Where are We in Recombinant Forest Biotech? Some Lessons about Science & Society in a Fractious and Changing World

Presented online at IUFRO Tree Biotechnology International Conference / Harbin, China

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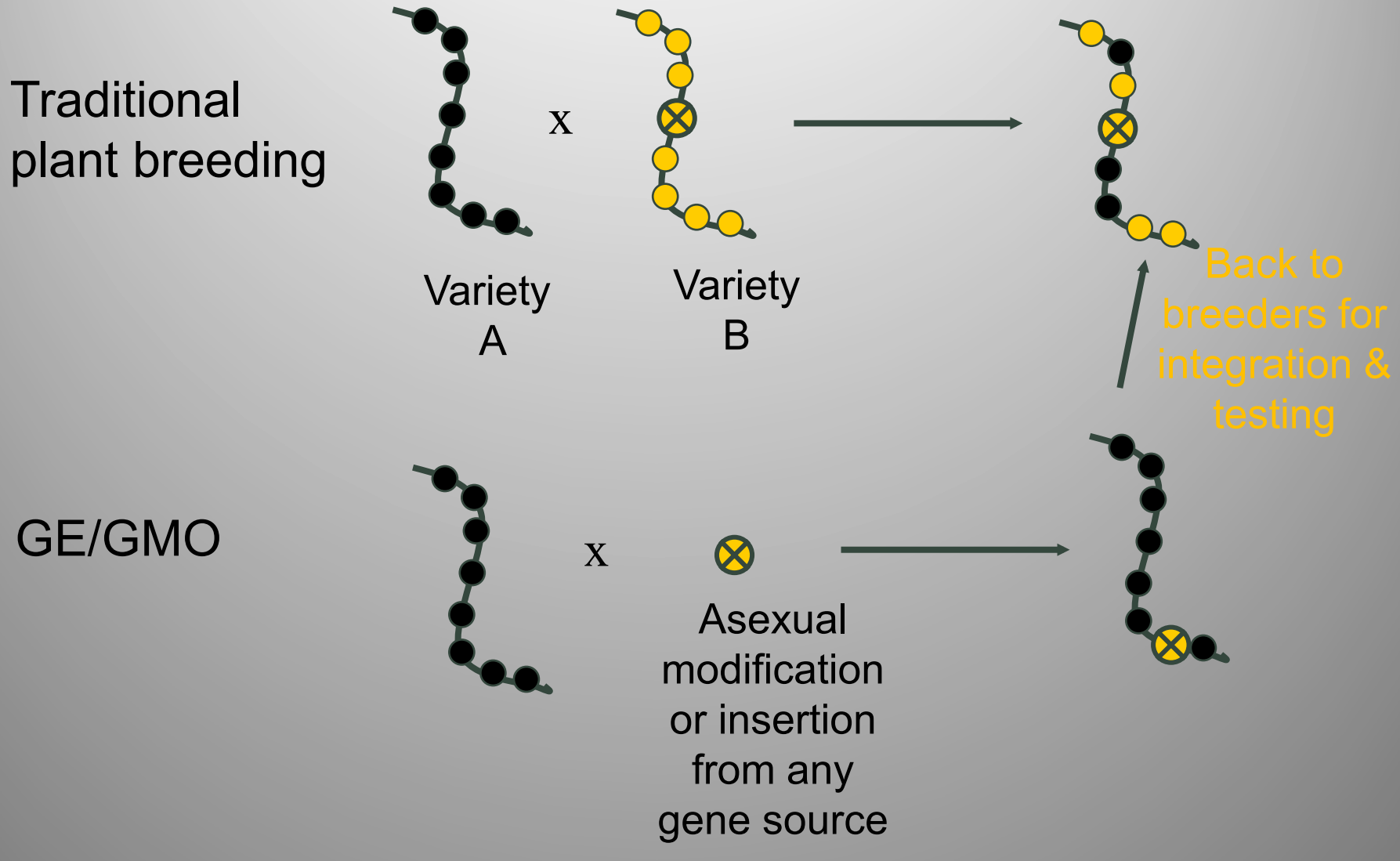
Agenda

- Definitions and overview
- The social thicket
- Gene flow as a bioethical dilemma
- Transformation/editing recalcitrance
- Recommended scientist priorities

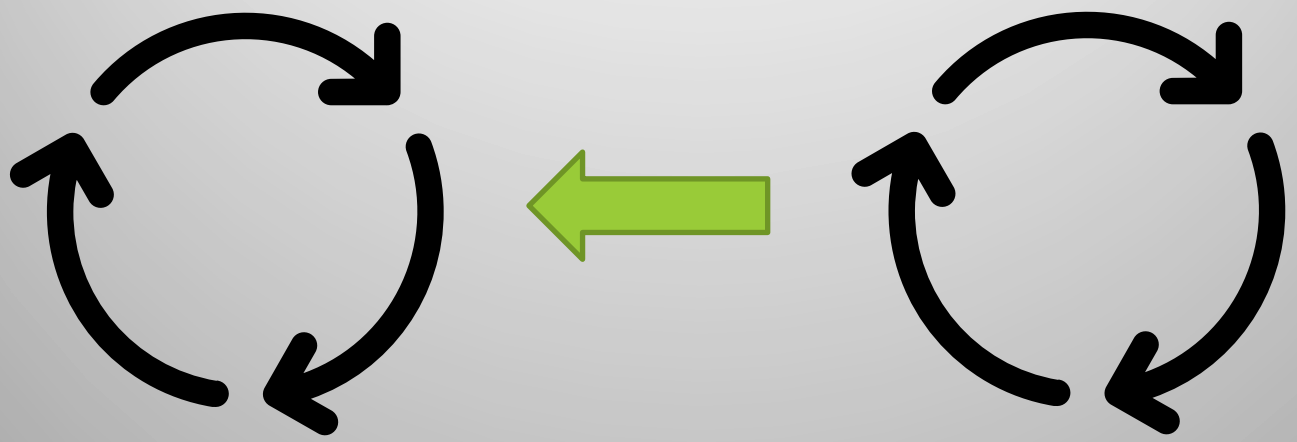
Gene edit/GMO (GE) = “biotech” for the purpose of this talk – not genomic breeding



Relationship of breeding and biotech

Breeding populations

Biotech innovations



Polygenic:
Growth rate and adaptation

Oligogenic:
Specific modifications and novel traits

These need to be integrated in a way that does not slow down conventional breeding, with climate change urgency, and its growing power due to physiological and genomic innovations

Why won't biotech deliver?

