Innovations and Novel Food Systems in Ukraine & Europe

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The OECD Co-operative Research Programme: Sustainable Agricultural and Food Systems

BETTER POLICIES FOR BETTER LIVES

Global Conference on
Sustainability in Agriculture & Food Systems
Innovation, Indicators & Implementation

The Ukraine Law on Genetically Engineered Organisms signed in 2007

The proposed new Law discussed in Parliament starting 2022

No legislation in place on genome editing

ЗАКОН УКРАЇНИ

Про державну систему біобезпеки при створенні, випробуванні, транспортуванні та використанні генетично модифікованих організмів

(Відомості Верховної Ради України (ВВР), 2007, № 35, ст.484)

{Із змінами, внесеними згідно із Законами
№ 1804-VI від 19.01.2010, ВВР, 2010, № 9, ст.90
№ 4441-VI від 23.02.2012, ВВР, 2012, № 42, ст.529
№ 5456-VI від 16.10.2012, ВВР, 2013, № 46, ст.640
№ 1170-VII від 27.03.2014, ВВР, 2014, № 22, ст.816
№ 1193-VII від 09.04.2014, ВВР, 2014, № 23, ст.873
№ 1602-VII від 22.07.2014, ВВР, 2014, № 41-42, ст.2024
№ 222-VIII від 02.03.2015, ВВР, 2015, № 23, ст.158
№ 2059-VIII від 23.05.2017, ВВР, 2017, № 29, ст.315
№ 2530-VIII від 06.09.2018, ВВР, 2018, № 41, ст.320
№ 124-IX від 20.09.2019, ВВР, 2019, № 46, ст.295
№ 440-IX від 14.01.2020, ВВР, 2020, № 28, ст.188
№ 2849-IX від 13.12.2022}

Проект Закону про державне регулювання генетично-інженерної діяльності та державний контроль за обігом генетично модифікованих організмів і генетично модифікованої продукції для забезпечення продовольчої безпеки

https://bch.cbd.int/en/countries/UA/LAW

‘The biotechnology regulatory system in Ukraine is still not fully developed, but the country is gradually adjusting its domestic policies to align with the European Union’s regulations. Agricultural biotechnology is a disputed item in Ukraine. Currently, no GE events are officially approved for agricultural and food production. Therefore, no GE products can be legally imported into Ukraine, which restricts trade in some agricultural and food commodities from the United States. The Government of Ukraine does not permit the cultivation of GE crops, however, there are reports of unregistered GE production for certain crops.’
Denys Sobolev
Date: November 14, 2022 USDA Report Number: UP2022-0078 Report Name: Biotechnology and Other New Production Technologies Annual Country: Ukraine

https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Biotechnology%20and%20Other%20New%20Production%20Technologies%20Annual_Kyiv_Ukraine_UP2022-0078.pdf

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https://bch.cbd.int/en/countries/UA/LAW

UA Law Draft of 5839 від 05.08.2021
https://itd.rada.gov.ua/billInfo/Bills/CardByRn?regNum=5839&conv=9

Plant Biotechnology in Ukraine

Main research institutes, National Academy of Science of Ukraine

- Institute of Cell Biology and Genetic Engineering
- Institute of Molecular Biology
- Institute of Food Biotechnology and Genomics

In 70-80ies – world leadership in somatic hybridization; first in USSR works on genetic transformation of plants

In 90ies – exodus to Western academic labs and companies; many maintain contacts and help colleagues in Ukraine

Work(ed) at universities of California, Stanford, Cambridge, Oxford, Munich, Melbourne, Tokyo, institutes Max-Planck, Leibnitz, John Innes, CNRS, INRA…

Work(ed) at Bayer, Monsanto, Syngenta, BASF, American Cyanamid, KWS…

Founded/manage several plant biotech companies.

EU Companies Founded and Led by Ukrainians

Icon Genetics GmbH, Germany
CEO Victor Klimyuk
Plant Biotechnology
Founded 1999

NOMAD Bioscience GmbH, Germany
NOMADS UAB Lithuania
CEO Yuri Gleba
CSO Anatoli Giritch
Plant Biotechnology
Founded 2008-2012

NAMBAWAN Biotech GmbH, Germany
NAMBAWAN SLU, Spain
CEO Yuri Gleba
COO Anatoli Giritch
Plant Biotechnology
Founded 2021-3

ScreenSYS GmbH, Germany
CEO Oleksandr Dovzhenko
Plant Biotechnology
Founded 2022

IP and Publications

>550 issued patents representing >55 patent families in 26 countries
10 product approvals as GRAS food substances/food processing aids by FDA and FEMA

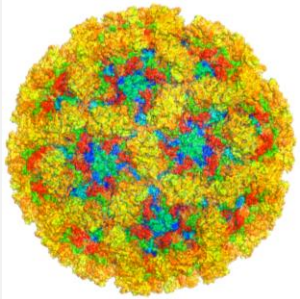
- Nature Sci. Rep., 12:5865 (2022)
- Nature Plants, 7, 159 (2021)
- Nature Sci. Rep., 9, 15422 (2019)
- Nature Sci. Rep., 8:4078 (2018)
- Nature Sci. Rep., 8:10589 (2018)
- Proc. Natl. Acad. Sci. USA, 112, 1513311 (2015)
- Proc. Natl. Acad. Sci. USA, 111, 1402836 (2014)
- Proc. Natl. Acad. Sci. USA, 108, 14061 (2011)
- PLoS One, 6, 19722 (2011)
- PLOS One, 4, 5553 (2009)
- PLOS One, 3, 3647 (2008)
- Proc. Natl. Acad. Sci. USA, 104, 6864 (2007)
- Proc. Natl. Acad. Sci. USA, 103, 17678 (2006)
- Proc. Natl. Acad. Sci. USA, 103, 14701 (2006)
- Proc. Natl. Acad. Sci. USA, 103, 861 (2006)
- Nature Biotechnology, 23, 718 (2005)
- Proc. Natl. Acad. Sci. USA, 101, 6852 (2004)
- Nature Biotechnology, 22, 461 (2004)
- Nature Biotechnology, 21, 224 (2003)
- Proc. Natl. Acad. Sci. USA, 99,5301 (2002)
- Nature Biotechnology, 18, 1303 (2000)
- Nature Biotechnology, 17, 466 (1999)
- Proc. Natl. Acad. Sci. USA, 96,5973 (1999)
- Proc. Nati. Acad. Sci. USA, 84, 3709 (1987)

Plant-Made Pharmaceuticals/Food Additives: Entered Market Phase

NOMAD

Over 600 proteins including difficult to express ones:

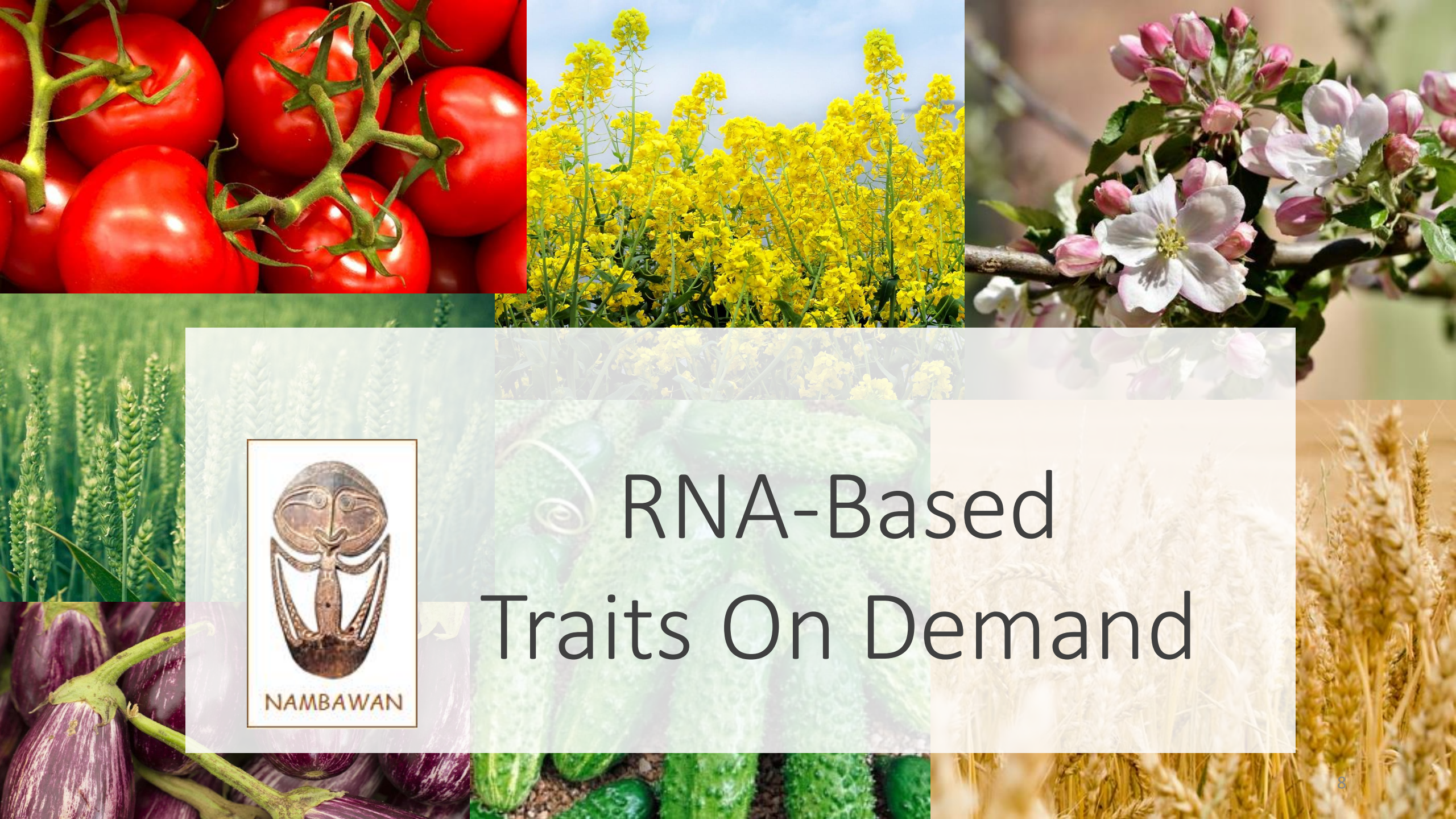
- Antibodies
  - Novel therapeutic MABs
  - Biosimilars
  - MABs for diagnostics
- Vaccines
  - Antigens
  - Virus-like particles
- Antibacterial and antiviral proteins
  - Bacteriocins
  - Lectins
- Diagnostic proteins
- Food additive proteins
  - Thaumatins
  - Enzymes
- Industrial proteins
  - Cellulases
- Biopolymers, bioscaffolds



most recent trials rely on transient production technology!

