Biotechnology in a Changing Climate: Just another technological fix!?

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"We have recently advanced our knowledge of genetics to the point where we can manipulate life in a way never intended by nature.

We must proceed with the utmost caution in the application of this new found knowledge"

Luther Burbank

1906

My Greatest Discovery in Fifty Years

Famous Plant Wizard, Celebrating Half a Century of Useful Labor, Tells How He Believes We Can Develop Better "Human Plants"

By Luther Burbank, Sc.D., Especially written for POPULAR SCIENCE MONTHLY

ON THE seventh day of March, I was 74 years of age. On that day, I celebrated the conclusion of half a century of ceaseless experimentation with plant life.

In those 50 years, millions of plants—grasses, flowers, vegetables, grains, and trees—have passed through my hands, and from them I have selected a few, seemingly a very, very few, for preservation, reproduction, improvement, development, to such a point that they may render the utmost service of food, beauty, and enjoyment to man.

Plants Teach Man

To me, they have become like a vast army of individuals, marching onward, guided by selection, toward a goal of improvement. From my first creation—a potato that is now grown by the millions of bushels all over the habitable globe—to the latest of more than a dozen varieties of new and commercially valuable fruits—of which more than 100 carloads were shipped last year from California alone—there has been growing

The Grand Old Man at 74

fact. It has been p... time on time, and I ... crystallized it into two statements, one the corollary of the other:

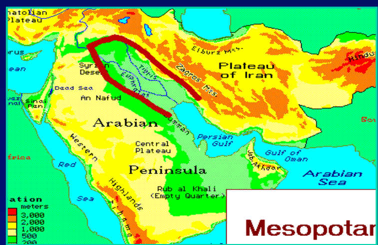
First, that plants are pliable and under the control of man; and that they can be bred and trained and developed, just as animals can be bred and improved and trained.

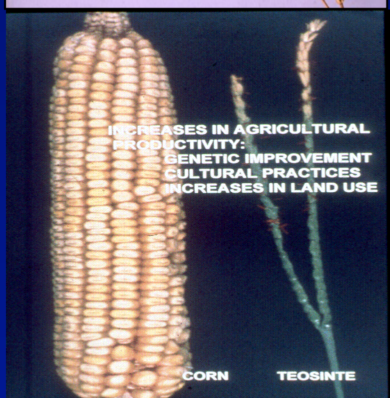
Second, that the human plant—the child—can be trained, developed, and improved, just as the skilled gardener, or the trained botanist, trains, develops, and improves the best that is in each one of his plants.

The Hope of Progress

During the course of many years of investigation into the plant life of the world, creating new forms, modifying old ones, adapting others to new connections, and blending still others, I have been impressed constantly with the similarity between the organization and development of plant and human life. While I have never lost sight of the principle

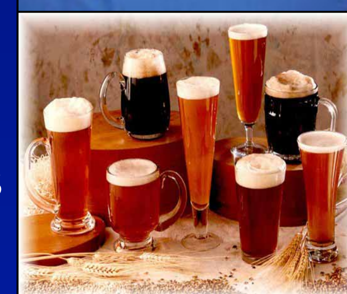
Myth: Agricultural technology is new

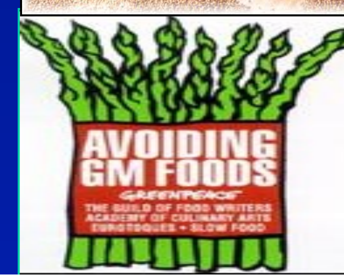




8,000 BC
19^{th} C
Ea 20^{th} C
Md 20^{th} C
1930s
1940s
1950s
1970s
1980
1990s
21^{st} CC

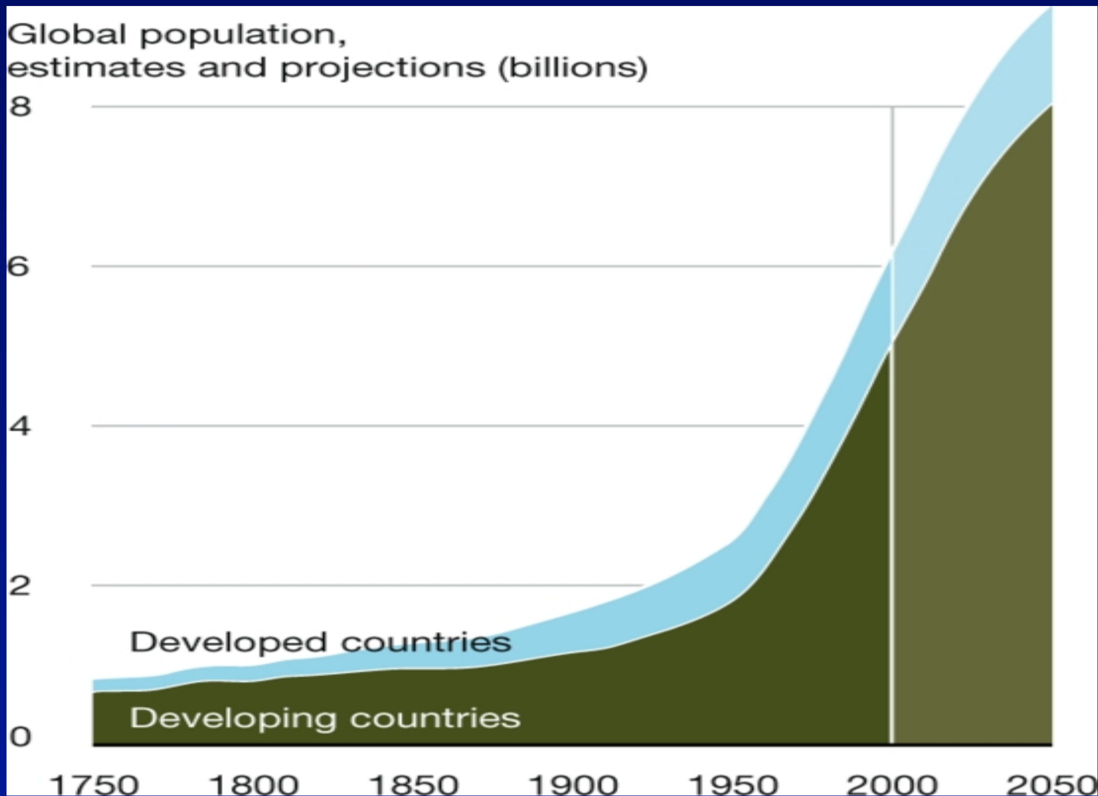
- Cultivation
- Selective cross breeding
- Cell culture
- Somaclonal variation
- Embryo rescue
- Mutagenesis and selection
- Anther culture
- Recombinant DNA
- Marker assisted selection
- ---omics - Bioinformatics
- Novel Breeding
- RNAi/ GEENs/ Epigenetics
- Network engineering
- Synthetic biology
- Systems biology



