Paper and Patent Trends

(2015.10.22 ~ 2015.11.11)

Puna Maya Maharjan

2015. 10. 12

Paper Trend (PubMed Search)

- Brassinosteroids (4)
- CRISPR-Cas9 and plant (6)
- Herbicide (2)
- Totipotency, plant (0)
- Maize transformation (0)
- Rice transformation (2)
- C4 Photosynthesis (5)
- Anti-cancer, plant (8)
- In planta, transformation (1)
- Molecular Pharming(farming) (2)
- Cytochrome P450 (2)
- Herbal drug (4)
- Natural product, plant (4)
- Setaria (1)

Brassinosteroids 1

Development. 2015 Oct 22. pii: dev.124347. [Epub ahead of print]

ATAF2 integrates Arabidopsis brassinosteroid inactivation and seedling photomorphogenesis.

Peng H[1], Zhao J[2], Neff MM[3].

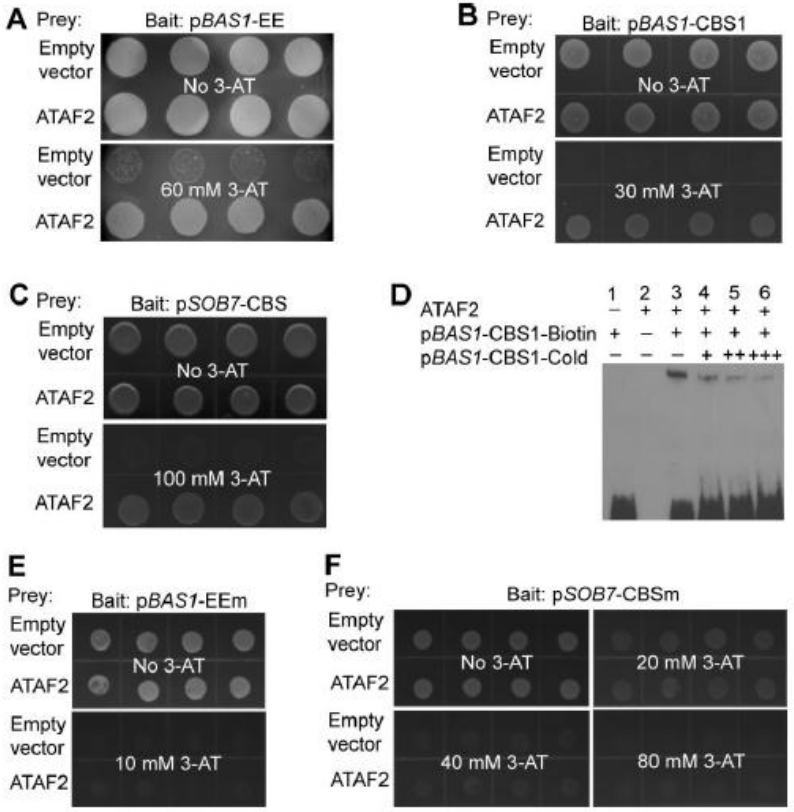
Author information

Abstract

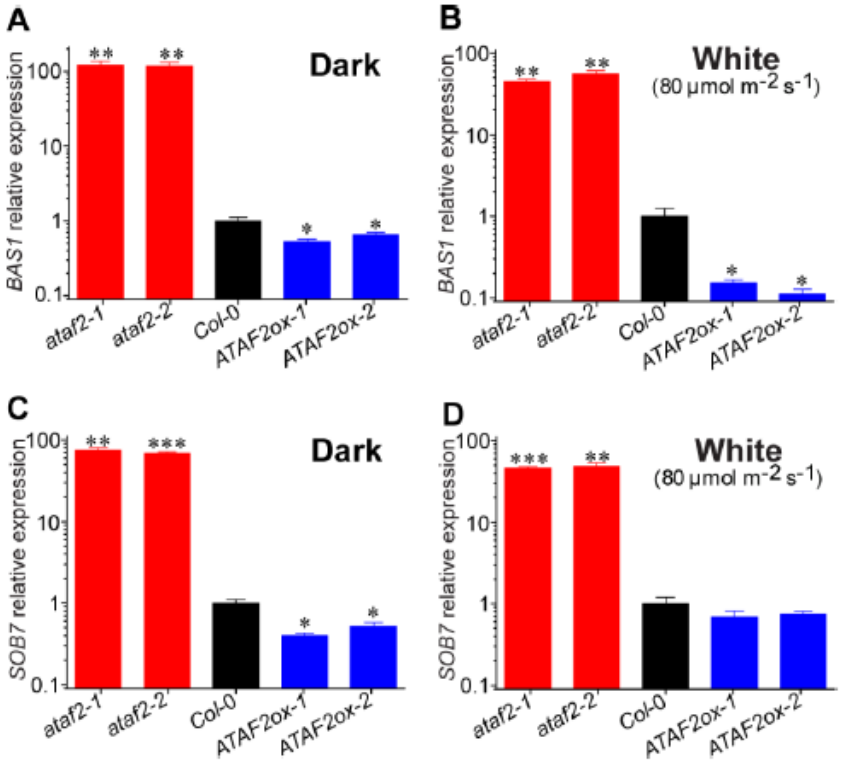
The Arabidopsis thaliana hypocotyl is a robust system for studying the interplay of light and plant hormones, such as brassinosteroids (BRs), in the regulation of plant growth and development. Since BRs cannot be transported between plant tissues, their cellular levels must be appropriate for given developmental fates. BR homeostasis is maintained in part by transcriptional feedback-regulation loops that control the expression of key metabolic enzymes, including the BR-inactivation enzymes CYP734A1/CYP72B1/BAS1 and CYP72C1/SOB7. In this research, the NAC transcription factor (TF), ATAF2, is found to bind the promoters of BAS1 and SOB7 to suppress their expression. ATAF2 restricts the tissue-specific expression of BAS1 and SOB7 in planta. ATAF2 loss- and gain-of-function seedlings have opposite BR response phenotypes for hypocotyl elongation. ATAF2 modulates hypocotyl growth in a light-dependent manner, with the photoreceptor phytochrome A playing a major role. The photomorphogenic phenotypes of ATAF2 loss- and gain-of-function seedlings can be suppressed by treatment with the BR biosynthesis inhibitor brassinazole (BRZ). Moreover, the disruption of BAS1 and SOB7 abolishes the short-hypocotyl phenotype of ATAF2 loss-of-function seedlings in low-fluence-rate white light, which demonstrates an ATAF2-mediated connection between BR catabolism and photomorphogenesis. The expression of ATAF2 is suppressed by both BRs and light, which demonstrates the existence of an ATAF2-BAS1/SOB7-BR-ATAF2 feedback-regulation loop as well as a light-ATAF2-BAS1/SOB7 -BR-photomorphogenesis pathway. ATAF2 also modulates root growth by regulating BR catabolism. Since ATAF2 was known to regulate plant defense and auxin biosynthesis, this TF acts as a central regulator of plant defense, hormone metabolism, and light-mediated seedling development.

http://www.ncbi.nlm.nih.gov/pubmed/26493403

ATAF 2 binds to promoter of *BAS1* and *SOB7*

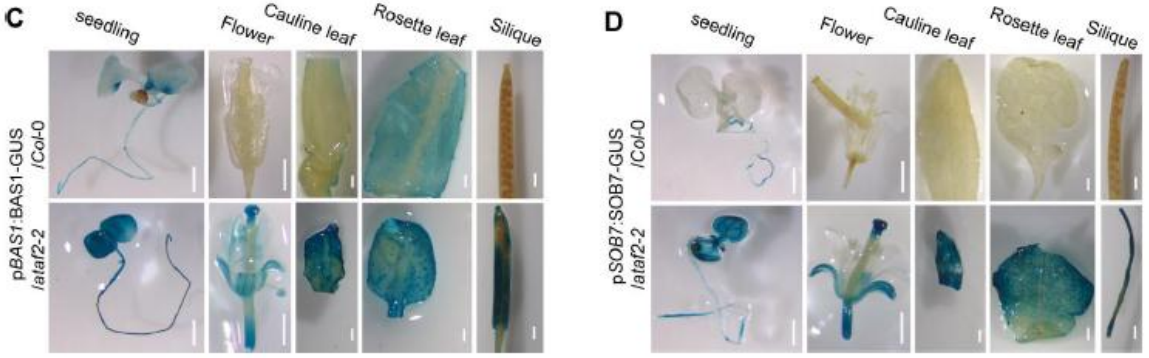


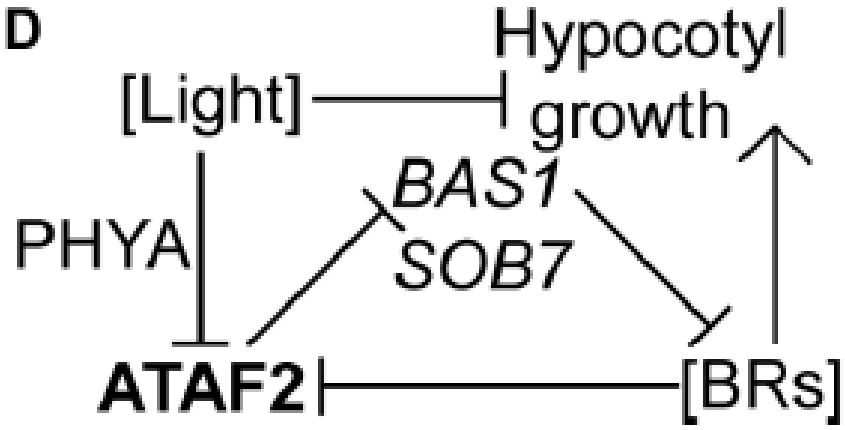
ATAF 2 suppress the expression of *BAS1* and *SOB7*



ATAF2 is repressor of BAS1 and SOB7 and

ATAF 2 restrict the tissue specific expression of *BAS1* and *SOB7*





Brassinosteroids 2

Mol Plant. 2015 Oct 27. pii: S1674-2052(15)00402-5. doi: 10.1016/j.molp.2015.10.007. [Epub ahead of print]

The brassinosteroid-activated BRI1 receptor kinase is switched off by dephosphorylation mediated by cytoplasm-localized PP2A B' subunits.

Wang R[1], Liu M[1], Yuan M[1], Oses-Prieto JA[2], Cai X[1], Sun Y[1], Burlingame AL[2], Wang ZY[3], Tang W[4].

