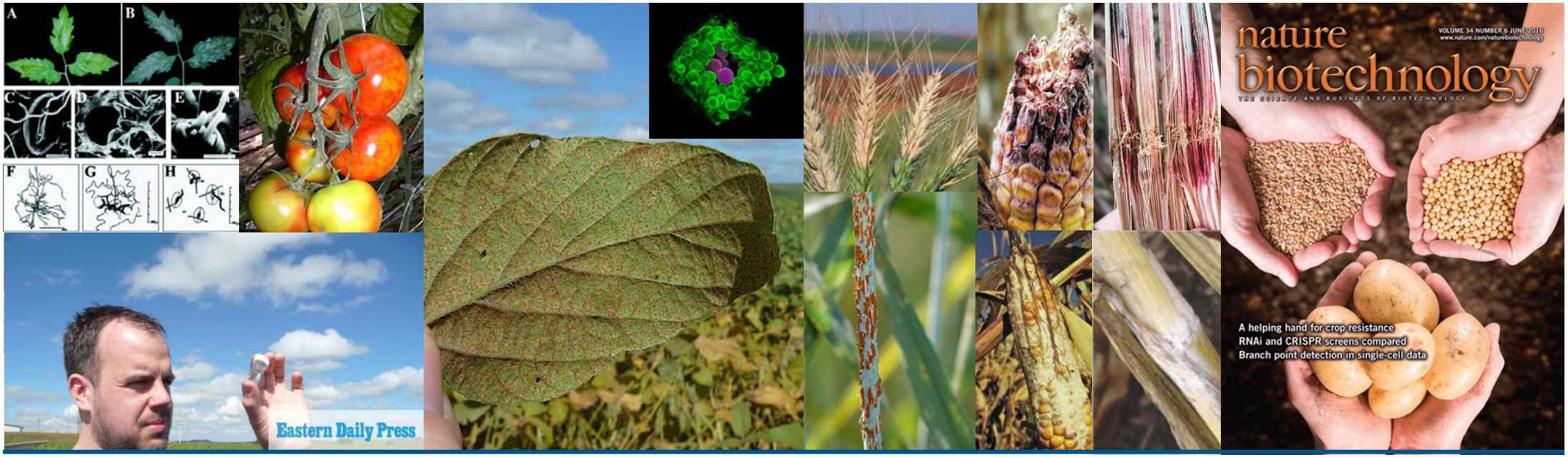


NICE TO MEET YOU

2BLADES
FOUNDATION

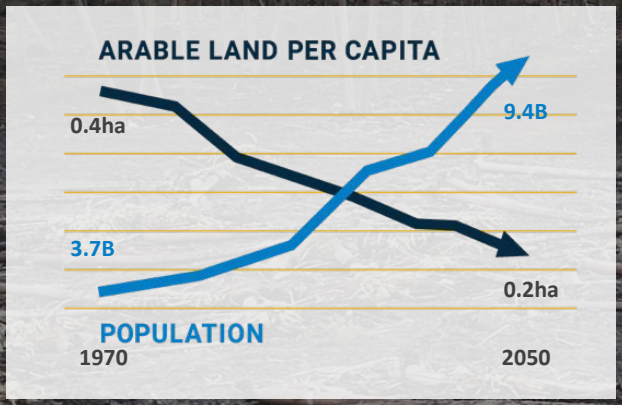
The Hidden Problem

Diseases are stealing our food

2BLADES FOUNDATION

Our Global Food Challenge

Less Land to Farm



Production at Risk from Crop Disease

10-15%
lost every year

Up to 100%
lost from catastrophic diseases

Source: https://www.census.gov/population/international/data/worldpop/table_population.php
http://www.dani2989.com/gold/potashgb.htm
*Photo – Dennis Gonsalves

Catastrophic Crop Diseases

	WHEAT 50% of Global Diet	**SOY** Top 10 Commodity	**POTATO** 3rd Most Important Crop
Disease	Stem Rust/Stripe Rust 	Asian Soybean Rust 	Late Blight 
Crop Loss	50-70% 90% varieties susceptible	Up to 80%	Up to 100%