It's a nexus of problems constraining progress

Nexus of problems, explained

- **Ethical unease:** Corporations, patents, transparency, plantation monocultures, GMOs, gene flow
- **rDNA regulations:** rDNA-based presumption of guilt and impairment of effective research and integration with breeding
- **No-GMO Certification:** Prevention of significant use in research, breeding, or products on certified lands
- **Transformation/edit capacity**: Inability to effectively address a diversity of species and genotypes in breeding programs in reliable, cost-effective manner
- **Gene control tools:** Reliable systems for control of gene expression, excision, editing, and stability when in routine use or for synthetic biology innovations
- **Field demonstrations:** Evidence that biotech modifications add significant value and do not compromise productivity in production environments

The social thicket: Regulations

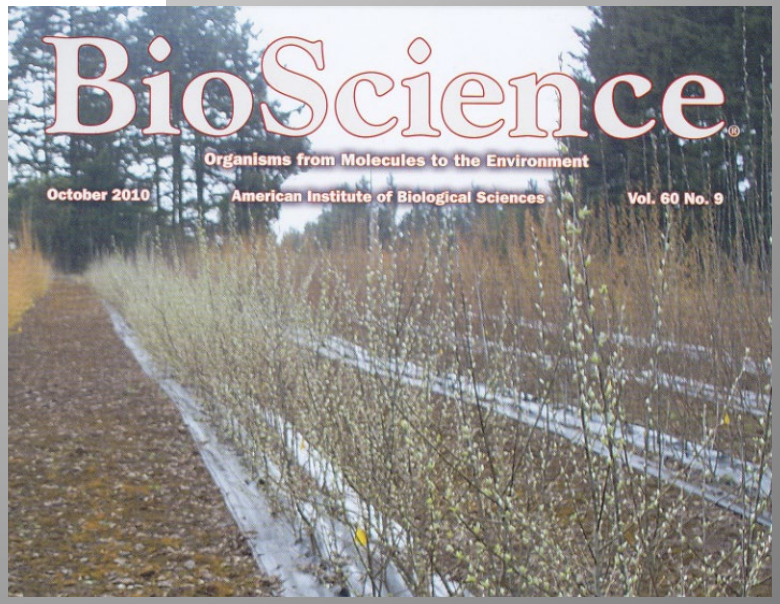
- Assumes the method used, vs. trait novelty and importance, is a suitable trigger for regulatory oversight
- Effectively treats a GMO insertion as guilty until proven innocent through extensive study
- Scientific reports, such as many from the USA National Academy of Sciences, have continually called for a trait/novelty based regulatory system, vs. one based on method

Much field research to develop new innovations, and understand risk, are hampered by method-based regulations

Far-reaching Deleterious Impacts of Regulations on Research and Environmental Studies of Recombinant DNA-modified Perennial Biofuel Crops in the United States

STEVEN H. STRAUSS, DREW L. KERSHEN, JOE H. BOUTON, THOMAS P. REDICK, HUIMIN TAN, AND ROGER A. SEDJO

Makes the incremental, trial and error, **adaptive research** that is the norm in forestry nearly impossible as each event or construct class requires regulatory review and decisions before any release to environment is allowed – a critical obstacle to the physiological "tinkering" needed for key traits like drought, heat, and cold tolerance—or wood engineering



Provided by Arborgen

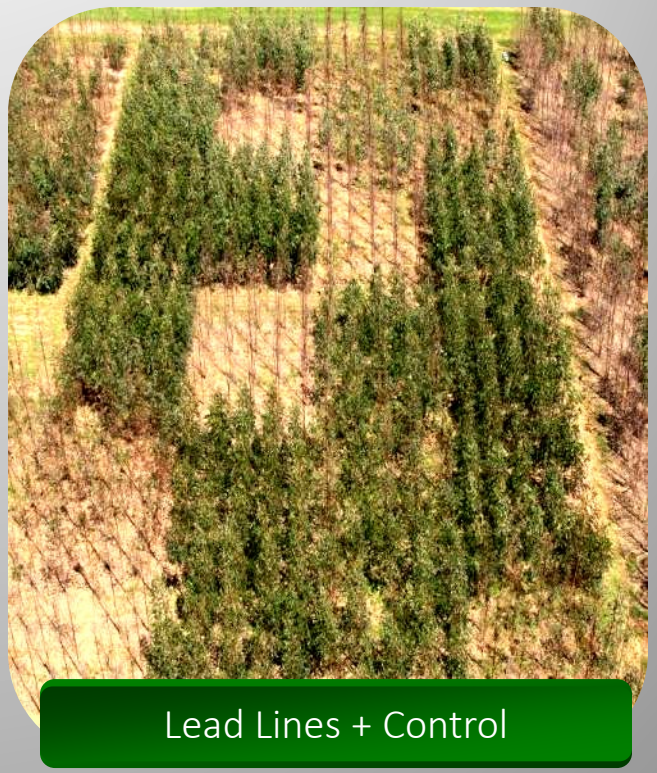
Cold tolerant, male-sterile GE *Eucalyptus*

