Genetic Engineering Novel Crop Plants: Unlimited Horizons

Bob Goldberg
9/19/08

"The Bravest are surely those who have the clearest vision of what is before them, glory and danger alike, and yet notwithstanding go out to meet it"

Thucydides 400 BC

Today's Headlines

The New York Times

Los Angeles Times

A Global Need for Grain That Farms Can't Fill

Published: March 9, 2008

Economist.com

High Rice Cost Creating Fears of Asia Unrest

By KEITH BRADSHER
Published: March 29, 2008

U.S.News & WORLD REPORT

CNN.com

THE FOOD CHAIN
A Drought in Australia, a Global Shortage of Rice

Across Globe, Empty Bellies Bring Rising Anger

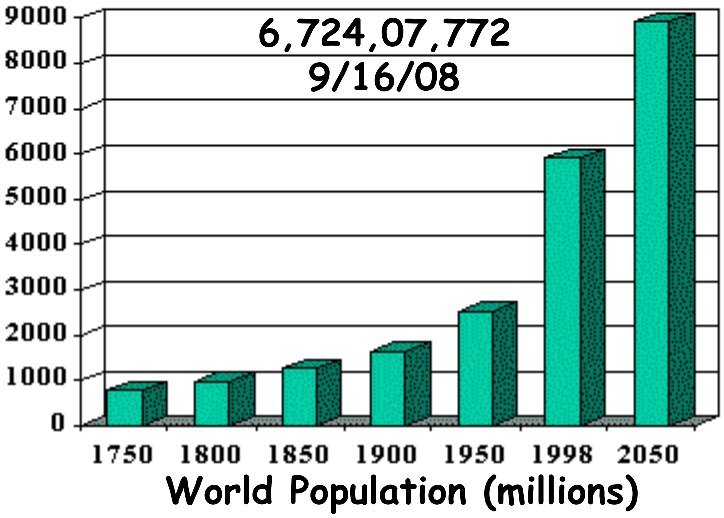
Newsweek

updated 10:42 p.m. EDT, Mon April 14, 2008

Riots, instability spread as food prices skyrocket

The Washington Post

As Discussed Here.....We Face Challenges In Agriculture Even Greater Than Those in Today's Headlines



OVER THE NEXT 50 YEARS WE WILL NEED TO PRODUCE MORE FOOD THAN IN THE WHOLE OF HUMAN HISTORY

AND DO IT WITH FEWER INPUTS ON LESS ARABLE LAND!!!!

CROP YIELDS NEED TO BE INCREASED SIGNIFICANTLY!!

How Will Crop Yields Be Increased in the Future?

As We Always Have…….By Using the Best Cutting-Edge Science and Technology…..Such Has Been Described at this Meeting!!

(One thing we can be sure of-we can't predict what new technology will be the driver 50-100 years out)

In the Beginning....

Seed

As Outlined Here…..It is Critical to Use a Variety of Approaches to Identify Genes and Processes That Will Help Increase Crop Yields and Food Production Significantly in the 21st Century

Yield (Developmental Traits)

- Seed Number
- Seed Size
- Growth Rate
- Organ Size (More Seeds)
- Plant Architecture
- Flowering Time
- Senescence
- Maturity
- Stature

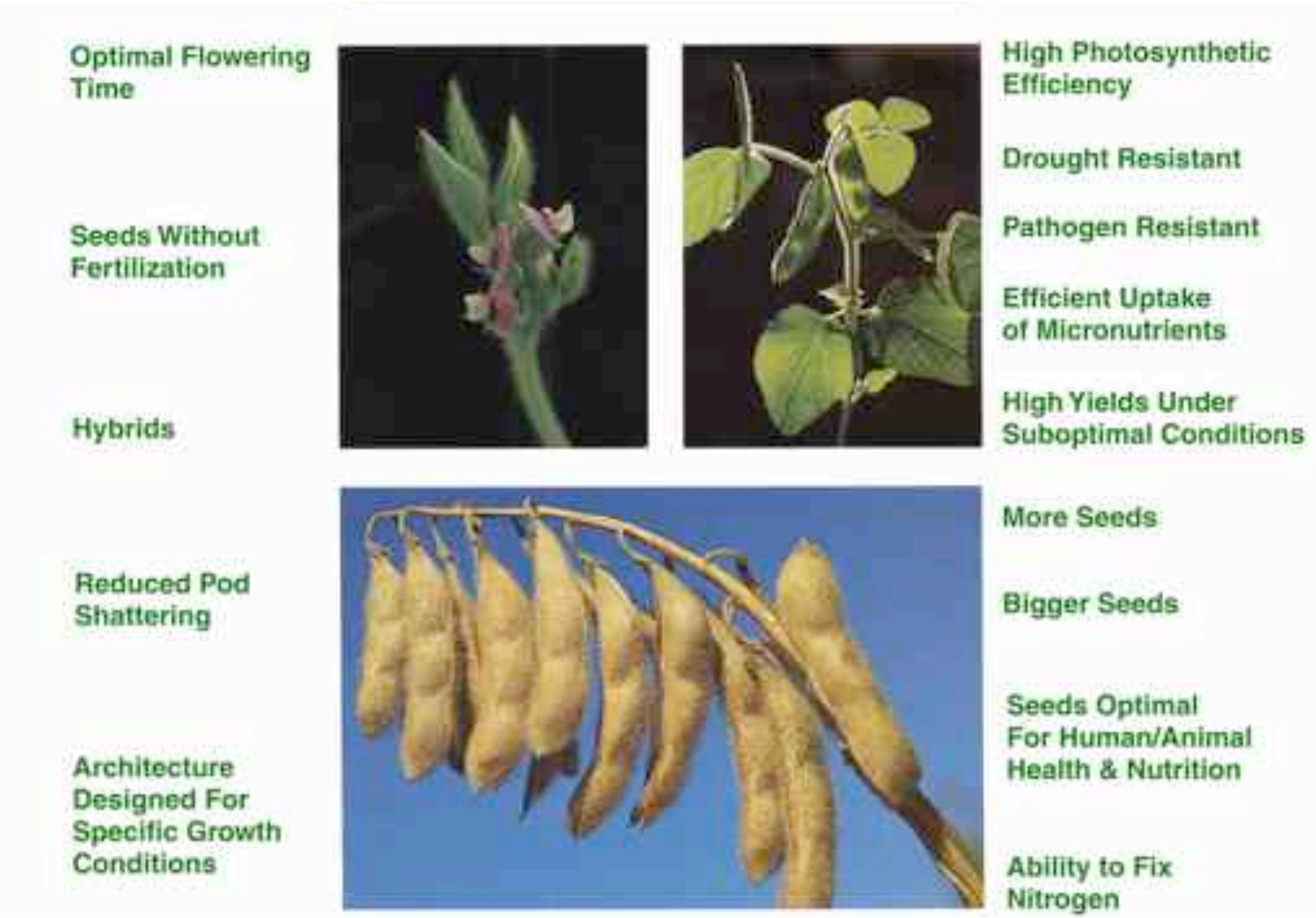
Yield (Stress Traits)

- Nutrient Uptake
- Drought Resistance
- Heat Resistance
- Cold Tolerance
- Salt Tolerance
- Shade Tolerance
- Disease Resistance

From "Low-Tech" to High-Tech

From Lab to Improved Seeds For Farmers

…….And Use Breeding and Genetic Engineering to Introduce These "Yield" Genes Into Existing Crops



This WILL Happen……Sooner Than Later!

