**Information and supporting documentation**

relevant to (i) the trends in new technological developments in synthetic biology referred to in paragraph 6 of decision 15/31, which correspond to the trends identified in the report of the 2019 Ad Hoc Technical Expert Group on Synthetic Biology (Report of the Ad Hoc Technical Expert Group on Synthetic Biology (https://www.cbd.int/doc/c/2074/26e7/a135b1b57dabe8e8ed669324/synbio-ahteg-2019-01-03-en.pdf, Section I, paragraph 5); (ii) any additional trend that should be considered.

1. New CRISPR-Cas system with on-off switch cuts proteins

Researchers from TU Delft in the group of Stan Brouns have discovered a CRISPR-Cas system that cuts proteins instead of DNA. The discovery opens the door to the development of a range of biotechnological and medical applications, for example, for sensing RNA molecules in pathogens.

Craspase is a CRISPR RNA-guided, RNA-activated protease / CHUNYI HU [et al.] // SCIENCE. - 25 Aug 2022. - Vol 377, Issue 6612. - pp. 1278-1285. - DOI: 10.1126/science.add50. - https://www.science.org/doi/10.1126/science.add5064

2. Synthetic genetic circuits as a means of reprogramming plant roots / [et al.] . - 2022. - Vol 377, Issue 6607. - pp. 747-751. - DOI: 10.1126/science.abo4326. - https://www.science.org/doi/10.1126/science.abo4326.

3. Biocircuits in plants and eukaryotic algae / Mayna da Silveira Gomide [et al.] //Front. Plant Sci. – 2022. - Sec. Technical Advances in Plant Science. - Volume 13. - https://doi.org/10.3389/fpls.2022.982959. - https://www.frontiersin.org/articles/10.3389/fpls.2022.982959/full.

4. Lloyd, J.P.B., Ly, F., Gong, P. et al. Synthetic memory circuits for stable cell reprogramming in plants. Nat Biotechnol 40, 1862–1872 (2022). https://doi.org/10.1038/s41587-022-01383-2

Synthetic gene circuits have the potential to integrate multiple customizable input signals through a processing unit constructed from biological parts to produce a predictable and programmable output. In the article a suite of functional recombinase-based gene circuits for use in plants is presented.

5. Williams, R.L., Murray, R.M. Integrase-mediated differentiation circuits improve evolutionary stability of burdensome and toxic functions in E. coli. Nat Commun 13, 6822 (2022). https://doi.org/10.1038/s41467-022-34361-y

6. Joshi, S.HN., Yong, C. & Gyorgy, A. Inducible plasmid copy number control for synthetic biology in commonly used E. coli strains. Nat Commun 13, 6691 (2022). https://doi.org/10.1038/s41467-022-34390-7

7. Pandi, A., Diehl, C., Yazdizadeh Kharrazi, A. et al. A versatile active learning workflow for optimization of genetic and metabolic networks. Nat Commun 13, 3876 (2022). https://doi.org/10.1038/s41467-022-31245-z

8. Broto, A., Gaspari, E., Miravet-Verde, S. et al. A genetic toolkit and gene switches to limit Mycoplasma growth for biosafety applications. Nat Commun 13, 1910 (2022). https://doi.org/10.1038/s41467-022-29574-0

9. Sebesta J, Xiong W, Guarnieri MT and Yu J (2022) Biocontainment of Genetically Engineered Algae. Front. Plant Sci. 13:839446. doi: 10.3389/fpls.2022.839446. - https://www.frontiersin.org/articles/10.3389/fpls.2022.839446/full

At industrial scale, genetically engineered algae may be cultivated outdoors in open ponds or in closed photobioreactors. In either case, industry would need to address a potential risk of the release of the engineered algae into the natural environment, resulting in potential negative impacts to the environment.

Feld trial of GE-algae. https://today.ucsd.edu/story/first_epa_approved_outdoor_field_trial_for_genetically_engineered_algae

10. Grama, S.B.; Liu, Z.; Li, J. Emerging Trends in Genetic Engineering of Microalgae for Commercial Applications. *Mar. Drugs* 2022, *20*, 285. https://doi.org/10.3390/md20050285. - https://www.mdpi.com/1660-3397/20/5/285.

11. Matsuo M, Toyota T, Suzuki K, Sugawara T. Evolution of Proliferative Model Protocells Highly Responsive to the Environment. Life. 2022; 12(10):1635. https://doi.org/10.3390/life12101635. - https://www.mdpi.com/2075-1729/12/10/1635.

12. Oberhofer G, Ivy T, Hay BA. Gene drive that results in addiction to a temperature-sensitive version of an essential gene triggers a population collapse in Drosophila, Proc Natl Acad Sci 2021 118 (49) e2107413118. https://www.pnas.org/content/118/49/e2107413118

In the article it was demonstrated the replacement of a fly population with a temperature-dependent Cleave and Rescue (ClvR) drive element, followed by suppression of the population as the temperature is changed.

13. A network approach to genetic circuit designs / Matthew Crowther, Anil Wipat, Ángel Goñi-Moreno // bioRxiv. -

2021.09.14.460206; doi: https://doi.org/10.1101/2021.09.14.460206. - https://www.biorxiv.org/content/10.1101/2021.09.14.460206v2.full

14. Japan's Genome-Edited fish and tomato approved on the market. – ISAAA website. - saaa.org/blog/entry/default.asp?BlogDate=1/19/2022#:~:text=Puffers%20of%20the%20genus%20Fugu,using%20CRISPR%20gene%20editing%20technology

15. Nwokeoji, A.O., Nwokeoji, E.A., Chou, T. *et al.* A novel sustainable platform for scaled manufacturing of double-stranded RNA biopesticides. *Bioresour. Bioprocess.* 9, 107 (2022). https://doi.org/10.1186/s40643-022-00596-2

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