TEXAS A&M UNIVERSITY
Veterinary Medicine
& Biomedical Sciences

Engineering Transformative and Sustainable Food Animal Agriculture

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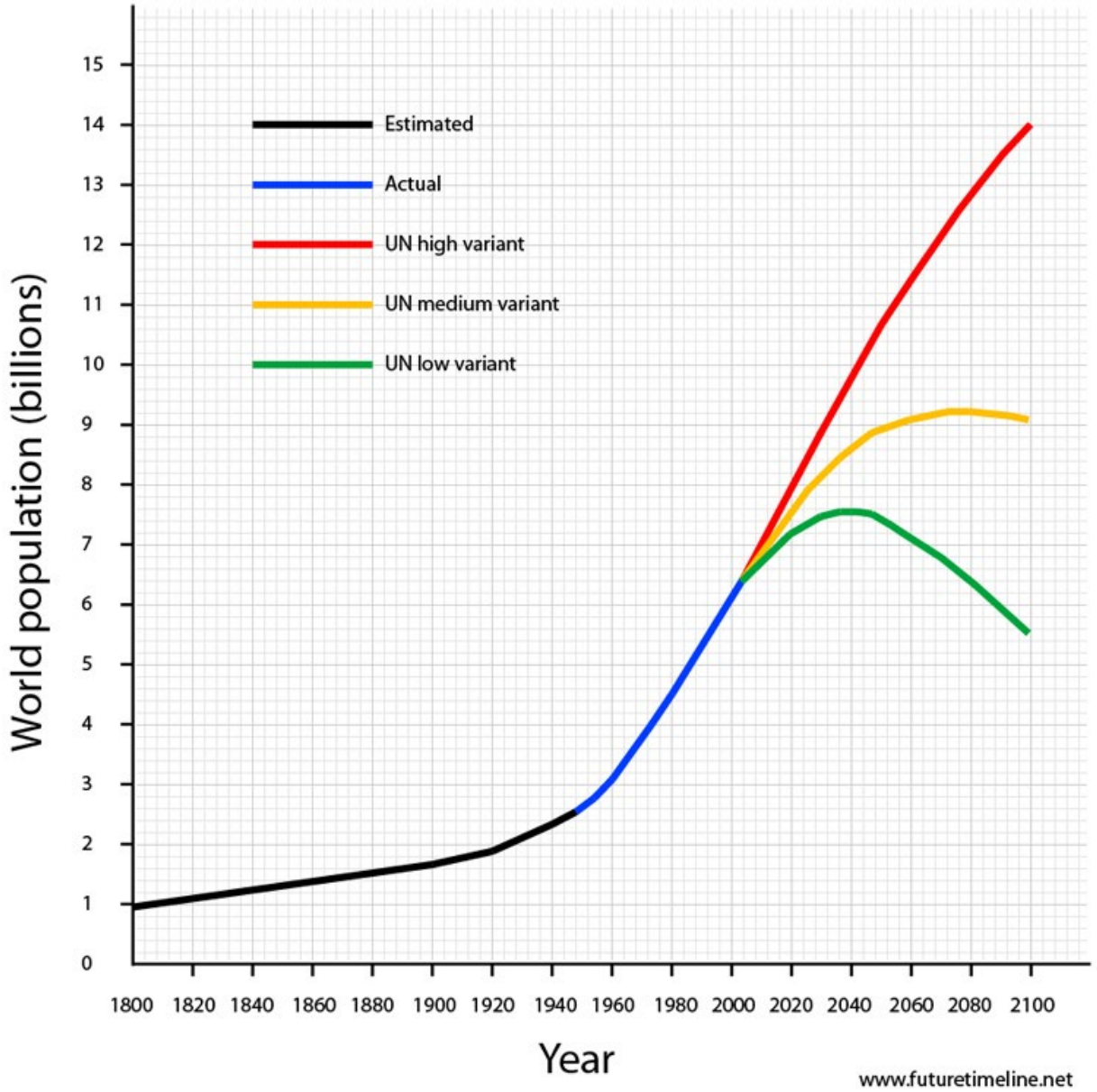
USDA Agricultural Outlook Forum, February 21, 2020, Arlington, VA

How do you sustainably feed 9 billion people in 2050 with less resources in an adverse environment?