Several products advanced:

- Glucocerebrosidase/Protalix, approved
- Anti-caries Mab/Planet, approved
- Fabry Disease Therapy/Protalix, Phase I-II
- Anti-TNF Therapy/Protalix, Phase I
- Anti-HIV Griffithsin/UoL, Phase I
- **Norovirus Vaccine Icon-Denka, Phase I**
- **NHL Vaccine/Icon-Bayer, Phase I**
- Influenza Vaccine/Medicago, Phase II-III
- Influenza Vaccine/iBio, Phase I
- Anti-Ebola Mab, Mapp, Phase I-II
- **Bacteriocins Nomad, 5 GRAS status**
- **Thaumatin II Nomad, 5 GRAS status**



NAMBAWAN

RNA-Based Traits On Demand

The Problem

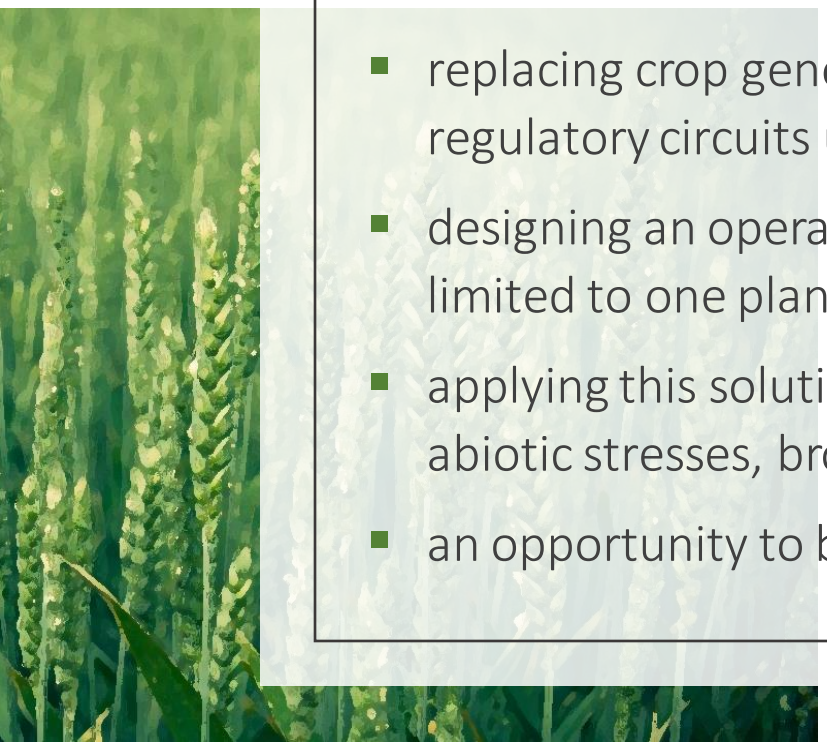
of modern breeding

- Traditional plant breeding technology is severely limited because of long times, usually more than a decade, required to develop and register a new variety, and associated high costs & low throughput
- Even for biotechnology-based transgenic crops, it takes years alone to generate a transformation event and to backcross it into commercial varieties
- Current changes in climate along with planet overpopulation & destabilization result in pathogen pandemics in humans, animals & plants as well as abiotic stresses in plants – all of those require fast responses from us that can't be delivered by existing technologies

What if

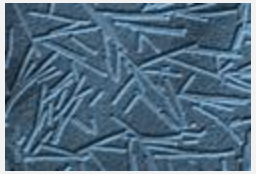
we could quickly re-program crop agronomic performance without changing plant genome

- replacing crop genome modification with a quick modulation of plant regulatory circuits using RNA viral replicons, thus generating a needed trait
- designing an operator control of plant performance that is fast, reversible, limited to one plant generation, inexpensive, easy to implement & scalable
- applying this solutions to deal with unexpected plant pathogen pandemics, abiotic stresses, broadly adaptable to major and orphan crops
- an opportunity to build a high value, sustainable, novel agriculture business



Principles Of RNA-Based Transient Crop Modification

1st generation process: *Agrobacteria* deliver DNA templates which plant cell transcribes into RNA replicons that move within a plant and express traits transiently



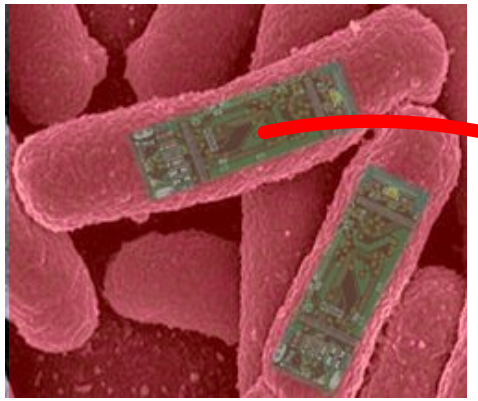
2nd generation process: packaged RNA replicons are made in a host plant (*N. benthamiana*), purified and used on a crop for transient trait induction

The whole process is analogous to what occurs when information is transferred from a flash drive to a computer CPU and processed

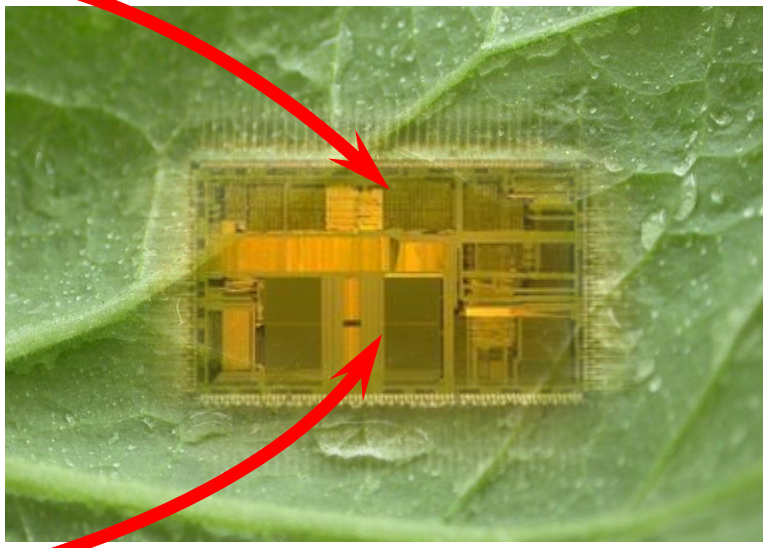
Flash drive, 254 GB memory

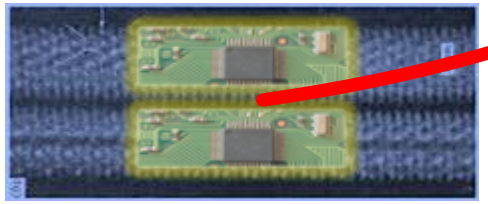
3 GHz CPU, 1 TB memory

NOMADIC® Technology!



bacteria deliver information in a form of T-DNA





RNA vector delivers information ready to be mobilized and used

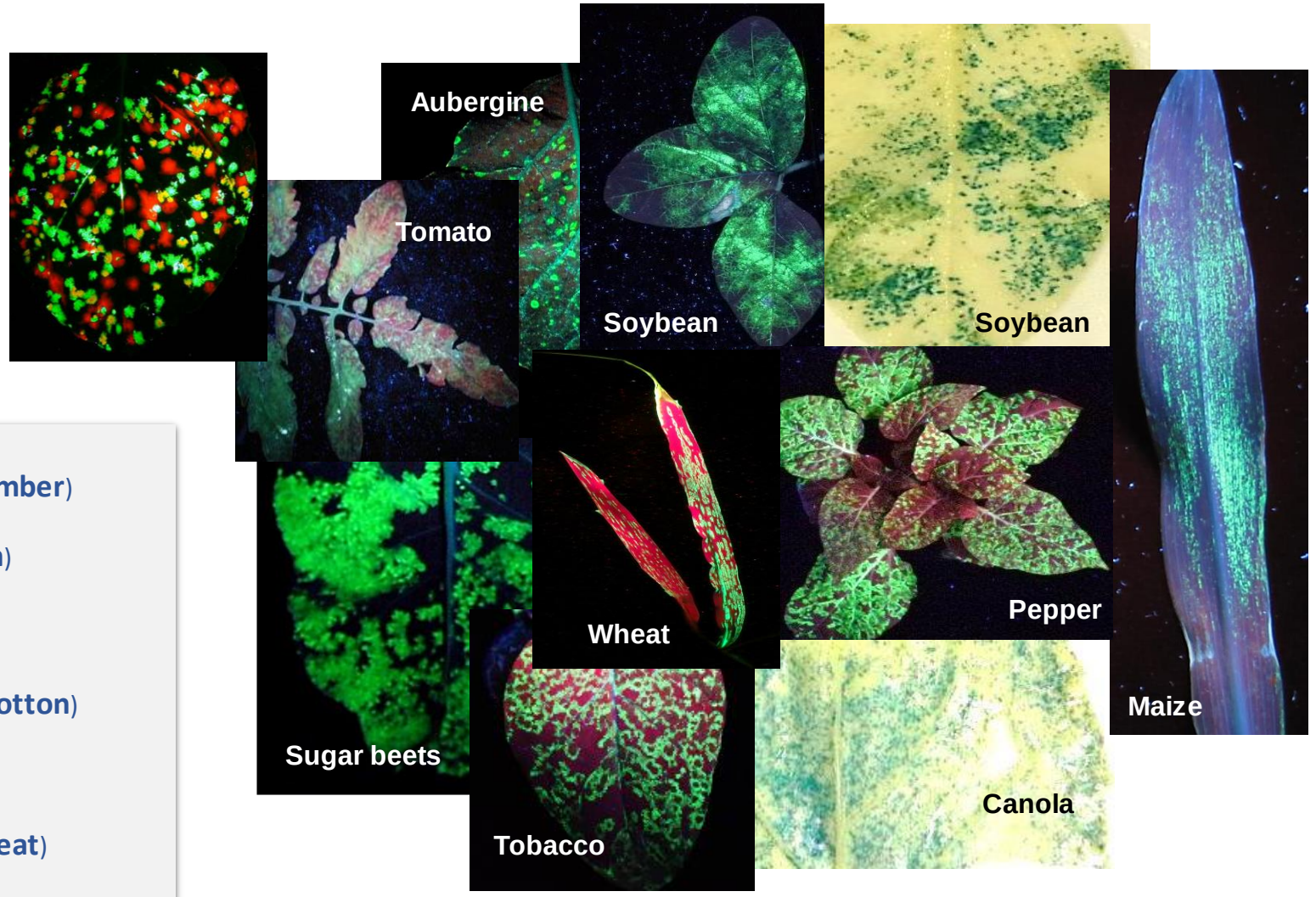
NOMADIC® RNA Vectors Work With Most Major Crops

15 plant families, including:

Solanaceae
Capsicum annuum (**pepper**)
Lycopersicon esculentum (**tomato**)
Nicotiana (6 **tobacco** species)
Solanum melongena (**aubergine**)
Solanum tuberosum (**potato**)
Chenopodiaceae
Beta vulgaris (**sugar beets**)
Spinacea oleracea (**spinach**)
Brassicaceae
Brassica napus (**canola**)
Brassica oleracea (**cabbage**)

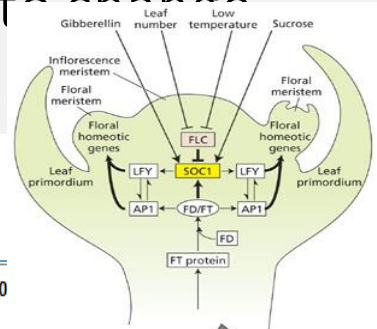
Cucurbitaceae
Cucumis sativus (**cucumber**)
Fabaceae
Glycine max (**soybean**)
Vicia faba (**beans**)
Pisum sativum (**pea**)
Malvaceae
Gossypium hirsutum (**cotton**)