Big Changes in the US Over The Past 100 Years

"We've Come a Long Way Baby"

	1900	2008
Life Expectancy	48 (women)	79 (women)
Average Family Income (2008 Dollars)	$8,000	$50,000
Gasoline Use Per Capita	34 gallons	1,100 gallons
Flush Toilets Per Housing Unit	10%	99%
High School Grads	13%	90%
Farm Workers	55%	1.5%

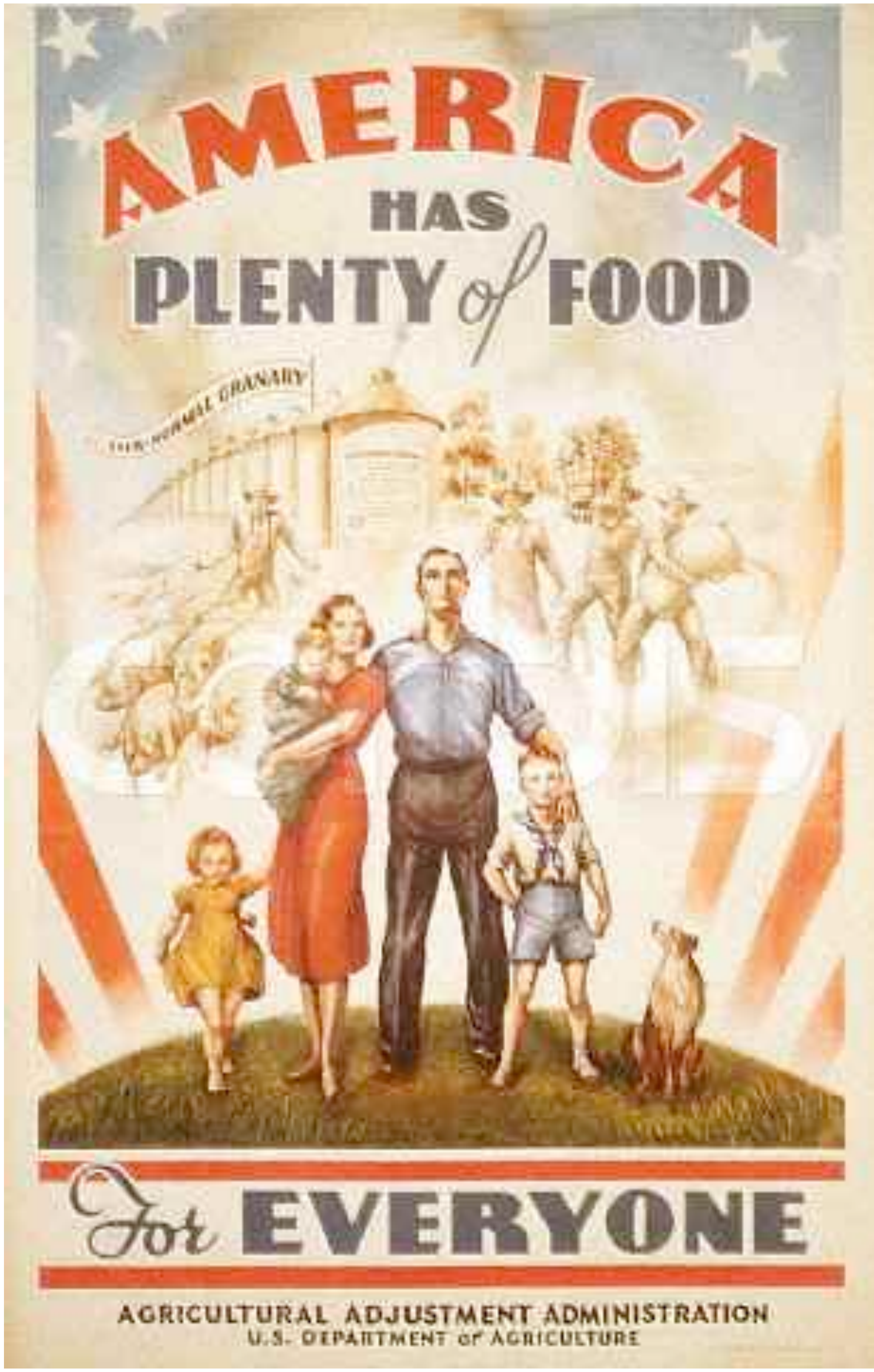
CROP YIELD INCREASES HAVE "ROCKETED UPWARDS" OVER THE LAST 100 YEARS AND CONTRIBUTED TO A LONGER AND "BETTER" LIFE

% Farm Workers	% Income on Food	Year	Crop Yield	Life Span
55%	50% →	1900	100	← 48 Years
		1920	115	
		1940	145	
		1950	200	
1.5%	9% →	2008	300	← 79 Years

1930: 30 bushels/acre
1930: 1 farmer fed 10 people

2008: 150 bushels/acre
2008: 1 farmer feeds 200 people

Conclusion: Crop yield increased ~ 300% over the past 100 years and lead to a similar reduction in food costs!!!!!



How Was This Accomplished Over the Past 100 Years?

What Role Did Science & Technology Play?

What About in the Future When There are 350 Million People in the USA and 9 Billion in the World?

WHAT TECHNOLOGIES CAUSED AN INCREASE IN CROP YIELDS OVER THE PAST 100 YEARS?

- PLANT BREEDING (New Hybrids-Green Revolution)
- IRRIGATION
- FERTILIZERS
- PESTICIDES & HERBICIDES
- MECHANIZATION (e.g., Tractor)
- GLOBAL POSITIONING AND SATELLITE IMAGING
- GENOMICS & GENETIC ENGINEERING (New Traits)

These technologies have resulted in a 300% increase in US crop productivity during the 20th-21st century! Need to sustain this yield increase by applying the best technology and agricultural practices!

Genetics Has Also Changed Dramatically Over the Past 100 Years!!

1900: Rediscovery of Mendel's Work

DeVries, Correns and Tschermak independently rediscover Mendel's work.

Three botanists - Hugo DeVries, Carl Correns and Erich von Tschermak - independently rediscovered Mendel's work in the same year, a generation after Mendel published his papers. They helped expand awareness of the Mendelian laws of inheritance in the scientific world.

The three Europeans, unknown to each other, were working on different plant hybrids when they each worked out the laws of inheritance. When they reviewed the literature before publishing their own results, they were startled to find Mendel's old papers spelling out those laws in detail. Each man announced Mendel's discoveries and his own work as confirmation of them.

1909: The Word Gene Coined

Danish botanist Wilhelm Johannsen coined the word gene to describe the Mendelian units of heredity.

He also made the distinction between the outward appearance of an individual (phenotype) and its genetic traits (genotype).

Four years earlier, William Bateson, an early geneticist and a proponent of Mendel's ideas, had used the word genetics in a letter; he felt the need for a new term to describe the study of heredity and inherited variations. But the term didn't start spreading until Wilhelm Johannsen suggested that the Mendelian factors of inheritance be called genes.

The proposed word traced from the Greek word genos, meaning "birth". The word spawned others, like genome.

1911: Fruit Flies Illuminate the Chromosome Theory

Using fruit flies as a model organism, Thomas Hunt Morgan and his group at Columbia University showed that genes, strung on chromosomes, are the units of heredity.

Morgan and his students made many important contributions to genetics. His students, who included such important geneticists as Alfred Sturtevant, Hermann Muller and Calvin Bridges, studied the fruit fly *Drosophila melanogaster*. They showed that chromosomes carry genes, discovered genetic linkage - the fact that genes are arrayed on linear chromosomes - and described chromosome recombination.

In 1933, Morgan received the Nobel Prize in Physiology or Medicine for helping establish the chromosome theory of inheritance.

Early Fly drawing

Portrait of Morgan at Work

Photo of Morgan's fly room at Columbia University

2000: *Drosophila* and *Arabidopsis* genomes sequenced

Drosophila melanogaster (fruit fly)has been a primary tool for geneticists since the early part of the twentieth century. The sequencing of its genome is the result of a collaborative effort between the *Drosophila* Genome Project Group, led by Gerald Fink at the University of California, Berkeley and researchers from Celera Genomics Corporation led by Craig Venter. The *Drosophila* genome is estimated to have approximately 13,600 genes as compared to 20,000—25,000 genes in humans. The popularity of *Drosophila* as an experimental organism ensures that its genome sequence will be a valuable resource for research in genetics and medicine. Many genes of *Drosophila* have been conserved through evolution and have human counterparts. This means that scientists can perform experiments using flies and apply their findings to human biology.

Arabidopsis thaliana is the first plant to have its genome sequenced. This plant from the mustard family has become the plant biologists' equivalent of the laboratory mouse. Its genome was completed by the collective efforts of an international group of researchers called the *Arabidopsis* Genome Initiative. The *Arabidopsis* genome has an estimated 25,000 genes—apparently even more than humans. Although not a crop plant, *Arabidopsis* was chosen as a model organism because its genome is small and it has relatively little of the noncoding, so-called junk, DNA. It does, however, share very similar biochemistry to crop plants such as rice or barely. The study of its sequence is expected to have widespread applications for agriculture and medicine.

2004: Refined Analysis of Complete Human Genome Sequence

The International Human Gene Sequencing Consortium led in the United States by the National Human Genome Research Institute and the Department of Energy published a description of the finished human gene sequence. The analysis reduced the estimated number of genes (which as recently as the mid-1990's had been ~100,000) from 35,000 to only 20,000-25,000. The fact that the human genome has far fewer genes than was originally thought suggests that humans "get more" out of their genetic information than do other animals. For example, the average human gene is able to produce three different gene products.