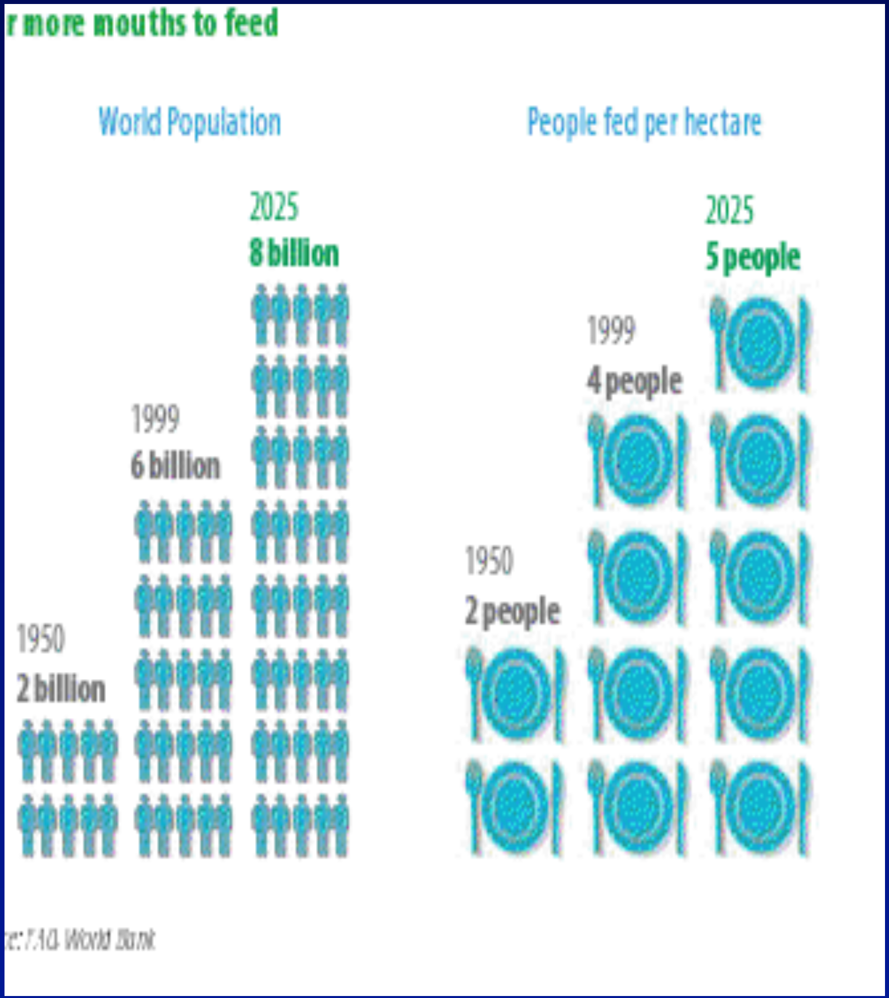


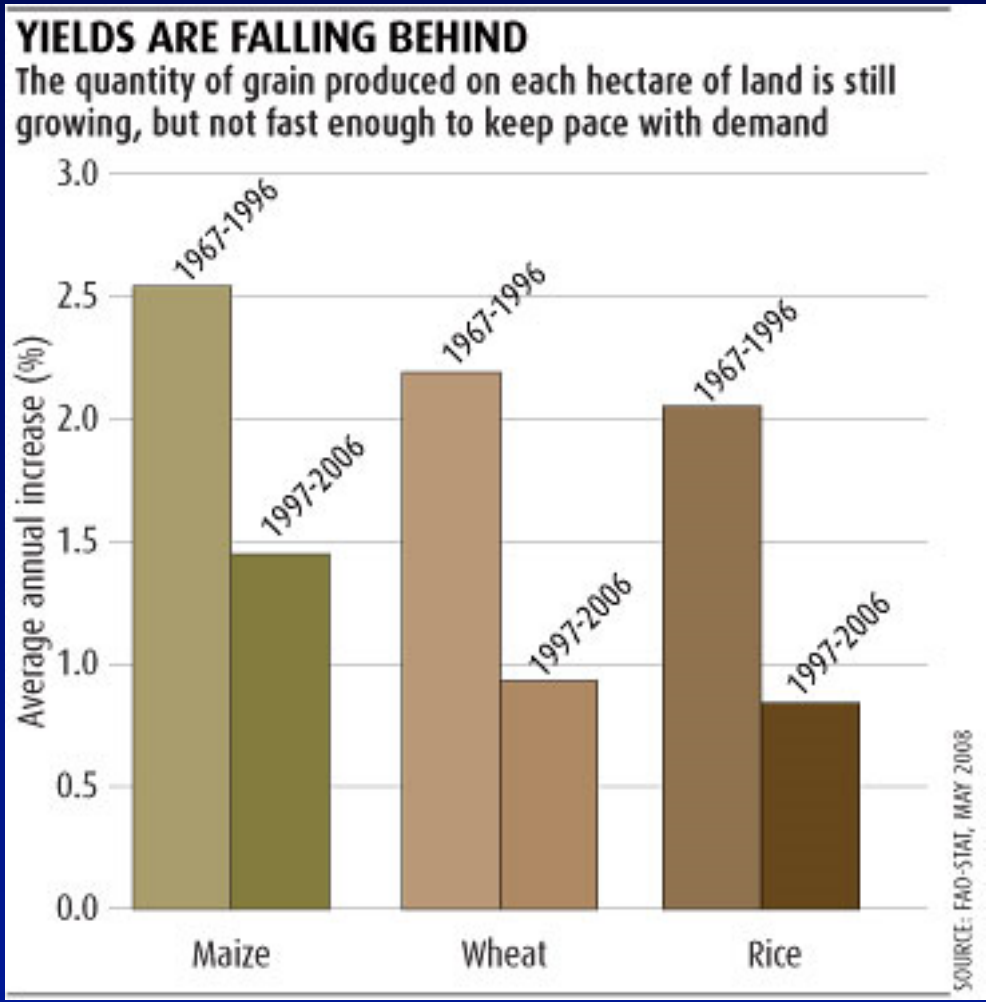
Why do we need Biotechnology

Greatest grand challenge of our time!
Population of 9 billion by 2050!
70-100% more food required.



- Need: Affordable, high yielding, high quality food, feed, fuel, fiber, sustainably produced
- Challenges: Changing climate, diminishing resources – degraded land, less water, less fuel, less fertilizer, less pesticides
- Sustainable intensification



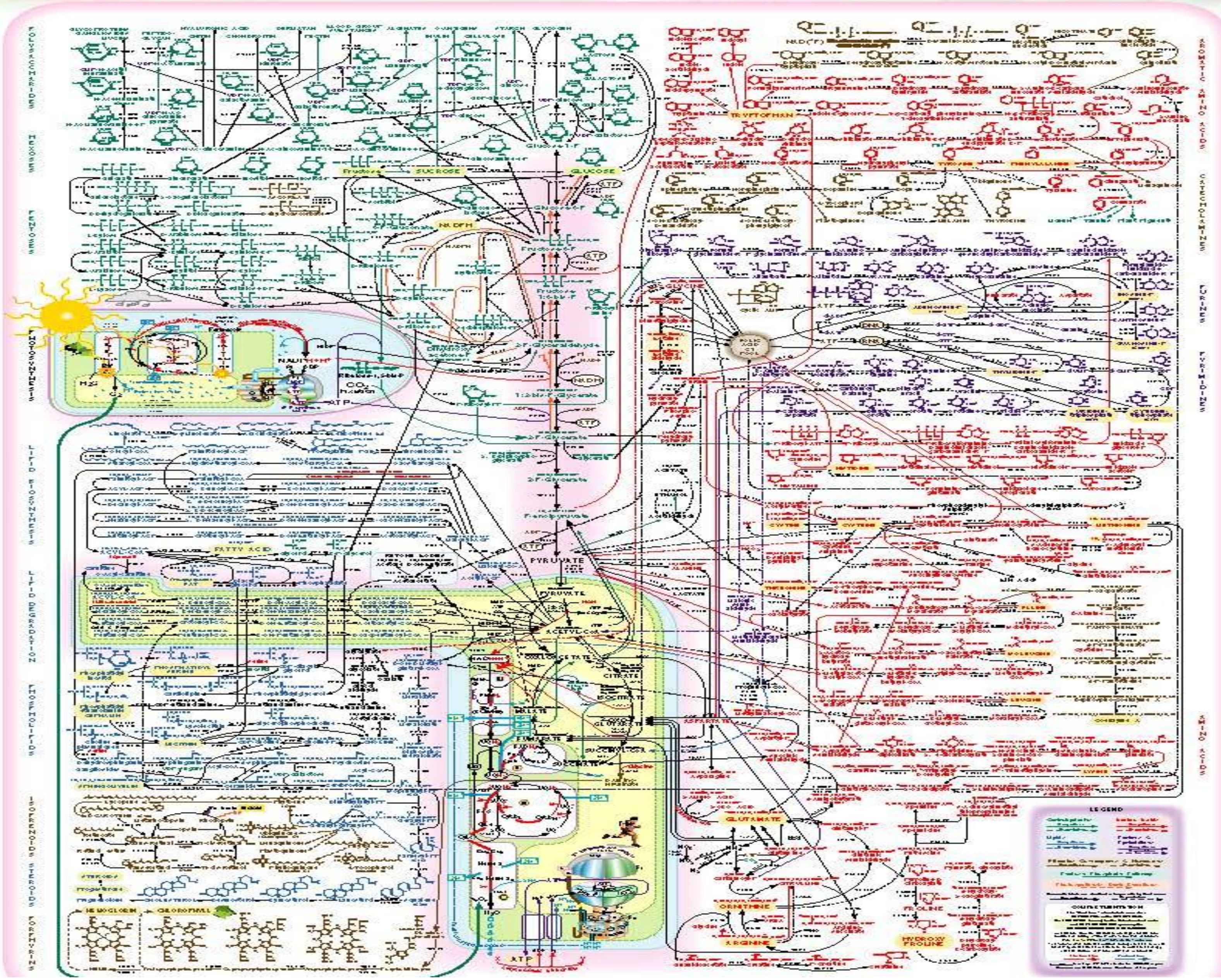


Production must double over the next 25 years to feed all these people
“physiological” optimum using traditional breeding already maximized for many crops

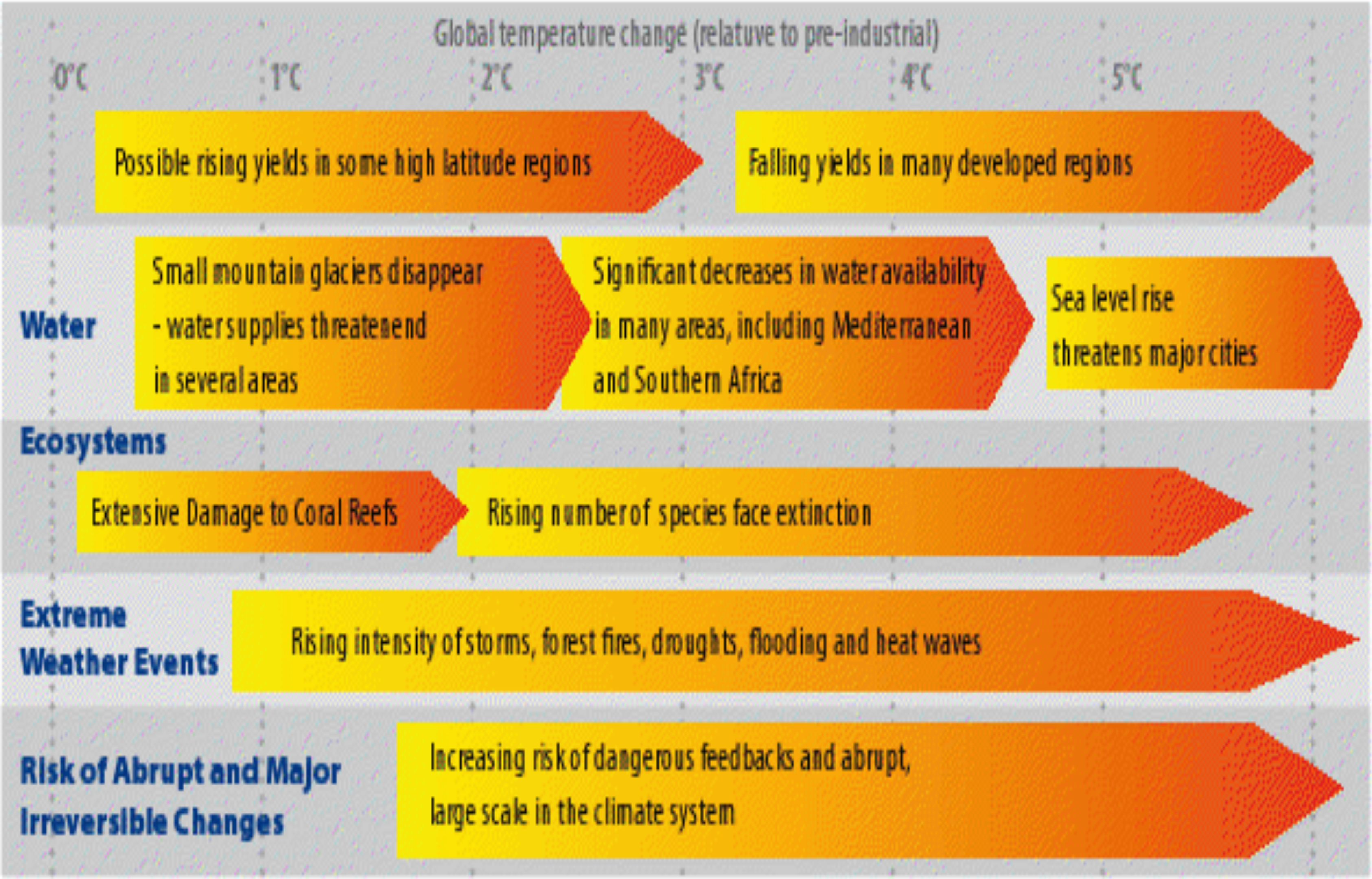
The Future: Smart Plants Smart Environments

- **Smart plants: Systems biology reductive and holistic approaches to identify, modify, introgress and subsequently simultaneously introduce /study / modify/ the expression/interaction of genes and the realtime response of plants to their environment**