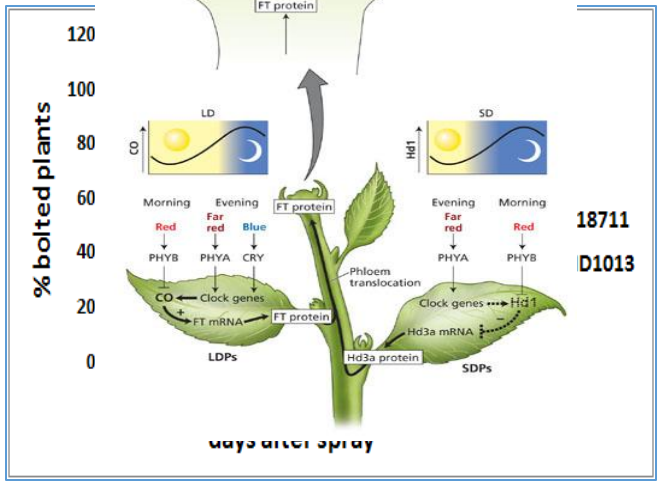
Gramineae
Zea mays (**corn**)
Triticum aestivum (**wheat**)
Amaryllidaceae
Allium sativum (**garlic**)

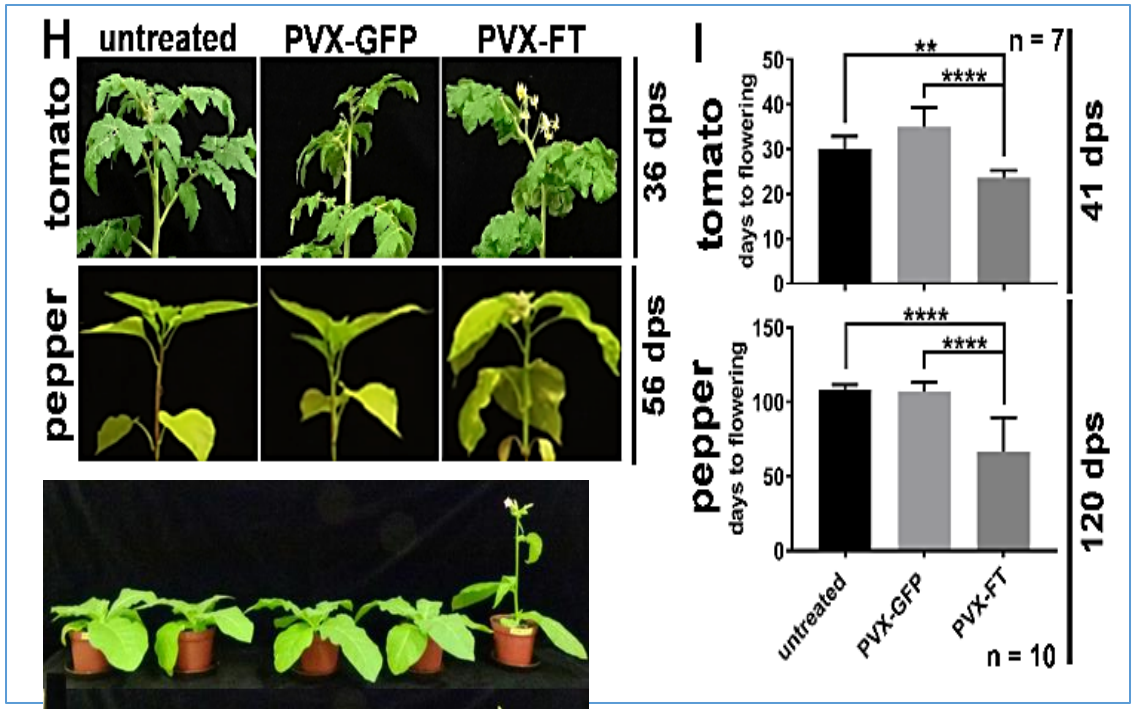


Flowering Control, Transiently: ‘Florigens’

Easy control of flowering, fruit set time
Relieves vernalization
Works with multiple crops
Tested over 40 genes, ‘on’ and ‘off’ switches
Allows to shorten life cycle, to change seed/green biomass ratio

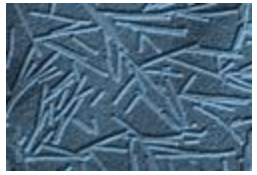


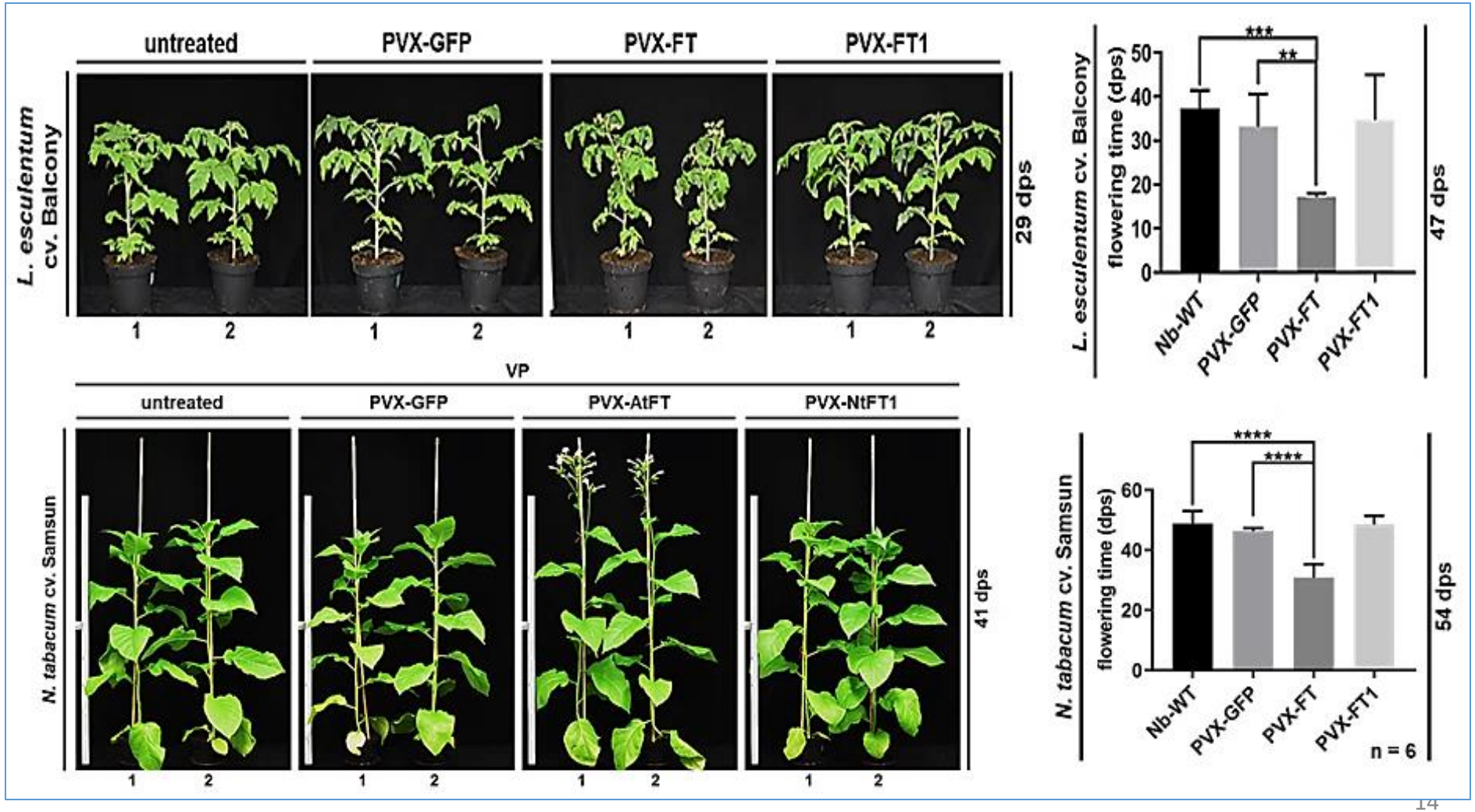




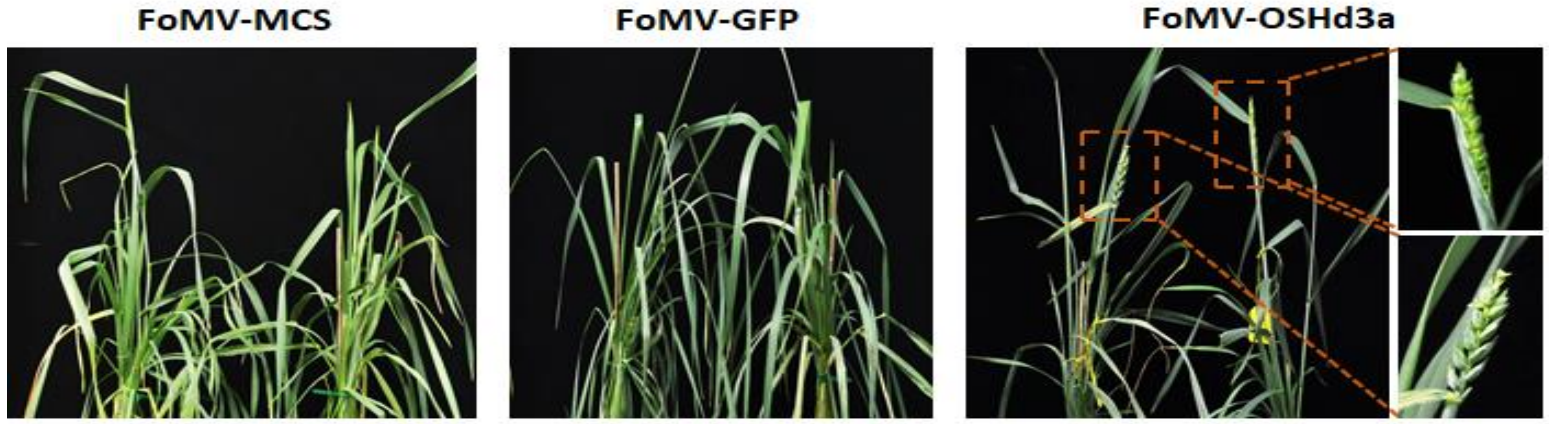
untreated - AIB - ICF320 - PVX-GFP - PVX-FT

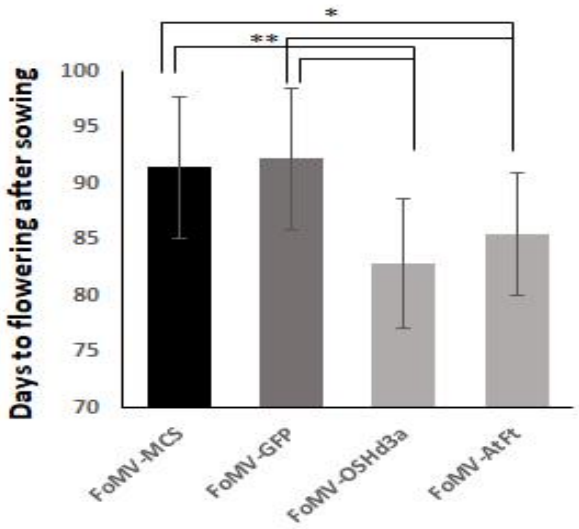
Spraying Tomato & Tobacco with RNP Particles: Flowering Time