Results from first winter in South Carolina

Control

Lead Line

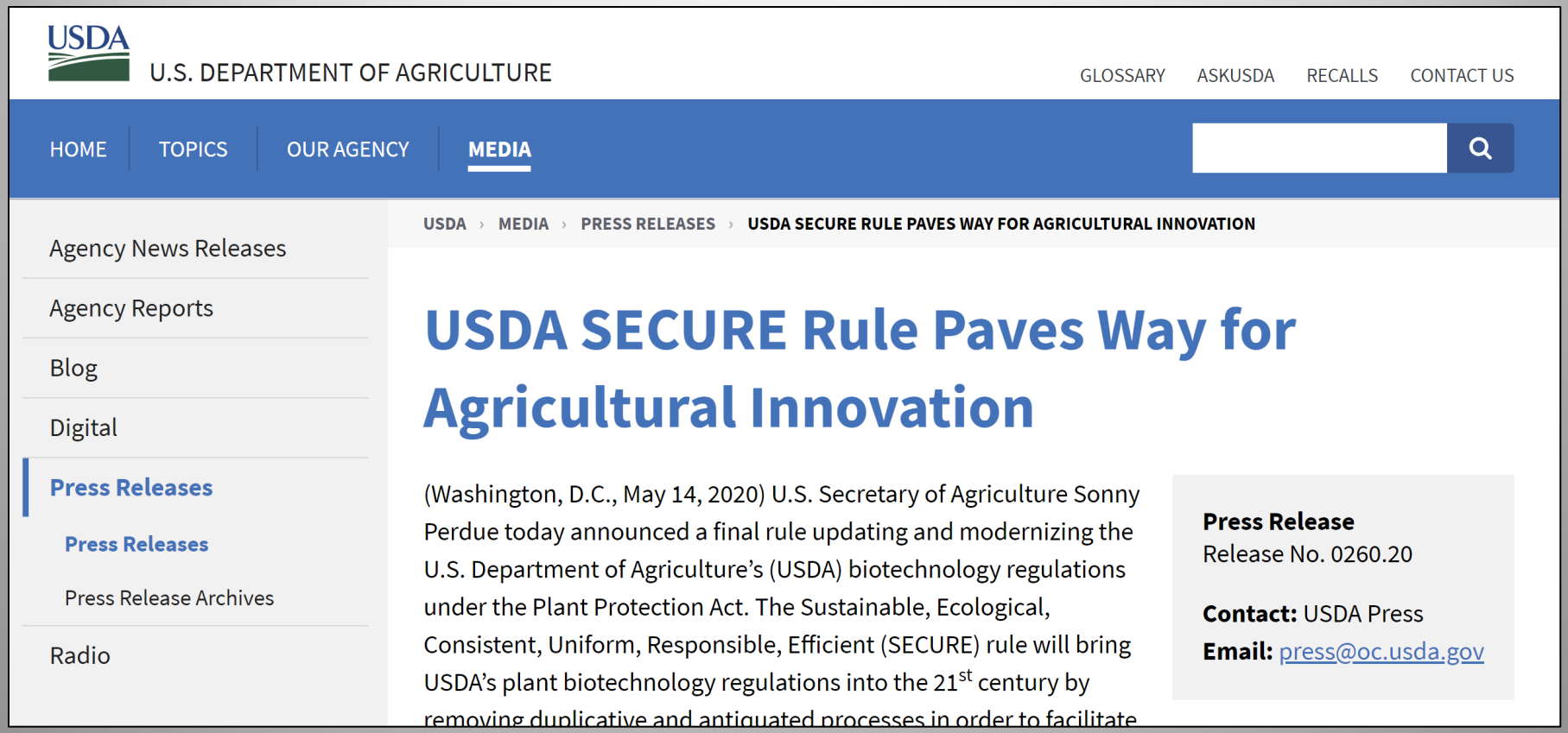
Results from second winter in Alabama



Lead Lines + Control

But technology seemed to fail in subsequent years. Sadly there was no further "tweaking" of genes and promoters undertaken to improve/evolve the trait – in part due to costly task of regulated field trial management and approvals, and of getting even a single insertion event approved for commercial use

The ~new 2020 USDA SECURE system is more enlightened – but improvement likely to be small



USDA U.S. DEPARTMENT OF AGRICULTURE

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USDA › MEDIA › PRESS RELEASES › USDA SECURE RULE PAVES WAY FOR AGRICULTURAL INNOVATION

USDA SECURE Rule Paves Way for Agricultural Innovation

(Washington, D.C., May 14, 2020) U.S. Secretary of Agriculture Sonny Perdue today announced a final rule updating and modernizing the U.S. Department of Agriculture's (USDA) biotechnology regulations under the Plant Protection Act. The Sustainable, Ecological, Consistent, Uniform, Responsible, Efficient (SECURE) rule will bring USDA's plant biotechnology regulations into the 21st century by removing duplicative and antiquated processes in order to facilitate

Press Release
Release No. 0260.20

Contact: USDA Press
Email: press@oc.usda.gov

The social thicket: Market certification

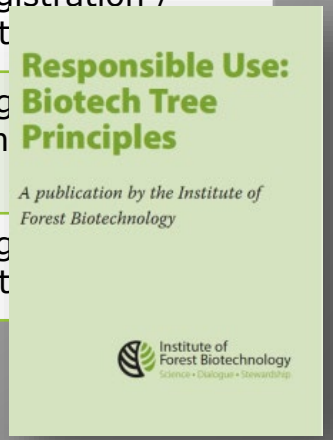
<u>A big deal</u>:
Many of the most highly managed forests and their products are certified

~500 million hectares,
~13% global forest area

Started by the Forest Stewardship Council, major principle:
"genetically modified trees are prohibited"

All major forest certification systems banned GE trees over time

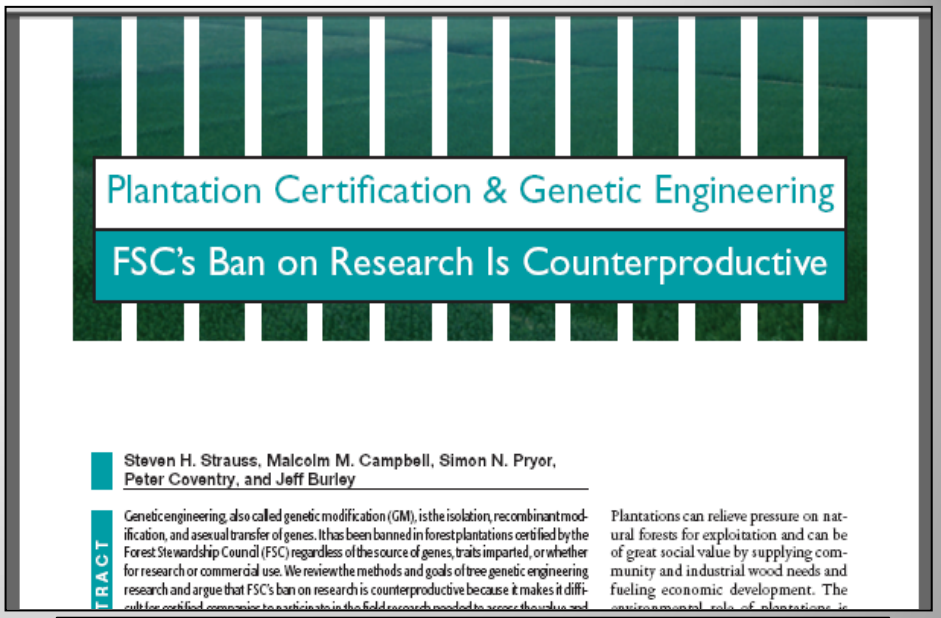
System	Region	GM Tree Approach / Reason
PEFC : Programme for Endorsement of Forest Certification	International	**Banned** / Precautionary approach based on lack of data
FSC : Forest Stewardship Council	International	**Banned** / Precautionary approach based on lack of data
CerFlor : Certificação Florestal	Brazil	**Banned** via PEFC registration / No additional rationale
CertFor : Certficación Forestal	Chile	**Banned** via PEFC registration / No additional rationale
SFI : Sustainable Forestry Initiative	North America	**Banned** via PEFC registration / Awaiting risk-benefit data
ATFS : American Tree Farm System	USA	**Banned** via PEFC registration / No additional rat
CSA : Canadian Standards Association	Canada	**Banned** via PEFC reg Allows public to determ
CFCC : China Forest Certification Council	China	**Banned** via PEFC reg No additional rat