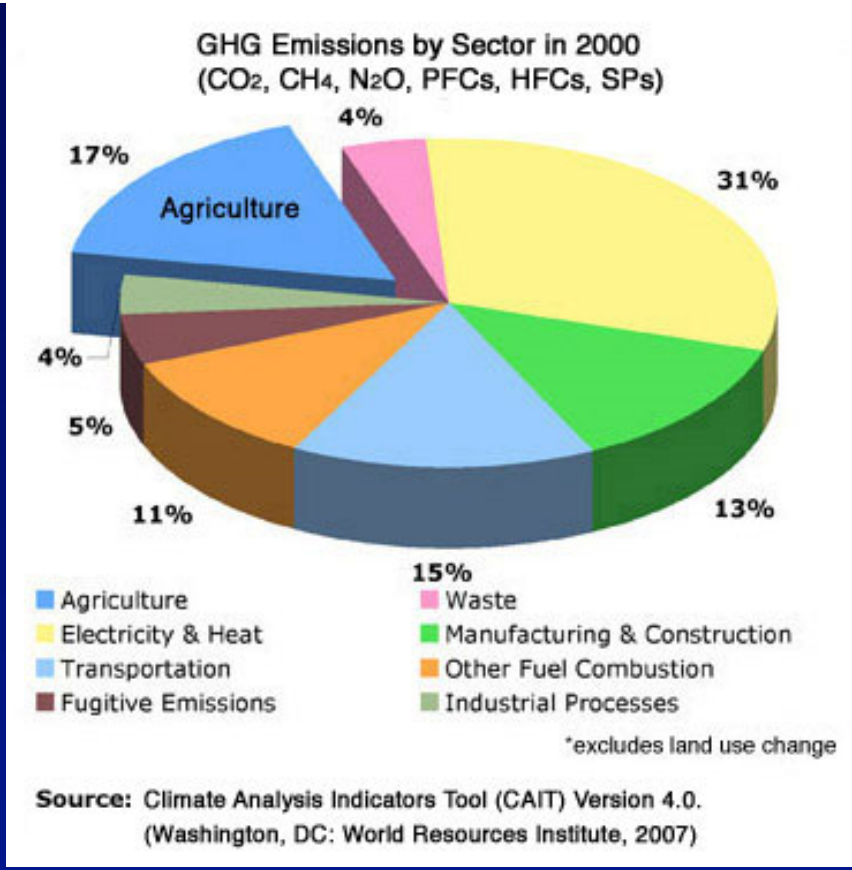
Metabolic Pathways



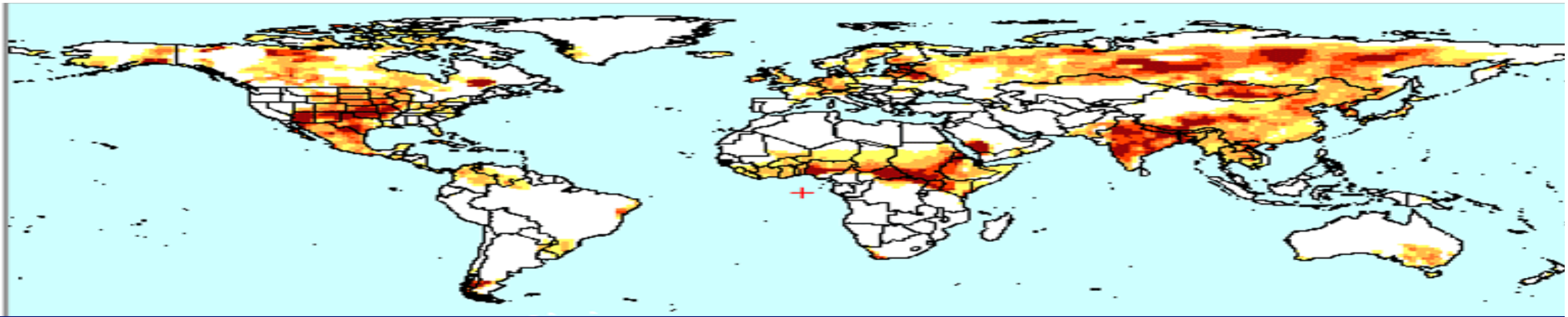
Projected Impacts of Climate Change



Source: Stern Review on the Economics of Climate 2006



- **Agriculture is a major source of greenhouse gas emissions. Practices - deforestation, cattle feedlots and fertilizer use - currently account for about 25% of greenhouse gas emissions.**
- **Agriculture accounts for 14% of CO_2 emission. Agriculture is also a major source of methane (CH_4) and nitrous oxide (N_2O), with estimates showing that it accounts for 48% of methane emissions and 52% of N_2O emissions.**



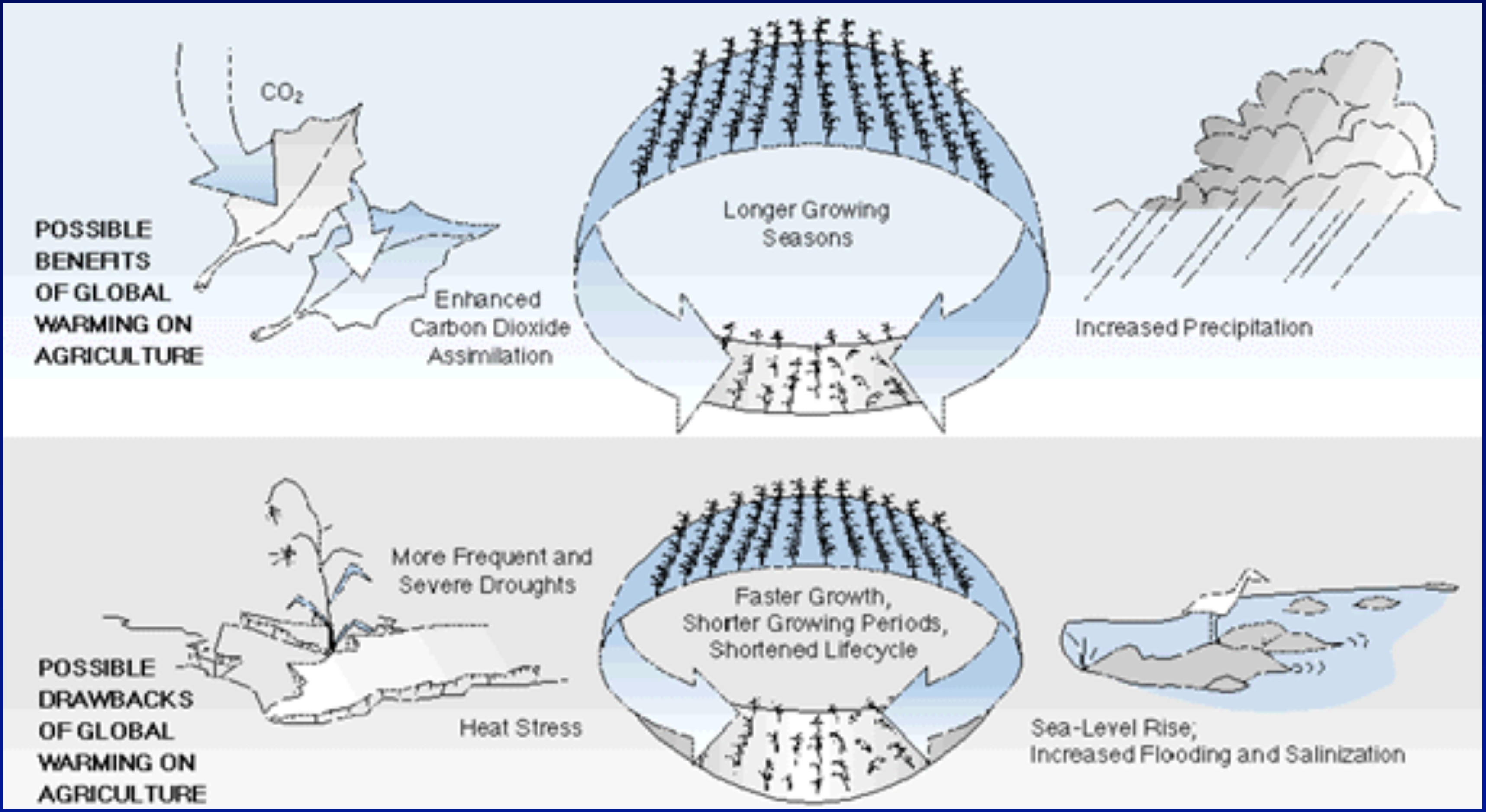
Given the impacts of climate change on agricultural productivity and the part played by agriculture practices in global warming, agricultural techniques must play a substantial part in the fight against climate change. Green biotechnology offers a “toolbox” which can help farmers limiting greenhouse gas emissions as well as adapting their agricultural techniques to shifting climates.

The three major contributions of green biotechnology to the mitigation of the impact of climate change are:

1. Greenhouse gas reduction

2. Crop adaptation (Environmental stress, changing niches)

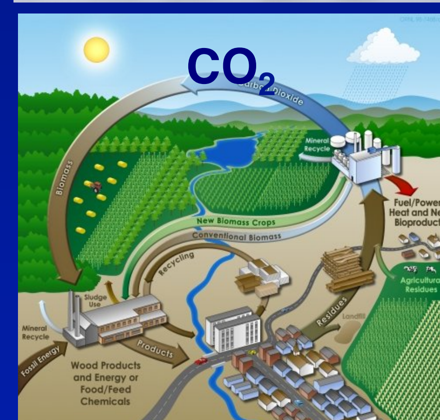
3. Protection and increase yield in less desirable and marginal soils



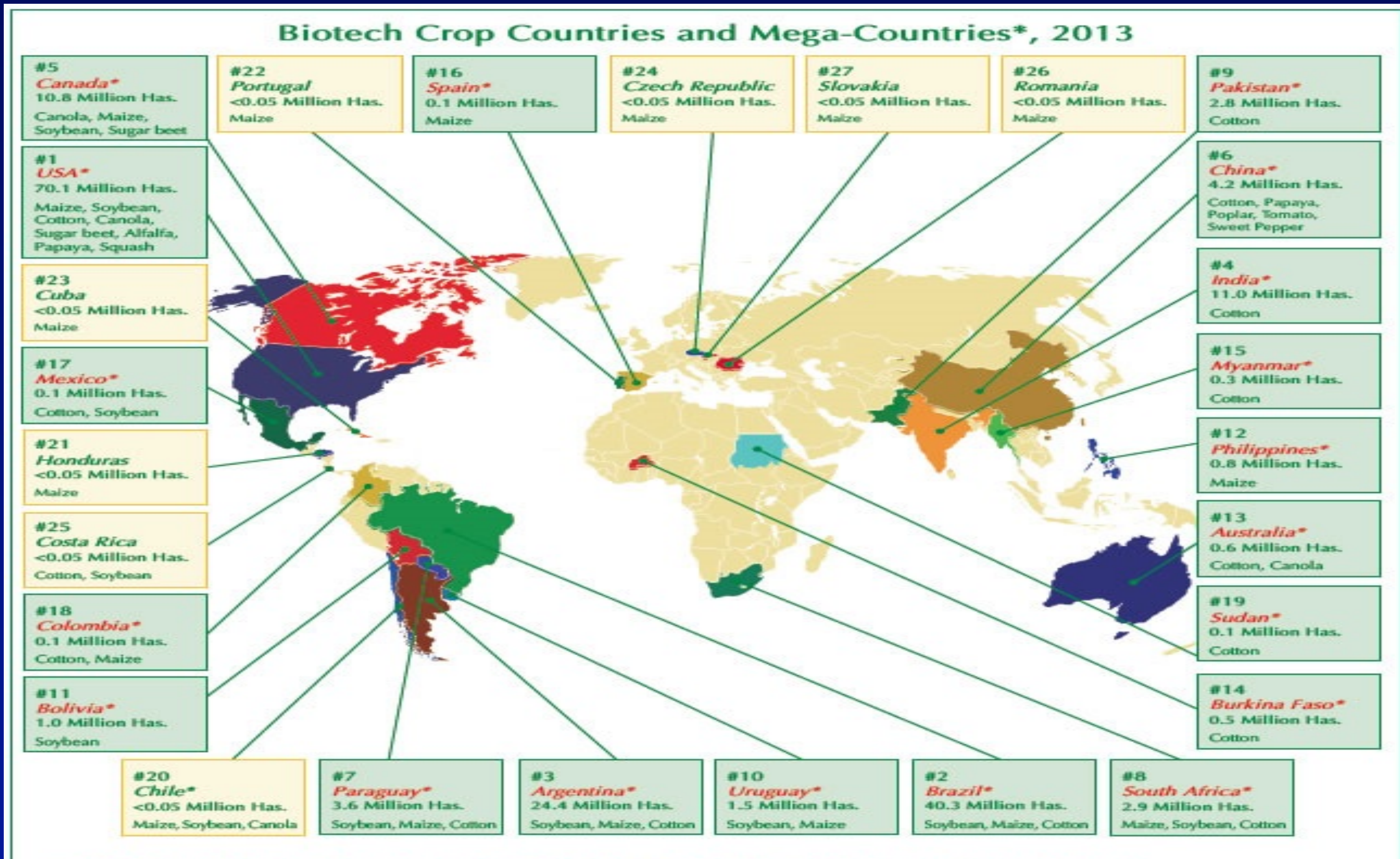
Possible benefits and drawbacks of climate change on agriculture, based on an illustration in *Scientific American*.