2BLADES FOUNDATION

Fundamental Impact on Livelihoods

FOR LARGE SCALE FARMERS

Chemical use

Large scale production impact

FOR SMALL HOLDER FARMERS

Food loss

Income loss

Unsafe chemicals

FOR ALL

Malnutrition

Rising food prices and economic instability

Civil unrest and political instability

NOT PRO-GM OR PRO-GE
BUT PRO TECHNOLOGY
THAT CAN MAKE A DIFFERENCE

2BLADES
FOUNDATION

Proven Solutions to Crop Disease

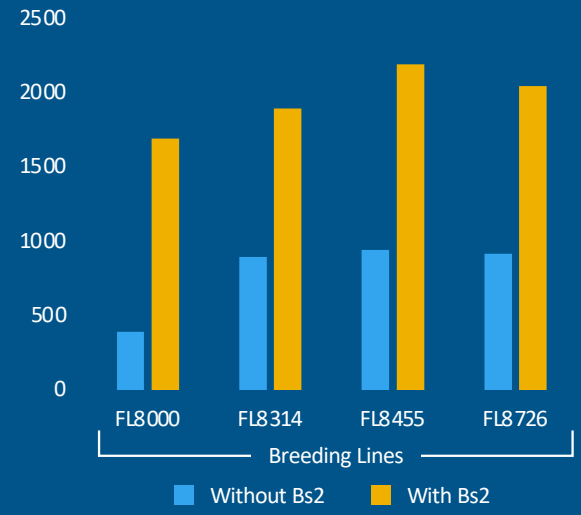
Tomatoes Infected with Bacterial Spot

Control plants
WITHOUT Bs2 gene

Control plants
WITH Bs2 gene

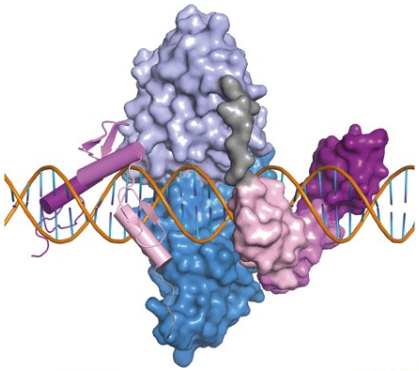
Yield

2x Improvement

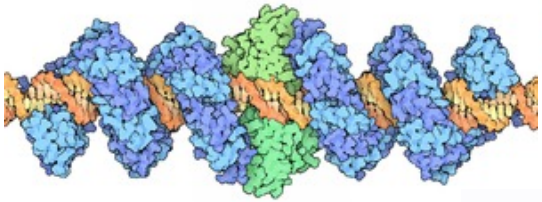


2BLADES FOUNDATION

ZINC FINGERS



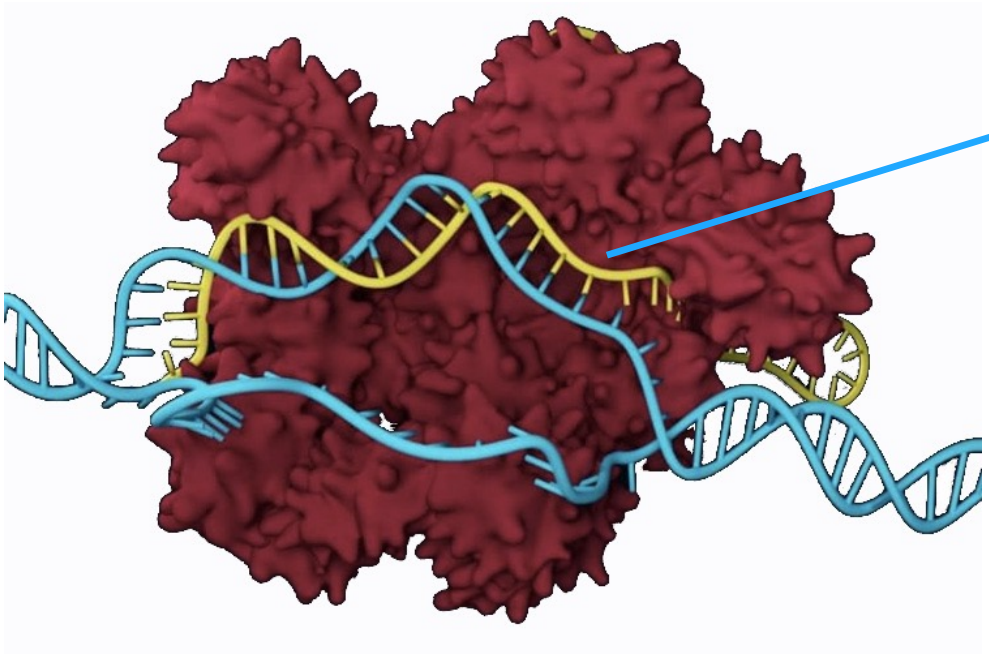
TALENS



2BLADES
FOUNDATION

CRISPR-CAS9

CRISPR-CAS9



Guide RNA enables modularity

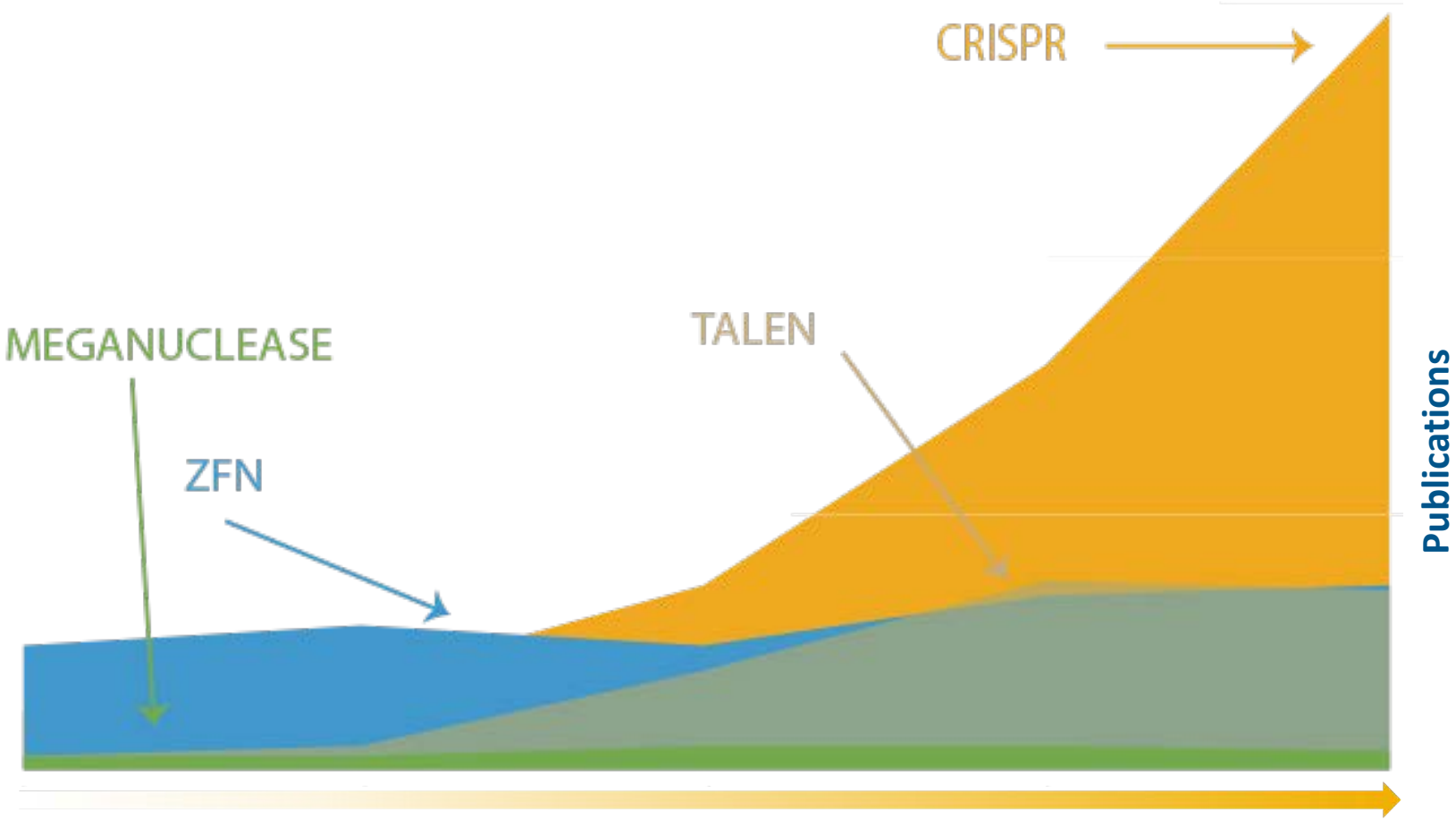
THE GENOME EDITING PARADOX:
REVOLUTIONARY
DISRUPTIVE
OVERHYPED

THE GENOME EDITING PARADOX:

REVOLUTIONARY

DISRUPTIVE

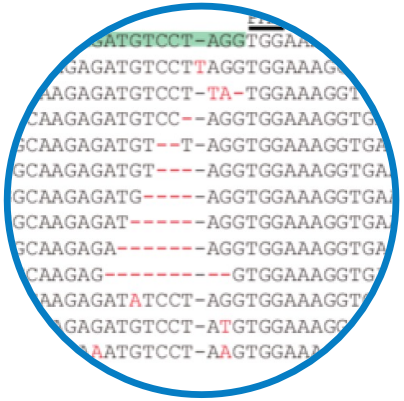
OVERHYPED



2BLADES FOUNDATION

EXISTING CAPABILTIES

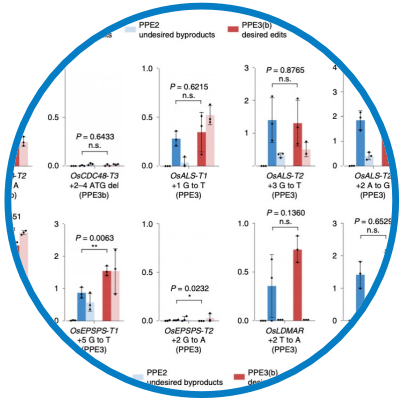
Simple editing



100%

Double strand breaks, gene “deletion”

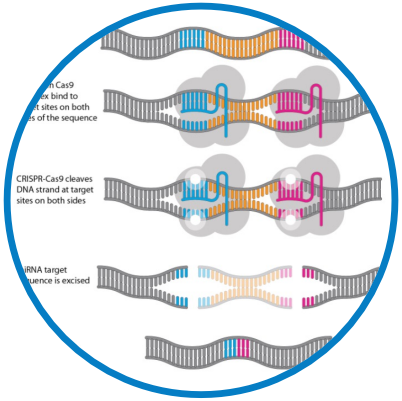
Prime editing



100%

Prime editing, or nicking the DNA leading to more specific edits

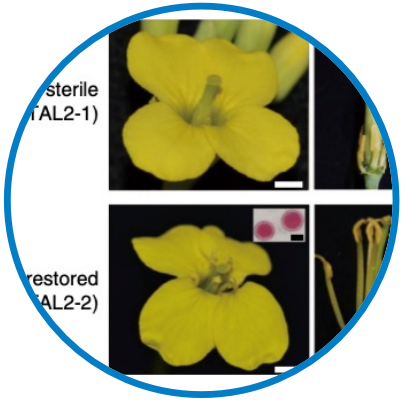
miRNA Editing



100%

complete excision of the miRNA

Organelle editing



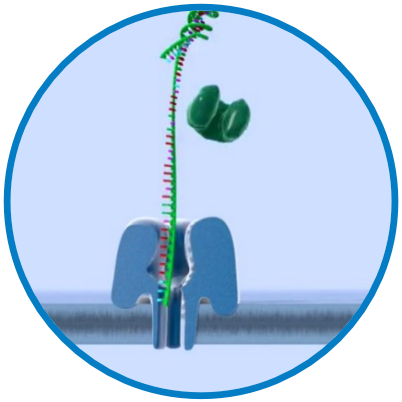
100%

Uses TALENs with localization signals

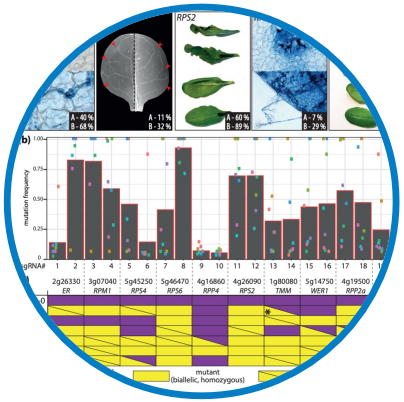
2BLADES
FOUNDATION

EXISTING CAPABILTIES

Targeted sequencing

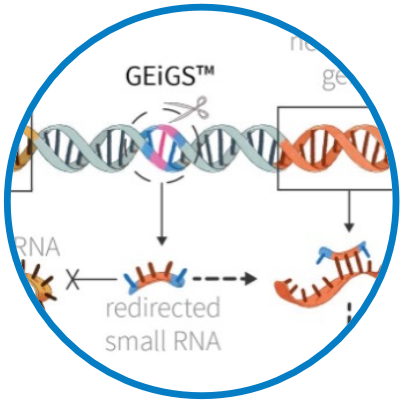


Multiplex editing zCas9i



de novo induction of gene-edited meristems

Gene Editing induced Gene Silencing



100%

Targeted sequencing using nanopore

80%

Removes need for tissue culture step in genome edits

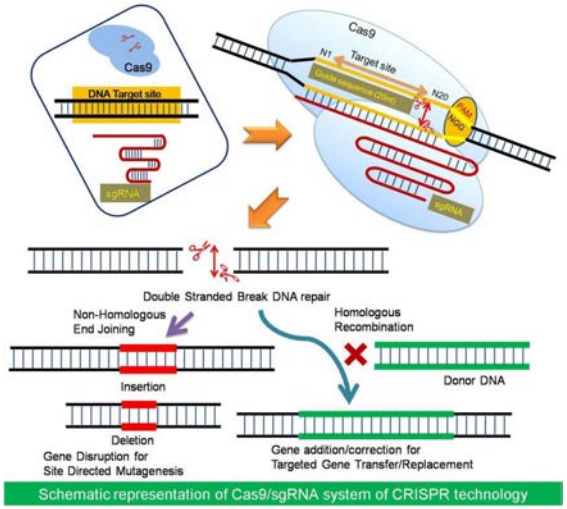
100%

Assembly of nuclease constructs expressing up to 32 sgRNAs

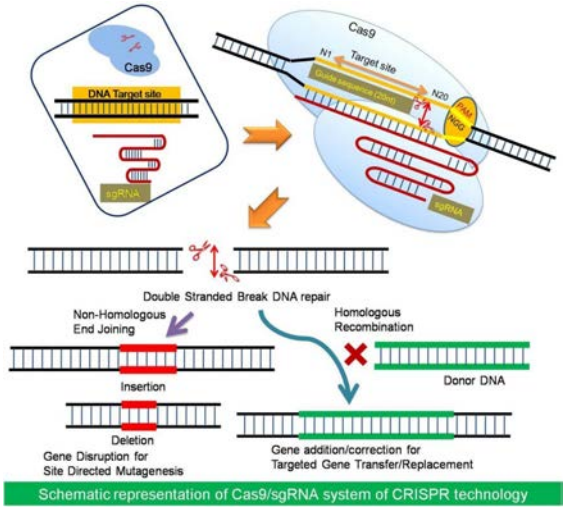
100%

Activity of non-coding genes towards target genes

2BLADES FOUNDATION



Marker free homologous recombination of large DNA fragments

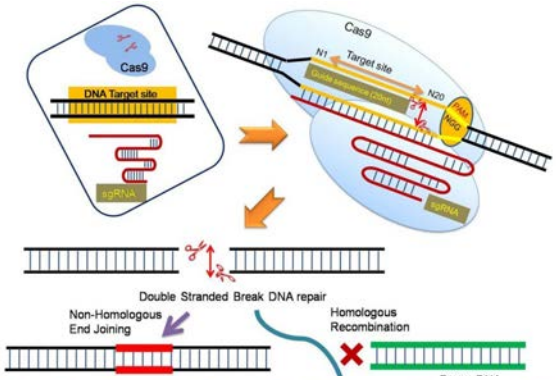


Schematic representation of Cas9/sgRNA system of CRISPR technology

Marker free homologous recombination of large DNA fragments

Happens at extremely low Frequency (0.01%)

Marker free homologous recombination of large DNA fragments



Happens at extremely low Frequency (0.01%)

HIGH

IMPACT

TARGETS

2n=3x

2n = 4x

2n = 8×

(2n)=(6x)

2BLADES
FOUNDATION

THE GENOME EDITING PARADOX:

REVOLUTIONARY

DISRUPTIVE

OVERHYPED

NATURE | NEWS

Gene-edited CRISPR mushroom escapes US regulation

A fungus engineered with the CRISPR–Cas9 technique can be cultivated and sold without further oversight.