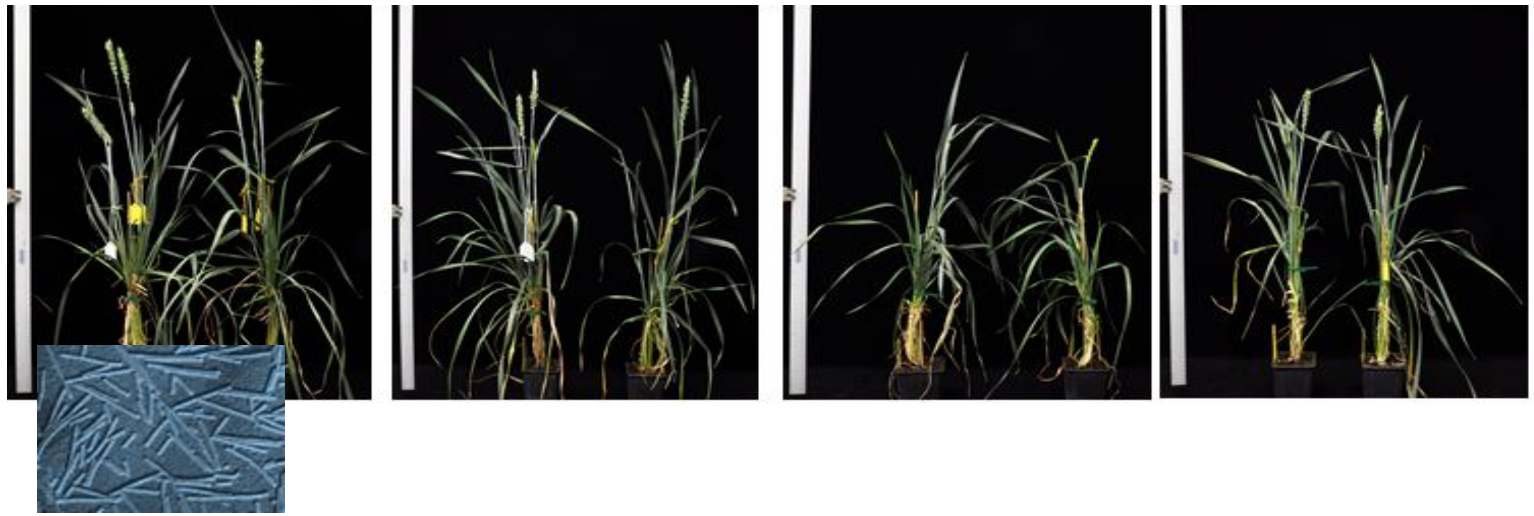


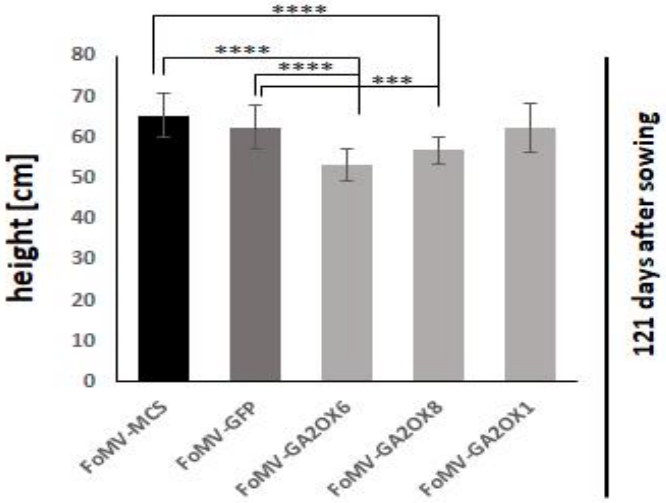


Control of Flowering and Dwarfism in Wheat

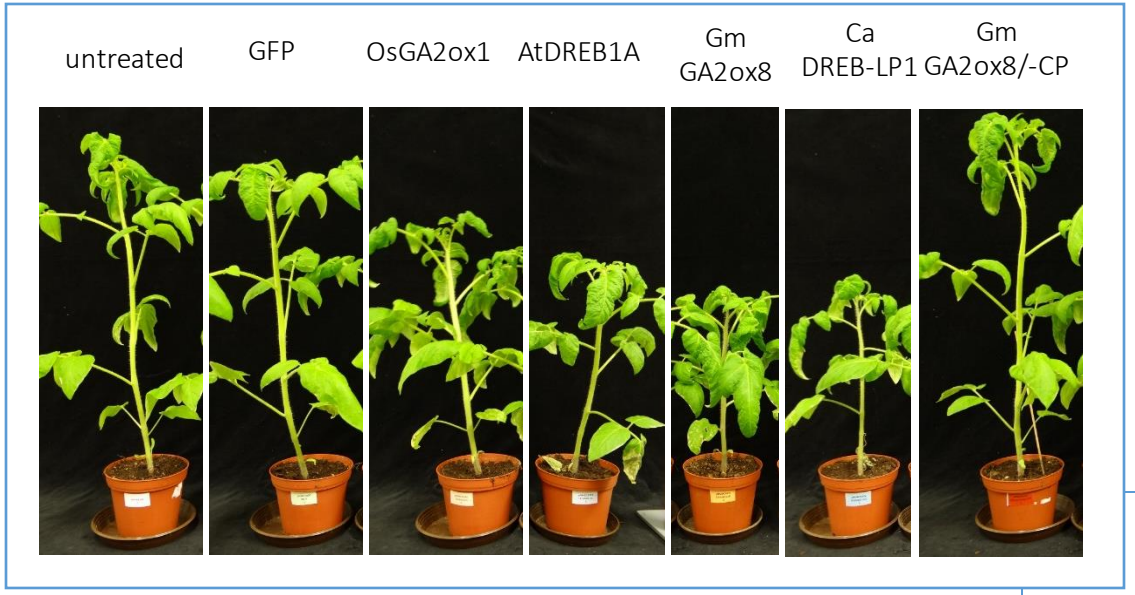


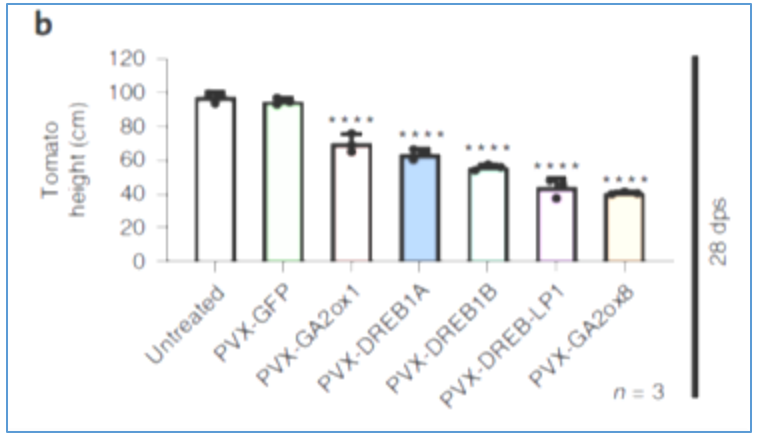


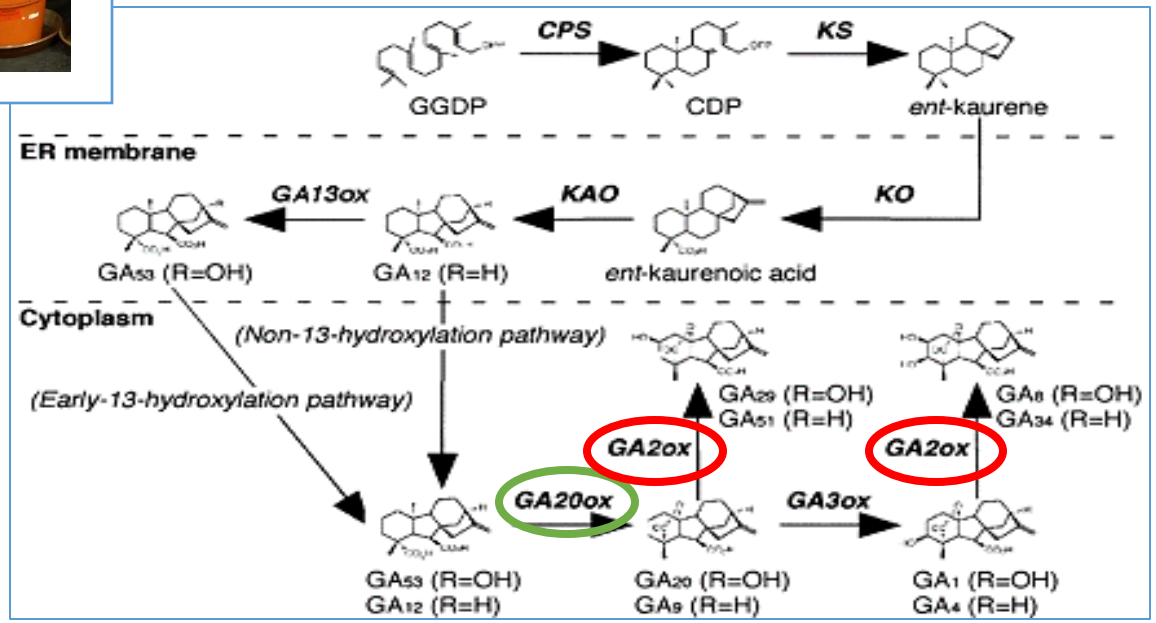




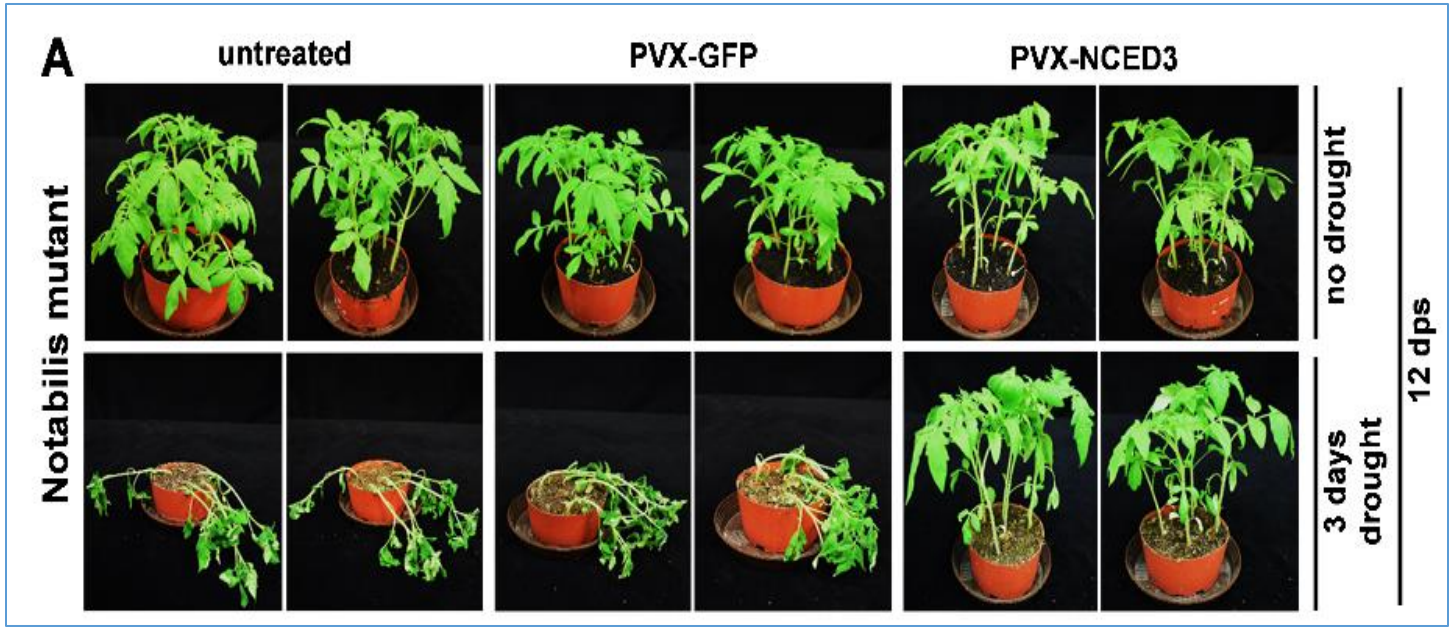
Dwarfism: Manipulating Gibberellin Pathway

