non-GM through breeding
- In development:
 - GM soybean resistant against Asian Soybean Rust
 - Disease resistant corn plants

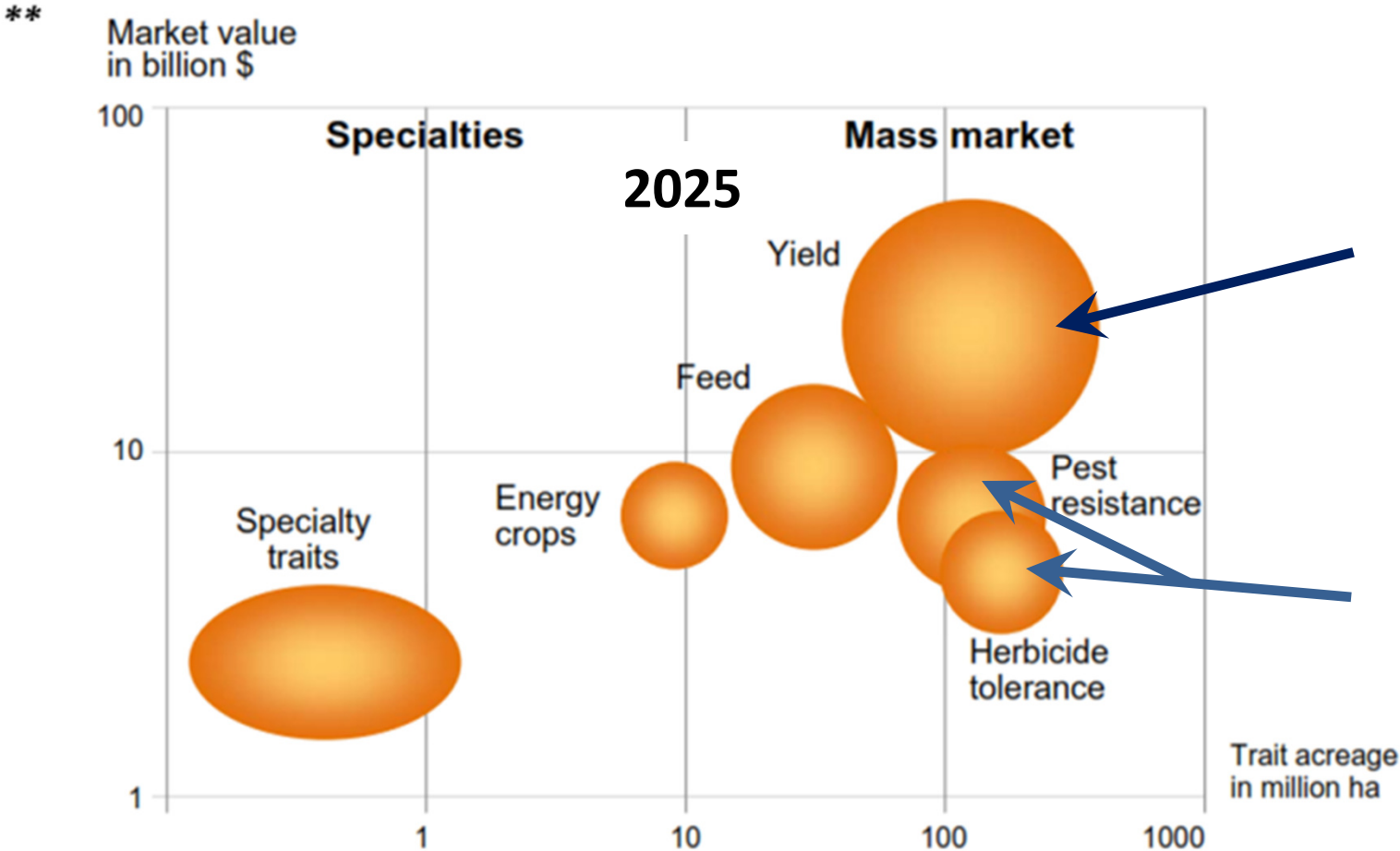


2nd Generation Ag Biotech – Complex Quality Traits

- Golden rice (IRRI)
 - Humanitarian project: β -carotene rice
 - Long R&D timelines
- Healthy fatty acids from canola (BASF)
 - Production of LC-PUFAs in canola through metabolic engineering of an entire pathway (8 genes!)
- Much more complicated than anticipated
- Complex interactions with crop metabolism
- Metabolic engineering & synthetic biology enabled
- Note: most other GM quality traits were discontinued