De-risked (replicating RNAi and mutagenesis results)

- Reduced oxidative browning (PPO)
  - Apple, Potato
- High and Low-amylose starch (starch branching enzyme and synthesis genes)
  - Barley, Maize, Wheat, Potato, Rice
- Mildew resistance (MLO)
  - Already produced via tilling
  - Wheat, Grape, Strawberry
- Bacterial Resistance
  - SWEET genes
- Viral resistance (eIF4E)
  - Tomato, Cucumber

THE GENOME EDITING PARADOX:

REVOLUTIONARY

DISRUPTIVE

OVERHYPED

TRAITS ARE BECOMING MORE AND MORE TRACTABLE

FOUNDATION

TRAITS ARE BECOMING MORE AND MORE TRACTABLE

THE UP AND COMING BOTTLENECKS

FOUNDATION

TRAITS ARE BECOMING MORE AND MORE TRACTABLE

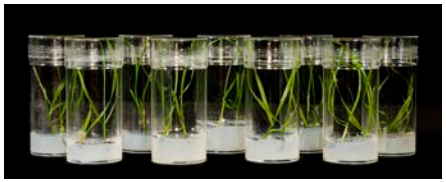
THE UP AND COMING BOTTLENECKS

TECHNOLOGY FOR IMPLEMENTATION IS NOT

2BLADES FOUNDATION

TRAITS ARE BECOMING MORE AND MORE TRACTABLE

THE UP AND COMING BOTTLENECKS



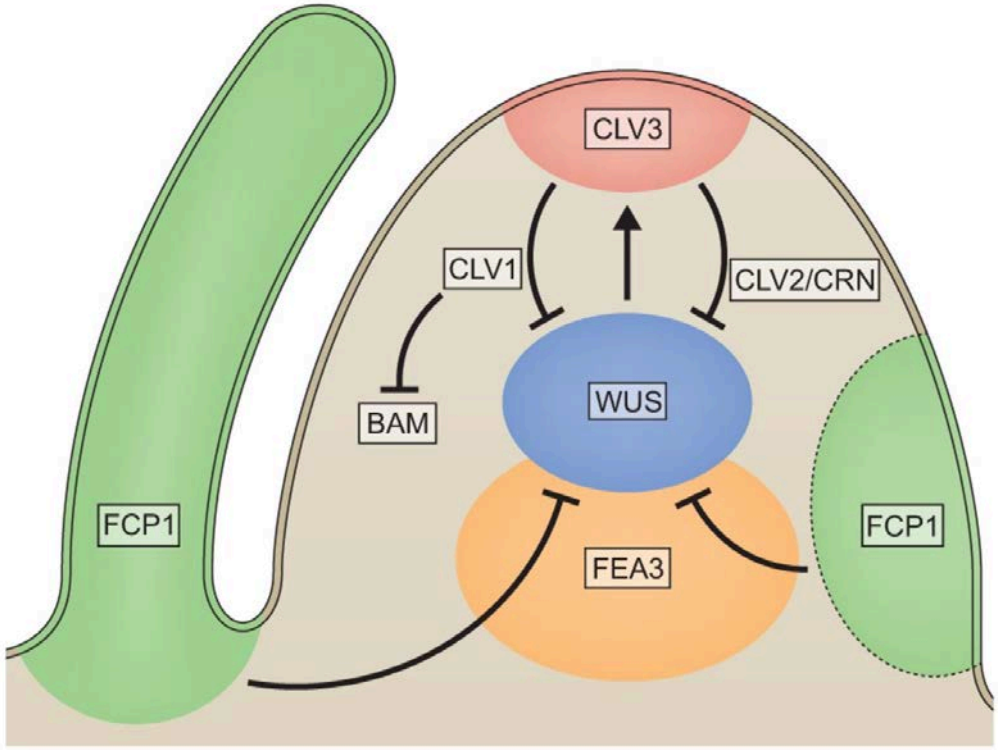
TECHNOLOGY FOR IMPLEMENTATION IS NOT

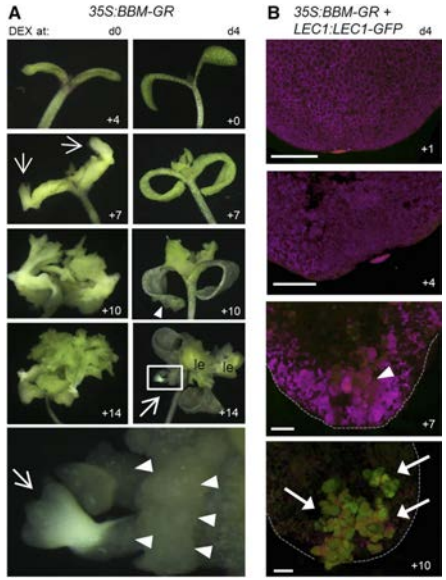
2BLADES FOUNDATION

FOUNDATION

PLANT TRANSFORMATION FOR ALL CROPS

WHY IS IT THAT SOME CROPS CAN BE READILY TRANSFORMED WHILE OTHERS DO NOT?





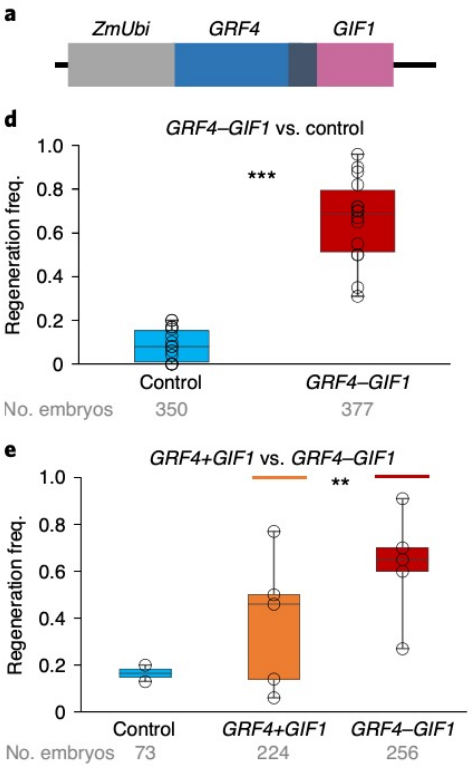
overexpression of *Wuschel* and *Baby boom*

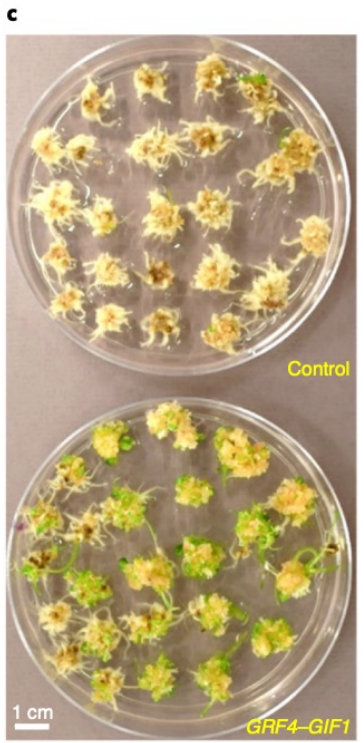
Letter | Published: 12 October 2020

A GRF–GIF chimeric protein improves the regeneration efficiency of transgenic plants

Juan M. Debernardi, David M. Tricoli, Maria F. Ercoli, Sadiye Hayta, Pamela Ronald, Javier F. Palatnik & Jorge Dubcovsky

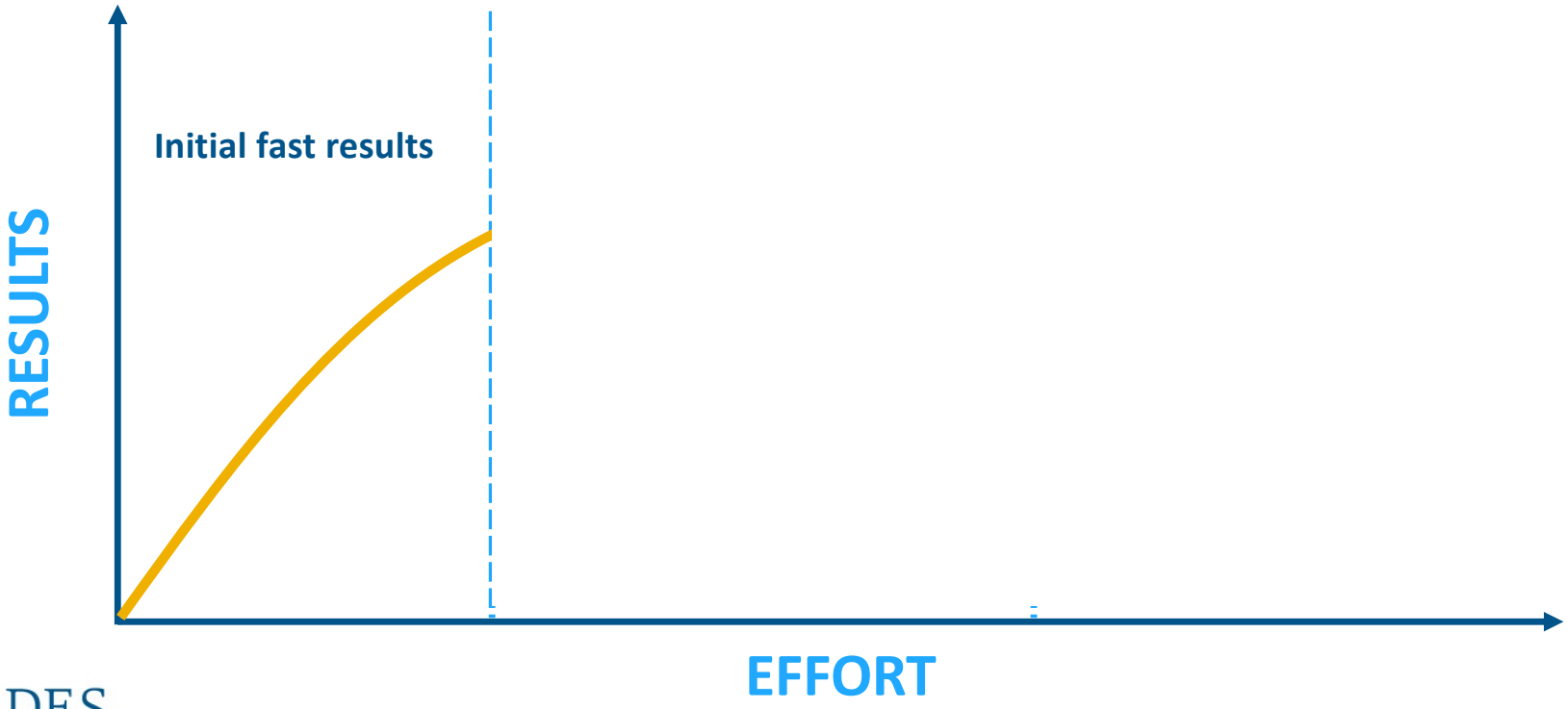
Nature Biotechnology (2020) | Cite this article



