

Supporting document #1 to EPSO contribution to Stakeholder consultation on new genomic techniques to contribute to a Commission study requested by the Council

Support for answers to all sections (Q1 to Q29).

REFERENCES

- AFBV-WGG (2020) Proposal by AFBV and WGG for amendments to GMO legislation (<https://www.wgg-ev.de/info/korrespondenz-international/open-letter-eu-kommission-02-2020/>)
- Altpeter F, Springer NM, Bartley LE, Blechl AE, Brutnell TP, Citovsky V, Conrad LJ, Gelvin SB, Jackson DP, Kausch AP, Lemaux PG, Medford JI, Orozco-Cárdenas ML, Tricoli DM, Van Eck J, Voytas DF, Walbot V, Wang K, Zhang ZJ, Stewart CN (2016) Advancing Crop Transformation in the Era of Genome Editing. *The Plant Cell*, 28: 1510–1520. [doi.org/10.1105/tpc.16.00196]
- Anderson, JA, Gipmans, M, Hurst, S, Layton, R, Nehra, N, Pickett, J et al., (2016): Emerging Agricultural Biotechnologies for Sustainable Agriculture and Food Security. *J Agric Food Chem* 64:383–393. [DOI: 10.1021/acs.jafc.5b04543].
- Andersson M, Turesson H, Nicolai A, et al., (2017) Efficient targeted multiallelic mutagenesis in tetraploid potato (*Solanum tuberosum*) by transient CRISPR-Cas9 expression in protoplasts. *Plant Cell Rep* 36:117–128. [doi.org/dx.doi.org/10.1007/s00299-016-2062-3].
- Andersson M, Turesson H, Olsson N Fält AS, Ohlsson P, Gonzalez MN, Samuelsson M, Hofvander P (2018) Genome editing in potato via CRISPR-Cas9 ribonucleoprotein delivery. *Physiol Plant* 164:378-384. [doi.org/10.1111/ppl.12731].
- Aznar-Moreno, JA, Durrett, TP (2017): Simultaneous Targeting of Multiple Gene Homeologs to Alter Seed Oil Production in *Camelina sativa*. *Plant Cell Physiol* 58:1260–1267. [DOI: 10.1093/pcp/pcx058].
- Batista R, Saibo N, Lourenço T, Margarida Oliveira (2008) Microarray analyses reveal that plant mutagenesis may induce more transcriptomic changes than transgene insertion *PNAS* 105:3640-3645. [doi.org/10.1073/pnas.0707881105]
- Bechtold S (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.* 9:1724. [doi: 10.3389/fpls.2018.01724]
- Blanvillain-Baufumé, S, Reschke, M, Solé, M, Auguy, F, Doucoure, H, Szurek, B et al., (2017): Targeted promoter editing for rice resistance to *Xanthomonas oryzae* pv. *oryzae* reveals differential activities for SWEET14-inducing TAL effectors. *Plant Biotech J* 15:306–317. [DOI: 10.1111/pbi.12613].
- Braatz, J, Harloff, H-J, Mascher, M, Stein, N, Himmelbach, A, Jung, C (2017): CRISPR-Cas9 Targeted Mutagenesis Leads to Simultaneous Modification of Different Homoeologous Gene Copies in Polyploid Oilseed Rape (*Brassica napus*). *Plant Physiol* 174:935–942. [DOI: 10.1104/pp.17.00426].
- Bratlie S, Halvorsen K, Myskja BK, Mellegård H, Bjorvatn C, Frost P, Heiene G, Hofmann B,, Holst-Jensen A, Holst-Larsen T,O, Malnes RS, Paus B, Sandvig B, Sjøli SI, Skarstein B, Thorseth MB, Vagstad N, Våge DI, Borge OJ. (2019) A novel governance framework for GMO: A tiered, more flexible regulation for GMOs would help to stimulate innovation and public debate. *EMBO Rep* pii: e47812. [doi: 10.15252/embr.201947812].
- Broad Institute (2017) DuPont Pioneer and Broad Institute Join Forces to Enable Democratic CRISPR Licensing in Agriculture (<https://www.broadinstitute.org/news/dupont-pioneer-and-broad-institute-join-forces-enable-democratic-crispr-licensing-agriculture>)
- Broad Institute (2019) Questions and answers about CRISPR patents. (<https://www.broadinstitute.org/crispr/journalists-statement-and-background-crispr-patent-process>)
- Bull, SE, Seung, D, Chanez, C, Mehta, D, Kuon, J-E, Truernit, E et al., (2018): Accelerated ex situ breeding of GBSS- and PTST1-edited cassava for modified starch. *Sci Adv* 4, eaat6086. [DOI: 10.1126/sciadv.aat6086].