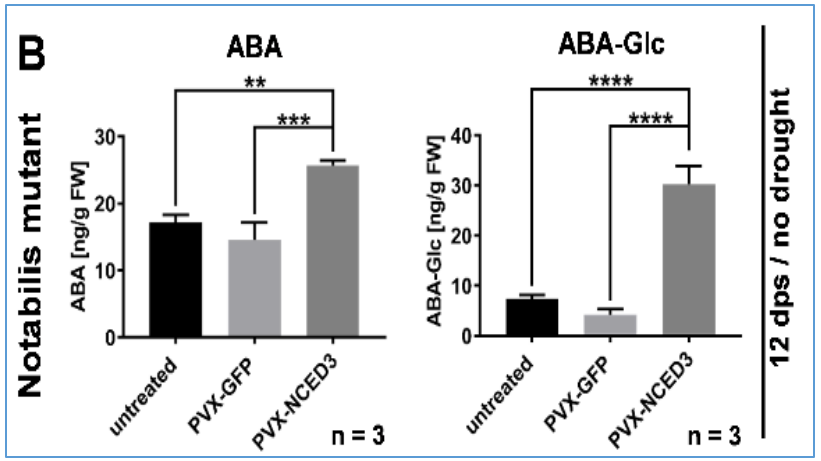


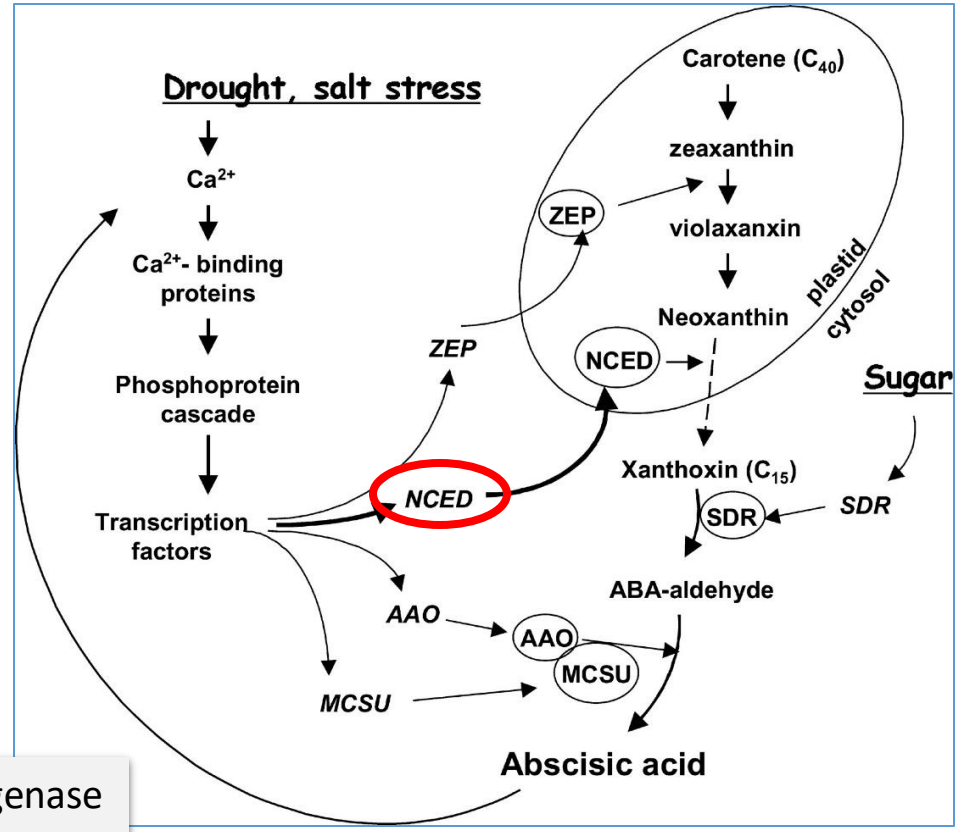




Drought Tolerance: Manipulating Abscisic Acid Pathway - ‚*Trait-On-Demand*‘

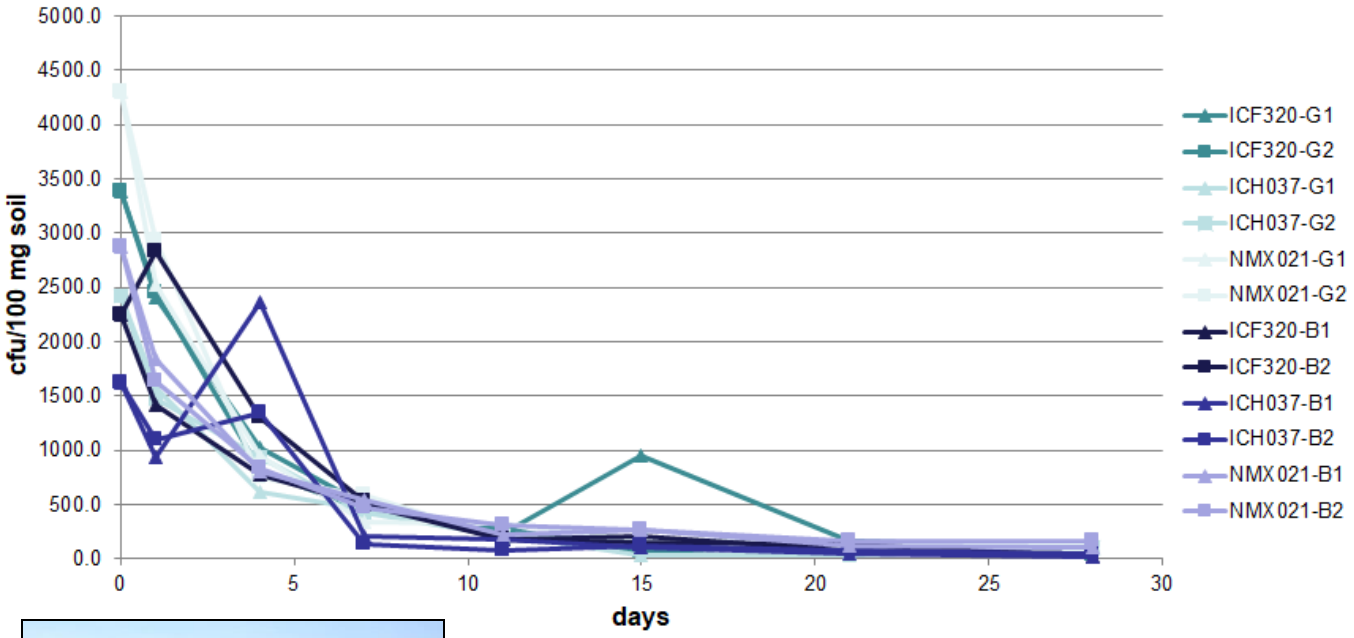




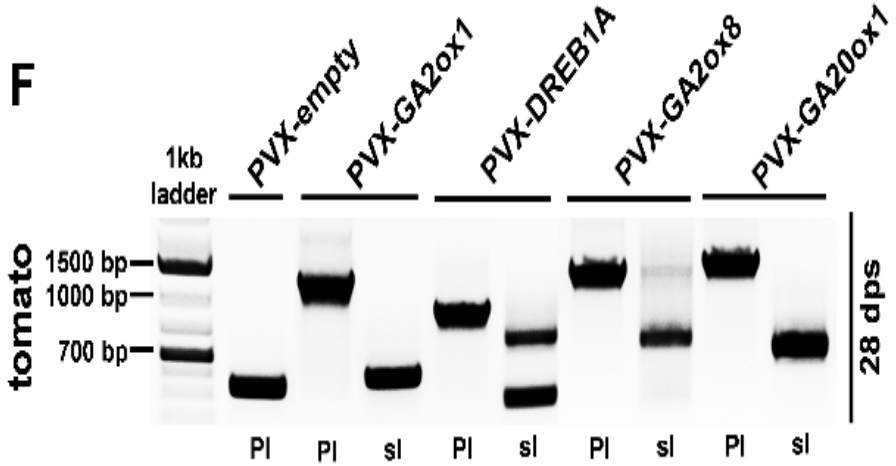


NCED: 9-cis-epoxycarotenoid dioxygenase
notabilis: NCED deficient mutant

Agrobacterium and Viral Vectors Are Self-Limiting: Quick Loss During Release or Systemic Move