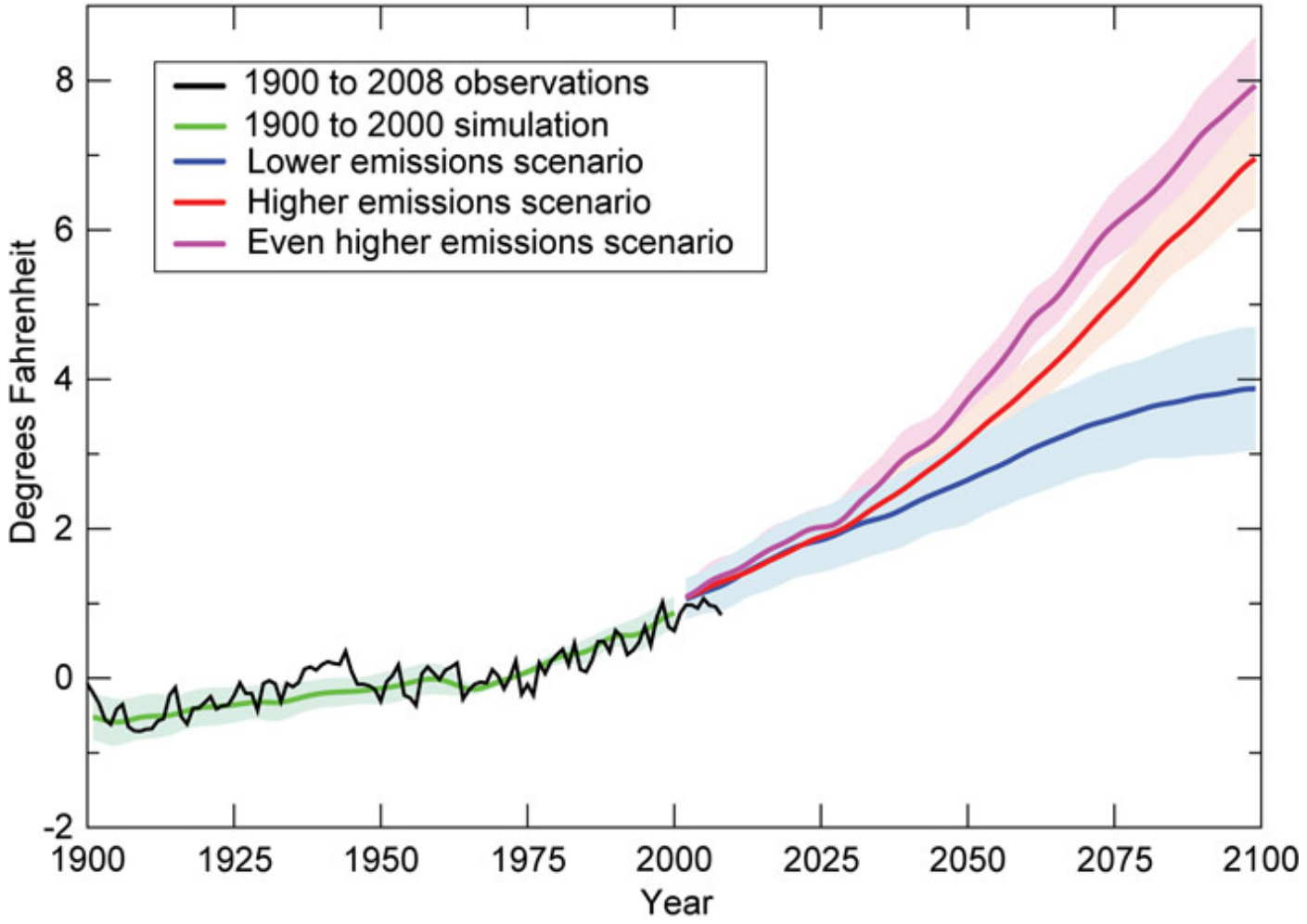
World Population Continues to Increase



Climate Change is Real

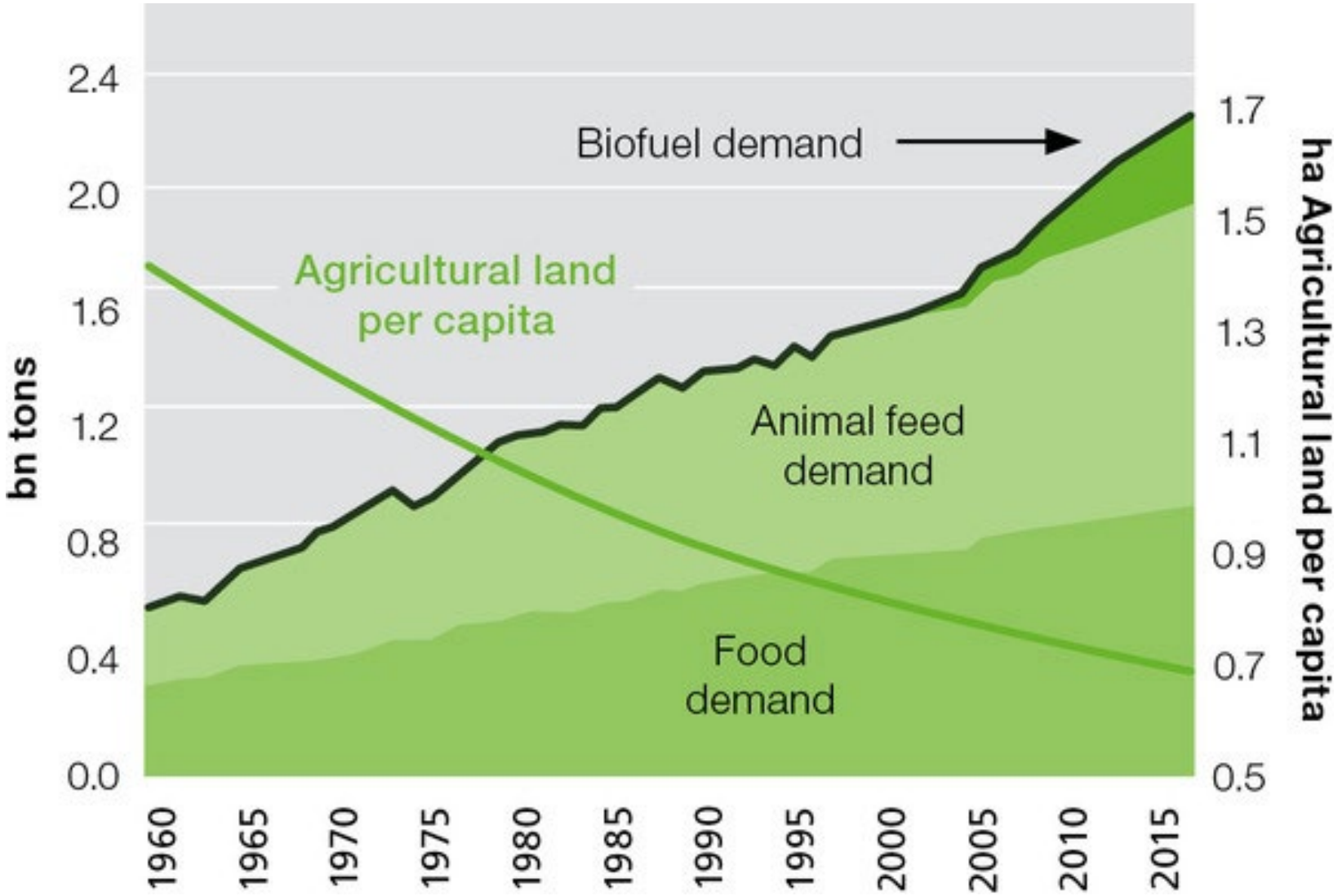
- Increased frequency and intensity of drought
- Increased frequency and intensity of devastating storms
- Rising sea levels
- Water shortages