Adam Costanza, Institute for Forest Biotechnology

In 2001 forest genetic and biotech scientists publicly criticized FSC for their complete ban on GMOs – because it does not allow relevant breeding research with them on certified lands

Helped motivate FSC to create a very narrow research exemption in 2011



Plantation Certification & Genetic Engineering

FSC's Ban on Research Is Counterproductive

Steven H. Strauss, Malcolm M. Campbell, Simon N. Pryor, Peter Coventry, and Jeff Burley

Genetic engineering, also called genetic modification (GM), is the isolation, recombinant modification, and asexual transfer of genes. It has been banned in forest plantations certified by the Forest Stewardship Council (FSC) regardless of the source of genes, traits imparted, or whether for research or commercial use. We review the methods and goals of tree genetic engineering research and argue that FSC's ban on research is counterproductive because it makes it difficult for certified companies to participate in the field research needed to assess the value and

Plantations can relieve pressure on natural forests for exploitation and can be of great social value by supplying community and industrial wood needs and fueling economic development. The

FSC-POL-01-004 (V2-0) POLICY FOR THE ASSOCIATION OF ORGANIZATIONS W FSC

Code	INT-POL-01-004_01
Requirement (s)	Clause 1.e
Publication date	11 July 2011

Does research on GMOs by FSC certificate holders or affiliated organizations constitute a breach of the FSC Policy on Association?

The FSC Policy on Association had its origins in the FSC Partial Certification Policy and is intended to prevent green washing by companies that are not committed to FSC certification. The Policy states that FSC shall not be associated with organizations that are directly or indirectly involved in the introduction of genetically modified organisms in forestry operations. Research, as defined in this document, does not constitute a breach to the FSC Policy on Association since the concept of operations is related to the standard commercial activities of an organization and as such does not include research efforts.

For the purpose of this clarification, research is understood as activities that:

- have a clear investigative purpose (i.e. test a hypothesis),
- are carried out on a limited scale and with defined timelines that are compatible to the scope of the research,
- are conducted following all related legal requirements, including safeguards and permits.

Decision making process: The above interpretation was approved by the FSC Board of Directors at the 57th meeting.

In 2015, as evidence of growing pest epidemics and climate stress mounted, we pressed the issue further in another policy essay

Traces of the emerald ash borer on the trunk of a dead ash tree in Michigan, USA. This non-native invasive insect from Asia threatens to kill most North American ash trees.

BIOTECHNOLOGY

Genetically engineered trees: Paralysis from good intentions

Forest crises demand regulation and certification reform

By **Steven H. Strauss[1]*, Adam Costanza[2], Armand Séguin[3]**

Intensive genetic modification is a long-standing practice in agriculture, and, for some species, in woody plant horticulture and forestry (*1*). Current regulatory systems for genetically engineered recently initiated an update of the Coordinated Framework for the Regulation of Biotechnology (*2*), now is an opportune time to consider foundational changes.

Difficulties of conventional tree breeding make genetic engineering (GE) methods relatively more advantageous for forest trees than for annual crops (*3*). Obstacles

Although only a few forest tree species might be subject to GE in the foreseeable future, regulatory and market obstacles prevent most of these from even being subjects of translational laboratory research. There is also little commercial activity: Only two types of pest-resistant poplars are authorized for commercial use in small areas in China and two types of eucalypts, one approved in Brazil and another under lengthy review in the USA (*5*).

METHOD-FOCUSED AND MISGUIDED. Many high-level science reports state that the GE method is no more risky than conventional breeding, but regulations around the world essentially presume that GE is hazardous and requires strict containment

…also with little effect

Petition created about GMO/gene edit ban by certification programs – implemented by Alliance for Science at Cornell University, USA