In field experiments, *Agrobacterium* is rapidly lost to local bacterioflora

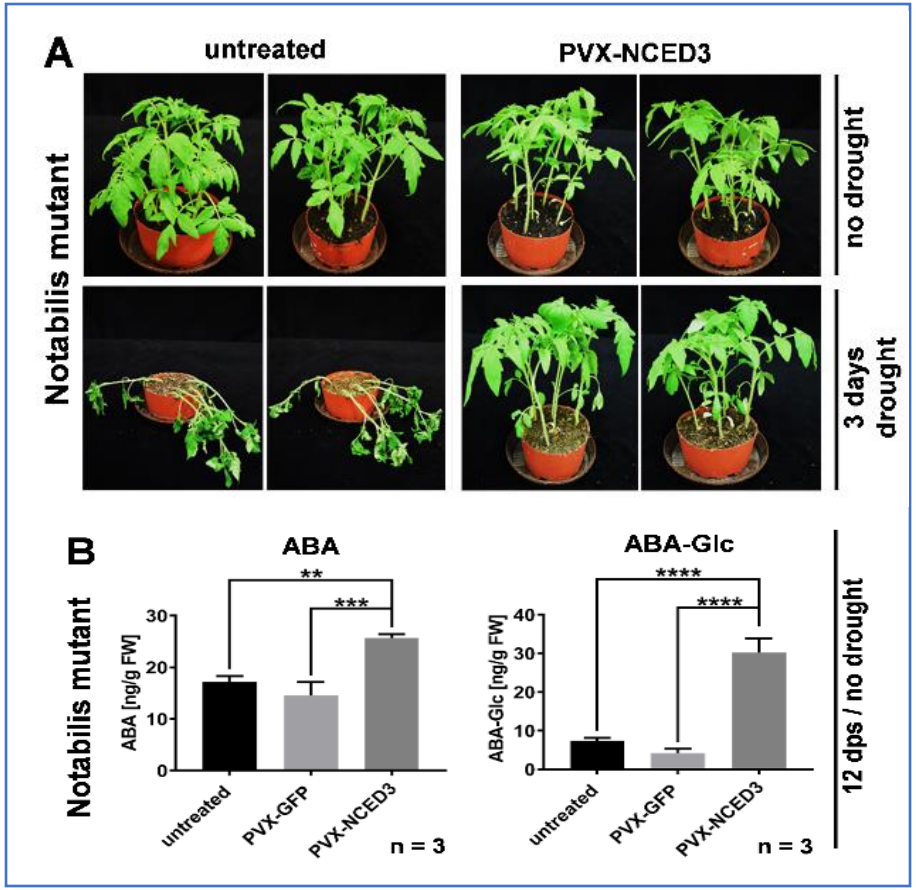


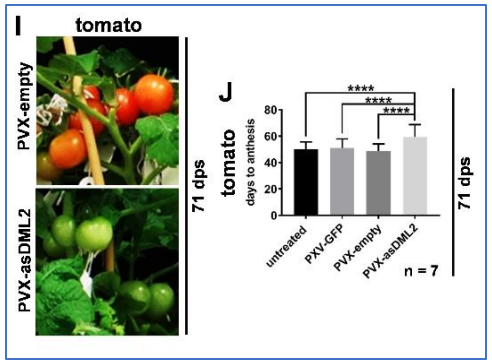
Gene inserts with GC content different from that of PVX are quickly lost during systemic movement

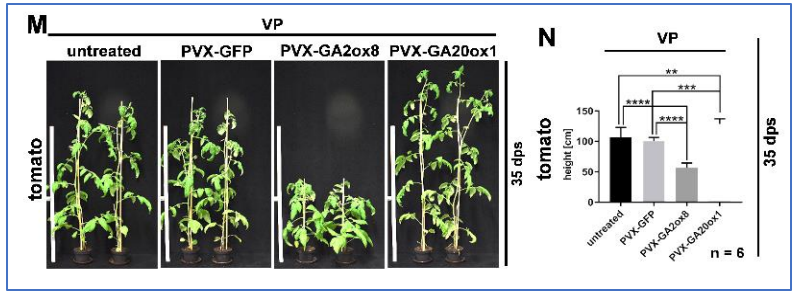
NOMAD's Plant Trait Reprogramming for Tomorrow

NOMAD with attractive production platforms magnICON® and NOMADIC®

- Transient reprogramming of plants for agronomic performance
- Universal applicability
- Traits-on-demand: control of flowering/fruit set; semi-dwarfism; drought resistance, fruit maturation, insect resistance, you name it
- Proof of principle with multiple crops plants including wheat, beans, tomato, potato, etc.
- Seminal paper in Nature Plants in 2021
- Delivery mediated by *Agrobacterium* or packaged RNA viral vector
- Safe, no plant genome modification, RNA based, no DNA release to environment; limited to one plant generation







Sweet & Taste Modifying Proteins

The Threat

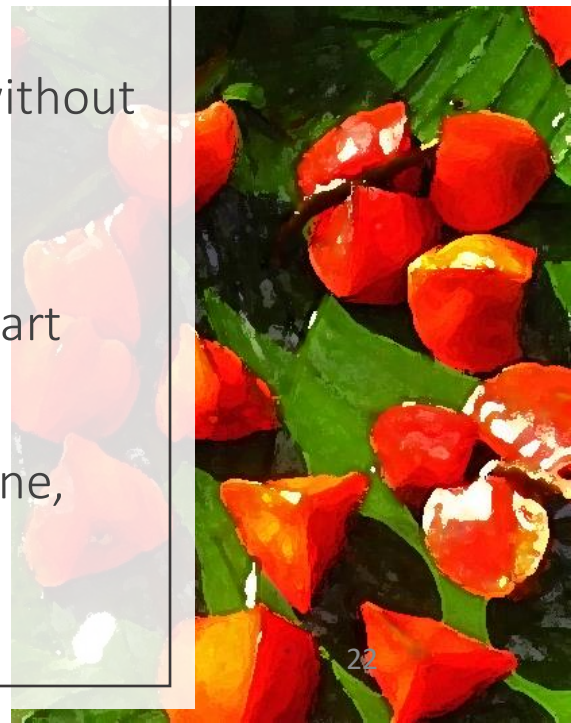
of unhealthy food

- Our current diet is unhealthy and unsustainable, primarily because it relies on excessive consumption of sugar & artificial sweeteners in our food and drinks
- Sugar is the main cause of obesity, overweight, diabetes, coronary/heart diseases
- Sugar market at US$75 B/y dwarfs markets of any single medicine
- Global area used for cultivation of sugar cane and sugar beets currently exceeds 31 million hectares (approx. the size of Germany)
- In addition, at least 2.5 million hectares of corn is grown in USA for corn syrup

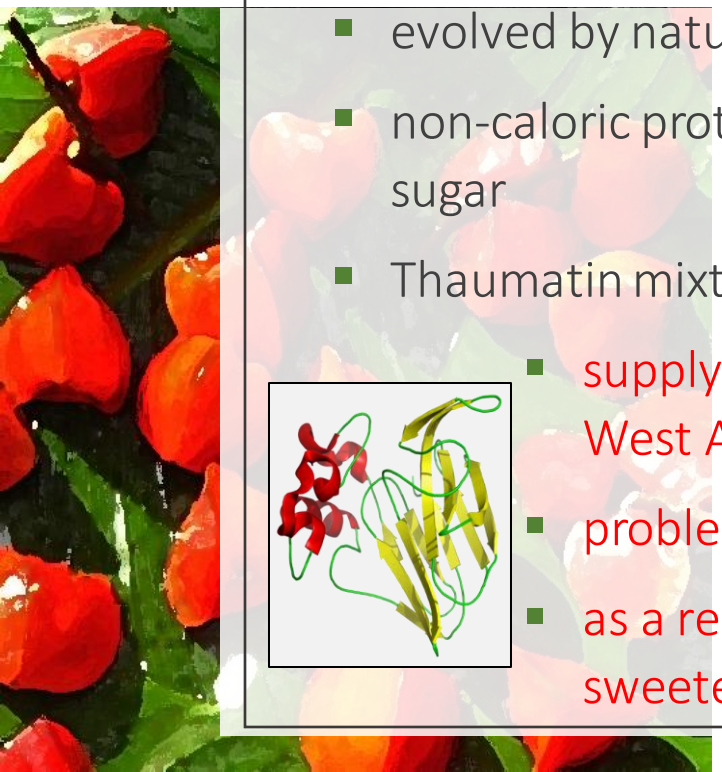
What if

we could replace half of the sugar with natural non-caloric super sweet proteins

- bringing the sugar consumption to healthy and medically correct levels without changing the sweetness and taste of food and drinks, and without use of artificial sweeteners
- eliminating the main cause of obesity, overweight, diabetes, coronary/heart diseases, etc.
- saving tens of million hectares of the land used for cultivation of sugar cane, sugar beet and corn (corn syrup); stop exploiting of tropical rainforests
- opportunity to build a high value, sustainable, novel food company



Thaumatins & Brazzeins



intensely sweet non-caloric proteins invented by nature

- evolved by nature and used by indigenous people for millennia as a sweetener
- non-caloric proteins (not sugars) thousands of times sweeter on a weight basis than sugar
- Thaumatin mixtures approved as sweeteners and taste modifiers and used but:
  - supply is limited (isolated from katemfe fruits collected in rainforests of West Africa)
  - problems with supply security
  - as a result, marketed products are too expensive to compete with artificial sweeteners or sugar, currently used in niche markets as taste modifiers

Thaumatin II

health smart, climate smart food

- Natural non-caloric sweetener/flavor modifier produced in plants
- Sweetest known natural substance: up to 11.000 times sweeter than sugar (w/w)
- Can replace: ≥35% of sugar without taste changes; 50% - with light lingering aftertaste; similar when replacing corn syrup
- Initial market as taste modifier, can address up to a half of $75 billion/year sugar market as a sweetener
- Major patents filed; FTO, exclusivity; favorable techno-economics
- Unlimited supply; requires only 0.05% of land used for sugar cane and sugar beets plantings today
- Interest from a world top three soft drink manufacturers, world top three food additive companies

Thaumatin II

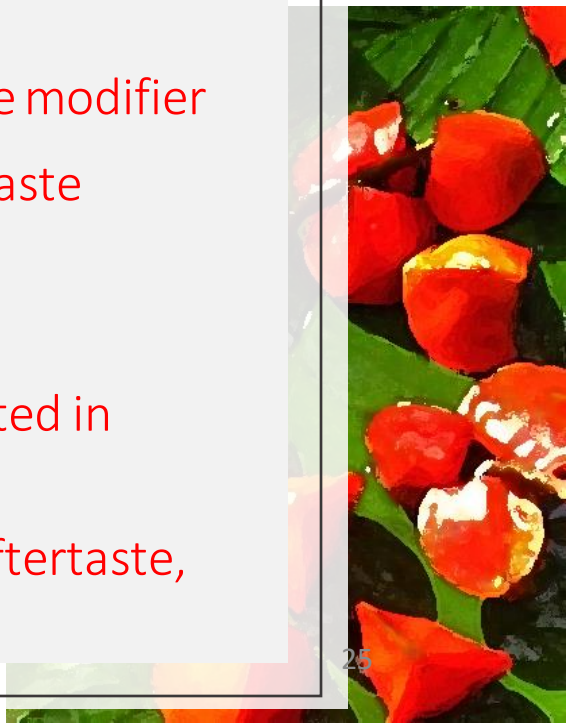
versus current commercial Thaumatin

Thaumatin II potential

- Unlimited supply
- Supply security
- COGs allow to compete with sugar
- Health benefits through replacing sugar
- Ecological benefits
  - 0.05% of agriculture land used by sugar beets and sugar cane needed
- Correct taste similar to pure sugar

