表2. NBT応用植物に関する文献調査結果(TALEN) （その3）

| Year | Applied plant species |
|---|---|
| ID | Affiliation, country |
| Identifiers | Title |
| Category | Description |
| | Details |
| 2012<br>17<br><br>PMID:23078195<br><br>TALEN | rice<br>Colorado State University, CO, USA<br>Transcription activator-like (TAL) effectors targeting OsSWEET genes enhance virulence on diverse rice (Oryza sativa) varieties when expressed individually in a TAL effector-deficient strain of Xanthomonas oryzae.<br>Verdier V, Triplett LR, Hummel AW, Corral R, Cernadas RA, Schmidt CL, Bogdanove AJ, Leach JE.<br>New Phytol. 2012 Dec;196(4):1197-207. doi: 10.1111/j.1469-8137.2012.04367.x. Epub 2012 Oct 18. |
| 2012<br>18<br>PMID:22565958<br>TALEN | rice<br>Iowa State University, IA, USA<br>High-efficiency TALEN-based gene editing produces disease-resistant rice.<br>Li T, Liu B, Spalding MH, Weeks DP, Yang B.<br>Nat Biotechnol. 2012 May 7;30(5):390-2. doi: 10.1038/nbt.2199. No abstract available. |
| 2012<br>19<br>PMID:22271303<br>TALEN | tobacco<br>King Abdullah University of Science and Technology, Thuwal, Saudi Arabia<br>Rapid and highly efficient construction of TALE-based transcriptional regulators and nucleases for genome modification.<br>Li L, Piatek MJ, Atef A, Piatek A, Wibowo A, Fang X, Sabir JS, Zhu JK, Mahfouz MM.<br>Plant Mol Biol. 2012 Mar;78(4-5):407-16. doi: 10.1007/s11103-012-9875-4. Epub 2012 Jan |
| 2011<br>20<br>PMID:21493687<br><br>TALEN | Arabidopsis<br>University of Minnesota, MN, USA<br>Efficient design and assembly of custom TALEN and other TAL effector-based constructs for DNA targeting.<br>Cermak T, Doyle EL, Christian M, Wang L, Zhang Y, Schmidt C, Baller JA, Somia NV, Bogdanove AJ, Voytas DF.<br>Nucleic Acids Res. 2011 Jul;39(12):e82. doi: 10.1093/nar/gkr218. Epub 2011 Apr 14.<br>Erratum in: Nucleic Acids Res. 2011 Sep 1;39(17):7879. |
| 2011<br>21<br>PMID:21262818<br><br>TALEN | tobacco<br>King Abdullah University of Science and Technology, Thuwal, Saudi Arabia<br>De novo-engineered transcription activator-like effector (TALE) hybrid nuclease with novel DNA binding specificity creates double-strand breaks.<br>Mahfouz MM, Li L, Shamimuzzaman M, Wibowo A, Fang X, Zhu JK.<br>Proc Natl Acad Sci U S A. 2011 Feb 8;108(6):2623-8. doi: 10.1073/pnas.1019533108. Epub 2011 Jan 24. |