Endorsed by the largest scientific society of plant biologists in the world

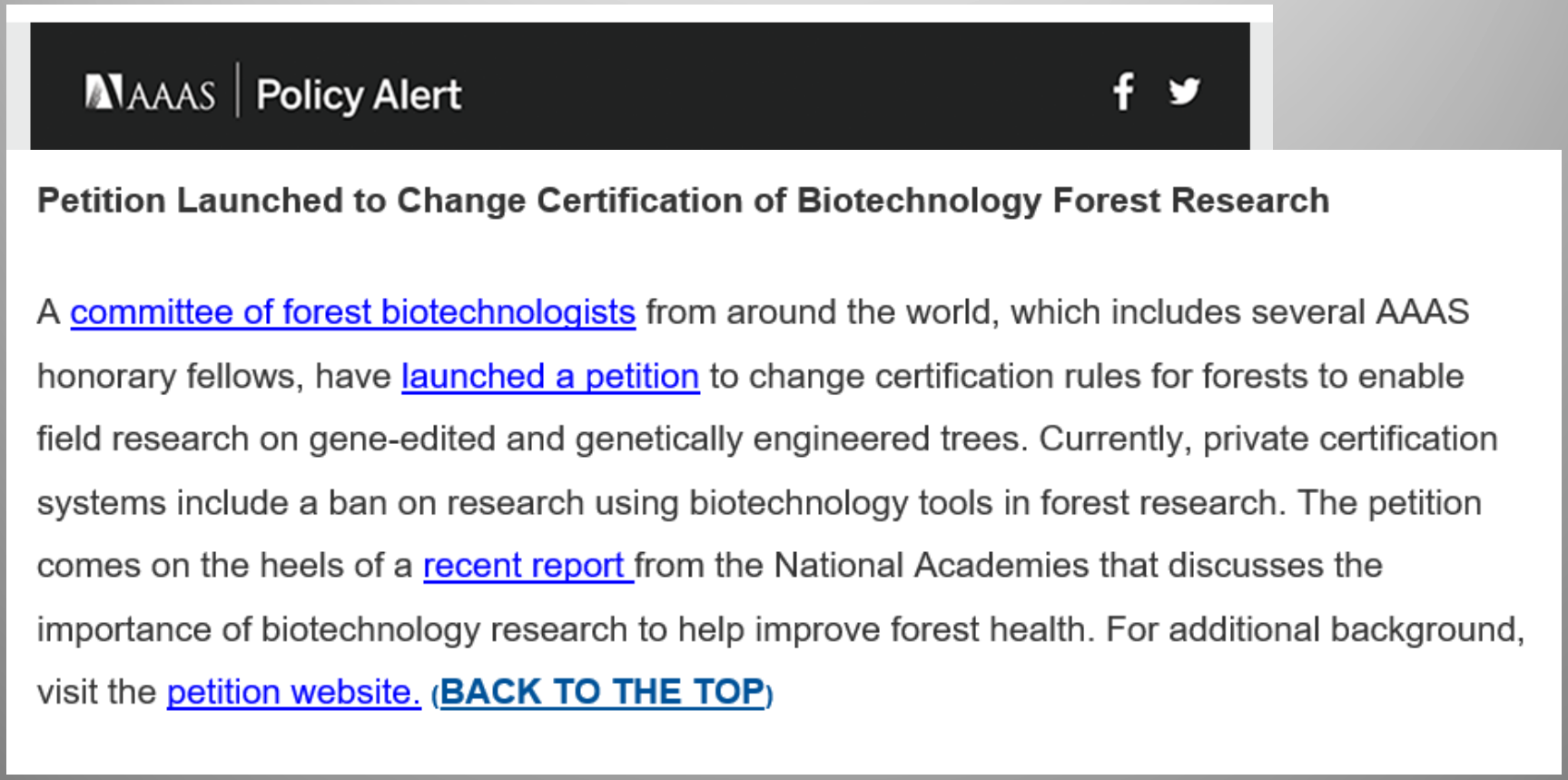
American Society of Plant Biologists

ASPB has studied and endorsed the petition.

members to support a petition to change certification rules for forests to enable field research on biotech (gene edited, genetically engineered) trees. Amazingly, all of the private certification systems have a complete ban in place that extends to research, at a time when forest health is in growing crisis due to expanding pests and climate change. Biotech is not a panacea, but its also too powerful to ignore—and can sometimes provide powerful solutions where other approaches fail.The petition follows the release of a major report on The Potential for Biotechnology to Address Forest Health from the USA National Academy of Sciences that has identified biotechnologies as a key tool for helping to manage forest health and associated pest epidemics.

ASPB has studied and endorsed the petition.

Alerts to tens of thousands of scientists sent by American Association for the Advancement of Science - AAAS (worlds largest general scientific society)



AAAS | Policy Alert

Petition Launched to Change Certification of Biotechnology Forest Research

A committee of forest biotechnologists from around the world, which includes several AAAS honorary fellows, have launched a petition to change certification rules for forests to enable field research on gene-edited and genetically engineered trees. Currently, private certification systems include a ban on research using biotechnology tools in forest research. The petition comes on the heels of a recent report from the National Academies that discusses the importance of biotechnology research to help improve forest health. For additional background, visit the petition website. (**BACK TO THE TOP**)

1,161 signatures, majority PhDs

Support modern forest biotechnology research

May 30 2018 Cornell Alliance for Science Closed on Jun 11 2019

https://www.gopetition.com/petitions/petition-in-support-of-modern-forest-biotechnology.html

Letter published in *Science* about it (September 2019)

Certification for gene-edited forests

Forest certification bodies were established to provide consumers with confidence that they are purchasing
sourced wood products. Over
hectares of forests, or about
l forest area, are certified
rgest certification systems
ver, certification bodies have
excluded all genetically
or gene-edited (GE) trees from
, including from field research
lands that is essential for
ng local benefits and impacts
ing forest biotechnology
om around the world, with
of more than 1000 globally
atories to a recent detailed
call for all forest certification
romptly examine and modify
s.
ce mounting stresses posed
ests and climate change (*6*).

Engineering, and Medicine recently completed an in-depth study on forest health and biotechnology, concluding that the potential benefits are numerous and rapidly increasing (*12*). Our forests are in dire need of assistance, and GE trees hold tremendous potential as a safe and powerful tool for promoting forest resilience and sustainability.

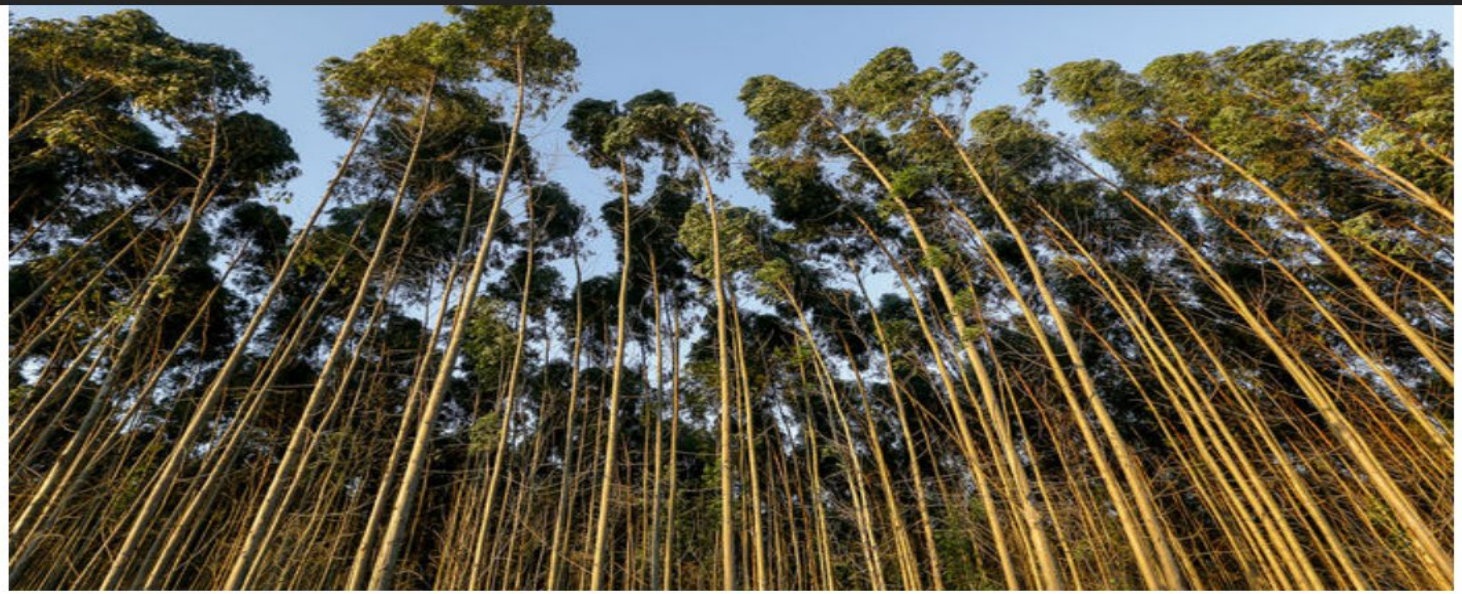
Steven H. Strauss[1]*, Wout Boerjan[2], Vincent Chiang[3], Adam Costanza[4], Heather Coleman[5], John M. Davis[6], Meng-Zhu Lu[7], Shawn D. Mansfield[8], Scott Merkle[9], Alexander Myburg[10], Ove Nilsson[11], Gilles Pilate[12], William Powell[13], Armand Seguin[14], Sofia Valenzuela[15]

