The ultimate in Genetic Engineering

SCIENCE'S COMPASS

POLICY FORUM: GENETICS

Ethical Considerations in Synthesizing a Minimal Genome

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"The prospect of constructing minimal and new genomes does not violate any fundamental moral precepts or boundaries, but does raise questions..."

Will it be possible to create "life" beginning with a genome sequence?

(1) Create new organisms to study critical Life processes — origins of life, bacterial evolution, control of cell metabolism, etc.

(2) Designer bacteria for specific tasks — e.g., breakdown of environmental toxins

(3) How does this experiment change our views of what life is? OR does it!?

What is Genetic Engineering?

Directed Genetic Change

a. Classical Breeding - new gene combinations

b. Molecular Genetic Engineering - DNA technology

(1) Reconstructing genes
(2) Modifying genes
(3) Synthesizing genes
(4) Combining genes from different organisms
(5) Cross species barrier! Mouse genes → plants!
(6) Synthesizing whole genomes!!

Altering Genetic Makeup of an organism for:

(1) Basic Science
(2) Medicine
(3) Agriculture
(4) Environment
(5) Biology factories
(6) The Law
(7) Commerce
etc.!

IN ITS SIMPLEST FORM

GENETIC Engineering

Means.....

(1) ISOLATING A Gene FROM a CHROMOSOME of An Organism AND

(2) CLONING (REPLICATING IDENTICAL COPIES) the Gene in BACTERIAL CELLS (CLONING DNA/genes in cells - not cell/organism cloning)

(3) TO: (1) Study A/That Gene

(2) ultimately Find out what it Does

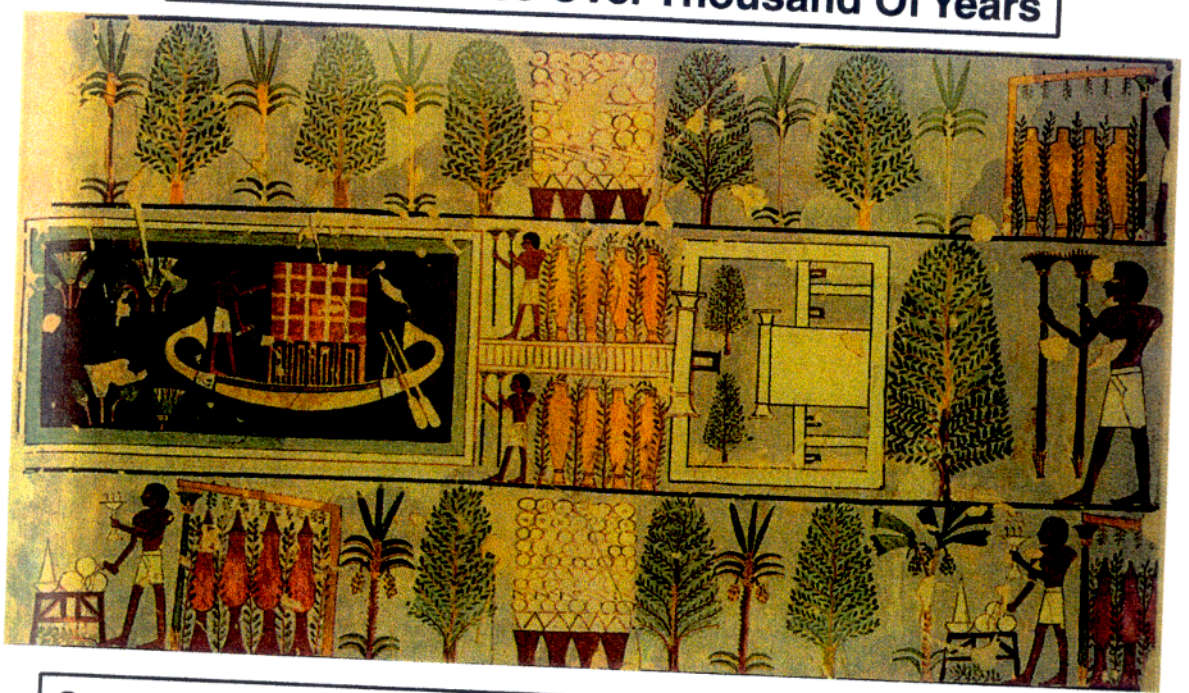
Using Bacteria As FACTORIES to Produce Large Amounts of ONE Gene For Study

BUT THE USE, BENEFITS, AND IMPLICATIONS ARE MUCH, MUCH Bigger!

GENETIC MANIPULATION / ENGINEERING

ANYTHING NEW?