- Increased stress on livestock and decreased production



USGCRP 2009

We Need More Food With Less Land



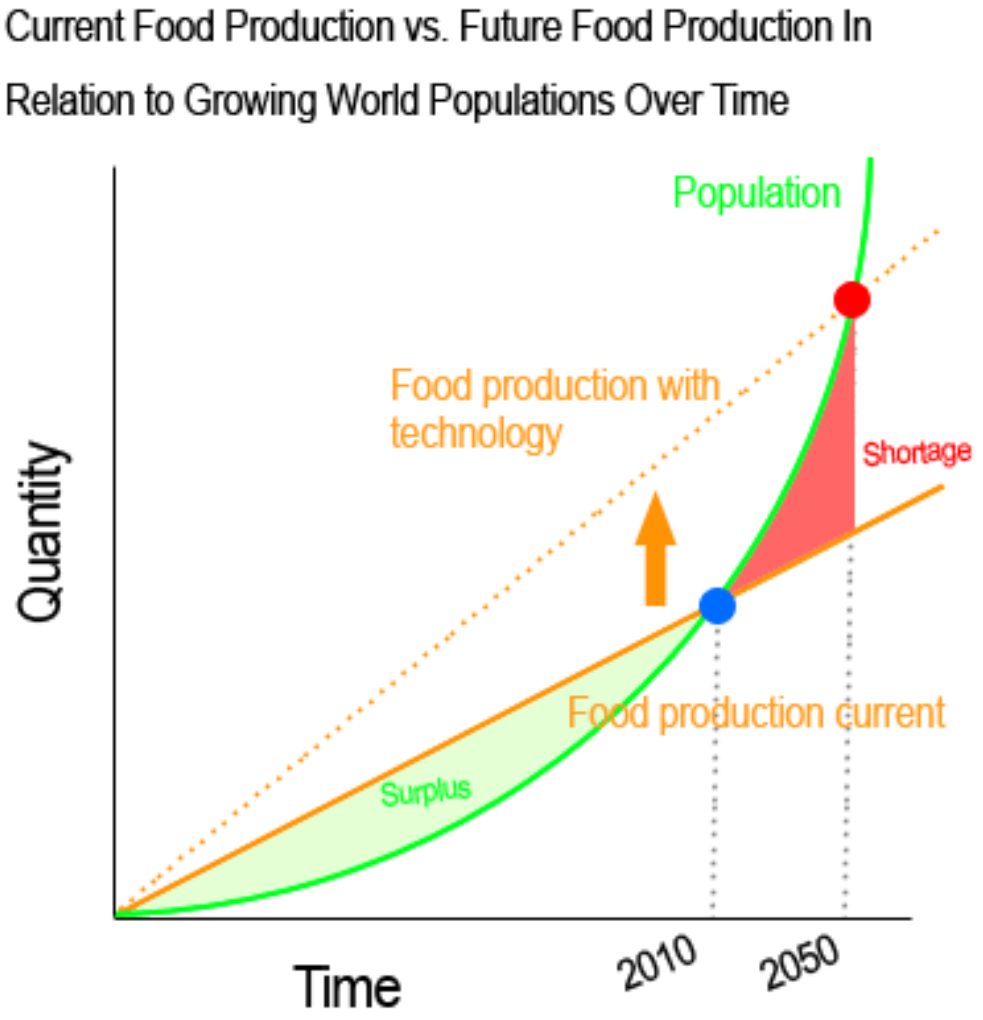
The World Bank, World Resources Institute

The Potential Of Genetically Engineered Livestock

- GE animals with new traits like:
  - Enhanced growth and production
  - Disease resistance
  - Drought and heat tolerance
  - Insect tolerance

- … will allow for high quality food to be produced in parts of the world where disease, climate, or accessibility of forage material have previously limited the ability to raise food animals.

FDA Guidance January 2009



Goals of Genetic Engineering In Livestock Production

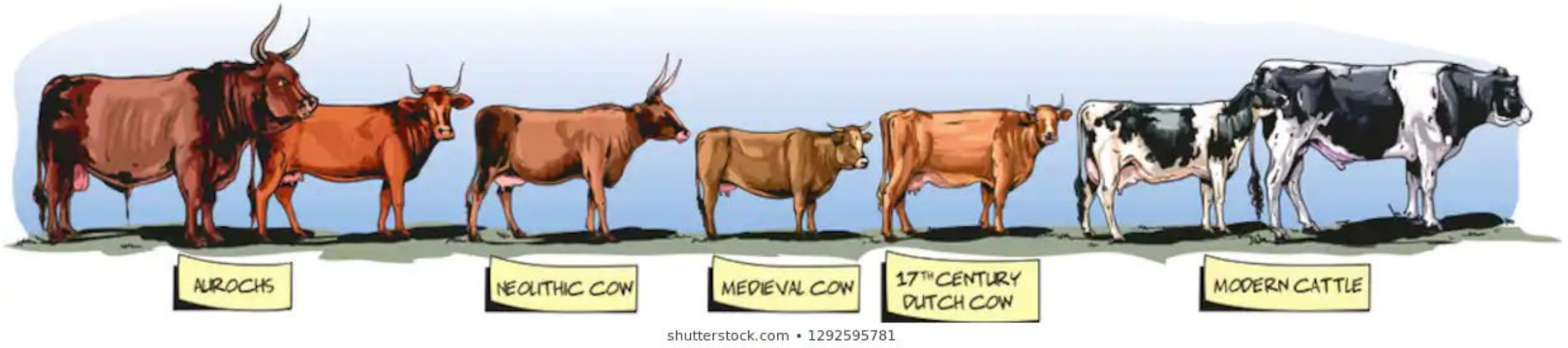
- Produce regionally adapted, pest and disease resistant livestock with improved performance traits that meet consumer demands
  - Efficiently convert grass to high value protein
    - Increased product (meat and milk) per animal
    - Improved quality and health benefits of products
    - Decrease the current practice of feeding human foods to animals
    - Reduce the environmental impact





Random Mutations Occur in Each New Offspring Produced from Natural Matings

- Approximately 44-83 random de novo mutations occur in the mammalian genome every generation.
- This is the driving force behind evolution and the ability to select livestock for improved traits.