[1]Department of Forest Ecosystems and Society, Oregon State University, Corvallis, OR 97331, USA. [2]Department of Plant Biotechnology and Bioinformatics, Ghent University and Center for Plant Systems Biology, VIB, 9052 Ghent, Belgium. [3]Department of Forestry and Environmental Resources, North Carolina State University, Raleigh, NC 27695, USA. [4]Chapel Hill, NC 27517, USA. [5]Department of Biology, Syracuse University, Syracuse, NY 13244, USA. [6]School of Forest Resources and Conservation, University of Florida, Gainesville, FL 32611, USA. [7]State Key Laboratory of Subtropical Silviculture, School of Forestry and Biotechnology, Zhejiang A&F University, Hangzhou 311300, China. [8]Forest Sciences Centre, University

standard-pefc-st-2002-2013.

Gene-edited and genetically engineered trees, such as these poplars, should be allowed in certified forests.

News article also published in Science



Productivity of eucalyptus plantations could be increased with trees genetically modified for faster growth.
CASADAPHOTO/SHUTTERSTOCK.COM

Scientists say sustainable forestry organizations should lift ban on biotech trees

By Erik Stokstad | Aug. 23, 2019 , 5:45 PM

The result: It helped to initiate a reconsideration of GMO policy by FSC

"FSC GE learning process" as an "associated use" – whereby a certified company can apply to do research, on non-certified land, but not use any GMO materials in products

A small, slow, and limited start, with strong emphasis on risk management vs. opportunity assessment

What is the value given extensive research already published? Is this better than the last ~30 years of stasis, or just a further delay tactic?

The problem of gene flow

- Gene flow, either as whole propagules like seeds, or via pollen where there are compatible relatives, creates special problems for GE acceptance
- Long distance dispersal of pollen, and sometimes seeds, common for trees
- Potential impacts on wild populations, ferals, exotics, invasives
  - Possible long term, evolutionary change a special ethical concern
- Movement onto other lands and products where their presence is unwelcomed or economically problematic

My lab has studied many containment technologies over the years

CRISPR to the rescue ?

Plant Biotechnology Journal
Open Access

Research Article | Open Access

Genetic containment in vegetatively propagated forest trees: CRISPR disruption of *LEAFY* function in *Eucalyptus* gives sterile indeterminate inflorescences and normal juvenile development

Estefania Elorriaga, Amy L. Klocko, Cathleen Ma, Marc du Plessis, Xinmin An, Alexander A. Myburg, Steven H. Strauss

First published: 27 March 2021 | https://doi.org/10.1111/pbi.13588 | Citations: 1

Much more in presentations by Amy Klocko and Estefania and Elorriaga !

But sterility can also have serious impacts on biodiversity, impair breeding, and with complex public perception

