Sunday Evening News No. 103

Week 46 (2018-11-12 / 11-18)

Selected and edited by ***BGF*** Jany

Dear all,
in my opinion, the most important press release in Europa in the field of genetic engineering and biotechnology

Commission and SAM: **A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive**
https://ec.europa.eu/info/publications/status-products-derived-gene-editing-and-implications-gmo-directive_en

Statement by the Group of Chief Scientific Advisors: **A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive**
https://ec.europa.eu/info/sites/info/files/2018_11_gcsa_statement_gene_editing_1.pdf

Commission's Chief Scientific Advisors publish statement on the regulation of gene editing
https://ec.europa.eu/info/news/commissions-chief-scientific-advisors-publish-statement-regulation-gene-editing-2018-nov-13_en

Press releases and media reports

Neergaard L.: **Gene-edited foods are coming, but how will they be regulated, and will consumers eat them?**
https://geneticliteracyproject.org/2018/11/16/gene-edited-foos-are-coming-but-how-will-they-be-regulated-and-will-consumers-eat-them/
http://www.post-gazette.com/life/food/2018/11/14/Gene-edited-food-is-coming-biotech-shoppers-buy-GMOs-market/stories/201811140088

GM Watch: Bound to fail: **The flawed scientific foundations of agricultural genetic engineering (part 1)**
The GMO food venture is bound to fail because it is based on flawed scientific foundations. This was the message of a public talk given by Dr Angelika Hilbeck, researcher at ETH Zurich, Switzerland, and a board member and co-founder of the European Network of Scientists for Social and Environmental Responsibility (ENSSER), on the evening before the 9th GMO Free Europe conference in Berlin this September.
https://www.gmwatch.org/en/news/latest-news/18582

Inzé D.: **EU legislation must safeguard precision plant breeding technologies**
European plant scientists are hindered by an outdated regulatory framework that is at odds with recent scientific evidence, writes Dirk Inzé.
https://www.theparliamentmagazine.eu/articles/partner_article/eu-legislation-must-safeguard-precision-plant-breeding-technologies

Voormolen S.: **Should Europe's 17-year-old GMO regulations apply to CRISPR-edited crops?**
https://geneticliteracyproject.org/2018/11/13/should-europes-17-year-old-gmo-regulations-apply-to-crispr-edited-crops/

Li Y.: **How scientists are using CRISPR to create non-GMO crops**
https://geneticliteracyproject.org/2018/11/15/how-scientists-are-using-crispr-to-create-non-gmo-crops/

As always you will find the daily up-date of the press releases at: https://www.biotech-gm-food.com/presse

For information:
In agreement with WGG and VBIO and due to a blocking period for a press release on an open letter to the Ministers of Agriculture as well as Research, I will send you on Monday 19.11.2018. 12:00 pm a Sunday Evening News Special.

Publication

Addendum from last week: Complete citation
Faltus T. (2018): **Das Mutagenese-Urteil des EuGH schwächt die rechtssichere Anwendung der Gentechnik.** ZUR 10, 524-533 pdf-file available

Ruffell D. (2018): **The EU Court of Justice extends the GMO Directive to gene edited organisms.** FEBS Lett. doi: 10.1002/1873-3468.13293.
https://www.ncbi.nlm.nih.gov/pubmed/30426476 pdf-file available

Australian Government/Department of Health: **Third Review of the National Gene Technology Scheme**
The Third Review (the Review) of the National Gene Technology Scheme (the Scheme) was conducted by a collaboration of Commonwealth, state and territory officials on behalf of all Australian governments, assisted by an independent Expert Advisory Panel.
http://www.health.gov.au/internet/main/publishing.nsf/Content/gene-technology-review