Acuna-Hildago et al., 2016

Classic Genetic Selection

Pedigree Information

Sitz Traveler 8180
#11367940

- **G D A R Traveler 71**
  #10988296
  - **Traveler 1146 G D A R**
    #9995320
  - **G D A R Miss Blackcap 567**
    10717922
- **Sitz Everelda Entense 1137**
  10912116
  - **G D A R Rainmaker 340**
    #10388929
  - **Sitz Everelda Entense 2335**
    10681191

G A R Precision 706
12716497

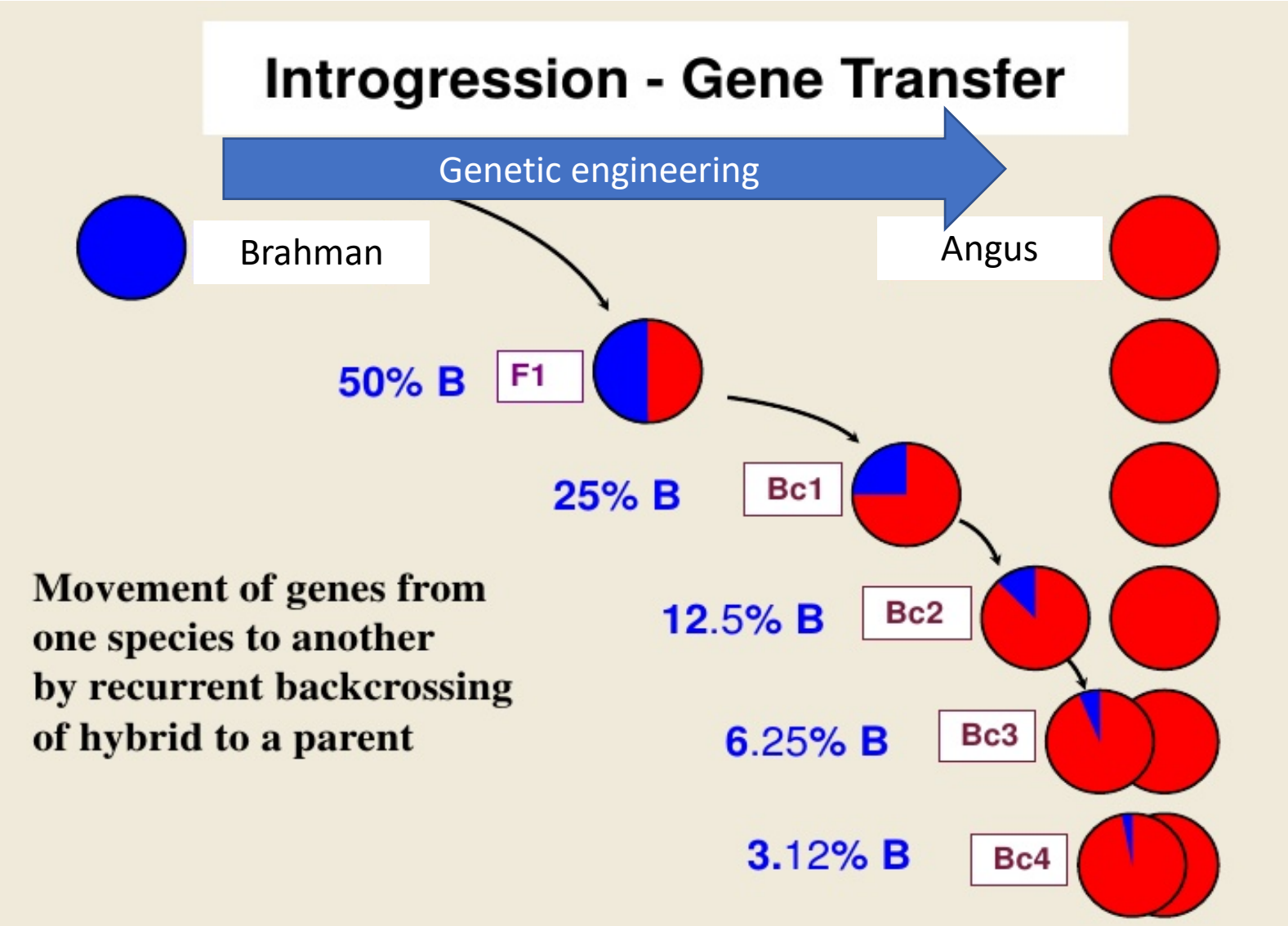
- **G A R Precision 1680**
  #11520398
  - **Tehama Bando 155**
    #9891499
  - **9J9 G A R 856**
    10895323
- **G A R Ext 2114**
  +12356151
  - **N Bar Emulation EXT**
    #10776479
  - **G A R Scotch Cap 867**
    #11047903

Limits to Classical Genetic Selection

- You can not select for a trait that does not exist in the population.
- Exposing a herd to a pathogen to discover individuals that are resistance is not practical.
- Breeding to introduce a desirable trait can lead to development of deleterious traits.