- Casacuberta, J.M. and Puigdomenech, P. (2018) Proportionate and scientifically sound risk assessment of gene-edited plants. *EMBO Rep.* 19, e46907. [doi: 10.15252/embr.201846907]
- CCCE Comité Consultatif Commun d'Ethique INRA-CIRAD-IFREMER (2018). Les nouvelles techniques

- d'amélioration génétique des plantes. <https://wwz.ifremer.fr/content/download/116511/file/Avis-11-Comite-Ethique.pdf>
- Chen K, Wang Y, Zhang R, Zhang H, Gao C (2019) CRISPR/Cas Genome Editing and Precision Plant Breeding in Agriculture. *Ann Rev Plant Biol* 70:667-697 [doi.org/10.1146/annurev-arplant-050718-100049]
- CNB Comisión Nacional de Bioseguridad (2019) https://www.miteco.gob.es/es/calidad-y-evaluacion-ambiental/temas/biotecnologia/informefinalmutagenesisdirigida_tcm30-489610.pdf
- Cohen J (2017) Round one of CRISPR patent legal battle goes to the Broad Institute Science. [[doi:10.1126/science.aal0770](https://doi.org/10.1126/science.aal0770)]. (<https://www.sciencemag.org/news/2017/02/round-one-crispr-patent-legal-battle-goes-broad-institute#>)
- Conseil d'Etat (2020) Organismes obtenus par mutagenèse. (<https://www.conseil-etat.fr/ressources/decisions-contentieuses/dernieres-decisions-importantes/conseil-d-etat-7-fevrier-2020-organismes-obtenus-par-mutagenese>)
- Coumoul X, Servien R, Juricek L, Kaddouch-Amar Y, Lippi Y, Berthelot L, Naylies C, Morvan ML, Antignac JP, Desdoits-Lethimonier C, Jegou B, Tremblay-Franco M, Canlet C, Debrauwer L, Le Gall C, Laurent J, Gouraud PA, Cravedi JP, Elisabeth Jeunesse E, Savy N, Dandere-Abdoulkarim K, Arnich N, Fourès F, Cotton J, Broudin S, Corman B, Moing A, Laporte B, Richard-Forget F, Barouki R, Rogowsky P, Salles B (2018) The GMO90+ project: absence of evidence for biologically meaningful effects of genetically modified maize based-diets on Wistar rats after 6-months feeding comparative trial. *Toxicol Sci* 168:315-338. [[doi: 10.1093/toxsci/kfy298](https://doi.org/10.1093/toxsci/kfy298)].
- Custers R, Casacuberta JM, Eriksson D, Sági L and Schiemann J (2019) Genetic Alterations That Do or Do Not Occur Naturally; Consequences for Genome Edited Organisms in the Context of Regulatory Oversight. *Front Bioeng Biotechnol* 6:213. [[doi: 10.3389/fbioe.2018.00213](https://doi.org/10.3389/fbioe.2018.00213)]
- DCE Danish Council on Ethics (2019) GMO and ethics in a new era. (<http://www.etiskraad.dk/english/publications/gmo-and-ethics-in-a-new-era>)
- Danilo, B, Perrot, L, Mara, K, Botton, E, Nogué, F, Mazier, M (2019): Efficient and transgene-free gene targeting using Agrobacterium-mediated delivery of the CRISPR/Cas9 system in tomato. *Plant Cell Rep* 38:459–462. [[DOI: 10.1007/s00299-019-02373-6](https://doi.org/10.1007/s00299-019-02373-6)].
- Das Bhowmik, SS, Cheng, AY, Long, H, Tan, GZH, Hoang, TML, Karbaschi, MR et al., (2019): Robust Genetic Transformation System to Obtain Non-chimeric Transgenic Chickpea. *Front Plant Sci* 10:524. [[DOI: 10.3389/fpls.2019.00524](https://doi.org/10.3389/fpls.2019.00524)].
- Darracq A, Vitte C, Nicolas S, Duarte J, Pichon JP, Aubert J, Wang X, Mary-Huard T, Chevalier C, Charcosset A, Bérard A, Le Paslier MC, Rogowsky P, Joets J (2018) Sequence analysis of European maize inbred line FV2 provides new insights into molecular and chromosomal characteristics of presence/absence variants. *BMC Genomics* 19:119. [doi.org/10.1186/s12864-018-4490-7].
- Dederer HG, Hamburger D (2019) Regulation of Genome Editing in Plant Biotechnology: A Comparative Analysis of Regulatory Frameworks of Selected Countries and the EU. Springer International Publishing. [[DOI: 10.1007/978-3-030-17119-3](https://doi.org/10.1007/978-3-030-17119-3)].
- EC European Commission (2000) Communication from the commission on the precautionary principle (<https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2000:0001:FIN:EN:PDF>).