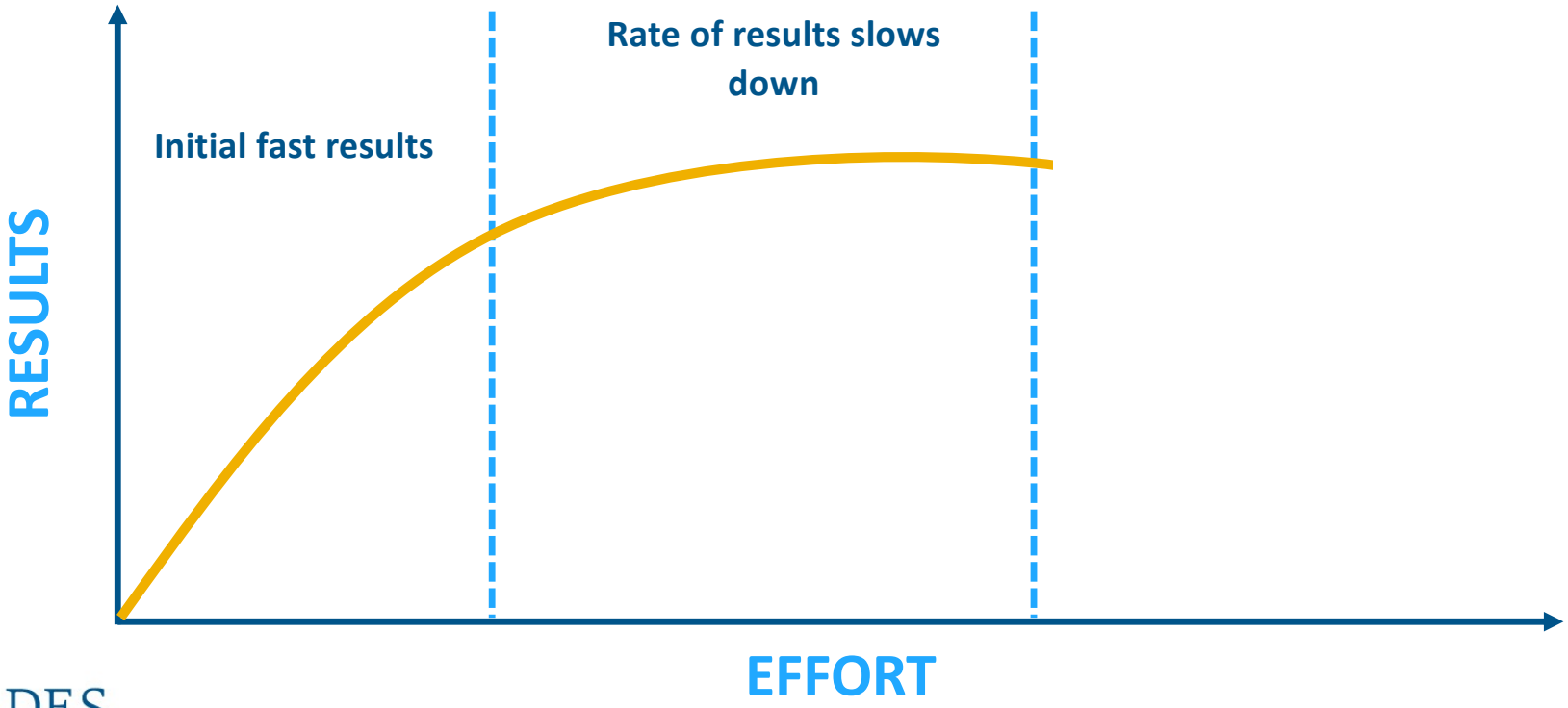


2BLADES FOUNDATION

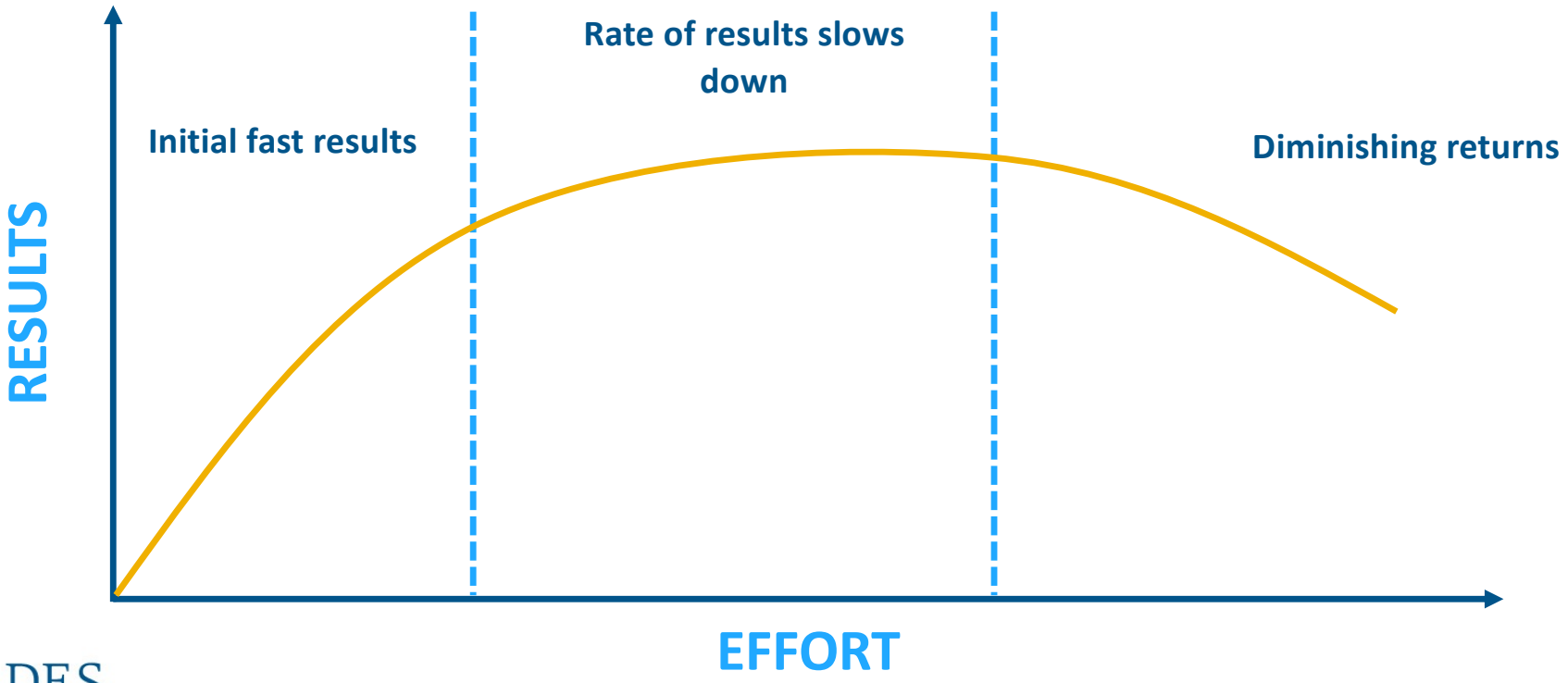
Law of Diminishing Returns



Law of Diminishing Returns



Law of Diminishing Returns



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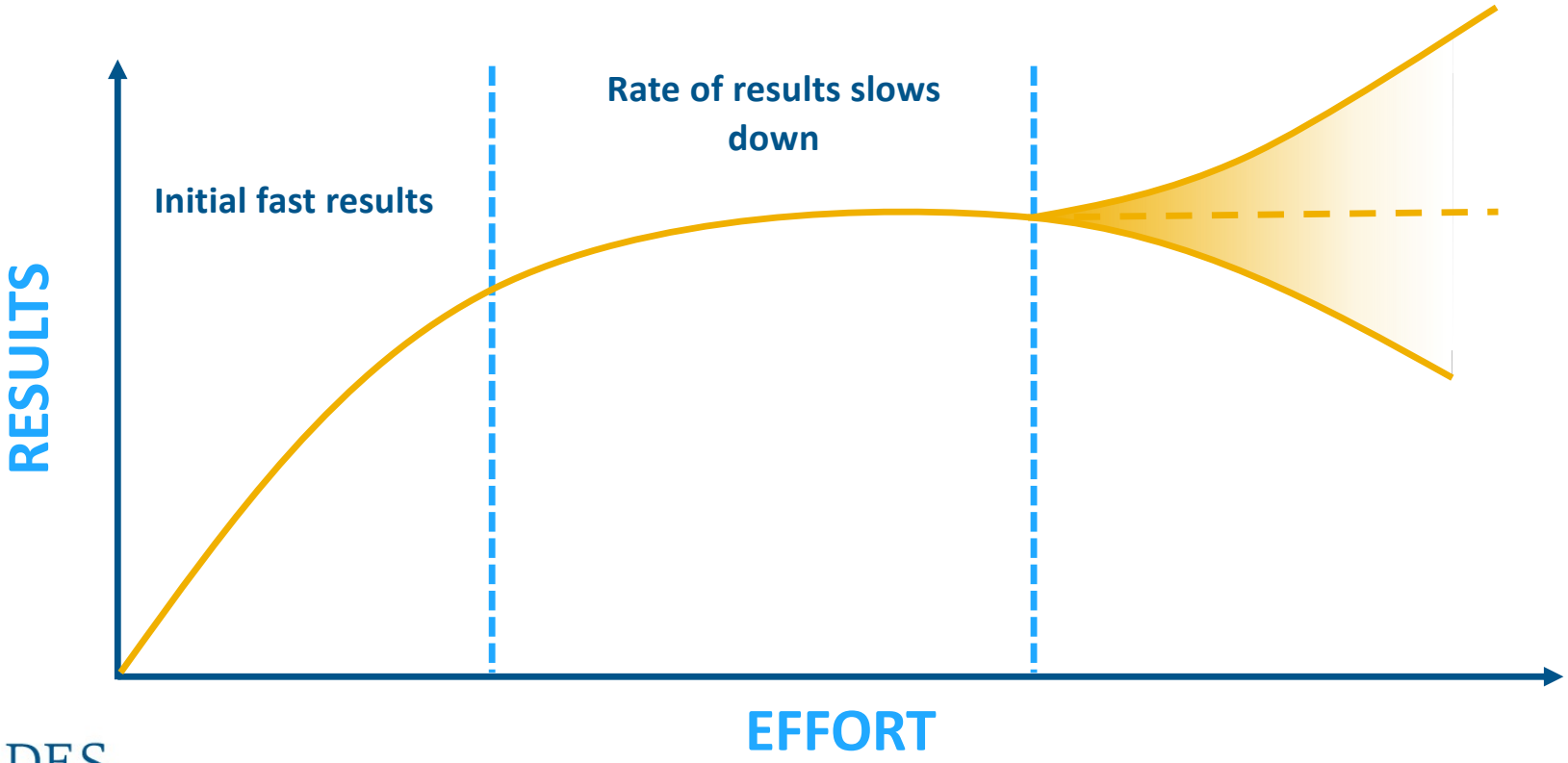
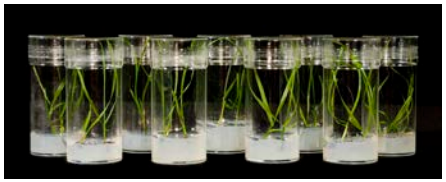
Law of Diminishing Returns



2BLADES FOUNDATION

TRAITS ARE BECOMING MORE AND MORE TRACTABLE

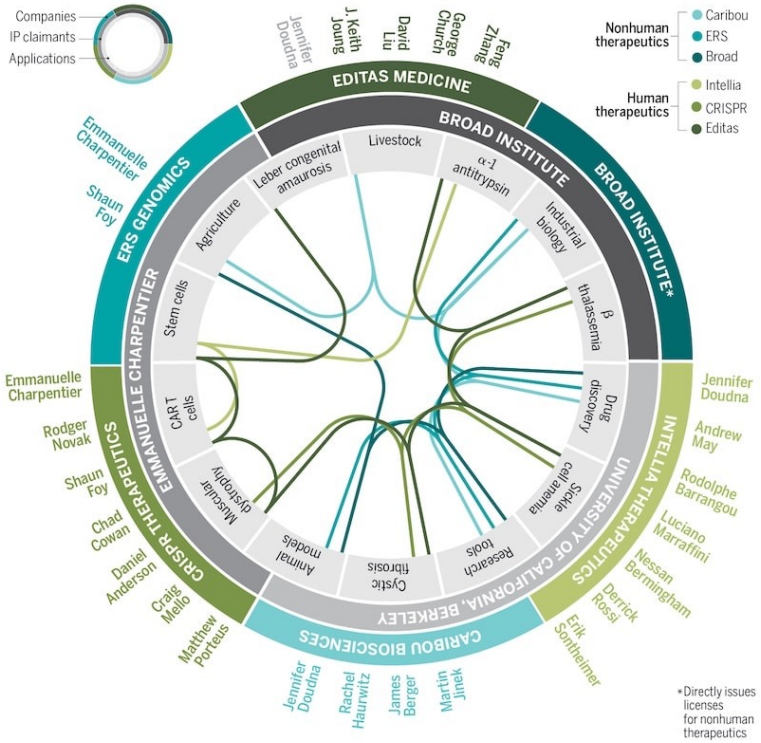
THE UP AND COMING BOTTLENECKS



LEGISLATION FOR IMPLEMENTATION IS NOT

2BLADES FOUNDATION

Who owns CRISPR?