Kumlehn J., Pietralla J., Hensel G., Pacher M., and Puchta H. (2018): **The CRISPR/Cas revolution continues: From efficient gene editing for crop breeding to plant synthetic biology**. J. Integr. Plant Biol: doi: [10.1111/jipb.12734]
Since the discovery that nucleases of the bacterial CRISPR/Cas system can be used as easily programmable tools for genome engineering, their application massively transformed different areas of plant biology. In this review, we assess the current state of their use for crop breeding to incorporate attractive new agronomical traits into specific cultivars of various crop plants. This can be achieved by the use of Cas9/12 nucleases for double strand break induction, resulting in mutations by non-homologous recombination. Strategies for performing such experiments – from the design of guide RNA to the use of different transformation technologies - are evaluated. Furthermore, we sum up recent developments regarding the use of nuclease-deficient Cas9/12 proteins, as DNA-binding moieties for targeting different kinds of enzyme activities to specific sites within the genome. Progress in base deamination, transcriptional induction and transcriptional repression, as well as in imaging in plants, is also discussed. As different Cas9/12 enzymes are at hand, the simultaneous application of various enzyme activities, to multiple genomic sites, is now in reach to redirect plant metabolism in a multifunctional manner and pave the way for a new level of plant synthetic biology.
https://onlinelibrary.wiley.com/doi/10.1111/jipb.12734

Shew A.M., Nalley L.L., Price H., Nayga R., Dixon B.L. (2018): **CRISPR versus GMOs: Public acceptance and valuation.** Global Food Security 19, 71-80; DOI: 10.1016/j.gfs.2018.10.005
CRISPR gene-editing has major implications for agriculture and food security. However, no studies have evaluated the public acceptance and valuation of CRISPR-produced food. As such, we conducted a multi-country assessment of consumers' willingness-to-consume (WTC) and willingness-to-pay (WTP) for CRISPR-produced food compared to conventional and genetically modified (GM) foods, respectively. In the USA, Canada, Belgium, France, and Australia, 56, 47, 46, 30, and 51% of respondents, respectively, indicated they would consume both GM and CRISPR food. We also found that biotechnology familiarity and perceptions of safety were the primary drivers for WTC CRISPR and GM food. Moreover, respondents valued CRISPR and GM food similarly-substantially less than conventional food-which could be detrimental for meeting future food demand.
https://www.researchgate.net/publication/328858808_CRISPR_versus_GMOs_Public_acceptance_and_valuation?pag:2:mrect:(113.16,655.51,55.45,7.69) pdf-file available

Jouanin A, Boyd L, Visser RGF and Smulders MJM (2018) **Development of Wheat With Hypoimmunogenic Gluten Obstructed by the Gene Editing Policy in Europe.** Front. Plant Sci. 9:1523.doi: 10.3389/fpls.2018.01523
Coeliac Disease (CD) is an auto-immune reaction to gluten in 1–2% of the human population. A gluten-free (GF) diet, excluding wheat, barley, and rye, is the only remedy. This diet is difficult to adhere to, partly because wheat gluten is added to many processed products for their viscoelastic properties. In addition, GF products are less healthy and expensive. Wheat products containing only hypoimmunogenic gluten proteins would be a desirable option. Various gluten peptides that trigger CD have been characterized. A single wheat variety contains around hundred gluten genes, producing proteins with varying numbers of epitopes. Gene editing using CRISPR/Cas9 can precisely remove or modify the DNA sequences coding for immunogenic peptides. Wheat with hypoimmunogenic gluten thus exemplifies the potential of gene editing for improving crops for human consumption where conventional breeding cannot succeed. We describe here, in relation to breeding

hypoimmunogenic wheat varieties, the inconsistencies of applying GM regulation in Europe for gene-edited plants while mutation breeding-derived plants are exempted. We explain that healthy products derived from this new technology may become available in the United States, Canada, Argentina and other countries but not in Europe, because of strict regulation of unintended GM risk at the expense of reduction the existing immunogenicity risks of patients. We argue that regulation of gene-edited plants should be based on scientific evidence. Therefore, we strongly recommend implementing the innovation principle. Responsible Research and Innovation, involving stakeholders including CD patient societies in the development of gene-editing products, will enable progress toward healthy products and encourage public acceptance.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6200864/pdf/fpls-09-01523.pdf