2nd Generation Ag Biotech – Abiotic Stress Tolerance & Yield Increase



2nd generation traits

1st generation traits, currently \$12B market

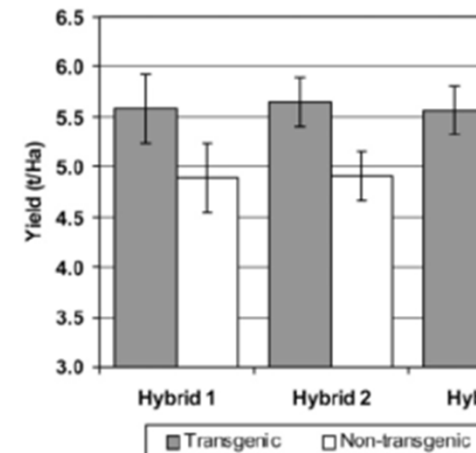
** from Monsanto/BASF collaboration presentation

Yield traits represent the largest opportunity in ag biotech

2nd Generation Ag Biotech – Abiotic Stress Tolerance & Yield Increase

- Excellent results and products from molecular breeding
 - AQUAmax™ corn from Pioneer
 - Artesian™ corn from Syngenta
 - Drought tolerant rice from IRRI
- Opportunity and Challenge for GM approaches:
 - Monsanto/BASF: largest partnership in the history of Ag Biotech R&D: \$2.5 billion(!)
 - HTP screens in model and crop plants
 - Field testing in crops (commercial germplasm)
 - First products: Droughtgard™ corn launched in 2013 (Cspb)
 - Benson Hill Biosystems:
 - Focus on yield improvement through improved photosynthesis

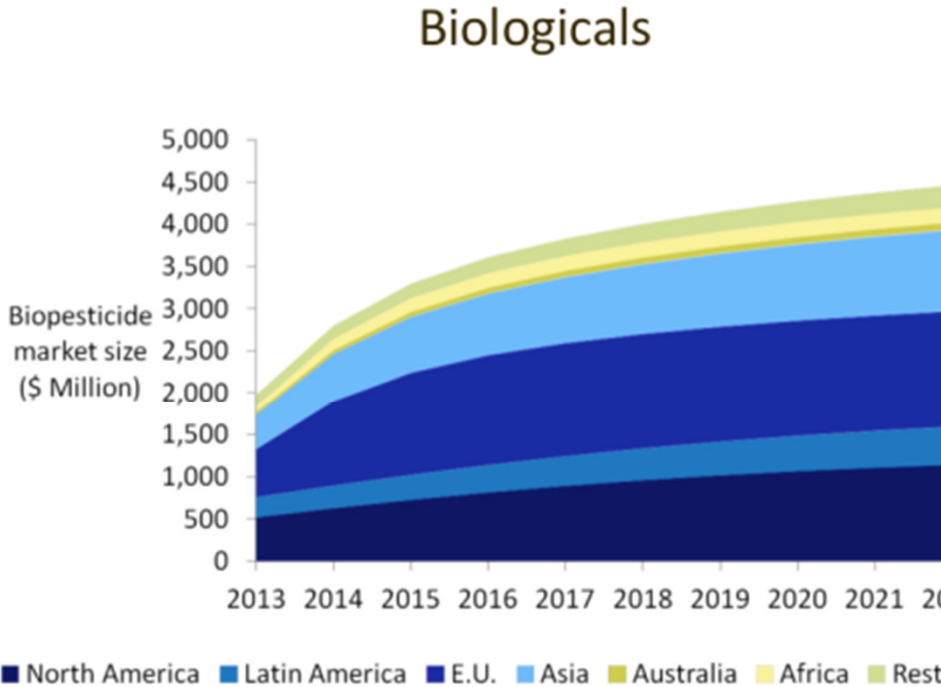
Bacterial RNA chaperone CspB confers drought tolerance in