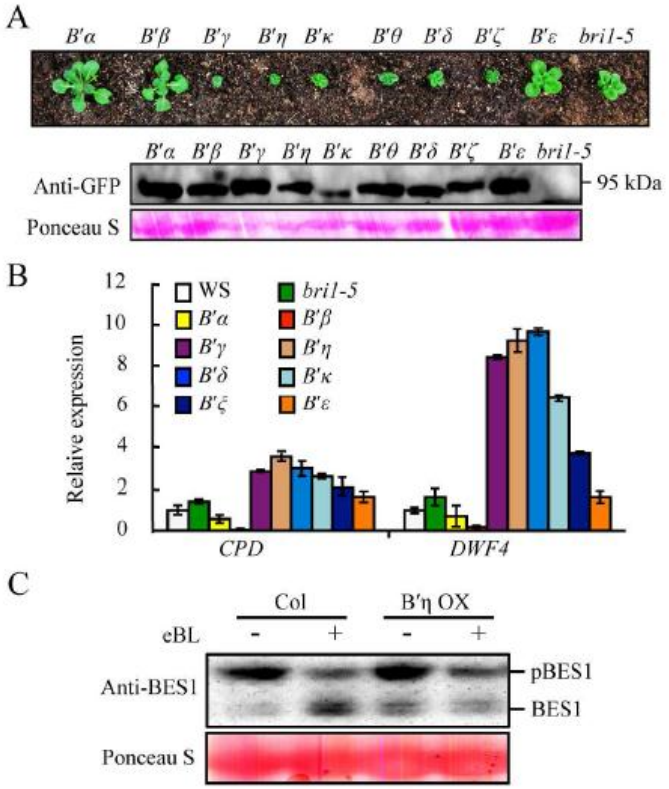
Author information

Abstract

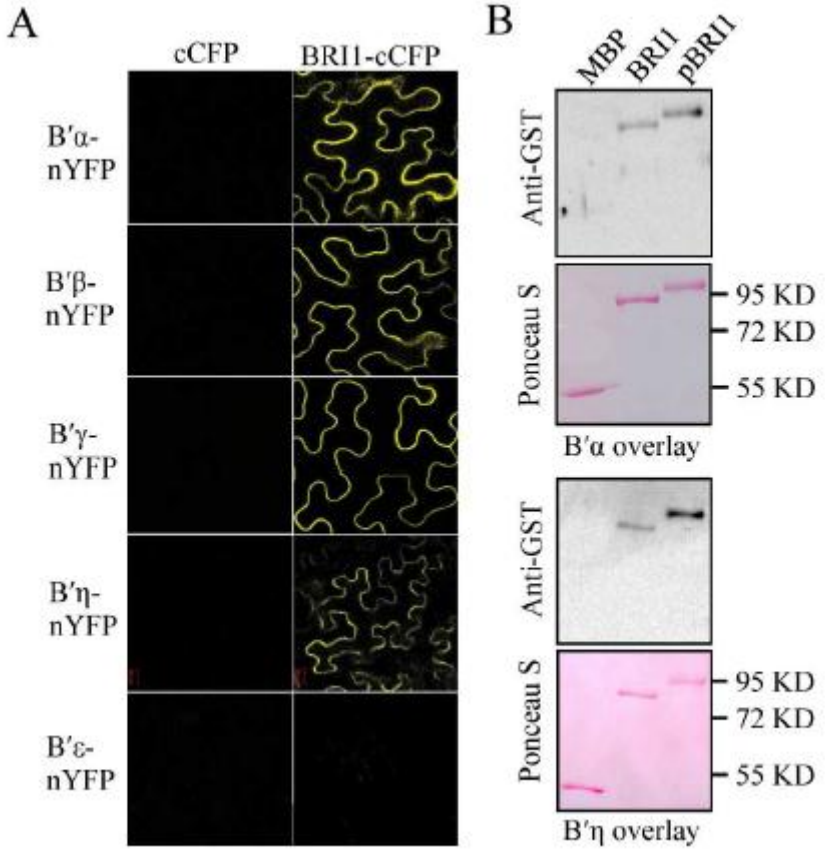
Brassinosteroid (BR) binding activates the receptor kinase BRI1 by inducing heterodimerization with its co-receptor kinase BAK1; however, the mechanisms that reversibly inactivate BRI1 remain unclear. Here we show that cytoplasm-localized PP2A B' regulatory subunits interact with BRI1 to mediate its dephosphorylation and inactivation. Loss-of-function and overexpression experiments showed that a group of PP2A B' regulatory subunits, represented by B'η, negatively regulate BR signaling by decreasing BRI1 phosphorylation. BR increases the expression levels of these B' subunits, and B'η interacts preferentially with phosphorylated BRI1, suggesting that the dynamics of BR signaling are modulated by the PP2A-mediated feedback inactivation of BRI1. Compared to PP2A B'α and B'β, which promote BR responses by dephosphorylating the downstream transcription factor BZR1, the BRI1-inactivating B' subunits showed similar binding to BRI1 and BZR1 but distinct subcellular localization. Alteration of the nuclear/cytoplasmic localization of the B' subunits revealed that cytoplasmic PP2A dephosphorylates BRI1 and inhibits the BR response, whereas nuclear PP2A dephosphorylates BZR1 and activates the BR response. Our findings not only identify the PP2A regulatory B subunits that mediate the binding and dephosphorylation of BRI1, but also demonstrate that the subcellular localization of PP2A specifies its substrate selection and distinct effects on BR signaling.

http://www.ncbi.nlm.nih.gov/pubmed/26517938

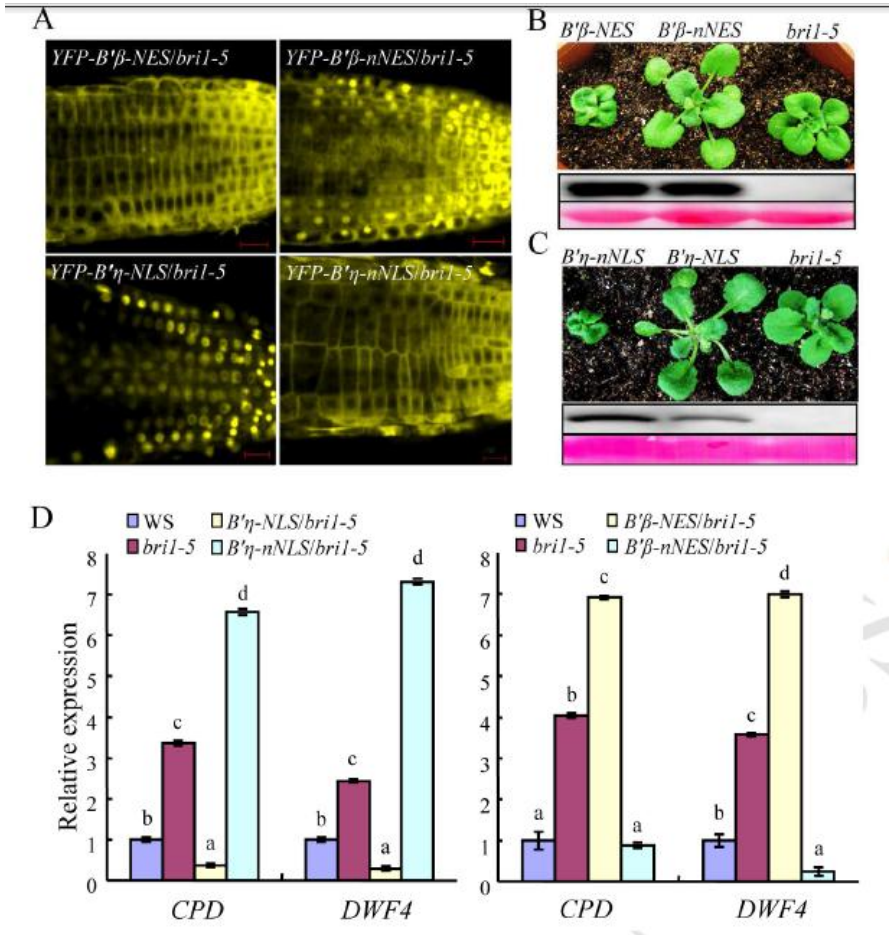
PP2A B′η, B′γ, B′κ, B′δ, B′ζ and B′θ negatively regulate BR signaling, whereas PP2A B′α and B′β positively regulate BR signaling



PP2A B′ subunits interact directly with active BRI1 BR signaling by dephosphorylating BRI1



The subcellular localization of PP2A B′ subunits determines their roles in the BR signaling pathway



B′η fused with a heterologous nuclear localization signal (B′η-NLS) and B′β fused to a nuclear exporting signal (B′β-NES

Brassinosteroids 3

BMC Plant Biol. 2015 Oct 13;15:247. doi: 10.1186/s12870-015-0617-z.

Two homolog wheat Glycogen Synthase Kinase 3/SHAGGY - like kinases are involved in brassinosteroid signaling.

Bittner T[1], Nadler S[2], Schulze E[3], Fischer-Iglesias C[4].

Author information

Abstract

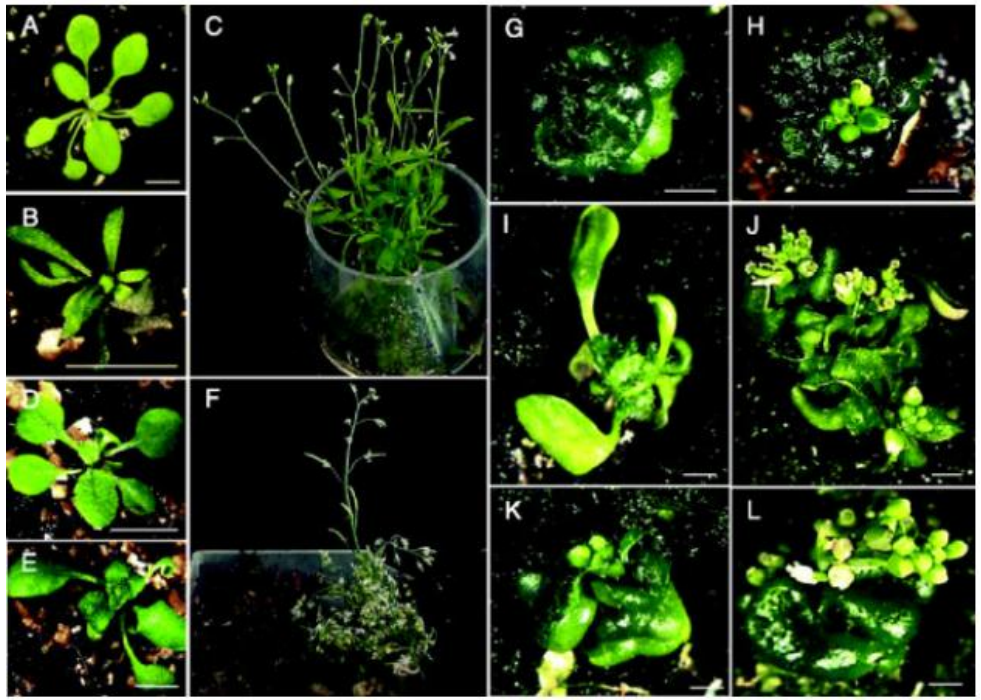
BACKGROUND: Glycogen Synthase Kinase 3/SHAGGY-like kinases (GSKs) are multifunctional non-receptor ser/thr kinases. Plant GSKs are involved in hormonal signaling networks and are required for growth, development, light as well as stress responses. So far, most studies have been carried out on Arabidopsis or on other eudicotyledon GSKs. Here, we evaluated the role of TaSK1 and TaSK2, two homolog wheat (Triticum aestivum) GSKs, in brassinosteroid signaling. We explored in addition the physiological effects of brassinosteroids on wheat growth and development.