Opportunities/challenges for biotech crops

- **Agronomic Traits**
  - **Biotic stress: Pests/disease/weeds/**
  - **Abiotic stress: Drought, heat, salinity, submergence, marginal soils**
  - **Yield: Nutrient efficiency, fossil genes**
- **Quality Traits**
  - **Improved post harvest characteristics – Shelf life, processing, taste – waste reduction**
  - **Improved nutrition – Improved functionality**
- **Renewable Resources**
  - **Biomass conversion, feedstocks, biofuels, phytoremediation concerns land/water use**
- **Plants as Factories**
  - **Pharmaceuticals/industrial products**



Myth: Biotech only helps “big industrial ag”

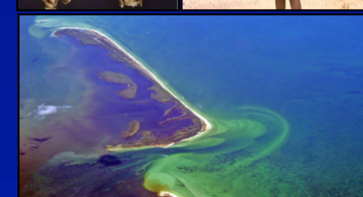


- Biotech Crops 2013: **430** million **acres**, up 7 million - 3% growth
- 27 countries (19 emerging economies) 18 M farmers 90% (16.5M) resource-poor
- US 70.1Mhas (173Mac), ~90% principal biotech crops
- BT corn. HT Soybean BT Cotton (27% stacked traits world wide)

Source: ISAAA

Relevant Benefits to date

- $177 million increase in farm productivity
  - 60% reduced costs; 40% increase in yield (377 million tons)
- 1 Billion lb reduction in pesticide active ingredient
- Saved 123 million hectares 1996-2012
- Conservation tillage
  - 93% reduction in erosion
  - 1 billion tons of top soil preserved
  - 70% reduction in herbicide run-off
  - 80% reduction in phosphorus in water
  - >50% reduction in fuel use
  - 59 billion lbs reduction in CO_2 emissions
  - ~11.8 million cars off the road
    - (Brookes and Barefoot (2014)
- BT corn 90% reduction in mycotoxin
- Phytase maize (China) decreased pollution

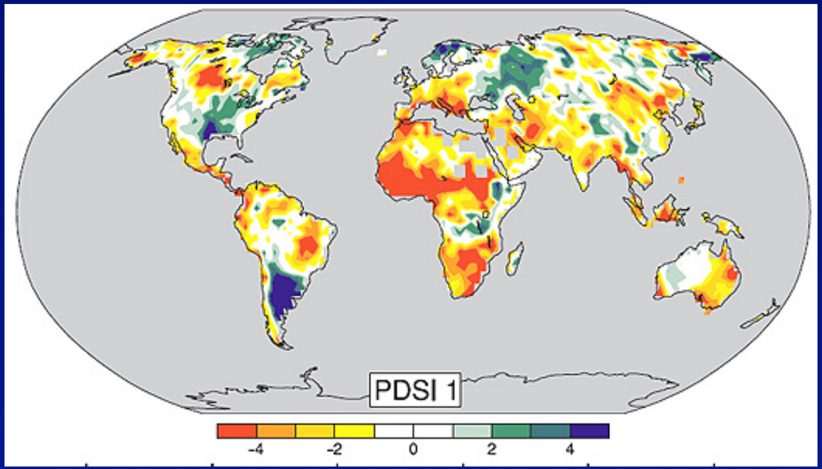


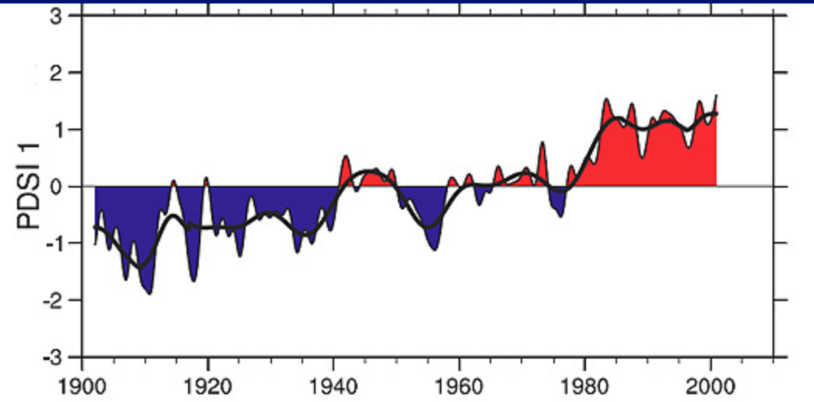
Abiotic Stress (Marginal Soils, environmental stresses): Crop Adaptation

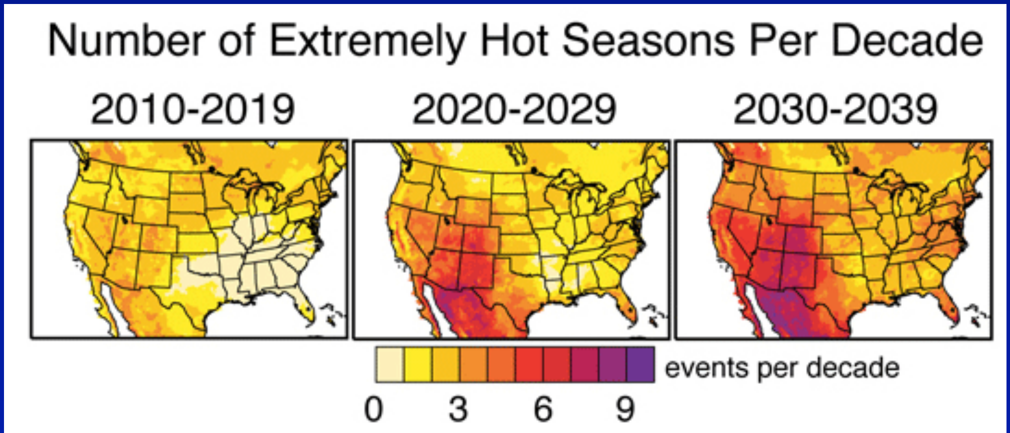
- Climate change poses a real challenge in terms of available agricultural land and fresh water use.
- Solutions must be developed to adapt crops to new conditions, such as marginal soils or harsher conditions such as cold, heat, drought, salinity, submergence.
- The agricultural sector uses a huge amount of available fresh water - 70% of the water currently consumed by humans is used in agriculture, and this is likely to increase as temperatures rise.
- 24.7 million acres of farmland worldwide lost each year due to salinity caused by irrigation . Crops limited by salinity on 40 % world's irrigated land (25 % US)
- In a warmer climate, plants will react to stresses, such as drought, by consuming large quantities of energy which is normally used for growth and seed production.

Abiotic stresses are the primary cause of crop-plants yield losses worldwide.

Decreased land precipitation and increased temperatures are contributing to more regions experiencing **drought** and heat waves affecting crops



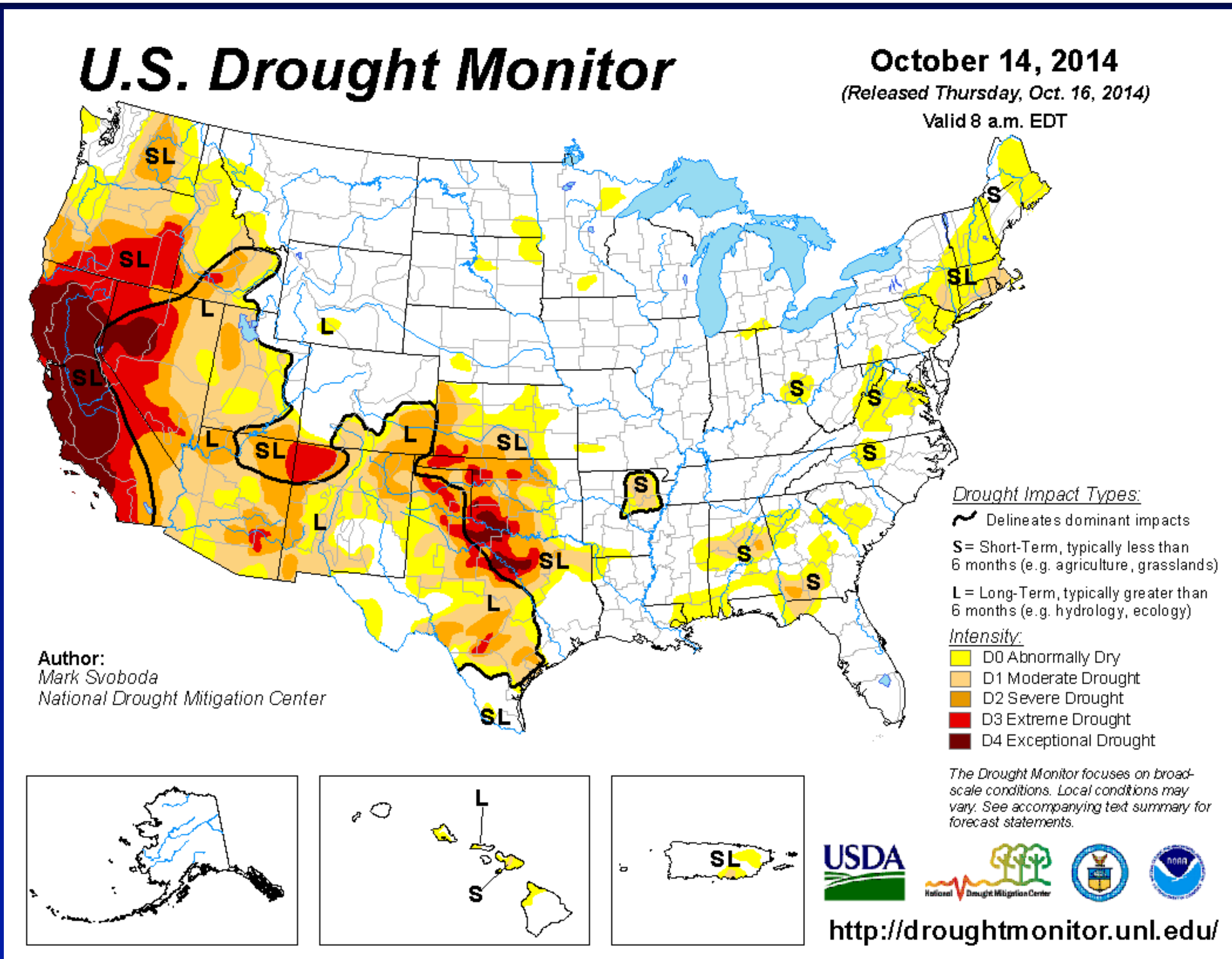




Global context

Abiotic stresses are the primary cause of crop-plants yield losses worldwide.