- EC European Commission (2019) The European Green Deal (https://ec.europa.eu/info/sites/info/files/european-green-deal-communication_en.pdf)
- EGESNT European Group of Ethics of Sciences and New Technologies (2008) Ethics of Modern Developments in Agricultural Technologies. https://ec.europa.eu/archives/bepa/european-group-ethics/docs/publications/opinion24_en.pdf
- Eom JS, Luo D, Atienza-Grande G, et al., (2019) Diagnostic kit for rice blight resistance. *Nat Biotechnol* 37:1372–1379. [doi.org/10.1038/s41587-019-0268-y].
- EPSO (2019) On the ECJ ruling regarding mutagenesis and the genetically modified organisms directive (<https://epsoweb.org/epsoweb/epsoweb-statement-on-the-court-of-justice-of-the-eu-ruling-regarding-mutagenesis-and-the-gmo-directive/2019/02/19/>)
- European Network of GMO Laboratories ENGL (2019) Detection of food and feed plant products obtained by

- new mutagenesis techniques, 26 March 2019 (JRC116289). (<https://gmo-crl.jrc.ec.europa.eu/doc/JRC116289-GE-report-ENGL.pdf>)
- González MN, Massa GA, Andersson M, et al., (2020) Reduced enzymatic browning in potato tubers by specific editing of a polyphenol oxidase gene *via* ribonucleoprotein complexes delivery of the CRISPR/Cas9 system. *Front Plant Sci* 10:1649. [doi.org/10.3389/fpls.2019.01649].
- Grohmann L, Keilwagen J, Duensing N, Dagand E, Hartung F, Wilhelm R, Bendiek J and Sprink T (2019) Detection and Identification of Genome Editing in Plants: Challenges and Opportunities. *Front. Plant Sci.* 10:236. [[doi: 10.3389/fpls.2019.00236](https://doi.org/10.3389/fpls.2019.00236)].
- Haberer G, Bauer E, Kamal N, Gundlach H, Fischer I, Seidel MA, Spannagl M, Marcon C, Ruban A, Urbany C, Nemdi A, Hochholdinger F, Ouzunova M, Houben A, Schön CC, Mayer KFX (2019) European maize genomes unveil pan-genomic dynamics of repeats and genes. *bioRxiv* [doi.org/10.1101/766444]
- Hahn F, Nekrasov V (2019) CRISPR/Cas precision: do we need to worry about off-targeting in plants? *Plant Cell Rep* 38:437–441. [doi.org/10.1007/s00299-018-2355-9].
- Hansson SO (2018) The Precautionary Principle. In: Möller N, Hansson SO, Holmberg J-E, Rollenhagen C, editors. *Handbook of Safety Principles*. Hoboken (US): John Wiley & Sons; 2018. p. 258-83. [doi.org/10.1002/9781119443070.ch12]
- Hansen SO (2019) A Science-Informed Ethics for Agricultural Biotechnology. *Crop Breed Genet Genom* 1:e190006. [doi.org/10.20900/cbagg20190006]
- Haverkort AJ, Boonekamp PM, Hutten R, et al., (2016) Durable late blight resistance in potato through dynamic varieties obtained by cisgenesis: scientific and societal advances in the DuRPh project. *Potato Res* 59:35–66. [doi.org/10.1007/s11540-015-9312-6].
- Holme IB, Wendt T, Gil-Humanes J, et al., (2017) Evaluation of the mature grain phytase candidate *HvPAPhy_a* gene in barley (*Hordeum vulgare* L.) using CRISPR/Cas9 and TALENs. *Plant Mol Biol* 95:111–121. [doi.org/10.1007/s11103-017-0640-6].
- INRA Institut National de la Recherche Agronomique (2018) Plant genome editing: INRA defines its strategy (<https://www.inrae.fr/en/news/plant-genome-editing-inra-defines-its-strategy>)
- Ishii T, Araki M (2017) A future scenario of the global regulatory landscape regarding genome-edited crops. *GM Crops Food* 8:44–56. [[DOI: 10.1080/21645698.2016.1261787](https://doi.org/10.1080/21645698.2016.1261787)]
- Jansing J, Schiermeyer A, Schillberg S, et al., (2019) Genome editing in agriculture: Technical and practical considerations. *Int J Mol Sci* 20:2888. [doi.org/10.3390/ijms20122888].
- Jiang, L, Li, DH, Jin, L, Ruan, Y, Shen, WH, Liu, CL (2018): Histone lysine methyltransferases BnaSDG8.A and BnaSDG8.C are involved in the floral transition in *Brassica napus*. In: *Plant J* 95 (4) :672–685. DOI: 10.1111/tbj.13978.
- Kausch, AP, Nelson-Vasilchik, K, Hague, J, Mookkan, M, Quemada, H, Dellaporta, S et al., (2019): Edit at will: Genotype independent plant transformation in the era of advanced genomics and genome editing. *Plant Sci* 281:186–205. [[DOI: 10.1016/j.plantsci.2019.01.006](https://doi.org/10.1016/j.plantsci.2019.01.006)].