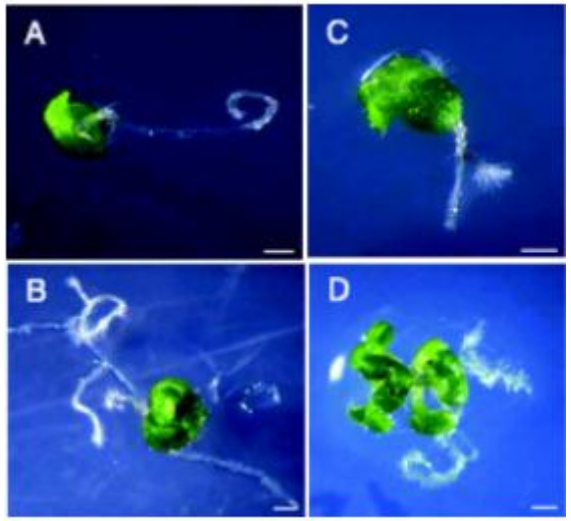
RESULTS: A bin2-1 like gain-of-function mutation has been inserted respectively in one of the homoeologous gene copies of TaSK1 (TaSK1-A.2-1) and in one of the homoeologous gene copies of TaSK2 (TaSK2-A.2-1). Arabidopsis plants were transformed with these mutated gene copies. Severe dwarf phenotypes were obtained closely resembling those of Arabidopsis bin2-1 lines and Arabidopsis BR-deficient or BR-signaling mutants. Expression of BR downstream genes, SAUR-AC1, CPD and BAS1 was deregulated in TaSK1.2-1 and TaSK2.2-1 transgenic lines. Severe dwarf lines were partially rescued by Bikinin beforehand shown to inhibit TaSK kinase activity. This rescue was accompanied with changes in BR downstream gene expression levels. Wheat embryos and seedlings were treated with compounds interfering with BR signaling or modifying BR levels to gain insight into the role of brassinosteroids in wheat development. Embryonic axis and scutellum differentiation were impaired, and seedling growth responses were affected when embryos were treated with Epibrassinolides, Propiconazole, and Bikinin.

CONCLUSIONS: In view of our findings, TaSKs are proposed to be involved in BR signaling and to be orthologous of Arabidopsis Clade II GSK3/SHAGGY-like kinases. Observed effects of Epibrassinolide, Propiconazole and Bikinin treatments on wheat embryos and seedlings indicate a role for BR signaling in embryonic patterning and seedling growth.

http://www.ncbi.nlm.nih.gov/pubmed/26458871

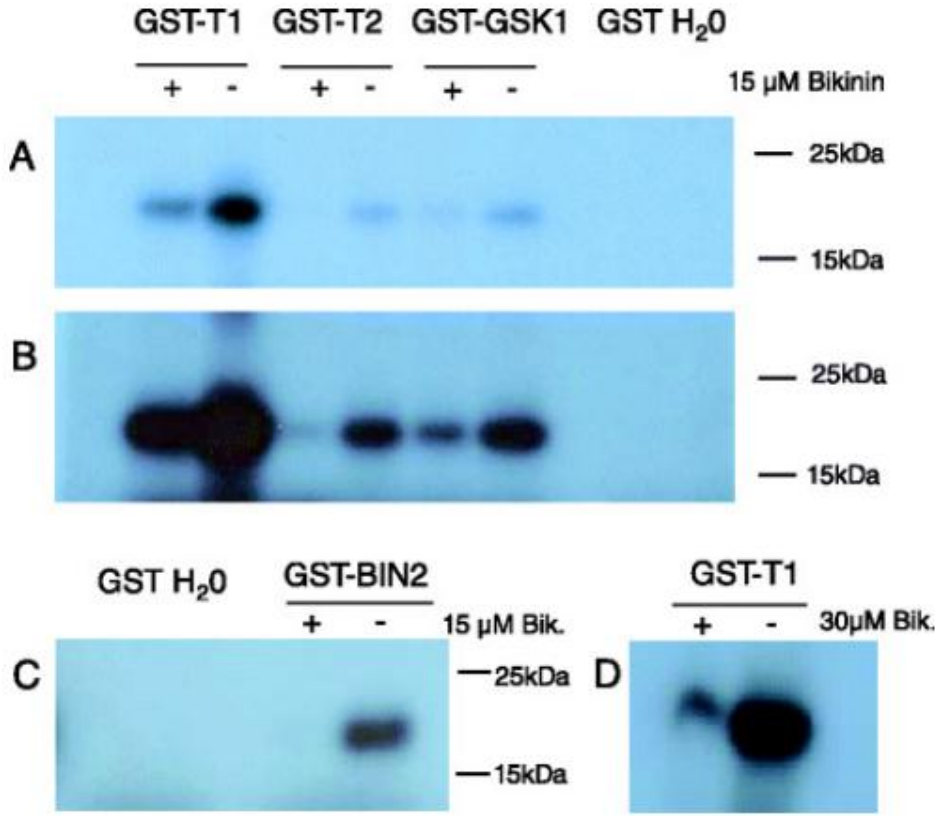
TaSK1.2-1 and TaSK2.2-1 **mutated gene copies expressed in *Arabidopsis* led to phenotypes reminiscent of BR-signaling mutant phenotypes**





Bikinin rescued
severe dwarf phenotypes

Bikinin inhibit kinase
activity of Wheat BIN2



Brassinosteroids 4

Front Plant Sci. 2015 Oct 8;6:833. doi: 10.3389/fpls.2015.00833. eCollection 2015.

Overexpression of OsDof12 affects plant architecture in rice (Oryza sativa L.).

Wu Q[1], Li D[2], Li D[3], Liu X[4], Zhao X[2], Li X[2], Li S[5], Zhu L[2].

Author information

Abstract

Dof (DNA binding with one finger) proteins, a class of plant-specific transcription factors, are involved in plant growth and developmental processes and stress responses. However, their biological functions remain to be elucidated, especially in rice (Oryza sativa L.). Previously, we have reported that OsDof12 can promote rice flowering under long-day conditions. Here, we further investigated the other important agronomical traits of the transgenic plants overexpressing OsDof12 and found that overexpressing OsDof12 could lead to reduced plant height, erected leaf, shortened leaf blade, and smaller panicle resulted from decreased primary and secondary branches number. These results implied that OsDof12 is involved in rice plant architecture formation. Furthermore, we performed a series of Brassinosteroid (BR)-responsive tests and found that overexpression of OsDof12 could also result in BR hyposensitivity. Of note, in WT plants the expression of OsDof12 was found up-regulated by BR treatment while in OsDof12 overexpression plants two positive BR signaling regulators, OsBRI1 and OsBZR1, were significantly down-regulated, indicating that OsDof12 may act as a negative BR regulator in rice. Taken together, our results suggested that overexpression of OsDof12 could lead to altered plant architecture by suppressing BR signaling. Thus, OsDof12 might be used as a new potential genetic regulator for future rice molecular breeding.

http://www.ncbi.nlm.nih.gov/pubmed/26500670

Phenotype of OX plants

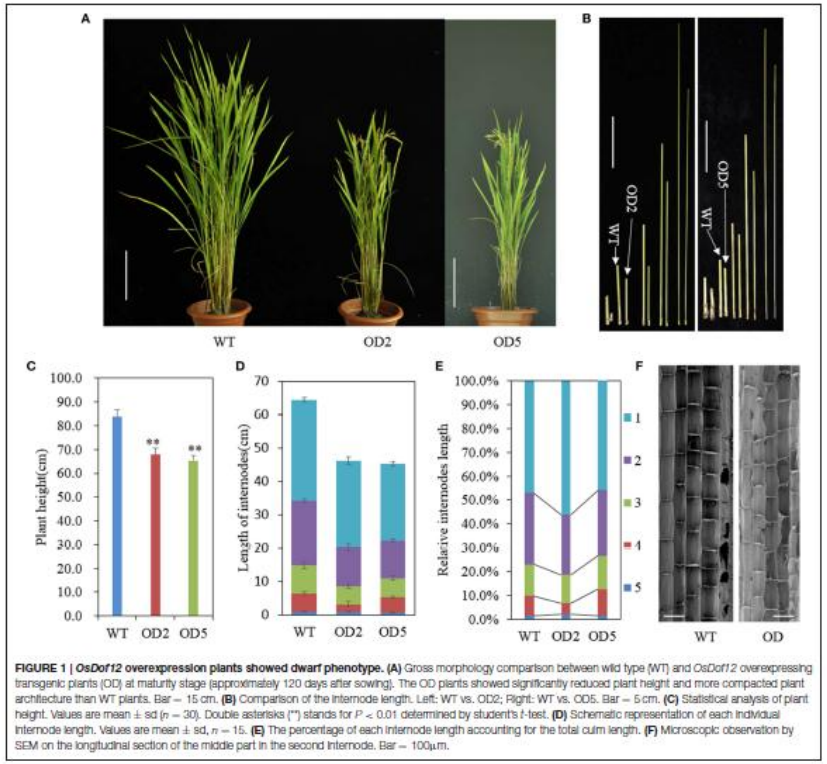


FIGURE 1 | *OsDof12* overexpression plants showed dwarf phenotype. (A) Gross morphology comparison between wild type (WT) and *OsDof12* overexpressing transgenic plants (OD) at maturity stage (approximately 120 days after sowing). The OD plants showed significantly reduced plant height and more compacted plant architecture than WT plants. Bar = 15 cm. **(B)** Comparison of the internode length. Left: WT vs. OD2; Right: WT vs. OD5. Bar = 5 cm. **(C)** Statistical analysis of plant height. Values are mean ± sd ($n = 30$). Double asterisks (**) stands for $P < 0.01$ determined by student's *t*-test. **(D)** Schematic representation of each individual internode length. Values are mean ± sd, $n = 15$. **(E)** The percentage of each internode length accounting for the total culm length. **(F)** Microscopic observation by SEM on the longitudinal section of the middle part in the second internode. Bar = 100μm.

