Editing Genes and Genomes

ITIF Tech Policy 202

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The Daily News

- 11 March. Why the future of gene-edited foods is in the balance: Regulators will decide the impact of the biggest advance in bioscience since genetic modification https://www.ft.com/content/12b978aa-0544-11e9-bf0f-53b8511afd73.
- 12 March. Animal gene editing breakthrough: Bringing Angus beef raised from US cattle to Brazil https://geneticliteracyproject.org/2019/03/12/animal-gene-editing-breakthrough-bringing-angus-beef-raised-from-us-cattle-to-brazil/.
- 12 March. Gene-edited food quietly arrives in restaurant cooking oil https://apnews.com/17f0f799580a483fbd1b2d69bcf2ba18.
- 13 March. Leaders call to Adopt a moratorium on heritable genome editing in humans https://www.nature.com/articles/d41586-019-00726-5.
- 19 March. Gene-edited foods are safe, Japanese panel concludes https://www.sciencemag.org/news/2019/03/gene-edited-foods-are-safe-japanese-panel-concludes.
- 19 March. Russian Academy of Sciences Director opposes equating CRISPR with GMOs https://www.archyworldys.com/director-of-the-institute-of-genetics-russian-academy-of-sciences-opposed-equating-crispr-with-gmos/.

Why Gene Editing Matters

1. Newly discovered/ ancient technique for making genetic changes with unprecedented precision.
2. Powerful tool for precision breeding in plants, animals, microbes.
3. Main tech platform for delivering new therapies for human disease .
4. Biology is THE 21st century platform; gene editing will likely be the primary vehicle.
5. A robust source of high-value jobs, outputs, and exports.
6. Immense national security implications.

What Is “Gene Editing” (“New Breeding Techniques”)?

- ZFN = Zinc Finger Nucleases
- TALENS = Transcription activator-like effector nucleases
- ODM = Oligonucleotide directed mutagenesis
- MEGA = meganucleases
- RdDM = RNA dependent DNA methylation
- RNAi/PTGS = small, interfering RNAs/Post translational gene silencing
- CRISPR-Cas9 = Clustered regularly interspaced short palindromic repeats
- Gene drives

Why Is CRISPR Important? What Can We Do With It?

- Researchers can tweak CRISPR so it can be used to target any specific DNA sequence (via “guide RNAs” – make your own!).
- It enables researchers to manage any DNA sequence of choice by changing, deleting, or inserting specific nucleotides or nucleotide sequences.
- If you can imagine a change you’d like to make to a DNA sequence, CRISPR allows you to make it.

Where Do We Find CRISPR In The Wild?

- There are at least 45 families of CAS genes/proteins
- “Libraries of tens of thousands of guide RNAs are available…”

—Elizabeth Pennisi, “The CRISPR Craze,” Science 23 Aug 2013:Vol. 341, Issue 6148, pp. 833-836

Copyediting genomes at will…

- “My initial gut reaction was 'Oh my god, this is terrible. It's so scary… But when you give it more thought and weigh it against the environmental changes that we have already made and continue to make, it would be a drop in the ocean.”