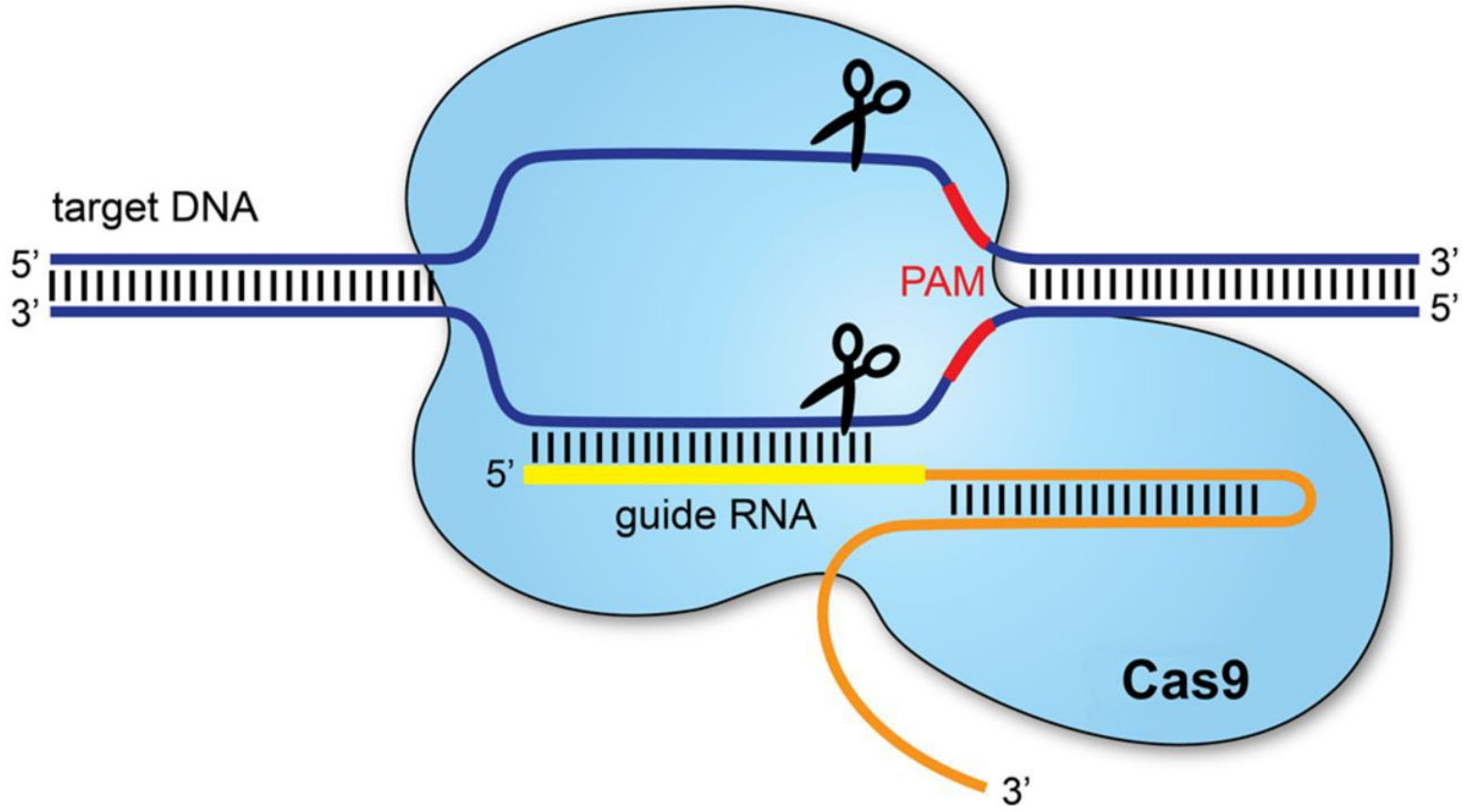
Slow, random, limited to traits already in the population

Traditional crossbreeding takes many years and leaves unwanted genetic elements



15 or more years and ~94 million residual DNA base pairs from Brahman

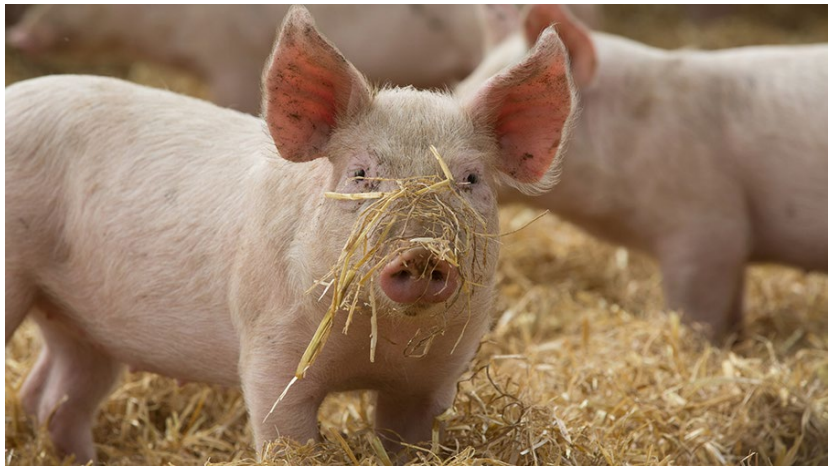
CRISPR/Cas and Other Gene Editing Tools Allow For Precise Genetic Changes



Technology is no longer a limiting factor.

Gene editing innovations that protect and improve performance in livestock production systems

- **Disease Resistance:**
  - **Pigs**
    - Porcine reproductive and respiratory syndrome virus
    - Porcine epidemic diarrhea virus/transmissible gastroenteritis virus
    - African swine fever virus
  - **Chicken**
    - Avian leucosis virus
    - Avian influenza virus
  - **Cattle**
    - Bovine spongioform encephalopathy (BSE)
    - Tuberculosis
    - Bovine respiratory disease
    - Mastitis



Gene editing innovations that protect and improve performance in livestock production systems

- **Environment**
  - Decreased phosphate polluction
- **Enhanced Production**
  - Heat tolerance
  - Polled (hornless) cattle
  - Reduction of milk allergens
  - Increase quantity and quality of meat
    - Increase growth rate of fish (AquaBounty salmon)

A Failed Regulatory Framework Limits Innovation In Animal Agriculture

Politics holds back animal engineers

Funds and approvals lag for transgenic livestock in US.