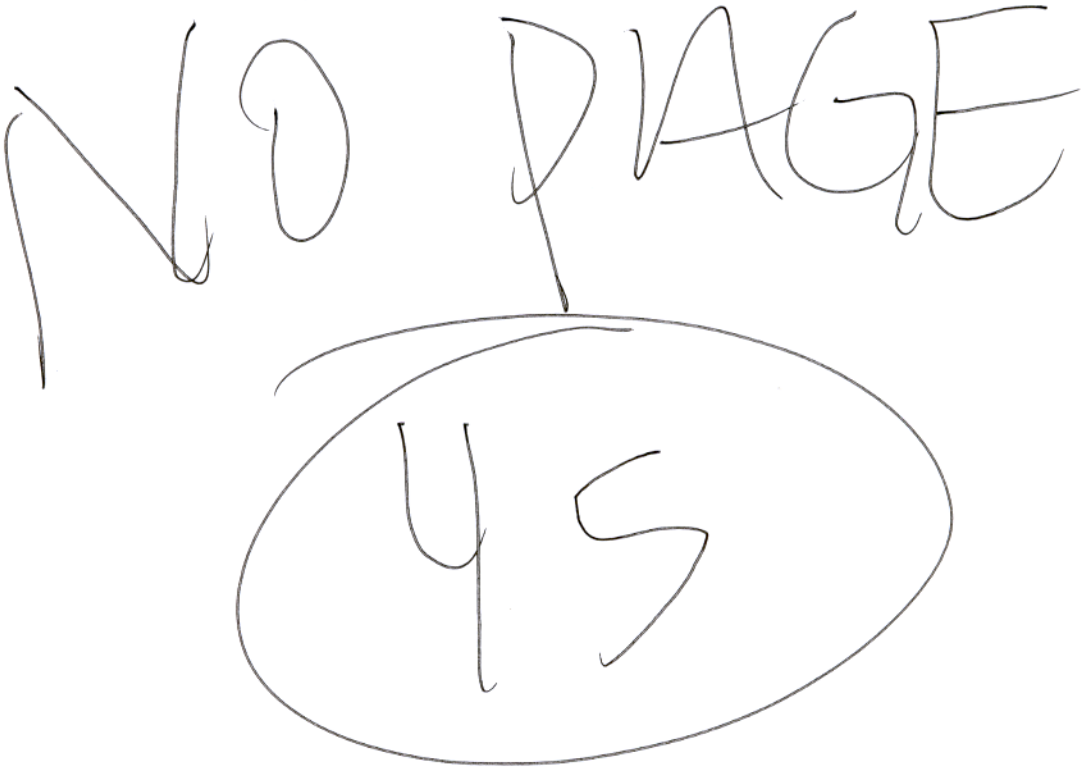
Breeding And Cultivation Of Plants Have Taken Place Over Thousand Of Years



Genetic Engineering is Not New

Crops of Egypt 400 B.C.

DNA Demo



FARM ANIMALS WERE ALSO "ENGINEERED" BY BREEDING WILD RELATIVES

Notice Variability in traits —

Figure 11-2 The ancient Egyptians were successful cattle breeders. This miniature stable, which dates from about 2000 BC, shows longhorn cattle. Other cattle breeds had short horns or no horns. *(Metropolitan Museum of Art, Rogers Fund and Edward S. Harkness Gift, 1920)*

CATTLE BREEDING in Egypt 4000 years Ago!

Manipulating Existing Genetic Variability

Variability Brought About By Chance Mutation!

Biologists chase down pooches' genetic and social past

A Shaggy Dog History

Dog father. Dogs might have evolved from an ancestor of this Chinese wolf.

Traced Using DNA Testing!

CAV only arise by selecting for existing variability

What are the genetic differences & How did they Arise?

Science V. 298 (2002)