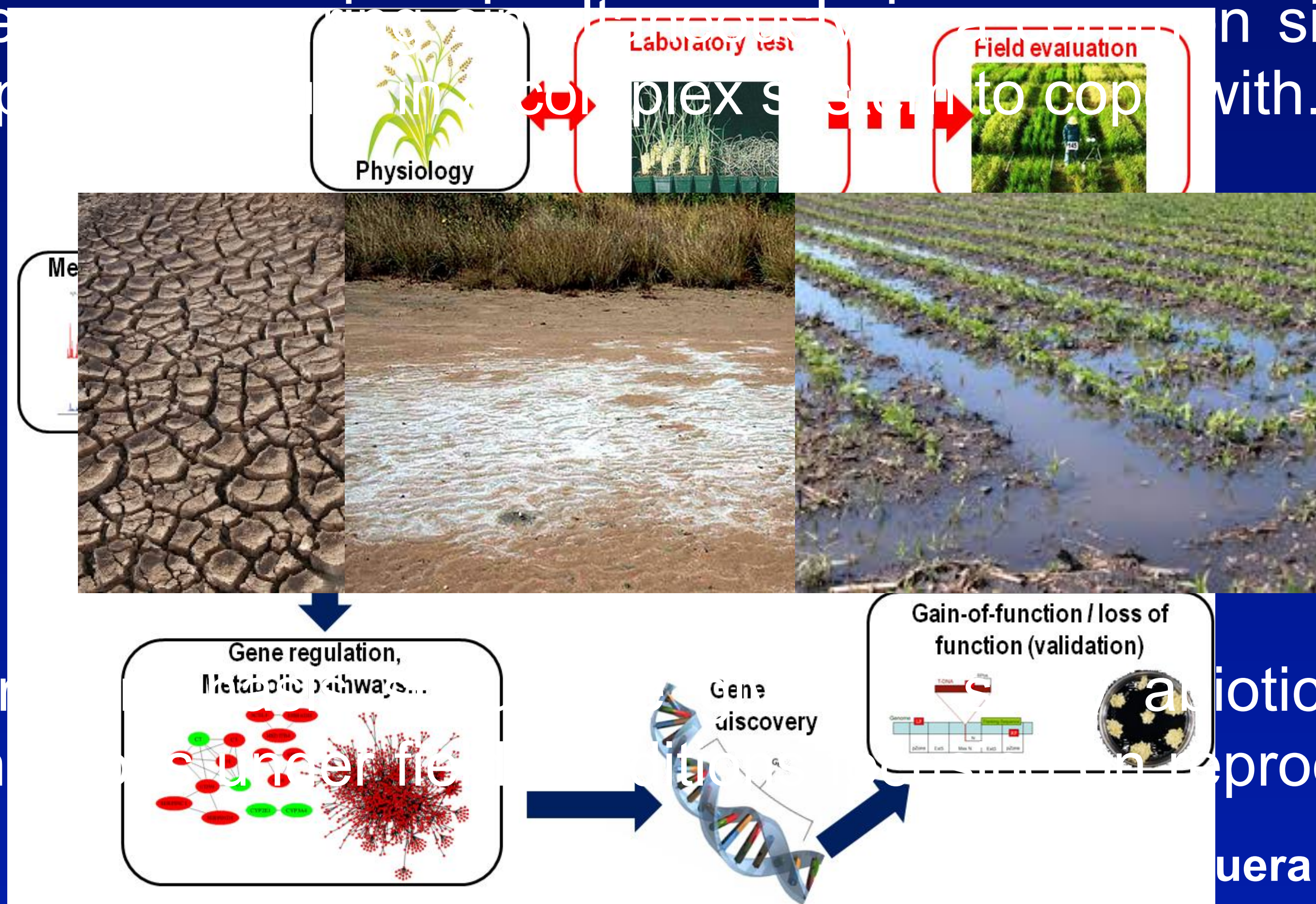
“Agriculture in drought”



Engineering abiotic stress tolerance

Numerous genes related to plant response to **abiotic stress** have been identified and characterized but most efforts to transform genes to crops have failed under field conditions

► Stre… n situation for crop… to cope with.



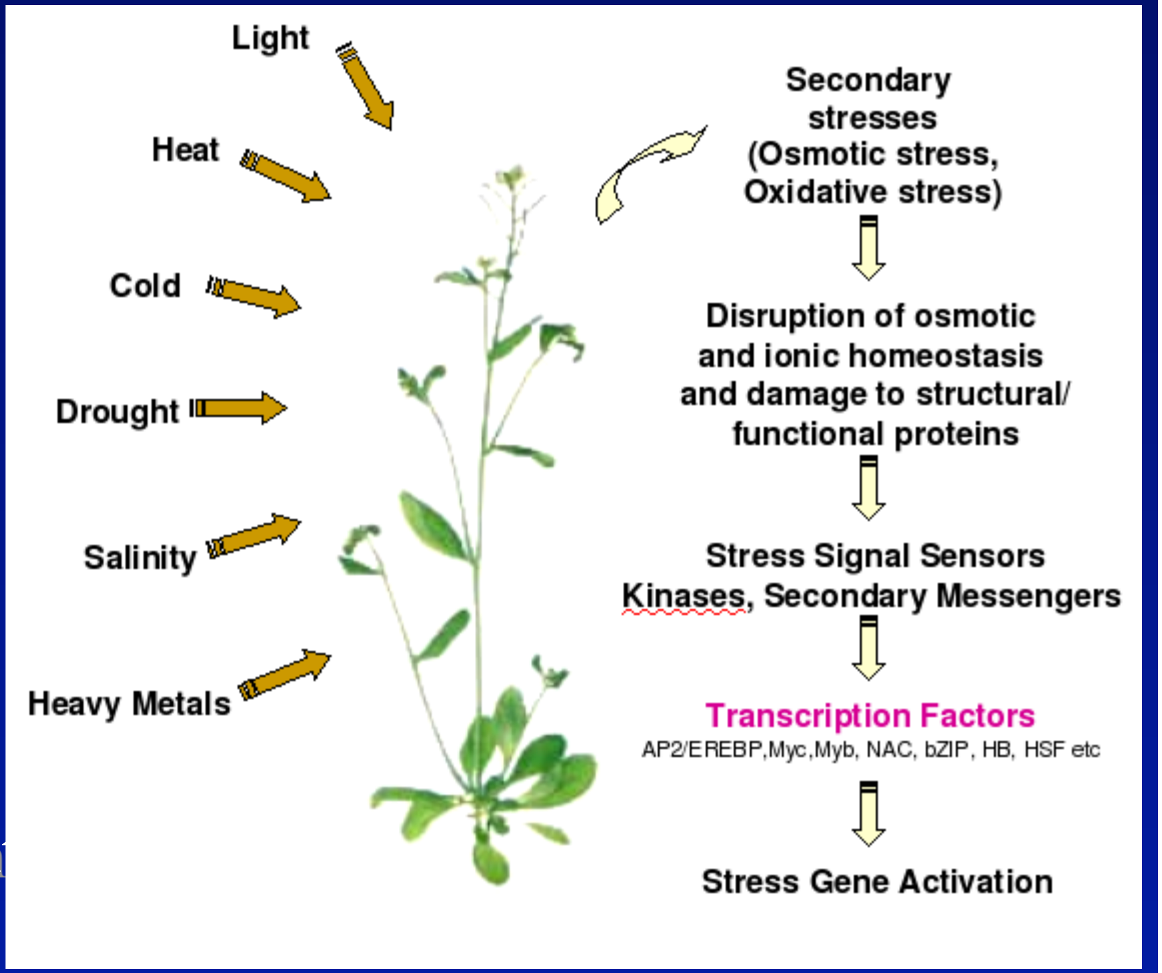
► Mor… abiotic-stress toleran… reproductive stage.

…uera et al. 2011

Abiotic stress limiting factor for crops reaching genetic potential

Abiotic Stress: Drought, Cold, Heat, Salinity

- Improved water conservation –
- Fewer crop losses –
- Higher yields on all acres through improved water utilization –
- Expand in drylands
- BASF Drought-tolerant corn 12 bushels more an acre

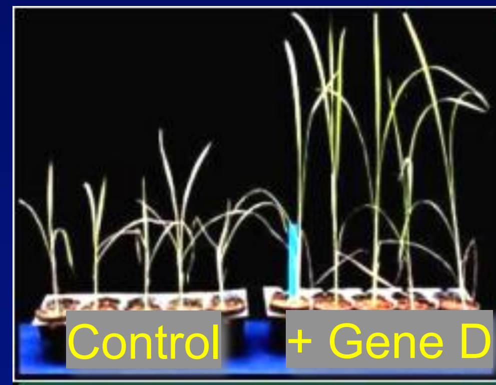


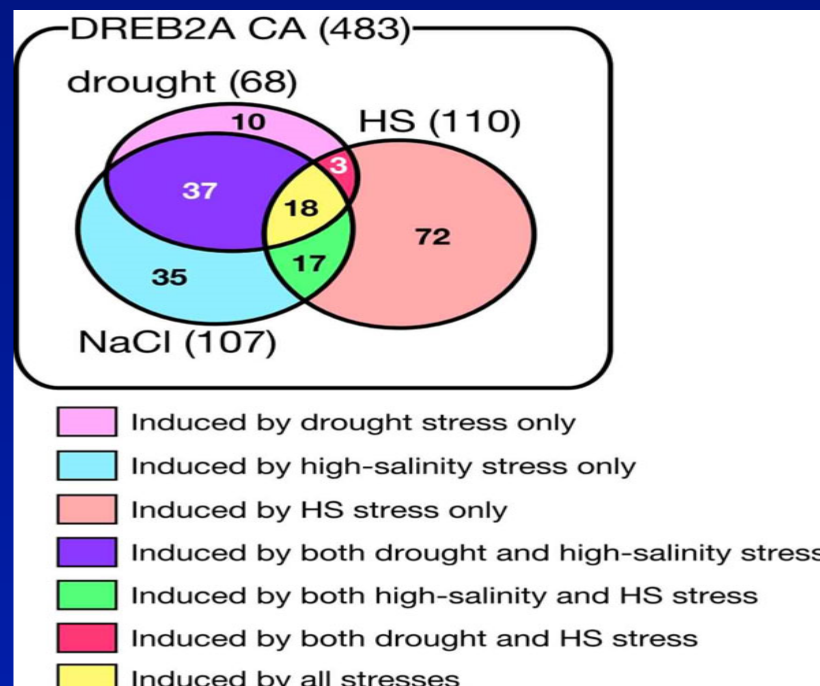
Abiotic stress limiting factor for crops reaching genetic potential