表3. NBT応用植物に関する文献調査結果(CRISPR) （その1）

query: CRISPR, cas9, plant, arabidopsis, nicotiana

| Year | Applied plant species |
|---|---|
| ID | Affiliation, country |
| Identifiers | Title |
| Category | Description |
| | Details |
| 2015<br>1<br>PMID:25578968<br>CRISPR | Arabidopsis<br>National Institute of Biological Sciences, Beijing, China<br>Two novel NAC transcription factors regulate gene expression and flowering time by associating with the histone demethylase JMJ14.<br>Ning YQ, Ma ZY, Huang HW, Mo H, Zhao TT, Li L, Cai T, Chen S, Ma L, He XJ.<br>Nucleic Acids Res. 2015 Jan 10. doi:pii: gku1382. [Epub ahead of print] |
| 2015<br>2<br>PMID:25403732<br>CRISPR/TALEN | Nicotiana benthamiana, Arabidopsis<br>Weizmann Institute of Science, Rehovot, Israel<br>Comparative assessments of CRISPR-Cas nucleases' cleavage efficiency in planta.<br>Johnson RA, Gurevich V, Filler S, Samach A, Lewy AA.<br>Plant Mol Biol. 2015 Jan;87(1-2):143-56. doi: 10.1007/s11103-014-0266-x. Epub 2014 Nov 18. |
| 2015<br>3<br>PMID:25344637<br>CRISPR | tobacco<br>Southwest University, Chongqing, China<br>CRISPR/Cas9-mediated targeted mutagenesis in Nicotiana tabacum.<br>Gao J, Wang G, Ma S, Xie X, Wu X, Zhang X, Wu Y, Zhao P, Xia Q.<br>Plant Mol Biol. 2015 Jan;87(1-2):99-110. doi: 10.1007/s11103-014-0263-0. Epub 2014 Oct 26. |
| 2015<br>4<br>PMID:25269397<br>CRISPR | Arabidopsis<br>Max Planck Institute for Plant Breeding Research, Cologne, Germany<br>Site-directed mutagenesis in Arabidopsis thaliana using dividing tissue-targeted RGEN of the CRISPR/Cas system to generate heritable null alleles.<br>Hyun Y, Kim J, Cho SW, Choi Y, Kim JS, Coupland G.<br>Planta. 2015 Jan;241(1):271-84. doi: 10.1007/s00425-014-2180-5. Epub 2014 Oct 1. |
| 2014<br>5<br>PMID:25432517<br>CRISPR | corn, Arabidopsis<br>China Agricultural University, Beijing, China<br>A CRISPR/Cas9 toolkit for multiplex genome editing in plants.<br>Xing HL, Dong L, Wang ZP, Zhang HY, Han CY, Liu B, Wang XC, Chen QJ.<br>BMC Plant Biol. 2014 Nov 29;14(1):327. [Epub ahead of print] |
| 2014<br>6<br>PMID:25398353<br>CRISPR | Arabidopsis, tobacco<br>Harvard Medical School, Boston, Massachusetts, USA<br>Cas9-based genome editing in Arabidopsis and tobacco.<br>Li JF, Zhang D, Sheen J.<br>Methods Enzymol. 2014;546:459-72. doi: 10.1016/B978-0-12-801185-0.00022-2. |
| 2014<br>7<br>PMID:25392068<br>CRISPR | rice<br>NIAS, Tsukuba, Japan<br>Multigene Knockout Utilizing Off-Target Mutations of the CRISPR/Cas9 System in Rice.<br>Endo M, Mikami M, Toki S.<br>Plant Cell Physiol. 2014 Nov 11. doi:pii: pcu154. [Epub ahead of print] |
| 2014<br>8<br>PMID:25327456<br>CRISPR | Arabidopsis<br>Karlsruhe Institute of Technology, Karlsruhe, Germany<br>The CRISPR/Cas system can be used as nuclease for in planta gene targeting and as paired nickases for directed mutagenesis in Arabidopsis resulting in heritable progeny.<br>Schiml S, Fauser F, Puchta H.<br>Plant J. 2014 Dec;80(6):1139-50. doi: 10.1111/tpj.12704. Epub 2014 Nov 11. |

2015: data of 2015/1/1～2/24

表3. NBT応用植物に関する文献調査結果(CRISPR) （その2）

| Year | Applied plant species |
|---|---|
| ID | Affiliation, country |
| Identifiers | Title |
| Category | Description |
| | Details |
| 2014<br>9<br>PMID:25232936<br>CRISPR | rice, wheat<br>Chinese Academy of Sciences, Beijing, China<br>Genome editing in rice and wheat using the CRISPR/Cas system.<br>Shan Q, Wang Y, Li J, Gao C.<br>Nat Protoc. 2014 Oct;9(10):2395-410. doi: 10.1038/nprot.2014.157. Epub 2014 Sep 18. |
| 2014<br>10<br>PMID:25225186<br>CRISPR | tomato<br>Boyce Thompson Institute for Plant Science, NY, USA<br>Efficient gene editing in tomato in the first generation using the clustered regularly interspaced short palindromic repeats/CRISPR-associated9 system.<br>Brooks C, Nekrasov V, Lippman ZB, Van Eck J.<br>Plant Physiol. 2014 Nov;166(3):1292-7. doi: 10.1104/pp.114.247577. Epub 2014 Sep 15. No abstract available. |
| 2014<br>11<br>PMID:25200087<br>CRISPR | rice<br>Iowa State University, Ames, IA, USA<br>Large chromosomal deletions and heritable small genetic changes induced by CRISPR/Cas9 in rice.<br>Zhou H, Liu B, Weeks DP, Spalding MH, Yang B.<br>Nucleic Acids Res. 2014;42(17):10903-14. doi: 10.1093/nar/gku806. Epub 2014 Sep 8. |
| 2014<br>12<br>PMID:25146436<br>CRISPR | grapefruit<br>University of Florida, FI, USA<br>Xcc-facilitated agroinfiltration of citrus leaves: a tool for rapid functional analysis of transgenes in citrus leaves.<br>Jia H, Wang N.<br>Plant Cell Rep. 2014 Dec;33(12):1993-2001. doi: 10.1007/s00299-014-1673-9. Epub 2014 Aug 22. |
| 2014<br>13<br>PMID:25038773<br>CRISPR/TALEN | bread wheat<br>Chinese Academy of Sciences, Beijing, China<br>Simultaneous editing of three homoeoalleles in hexaploid bread wheat confers heritable resistance to powdery mildew.<br>Wang Y, Cheng X, Shan Q, Zhang Y, Liu J, Gao C, Qiu JL.<br>Nat Biotechnol. 2014 Sep;32(9):947-51. doi: 10.1038/nbt.2969. Epub 2014 Jul 20. |
| 2014<br>14<br>PMID:24920971<br>CRISPR | rice<br>Anhui University, Hefei, China<br>Gene targeting using the Agrobacterium tumefaciens-mediated CRISPR-Cas system in rice.<br>Xu R, Li H, Qin R, Wang L, Li L, Wei P, Yang J.<br>Rice (N Y). 2014;7(1):5. doi: 10.1186/s12284-014-0005-6. |
| 2014<br>15<br>PMID:24918588<br>CRISPR | Arabidopsis<br>University of Nebraska, Nebraska, USA<br>Efficient CRISPR/Cas9-mediated gene editing in Arabidopsis thaliana and inheritance of modified genes in the T2 and T3 generations.<br>Jiang W, Yang B, Weeks DP.<br>PLoS One. 2014;9(6):e99225. doi: 10.1371/journal.pone.0099225. |
| 2014<br>16<br>PMID:24868032<br>CRISPR | tomato, Arabidopsis<br>University of California, Davis, California, USA<br>Hairy root transformation using Agrobacterium rhizogenes as a tool for exploring cell type-specific gene expression and function using tomato as a model.<br>Ron M, Kajala K, Pauluzzi G, Wang D, Reynoso MA, Zumstein K, Garcha J, Winte S, Masson H, Inagaki S, Federici F, Sinha N, Deal RB, Bailey-Serres J, Brady SM.<br>Plant Physiol. 2014 Oct;166(2):455-69. doi: 10.1104/pp.114.239392. Epub 2014 May 27. |