The finished sequence contains 2.85 billion nucleotides interrupted by only 341 gaps. It covers 99 percent of the genome with an accuracy of 1 error per 100,000 bases. Researchers confirmed the existence of 19,599 protein-coding genes and identified 2,188 other DNA segments that are thought to be protein-coding genes. Although the genome sequence is described as "finished," it isn't perfect. The small gaps that remain cannot be sequenced by the industrial-scale methods used by the Human Genome Project. Filling in these gaps will have to await a series of small targeted efforts by researchers using other techniques and possibly new technologies. The finished genome sequence can be freely accessed through public databases and may be used by researchers without restrictions.

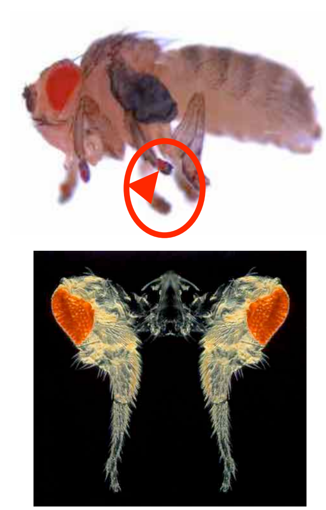
Modern Genetic Engineering Has Come a Long Way Since Its Origins in 1973!

Gene Transplants Seen Helping Farmers and Doctors;

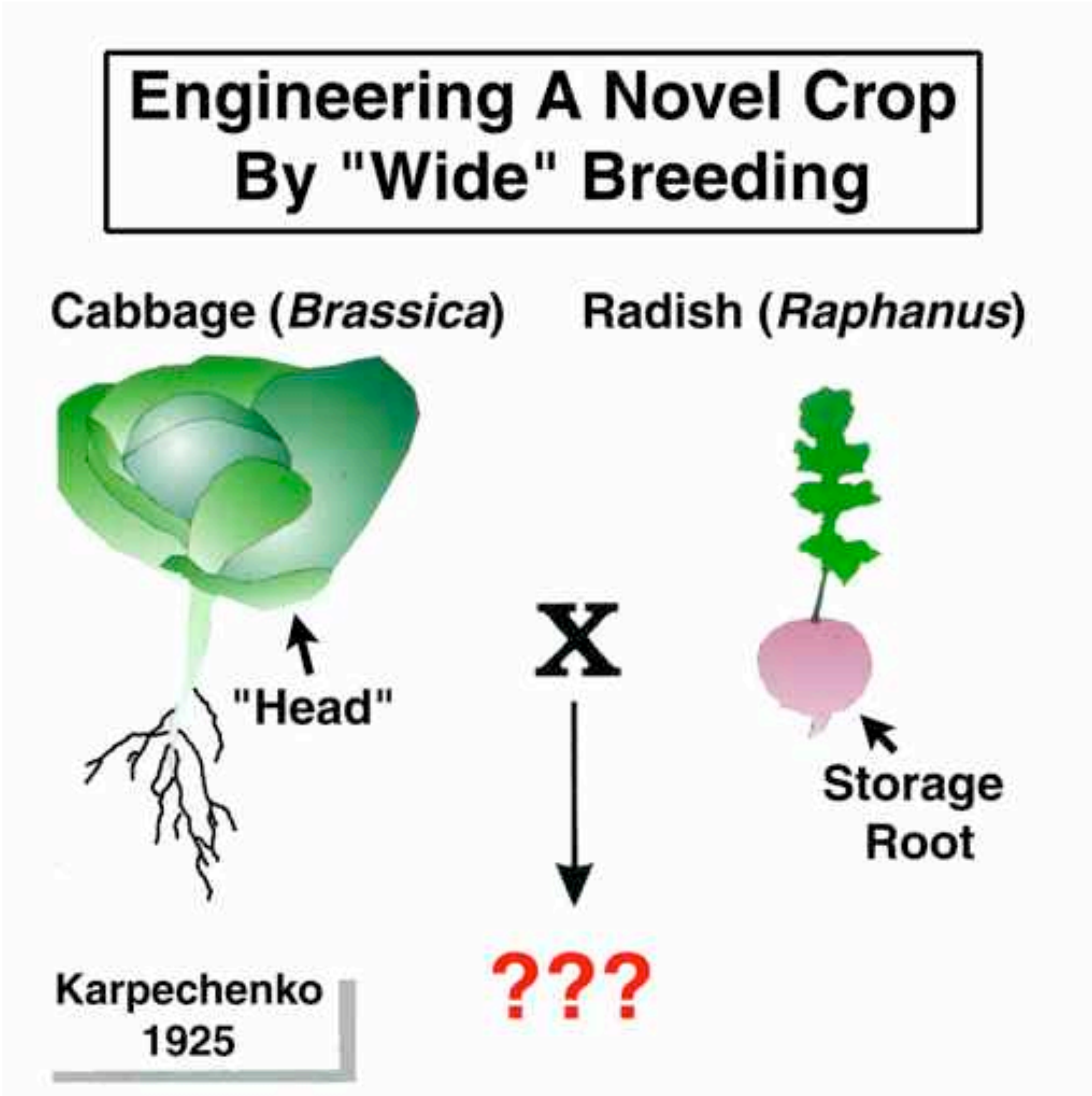
By VICTOR K. McELHENY
May 20, 1974, Monday
Page 61, 1335 words

NY Times-1974

Biochemists working in California have developed a practical method of transplanting genes, the chemical units of heredity, from cells as complex as those of animals into the extremely simple, fast-multiplying cells known as bacteria. [END OF FIRST PARAGRAPH]

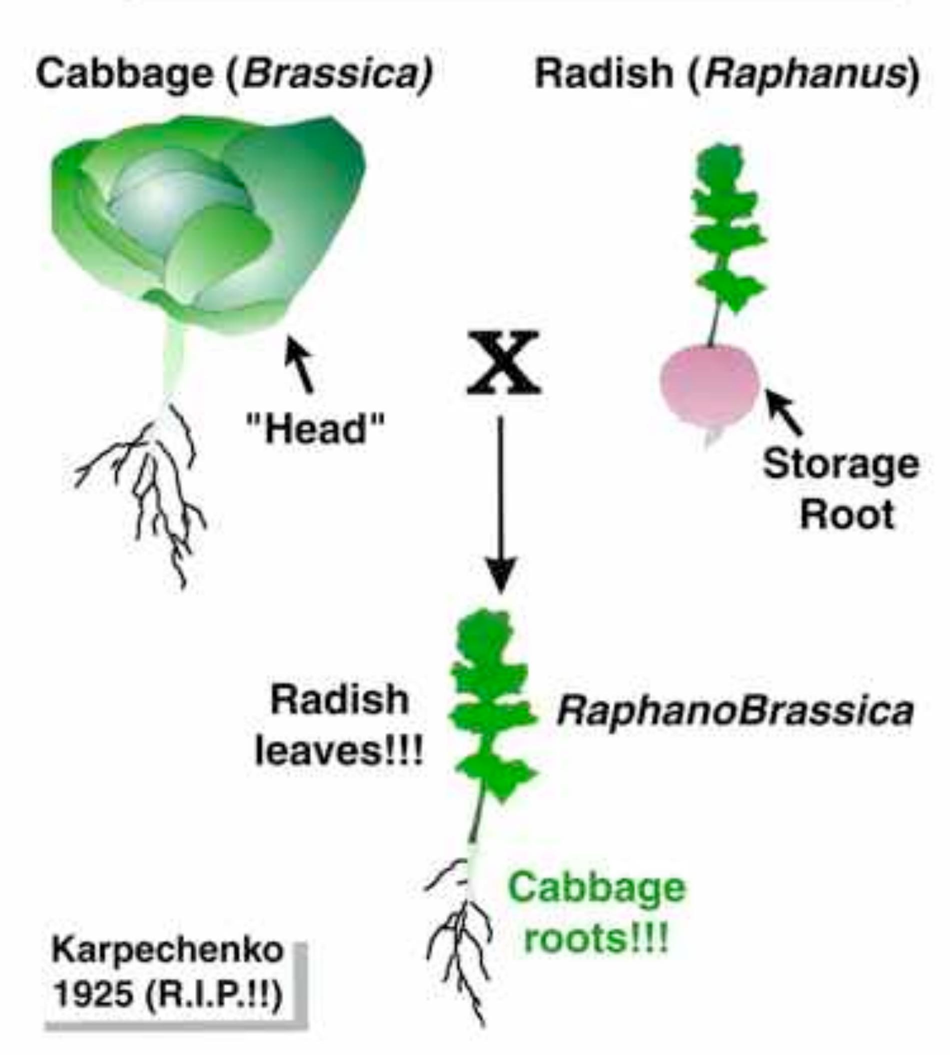


So Has Genetic Engineering in Plants…..