OX plants showed altered BR sensitivity

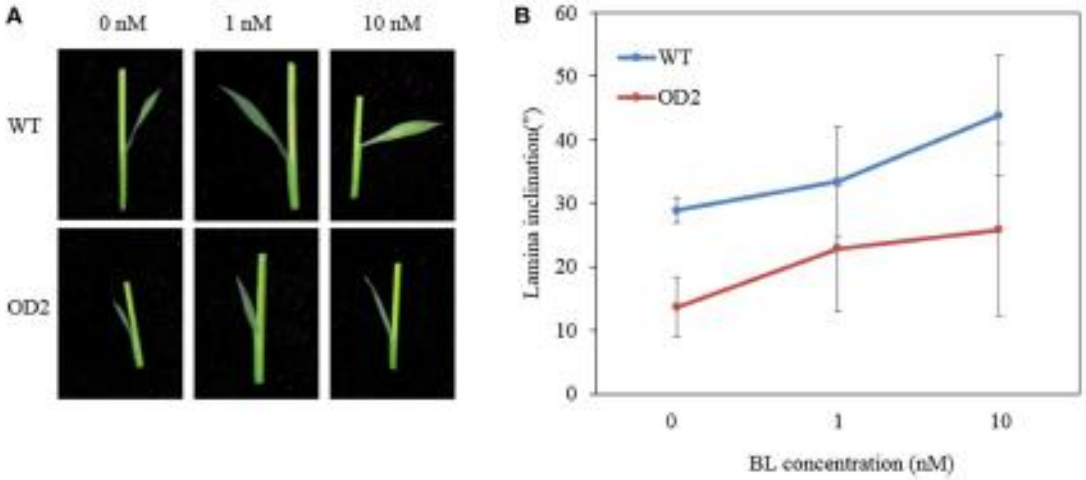


FIGURE 4 | Lamina joint bending analysis. (A) The second lamina joint morphology in WT and OD2 plants grown on BL contained half-strength MS for 7 days. **(B)** Quantification of the second lamina angel bending as shown in **(A)**, values are mean ± sd, $n = 20$.

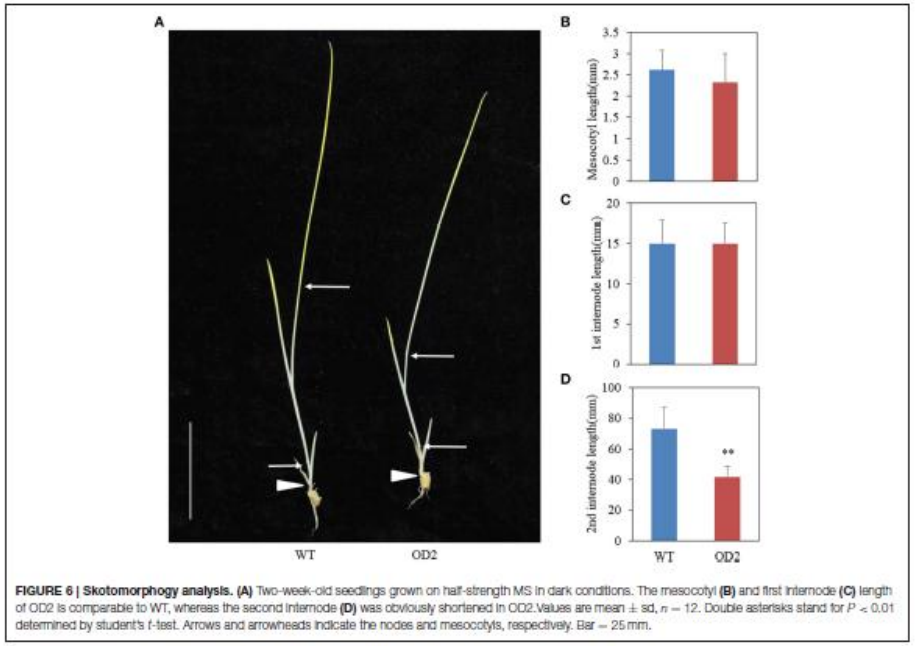


FIGURE 6 | Skotomorphogy analysis. (A) Two-week-old seedlings grown on half-strength MS in dark conditions. The mesocotyl **(B)** and first internode **(C)** length of OD2 is comparable to WT, whereas the second internode **(D)** was obviously shortened in OD2.Values are mean ± sd, $n = 12$. Double asterisks stand for $P < 0.01$ determined by student's *t*-test. Arrows and arrowheads indicate the nodes and mesocotyls, respectively. Bar = 25 mm.

The second internode length in OD plants was much less than that in WT plants

Brassinosteroids 5

Plant Cell Rep. 2015 Oct 30. [Epub ahead of print]

Brassinosteroid (BR) biosynthetic gene lhdd10 controls late heading and plant height in rice (Oryza sativa L.).

Liu X[1], Feng ZM[1], Zhou CL[1], Ren YK[1], Mou CL[1], Wu T[1], Yang CY[1], Liu SJ[1], Jiang L[2], Wan JM[3,4].

Author information

Abstract

KEY MESSAGE: A Brd2 allele suppresses heading date by altering the expression of heading date regulators such as OsMADS50 , and also negatively regulates chlorophyll biosynthesis. Heading date and plant height are important determinants of yield in rice (Oryza sativa L.). In this study, we characterized a late heading, dwarf mutant known as lhdd10 selected following ethyl methane sulfonate (EMS)-treatment of ssp. indica cultivar 93-11. lhdd10 showed late heading, dwarfness and slightly darker-green leaves than wild-type 93-11 under long-day and short-day conditions. We isolated lhdd10 by map-based cloning; it encoded a putative FAD-linked oxidoreductase protein (a brassinosteroid biosynthetic gene) that localized to the nucleus. LHDD10 was constitutively expressed in various tissues, but more so in shoot apices and panicles. Our data showed that lhdd10 influences heading date by controlling the expression of heading date regulators, such as OsMADS50 in both LD and SD conditions. lhdd10 also negatively regulated expression of chlorophyll biosynthetic genes to reduce the chlorophyll content. Our data indicated that BRs play important roles in regulating heading date and chlorophyll biosynthesis. This work provides material that will allow study of how BRs regulate heading date in rice.

http://www.ncbi.nlm.nih.gov/pubmed/26518431

Phenotype of lhdd10 mutant

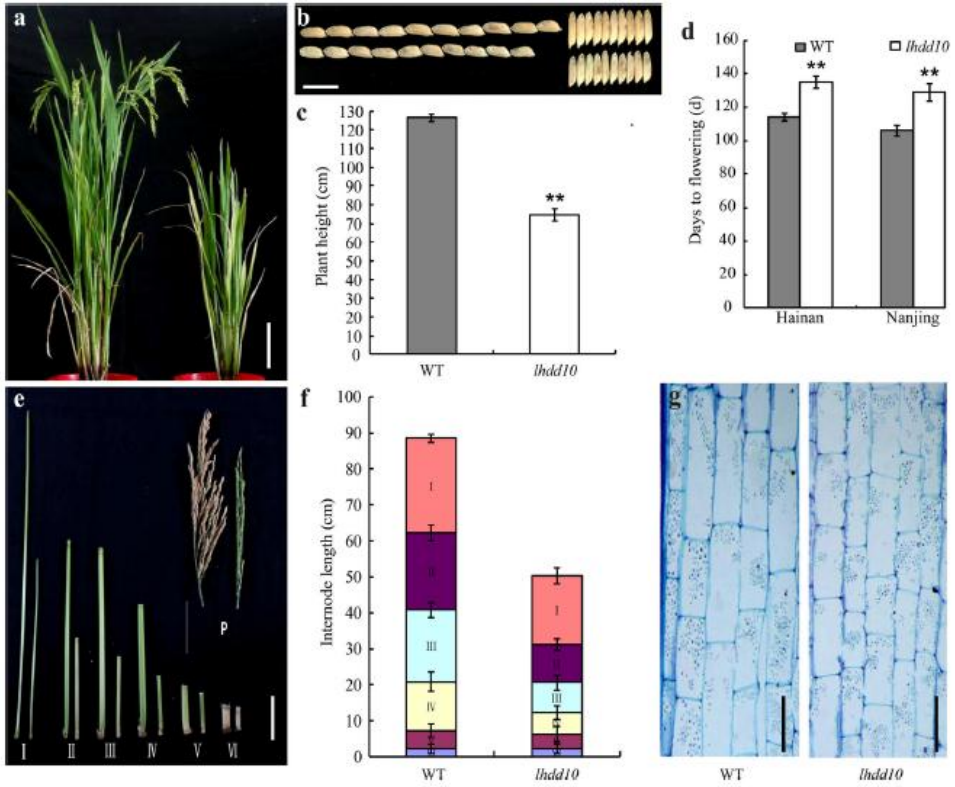
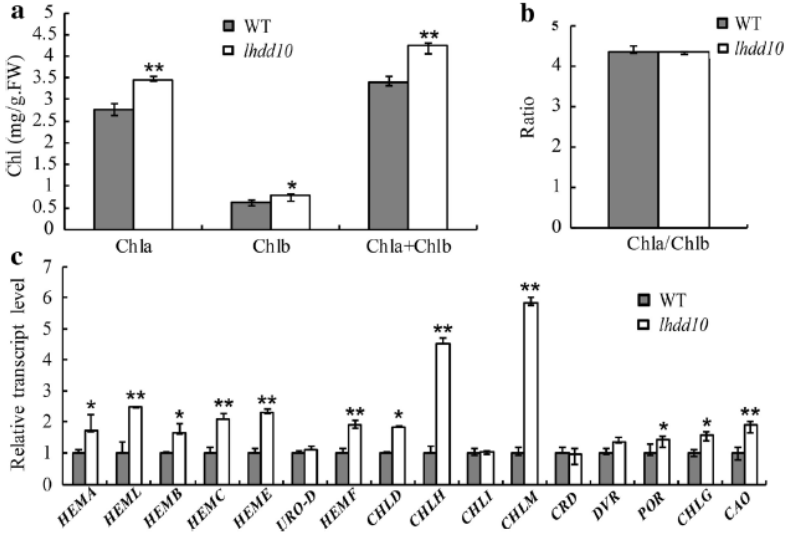


Fig. 1 Comparative phenotypes of WT (*left*) and the *lhdd10* mutant (*right*). **a** At 110 days from planting; WT (*left*) and mutant (*right*). *Bars* 10 cm. **b** Grains from the main panicles. *Bars* 1 cm. **c** Plant height at heading. **d** Days to flowering when grown under LDs and SDs. **e** and **f** Internode lengths at 140 days after planting. *Bars* 5 cm. **g** Parenchyma cells from the second internodes of WT and *lhdd10* observed in paraffin sections. *Bars* 20 μm. *Double asterisk* indicates significant differences between WT and *lhdd10* at $P = 0.01$ by Student's *t* test in (**c**) and (**d**)