  -- Micky Eubanks, Texas A&M

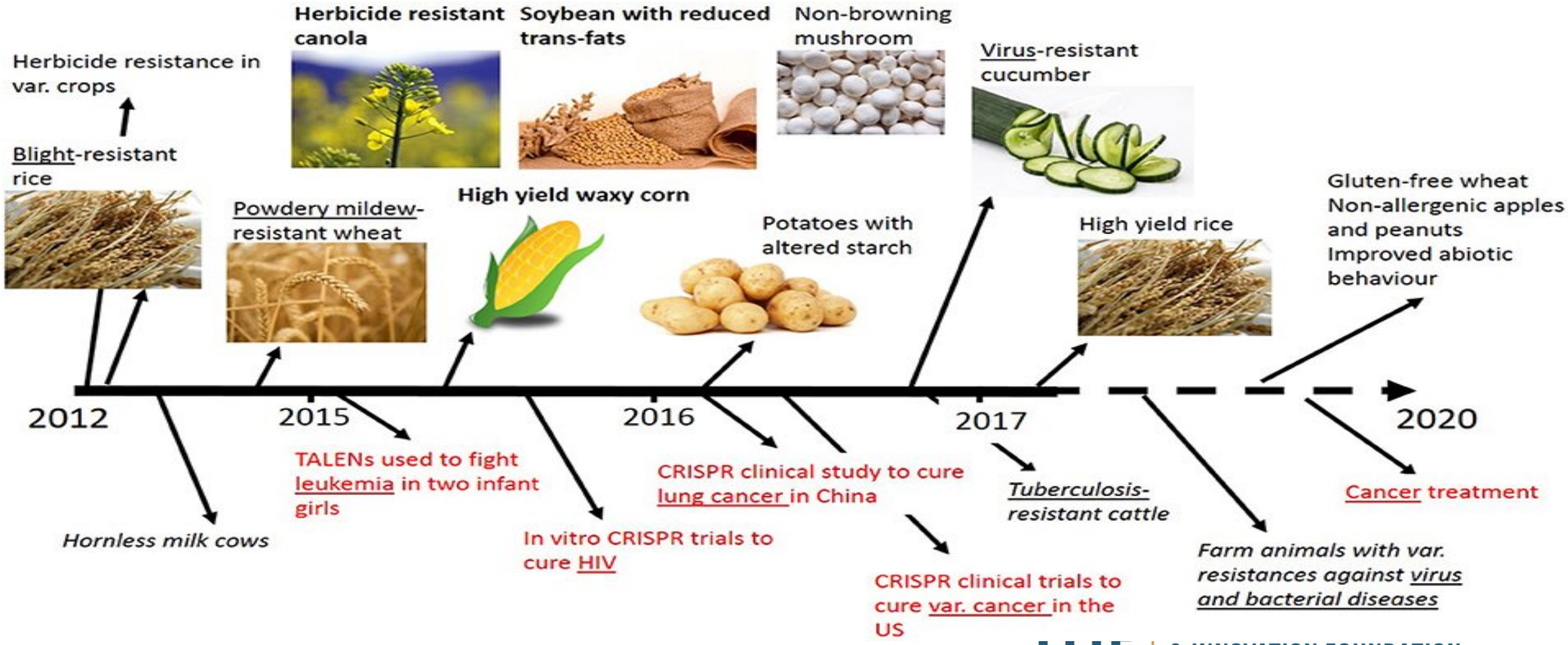
- “A dream come true for plant breeders…”

  --A. Gal-On

AGRICULTURAL APPLICATIONS

BIOMEDICAL APPLICATIONS

Gene Editing Timeline



How Researchers Already Have Used CRISPR

- Make programmable transcription factors to turn genes on/off.
- Gene therapy: curing tyrosinaemia in mice; β-thalassaemia (23,714 entries in https://www.omim.org/statistics/entry).
- Vitamin enriched oranges; micronutrient enhanced grains; oil-profile modified oilseeds.
- CRISPR gene drives (2015) targeting mosquitoes, ticks, invasive plants, weeds.
- PERV deletion in pigs.
- CRISPR used to gene edit human embryos (2015).
- T-cell augmented cancer therapy clinical trial (2016).

What Else Could We Do?

- Cure HIV
- Cure genetic diseases like CF, MD, sickle cell anemia, Huntington's… (OMIM = 23,714)
- Cure cancer(s) (restore p53-mediated tumor suppression)
- Make mosquitoes immune to malaria/Dengue/Yellow Fever/Zika
- Drive mosquito species to extinction
- If it has any genetic basis….

Significant recent policy developments

- **Secretary Perdue Issues USDA Statement on Plant Breeding Innovation** https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation (28 March, 2018)
- **Retraction: "Unexpected mutations after CRISPR–Cas9 editing in vivo"** Nature Methods vol 5, page 394 (2018) https://www.nature.com/articles/nmeth0518-394a (27 April)
- **UC Berkeley vs Broad Institute patent litigation** https://www.nature.com/articles/d41586-018-06656-y (10 September 2018)
- **CRISPR-Cas12a More Precise Than CRISPR-Cas9** https://www.genengnews.com/topics/genome-editing/crispr-cas12a-more-precise-than-crispr-cas9/81256099/?utm_medium=newsletter (3 August, 2018)
- **European Court of Justice ruling on gene editing** https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf (25 July, 2018)

Policy Considerations/Topics for Discussion

- How can we anticipate/prevent/mitigate/manage what could go wrong?
- What kind of regulation is appropriate for products of gene editing technologies?
  - R = H x E; Are there any novel hazards? Are there any unreasonable risks? (FDA is blowing it).
  - Are there opportunity costs associated with getting regulation wrong?
- How should human applications be governed?
  - Curing/preventing disease vs CRISPR babies.
  - Who owns genetic information? What privacy rules should apply?
- What level of R&D support is appropriate?
- International Trade Implications: WTO/SPS.
- National security implications.

Key Take-aways

1. Gene editing/modern biology has huge potential for good.
2. Novel hazards and unreasonable risks have been slow to emerge.
3. U.S. leadership cannot be taken for granted.
4. Countries must make science-based/hazard-risk driven regulation a priority.

Keeping Up To Date

1. Pivotal & Recent Developments in Gene Editing
2. CRISPR Babies: A Catalogue of Noteworthy Commentary and Analysis
3. Broad Institute - CRISPR Timeline

Thank You!

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