Abiotic Stress: Drought, ColdHeat, Salinity

- WEM decreased yield loss under drought conditions
- 30% yield advantage compared to conventional hybrids under drought conditions
- Transcription factor (Tf) DREB2A water-stress-responsive /heat-stress-responsive
- Nuclear Factor Y B subunit
- Homeodomain-leucine zipper (HD-Zip) transcription factors respond to H_2O & osmotic stress, exongenous abscisic acid

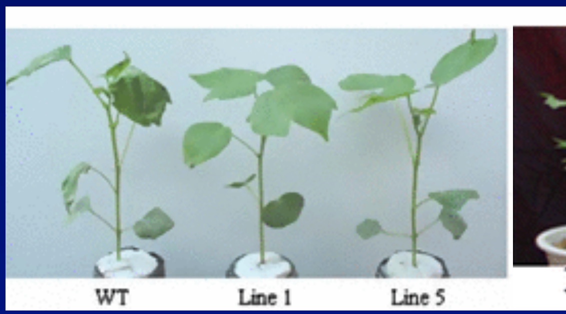
Drought Stressed Rice

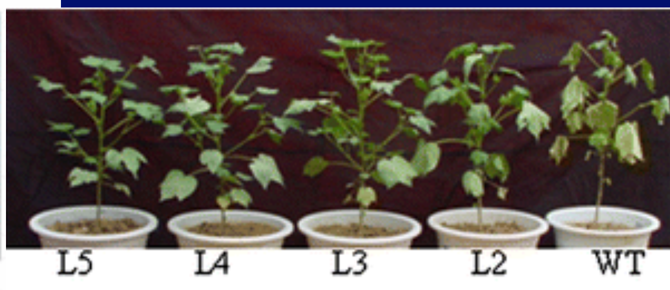




Engineering abiotic stress tolerance

- **Genes associated with osmoregulation.**
  Accumulation of Glycinebetaine, polyamines, proline , trehalose,….



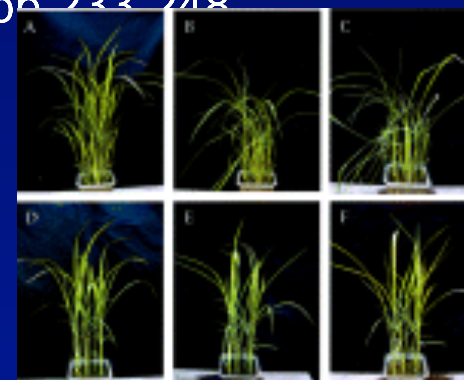


Molecular Breeding, 2007, Volume 20, Issue 3, pp 233-248

- **Detoxification of reactive oxygen species (ROS).**

Increasing antioxidant capacity by expressing antioxidant enzymes (i.e. SOD, CAT, APX..)

Physiologia Plantarum , 2002 .116(3) p317–327



WT

CAT

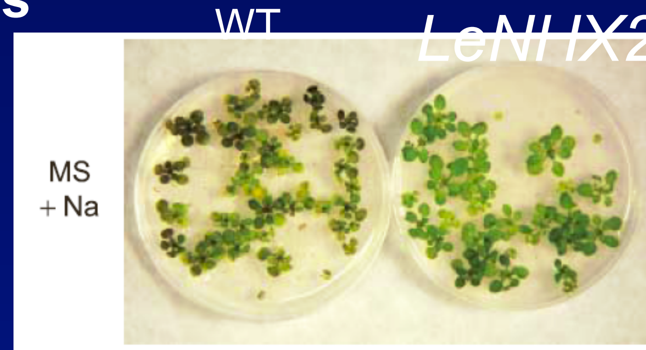
- **Manipulation of the expression of chaperones, heat-shock (HSP) proteins and late embryogenesis abundant (LEA) proteins.**

ROB5, a stress inducible gene isolated from bromegrass that encodes for a heat stable LEA group 3-like protein express in potato conferred heat stress (Molecular Breeding, 2010, 25(3) pp 527-540)

Engineering abiotic stress tolerance

- **Regulation of water and ion homeostasis**

Silencing or overexpression of aquaporins, uniporters, ion channels or antiporters (i.e. NHXs) …



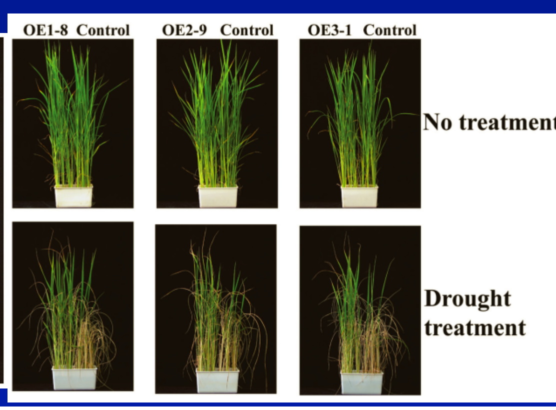
New Phytologist (2008) 179: 366–377

- **Manipulation of regulatory genes (Transcription Factors, TFs).**

Several families of TFs are involved in the regulation of stress responsive genes (ERF/AP2, bZIP, ,MYB, MADSbox,…)

PNAS 2006 103(35):12987-92

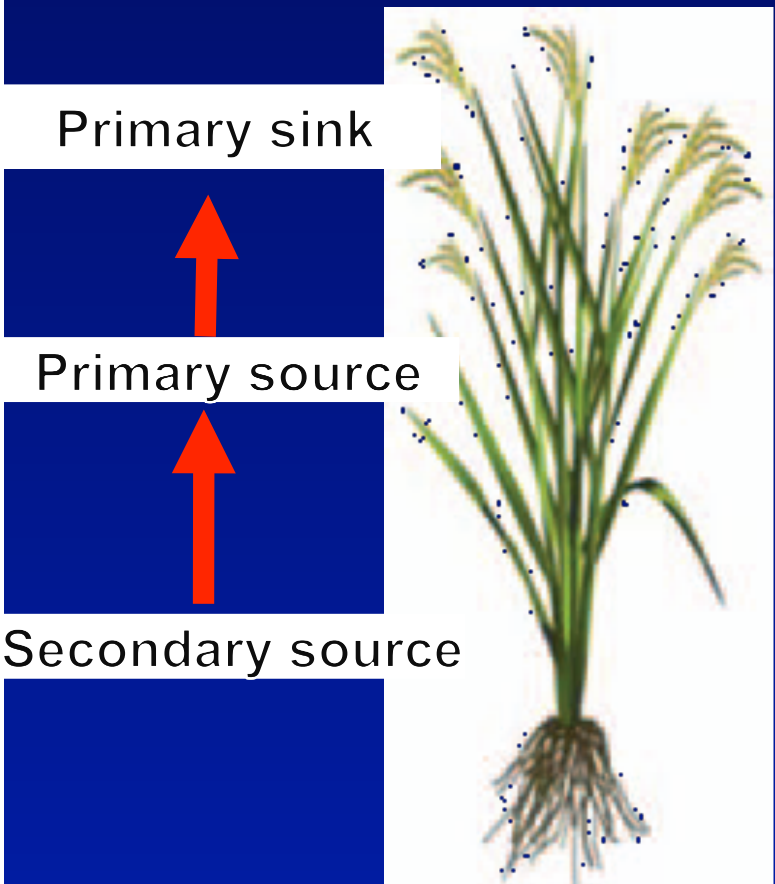
- **Modifications of hormone homeostasis**



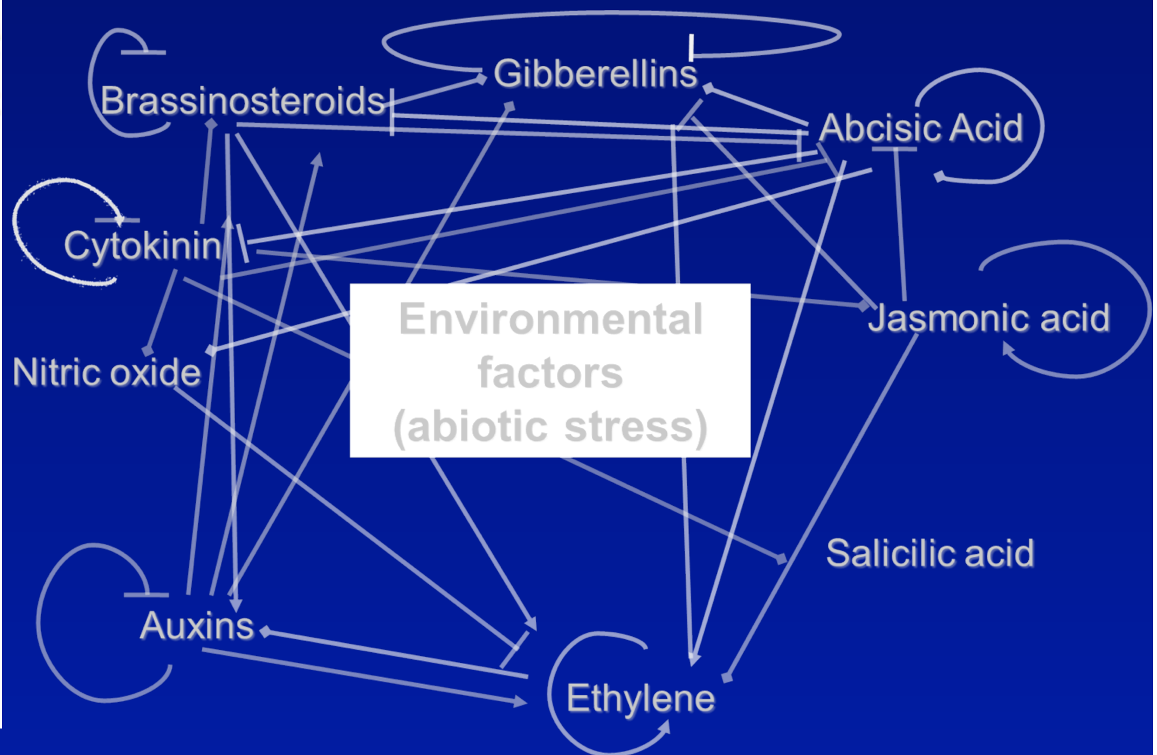
Phytohormones regulate every aspect of plant growth, development and plant responses to environmental changes.