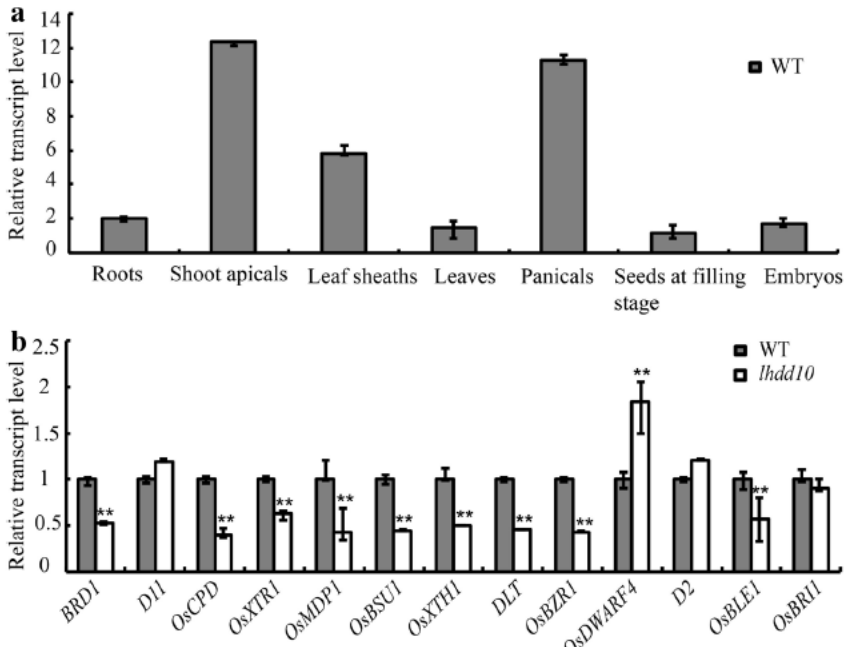
Trait	WT	*lhdd10*	*P* value
Plant height (cm)	126.44 ± 2.01	74.76 ± 3.54**	2.38E−11
Panicle length (cm)	23.18 ± 1.55	17.42 ± 0.72**	3.27E−6
Spikelet fertility (%)	95.69 ± 2.15	72.14 ± 2.10**	7.12E−4
1000 grain weight (g)	30.59 ± 0.86	26.03 ± 0.84**	1.77E−3
Grain number per main panicle	201.2 ± 11.49	73.43 ± 7.02**	2.29E−5
Primary branch number	11.4 ± 1.14	8.2 ± 0.49**	5.13E−4
Grain length (mm)	10.29 ± 0.16	9.07 ± 0.13**	5.57E−9
Grain width (mm)	2.71 ± 0.05	2.67 ± 0.09	0.62
Grain thickness (mm)	2.34 ± 0.33	2.20 ± 0.05**	3.23E−3
Number of tillers	6.8 ± 1.05	6.2 ± 1.30	0.35

Data are averages of 20 samples ± SD, ** indicates a significant difference between WT and *lhdd10* at $P = 0.01$

llhdd10 regulates chlorophyll biosynthesis



Expression pattern of lhdd10 and altered expression



CRISPR-Cas9 and plant 1

Nat Biotechnol. 2015 Nov;33(11):1162-4. doi: 10.1038/nbt.3389. Epub 2015 Oct 19.

DNA-free genome editing in plants with preassembled CRISPR-Cas9 ribonucleoproteins.

Woo JW[1], Kim J[2,3], Kwon SI[1], Corvalán C[4], Cho SW[3], Kim H[2], Kim SG[2], Kim ST[2], Choe S[1,4,5], Kim JS[2,3].

Author information

Abstract

Editing plant genomes without introducing foreign DNA into cells may alleviate regulatory concerns related to genetically modified plants. We transfected preassembled complexes of purified Cas9 protein and guide RNA into plant protoplasts of Arabidopsis thaliana, tobacco, lettuce and rice and achieved targeted mutagenesis in regenerated plants at frequencies of up to 46%. The targeted sites contained germline-transmissible small insertions or deletions that are indistinguishable from naturally occurring genetic variation.

http://www.ncbi.nlm.nih.gov/pubmed/26479191

CRISPR-Cas9 and plant (2)

Biochem Biophys Res Commun. 2015 Nov 6;467(1):76-82. doi: 10.1016/j.bbrc.2015.09.117. Epub 2015 Sep 25.

CRISPR/Cas9-mediated mutagenesis of the RIN locus that regulates tomato fruit ripening.

Ito Y[1], Nishizawa-Yokoi A[2], Endo M[2], Mikami M[3], Toki S[4].

Author information

Abstract

Site-directed mutagenesis using genetic approaches can provide a wealth of resources for crop breeding as well as for biological research. The clustered regularly interspaced short palindromic repeat (CRISPR)/CRISPR-associated 9 endonuclease (CRISPR/Cas9) system is a novel strategy used to induce mutations in a specific genome region; the system functions in a variety of organisms, including plants. Here, we report application of the CRISPR/Cas9 system to efficient mutagenesis of the tomato genome. In this study, we targeted the tomato RIN gene, which encodes a MADS-box transcription factor regulating fruit ripening. Three regions within the gene were targeted and mutations consisting either of a single base insertion or deletion of more than three bases were found at the Cas9 cleavage sites in T0 regenerated plants. The RIN-protein-defective mutants produced incomplete-ripening fruits in which red color pigmentation was significantly lower than that of wild type, while heterologous mutants expressing the remaining wild-type gene reached full-ripening red color, confirming the important role of RIN in ripening. Several mutations that were generated at three independent target sites were inherited in the T1 progeny, confirming the applicability of this mutagenesis system in tomato.

The CRIPSR/Cas9 system generated novel mutations in a tomato ripening regulator, *RIN*.

- **The mutations affected RIN protein accumulation and fruit ripening phenotypes.**
- **The mutations were successfully transmitted to the next generation.**

http://www.ncbi.nlm.nih.gov/pubmed/26408904

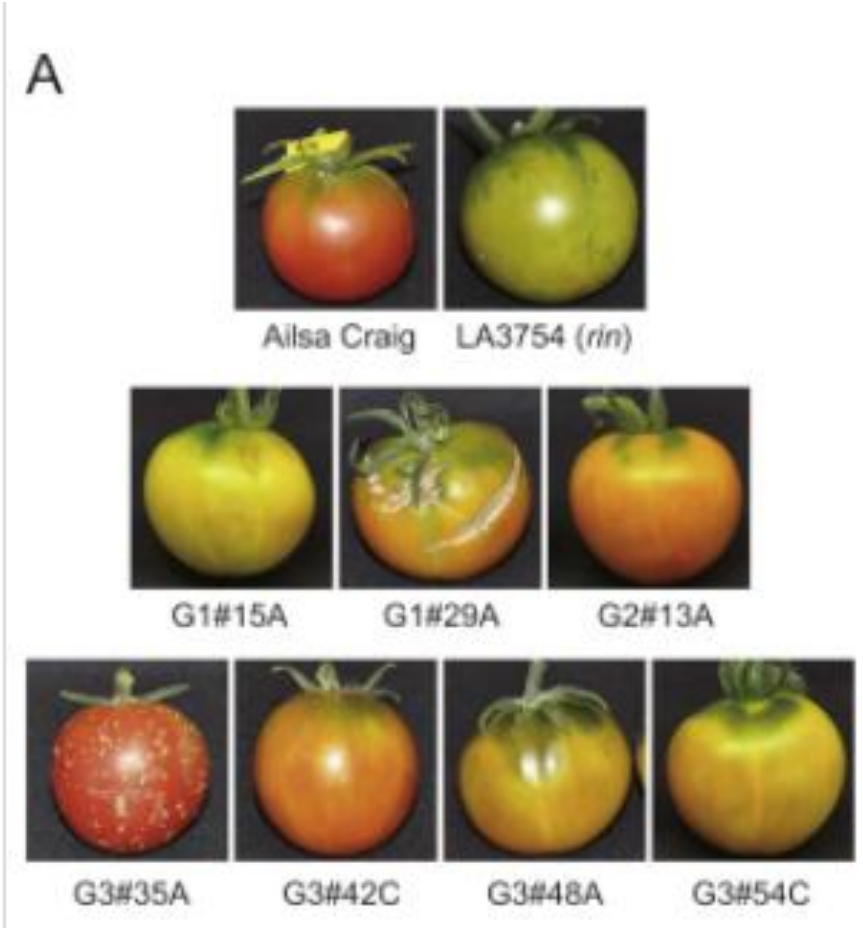
2.1. Plasmid construction

Targeting sites in the RIN gene were selected using the CRISPR-P program (http://cbi.hzau.edu.cn/cgi-bin/CRISPR) [16]. Oligonucleotide pairs for the target sequences (Supp. Table 1) were annealed and the resulting fragments were then cloned into the *Bbs*I site of a single-guide RNA (sgRNA) cloning vector, pUC19_AtU6oligo, in which the attL1::AtU6-26::gRNA::attL2 fragment from pEn-Chimera [17] lies between the two I-SceI sites of the vector. An all-in-one binary vector harboring a sgRNA, Cas9 and an NPTII expression construct was made as follows; first, a sgRNA expression construct, OsU3::gYSA, and a terminator sequence with a NPTII expression construct, OsAct1 3′ UTR::35S(P)::NPTII::hsp17.3(T), were prepared according to our previous report [18], and a Cas9 expression construct, PcUbi4-2(P)::Cas9::pea3A(T), was prepared from pDe -Cas9 [17]. Next, these three constructs were cloned into pPZP202 via an In-fusion® (Takara) cloning reaction, completing pZK_OsU3gYSA_FFCas9. Finally, the sgRNA expression cassette prepared in pUC19_AtU6oligo was excised at the I-SceI sites and replaced by OsU3::gYSA in pZK_OsU3gYSA_FFCas9, completing pZK_ AtU6gRNA _FFCas9.

Table 2.
Inheritance of target mutations into T1 plants.

Plant Line	T_0 genotype	T_1 segregation		
	allele[a]	No. of plants examined	Ratio of homozygous mu	
G1#15A	*rinG1-2, rinG1-5, rinG1-6, rinG1-7*	16	56.2%	(*rinG1-6*, 31.2%; *rinG1-*
G1#29A	*rinG1-5, WT*	13	69.2%	(*rinG1-5*, 69.2%)
G2#13A	*rinG2-1, rinG2-2*	14	57.1%	(*rinG2-1*, 28.6%; *rinG2-*
G3#35A	*rinG3-3 rinG3-4, WT*	21	0.0%	
G3#42C	*rinG3-5, rinG3-6, WT*	10	50.0%	(*rinG3-5*, 40.0%; *rinG3-*
G3#48A	*rinG3-6*	11	100.0%	(*rinG3-6*, 100%)
G3#54C	*rinG3-1, rinG3-6*	8	25.0%	(*rinG3-6* , 25.0%)

[a]Sequences of each allele were indicated in Table 1 and Supp. Table 2



CRISPR-Cas9 and plant 3

Plant Sci. 2015 Nov;240:130-42. doi: 10.1016/j.plantsci.2015.09.011. Epub 2015 Sep 11.