Nature, October 17, 2012

Gene-edited animals face US regulatory crackdown

Nature, January 19, 2017

Gene-edited animal creators look beyond US market

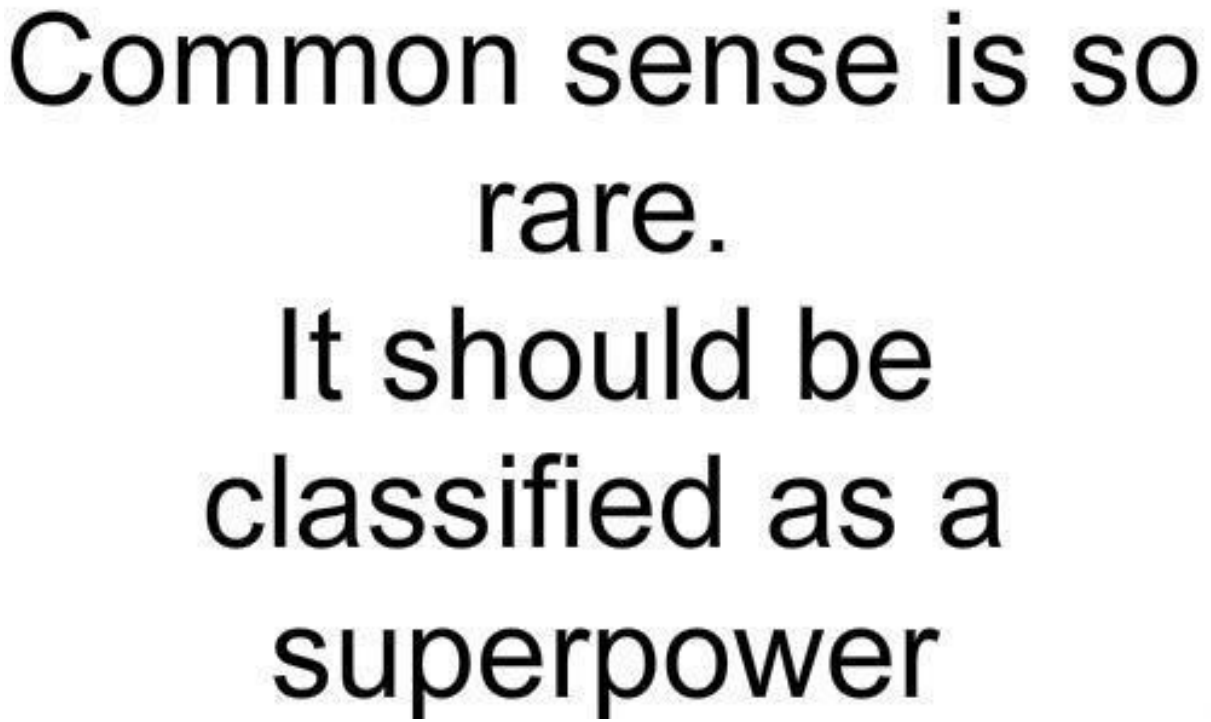
Tired of regulatory confusion and a lack of funding, some US researchers are taking their gene-edited livestock abroad.

Nature, February 20, 2019

Food and Drug Administration- Veterinary Innovation Program

https://www.fda.gov/animal-veterinary/animals-intentional-genomic-alterations/vip-veterinary-innovation-program

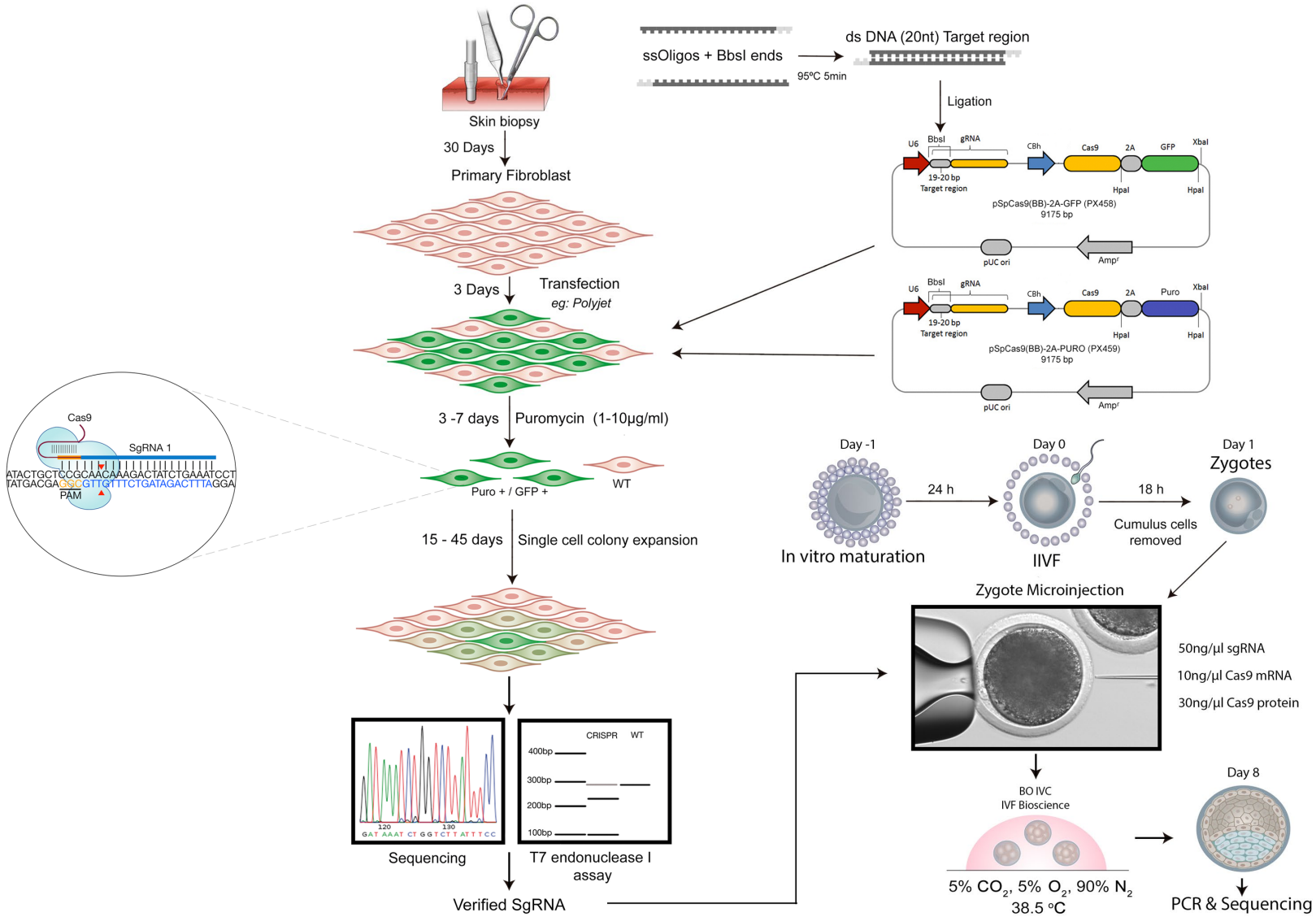
We must have clear risk based assessment of gene edited food, but only for those products that pose a reasonable risk