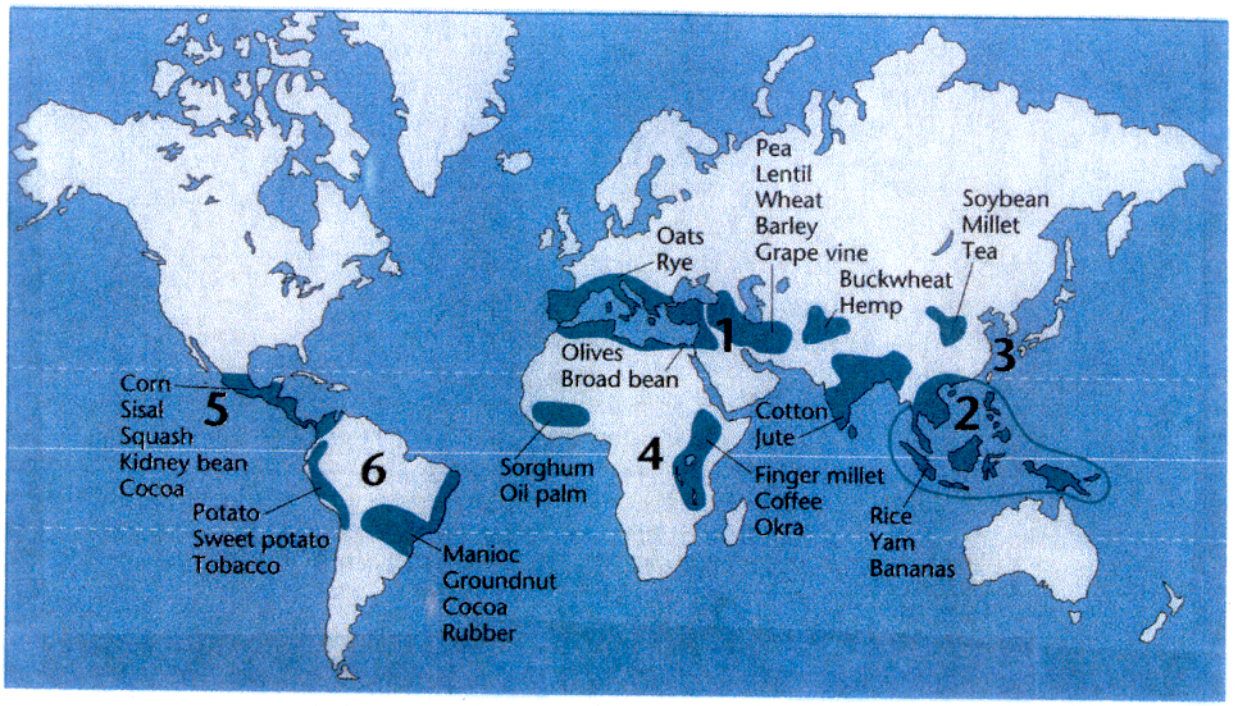
15,000 years ago in Europe Asia

Genetic VARIability

Common pedigree. From Chihuahuas (*left*) to Great Danes, dogs of all shapes and sizes share common ancestors.

MAJOR CROPS WERE "ENGINEERED" FROM NON-PRODUCTIVE WILD RELATIVES 13,000 years Ago!

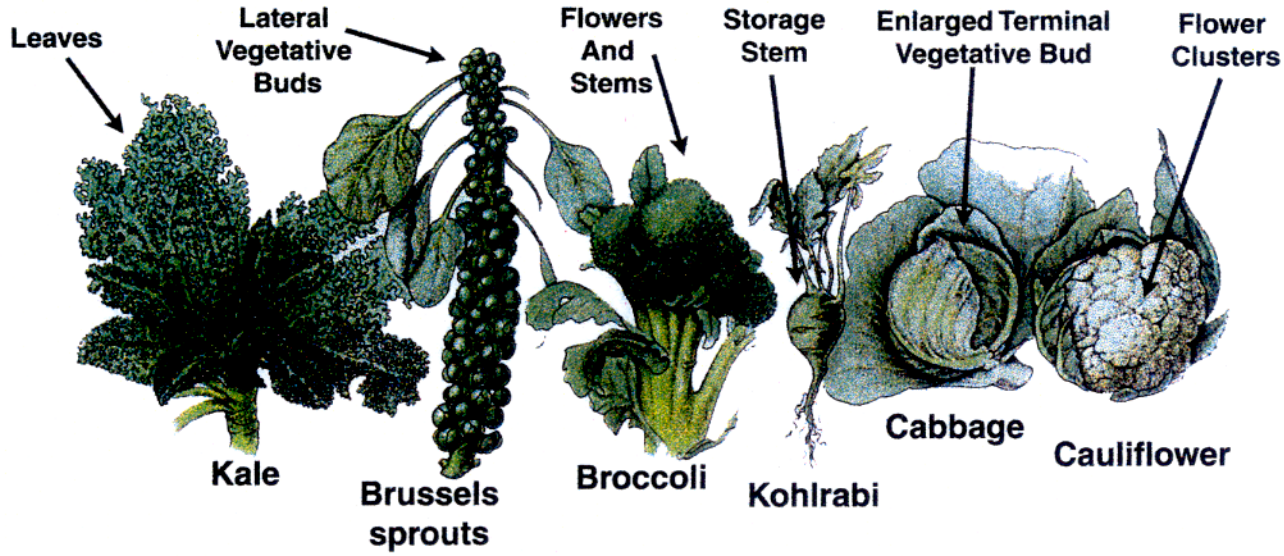
Regions Where Major Crops Were Established



Breeding involves gene Manipulation!

Using Existing Gene Variability!

Breeders Have Selected For Variability In Plant Control Genes To Generate Novel Crops