Karpechenko, G.D., 1927. The production of polyploid gametes in hybrids. Hereditas 9, 349–368.

With Unpredictable Results in the Beginning…



Real Soviet-Style Biology!!

Modern Plant Genetic Engineering is Less Than 30 Years Old!

The New York Times
nytimes.com

June 30, 1981

Protein Gene Is Transplanted From Bean to Sunflower

UPI

1981

The New York Times
nytimes.com

August 29, 1986

GENE-ALTERED PLANT TO GET TEST

AP

The crop will consist of only 20 plants, but experts say the tiny tobacco stand may lead to an inexpensive genetic way to fight costly plant-devastating insects.

The Rohm & Haas Company of Philadelphia, one of the world's largest producers of chemicals, announced Wednesday that the United States Department of Agriculture had approved the world's first field test of genetically altered caterpillar-resistant plants. The Agriculture Department confirmed that the approval had been granted.

Two other chemical companies, Ciba-Geigy and Agracetus, have been conducting similar tests with genetically altered plants resistant to weeds.

1986

The New York Times
nytimes.com

September 3, 1987

COMPANY NEWS; Insect-Resistant Plant Reported

REUTERS

LEAD: A Belgian company said it had made an important scientific breakthrough by altering plants genetically so they became poisonous to insects. Plant Genetic Systems of Ghent said its techeique could result in a big reduction in the spraying of farm crops with insecticides.

A Belgian company said it had made an important scientific breakthrough by altering plants genetically so they became poisonous to insects. Plant Genetic Systems of Ghent said its technique could result in a big reduction in the spraying of farm crops with insecticides.

P.G.S. said field trials of tobacco plants alterd with the gene of a natural, nontoxic insecticide showed that successive generations of the plants produced enough of the insecticide in their leaves to kill caterpillars.

1987

In the Beginning……

As Pointed Out at This Meeting…Plants Have Been Engineered For Large Numbers of Traits in Laboratories Around the World

Tens of Thousands of GE Experiments!!

Genetically Engineered Traits

Improving Pest and Weed Management

- Herbicide tolerance
- Virus resistance
- Insect resistance
- Bacterial resistance
- Fungal resistance

Chemical Free Crops

Improving Agronomic Properties

- Altering cold sensitivity
- Improving water stress tolerance
- Improving salt tolerance
- Improving nutrient uptake
- Drought Resistance*

Crops in Desert & Drought

Improving PostHarvest Qualities

- Delay of fruit ripening
- Delay of flower senescence/timing
- High-solids tomatoes
- High-starch potatoes
- Sweeter vegetables

Longer Lasting Crops

Improving Plant Breeding

- Male sterility; production of hybrid seeds

Improving Nutritional Quality

- High-methionine and high-lysine seeds
- Decaffeinated Coffee*
- Vitamin-enriched grains
- Allergen-free seeds/grains*

Healthier Crops

Molecular Farming

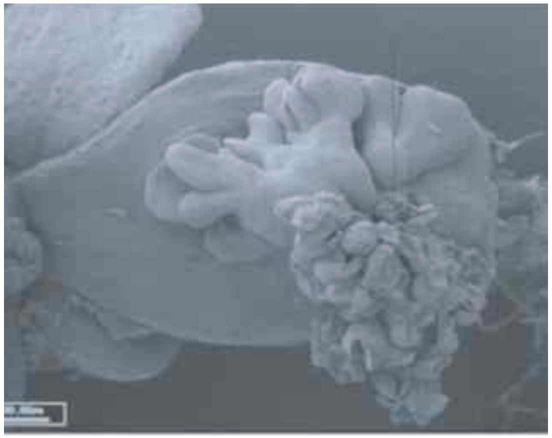
- Oils
- Starch
- Plastic
- Enzymes, Pharmaceuticals
- Ethanol/Transportation Fuel*

Crops as Factories & *Vaccines*

Detoxifying Contaminated Soils

Crops to Clean Environment

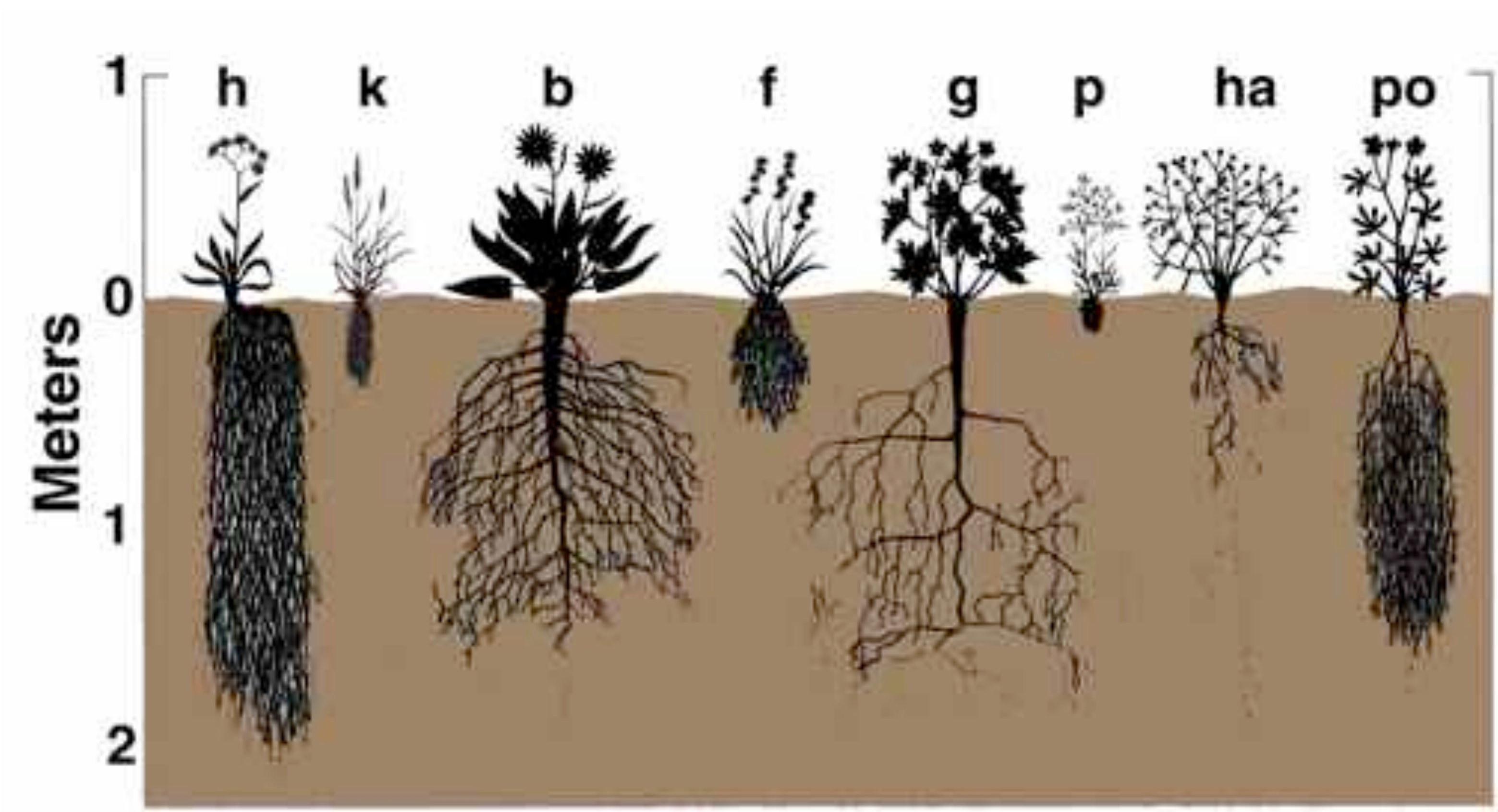
But Only a Few Have Helped Generate New Crops!
The "Simple Ones With Economic Drivers"



Genetic Engineering Has the Advantage of Allowing Everything That's Possible Biologically To Be Achieved