Wu S. et al. (2018): **A common genetic mechanism underlies morphological diversity in fruits and other plant organs.** *Nature Communications,* **9**, Article number: 734 (2018) (2018). DOI: 10.1038/s41467-018-07216-8
Shapes of edible plant organs vary dramatically among and within crop plants. To explain and ultimately employ this variation towards crop improvement, we determined the genetic, molecular and cellular bases of fruit shape diversity in tomato. Through positional cloning, protein interaction studies, and genome editing, we report that OVATE Family Proteins and TONNEAU1 Recruiting Motif proteins regulate cell division patterns in ovary development to alter final fruit shape. The physical interactions between the members of these two families are necessary for dynamic relocalization of the protein complexes to different cellular compartments when expressed in tobacco leaf cells. Together with data from other domesticated crops and model plant species, the protein interaction studies provide possible mechanistic insights into the regulation of morphological variation in plants and a framework that may apply to organ growth in all plant species.
https://www.nature.com/articles/s41467-018-07216-8.pdf

J. Merritt Melancon, University of Georgia: Researchers discover genes that give vegetables their shape
https://phys.org/news/2018-11-genes-vegetables.html#jCp

Pryor J.M. et al. (2018): **Ribonucleotide incorporation enables repair of chromosome breaks by nonhomologous end joining**. *Science* 361 (6407), 1126-1129;DOI: 10.1126/science.aat2477
The nonhomologous end–joining (NHEJ) pathway preserves genome stability by ligating the ends of broken chromosomes together. It employs end-processing enzymes, including polymerases, to prepare ends for ligation. We show that two such polymerases incorporate primarily ribonucleotides during NHEJ—an exception to the central dogma of molecular biology—both during repair of chromosome breaks made by Cas9 and during V(D)J recombination. Moreover, additions of ribonucleotides but not deoxynucleotides effectively promote ligation. Repair kinetics suggest that ribonucleotide-dependent first-strand ligation is followed by complementary strand repair with deoxynucleotides, then by replacement of ribonucleotides embedded in the first strand with deoxynucleotides. Our results indicate that as much as 65% of cellular NHEJ products have transiently embedded ribonucleotides, which promote flexibility in repair at the cost of more fragile intermediates.
http://science.sciencemag.org/content/361/6407/1126

University of North Carolina at Chapel Hill School of Medicine: By solving a mystery of gene repair, scientists uncover an exception to biology's rules
https://phys.org/news/2018-11-mystery-gene-scientists-uncover-exception.html#jCp

Zawedde BM, Kwehangana M and Oloka HK (2018): **Readiness for Environmental Release of Genetically Engineered (GE) Plants in Uganda**. Front. Bioeng. Biotechnol. 6:152;.doi: 10.3389/fbioe.2018.00152
Research and development of genetically engineered (GE) crops in Uganda was initiated in 2003 with the launch of a national agricultural biotechnology center at Kawanda in central Uganda. The country has now approved 17 field experiments for GE plants, which were first established in 2006 with the planting of a banana confined field trial that evaluated performance of plants modified to express resistance to black sigatoka disease. Researchers leading the GE experiments have indicated that some of these GE plants are ready for environmental release that is moving beyond confined field testing toward commercialization. The government of Uganda, over the past two decades, has supported processes to put in place an effective national biosafety framework including establishment of a supportive policy environment; creation of a clear institutional framework for handling applications and issuance of permits; building critical capacity for risk analysis; and providing options for public engagement during decision-making. Uganda is ready to make a biosafety decision regarding environmental release of GE plants based on the level of capacity built, progress with priority GE crop research in the country, and the advancement in biosafety systems. Enactment of a national biosafety law that provides for a coordinated framework for implementation by the relevant regulatory agencies will strengthen the system further. In addition, product developers need to submit applications for biosafety approval for environmental release of GE crops so that mechanisms are tested and improved through practice.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6207583/pdf/fbioe-06-00152.pdf

Borges B.J., Arantes O.M., A. Fernandes A.A.R., Broach J.R. and PATRICIA M. FERNANDES P.M. (2018): **Genetically Modified Labeling Policies: Moving Forward or Backward?** Front. Bioeng. Biotechnol. | doi: 10.3389/fbioe.2018.00181

One of the priorities to address food security is to increase the access of farmers to biotechnology, through the application of scientific advances, such as genetically modified organisms and food (GMF). However, the spread of (mis)information about their safety strengthens the clamor for mandatory GMF labeling. This paper provides an overview of food labeling policies, considering the principles suggested by the Codex Alimentarius Commission, and analyzes the consequences for the world food security of the Brazilian labeling policies compared to developed countries. We discuss the discriminatory application of GMF mandatory labeling in the absence of any scientific evidence as it has the potential of causing social harm and jeopardizes research, production, and distribution of food and consumers' right to information.
https://www.frontiersin.org/articles/10.3389/fbioe.2018.00181/abstract