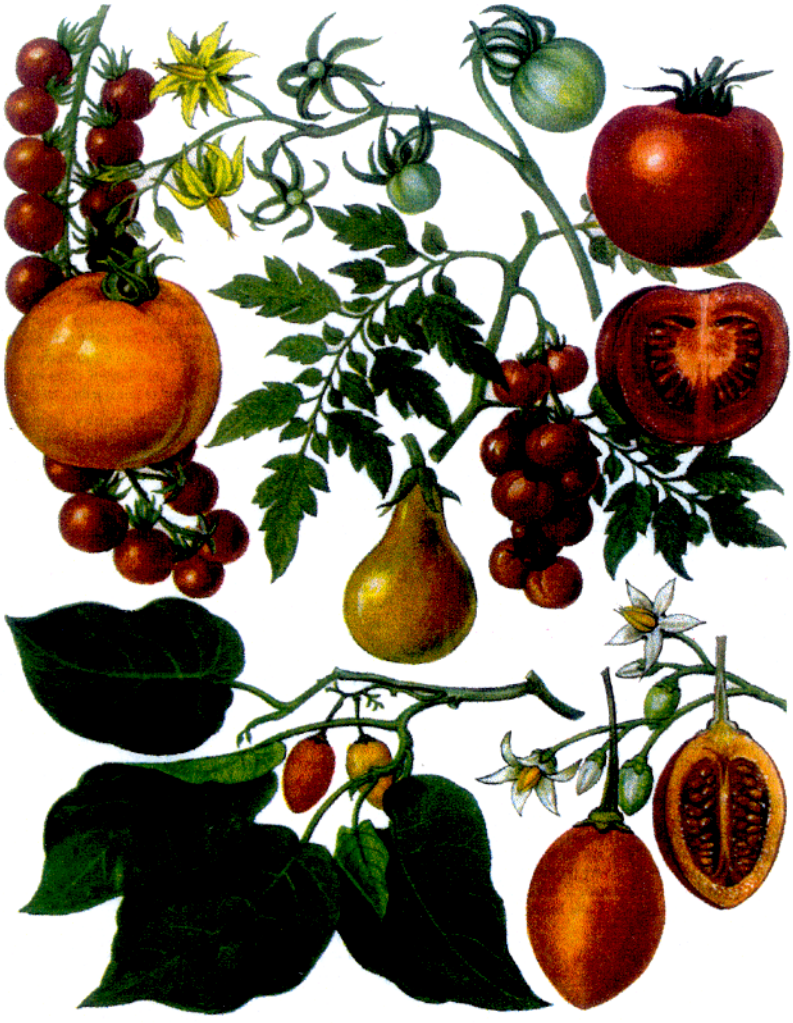


How Are These Plants Related?

Breeding For Parts of Plants!
What is Being Manipulated?

Breeding Uses Natural Variability of Genes As Raw Material

Tomato Genetic Diversity

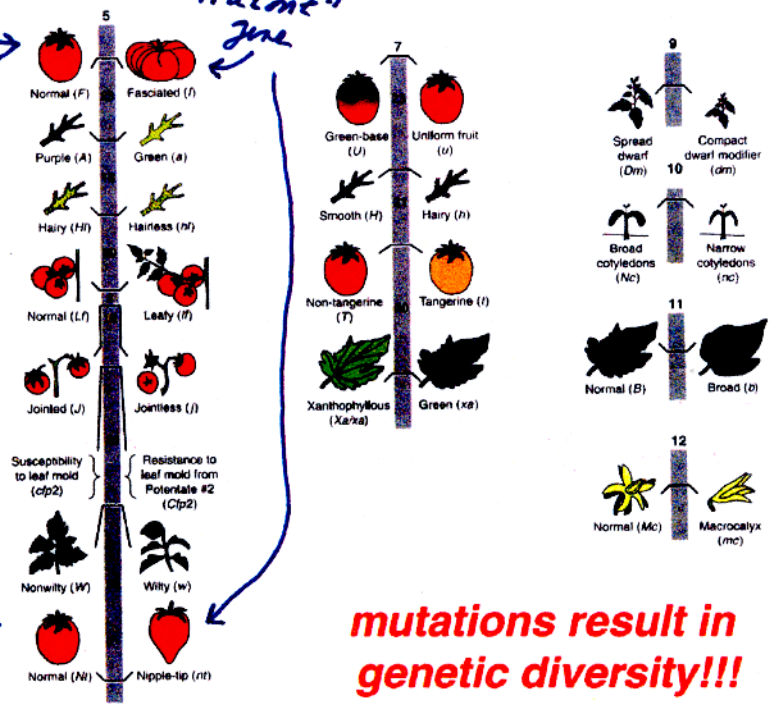


Diversity generated by Mutations in a gene that change its Chemical Sequence & Slightly Alters its function