Journal of Experimental Botany, Vol. 65, No. 2, pp. 453–464, 2014

Drought stress accelerate senescence of plants, modifying sink/source relationships

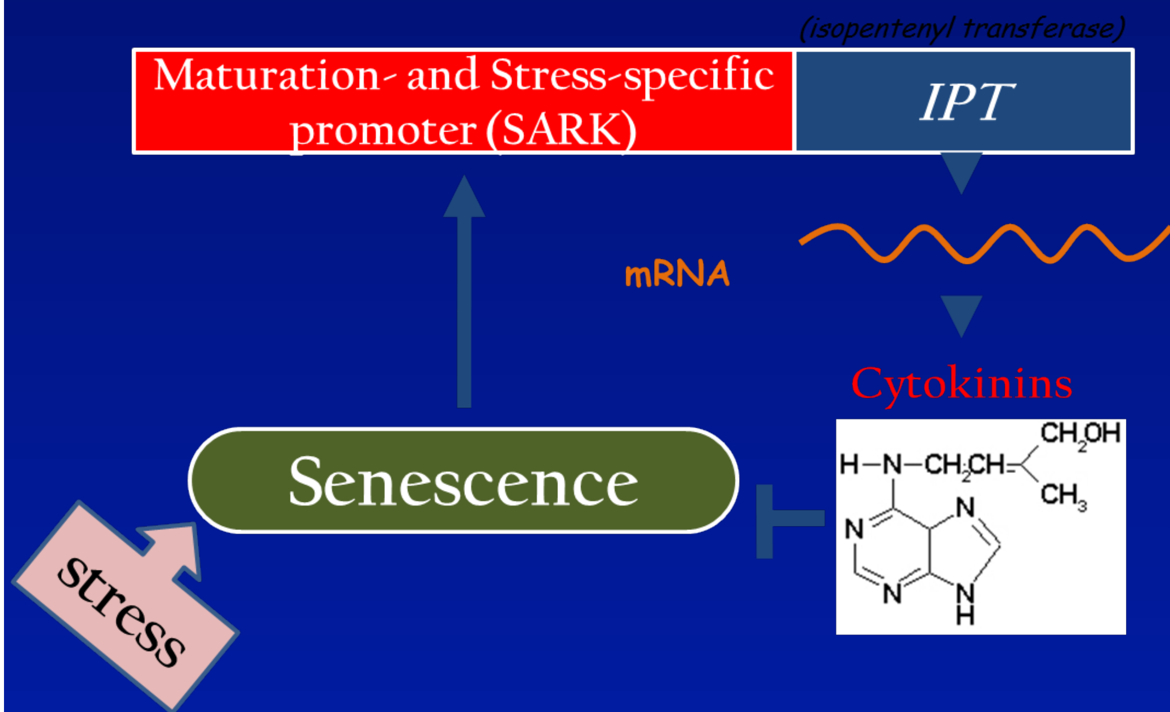


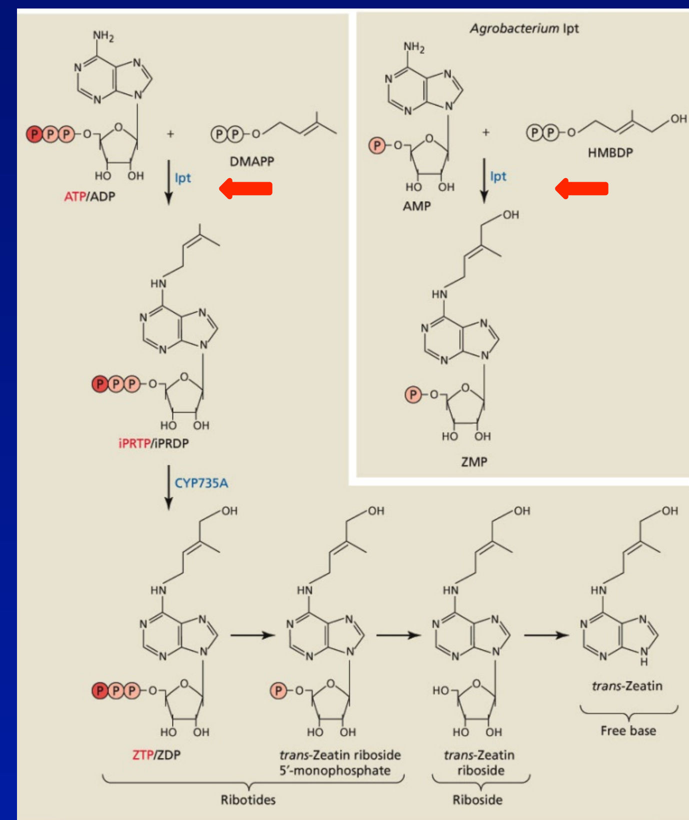
Hormones are key regulators of source/sink relationships



Hypothesis

It is possible to enhance the tolerance of plants to abiotic stress by delaying stress-induced senescence, increasing source fitness and improving source/sink relationships





Improved drought stress tolerance in Tobacco plants expressing *PSARK::IPT*

Rivero et al. 2007; 2009; 2010

Nicotiana tabacum **as a model plant**

Wild-type and transgenic plants expressing Isopentenyltransferase (IPT) under the control of SARK promoter after 15 days Drought followed by 7 days Re-watering.

Wild Type

P_{SARK}::*IPT*

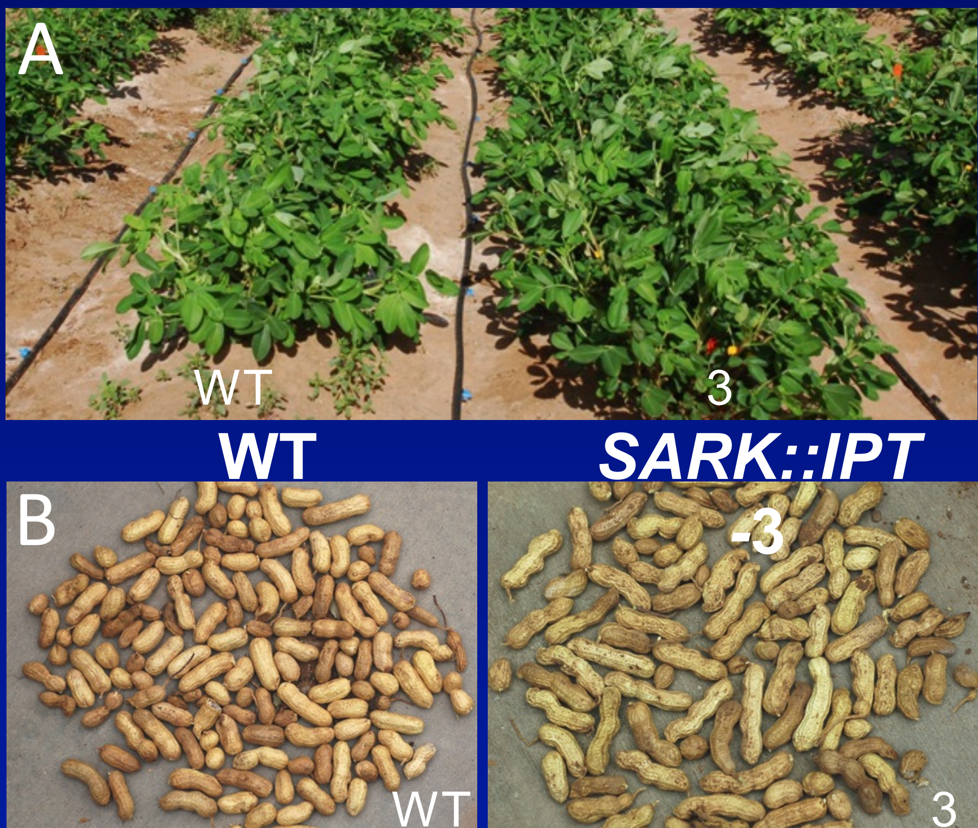
-Expression of *IPT* during drought alters **hormone homeostasis** and improves **source/sink relationships**.

-Induction of **CK** results in higher leaf starch and sucrose contents, and an **inhibition of sucrose degradation** that prevents the increase of glucose and fructose contents.

-Metabolite, enzyme and transcriptomic profiling revealed a **delay in stress associated degradation processes**, including **protein stability and chloroplast function**.

-The cytokinin dependent **coordination of C and N metabolism** ensured an adequate supply of energy, reducing power and organic compounds that ultimately **enhanced survival of P_{SARK}::*IPT* plants under water stress**.

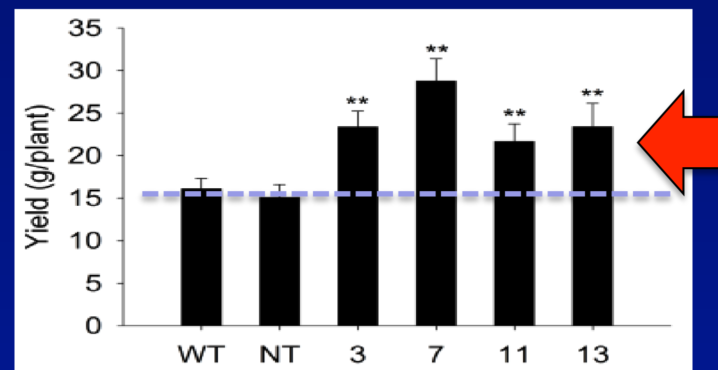
Regulated Expression of an Isopentenyltransferase Gene (IPT) in Peanut Significantly Improves Drought Tolerance and Increases Yield Under Field Conditions



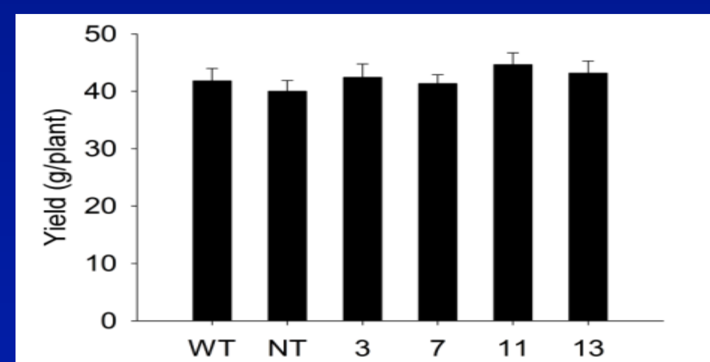
Wild-type and transgenic **peanut plants in the field** and phenotype of pods from these peanut plants.

Seed Yield

B. 2010 Field Trial (dryland)



C. 2010 Field Trial (irrigated)



Qin et al., (2011) Plant Cell Physiol 52:1904-14

Targeted inhibition of hormones using Chemical Genomics to identify stress response pathways

- Overall, the specific inhibition of either **GA, BR or Auxins**, negatively affected GY and plant biomass while the inhibition of **ABA or Ethylene** resulted in the improvement of GY and plant Biomass though the strengthening of source fitness in rice.

- These results will help identifying hormone related pathways that can be manipulated to improve rice productivity.

In progress

- Drought Tolerant Oilseed Rape engineered to reduce the levels PARP [poly(ADP-ribose) polymerase], a key stress-related protein in plants. Relative yield increases of up to +44% compared to non-drought tolerant varieties.
- Bayer CropScience . Mutation that changes the activity of farnesyltransferase. Maize, cotton, oilseed rape and rice, to develop a new generation of stress-tolerant, high-performance crop varieties
- Pioneer Hi-Bred International is developing hybrids and varieties that use water sources more efficiently and therefore perform better during water deficits.
- Maintaining yields during water stress will help preserve grower incomes and yield more grain for the food and energy value chain as well as reducing the need for irrigation.