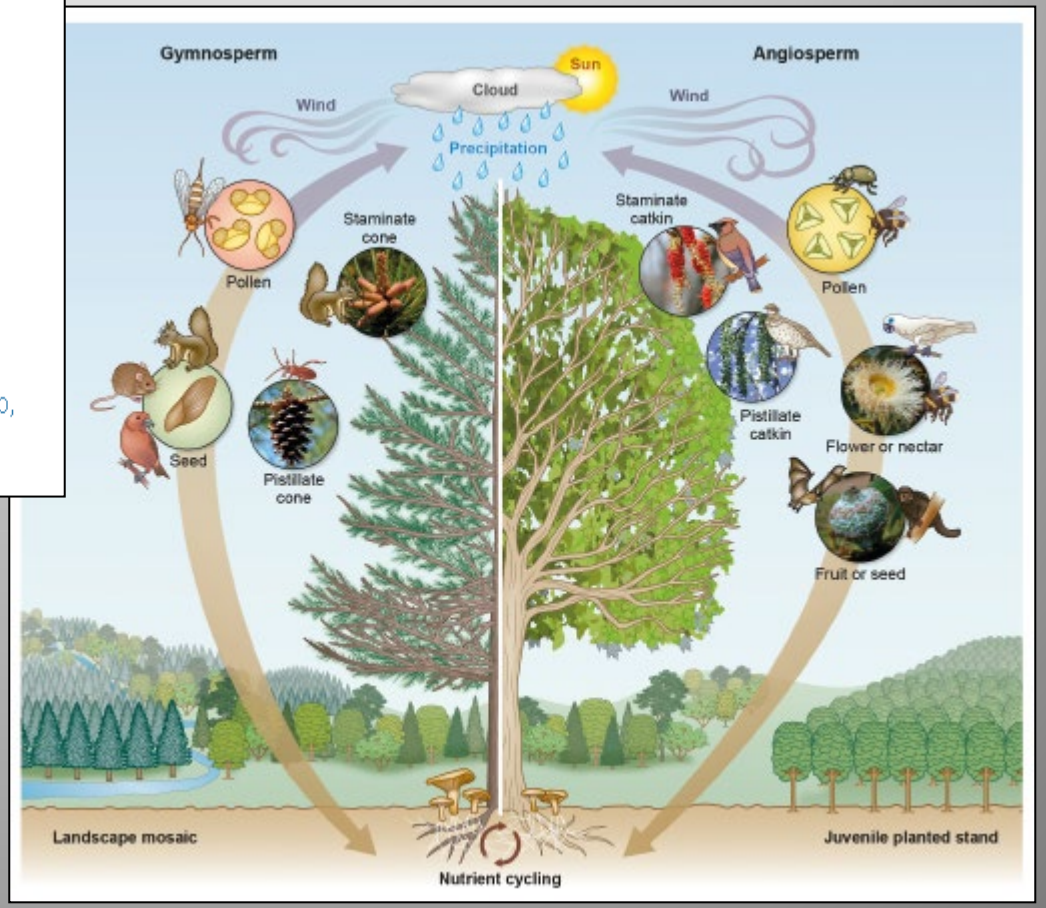
New Phytologist

Explore this journal >

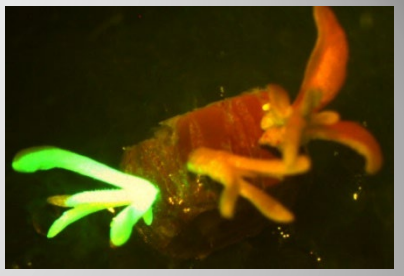
Tansley review

Reproductive modification in forest plantations: impacts on biodiversity and society

Steven H. Strauss ✉, Kristin N. Jones, Haiwei Lu, Joshua D. Petit, Amy L. Klocko, Matthew G. Betts, Berry J. Brosi, Robert J. Fletcher Jr, Mark D. Needham

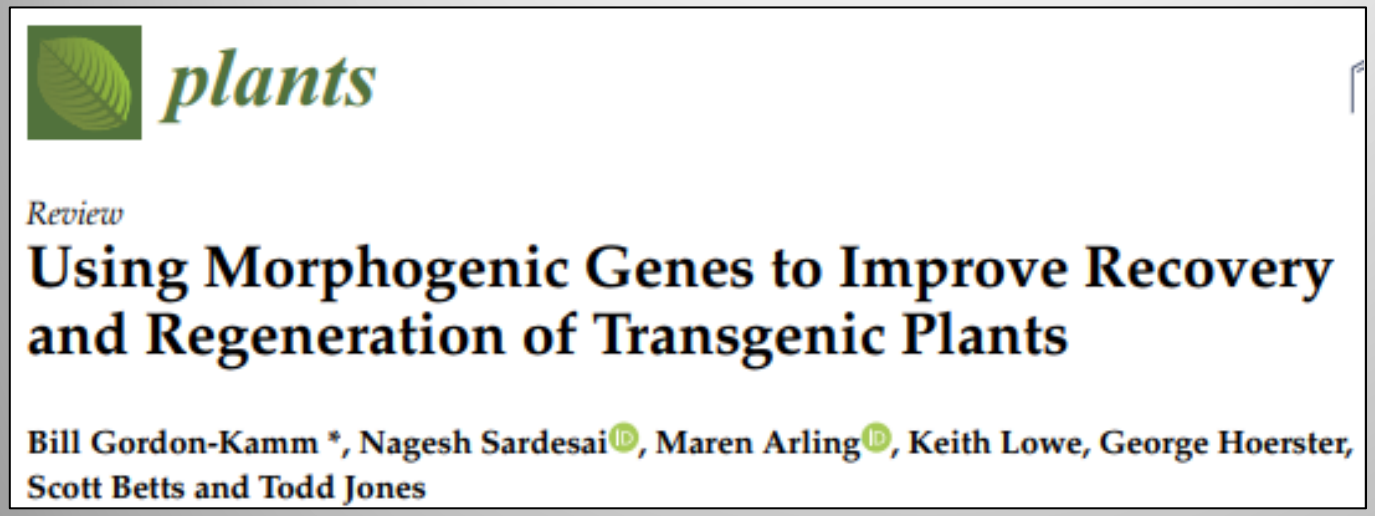


The problem of effective transformation / editing



- Transformation (and regeneration) difficult, costly, or impossible in many genotypes
- Forest trees highly diverse, tissues often recalcitrant to typical treatments due to developmental stage or physiology
- Problematic for obtaining “clean” gene edited progeny from diverse genotypes to avoid GMO regulation

“DEV” genes can work, but need much more research

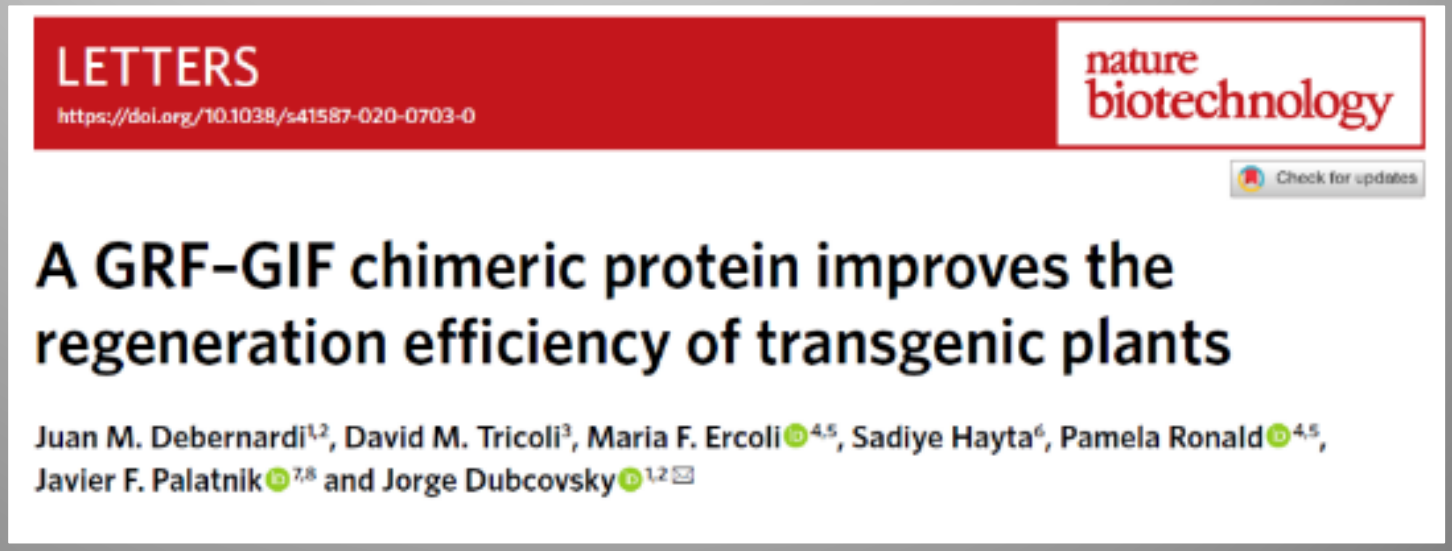


plants

Review

Using Morphogenic Genes to Improve Recovery and Regeneration of Transgenic Plants