Alternative Forms of the Same Gene Lead to Genetic Diversity

"normal" gene

"mutant" gene

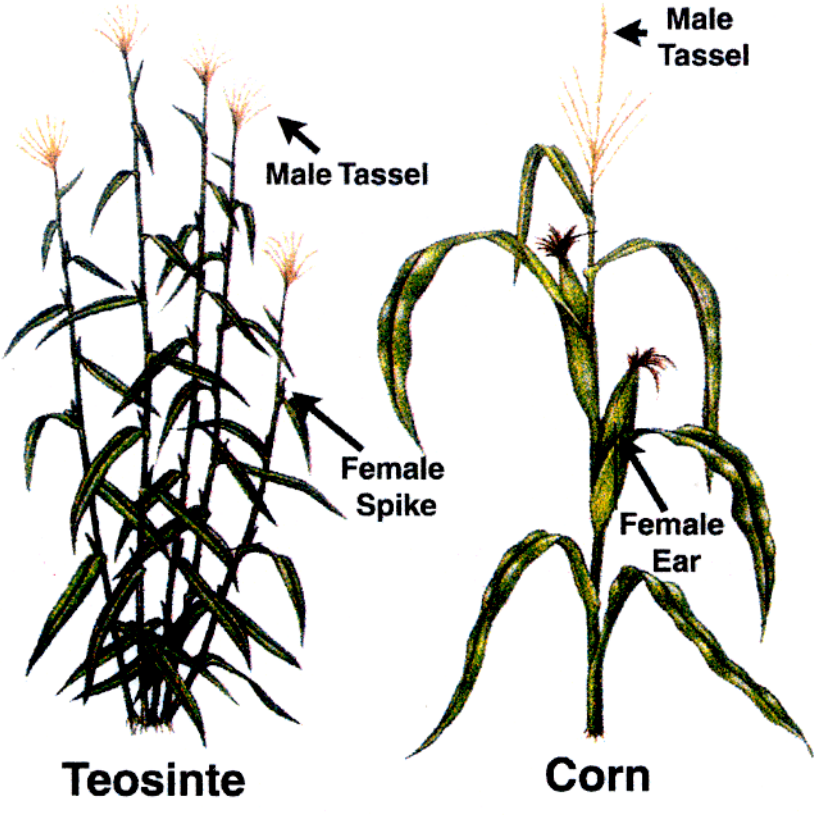


12 Chromosomes
Different Genes

mutations result in genetic diversity!!!

What is the Relationship Between the Mutant & Normal Gene?

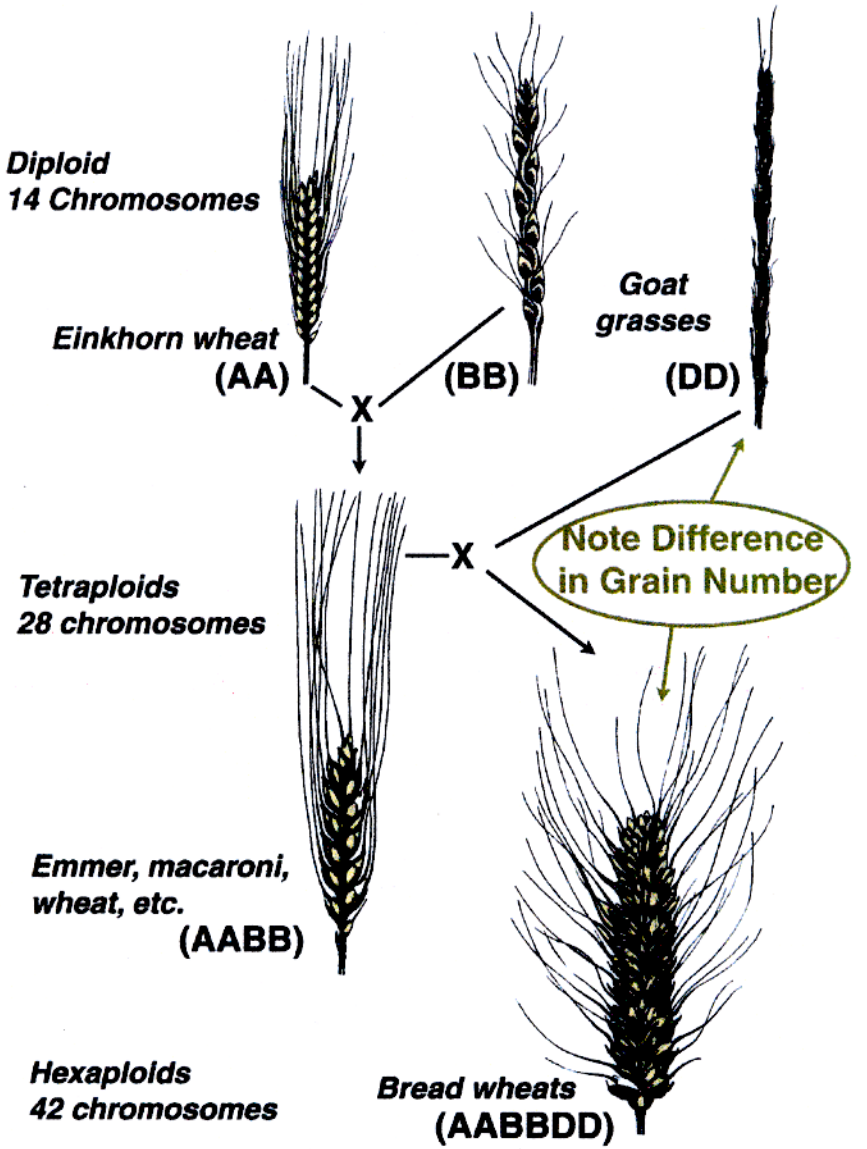
Corn And Its Ancestor Teosinte



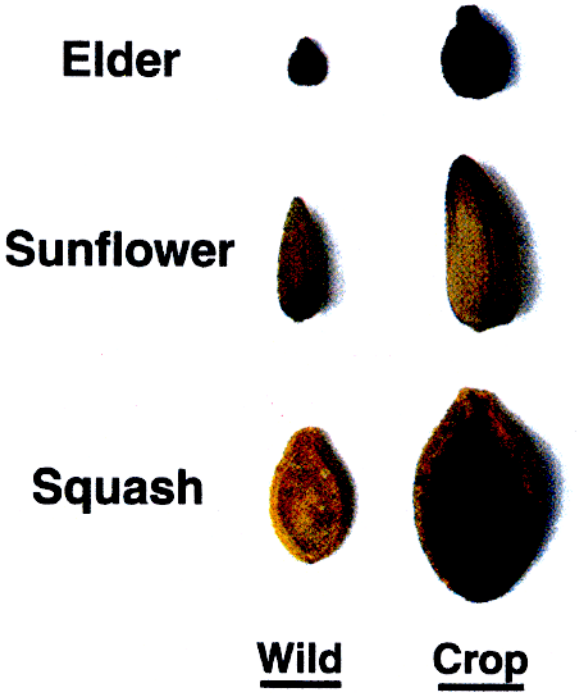
Note Differences in Plant Architecture Yet They Are The Same Species

ONLY 5 genes CAUSE these PLANTS to be different!