We Are Only Limited By Our Imagination and Knowledge of Biological Processes

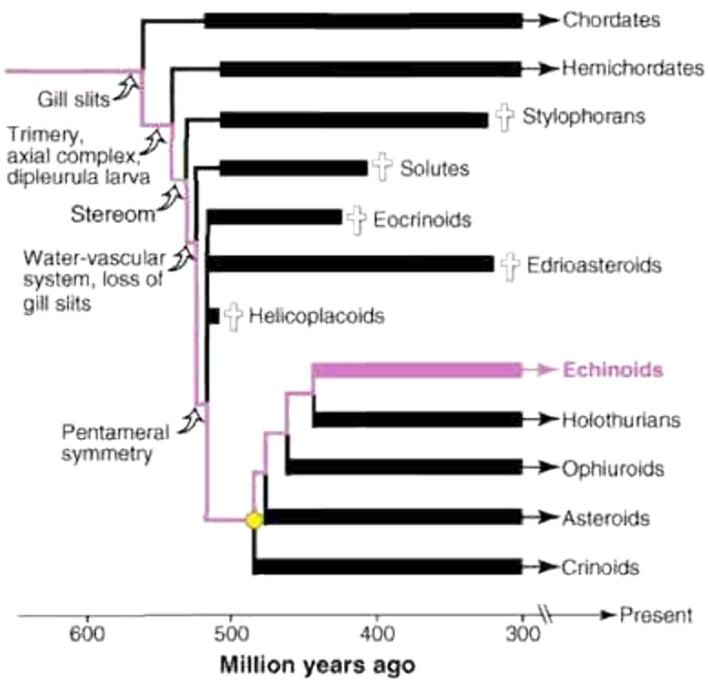
How Use Genetic Engineering To Change Plant Architecture or "Complex" Developmental Traits to Improve Crops?



For Example-Root Architecture?

…….or Make a Giant Seed?

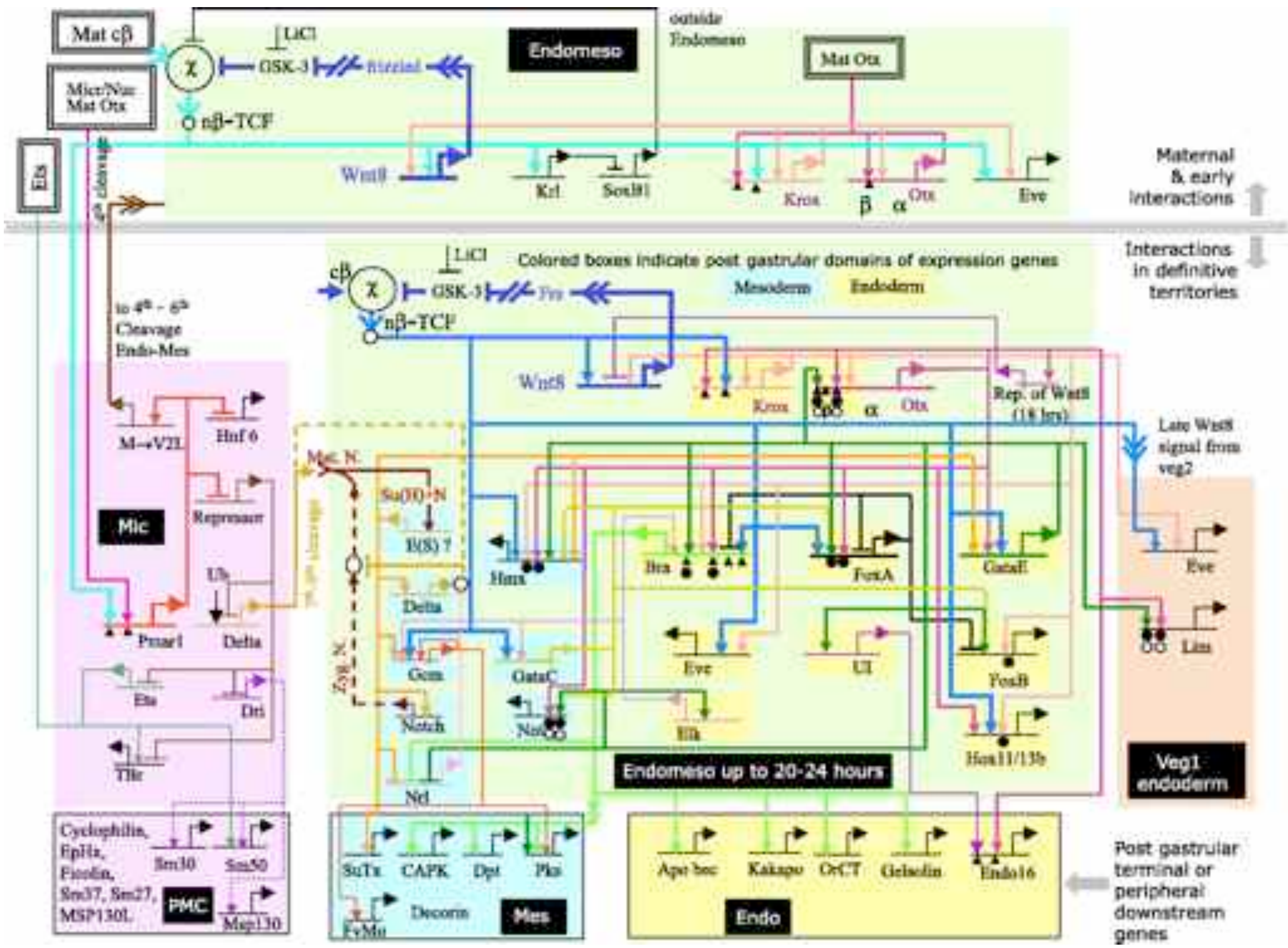
An Example From Sea Urchin and Starfish



Sea Urchin

Starfish

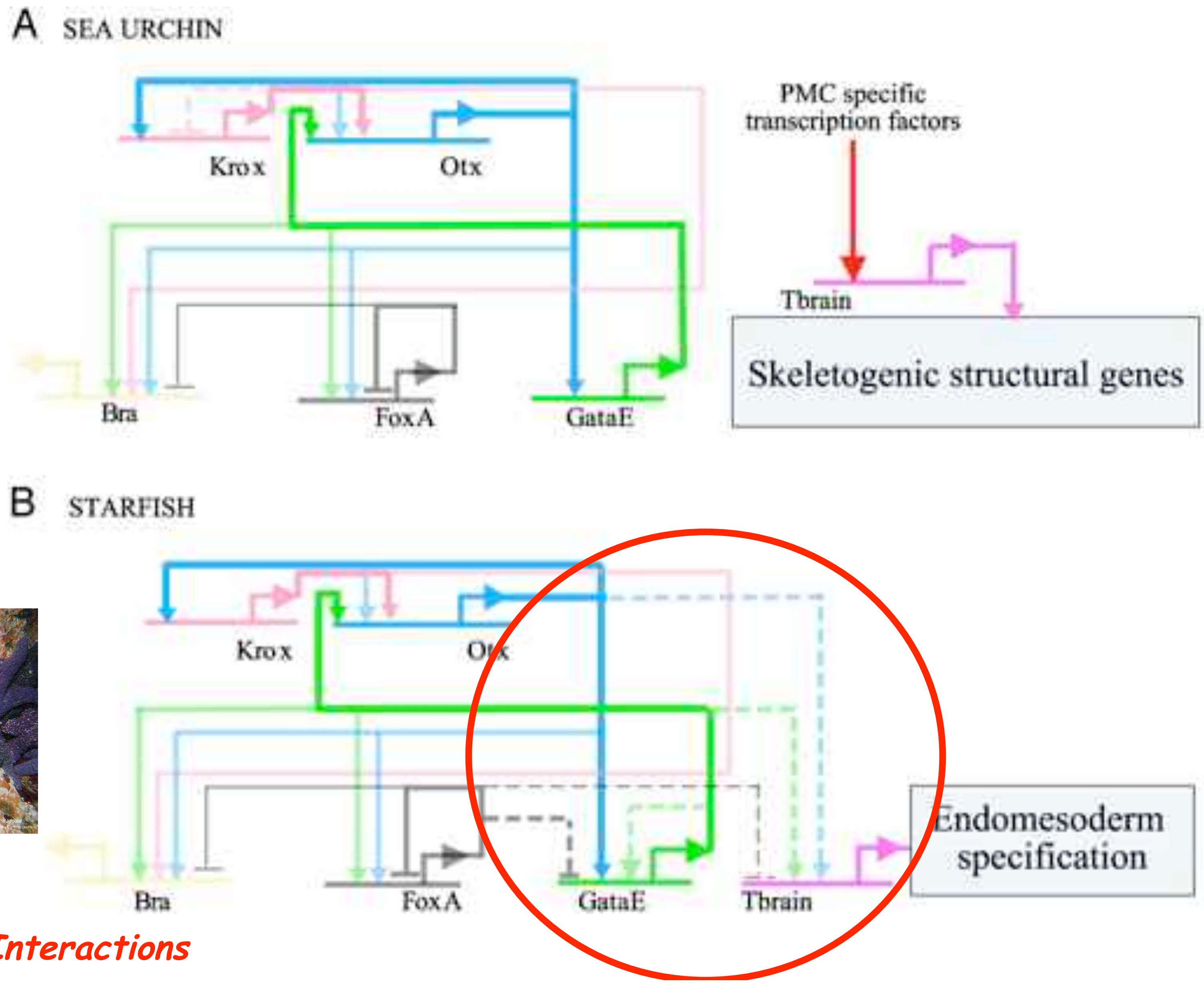
Regulatory Genes and Circuits Driving Early Sea Urchin Embryo Cell Differentiation and Development -- From FUNCTIONAL Genomics