Xu X. et al. (2018): **Structural basis for reactivating the mutant TERT promoter by cooperative binding of p52 and ETS1.** *Nature Communications* (2018). DOI: 10.1038/s41467-018-05644-0
Transcriptional factors ETS1/2 and p52 synergize downstream of non-canonical NF-κB signaling to drive reactivation of the −146C>T mutant *TERT* promoter in multiple cancer types, but the mechanism underlying this cooperativity remains unknown. Here we report the crystal structure of a ternary p52/ETS1/−146C>T *TERT* promoter complex. While p52 needs to associate with consensus κB sites on the DNA to function during non-canonical NF-κB signaling, we show that p52 can activate the −146C>T *TERT* promoter without binding DNA. Instead, p52 interacts with ETS1 to form a heterotetramer, counteracting autoinhibition of ETS1. Analogous to observations with the GABPA/GABPB heterotetramer, the native flanking ETS motifs are required for sustained activation of the −146C>T *TERT* promoter by the p52/ETS1 heterotetramer. These observations provide a unifying mechanism for transcriptional activation by GABP and ETS1, and suggest that genome-wide targets of non-canonical NF-κB signaling are not limited to those driven by consensus κB sequences.
https://www.nature.com/articles/s41467-018-05644-0.pdf
Agency for Science, Technology and Research (A*STAR), Singapore: Controlling the gene for the 'immortalizing enzyme'
https://phys.org/news/2018-11-gene-immortalizing-enzyme.html#jCp

Ohkanda J. et al. (2018): **Structural Effects of Fusicoccin upon Upregulation of 14-3-3-Phospholigand Interaction and Cytotoxic** Activity, Chemistry - A European Journal; DOI: 10.1002/chem.201804428
Fusicoccins (FCs) exhibit various cellular activities in mammalian cells, but details of the mechanism of action are not fully understood. In this study, we synthesized two pairs of model derivatives of FCs differing only in the presence and absence of a 12-hydroxyl group and evaluated their binding to a 14-3-3 protein together with various mode 1 and mode 3 phosphopeptide ligands. Our results demonstrate that the 12-hydroxyl group hampers binding to 14-3-3 with mode 1 phospholigands, presumably due to steric repulsion with the *i*+2 residue. Furthermore, cell-based evaluations showed that only non-substituted FCs exhibit significant cytotoxicity and all 12-hydroxyl derivatives were inactive, demonstrating a clear correlation with their ability to form ternary complexes with 14-3-3 and a mode 1 ligand. These results suggest that binding to 14-3-3 and a partner protein(s) possessing a mode 1 sequence plays a role in the mechanism of action of 12-non-substituted FCs.
https://onlinelibrary.wiley.com/doi/pdf/10.1002/chem.201804428

Shinshu University: Edited plant-based toxin possesses anti-tumor characteristics
https://phys.org/news/2018-11-plant-based-toxin-anti-tumor-characteristics.html#jCp

Guo J.et al. (2018): "Light-driven fine chemical production in yeast biohybrids," *Science* 362 (6416), 813-816; science.sciencemag.org/cgi/doi … 1126/science.aat9777
Inorganic-biological hybrid systems have potential to be sustainable, efficient, and versatile chemical synthesis platforms by integrating the light-harvesting properties of semiconductors with the synthetic potential of biological cells. We have developed a modular bioinorganic hybrid platform that consists of highly efficient light-harvesting indium phosphide nanoparticles and genetically engineered *Saccharomyces cerevisiae*, a workhorse microorganism in biomanufacturing. The yeast harvests photogenerated electrons from the illuminated nanoparticles and uses them for the cytosolic regeneration of redox cofactors. This process enables the decoupling of biosynthesis and cofactor regeneration, facilitating a carbon- and energy-efficient production of the metabolite shikimic acid, a common precursor for several drugs and fine chemicals. Our work provides a platform for the rational design of biohybrids for efficient biomanufacturing processes with higher complexity and functionality.
http://science.sciencemag.org/content/362/6416/813