CRISPR/Cas9-mediated genome editing and gene replacement in plants: Transitioning from lab to field.

Schaeffer SM[1], Nakata PA[2].

Author information

Review

Abstract

The CRISPR/Cas9 genome engineering system has ignited and swept through the scientific community like wildfire. Owing largely to its efficiency, specificity, and flexibility, the CRISPR/Cas9 system has quickly become the preferred genome-editing tool of plant scientists. In plants, much of the early CRISPR/Cas9 work has been limited to proof of concept and functional studies in model systems. These studies, along with those in other fields of biology, have led to the development of several utilities of CRISPR/Cas9 beyond single gene editing. Such utilities include multiplexing for inducing multiple cleavage events, controlling gene expression, and site specific transgene insertion. With much of the conceptual CRISPR/Cas9 work nearly complete, plant researchers are beginning to apply this gene editing technology for crop trait improvement. Before rational strategies can be designed to implement this technology to engineer a wide array of crops there is a need to expand the availability of crop-specific vectors, genome resources, and transformation protocols. We anticipate that these challenges will be met along with the continued evolution of the CRISPR/Cas9 system particularly in the areas of manipulation of large genomic regions, transgene-free genetic modification, development of breeding resources, discovery of gene function, and improvements upon CRISPR/Cas9 components. The CRISPR/Cas9 editing system appears poised to transform crop trait improvement.

http://www.ncbi.nlm.nih.gov/pubmed/26475194

CRISPR-Cas9 and plant 4

J Mol Biol. 2015 Oct 23. pii: S0022-2836(15)00606-3. doi: 10.1016/j.jmb.2015.10.014. [Epub ahead of print]

Origins of Programmable Nucleases for Genome Engineering.

Chandrasegaran S[1], Carroll D[2].

Author information

Abstract

Genome engineering with programmable nucleases depends on cellular responses to a targeted double-strand break (DSB). The first truly targetable reagents were the zinc finger nucleases (ZFNs) showing that arbitrary DNA sequences could be addressed for cleavage by protein engineering, ushering in the breakthrough in genome manipulation. ZFNs resulted from basic research on zinc finger proteins and the FokI restriction enzyme (which revealed a bipartite structure with a separable DNA-binding domain and a non-specific cleavage domain). Studies on the mechanism of cleavage by 3-finger ZFNs established that the preferred substrates were paired binding sites, which doubled the size of the target sequence recognition from 9 to 18bp, long enough to specify a unique genomic locus in plant and mammalian cells. Soon afterwards, a ZFN-induced DSB was shown to stimulate homologous recombination in cells. Transcription activator-like effector nucleases (TALENs) that are based on bacterial TALEs fused to the FokI cleavage domain expanded this capability. The fact that ZFNs and TALENs have been used for genome modification of more than 40 different organisms and cell types attests to the success of protein engineering. The most recent technology platform for delivering a targeted DSB to cellular genomes is that of the RNA-guided nucleases, which are based on the naturally occurring Type II prokaryotic CRISPR-Cas9 system. Unlike ZFNs and TALENs that use protein motifs for DNA sequence recognition, CRISPR-Cas9 depends on RNA-DNA recognition. The advantages of the CRISPR-Cas9 system-the ease of RNA design for new targets and the dependence on a single, constant Cas9 protein-have led to its wide adoption by research laboratories around the world. These technology platforms have equipped scientists with an unprecedented ability to modify cells and organisms almost at will, with wide-ranging implications across biology and medicine. However, these nucleases have also been shown to cut at off-target sites with mutagenic consequences. Therefore, issues such as efficacy, specificity and delivery are likely to drive selection of reagents for particular purposes. Human therapeutic applications of these technologies will ultimately depend on risk versus benefit analysis and informed consent.

http://www.ncbi.nlm.nih.gov/pubmed/26506267

CRISPR-Cas9 and plant 5

Nature. 2015 Nov 5;527(7576):110-3. doi: 10.1038/nature15544. Epub 2015 Oct 28.

Conformational control of DNA target cleavage by CRISPR-Cas9.

Sternberg SH[1], LaFrance B[2], Kaplan M[3], Doudna JA[1,2,3,4,5].

Author information

Abstract

Cas9 is an RNA-guided DNA endonuclease that targets foreign DNA for destruction as part of a bacterial adaptive immune system mediated by clustered regularly interspaced short palindromic repeats (CRISPR). Together with single-guide RNAs, Cas9 also functions as a powerful genome engineering tool in plants and animals, and efforts are underway to increase the efficiency and specificity of DNA targeting for potential therapeutic applications. Studies of off-target effects have shown that DNA binding is far more promiscuous than DNA cleavage, yet the molecular cues that govern strand scission have not been elucidated. Here we show that the conformational state of the HNH nuclease domain directly controls DNA cleavage activity. Using intramolecular Förster resonance energy transfer experiments to detect relative orientations of the Cas9 catalytic domains when associated with on- and off-target DNA, we find that DNA cleavage efficiencies scale with the extent to which the HNH domain samples an activated conformation. We furthermore uncover a surprising mode of allosteric communication that ensures concerted firing of both Cas9 nuclease domains. Our results highlight a proofreading mechanism beyond initial protospacer adjacent motif (PAM) recognition and RNA-DNA base-pairing that serves as a final specificity checkpoint before DNA double-strand break formation.

http://www.ncbi.nlm.nih.gov/pubmed/26524520

CRISPR-Cas9 and plant (6)

Genome Biol. 2015 Nov 6;16(1):232. doi: 10.1186/s13059-015-0796-9.

High-frequency, precise modification of the tomato genome.

Čermák T[1], Baltes NJ[2], Čegan R[3], Zhang Y[4], Voytas DF[5].

Author information

Abstract

BACKGROUND: The use of homologous recombination to precisely modify plant genomes has been challenging, due to the lack of efficient methods for delivering DNA repair templates to plant cells. Even with the advent of sequence-specific nucleases, which stimulate homologous recombination at predefined genomic sites by creating targeted DNA double-strand breaks, there are only a handful of studies that report precise editing of endogenous genes in crop plants. More efficient methods are needed to modify plant genomes through homologous recombination, ideally without randomly integrating foreign DNA.

RESULTS: Here, we use geminivirus replicons to create heritable modifications to the tomato genome at frequencies tenfold higher than traditional methods of DNA delivery (i.e., Agrobacterium). A strong promoter was inserted upstream of a gene controlling anthocyanin biosynthesis, resulting in overexpression and ectopic accumulation of pigments in tomato tissues. More than two-thirds of the insertions were precise, and had no unanticipated sequence modifications. Both TALENs and CRISPR/Cas9 achieved gene targeting at similar efficiencies. Further, the targeted modification was transmitted to progeny in a Mendelian fashion. Even though donor molecules were replicated in the vectors, no evidence was found of persistent extra-chromosomal replicons or off-target integration of T-DNA or replicon sequences.

CONCLUSIONS: High-frequency, precise modification of the tomato genome was achieved using geminivirus replicons, suggesting that these vectors can overcome the efficiency barrier that has made gene targeting in plants challenging. This work provides a foundation for efficient genome editing of crop genomes without the random integration of foreign DNA.

http://www.ncbi.nlm.nih.gov/pubmed/26541286

Herbicides 1

J Agric Food Chem. 2015 Oct 28. [Epub ahead of print]

Spot Spraying Reduces Herbicide Concentrations in Runoff.

Melland AR[1], Silburn DM[1,2], McHugh AD[3], Fillols E[4], Rojas-Ponce S[2], Baillie C[1], Lewis S[5].

Author information

Abstract

Rainfall simulator trials were conducted on sugar cane paddocks across dry-tropical and subtropical Queensland, Australia, to examine the potential for spot spraying to reduce herbicide losses in runoff. Recommended rates of the herbicides glyphosate, 2,4-D, fluoroxypyr, atrazine, and diuron were sprayed onto 0, 20, 40, 50, 70, or 100% of the area of runoff plots. Simulated rainfall was applied 2 days after spraying to induce runoff at one plant cane and three ratoon crop sites. Over 50% of all herbicides were transported in the dissolved phase of runoff, regardless of the herbicide's sediment-water partition coefficient. For most sites and herbicides, runoff herbicide concentrations decreased with decreasing spray coverage and with decreasing herbicide load in the soil and cane residues. Importantly, sites with higher infiltration prior to runoff and lower total runoff had lower runoff herbicide concentrations.

http://www.ncbi.nlm.nih.gov/pubmed/26479195

Herbicides 2

Arch Environ Contam Toxicol. 2015 Nov;69(4):577-85. doi: 10.1007/s00244-015-0171-6. Epub 2015 Jun 17.

Environmentally Relevant Concentrations of Atrazine and Ametrine Induce Micronuclei Formation and Nuclear Abnormalities in Erythrocytes of Fish.

Botelho RG[1], Monteiro SH[2], Christofoletti CA[3], Moura-Andrade GC[4], Tornisielo VL[4].

Author information

Abstract

A rapid and sensitive method using liquid chromatography coupled with mass spectrometry triple quadrupole direct aqueous injection for analysis of atrazine and ametrine herbicides in surface waters was developed. According to the validation method, water samples from six different locations in the Piracicaba River were collected monthly from February 2011 to January 2012 and injected into a liquid chromatographer/dual mass spectrometer without the need for sample extraction. The method was validated and shown to be precise and accurate; limits of detection and quantification were 0.07 and 0.10 μg L(-1) for atrazine and 0.09 and 0.14 μg L(-1) for ametrine. During the sampling period, concentrations of atrazine ranged from 0.11 to 1.92 μg L(-1) and ametrine from 0.25 to 1.44 μg L(-1). After analysis of the herbicides, Danio rerio were exposed a range of concentrations found in the river water to check the induction of micronuclei and nuclear abnormalities (NAs) in erythrocytes. Concentrations of atrazine and ametrine >1.0 and 1.5 μg L(-1), respectively, induced MN formation in D. rerio. Ametrine was shown to be more genotoxic to D. rerio because a greater incidence of NAs was observed compared with atrazine. Therefore, environmentally relevant concentrations of atrazine and ametrine found in the Piracicaba River are dangerous to the aquatic biota.

http://www.ncbi.nlm.nih.gov/pubmed/26081367

Rice transformation 1

Full text not available

Genet Mol Res. 2015 Oct 29;14(4):13667-78. doi: 10.4238/2015.October.28.29.

Drought-tolerant rice germplasm developed from an Oryza officinalis transformation-competent artificial chromosome clone.

Liu R[1], Zhang HH[1], Chen ZX[1], Shahid MQ[1], Fu XL[1], Liu XD[2].