Castiglioni et al. (2008) Plant Phys. 147:

Biologicals – From a Niche Product to a Key Market

- Enormous growth of market volume and capital invested
 - 2012: \$1.6 billion
 - 2016: \$3.2 billion
- Major investments & acquisitions in past years:
 - Bayer: Athenix & Agraquest
 - Syngenta: Pasteuria
 - BASF: Becker Underwood
 - Monsanto – Novozymes (BioAg Alliance)



Source: Lux Research

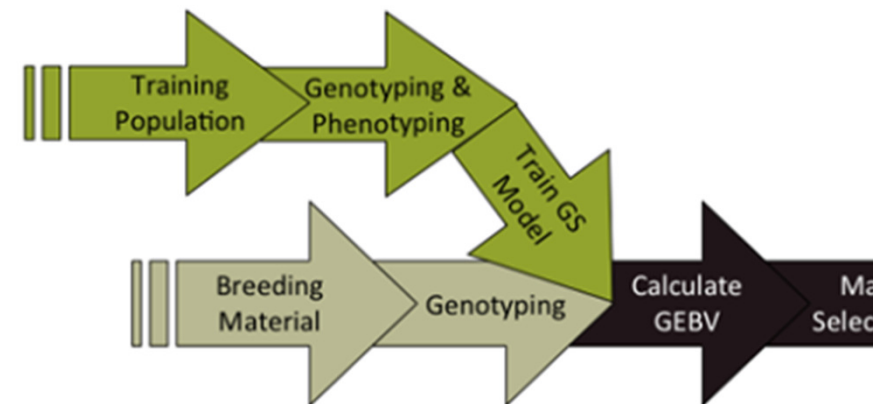
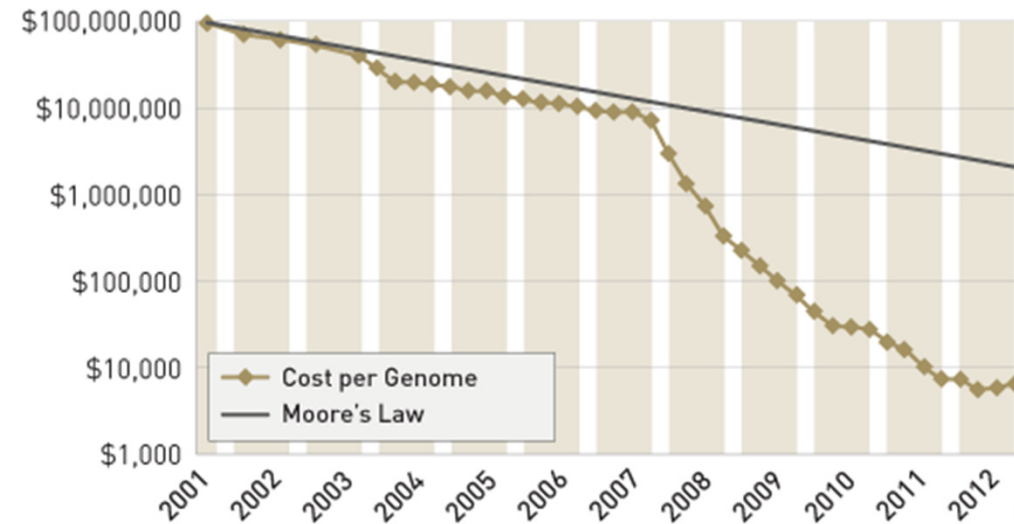
- Independent player:



- Sprayable RNAi
 - Monsanto’s BioDirect™ Technology

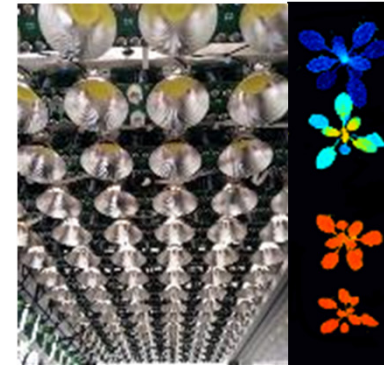
Breakthrough Technologies – Based on the Sequencing Revolution

- Sequencing costs per genome are 10,000X lower compared to 15 years ago
- Enabled Molecular Breeding:
 - Genotyping by Sequencing (GBS)
 - Transcriptomics (RNAseq)
 - Genomic Selection
 - Predict phenotypes in breeding and hybrid production
 - Much more advanced in cattle than in crops



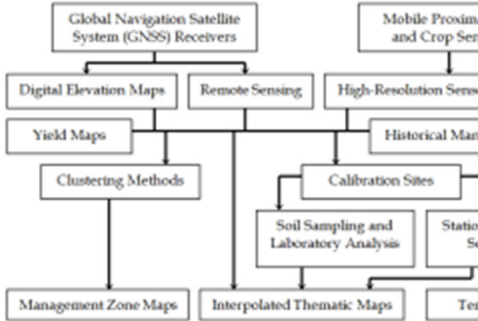
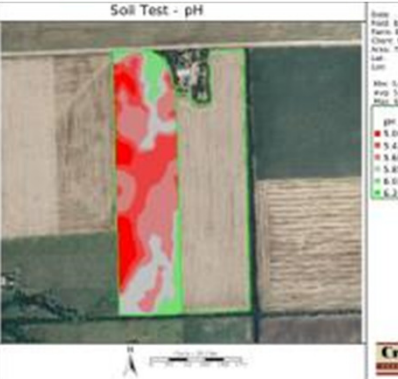
Breakthrough Technologies – Phenotyping: from Indoors to the Field

- State-of-the-art: automatized phenotyping
 - CropDesign/BASF
 - Monsanto, Syngenta, Pioneer
 - Keygene/LemnaTech (Phenolab)
 - Donald Danforth Plant Science Center
 - Photosynthetic Phenometrics (Michigan State University)
- Field-based Phenotyping
 - CSIRO's Phenomobile
 - Huazhong Agricultural University
 - University of Nebraska Lincoln



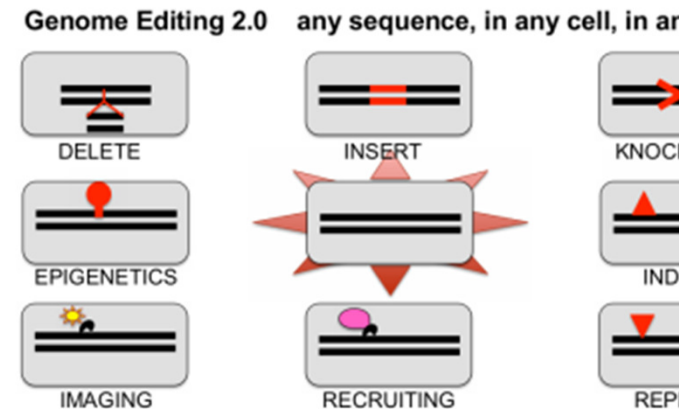
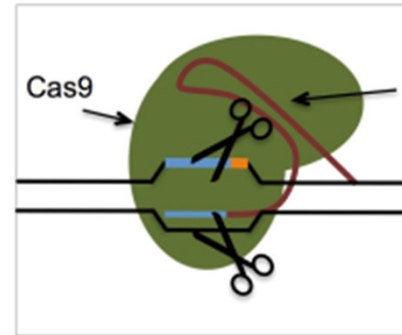
Breakthrough Technologies – Aerial Imaging and Big Data Integration