1700 PATENTS

100 NEW PATENTS

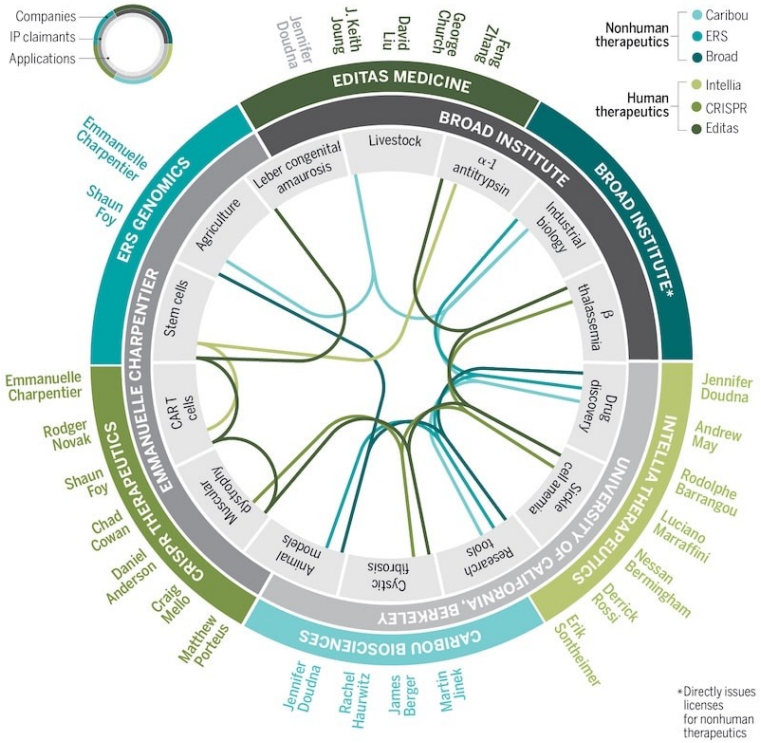
EACH MONTH

2BLADES FOUNDATION

Image credit: Labiotech and Science News

Who owns CRISPR?

"DEMOCRATIC LICENCE"
SCIENTIST
NON-COMMERCIAL

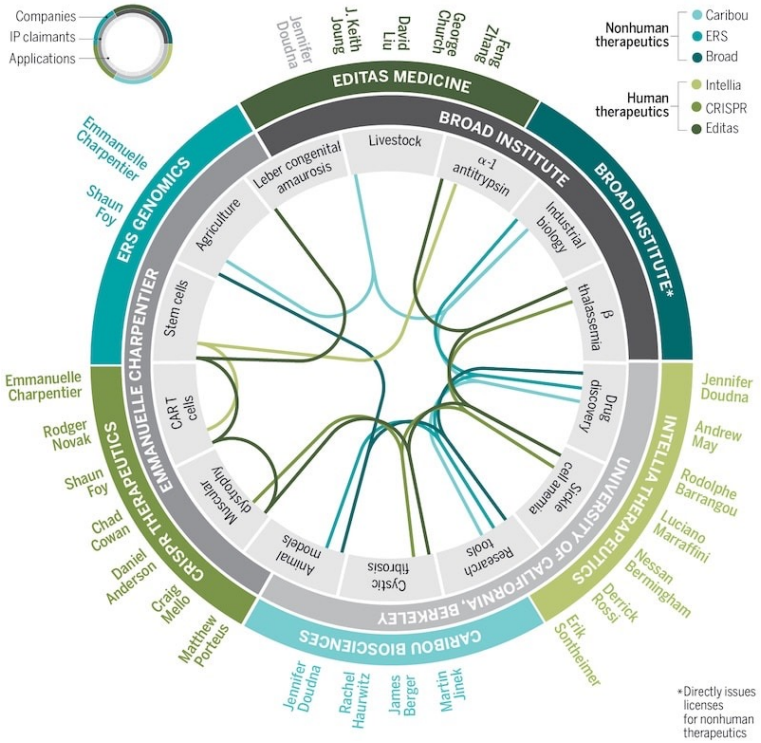


2BLADES FOUNDATION

Image credit: Labiotech and Science News

Who owns CRISPR?

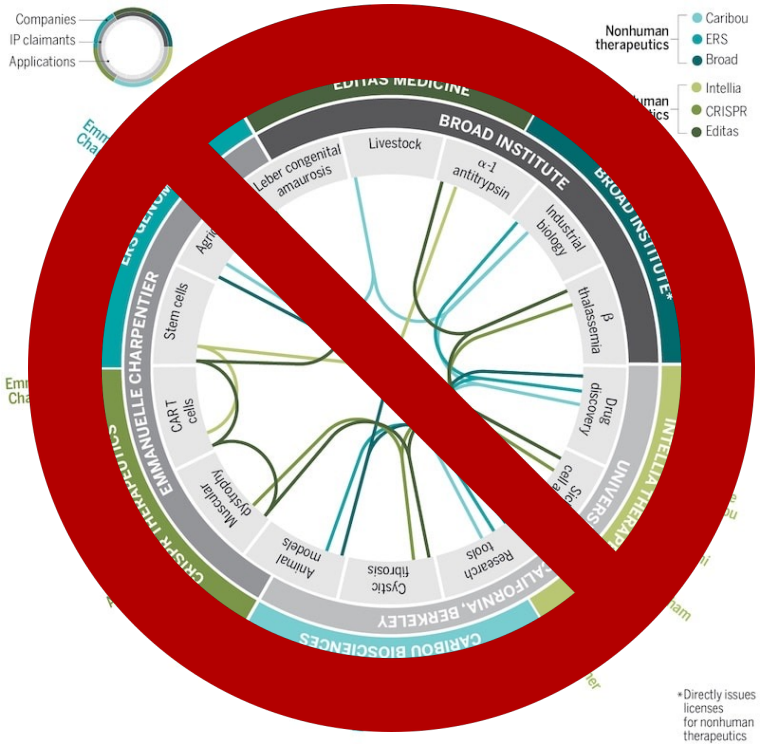
ROYALTIES PROPOSED BY LICENCE HOLDERS



2BLADES FOUNDATION

Image credit: Labiotech and Science News

Who owns CRISPR?

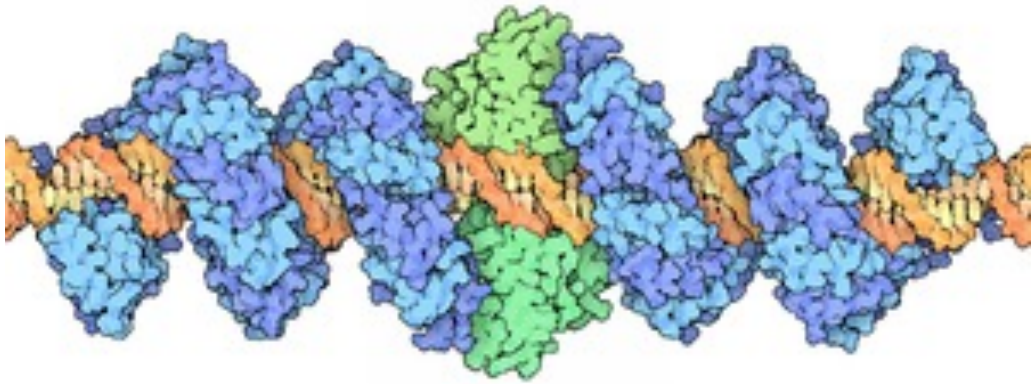


OFTEN MAKE COMMERCIAL INNOVATON A NON-STARTER

2BLADES FOUNDATION

Image credit: Labiotech and Science News

NON-EXCLUSIVE TIERED BASED LICENCING?