Author information

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Abstract

Oryza officinalis has proven to be a natural gene reservoir for the improvement of domesticated rice as it carries many desirable traits; however, the transfer of elite genes to cultivated rice by conventional hybridization has been a challenge for rice breeders. In this study, the conserved sequence of plant stress-related NAC transcription factors was selected as a probe to screen the O. officinalis genomic transformation-competent artificial chromosome library by Southern blot; 11 positive transformation-competent artificial chromosome clones were subsequently detected. By Agrobacterium-mediated transformation, an indica rice variety, Huajingxian 74 (HJX74), was transformed with a TAC clone harboring a NAC gene-positive genomic fragment from O. officinalis. Molecular analysis revealed that the O. officinalis genomic fragment was integrated into the genome of HJX74. The transgenic lines exhibited high tolerance to drought stress. Our results demonstrate that the introduction of stress-related transformation-competent artificial chromosome clones, coupled with a transgenic validation approach, is an effective method of transferring agronomically important genes from O. officinalis to cultivated rice.

http://www.ncbi.nlm.nih.gov/pubmed/26535682

Rice transformation 2

PLoS One. 2015 Nov 3;10(11):e0141530. doi: 10.1371/journal.pone.0141530. eCollection 2015.

Expression of the Rice Arginase Gene OsARG in Cotton Influences the Morphology and Nitrogen Transition of Seedlings.

Meng Z[1], Meng Z[1], Zhang R[1], Liang C[1], Wan J[2], Wang Y[3], Zhai H[1], Guo S[1].

Author information

Abstract

Arginase is the only enzyme capable of producing urea in plants. This enzyme also contributes to many important biological functions during plant growth and development, such as seed development, root development and plant nitrogen using. The unique rice arginase gene OsARG is known to affect nitrogen use efficiency and is also associated with higher yields in rice. In this study, we transformed OsARG into upland cotton R18 by Agrobacterium-mediated genetic transformation and analyzed the function of OsARG in transgenic cotton. Two independent OsARG expression transgenic cotton lines, ARG-26 and ARG-38, were obtained via transformation. Southern blot analysis indicated that two copies and one copy of the OsARG gene were integrated into the ARG-26 and ARG-38 genomes, respectively. Enzyme activity and RNA transcription analysis revealed that the OsARG gene is highly expressed in cotton. The nitric oxide content and the morphology of ARG-26 and ARG-38 seedlings were both affected by expression of the OsARG gene. Field experiments indicated that the polyamine and nitrogen content increased by more than two-fold in the T3 generation plants of the transgenic cotton lines ARG-26-2, ARG-26-7, ARG-38-8, and ARG-38-11, as compared with the control plants. After harvesting cotton fibers grown in field conditions, we analyzed the quality of fiber and found that the fiber length was increased in the transgenic lines. The average cotton fiber length for all of the transgenic cotton lines was two millimeters longer than the fibers of the control plants; the average cotton fiber lengths were 31.94 mm, 32.00 mm, 32.68 mm and 32.84 mm in the ARG-26ARG-26-2, ARG-26-7, ARG-38-8 and ARG-38-11 lines, respectively but the average fiber length of the control plants was 29.36mm. Our results indicate that the OsARG gene could potentially be used to improve cotton fiber length traits.

Genetic transformation and screening of cotton transformants

The method of cotton transformation and the tissue culture conditions used in this study were as previously described in Meng *et al* [19]. Hypocotyls were excised from 5- to 6-day-old seedlings and used as explants for callus induction. All offspring from each generation of transgenic cotton were screened via PCR and for the presence of the kanamycin resistance gene *Npt*II, and then bred via self-fertilization. The PCR primer pair *OsARG*-F and *OsARG*-R (S1 Table)

http://www.ncbi.nlm.nih.gov/pubmed/26528551

C4 plants 1

Plant Cell Environ. 2015 Nov 2. doi: 10.1111/pce.12665. [Epub ahead of print]

Evolutionary implications of C3 -C4 intermediates in the grass Alloteropsis semialata.

Lundgren MR[1], Christin PA[1], Gonzalez Escobar E[1], Ripley BS[2], Besnard G[3], Long CM[4], Hattersley PW[5], Ellis RP[6], Leegood RC[1], Osborne CP[1].

Author information

Abstract

C_4 photosynthesis is a complex trait resulting from a series of anatomical and biochemical modifications to the ancestral C_3 pathway. It is thought to evolve in a stepwise manner, creating intermediates with different combinations of C_4 -like components. Determining the adaptive value of these components is key to understanding how C_4 photosynthesis can gradually assemble through natural selection. Here, we decompose the photosynthetic phenotypes of numerous individuals of the grass Alloteropsis semialata, the only species known to include both C_3 and C_4 genotypes. Analyses of δ^{13} C, physiology, and leaf anatomy demonstrate for the first time the existence of physiological C_3 -C_4 intermediate individuals in the species. Based on previous phylogenetic analyses, the C_3 -C_4 individuals are not hybrids between the C_3 and C_4 genotypes analysed, but instead belong to a distinct genetic lineage, and might have given rise to C_4 descendants. C_3 A. semialata, present in colder climates, likely represents a reversal from a C_3 -C_4 intermediate state, indicating that, unlike C_4 photosynthesis, evolution of the C_3 -C_4 phenotype is not irreversible.

http://www.ncbi.nlm.nih.gov/pubmed/26524631

C4 plants 2

Plant Physiol. 2015 Nov;169(3):1850-61. doi: 10.1104/pp.15.00586. Epub 2015 Sep 15.

Temperature Responses of C4 Photosynthesis: Biochemical Analysis of Rubisco, Phosphoenolpyruvate Carboxylase, and Carbonic Anhydrase in Setaria viridis.

Boyd RA[1], Gandin A[1], Cousins AB[2].

Author information

Abstract

The photosynthetic assimilation of CO2 in C4 plants is potentially limited by the enzymatic rates of Rubisco, phosphoenolpyruvate carboxylase (PEPc), and carbonic anhydrase (CA). Therefore, the activity and kinetic properties of these enzymes are needed to accurately parameterize C4 biochemical models of leaf CO2 exchange in response to changes in CO2 availability and temperature. There are currently no published temperature responses of both Rubisco carboxylation and oxygenation kinetics from a C4 plant, nor are there known measurements of the temperature dependency of the PEPc Michaelis-Menten constant for its substrate HCO3 (-), and there is little information on the temperature response of plant CA activity. Here, we used membrane inlet mass spectrometry to measure the temperature responses of Rubisco carboxylation and oxygenation kinetics, PEPc carboxylation kinetics, and the activity and first-order rate constant for the CA hydration reaction from 10°C to 40°C using crude leaf extracts from the C4 plant Setaria viridis. The temperature dependencies of Rubisco, PEPc, and CA kinetic parameters are provided. These findings describe a new method for the investigation of PEPc kinetics, suggest an HCO3 (-) limitation imposed by CA, and show similarities between the Rubisco temperature responses of previously measured C3 species and the C4 plant S. viridis.

http://www.ncbi.nlm.nih.gov/pubmed/26373659

C4 plants 3

Plant Physiol. 2015 Nov;169(3):1755-65. doi: 10.1104/pp.15.01054. Epub 2015 Sep 2.

Changes in Whole-Plant Metabolism during the Grain-Filling Stage in Sorghum Grown under Elevated CO2 and Drought.

De Souza AP[1], Cocuron JC[1], Garcia AC[1], Alonso AP[2], Buckeridge MS[2].

Author information

Abstract

Projections indicate an elevation of the atmospheric CO2 concentration ([CO2]) concomitant with an intensification of drought for this century, increasing the challenges to food security. On the one hand, drought is a main environmental factor responsible for decreasing crop productivity and grain quality, especially when occurring during the grain-filling stage. On the other hand, elevated [CO2] is predicted to mitigate some of the negative effects of drought. Sorghum (Sorghum bicolor) is a C4 grass that has important economical and nutritional values in many parts of the world. Although the impact of elevated [CO2] and drought in photosynthesis and growth has been well documented for sorghum, the effects of the combination of these two environmental factors on plant metabolism have yet to be determined. To address this question, sorghum plants (cv BRS 330) were grown and monitored at ambient (400 µmol mol(-1)) or elevated (800 µmol mol(-1)) [CO2] for 120 d and subjected to drought during the grain-filling stage. Leaf photosynthesis, respiration, and stomatal conductance were measured at 90 and 120 d after planting, and plant organs (leaves, culm, roots, prop roots, and grains) were harvested. Finally, biochemical composition and intracellular metabolites were assessed for each organ. As expected, elevated [CO2] reduced the stomatal conductance, which preserved soil moisture and plant fitness under drought. Interestingly, the whole-plant metabolism was adjusted and protein content in grains was improved by 60% in sorghum grown under elevated [CO2].

Table I. *Biomass (g) and starch, fatty acids, and proteins contents (% of dry weight) of leaves, culm, roots, prop roots, and grains of sorghum 'BRS 330' at ambient and elevated CO_2 at 90 and 120 DAP*

Values are means ± SD of biological replicates. $n = 3$. Boldface values indicate significant statistical differences between treatments ($P < 0.05$). n.d., Not detected.

Organ	DAP	Biomass		Starch		Fatty Acids		Proteins	
		Ambient CO_2	Elevated CO_2	Ambient CO_2	Elevated CO_2	Ambient CO_2	Elevated CO_2	Ambient CO_2	Elevated CO_2
Leaves	90	23.54 ± 6.84	32.63 ± 5.4	n.d.	n.d.	1.49 ± 0.09	1.42 ± 0.04	14.4 ± 1.23	16.8 ± 0.45
	120	**17.75 ± 2.04**	**26.19 ± 3.8**	n.d.	n.d.	1.09 ± 0.07	1.23 ± 0.05	16.3 ± 2.01	19.1 ± 2.70
Culm	90	13.25 ± 4.51	15.49 ± 2.96	n.d.	n.d.	0.29 ± 0.02	0.30 ± 0.03	2.2 ± 0.26	1.9 ± 0.08
	120	13.69 ± 4.79	10.80 ± 1.96	n.d.	n.d.	0.22 ± 0.02	0.24 ± 0.00	2.0 ± 0.32	1.9 ± 0.32
Roots	90	10.74 ± 3.54	9.17 ± 2.03	n.d.	n.d.	0.29 ± 0.02	0.29 ± 0.01	**3.9 ± 0.15**	**3.4 ± 0.22**
	120	10.41 ± 4.34	14.25 ± 7.79	n.d.	n.d.	0.21 ± 0.00	0.21 ± 0.00	3.2 ± 0.15	3.6 ± 0.42
Prop roots	90	**5.46 ± 1.78**	**10.48 ± 1.2**	n.d.	n.d.	0.21 ± 0.01	0.19 ± 0.02	4.1 ± 0.69	3.1 ± 0.16
	120	2.76 ± 0.16	3.5 ± 0.72	n.d.	n.d.	0.18 ± 0.01	0.17 ± 0.01	2.5 ± 0.12	2.3 ± 0.28
Grains	90	34.74 ± 3.14	30.08 ± 7.51	57.4 ± 4.51	51.6 ± 6.06	**1.91 ± 0.14**	**1.32 ± 0.11**	**7.5 ± 0.53**	**10.1 ± 0.70**
	120	61.95 ± 16.92	46.91 ± 13.56	59.9 ± 1.15	57.3 ± 2.43	2.09 ± 0.03	2.10 ± 0.13	**5.1 ± 0.10**	**8.1 ± 0.68**