- Aerial Imaging
 - Drones, fixed-wing planes and multi-copters
 - Multiple sensors: RGB, LiDAR, Thermal IR, Hyperspectral Imaging
- Environmental Data
 - Weather data
 - Soil data
- Big Data Integration
 - Climate Corp/Monsanto
 - Many others



Breakthrough Technologies – Genome Editing

- ZFNs: Sangamo & Dow Agrosiences
- Meganucleases: Precision Biosciences, Collectis
- TALENs: 2Blades Foundation, Calyxt
- CRISPR/Cas:
 - Technology of the year 2014: CRISPR Craze
 - DNA encoded, RNA mediated
 - Versatile
 - Precise
 - Proof-of-concept in plants
 - Complicated patent portfolio;
Calyxt holds certain rights in plants



Future Trends – From Isolated Silos to Integrated Approaches



**1st Generation
single-gene GM
Traits (HT, IR)**

**2nd Generation
GM traits (FR, Yield)**

**Multi-genic
GM traits (Yield)**

**Advanced
mutagenesis**

**Genome
editing**

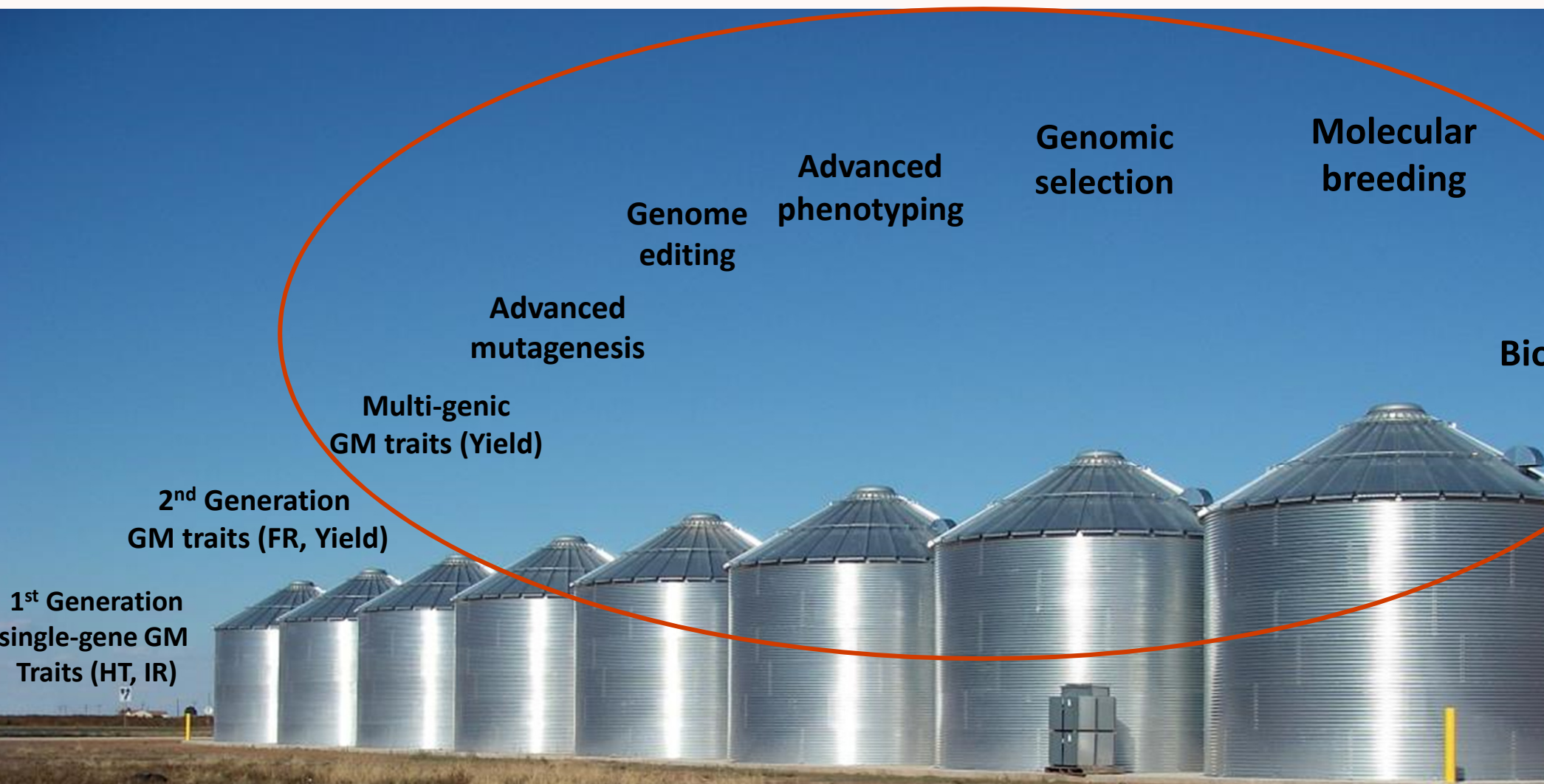
**Advanced
phenotyping**

**Genomic
selection**

**Molecular
breeding**

Bio

Future Trends – From Isolated Silos to Integrated Approaches

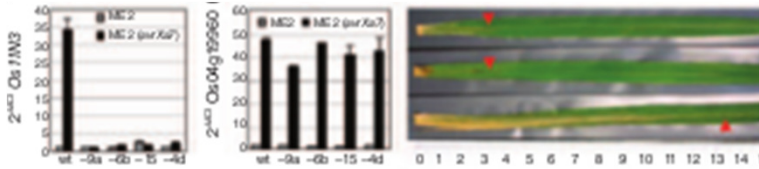


In the future, more integrated approaches will increase the innovation potential

Future Trends

- Integrated discovery platforms
 - Combining molecular breeding, multi-gene traits & genome editing
- Precision crops
 - Targeted integration for up- and down-regulation of genes
 - GM and non-GM products based on genome editing

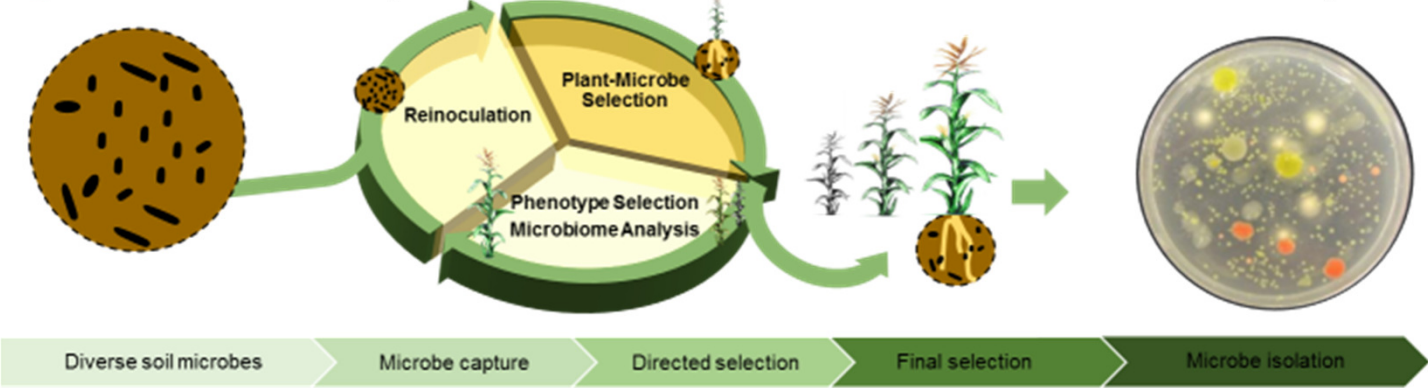
Proof-of-concept for functional traits through genome editing