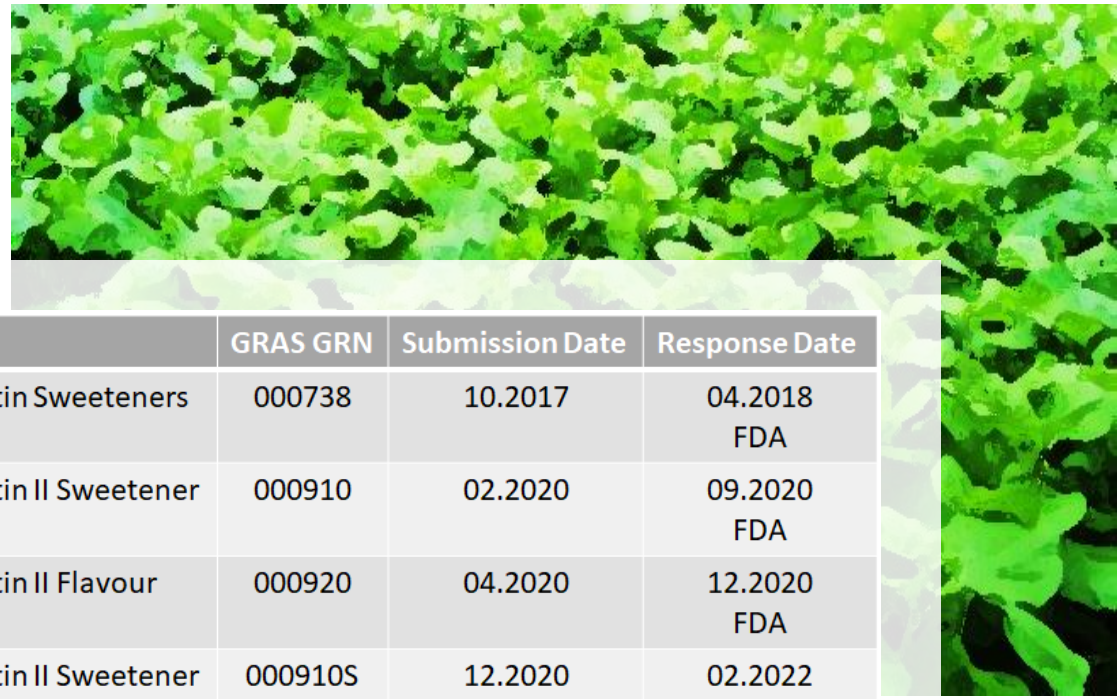
current commercial Thaumatin

- Limited supply
- Low supply security
- COGs allow to sell it as a taste modifier
- No health benefits (used as taste modifier only)
- No ecological benefits
  - Katemfe fruits are collected in tropical rainforests
- Sweetness delay, extended aftertaste, liquorice off-notes



Regulatory

- GRAS ('Generally Recognized As Safe') is regulatory approval path for food additives in USA
- Nomad has received four GRAS regulatory approvals for thaumatins by FDA and one by FEMA
- Nomad intends to have its Thaumatin II approved in other important regions/countries: EU, Japan, China, Canada, Australia
- Ongoing efforts to register thaumatin II as taste modifier in *Codex Alimentarius*, FAO/WHO
- We intend to register Brazzein III as GRAS



Product	GRAS GRN	Submission Date	Response Date
Thaumatin Sweeteners	000738	10.2017	04.2018 FDA
Thaumatin II Sweetener	000910	02.2020	09.2020 FDA
Thaumatin II Flavour modifier	000920	04.2020	12.2020 FDA
Thaumatin II Sweetener Supplement	000910S	12.2020	02.2022 FDA
Thaumatin II Flavour modifier	FEMA 510	11.2021	03.2022 FEMA

Pilot Production, Open Field

NAMBAWAN

Food Antibacterials

The Threat of contaminated food

In USA, foodborne diseases affect 50 million people yearly, with 56.000 hospitalizations, 3.000 deaths a year

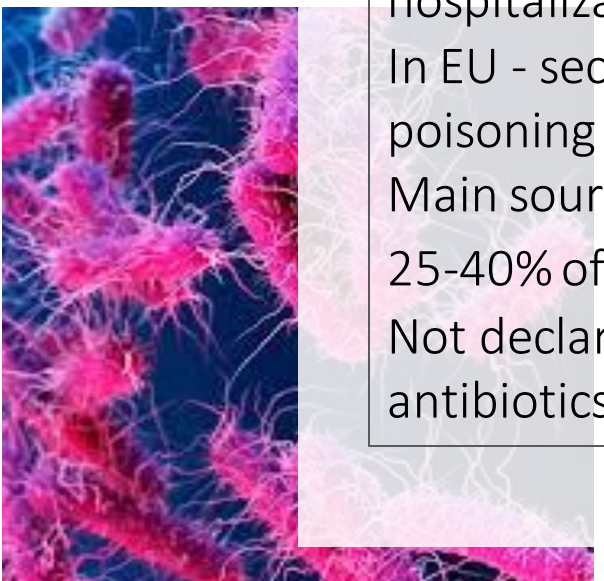
The most costly and deadly pathogen accounting for 35% of hospitalizations and 28% deaths is *Salmonella*

In EU - second most common pathogen and the main cause of food poisoning outbreaks

Main sources of pathogen: contaminated eggs, poultry and pig meat

25-40% of meat sold in supermarkets contains *Salmonella*

Not declared as a food adulterant (because lack of effective control); antibiotics are banned in animal husbandry & processing)



https://www.cdc.gov/foodborneburden/2011-foodborne-estimates.html
https://www.ecdc.europa.eu/en/all-topics-z/salmonellosis-non-typhi-non-paratyphi.html

Bacteriocins

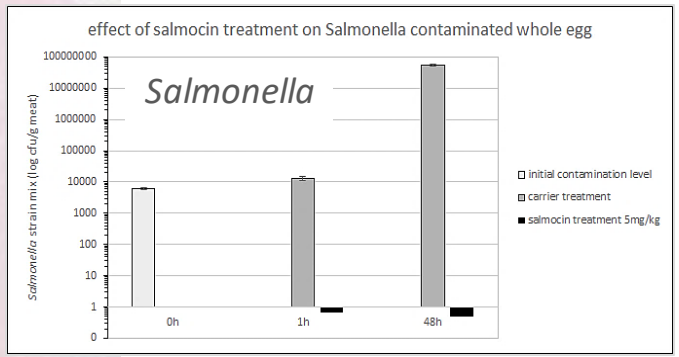
non-antibiotic biologics invented by nature

- Evolved by nature and used by bacteria themselves to fight related germs
- Up to one million times more active than antibiotics, completely safe for humans and animals, and easy to produce in green plants
- Highly specific, killing just one bacterial species
- Huge diversity of bacteriocins in bacterial genomes, with different mechanisms of action
- Active on all multi-drug resistant bacteria

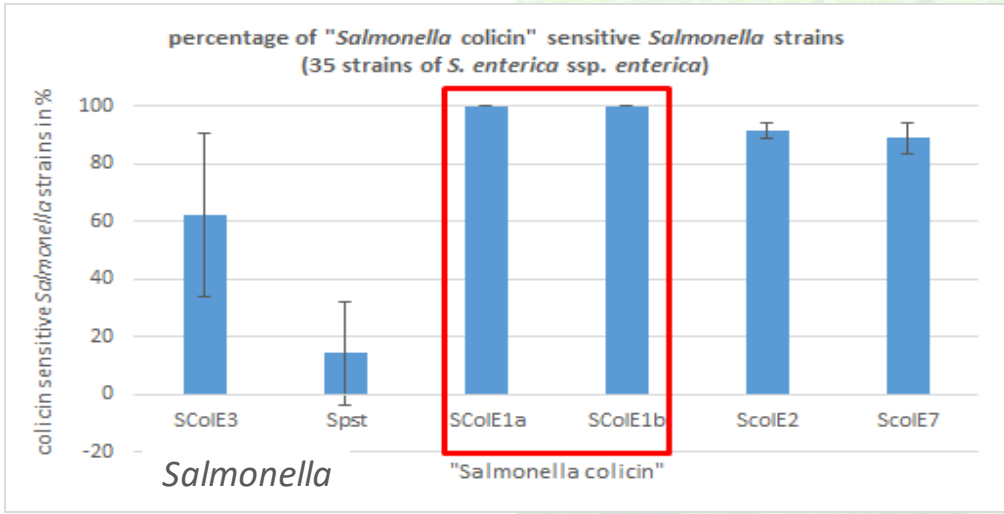
Bacteriocins

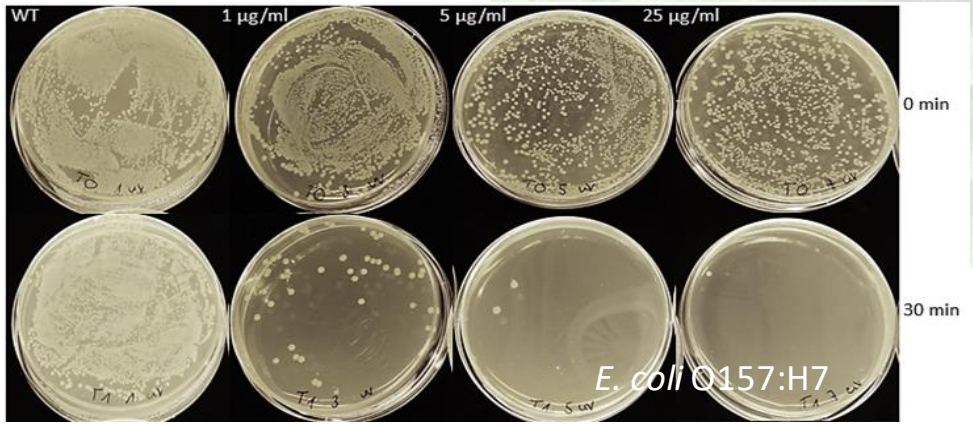
mined and extensively researched by our scientists

tested on different food matrices



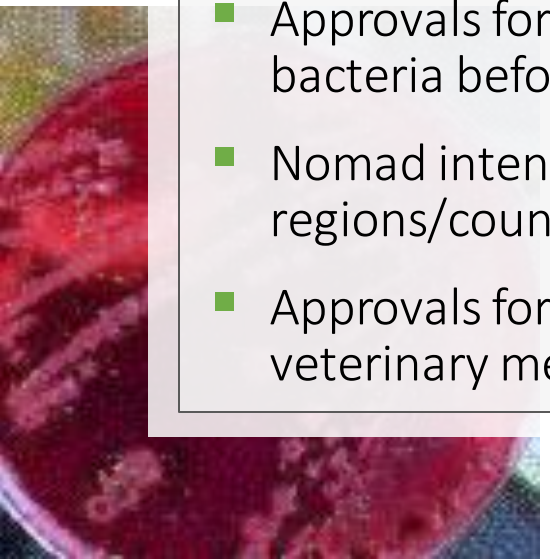
tested with all strains, *in vitro* & *in vivo*