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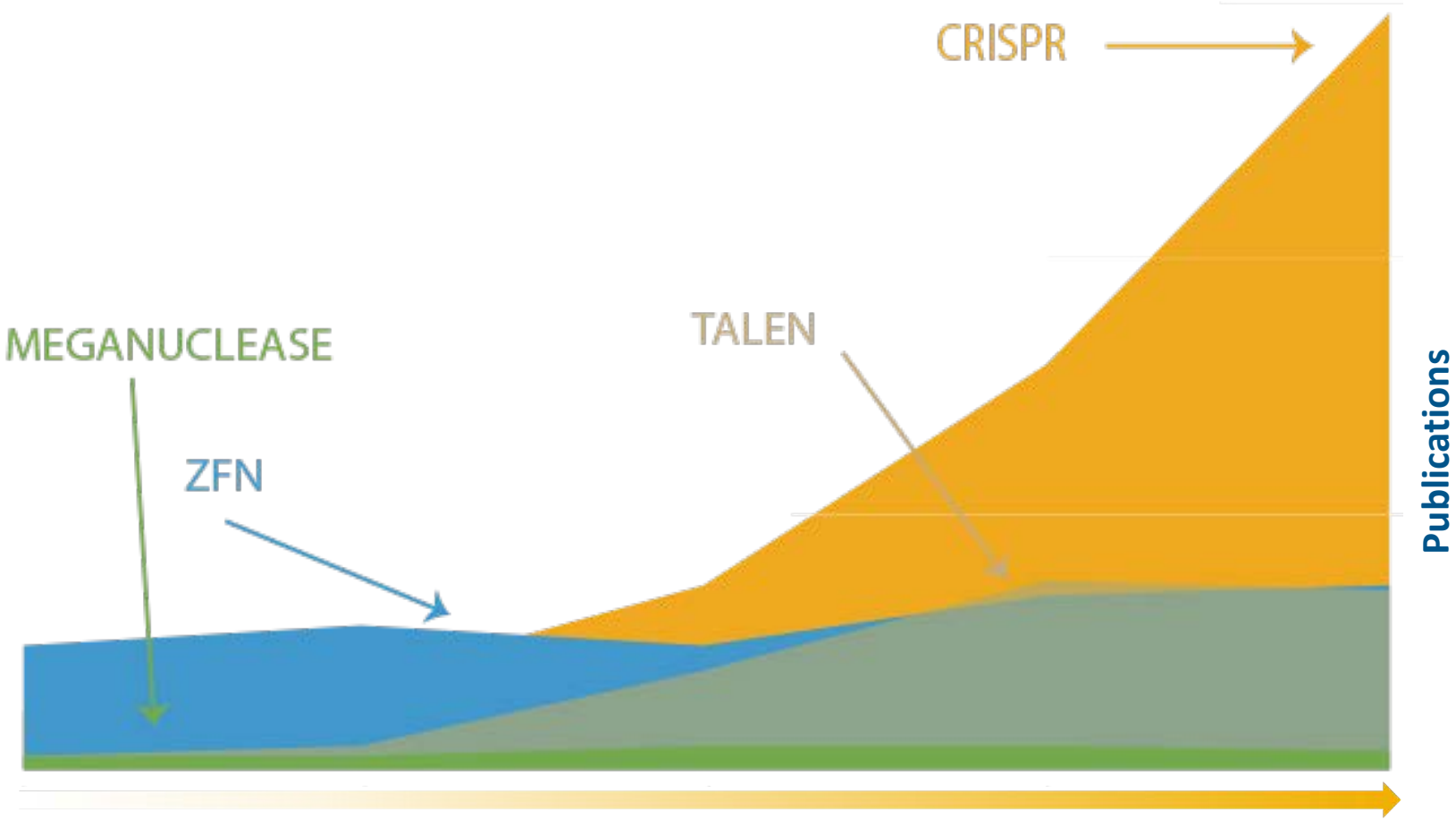
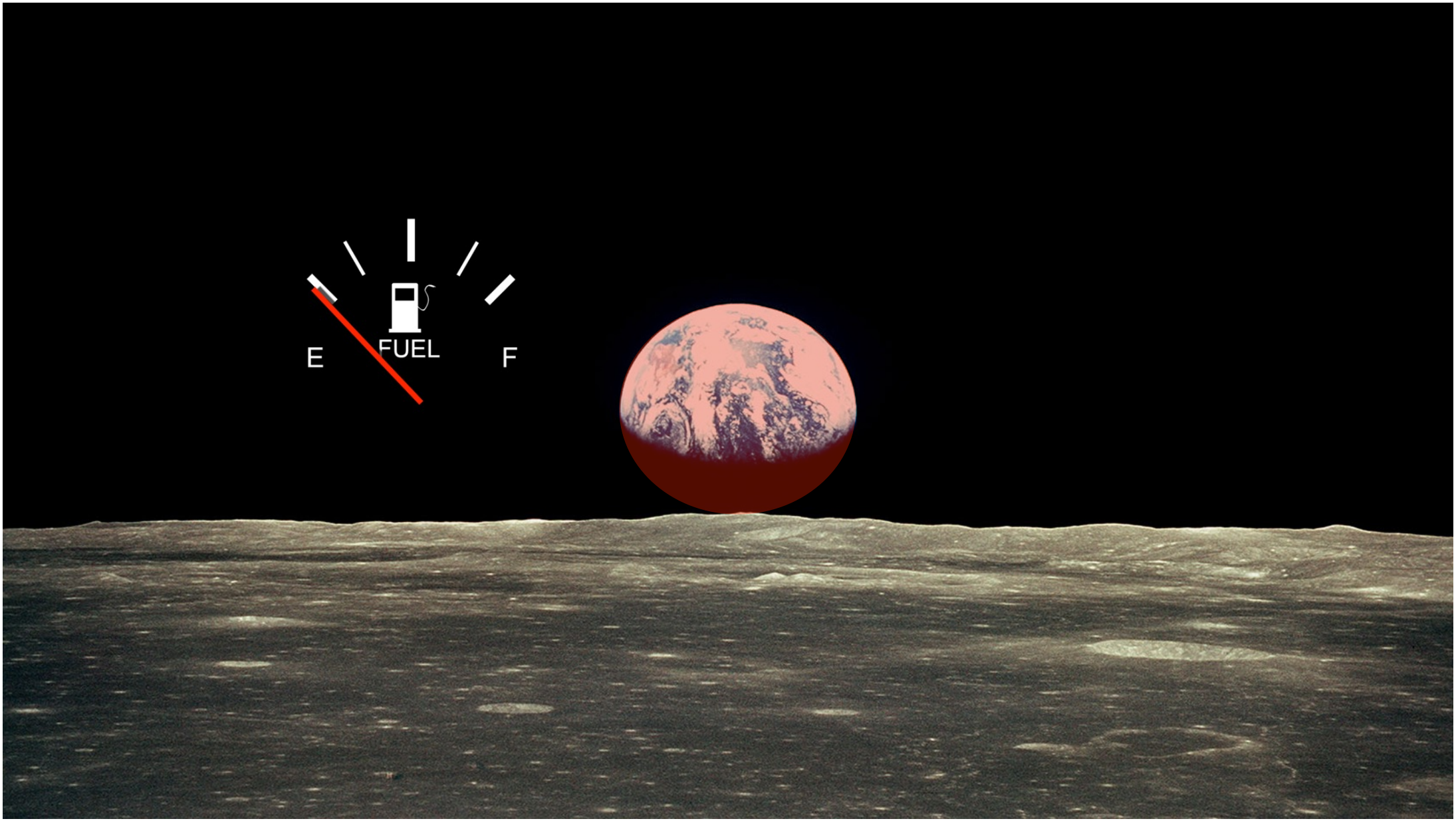
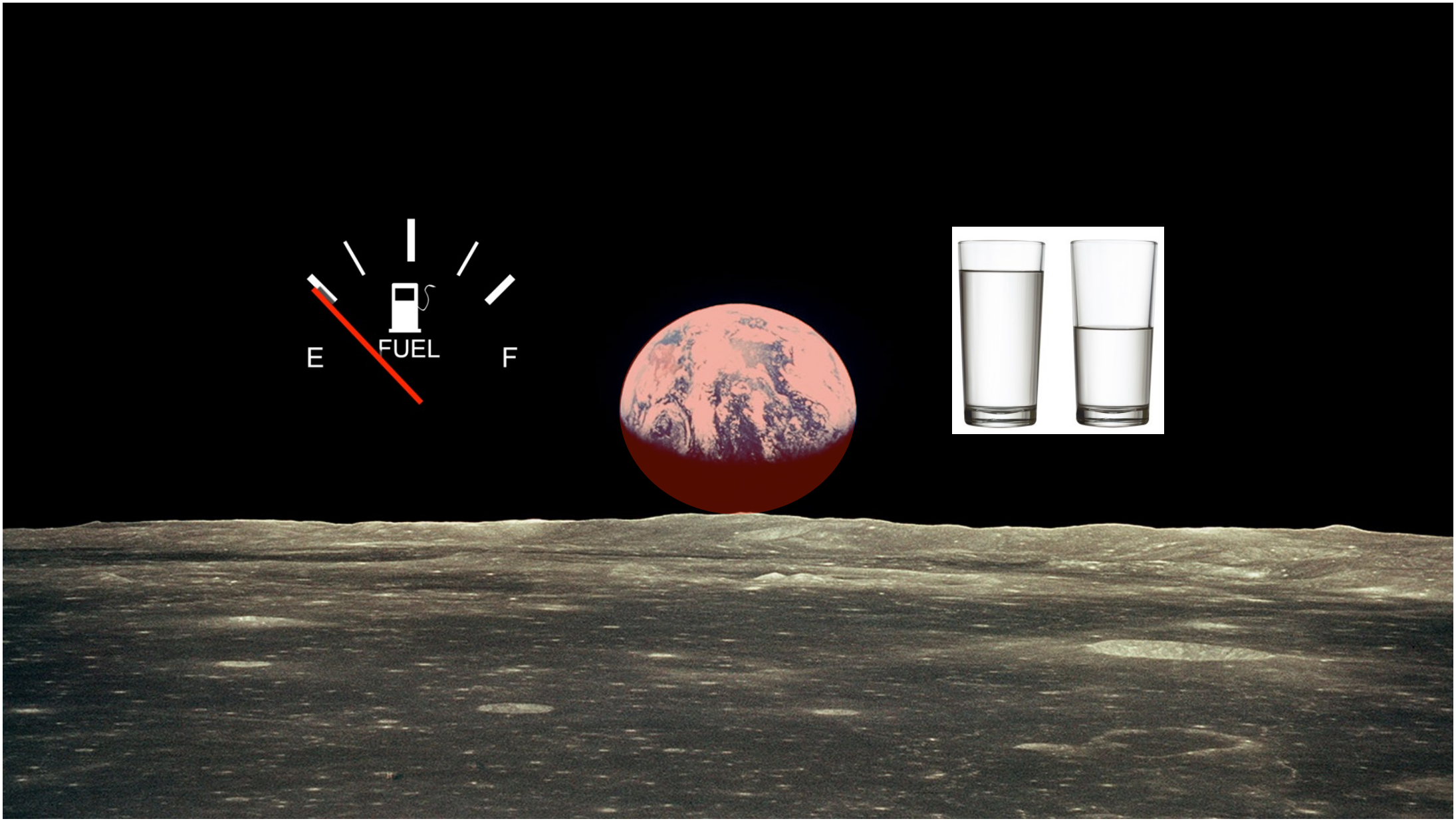
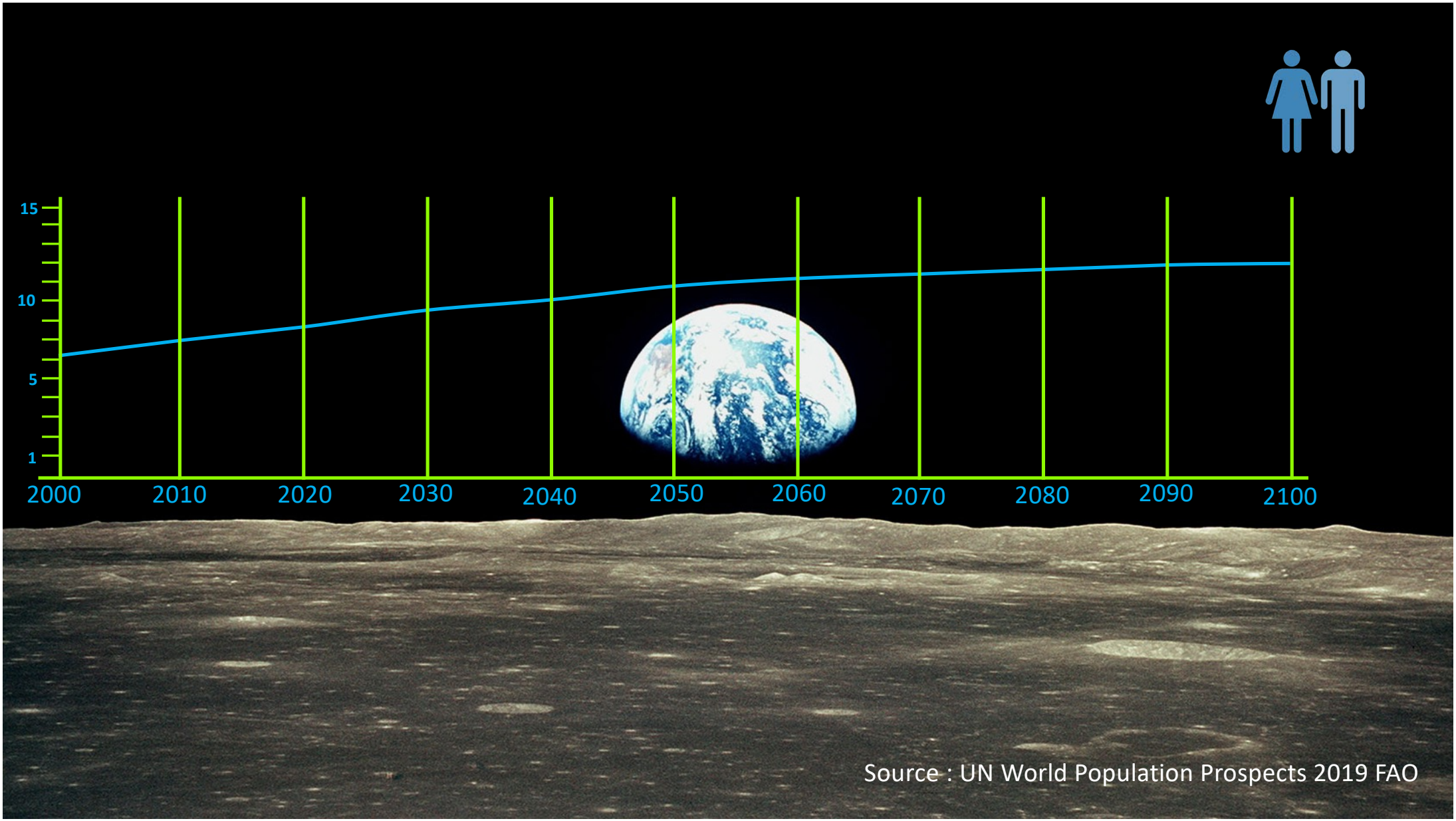