Harvard University: Solar panels for yeast cell biofactories
https://phys.org/news/2018-11-solar-panels-yeast-cell-biofactories.html#jCp

Rai A. K. Pandey A., Sahoo D. (2018): **Biotechnological potential of yeasts in functional food industry.** Trends in Food Science & Technology https://doi.org/10.1016/j.tifs.2018.11.016
Background: Biotechnological potential of yeasts can be evidenced by the rich history of its application in food fermentation. Several yeast species isolated from fermented foods have been characterised and applied as starter/co-starter in functional food industries. The outcome of modern research in the recent past on

nutraceuticals and development of functional foods using yeasts suggests its bright future in food biotechnology.
Scope and Approach: In this article, bioactive compounds produced using yeasts including β-glucan, carotenoids, glutathione, bioactive peptides, γ-aminobutyric acid, organic selenium, prebiotic oligosaccharides and free polyphenols, are discussed. Yeast species having probiotic potential as well as therapeutic properties are highlighted in the manuscript. Recent studies on metabolic engineering approaches applied to develop yeast strains with additional functional properties with higher industrial importance have also been reviewed.
Key Findings and Conclusions: The current review summarizes the importance of yeast in the production of functional food and development of bioprocesses for the production of high value nutraceuticals. The review also highlights the importance of yeast as a single starter as well as a component of mixed starter cultures in production of bioactive metabolites. However, there is a need of exploration of novel yeast strains that have the ability to produce novel and efficient biocatalysts from traditional fermented foods for advances in food industry bioprocesses.
https://www.sciencedirect.com/science/article/abs/pii/S0924224418304163

Carzoli A. K, Aboobucker S.I., Sandall L.L., Lübberstedt T.T. Suza W.P.(2018): **Risks and opportunities of GM crops: Bt maize example**. Global Food Security 19, 84-91; https://doi.org/10.1016/j.gfs.2018.10.004
The anticipated world population growth emphasizes a need to produce more food on less land. Cutting-edge technologies, including genetic engineering, can help to develop improved crop varieties and protect natural resources. In spite of the potential for genetically-modified (GM) crops to make crop production more efficient, they remain a polarizing issue due to safety concerns. This paper provides an overview of the risk assessment process. The safety of *Bacillus* thuringiensis (Bt) proteins is used as an example for how risk assessment is applied to GM crops. Risks associated with GM crops have proven to be low to non-existent. Developing countries would benefit from GM technologies as one tool to improve crop yields and reduce production challenges.
https://reader.elsevier.com/reader/sd/pii/S221191241830049X?token=588324546DBEE88B33F1DD001C784AF36483A7C9AA3E721C20F25C04E24B5086218FCD28AF4EE9B2D13A3BDDF2C6CF71

Sarah N. Bechtold S.N. (2018): **Beyond risk considerations: Where and how can a debate about non-safety related issues of genome editing in agriculture take place?** Front. Plant Sci. | doi: 10.3389/fpls.2018.01724
Having the potential to realize breeding objectives that were out of reach so far, genome editing (GE) surely constitutes a major advancement in the field of plant research, especially for the agricultural sector. Only recently has the debate about GE and its possible use in food and feed production transcended the scientific circle towards a political discussion. Considering the discussions about genetically modified organisms (GMOs) in the past, it is very likely that the public debate about genome edited food and feed products will be highly controversial. This article will show that the debate about genome editing is already risk-focused and that the resulting confinement structurally hampers a sound discussion of the values that are at stake. In contrast to this development I argue that a comprehensive deliberation of values is needed in the context of genome editing in agriculture. Moreover, those deliberations should be separated from risk analysis and allow for individual decisions within our value system. Finally I will discuss food labelling and consumer choice as an institution to support communication about values and to broaden the perspective on the agricultural use of genome editing and its products.
https://www.frontiersin.org/articles/10.3389/fpls.2018.01724/full

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Wie immer wird für Hinweise und der Zusendung von Publikationen und sonstigen Informationen gedankt. pdf-Dateien können meist direkt aus den links heruntergeladen werden.

Bitte besuchen sie auch die Webseite des Wissenschaftlerkreis Grüne Gentechnik e.V. (WGG): www.wgg-ev.de .

*As always, I thank you all for hints and for publications. M*ost of the pdf files can be downloaded directly from the links.

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