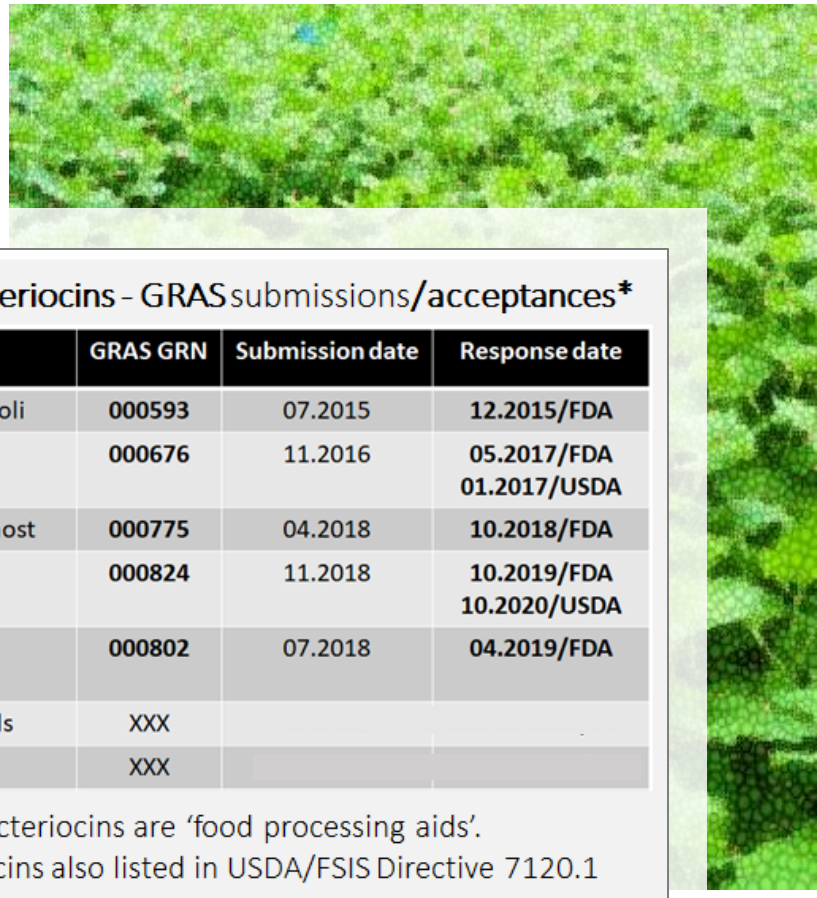




First-In-Class
Regulatory Approvals

- GRAS ('Generally Recognized As Safe') is a regulatory approval path for food substances in USA, the largest market
- Five GRAS regulatory approvals for products secured, two in preparation
- **Products approved as food processing aids** (no need for labelling)
- Approvals for treatment of live animals (removal of bacteria before harvesting) in development
- Nomad intends to seek approvals in other important regions/countries: EU, Japan, China
- Approvals for our products in new markets (e.g. veterinary medicines) are being explored



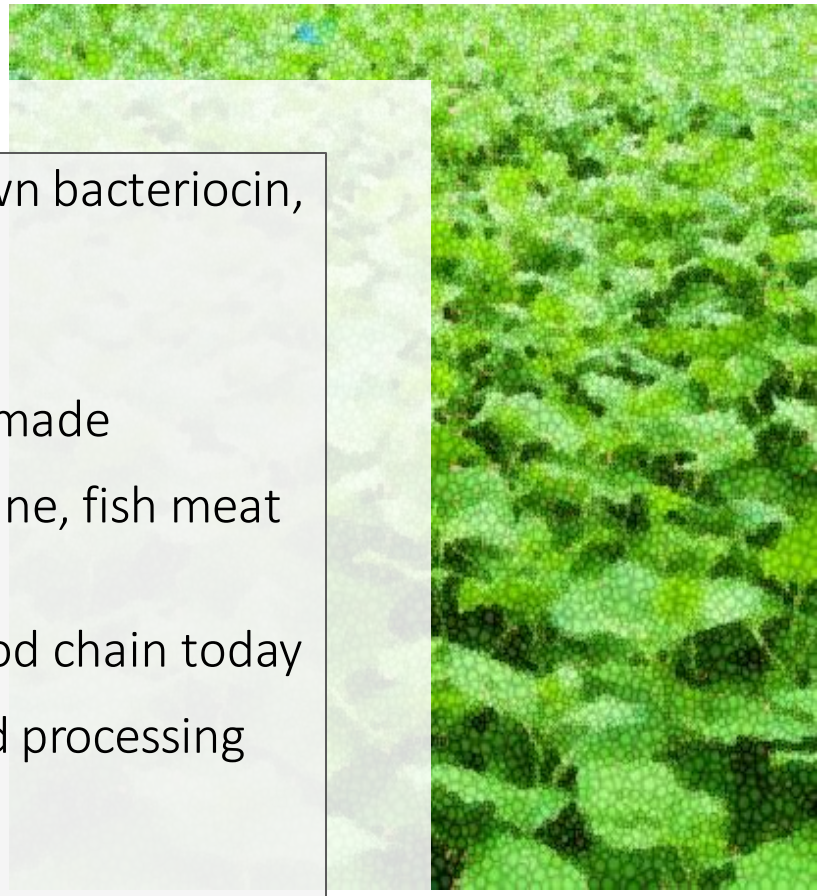


Nomad`s bacteriocins - GRAS submissions/acceptances*

Product/Origin	GRAS GRN	Submission date	Response date
Colicins/Escherichia coli	**000593**	07.2015	**12.2015/FDA**
Colicins/E.coli	**000676**	11.2016	**05.2017/FDA 01.2017/USDA**
Nicotiana as a GRAS host	**000775**	04.2018	**10.2018/FDA**
Salmocins/ Salmonella enterica	**000824**	11.2018	**10.2019/FDA 10.2020/USDA**
Endolysins, Clostridium phages	**000802**	07.2018	**04.2019/FDA**
Salmocins/live animals	XXX		
Colicins/live animals	XXX		

*All approved bacteriocins are 'food processing aids'.
Colicins & Salmocins also listed in USDA/FSIS Directive 7120.1

The Lead Product:
Salmocin E1b



- Natural protein, non-antibiotic, the most potent known bacteriocin, active in nanomolar concentrations
- Broadly active against **all** *Salmonella* pathovars
- Safe, doesn't damage natural gut microbiome, plant-made
- For control of *Salmonella* in processing of poultry, swine, fish meat and eggs as **food processing aid**
- Breakthrough product: no control of *Salmonella* in food chain today
- **180 - 1.990 million potential market (USA only)** – food processing plus treatment of live animals
- **Approved in USA** by FDA and USDA
- **NAMBAWAN intends to have NMW 02 on the U.S. market by 2024**

Where Do We Go From Here?

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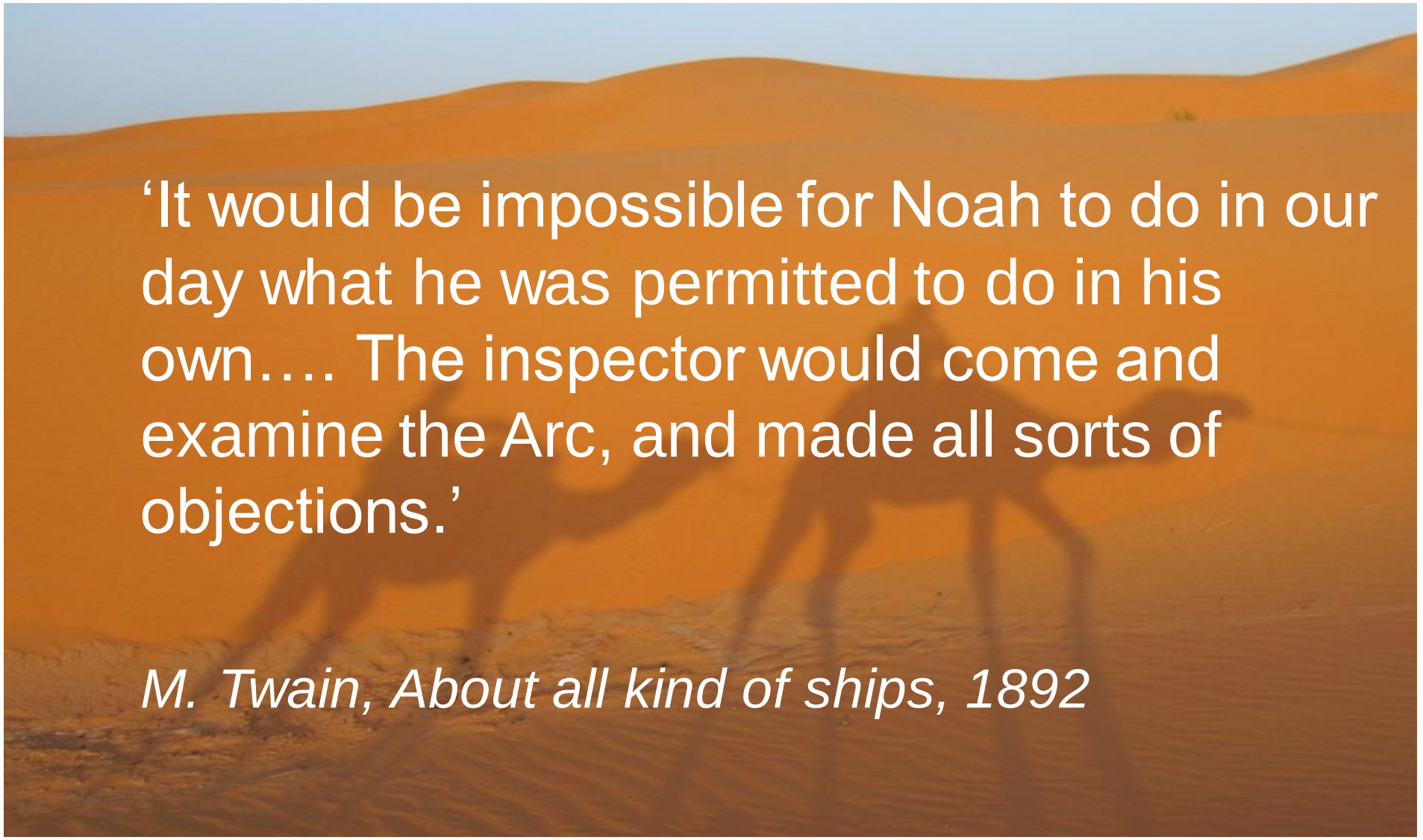






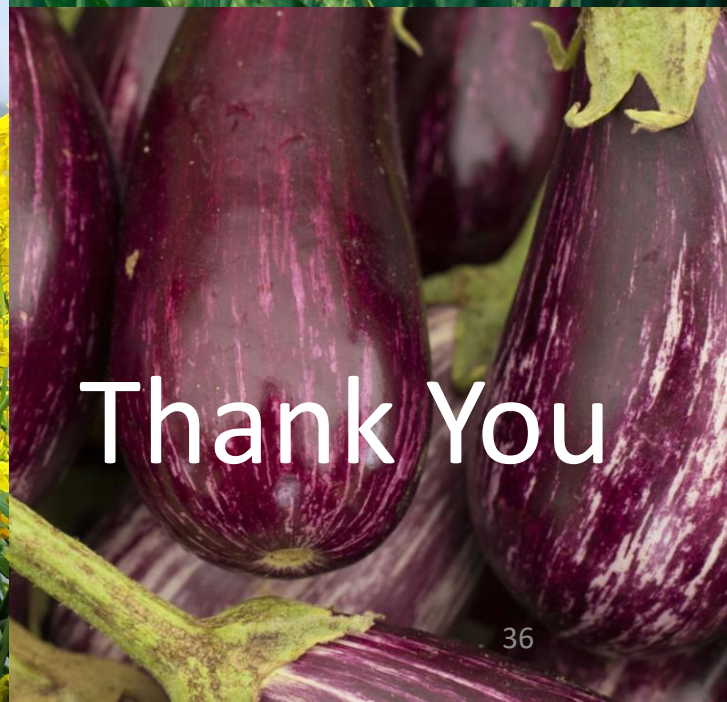

Thank You