"One of the wonderful things about transgenesis is that we can do all at once what evolution has taken millions of years to do."

Francis Ruddle

Targeting Bovine Myostatin by Microinjection



What is needed is legislation regulating varieties and their products based on their (new) characteristics and a reasonable a priori risk assessment, not the breeding methods that produced them. It is urgent legislation. We will sacrifice our agriculture and our food production if we fail to produce it.

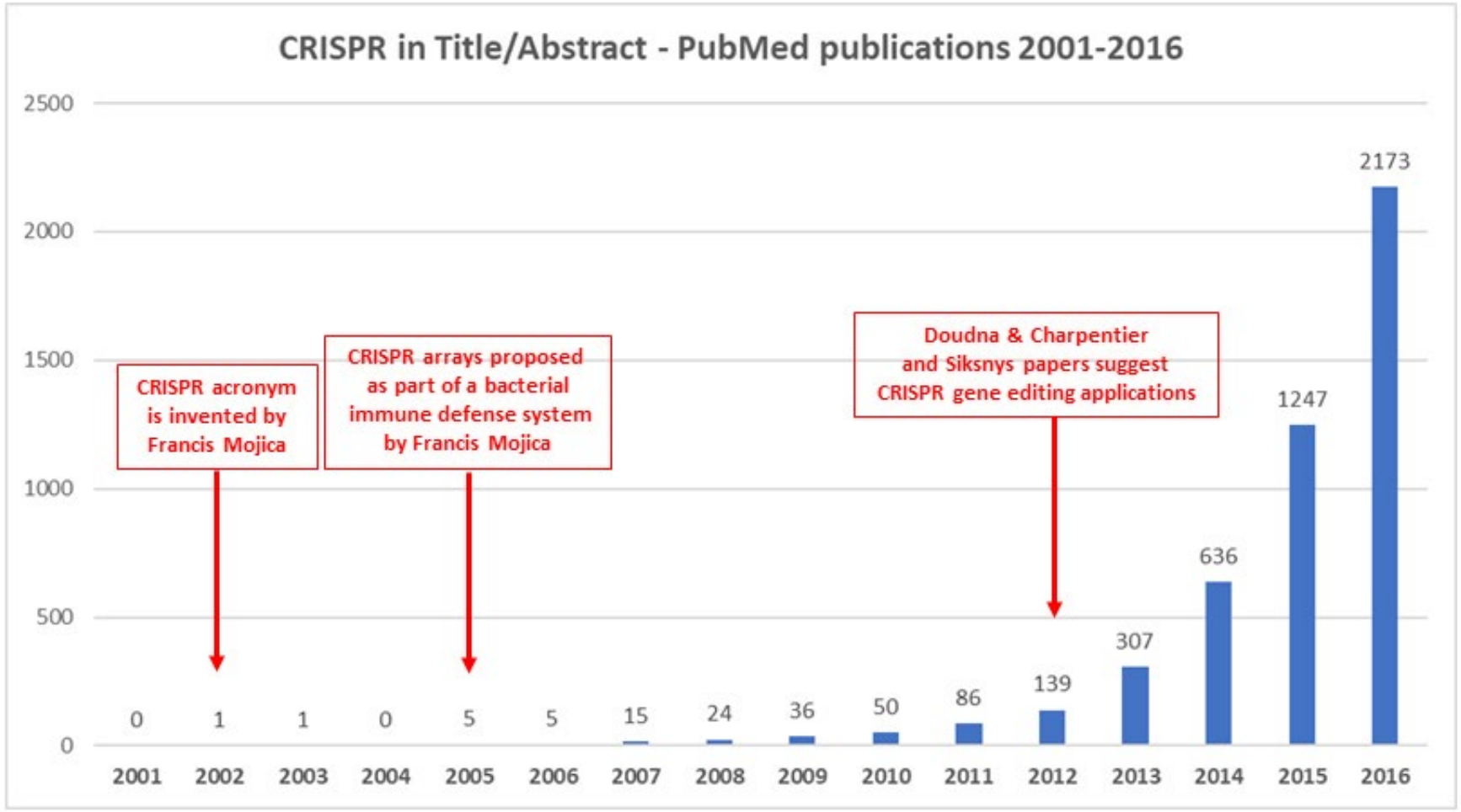
André Heitz | February 14, 2020

geneticliteracyproject.org

Table 1. Industry interests in Cas9-based technologies

Industry sector	Product/application	Company	Intellectual property
Food	Yogurt, cheese	Danisco (DuPont)	7 919 277; 8 361 725; 13/722 539;11/990 885
	Crops	Dow Agrosciences	PCT/US2013/039979 co-owned with Sangamo Biosciences
	Livestock	Recombinetics	PCT/US2014/0201857
	Crops	Cellectis Plant Sciences	Boston Children's Hosp., Institut Pasteur License
Laboratory	Research tools	System Biosciences	US 14/216 655