Eric Davidson et al. Science, 2007

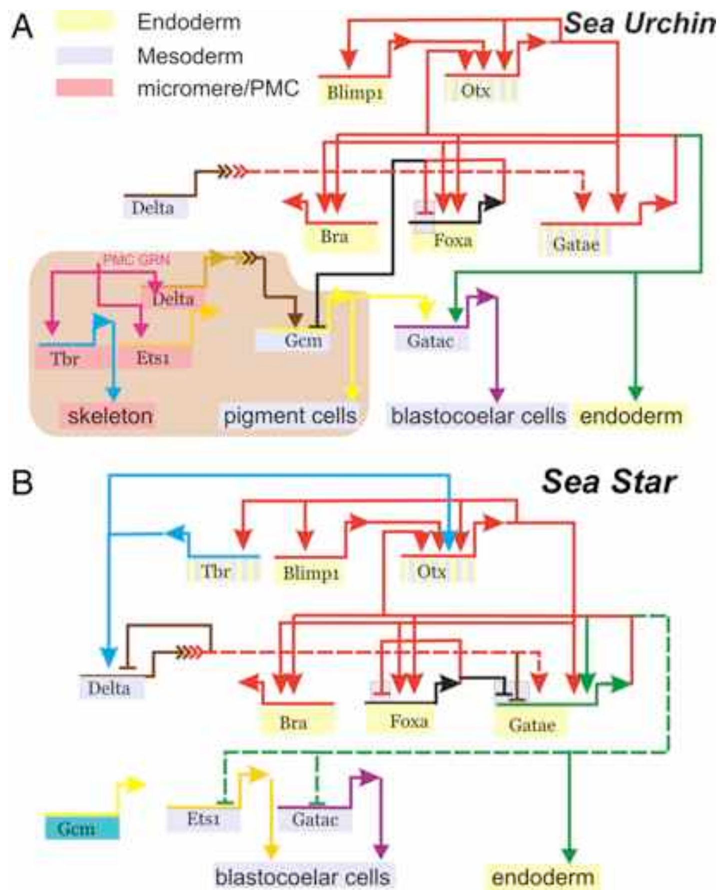
Knowledge of Cell-Specific TF mRNAs and Knock-Down Effects On Embryo Phenotype and TF mRNAs

Functional Dissection of a Shared Regulatory Circuit Between Sea Urchin and Starfish



Note Different Interactions

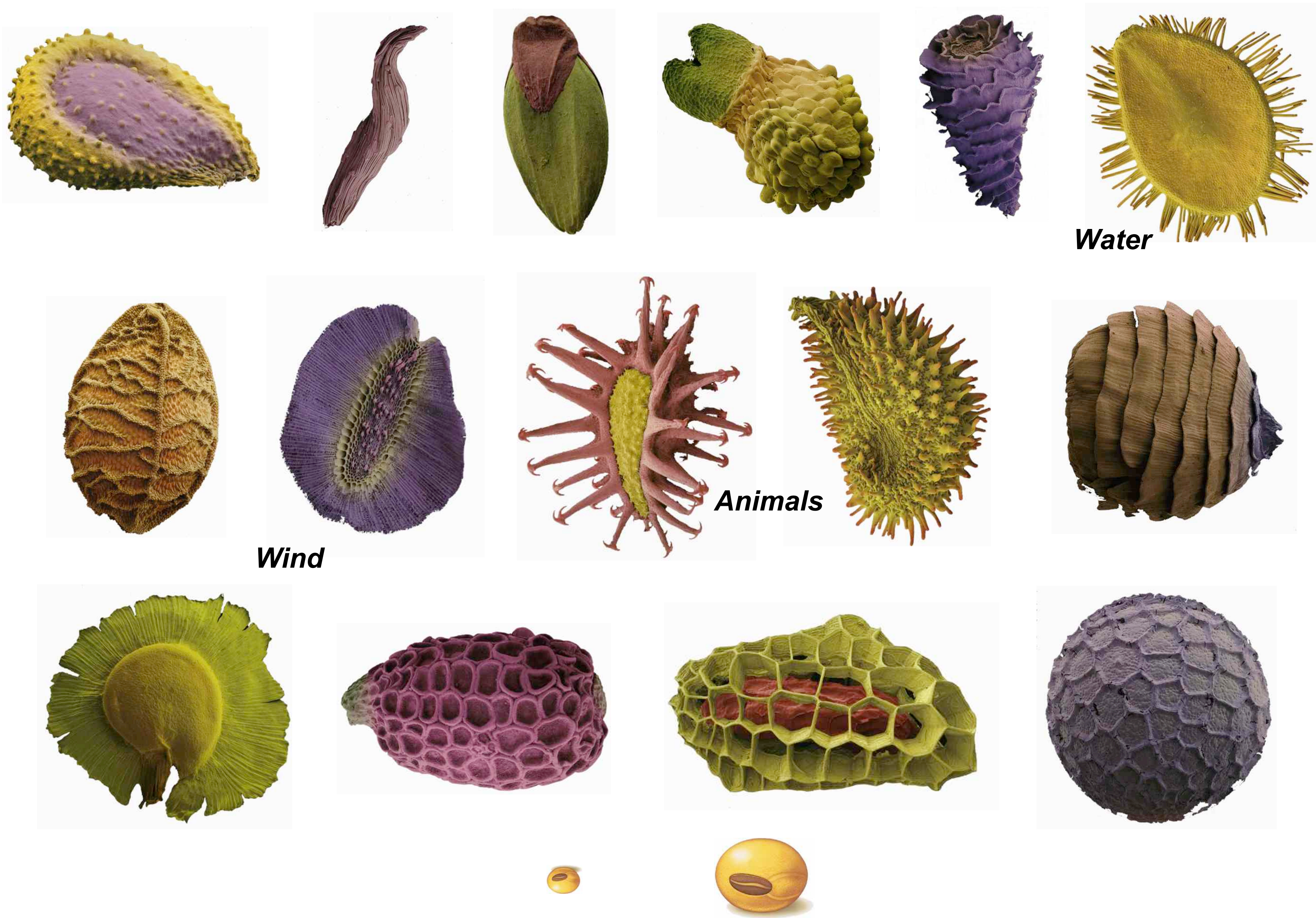
Different Regulatory Interactions Lead To Differential Activation of Downstream Sea Urchin Genes Leading to Novel Embryo Cell Types and Functions