- Jouanin A, Schaart JG, Boyd LA, et al., (2019) Outlook for coeliac disease patients: towards bread wheat with hypoimmunogenic gluten by gene editing of α - and γ -gliadin gene families. *BMC Plant Biol* 19:333. [doi.org/10.1186/s12870-019-1889-5].
- Kalaitzandonakes N, Alston JM, Bradford KJ. (2007) Compliance costs for regulatory approval of new biotech crops. *Nature Biotechnol*, 25: 509-511. [doi.org/10.1038/nbt0507-509].
- Kaya H, Mikami M, Endo A, Endo M, Toki S (2016) Highly specific targeted mutagenesis in plants using *Staphylococcus aureus* Cas9. *Sci Rep* 6:srep26871. [doi.org/10.1038/srep26871].
- Kim, JS (2018) Precision genome engineering through adenine and cytosine base editing. *Nat Plants* 4:148–151 (2018). [doi.org/10.1038/s41477-018-0115-z].
- Kis, A, Hamar, É, Tholt, G, Bán, R, Havelda, Z (2019): Creating highly efficient resistance against wheat dwarf virus in barley by employing CRISPR/Cas9 system. *Plant Biotech J* 17:1004–1006. [[DOI: 10.1111/pbi.13077](https://doi.org/10.1111/pbi.13077)].
- Le Buanec B, Ricroch A (2014). Intellectual Property Protection of Plant Innovation. In: Ricroch A., Chopra S., Fleischer S. (Editors) *Plant Biotechnology – Experience and Future Prospects*. Publisher: Springer ISBN

978-3-319-06892-3

- Ledford H (2017) Why the CRISPR patent verdict isn't the end of the story. *Nature* 542 [doi:10.1038/nature.2017.21510]. (<https://www.nature.com/news/why-the-crispr-patent-verdict-isn-t-the-end-of-the-story-1.21510>)
- Lemmon, Z.H., Reem, N.T., Dalrymple, J. Soyk S, Swartwood KE, Rodriguez-Leal D, Van Eck J, Lippman ZB (2018) Rapid improvement of domestication traits in an orphan crop by genome editing. *Nature Plants* 4:766–770. [doi.org/10.1038/s41477-018-0259-x].
- Lotz LAP, van de Wiel CCM, Smulders MJM (2020) Genetic engineering at the heart of agroecology. *Outlook Agric* 49:21-28. [doi.org/10.1177/0030727020907619].
- Li M, Li X, Zhou Z, et al., (2016a) Reassessment of the four yield-related genes *Gn1a*, *DEP1*, *GS3*, and *IPA1* in rice using a CRISPR/Cas9 system. *Front Plant Sci* 7:377. [doi.org/10.3389/fpls.2016.00377].
- Li Q, Zhang D, Chen M, et al., (2016b) Development of *japonica* photo-sensitive genic male sterile rice lines by editing *Carbon Starved Anther* using CRISPR/Cas9. *J Genet Genomics* 43:415–419. [doi.org/10.1016/j.jgg.2016.04.011].
- Li S, Gao F, Xie K, et al., (2016c) The OsmiR396c-OsGRF4-OsGIF1 regulatory module determines grain size and yield in rice. *Plant Biotechnol J* 14:2134–2146. [doi.org/10.1111/pbi.12569].
- Li R, Fu D, Zhu B, et al., (2018a) CRISPR/Cas9-mediated mutagenesis of *IncRNA1459* alters tomato fruit ripening. *Plant J* 94:513–524. [doi.org/10.1111/tpj.13872].
- Li R, Li R, Li X, et al., (2018b) Multiplexed CRISPR/Cas9-mediated metabolic engineering of γ -aminobutyric acid levels in *Solanum lycopersicum*. *Plant Biotechnol J* 16:415–427. [doi.org/10.1111/pbi.12781].
- Li T, Yang X, Yu Y, Si X, Zhai X, Zhang H, Dong W, Gao C, Xu C (2018c) Domestication of wild tomato is accelerated by genome editing. *Nat Biotechnol* 36:1160–1163. [doi.org/10.1038/nbt.4273].
- Li J, Manghwar H, Sun L, Wang P, Wang G, Sheng H, Zhang J, Liu H, Qin L, Rui H, Li B, Lindsey K, Daniell H, Jin S, Zhang X (2019) Whole genome sequencing reveals rare off-target mutations and considerable inherent genetic or/and somaclonal variations in CRISPR/Cas9-edited cotton plants. *Plant Biotechnol J* 17:858-868. [doi: 10.1111/pbi.13020. Epub 2018 Oct 30].