表3. NBT応用植物に関する文献調査結果(CRISPR) （その3）

| Year | Applied plant species |
|---|---|
| ID | Affiliation, country |
| Identifiers | Title |
| Category | Description |
| | Details |
| 2014<br>17<br>PMID:24854982<br>CRISPR | rice<br>Chinese Academy of Sciences, Shanghai, China<br>The CRISPR/Cas9 system produces specific and homozygous targeted gene editing in rice in one generation.<br>Zhang H, Zhang J, Wei P, Zhang B, Gou F, Feng Z, Mao Y, Yang L, Zhang H, Xu N, Zhu JK.<br>Plant Biotechnol J. 2014 Aug;12(6):797-807. doi: 10.1111/pbi.12200. Epub 2014 May 23. |
| 2014<br>18<br>PMID:24836556<br>CRISPR | Arabidopsis<br>Karlsruhe Institute of Technology, Karlsruhe, Germany<br>Both CRISPR/Cas-based nucleases and nickases can be used efficiently for genome engineering in *Arabidopsis thaliana*.<br>Fauser F, Schiml S, Puchta H.<br>Plant J. 2014 Jul;79(2):348-59. doi: 10.1111/tpj.12554. Epub 2014 Jun 17. |
| 2014<br>19<br>PMID:24710347<br>CRISPR | sweet orange<br>University of Florida, Fl, USA<br>Targeted genome editing of sweet orange using Cas9/sgRNA.<br>Jia H, Wang N.<br>PLoS One. 2014;9(4):e93806. doi: 10.1371/journal.pone.0093806. |
| 2014<br>20<br>PMID:24576457<br>CRISPR/TALEN | corn<br>Chinese Academy of Sciences, Beijing, China<br>Targeted mutagenesis in Zea mays using TALENs and the CRISPR/Cas system.<br>Liang Z, Zhang K, Chen K, Gao C.<br>J Genet Genomics. 2014 Feb 20;41(2):63-8. doi: 10.1016/j.jgg.2013.12.001. Epub 2013 Dec 14. |
| 2014<br>21<br>PMID:24550464<br>CRISPR | Arabidopsis<br>Chinese Academy of Sciences, Shanghai, China<br>Multigeneration analysis reveals the inheritance, specificity, and patterns of CRISPR/Cas-induced gene modifications in Arabidopsis.<br>Feng Z, Mao Y, Xu N, Zhang B, Wei P, Yang DL, Wang Z, Zhang Z, Zheng R, Yang L, Zeng L, Liu X, Zhu JK.<br>Proc Natl Acad Sci U S A. 2014 Mar 25;111(12):4632-7. doi: 10.1073/pnas.1400822111. Epub 2014 Feb 18. |
| 2014<br>22<br>PMID:24443494<br>CRISPR | liverwort<br>Kyoto University, Kyoto, Japan<br>CRISPR/Cas9-mediated targeted mutagenesis in the liverwort Marchantia polymorpha L.<br>Sugano SS, Shirakawa M, Takagi J, Matsuda Y, Shimada T, Hara-Nishimura I, Kohchi T.<br>Plant Cell Physiol. 2014 Mar;55(3):475-81. doi: 10.1093/pcp/pcu014. Epub 2014 Jan 18. |
| 2013<br>23<br>PMID:24122057<br>CRISPR | wheat<br>National Agri-Food Biotechnology Institute, Government of India, India<br>RNA-guided genome editing for target gene mutations in wheat.<br>Upadhyay SK, Kumar J, Alok A, Tuli R.<br>G3 (Bethesda). 2013 Dec 9;3(12):2233-8. doi: 10.1534/g3.113.008847. |
| 2013<br>24<br>PMID:23999856<br>CRISPR | rice<br>Peking University, Beijing, China<br>Targeted mutagenesis in rice using CRISPR-Cas system.<br>Miao J, Guo D, Zhang J, Huang Q, Qin G, Zhang X, Wan J, Gu H, Qu LJ.<br>Cell Res. 2013 Oct;23(10):1233-6. doi: 10.1038/cr.2013.123. Epub 2013 Sep 3. No abstract available. |