Domestication of Wheat



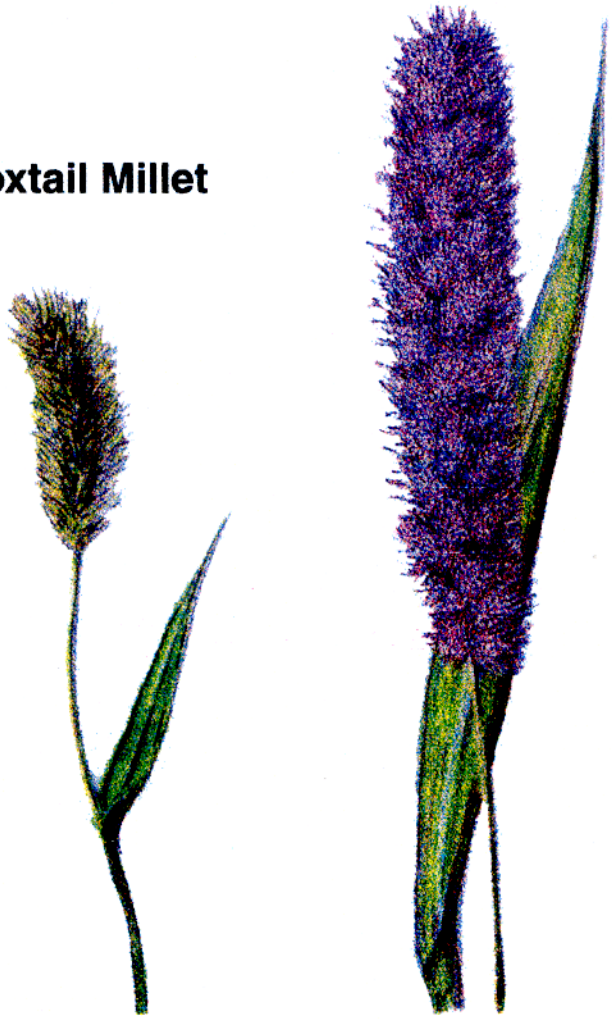
Domesticating Crops Caused Increased Seed Size



∴ Selected for genes controlling size of seeds! Because that's what WAS consumed –

Domesticating Crops Caused Increase Seed Head Size

Foxtail Millet



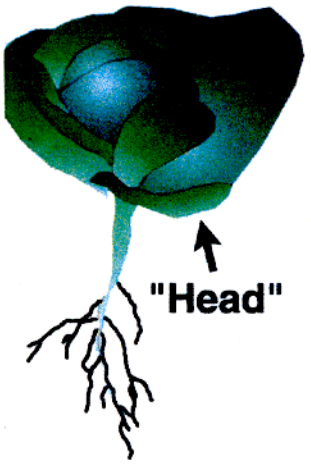
Wild **Domesticated**

∴ Breeding increased size of seeds
↓ number of seeds

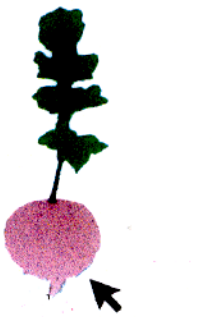
Breeding A "New organism"

Engineering A Novel Crop By "Wide" Breeding

Cabbage (*Brassica*)



Radish (*Raphanus*)