- Li et al., 2019. *Plant J*. [doi.org/10.1111/tpj.14117]
- Liang Z, Chen K, Zhang Y, Liu J, Yin K, Qiu JL, Gao C (2018) Genome editing of bread wheat using biolistic delivery of CRISPR/Cas9 in vitro transcripts or ribonucleoproteins. *Nat Protoc* 13:413-430. [doi: 10.1038/nprot.2017.145].
- Lin, Q., Zong, Y., Xue, C. et al., (2020) Prime genome editing in rice and wheat. *Nat Biotechnol* [doi.org/10.1038/s41587-020-0455-x]
- Macovei, A, Sevilla, NR, Cantos, C, Jonson, GB, Slamet-Loedin, I, Čermák, T et al., (2018): Novel alleles of rice eIF4G generated by CRISPR/Cas9-targeted mutagenesis confer resistance to Rice tungro spherical virus. In: *Plant biotechnology journal* 16 (11) :1918–1927. DOI: 10.1111/pbi.12927.
- Martin-Laffon J, Kuntz M, Ricroch A (2019) Worldwide CRISPR patent landscape shows strong geographical biases. *Nat Biotechnol* 37:613-620. [doi.org/10.1038/s41587-019-0138-7].
- Matveeva, TV, Otten, L (2019) Widespread occurrence of natural genetic transformation of plants by *Agrobacterium*. *Plant Mol Biol* 101: 415–437. [doi.org/10.1007/s11103-019-00913-y]
- Mock U, Hauber I, Fehse B (2016) Digital PCR to assess gene-editing frequencies (GEF-dPCR) mediated by designer nucleases. *Nat. Protoc.* 11:598-615 [doi: 10.1038/nprot.2016.027].
- Metje-Sprink J, Menz J, Modrzejewski D and Sprink T (2019) DNA-Free Genome Editing: Past, Present and Future. *Front Plant Sci* 9:1957. [doi.org/10.3389/fpls.2018.01957].
- Modrzejewski D, Hartung F, Sprink T, Krause D, Kohl C, Wilhelm R (2019) What is the available evidence for the range of applications of genome-editing as a new tool for plant trait modification and the potential occurrence of associated off-target effects: a systematic map. *Environ Evid* 8:27. [doi.org/10.1186/s13750-019-0171-5].
- Morineau, C, Bellec, Y, Tellier, F, Gissot, L, Kelemen, Z, Nogué, F, Faure, J-D (2017): Selective gene dosage by CRISPR-Cas9 genome editing in hexaploid *Camelina sativa*. In: *Plant biotechnology journal* 15 (6) :729–

739. DOI: 10.1111/pbi.12671.

- Mumm RH (2013) A Look at Product Development with Genetically Modified Crops: Examples from Maize. *J Agric Food Chem* 61:8254–8259 [doi.org/10.1021/jf400685y].
- Nekrasov V, Wang CM, Win J, et al., (2017) Rapid generation of a transgene-free powdery mildew resistant tomato by genome deletion. *Sci Rep* 7:482. [doi.org/10.1038/s41598-017-00578-x].
- Nieves-Cordones, M, Mohamed, S, Tanoi, K, Kobayashi, NI, Takagi, K, Vernet, A et al., (2017): Production of low-Cs⁺ rice plants by inactivation of the K⁺ transporter OsHAK1 with the CRISPR-Cas system. *Plant J* 92:43–56. [DOI: 10.1111/tpj.13632].
- Niggli U (2016) Die neue Gentechnik hat großes Potenzial (<https://taz.de/Oekoforscher-ueber-neue-Gentech-Methode/!5290509&SuchRahmen=Print/>)
- Njuguna, E, Coussens, G, Neyt, P, Aesaert, S, Storme, V, Demuyndck, K et al., (2019): Functional analysis of Arabidopsis and maize transgenic lines overexpressing the ADP-ribose/NADH pyrophosphohydrolase, AtNUDX7. *Intl J Dev Biol* 63:45–55. [DOI: 10.1387/ijdb.180360mv].
- Nogué F, Vergne P, Chèvre AM, Chauvin JE, Bouchabké-Coussa O, Déjardin A Chevreau E, Hibrand-Saint Oyant L, Mazier M, Barret P, Guiderdoni E, Sallaud C, Foucrier S, Devaux P, Rogowsky PM. (2019): Crop plants with improved culture and quality traits for food, feed and other uses. *Transgenic Res* 28:65–73. [DOI: 10.1007/s11248-019-00135-4].
- Oliva R, Ji C, Atienza-Grande G, et al., (2019) Broad-spectrum resistance to bacterial blight in rice using genome editing. *Nat Biotechnol* 37:1344–1350. [doi.org/10.1038/s41587-019-0267-z].