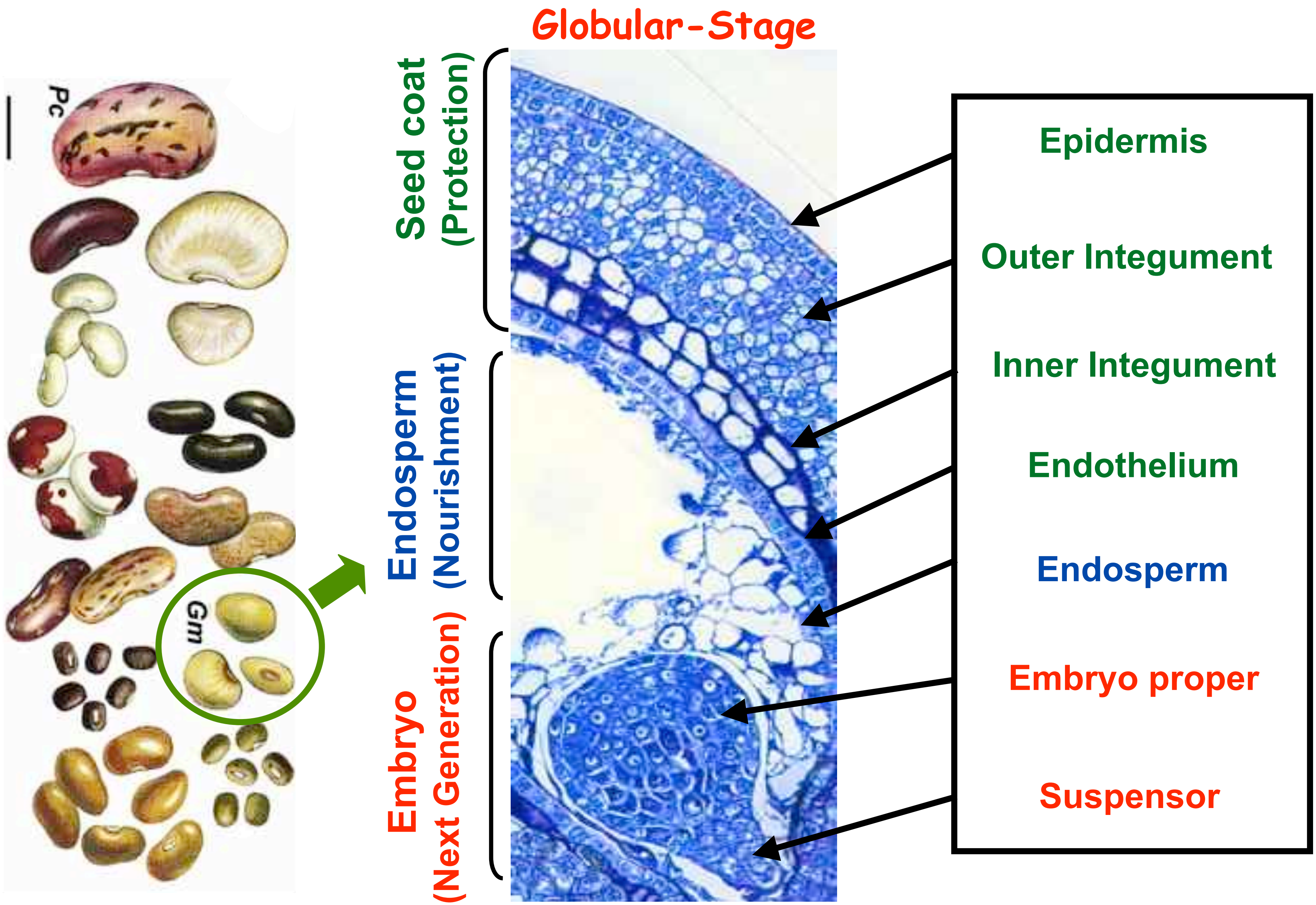
Evolution of Animal Architecture And Manipulation Targets

Hinman V. F., Davidson E. H. PNAS 2007;104:19404-19409

What About Seed Architecture and Size?

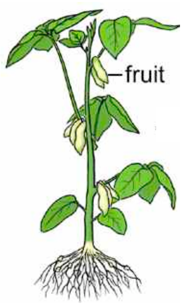


What Are the Genes Required to Make a Seed?



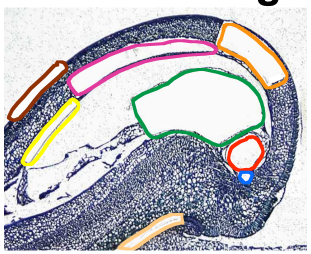
And How Are They Wired in a Plant Genome?

Profiling mRNAs in Every Tissue, Cell Type, and Compartment During All of Soybean and Arabidopsis Seed Development



Soybean

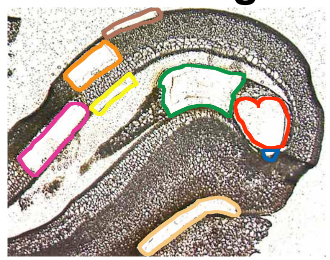
Globular-Stage



21,989
(1,552)

+

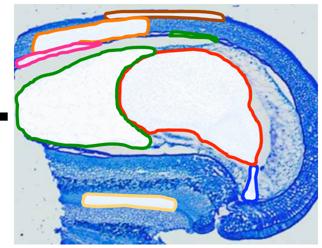
Heart-Stage



22,377
(1,538)

+

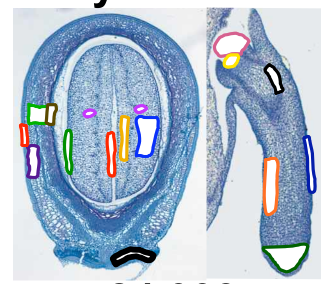
Cotyledon-Stage



22,903
(1,595)

+

Early Maturation



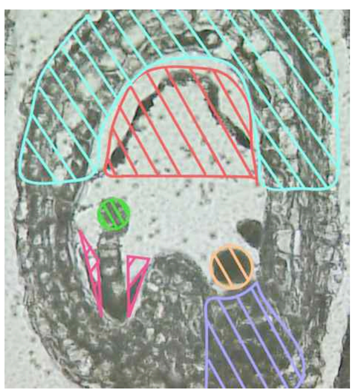
24,003
(1,685)

= **26,359**
(1,894)

(Transcription Factors)

Arabidopsis

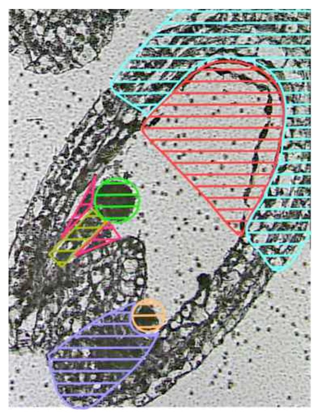
Pre-Globular-Stage



14,538
(1,199)

+

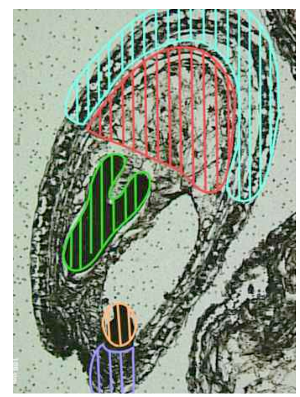
Globular-Stage



15,156
(1,259)