	Expression systems	Sigma-Aldrich	PCT/US2013/073307
	Research tools	GE Healthcare	Broad License
	Animal models	Sage	Caribou, Broad License
	Research tools	ThermoFisher	Cellectis Sublicense
	Animal models	Taconic	Broad License
Sublicensing	Ag, Industrial, Bio	Caribou	PCT/US2013/053287
Medical	Pharmaceuticals	Novartis	Caribou License
	In vitro applications only	Cellectis	Boston Children's Hosp., Institut Pasteur License
	Target validation	AstraZeneca	Open Innovation Model
	Therapeutics	Crispr Therapeutics	PCT/US2013/032589
	Monogenic diseases	Sangamo Biosciences	PCT/US2013/032381; PCT/US2013/039979; PCT/US2013/028348
	Therapeutics	Intellia	Caribou License
	Therapeutics	Editas	Broad, Duke, MGH Licenses

CRISPR is Not New Anymore

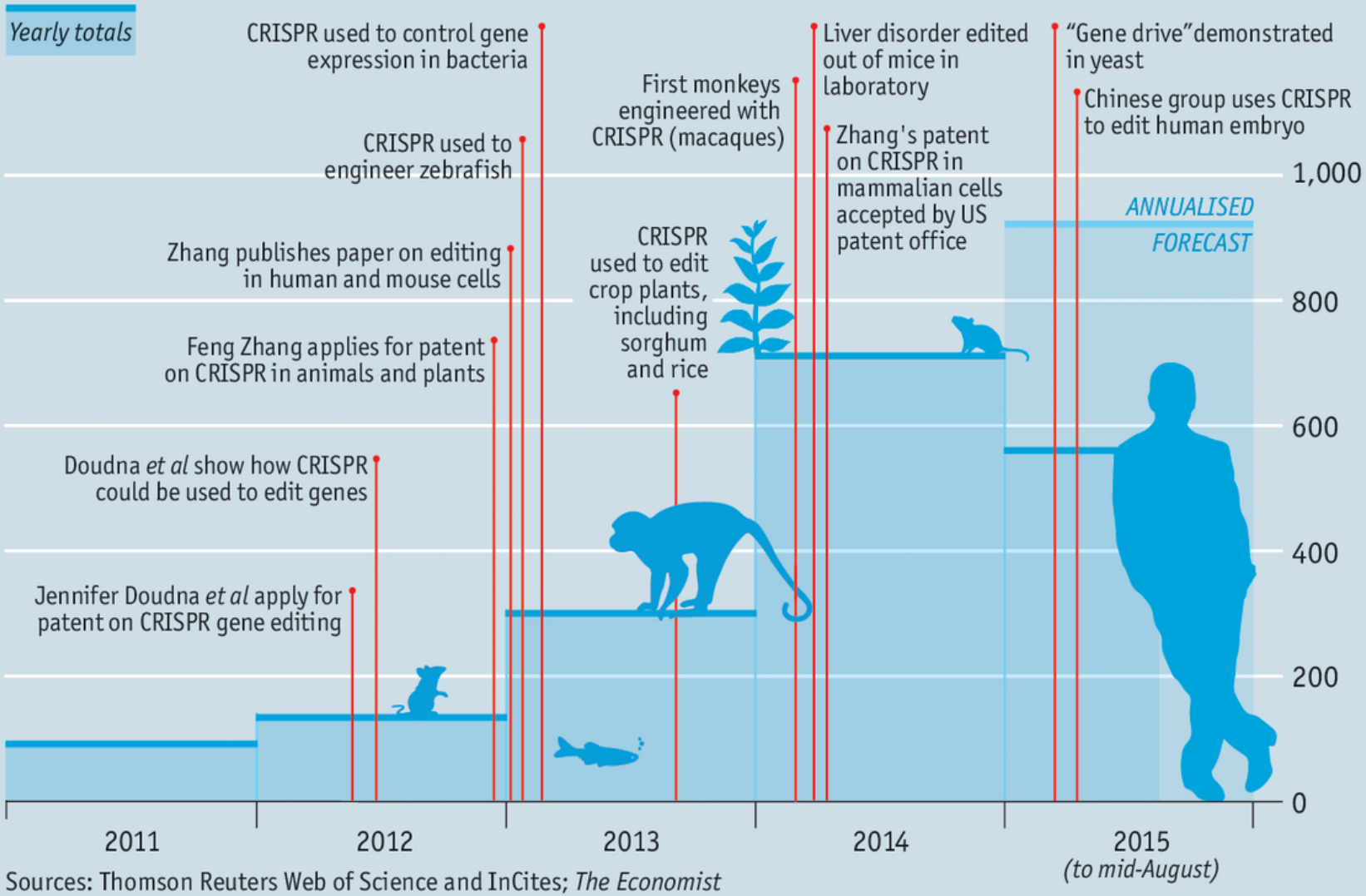


Now approximately 100 new publications per week!

http://wwwuser.cnb.csic.es/~montoliu/CRISPR/

Stepping up

Number of **CRISPR** papers published and some research highlights



Sources: Thomson Reuters Web of Science and InCites; *The Economist*