- Olsen KM, Wendel JF (2013). A bountiful harvest: genomic insights into crop domestication phenotypes. *Annu. Rev. Plant Biol.* 64:47–70. [doi: 10.1146/annurev-arplant-050312-120048]
- Ortigosa, A, Gimenez-Ibanez, S, Leonhardt, N, Solano, R (2019): Design of a bacterial speck resistant tomato by CRISPR/Cas9-mediated editing of SJJAZ2. *Plant Biotech J* 17:665–673. [DOI: 10.1111/pbi.13006].
- Ossowski, S, Schneeberger K, Lucas-Lledó JI, Warthmann N, Clark RM, Shaw RG, Weigel D, Lynch M (2010) The rate and molecular spectrum of spontaneous mutations in Arabidopsis thaliana. *Science* 327, 92–94. [doi: 10.1126/science.1180677].
- Park J, Yoo CG, Flanagan A, et al., (2017) Defined tetra-allelic gene disruption of the 4-coumarate:coenzyme A ligase 1 (Pv4CL1) gene by CRISPR/Cas9 in switchgrass results in lignin reduction and improved sugar release. *Biotechnol Biofuels* 10:284. [doi.org/10.1186/s13068-017-0972-0].
- Pérez, L, Soto, E, Farré, G, Juanos, J, Villorbina, G, Bassie, L et al., (2019): CRISPR/Cas9 mutations in the rice Waxy/GBSSI gene induce allele-specific and zygosity-dependent feedback effects on endosperm starch biosynthesis. *Plant Cell Rep* 38:417–433. [DOI: 10.1007/s00299-019-02388-z].
- Pont C, Wagner S, Kremer A, Orlando L, Plomion C, Salse J (2019) Paleogenomics: reconstruction of plant evolutionary trajectories from modern and ancient DNA. *Genome Biol* 20:29. [doi: 10.1186/s13059-019-1627-1].
- Puchta, H (2005): The repair of double-strand breaks in plants: mechanisms and consequences for genome evolution. *J Exp Bot* 56:1–14. [DOI: 10.1093/jxb/eri025].
- Puchta H (2017) Applying CRISPR/Cas for genome engineering in plants: the best is yet to come. *Curr Opin Plant Biol.* 36:1-8. [doi: 10.1016/j.pbi.2016.11.011.]
- Quispe-Huamanquispe, DG, Gheysen, G, Yang, J, Jarret R, Rossel G, Kreuze JF (2019) The horizontal gene transfer of *Agrobacterium* T-DNAs into the series *Batatas* (Genus *Ipomoea*) genome is not confined to hexaploid sweetpotato. *Sci Rep* 9, 12584 (2019). [doi.org/10.1038/s41598-019-48691-3].
- Ricroch A, Clairand P, Harwood W (2017) Use of CRISPR systems in plant genome editing: toward new opportunities in agriculture. *Emerg Top Life Sci* 1:169–182. [doi.org/10.1042/ETLS20170085].
- Ricroch A (2020) Organic vs. GMOs: six recurring a priori of an ideological debate. *European Scientist* (<https://www.europeanscientist.com/en/environment/organic-vs-gmos-six-recurring-a-priori-of-an-ideological-debate/>)
- Rogowsky P (2017) Use of CRISPR-Cas9 in plant science. *Potato Res* 60:353–360. [doi.org/10.1007/s11540-018-9387]

- Salomon, S, Puchta, H (1998): Capture of genomic and T-DNA sequences during double-strand break repair in somatic plant cells. *EMBO J* 17:6086–6095. [DOI: 10.1093/emboj/17.20.6086].
- SAM Scientific Advisory Mechanism (2017) New techniques in agricultural biotechnology (https://ec.europa.eu/research/sam/pdf/topics/explanatory_note_new_techniques_agricultural_biotechnology.pdf)
- Sashidhar N, Harloff HJ, Potgieter L, Jung C (2020) Gene editing of three *BnITPK* genes in tetraploid oilseed rape leads to significant reduction of phytic acid in seeds. *Plant Biotechnol J*. [doi.org/10.1111/pbi.13380].
- Sánchez-León S, Gil-Humanes J, Ozuna C V, et al., (2018) Low-gluten, nontransgenic wheat engineered with CRISPR/Cas9. *Plant Biotechnol J* 16:902–910. [doi.org/10.1111/pbi.12837].
- SBA Swedish Board of Agriculture (2018) Consequences of the EC-ruling according to Swedish companies and research groups. (https://www.upsc.se/documents/News/News_2019/Attachment_1.pdf).
- Schiemann J, Dietz-Pfeilstetter A, Hartung F, Kohl C, Romeis J, Sprink T (2019) Risk Assessment and Regulation of Plants Modified by Modern Biotechniques: Current Status and Future Challenges. *Annu Rev Plant Biol* 70:699-726 [doi.org/10.1146/annurev-arplant-050718-100025].