表3. NBT応用植物に関する文献調査結果(CRISPR) （その4）

| Year | Applied plant species |
|---|---|
| ID | Affiliation, country |
| Identifiers | Title |
| Category | Description |
| | Details |
| 2013<br>25<br>PMID:23999092<br>CRISPR | Arabidopsis, tobacco, sorghum , rice<br>Iowa State University, IA, USA<br>Demonstration of CRISPR/Cas9/sgRNA-mediated targeted gene modification in Arabidopsis, tobacco, sorghum and rice.<br>Jiang W, Zhou H, Bi H, Fromm M, Yang B, Weeks DP.<br>Nucleic Acids Res. 2013 Nov;41(20):e188. doi: 10.1093/nar/gkt780. Epub 2013 Sep 2. |
| 2013<br>26<br>PMID:23963532<br>CRISPR | Arabidopsis, rice<br>Chinese Academy of Sciences, Shanghai, China<br>Application of the CRISPR-Cas system for efficient genome engineering in plants.<br>Mao Y, Zhang H, Xu N, Zhang B, Gou F, Zhu JK.<br>Mol Plant. 2013 Nov;6(6):2008-11. doi: 10.1093/mp/sst121. Epub 2013 Aug 22. No abstract available. |
| 2013<br>27<br>PMID:23958582<br>CRISPR | Arabidopsis, rice<br>Chinese Academy of Sciences, Shanghai, China<br>Efficient genome editing in plants using a CRISPR/Cas system.<br>Feng Z, Zhang B, Ding W, Liu X, Yang DL, Wei P, Cao F, Zhu S, Zhang F, Mao Y, Zhu JK.<br>Cell Res. 2013 Oct;23(10):1229-32. doi: 10.1038/cr.2013.114. Epub 2013 Aug 20. No abstract available. |
| 2013<br>28<br>PMID:23956122<br>CRISPR | rice<br>Pennsylvania State University, PA, USA<br>RNA-guided genome editing in plants using a CRISPR-Cas system.<br>Xie K, Yang Y.<br>Mol Plant. 2013 Nov;6(6):1975-83. doi: 10.1093/mp/sst119. Epub 2013 Aug 17. |
| 2013<br>29<br>PMID:23929340<br>CRISPR | Nicotiana benthamiana<br>The Sainsbury Laboratory, Norwich, UK<br>Targeted mutagenesis in the model plant Nicotiana benthamiana using Cas9 RNA-guided endonuclease.<br>Nekrasov V, Staskawicz B, Weigel D, Jones JD, Kamoun S.<br>Nat Biotechnol. 2013 Aug;31(8):691-3. doi: 10.1038/nbt.2655. No abstract available. |
| 2013<br>30<br>PMID:23929339<br>CRISPR | Arabidopsis, Nicotiana benthamiana<br>Massachusetts General Hospital, Massachusetts, USA<br>Multiplex and homologous recombination-mediated genome editing in Arabidopsis and Nicotiana benthamiana using guide RNA and Cas9.<br>Li JF, Norville JE, Aach J, McCormack M, Zhang D, Bush J, Church GM, Sheen J.<br>Nat Biotechnol. 2013 Aug;31(8):688-91. doi: 10.1038/nbt.2654. No abstract available. |
| 2013<br>31<br>PMID:23929338<br>CRISPR | rice<br>Chinese Academy of Sciences, Beijing, China<br>Targeted genome modification of crop plants using a CRISPR-Cas system.<br>Shan Q, Wang Y, Li J, Zhang Y, Chen K, Liang Z, Zhang K, Liu J, Xi JJ, Qiu JL, Gao C.<br>Nat Biotechnol. 2013 Aug;31(8):686-8. doi: 10.1038/nbt.2650. No abstract available. |