CRISPR
TALEN
MEGANUCLEASE
ZFN
Publications
Time


Bill Anders, Apollo 8


E
FUEL
F


E
FUEL
F


15
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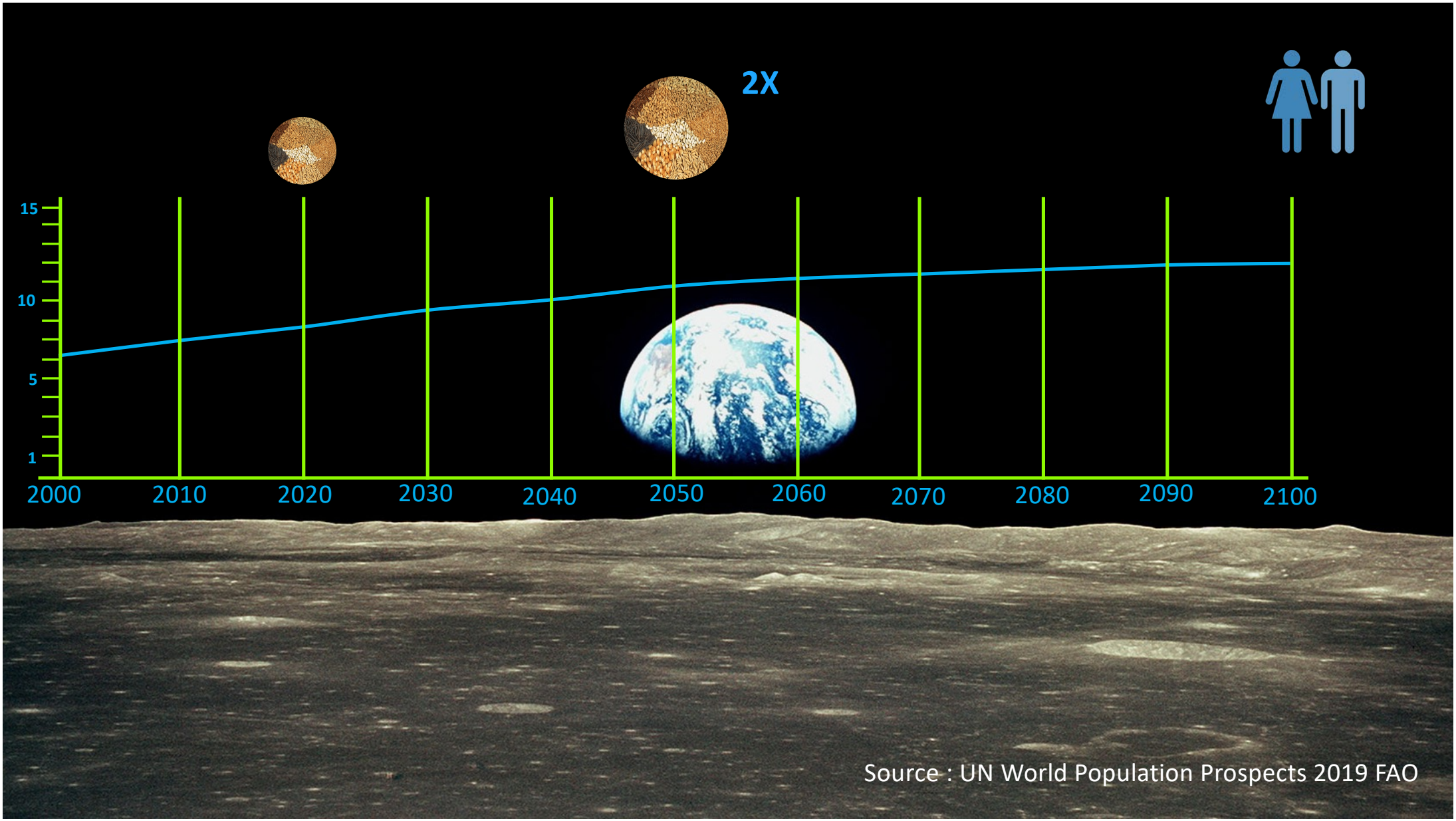
Source : UN World Population Prospects 2019 FAO


2X
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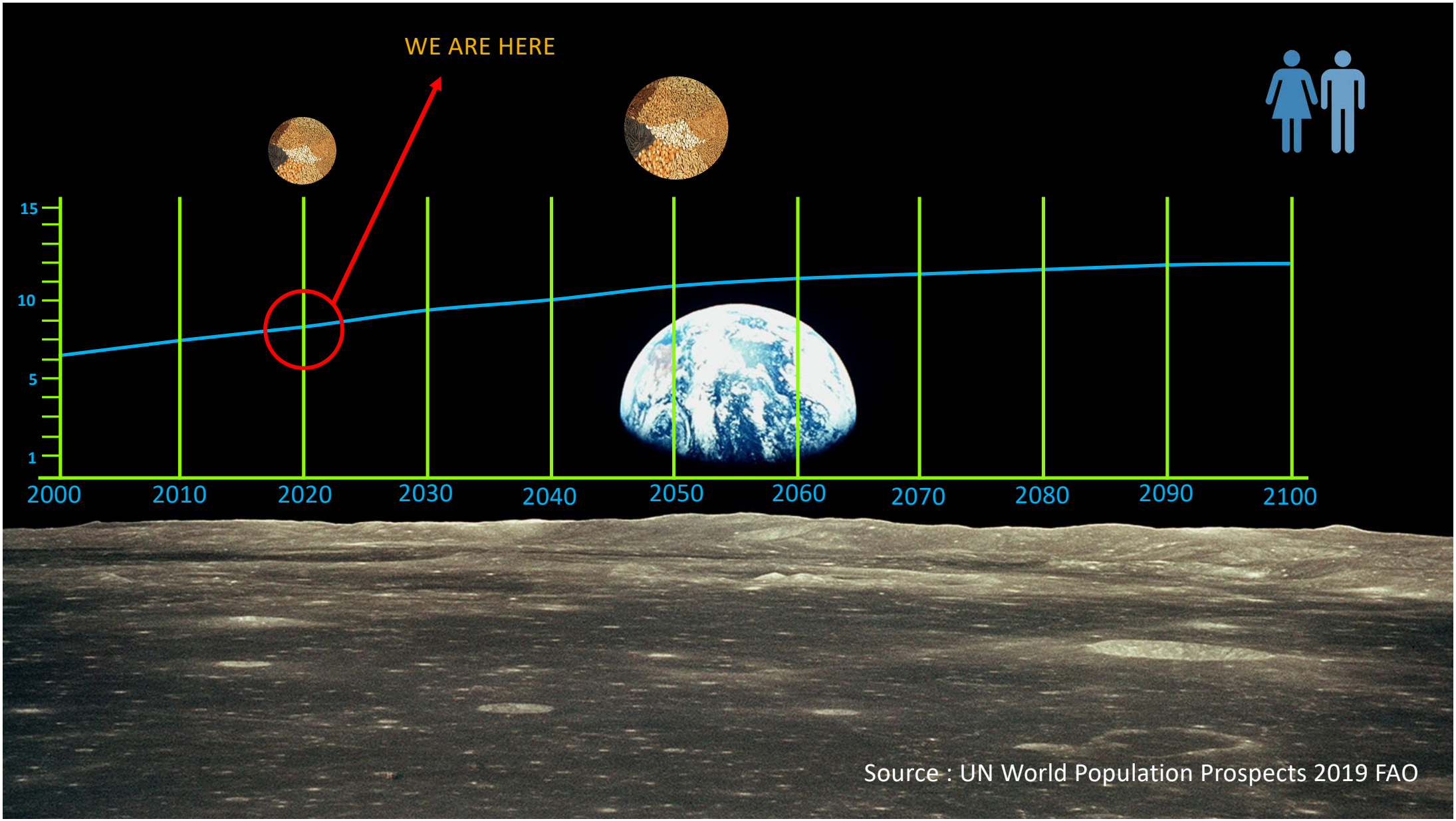
Source : UN World Population Prospects 2019 FAO