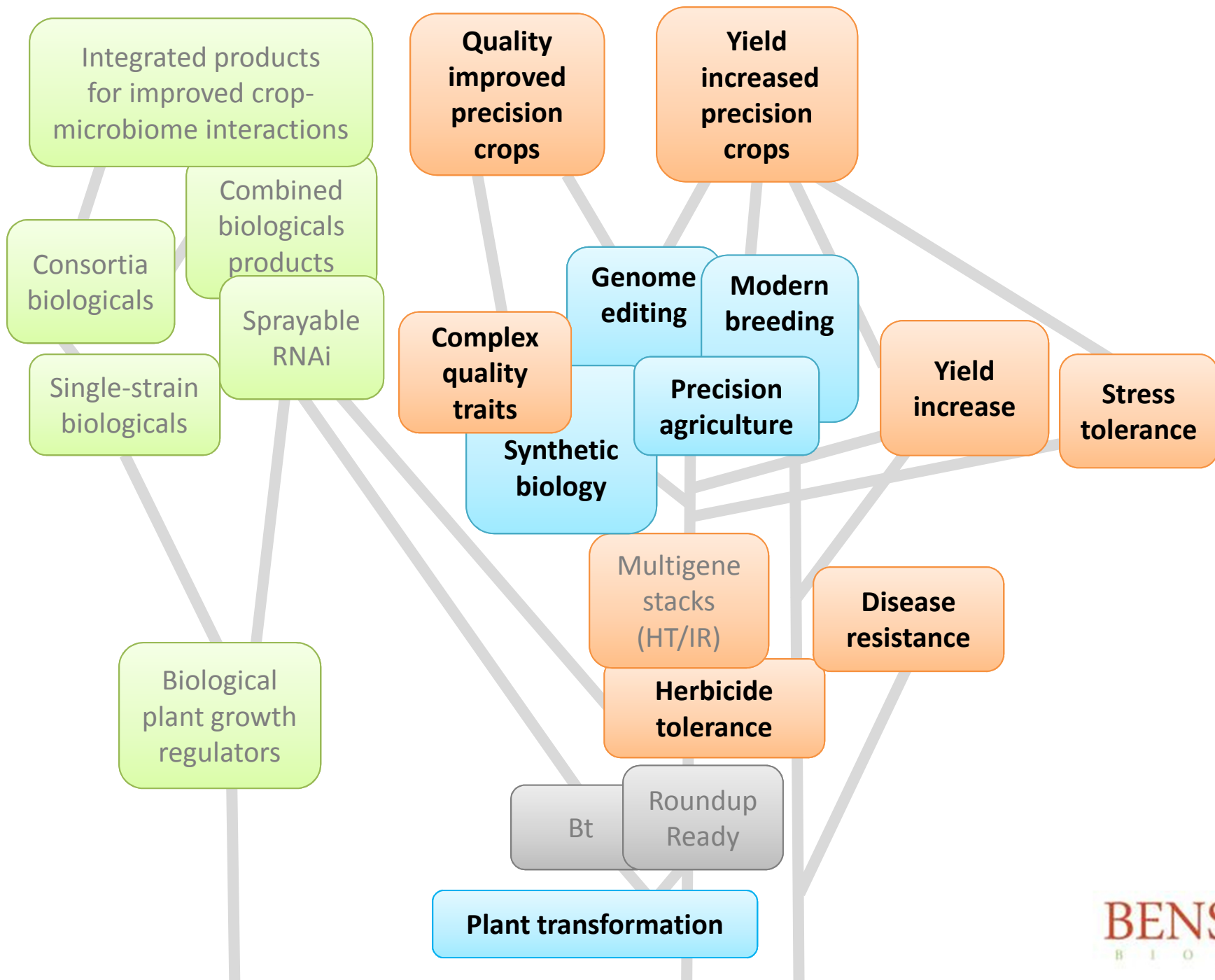
Li et al (2013) Nature Biotechnology 30: 390

Crop-microbiome Interactions

BioConsortia's proprietary Advanced Microbial Selection system



Formulations
biologicals w/
agrochemicals



Thank You

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