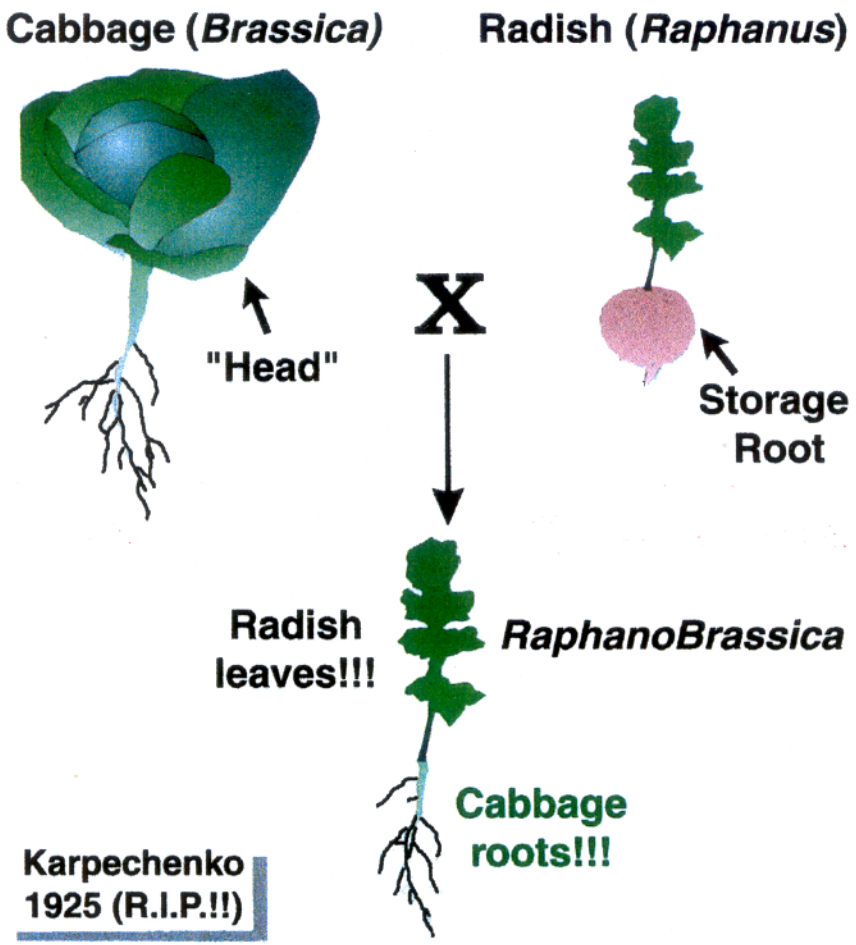


X

???

Karpechenko
1925

Engineering A Novel Crop By "Wide" Breeding



Result shows the unpredictability of classical Breeding Approaches

And Attempts Have Been Made to "Select" out "Bad" Genes in Man.....

Eugenics → Directed Genetic Change in Man

1. Positive – Add "good" genes
2. Negative – Remove "bad" genes

By: Preventing individuals from having children (negative)

OR

Encouraging individuals with the "correct" traits to have children (positive .... or is it.??)

Don't we all do this to a certain extent?

Are there "GOOD" & "BAD" Genes?

BUCK VS. BELL

better "left behind in the cast-off junk of ignorant efforts, with which the past is filled."[41]

By the outbreak of the First World War, sterilization laws were in such dispute as to have been de facto suspended in their operation in a number of states. The courts had also declared unconstitutional not only the stringent Iowa statute but less sweeping measures in six other states. Advocates of eugenic sterilization, frustrated at the legal impasse, wanted to take the issue to the Supreme Court. In Virginia, eugenicists helped draw up a sterilization statute, passed by the legislature in March 1924, that was designed to meet the constitutional objections. The opportunity to press a test case arose that June, when a seventeen-year-old girl named Carrie Buck, who seemed definable as a "moral imbecile," was committed to the Virginia Colony for Epileptics and Feebleminded, in Lynchburg.[42]

Carrie's mother, Emma, had lived at the Colony since 1920 and was also certified to be feebleminded. Carrie herself had conceived a child out of wedlock, and shortly before her commitment, she gave birth to a daughter, Vivian. Carrie was given the Stanford revision of the Binet-Simon I.Q. test and was found to have a mental age of nine years, well within Henry Goddard's definition of "moron." Carrie's mother was found to have a mental age of slightly under eight years. Thus, according to these results, there was mental deficiency in two successive generations. If Vivian could be shown to be feebleminded too, Carrie would be a perfect subject for a test of the Virginia sterilization statute. In September 1924, the Colony's board of directors ordered Carrie Buck sterilized, and a court-appointed guardian initiated legal proceedings by appealing the order in a suit on

's behalf against the superintendent of the Colony, Albert S. Priddy.[43]

In preparing their case, Virginia officials consulted Harry Laughlin at the Eugenics Record Office. Laughlin examined the pedigrees of Carrie, her mother, and her daughter, and information about them given him by Colony officials, and—without ever having seen them in person—provided an expert deposition that Carrie's alleged feeblemindedness was primarily hereditary. Carrie and her forebears, Laughlin submitted, "belong to the shiftless, ignorant, and worthless class of anti-social whites of the South." At the time of Laughlin's deposition, however, there was no evidence at all that Vivian was mentally deficient. To clarify the matter, Caroline E. Wilhelm, a Red Cross worker who had placed Vivian in a foster home, was prevailed upon to examine her there. At the initial hearing, in the Circuit Court of Amherst County, she testified that there was "a look" about Vivian (who at the time of the visit was seven months old) which was "not quite normal." Evidence also came from Arthur Estabrook of the Eugenics Record Office, who had subjected Vivian to a mental test for an infant and concluded that she was below average for a child her age. In the court

proceeding, Estabrook testified that the feeblemindedness in the Buck line conformed to the Mendelian laws of inheritance, and the judge upheld the sterilization order.[44]