Bill Gordon-Kamm *, Nagesh Sardesai, Maren Arling, Keith Lowe, George Hoerster, Scott Betts and Todd Jones

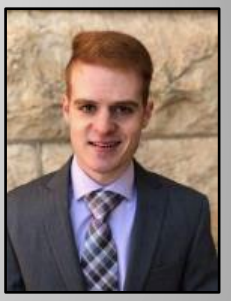


LETTERS
https://doi.org/10.1038/s41587-020-0703-0
nature biotechnology
Check for updates

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

Juan M. Debernardi[1,2], David M. Tricoli[3], Maria F. Ercoli[4,5], Sadiye Hayta[6], Pamela Ronald[4,5], Javier F. Palatnik[7,8] and Jorge Dubcovsky[1,2]

Populus GRF-GIF promoted transgenic shoot regeneration in recalcitrant *P. alba* '6K10'

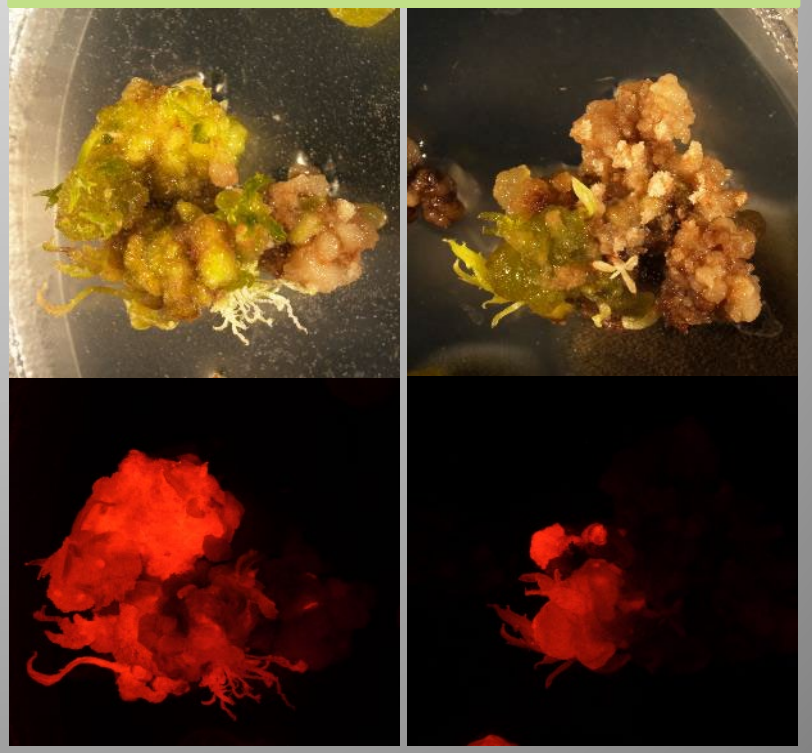


Control (dsRed + *hpt*)

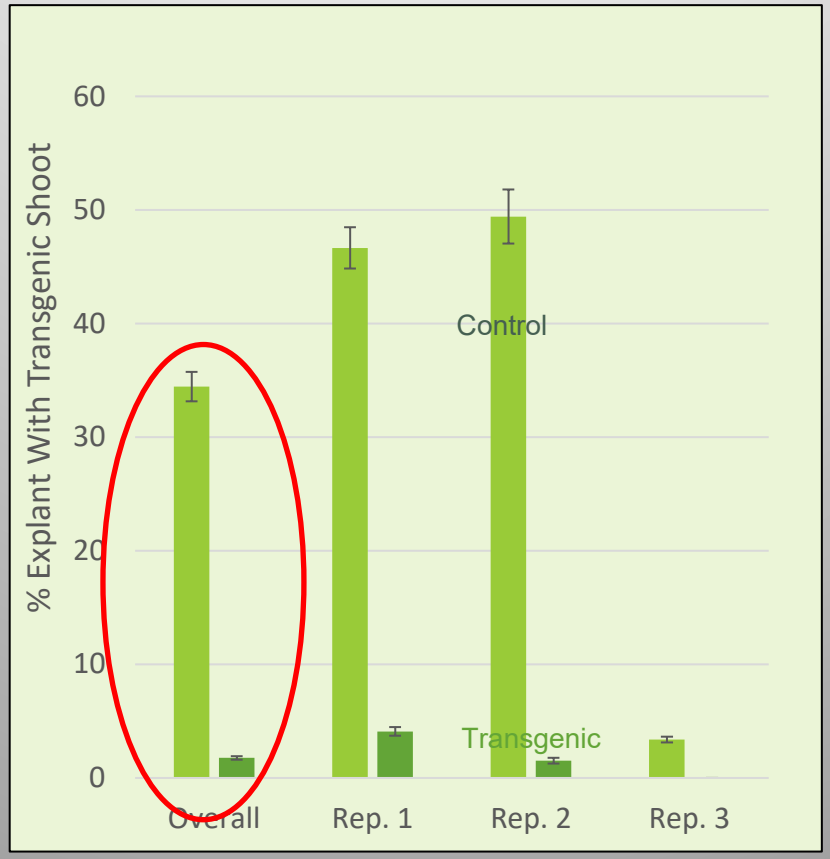
Bright field

dsRed

2x35S:PtGRF4-GIF1



But *Citrus 4-mut* GRF-GIF strongly inhibited shoot formation in poplar clone 353-53 (*P. tremula x tremuloides*)



Error bars = SE

What is needed to make biotech relevant?

- Basic science on gene-trait controls, gene control tools, synthetic biology
- Overcome the transformation bottleneck – research new tools (e.g., DEV genes and viral editing tools)
- Conduct extensive, public field research with a wide variety of product and stress-reduction genes
- Tie-down (demonstrate, confirm) genetic containment in the field – including to elaborate and expand options and management
- Organized action by scientists to make the case to the public and other scientists that these tools can matter

Thanks to the organizers of this meeting…
For industry and scientific grant support…
For my illustrious coworkers in Oregon…
And warm greetings to my many friends and colleagues at this meeting, and in China