- Sedeek, KEM, Mahas, A, Mahfouz, M (2019): Plant Genome Engineering for Targeted Improvement of Crop Traits. *Frontiers Plant Sci* 10:114. [DOI: 10.3389/fpls.2019.00114].
- Shan S, Soltis PS, Soltis DE, Yang B (2020) Considerations in adapting CRISPR/Cas9 in nongenetic model plant systems. *Applications in Plant Sciences* 8(1): e11314. [doi:10.1002/aps3.11314].
- Sherkow J (2015) Law, history and lessons in the CRISPR patent conflict. *Nat Biotechnol* 33:256–257. [doi.org/10.1038/nbt.3160].
- Soyk, S, Müller, NA, Park, SJ, Schmalenbach, I, Jiang, K, Hayama, R, Zhang L, Van Eck J, Jiménez-Gómez JM, Lippman ZB. (2017): Variation in the flowering gene SELF PRUNING 5G promotes day-neutrality and early yield in tomato. *Nat Genet* 49:162–168. [DOI: 10.1038/ng.3733].
- Steinberg P, van der Voet H, Goedhart PW, Kleter G, Kok EJ, Pla M, Nadal A, Zeljenková D, Aláčková R, Babincová J, Rollerová E, Jaďudová S, Kebis A, Szabova E, Tulinská J, Líšková A, Takácsová M, Mikušová ML, Krivošíková Z, Spök A, Racovita M, de Vriend H, Alison R, Alison C, Baumgärtner W, Becker K, Lempp C, Schmicke M, Schrenk D, Pötting A, Schiemann J, Wilhelm R (2019) Lack of adverse effects in subchronic and chronic toxicity/carcinogenicity studies on the glyphosate-resistant genetically modified maize NK603 in Wistar Han RCC rats. *Arch Toxicol*. 93:1095-1139. [doi: 10.1007/s00204-019-02400-1].
- Sun YW, Jiao GA, Liu ZP, et al., (2017) Generation of high-amylose rice through CRISPR/Cas9-mediated targeted mutagenesis of starch branching enzymes. *Front Plant Sci* 8:298. [doi.org/10.3389/fpls.2017.00298].
- Swierstra T (2017) Introduction to the Ethics of New and Emerging Science and Technology. In book: *Handbook of Digital Games and Entertainment Technologies* [DOI: 10.1007/978-981-4560-50-4_33]
- Tang L, Mao B, Li Y, Lv Q, Zhang L, Chen C, He H, Wang W, Zeng X, Shao Y, Pan Y, Hu Y, Peng Y, Fu X, Li H, Xia S, Zhao B (2017) Knockout of *OsNramp5* using the CRISPR/Cas9 system produces low Cd-accumulating indica rice without compromising yield. *Sci Rep* 7:14438. [doi.org/10.1038/s41598-017-14832-9.]
- Tang X, Liu G, Zhou J, Ren Q, You Q, Tian L, Xin X, Zhong Z, Liu B, Zheng X, Zhang D, Malzahn A, Gong Z, Qi Y, Zhang T, Zhang Y (2018) A large-scale whole-genome sequencing analysis reveals highly specific genome editing by both Cas9 and Cpf1 (Cas12a) nucleases in rice. *Genome Biol* 19:84. [doi: 10.1186/s13059-018-1458-5].
- Veillet, F., Chauvin, L., Kermarrec, M.-P., Sevestre, F., Merrer, M., Terret, Z., Szydlowski, N., Devaux, P., Gallois, J.-L., and Chauvin, J.-E. (2019). The *Solanum tuberosum* GBSSI gene: a target for assessing gene and base editing in tetraploid potato. *Plant Cell Rep*. 38, 1065–1080. [doi: 10.1007/s00299-019-02426-w.]
- Veillet, F., Perrot, L., Guyon-Debast, A., Kermarrec, M.-P., Chauvin, L., Chauvin, J.-E., Gallois, J.-L., Mazier, M., and Nogué, F. (2020). Expanding the CRISPR Toolbox in *P. patens* Using SpCas9-NG Variant and Application for Gene and Base Editing in Solanaceae Crops. *Int. J. Mol. Sci*. 21. [doi: 10.3390/ijms21031024].

- Wang Y, Cheng X, Shan Q, et al., (2014) Simultaneous editing of three homoeoalleles in hexaploid bread wheat confers heritable resistance to powdery mildew. *Nat Biotechnol* 32:947–951. [doi.org/10.1038/nbt.2969]
- Wang, F, Wang, C, Liu, P, Lei, C, Hao, W, Gao, Y et al., (2016): Enhanced Rice Blast Resistance by CRISPR/Cas9-Targeted Mutagenesis of the ERF Transcription Factor Gene OsERF922. *PLoS One* 11, e0154027. [DOI: 10.1371/journal.pone.0154027].