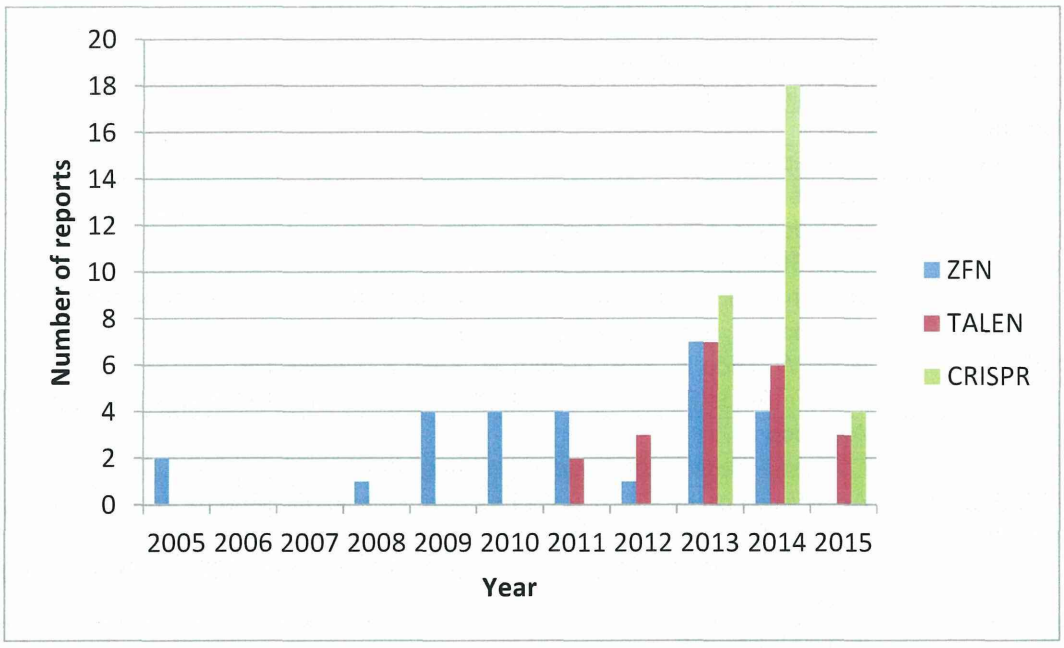


図1. NBT(ZFN, TALEN, CRISPR)の植物関連論文数の推移（植物に対する実施報告数）

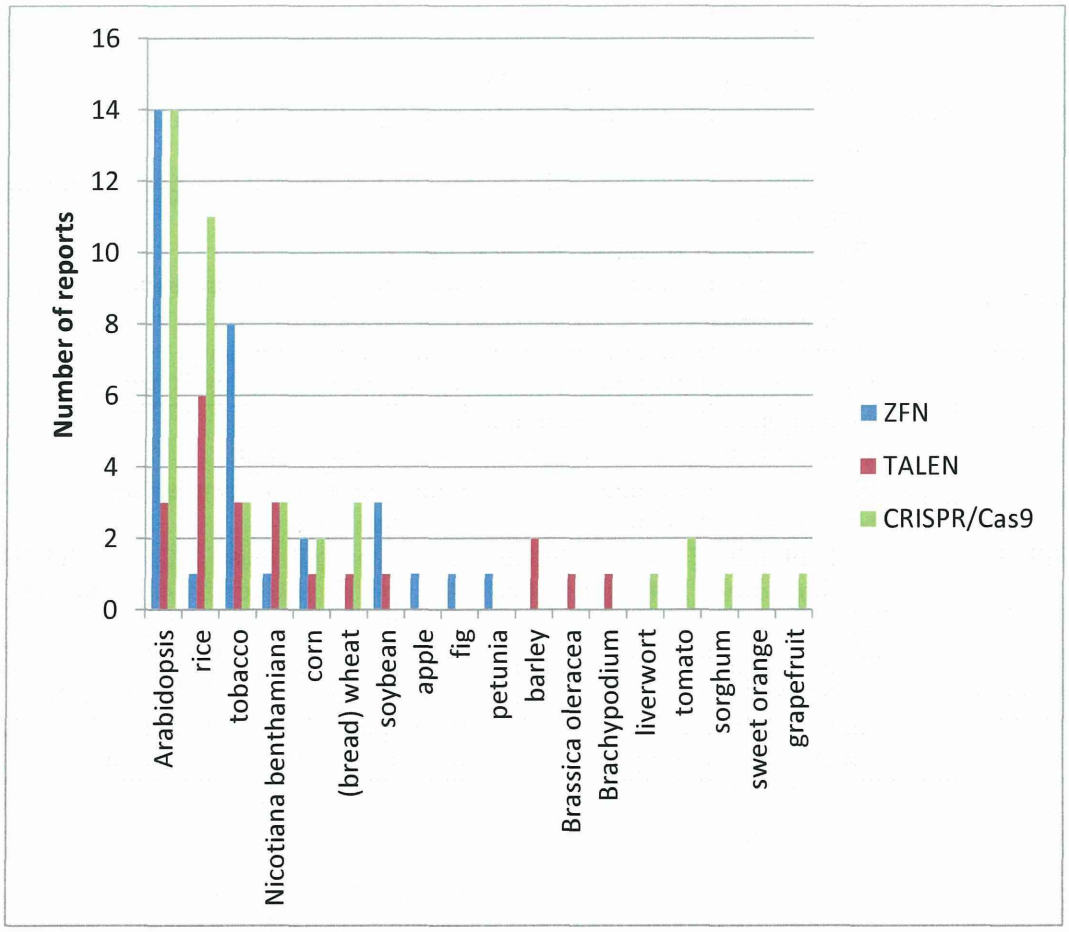


図2. NBT(ZFN, TALEN, CRISPR)の対象植物別報告数

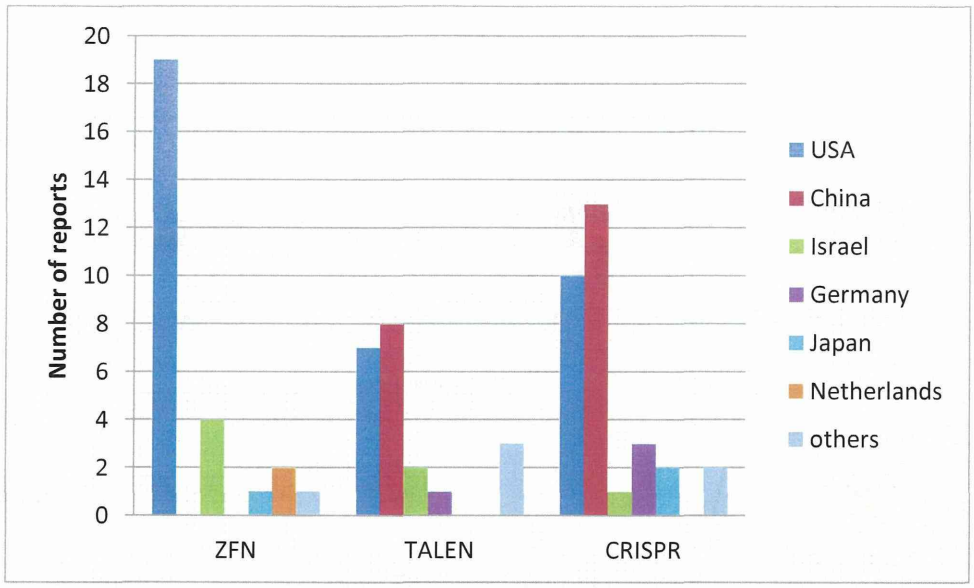


図3. 植物に対し実施されたNBT(ZFN, TALEN, CRISPR)の技術カテゴリー及び国別報告数

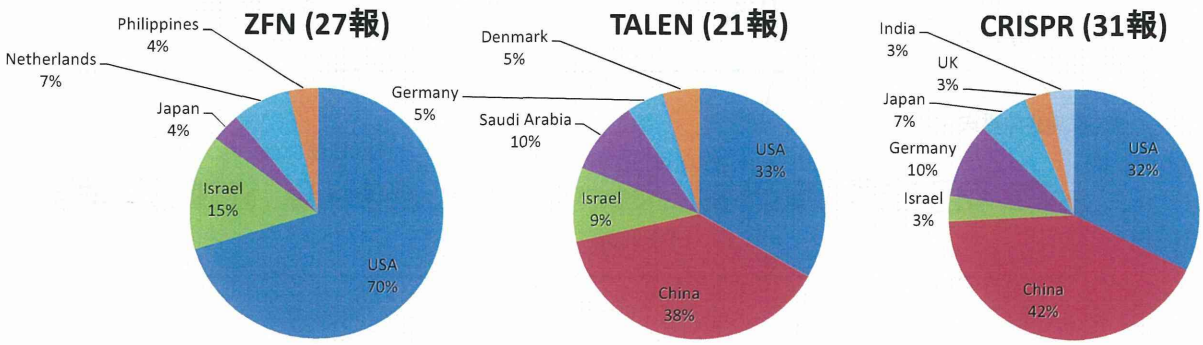


図4. 植物に対し実施されたNBT(ZFN, TALEN, CRISPR)の技術カテゴリー及び国別報告数の割合

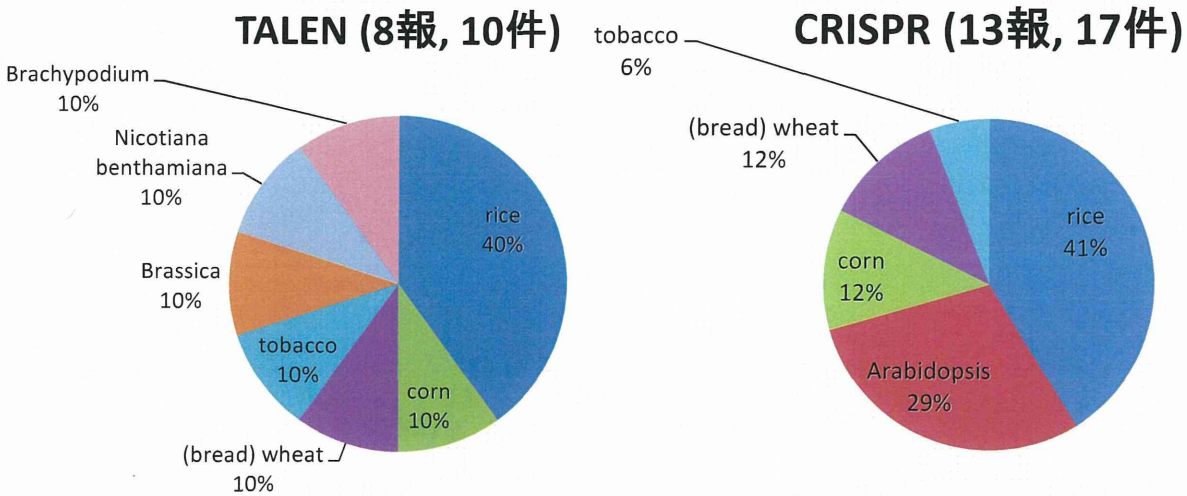


図5. 中国が実施したNBT(TALEN, CRISPR)の対象植物種の割合

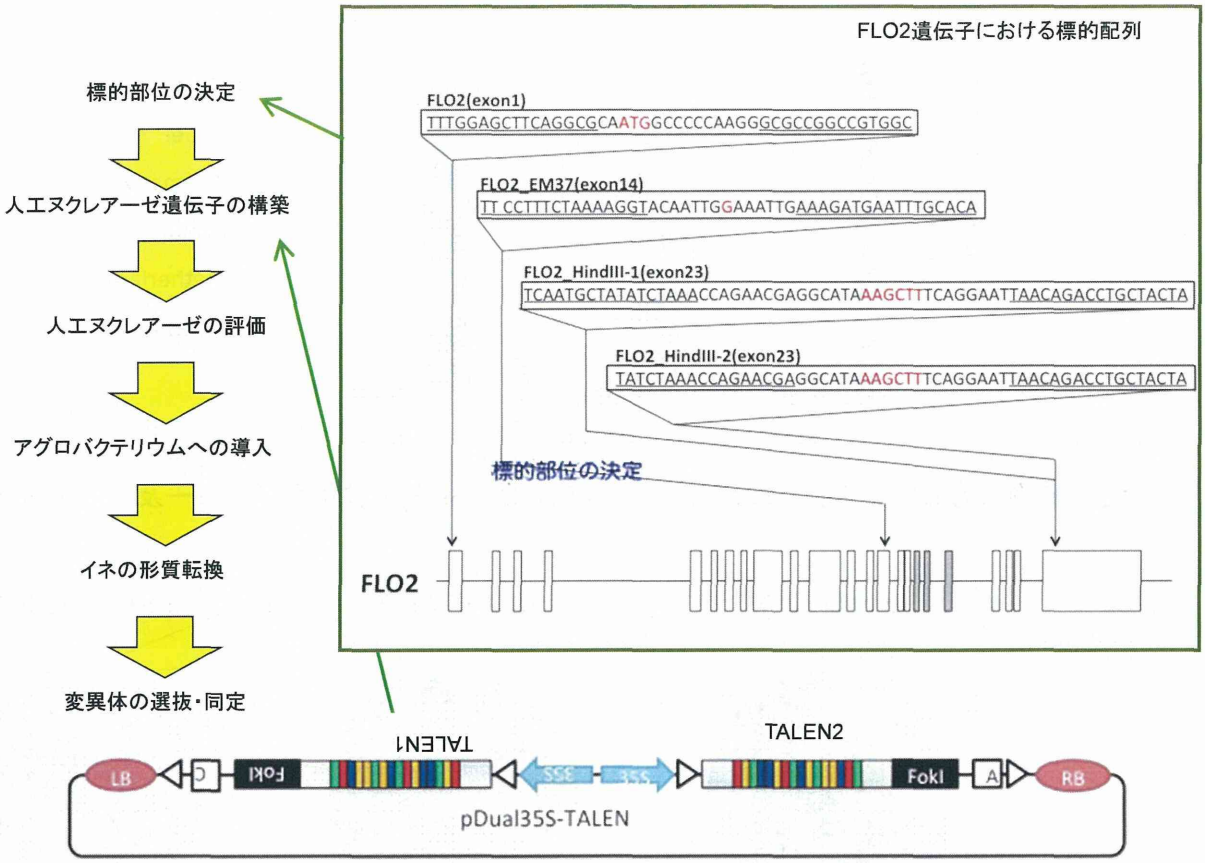


図6. *FLO2*遺伝子を標的とした人工ヌクレアーゼの標的配列の決定と変異体取得の戦略

# III. 研究成果の刊行に関する一覧表

# 平成26年度　研究成果の刊行に関する一覧表

書籍

| 著者氏名 | 書籍タイトル名 | 書籍全体の編集者名 | 書籍名 | 出版社名 | 出版地 | 出版年 | ページ |
|---|---|---|---|---|---|---|---|
| なし | | | | | | | |

雑誌

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻名 | ページ | 出版年 |
|---|---|---|---|---|---|
| Li HL, Fujimoto N, Sasakawa N, Shirai S, Ohkame T, Sakuma T, Tanaka M, Amano N, Watabnabe A, Sakurai H, Yamamoto T, Yamanaka S and Hotta A. | Precise Correction of the Dystrophin Gene in Duchenne Muscular Dystrophy Patient Induced Pluripotent Stem Cells by TALEN and CRISPR-Cas9. | Stem Cell Reports | 4 | 143-154 | 2015 |