WE ARE HERE
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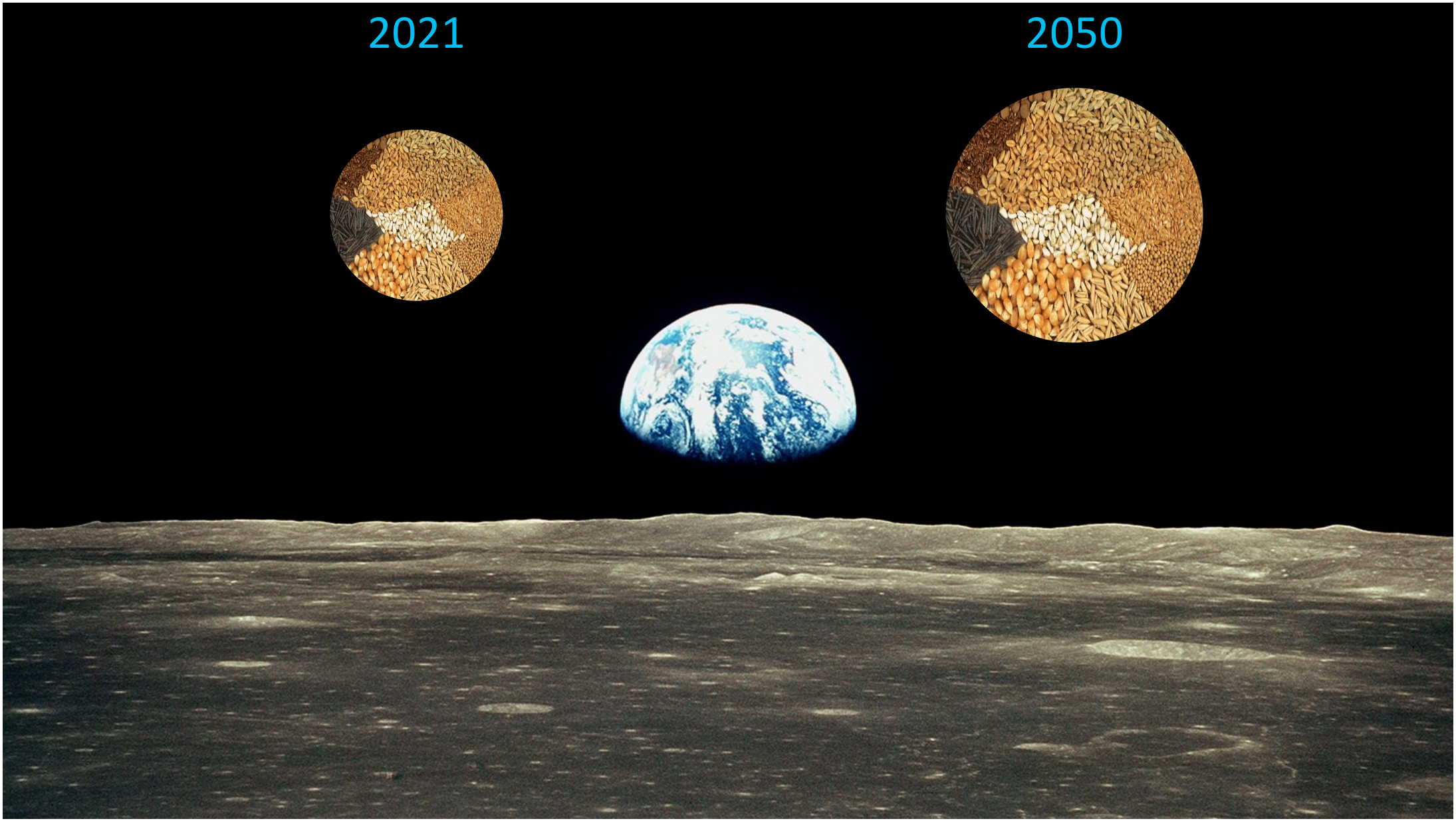
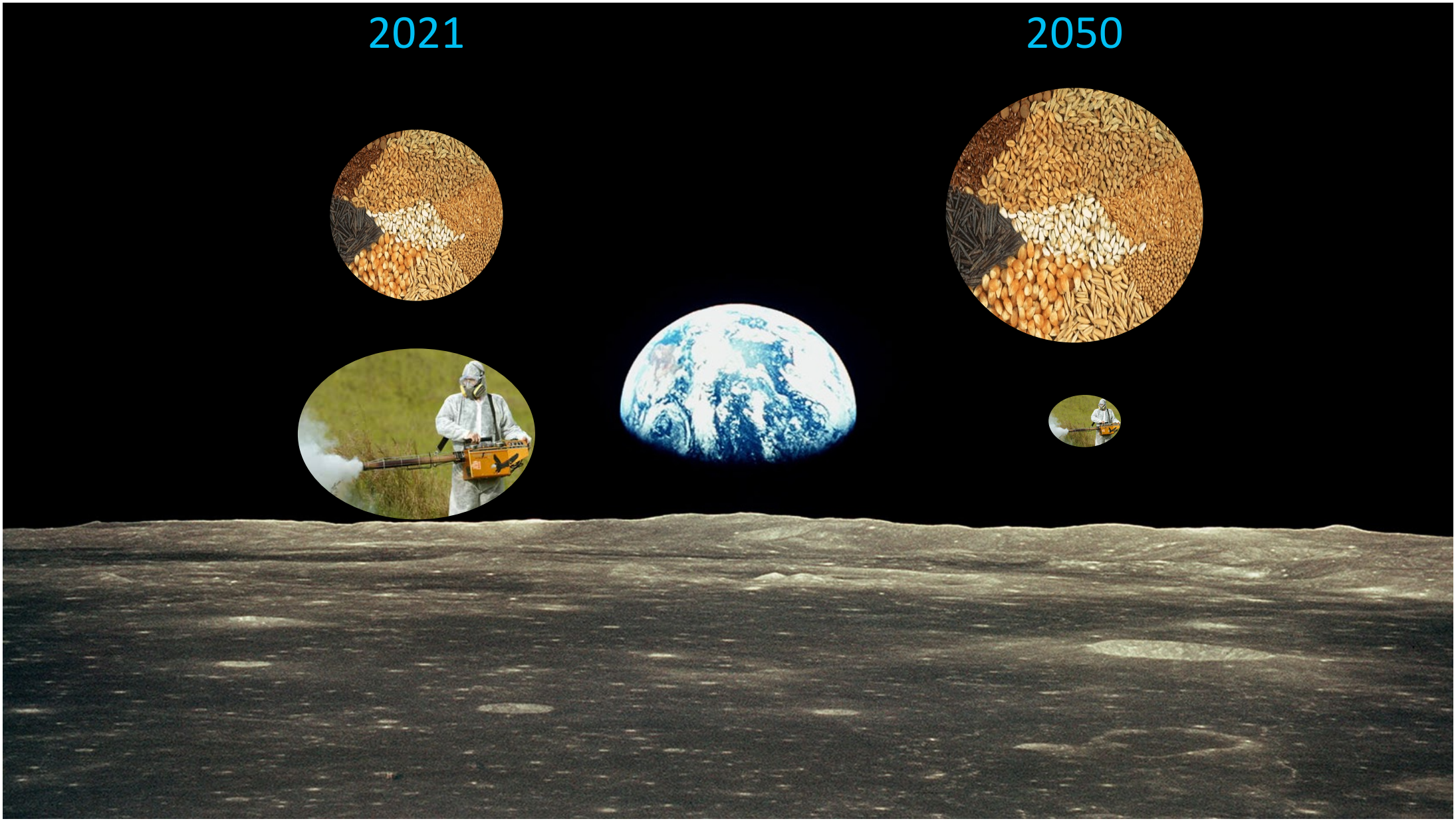
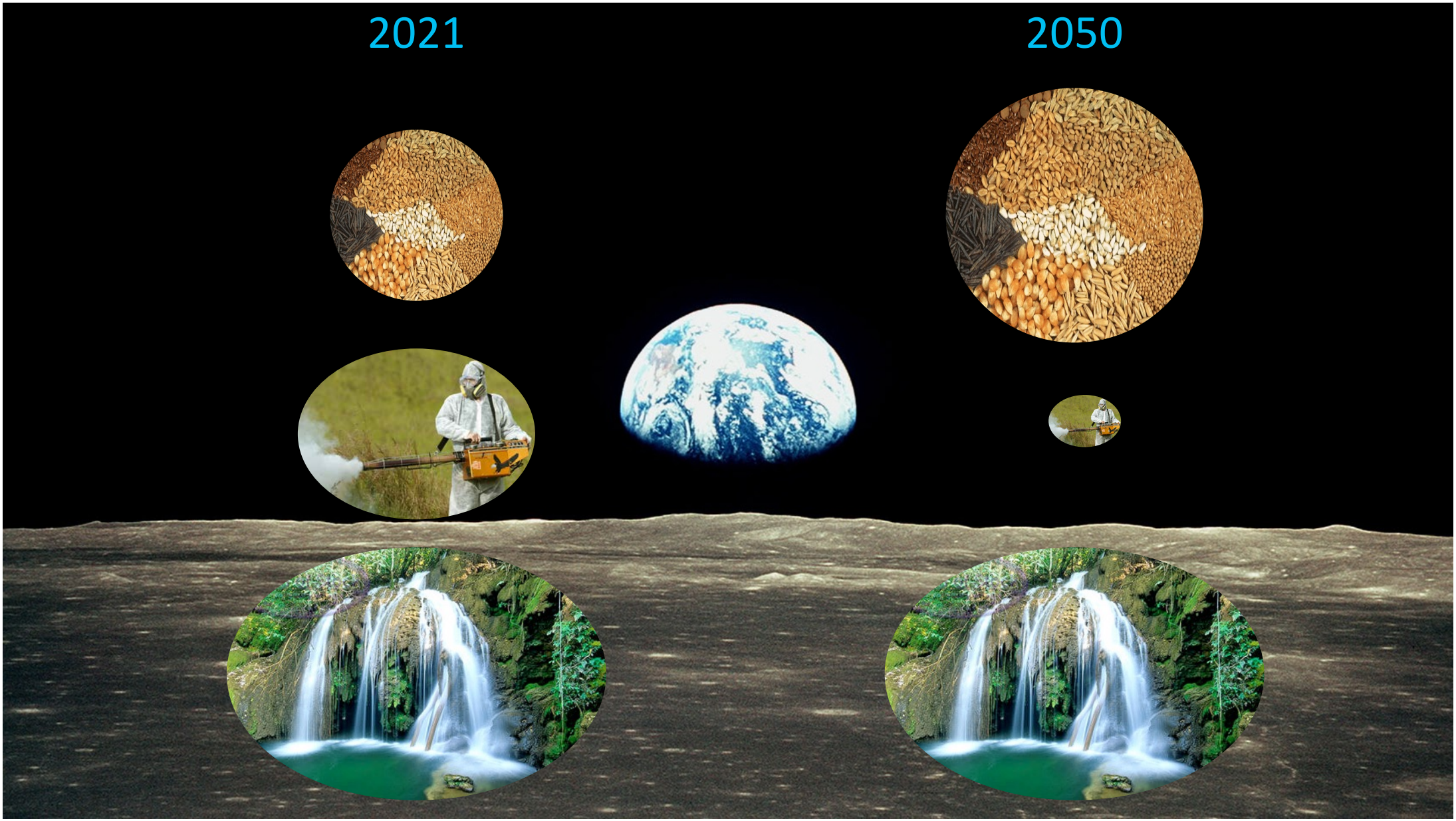
2100
Source : UN World Population Prospects 2019 FAO


2021
2050


2021
2050


2021
2050

- **Statement 1:** The innovation that comes with genome editing technology can hardly be overstated. However downstream bottlenecks need to be tackled to bring the science into practice.

- **Statement 2:** We cannot send mixed messages to a well-informed public. Therefore, we need to be factual and:
  - Focus legislation on the end-product and not the method
  - Regulation should be trait-based for any trait that could not be made with traditional technology (breeding, mutagenesis, TILLING, crossing, tissue culture, hybridisation, etc.)
  - Organisms modified by GE that do not contain foreign DNA should not be regulated as GMO.

- **Statement 3:** To face the challenges of the coming decades, we need a fundamental different approach in our mindset and revenue model for enabling technologies such as genome editing.


Bill Anders, Apollo 8