- Wang, W, Simmonds, J, Pan, Q, Davidson, D, He, F, Battal, A et al., (2018): Gene editing and mutagenesis reveal inter-cultivar differences and additivity in the contribution of TaGW2 homoeologues to grain size and weight in wheat. *Theor Appl Genet* 131:2463–2475. [DOI: 10.1007/s00122-018-3166-7].
- Wang X, Tang T, Miao Q, Xie S, Chen X, Tang J, Peng C, Xu X, Wei W, You X, Xu J (2019a) Detection of transgenic rice line TT51-1 in processed foods using conventional PCR, real-time PCR, and droplet digital PCR *Food Control* 98:380-388. [doi.org/10.1016/j.foodcont.2018.11.032]
- Wang R, Tavano EC da R, Lammers M, et al., (2019b) Re-evaluation of transcription factor function in tomato fruit development and ripening with CRISPR/Cas9-mutagenesis. *Sci Rep* 9:1696. [doi.org/10.1038/s41598-018-38170-6].
- Wang H, Sun S, Ge W, Zhao L, Hou B, Wang K, Lyu Z, Chen L, Xu S, Guo J, Li M, Su P, Li X, Wang G, Bo C, Fang X, Zhuang W, Cheng X, Wu J, Dong L, Chen W, Li W, Xiao G, Zhao J, Hao Y, Xu Y, Gao Y, Liu W, Liu Y, Yin H, Li J, Li X, Zhao Y, Wang X, Ni F, Ma X, Li A, Xu SS, Bai G, Nevo E, Gao C, Ohm H, Kong L (2020) Horizontal gene transfer of Fhb7 from fungus underlies Fusarium head blight resistance in wheat. *Science* pii: eaba5435[Epub ahead of print]. [doi: 10.1126/science.aba5435].
- Weale A (2010) Ethical arguments relevant to the use of GM crops. *New Biotechnol* 27:582-587. [doi:10.1016/j.nbt.2010.08.013]
- Whelan AI, Gutti P and Lema MA (2020) Gene Editing Regulation and Innovation Economics. *Front Bioeng Biotechnol* 8:303. [doi: 10.3389/fbioe.2020.00303].
- Wiegand, A, Prüfer, D, Schulze Gronover, C (2019): Loss of function mutation of the Rapid Alkalinization Factor (RALF1)-like peptide in the dandelion *Taraxacum koksaghyz* entails a high-biomass taproot phenotype. *PLoS One* 14, e0217454. [DOI: 10.1371/journal.pone.0217454].
- Xu, Z, Xu, X, Gong, Q, Li, Z, Li, Y, Wang, S et al., (2019): Engineering Broad-Spectrum Bacterial Blight Resistance by Simultaneously Disrupting Variable TALE-Binding Elements of Multiple Susceptibility Genes in Rice. *Mol Plant* 12:1434–1446. [DOI: 10.1016/j.molp.2019.08.006].
- Xu W, Yang Y, Liu Y, Kang G, Wang F, Li L, Lv X, Zhao S, Yuan S, Song J, Wu Y, Feng F, He X, Zhang C, Song W, Zhao J, Yang J (2020) Discriminated sgRNAs-Based SurroGate System Greatly Enhances the Screening Efficiency of Plant Base-Edited Cells. *Mol Plant* 13:169-180. [doi.org/10.1016/j.molp.2019.10.007].
- Yin K, Gao, C, Qiu J (2017) Progress and prospects in plant genome editing. *Nature Plants* 3:17107. [doi.org/10.1038/nplants.2017.107]
- Zhan, X, Zhang, F, Zhong, Z, Chen, R, Wang, Y, Chang, L et al., (2019): Generation of virus-resistant potato plants by RNA genome targeting. *Plant Biotechnol J* 17:1814–1822. [DOI: 10.1111/pbi.13102].
- Zhang, M, Liu, Q, Yang, X, Xu, J, Liu, G, Yao, X et al., (2020): CRISPR/Cas9-mediated mutagenesis of Clpsk1 in watermelon to confer resistance to *Fusarium oxysporum* f.sp. *niveum*. *Plant Cell Rep* 39:589–595. [DOI: 10.1007/s00299-020-02516-0].
- Zhou XH, Jacobs TB, Xue LJ, et al., (2015) Exploiting SNPs for biallelic CRISPR mutations in the outcrossing woody perennial *Populus* reveals 4-coumarate: CoA ligase specificity and redundancy. *New Phytol* 208:298–301. [doi.org/10.1111/nph.13470].
- Zsögön A, Čermák T, Naves ER, et al., (2018) De novo domestication of wild tomato using genome editing. *Nat Biotechnol* 36:1211–1216. [doi.org/10.1038/nbt.4272].