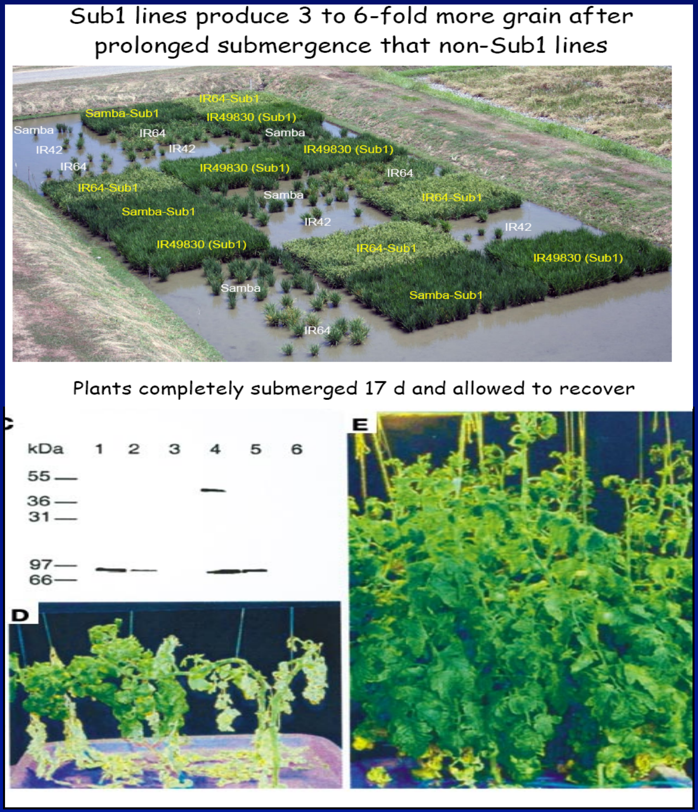
Climate change can prevent crops from reaching their potential

- **Submergence sub -1 gene produces 6X grain - save 3 mil tons rice**

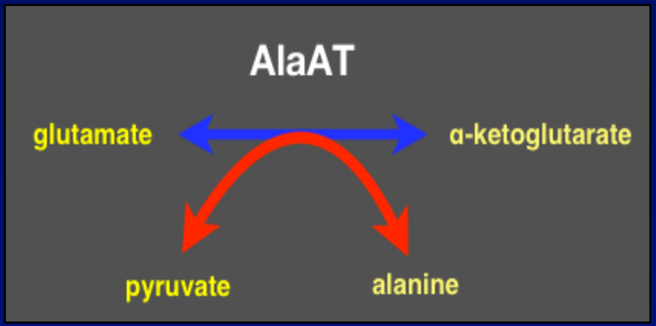
- **Arabidopsis antiporter gene used to create plants that can grow and yield fruit in irrigation water that is more than 50 times saltier than normal (1/3 as salty as sea water).**

- **Cold: Engineering with COR15a Tf, role in freezing tolerance.**

- **Plants engineered with Choline oxidase (codA) tolerated saline and cold**



Nutrient access implications



- **Arcadia has produced plants with increased Nitrogen Use Efficiency (NUE). These plants yield the same as conventional plants, but use 30% less nitrogen and are licensed to China.**

- **Phosphite rather than phosphate also control weeds**

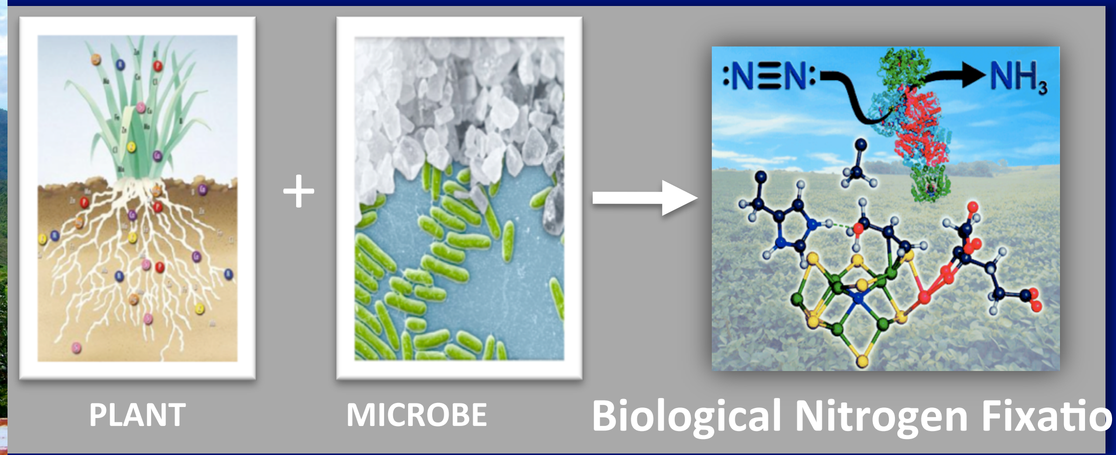
- **Plant Microbiome- Engineering plants for natural Nitrogen fixation**

Biological Nitrogen Fixation – bacteria harness the sun

$$N_2 + 8H^+ + 8e^- + 16\ ATP \longrightarrow 2NH_3 + H_2 + 16\ ADP + 16\ Pi$$

N_2 Fixation an energy "expensive" reaction

N_2 and Plant-associated bacteria in a novel glycan



<u>Hypothesis:</u> indigenous landraces of corn grown in isolated regions of Mexico co-evolved diazotrophic microbiomes that contribute to plant performance due to nitrogen deficiency in the soil.

Biotic Stresses also changing in response to Climate change

- Potato Late Blight – 75% crop loss
  - 2 genes from wild potato - Less spray, less loss = $4.3 billion potential savings
- Hawaiian Papaya
  - Biotechnology saved the industry in Hawaii No natural resistance so traditional breeding will not work Removes viral reservoir thus protects all growers
- Apple
  - Fireblight: Peptide alternative to antibiotic sprays
  - Applescab: Chitinase alternative to fungicides
- Citrus Greening
  - No natural resistance so traditional breeding will not work – biotech the only solution
- Grapes - Pierce's disease
  - Fusion of two genes innate immunity and membrane lysis - Preferable to spraying malathion

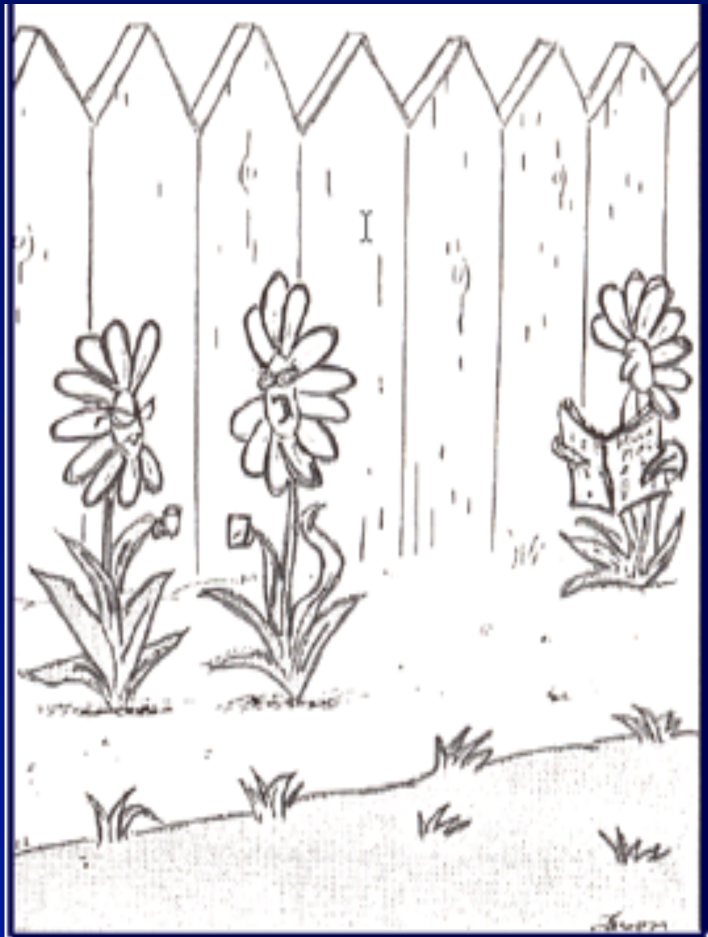
Myth: Biotech crops are not regulated

- Most thoroughly regulated of any process in crop breeding – USDA (APHIS), EPA, FDA
  - Commercialization: 7 to 10 years, at least 9 stages
- Biotech crops and foods more thoroughly tested than conventional varieties which have "GRAS" status
- >150 livestock feeding studies
- Substantially equivalent to parent in composition, nutritional content, allergenicity potential, protein digestibility, anti-nutritional effects, toxicity studies
  - Highly sensitive profiling technology shows GM crop more like parent than ANY other breeding technique
- International consensus: OECD, CBD, CODEX

Potential Relative Risks with Biotechnology

- **Health/ Food Safety http://www.ilsi.org/AboutILSI/ifbic.htm**
  - Novel Toxins
  - Novel Allergens
  - Instability
  - Lack of specificity – pleiotropic effects
  - Antibiotic Resistance
  - Diminished Nutrition Value
  - Lack of knowledge of components
  - Gene Flow- Active Therapeutics
  - Transgenic animals (Mammals, Fowl, Fish, arthropods)

- **Environmental Impact**
  - Gene Flow – genetic pollution novel pests/weeds
  - Novel Pathogens
  - Effect on non-target species
  - Loss of effectiveness
  - Pest pressure shifts
  - Reduced diversity - Monocultures
  - Coexistence – economic construct
  - Feral animals – interbreeding, displacement, niche disruption



"I don't have any hard evidence, Connie--but my intuition tells me that Ed's been cross-pollinating.

Risk Management

- Antibiotic Resistance (perceived not scientific)
  - Transposon tagging
  - Positive selection – exclusive energy source
- Gene Flow-
  - Space
  - Male sterility
  - "Terminator" technology
  - Chloroplast transformation
- Lack of specificity – pleiotropic effects (expected, unexpected)
  - Site-specific recombination
  - Cre-Lox
- Effect on non-target species
  - Tissue specific expression
  - Chloroplast transformation
- Loss of effectiveness – resistance management
  - Refugia
  - Gene Pyramiding, Gene shuffling
- Reduced diversity
  - More sources of genetic diversity – rescue heritage varieties and landraces
- Novel animals – Food safety, feral potential
  - Physical and Biological containment

Relative Risk V. Benefit

- Out of the world's total land area of 13 billion hectares (ha), 12% is cultivated but the future expansion of farmland for food production will be slower than in the past. (FAO)
- In the next 30 years, developing countries will need an additional 120 million ha for crops according to the FAO, this means, less new land will be opened up than in the past.
- Some countries and communities will face problems related to land scarcity. This will strengthen their dependency to food and feed import.
- Genetically modified crop varieties are the most cost-effective way to sustain farming in marginal areas and to restore degraded lands to production.
- If we want to feed the world without destroying our resources, science and technology should drive the development of modern agriculture.

Professional scientific and/or medical bodies with an opinion on safety of GMOs

- <u>Generally Positive</u>
  - The U.S. National Research Council (NRC)
  - U.S. National Academy of Sciences (NAS)
  - The American Medical Association, (AMA)
  - U.S. Department of Agriculture (USDA)
  - U.S. Environmental Protection Agency (EPA)
  - U.S. Food and Drug Administration (FDA)
  - European Food Safety authority (EFSA)
  - American Society for Plant Biology (ASPB)
  - World Health Organization (WHO)
  - Food and Agriculture Organization (FAO)
  - Royal Society (London)
  - Brazil National Academy of Science,
  - Chinese National Academy of Science
  - Indian National Academy of Science
  - Mexican Academy of Science
  - Third World Academy of Sciences
- <u>Generally Negative</u>

Threats that harm and those that upset are often quite different

It is all about Adaptation!