+

Cotyledon-Stage



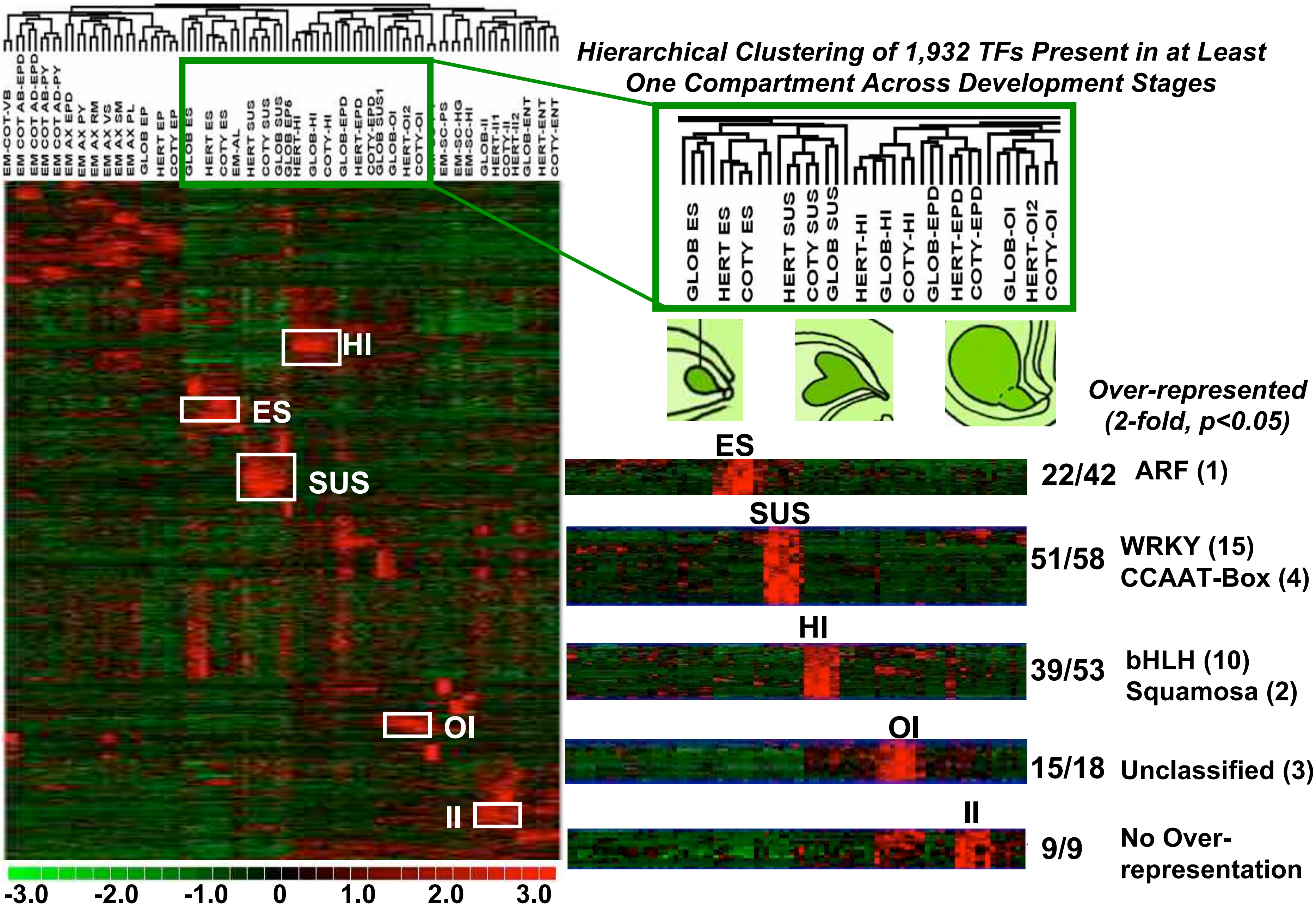
14,456
(1,210)

= **16,660**
(1,450)

~75 Compartments, Tissues, & Cells Profiled

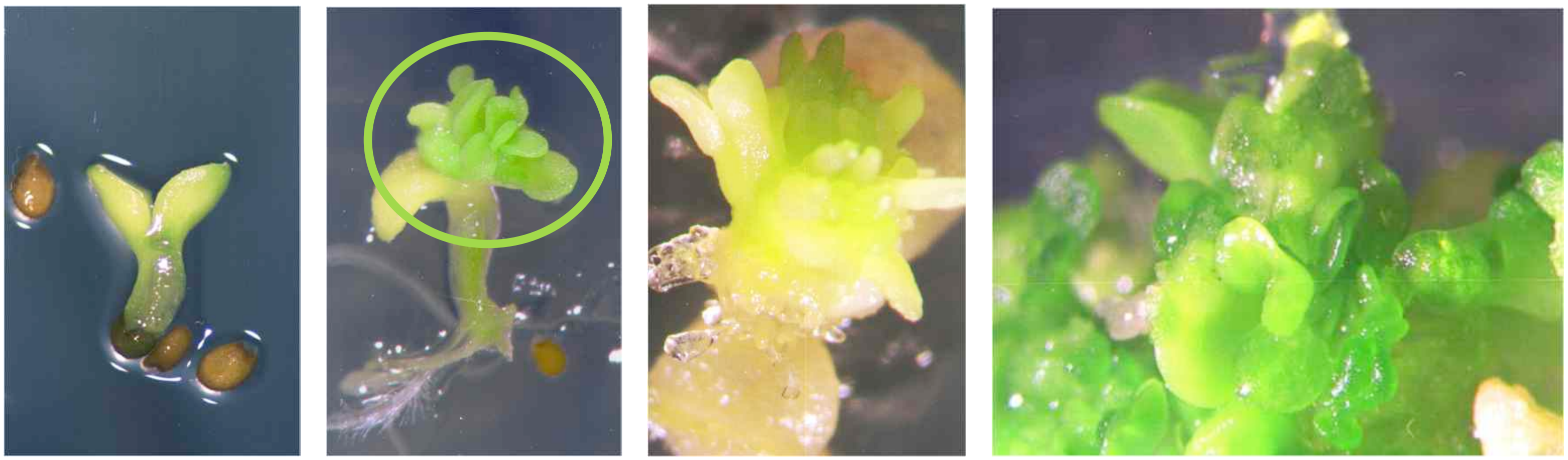
UCLA UCDAVIS UNIVERSITY OF CALIFORNIA NSF

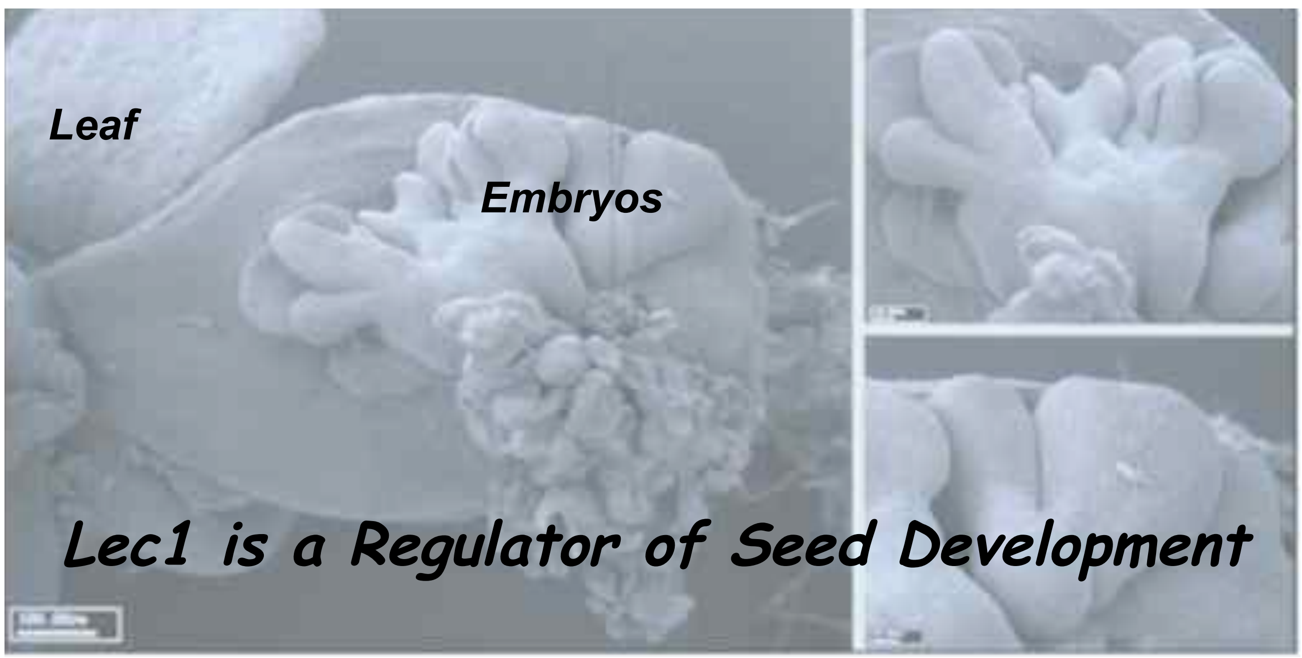
Spatial Patterns of Transcription Factor mRNA Accumulation During Early Soybean Seed Development



http://estdb.biology.ucla.edu/seed

Using TF Candidates To 'Engineer" Embryos on Leaves!





Lotan et al., Cell, 1998; Lee et al., PNAS, 2003; Kwong et al., Plant Cell, 2003

Future Challenges

- Efficient and Precise Genetic Engineering Technologies
    - Replacement
    - Mini-Chromosomes
    - Knock-Downs & Models to Functionally Test TFs Rapidly
- Knowledge of Gene Processes and Regulatory Circuits
    - Systems Biology-Integrating Plant Processes (It's not BS!)
    - Will Allow Rationale Approaches to Genetic Engineering
    - Will Allow Hypothesis-Based Approaches to Improving Plants
- Education
    - Young Scientists for the Future
    - Public
    - Decision Makers
- Fight Anti-Scientific Thinking That Continues to Hold Back Use of Genetic Engineering to Improve Agriculture and Humanity
- Build a Structure to Translate 1000s of New Genetic Discoveries to New Crops For Farmers
    - Re-Think and Re-Structure How Ag Research Done in US Public Institutions

The End…………….

….or is it the Beginning!