| Nakade S, Tsubota T, Sakane Y, Kume S, Sakamoto N, Obara M, Daimon T, Sezutsu H, Yamamoto T, Sakuma T and Suzuki K. | Microhomology-mediated end-joining-dependent integration of donor DNA in cells and animals using TALENs and CRISPR/Cas9. | Nature Communications | 5 | 5560 | 2014 |
| Ochiai H, Sugawara T, Sakuma T and Yamamoto T. | Stochastic promoter activation affects Nanog expression variability in mouse embryonic stem cells. | Scientific Reports | 4 | 7125 | 2014 |
| Ninagawa S, Okada T, Sumitomo Y, Kamiya Y, Kato K, Horimoto S, Ishikawa T, Takeda S, Sakuma T, Yamamoto T and Mori K. | EDEM2 initiates mammalian glycoprotein ERAD by catalyzing the first mannose trimming step. | Journal of Cell Biology | 206 | 347-356 | 2014 |
| Sakuma T, Nishikawa A, Kume S, Chayama K and Yamamoto T. | Multiplex genome engineering in human cells using all-in-one CRISPR/Cas9 vector system. | Scientific Reports | 4 | 5400 | 2014 |
| Takabatake, R., Onishi, M., Futo, S., Minegishi, Y., Noguchi, A., Nakamura, K., Kondo, K., Teshima, R., Mano, J., Kitta, K. | Comparison of the specificity, stability, and PCR efficiency of six rice endogenous sequences for detection analyses of genetically modified rice. | Food Control | 50 | 949-955 | 2015 |
| Kondo, K., Nakamura, K. | Scientific review on novel genome editing techniques | Food Hygiene and Safety Science | 55 | 231-246 | 2014 |
| Kitagawa, M., Nakamura, K., Kondo, K., Ubukata, S., Akiyama, H. | Examination on the detection of common DNA sequence of genetically modified tomatoes in processed vegetable foods. | Food Hygiene and Safety Science | 55 | 247-253 | 2014 |
| Noguchi, A., Akiyama, H., Nakamura, K., Sakata, K., Minegishi, Y., Mano, J., Takabatake, R., Futo, S., Kitta, K., Teshima, R., Kondo, K., Nishimaki-Mogami, T. | A novel trait-specific real-time PCR method enables quantification of genetically modified (GM) maize content in ground grain samples containing stacked GM maize. | European Food Research and Technology | DOI 10.1007/s00217-014-2340-7 | | 2014 |

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻名 | ページ | 出版年 |
|---|---|---|---|---|---|
| Minegishi, Y., Mano, J., Takabatake, R., Nakamura, K., Kondo, K., Kato, Y., Kitta, K., Akiyama, H. | Development of pBT63, a positive control plasmid for qualitative detection of genetically modified rice. | Japanese Journal of Food Chemistry and Safety | 21 | 48-56 | 2014 |
| Tanaka, H., Kitazaki, Y., Nakamura, K., Akiyama, H., Akashi, R. | Development of a simple detection method for genetically modified papaya PRSV-YK | Ikushugaku Kenkyu | 16 | 158-161 | 2014 |
| Mano, J., Hatano, S., Futo, S., Minegishi, Y., Ninomiya, K., Nakamura, K., Kondo, K., Teshima, R., Takabatake, R., Kitta, K. | Development of direct real-time PCR system applicable to a wide range of food and agricultural products. | Food Hygiene and Safety Science | 55 | 25-33 | 2014 |