The case—now known as *Buck* v. *Bell*, because Priddy had in the meantime died and been replaced as the defendant by the Colony's new superintendent, John H. Bell—was carried to the Virginia Supreme Court of Appeals in 1925, and the sterilization order was again upheld. In April 1927 it was argued before the United States Supreme Court. Carrie's defense counsel, I. P. Whitehead, a onetime member of the board of directors of the Colony, attacked the sterilization statute, warning that under this type of law a "reign of doctors will be inaugurated and in the name of science new classes will be added, even races may be brought within the scope of such a regulation and the worst forms of tyranny practiced." Nevertheless, the Court was persuaded not only that Carrie Buck and her mother were "feebleminded" but also—because Vivian was, too (or so all the experts said)—that the feeblemindedness was heritable. The Court, whose membership ranged in political conviction from William Howard Taft to Louis D. Brandeis, upheld the Virginia statute by a vote of eight to one. The sole dissenter was Justice Pierce Butler, a conservative, and he kept his minority opinion to himself. The decision declared that sterilization on eugenic grounds was within the police power of the state, that it provided due process of law, and that it did not constitute cruel or unusual punishment.[45]

The Court's opinion was written by Justice Oliver Wendell Holmes, an enthusiast of science as a guide to social action, who managed to find a link between eugenics and patriotism: "We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be strange if it could not call upon those who already sap the strength of the State for these lesser sacrifices . . . in order to prevent our being swamped with incompetence. . . . The principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes." With deliberate punch Holmes asserted: "Three generations of imbeciles are enough."[46]

Eugenicists naturally rejoiced at *Buck* v. *Bell*. For some years prior to the decision, the American Eugenics Society had promoted what it thought might be a constitutional revision of the faulty sterilization statutes. Apart from procedural and technical changes, the revisions centered on making the laws eugenic rather than punitive in intent. After *Buck* v. *Bell*, what was constitutional was clear. By the end of the nineteen-twenties, sterilization laws were on the books of twenty-four states, with the South no longer a regional exception. (Though now severely restricted by federal regulation, they are still on the books of twenty-two states today.) The laws were not uniformly enforced, but Carrie Buck was sterilized soon after the Court's

decision, and officials at the Virginia Colony subjected other inmates to the procedure—a total of about a thousand in the next ten years. By the mid-thirties, some twenty thousand sterilizations had been legally performed in the United States.[47]

Buck v. *Bell* generally stimulated either favorable, cautious, or—most commonly—no editorial comment. Few if any newspapers took notice of the impact of the decision on civil liberties in the United States. The I.Q. tests used in the Buck case have long since been discredited as indicators purely of general intelligence. With regard to the allegedly hereditary nature of mental defect in the Buck line, it is of interest that Carrie's daughter Vivian went through the second grade before she died of an intestinal disorder in 1932. Her teachers reportedly considered her very bright.[48]

BUCK VS. BELL

BUCK v. BELL

274 U.S. 200 (1927).

MR. JUSTICE HOLMES delivered the opinion of the Court.

This is a writ of error to review a judgment of the Supreme Court of Appeals of the state of Virginia, affirming a judgment of the Circuit Court of Amherst County, by which the defendant in error, the superintendent of the State Colony for Epileptics and Feeble Minded, was ordered to perform the operation of salpingectomy upon Carrie Buck, the plaintiff in error, for the purpose of making her sterile. The case comes here upon the contention that the statute authorizing the judgment is void under the Fourteenth Amendment as denying to the plaintiff in error due process of law and the equal protection of the laws.

Carrie Buck is a feeble minded white woman who was committed to the State Colony above mentioned in due form. She is the daughter of a feeble minded mother in the same institution, and the mother of an illegitimate feeble minded child. She was eighteen years old at the time of the trial of her case in the Circuit Court, in the latter part of 1924. An Act of Virginia, approved March 20, 1924, recites that the health of the patient and the welfare of society may be promoted in certain cases by the sterilization of mental defectives, under careful safeguard, & c.; that the sterilization may be effected in males by vasectomy and in females by salpingectomy, without serious pain or substantial danger to life; that the Commonwealth is supporting in various institutions many defective persons who if now discharged would become a menace but if incapable of procreating might be discharged with safety and become self-supporting with benefit to themselves and to society; and that experience has shown that heredity plays an important part in the transmission of insanity, imbecility, & c. The statute then enacts that whenever the superintendent of certain institutions including the above named State Colony shall be of opinion that it is for the best interests of the patients and of society that an inmate under his care should be sexually sterilized, he may have the operation performed upon any patient afflicted with hereditary forms of insanity, imbecility, & c., on complying with the very careful provisions by which the act protects the patients from possible abuse.

The superintendent first presents a petition to the special board of directors of his hospital or colony, stating the facts and the grounds for his opinion, verified by affidavit. Notice of the petition and of the time and place of the hearing in the institution is to be served upon the inmate, and also upon his guardian, and if there is no guardian the superintendent is to apply to the Circuit Court of the County to appoint one. If the inmate is a minor notice also is to be given to his parents if any with a copy of the petition. The board is to see to it that the inmate may attend the hearings if desired by him or his guardian. The evidence is all to be reduced to writing, and after the board has made its order for or against the operation, the superintendent, or the inmate, or his guardian, may appeal to the Circuit Court of the County. The Circuit Court may consider the record of the board and the evidence before it and such other admissible evidence as may be offered, and may affirm, revise, or reverse the order of the board and enter such order as it deems just. Finally any party may apply to the Supreme Court of Appeals, which, if it grants the appeal, is to hear the case upon the record of the trial in the Circuit Court and may enter such order as it thinks the