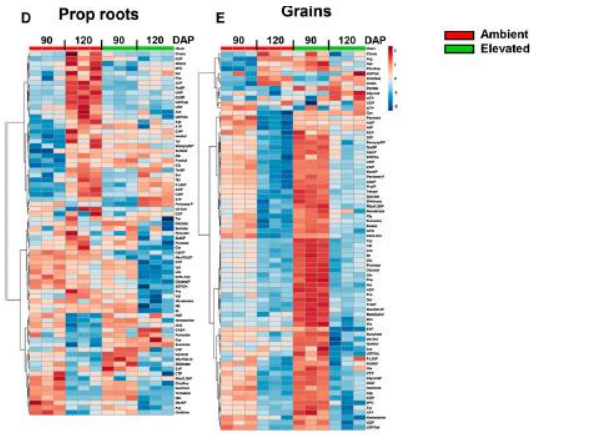

Figure 7. Heat maps showing the variation in the amount of metabolites in sorghum 'BRS 330' grown under ambient and elevated [CO_2] at 90 and 120 DAP in leaves (A), culm (B), roots (C), prop roots (D), and grains (E). 2/3PGA, 2- or 3-phosphoglycerate; 6PG, 6-phosphogluconate; AKG, α-ketoglutarate; cis-aco, cis-aconitate; Deoxyxyl5P, deoxyxylulose-5-phosphate; E4P, erythrose-4-phosphate; F1,6bP, Fru-1,6-bisP; Fru6P, Fru-6-P; GABA, γ-aminobutyric acid; Gal1p, Gal-1-P; Glc6P, Glc-6-P; Glycerol3P,

C4 plants

J Exp Bot. 2015 Nov;66(21):6535-49. doi: 10.1093/jxb/erv371. Ep

Constraints to the potential efficiency of biochemistry to canopy physiology and c

Yin X[1], Struik PC[2].

Author information

Abstract

A new simple framework was proposed to quantify the the need to account for (i) efficiency gain when scaling closure during early and late phases of the crop cycle. physiological steps. For a given amount of daily radiati of the photosynthetic light response. Due to the higher photochemical quenching, compared with C3 leaves. T this difference in the curvature of the light response, ca profile in the canopy, and productivity gain from future higher in C3 than in C4 species. The indicative efficien C4 crops, respectively, when grown under well-manag high as 3.6 and 4.1% for C3 and C4 crops, respectivel

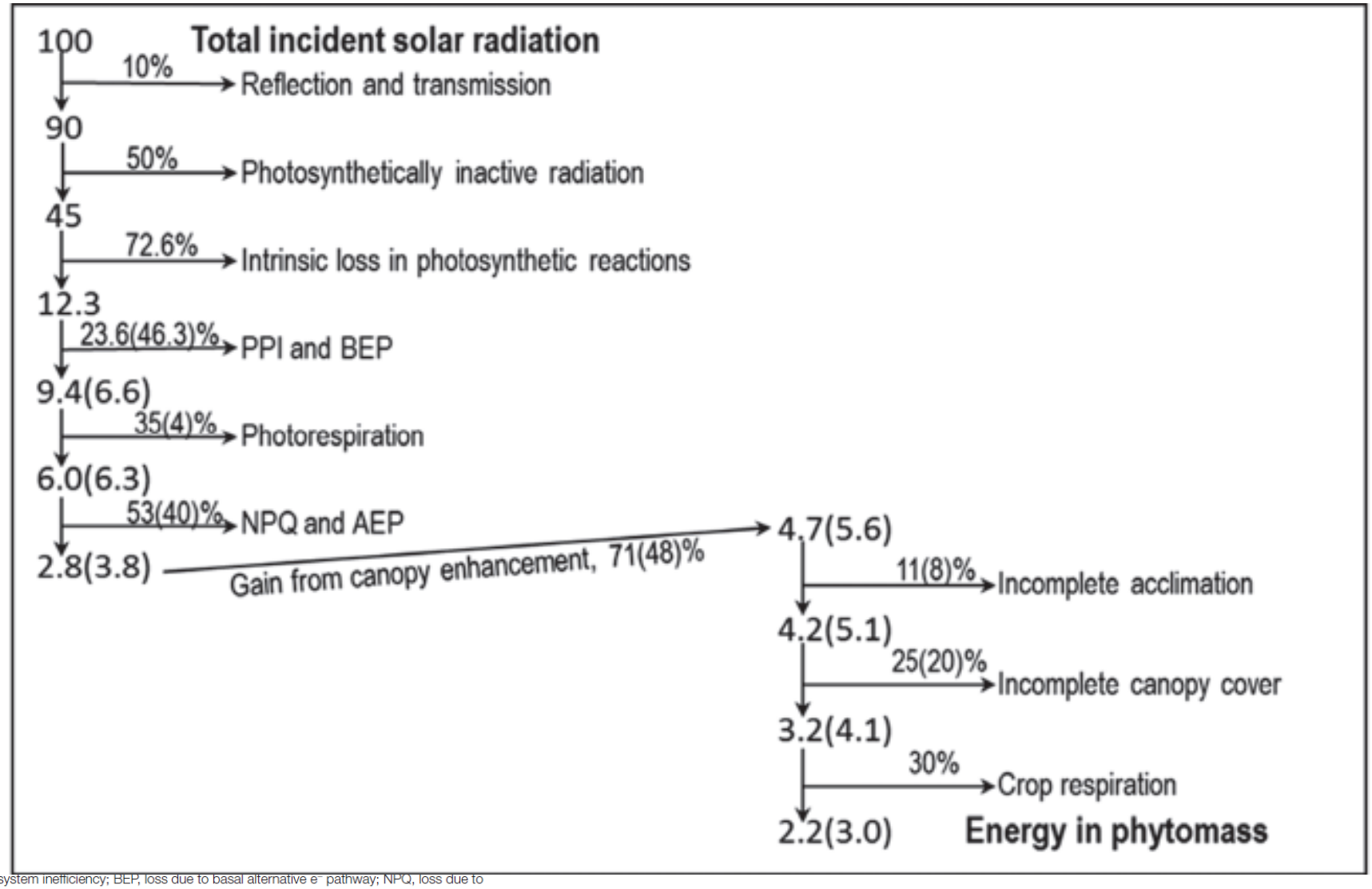

Fig. 5. Indicative values for losses (%) estimated from our two-se phytomass energy by present C_3 (values outside brackets) and C, the first series represents the theoretical maximum efficiency (%) first series refer to daily average efficiency (%) for uppermost leave total incident solar radiation=20 MJ m^{-2} d^{-1}, direct-light fraction=C atmospheric [CO_2]=400 μmol mol^{-1}. PPI, loss due to primary photosystem inefficiency; BEP, loss due to basal alternative e^- pathway; NPQ, loss due to non-photochemical quenching; AEP, loss due to additional alternative e^- pathway.

http://www.ncbi.nlm.nih.gov/pubmed/26224881

C4 plants 5

Glob Chang Biol. 2015 Nov;21(11):4237-49. doi: 10.1111/gcb.13013. Epub 2015 Sep 23.

Canopy warming caused photosynthetic acclimation and reduced seed yield in maize grown at ambient and elevated [CO2].

Ruiz-Vera UM[1], Siebers MH[1], Drag DW[1], Ort DR[1,2], Bernacchi CJ[1,2].

Author information

Abstract

Rising atmospheric CO2 concentration ([CO2]) and attendant increases in growing season temperature are expected to be the most important global change factors impacting production agriculture. Although maize is the most highly produced crop worldwide, few studies have evaluated the interactive effects of elevated [CO2] and temperature on its photosynthetic physiology, agronomic traits or biomass, and seed yield under open field conditions. This study investigates the effects of rising [CO2] and warmer temperature, independently and in combination, on maize grown in the field throughout a full growing season. Free-air CO2 enrichment (FACE) technology was used to target atmospheric [CO2] to 200 μmol mol(-1) above ambient [CO2] and infrared heaters to target a plant canopy increase of 3.5 °C, with actual season mean heating of ~2.7 °C, mimicking conditions predicted by the second half of this century. Photosynthetic gas-exchange parameters, leaf nitrogen and carbon content, leaf water potential components, and developmental measurements were collected throughout the season, and biomass and yield were measured at the end of the growing season. As predicted for a C4 plant, elevated [CO2] did not stimulate photosynthesis, biomass, or yield. Canopy warming caused a large shift in aboveground allocation by stimulating season-long vegetative biomass and decreasing reproductive biomass accumulation at both CO2 concentrations, resulting in decreased harvest index. Warming caused a reduction in photosynthesis due to down-regulation of photosynthetic biochemical parameters and the decrease in the electron transport rate. The reduction in seed yield with warming was driven by reduced photosynthetic capacity and by a shift in aboveground carbon allocation away from reproduction. This field study portends that future warming will reduce yield in maize, and this will not be mitigated by higher atmospheric [CO2] unless appropriate adaptation traits can be introduced into future cultivars.

http://www.ncbi.nlm.nih.gov/pubmed/26119211

Anticancer plant 1

Life Sci. 2015 Nov 2. pii: S0024-3205(15)30061-8. doi: 10.1016/j.lfs.2015.10.035. [Epub ahead of print]

Chrysin rich Scutellaria discolor Colebr. induces cervical cancer cell death via the induction of cell cycle arrest and caspase-dependent apoptosis.

Laishram S[1], Moirangthem DS[1], Borah JC[1], Pal BC[1], Suman P[2], Gupta SK[2], Kalita MC[3], Talukdar NC[4].

Author information

Abstract

AIMS: Scutellaria discolor Colebr. has been extensively used in traditional medicine against several diseases. The purpose of this study was to investigate the anticancer potential of S. discolor and to isolate the bioactive principle responsible for the anticancer activity.

METHODS: Cytotoxicity experiments were performed on cancer and normal cells using MTT assay. The mechanism of cell death was evaluated using real time PCR array, fluorescence microscopy, flow cytometry and Western blotting. MTT assay guided isolation (partition and column chromatography) was performed to identify the antiproliferative principle. Quantification of the active principle was done using HPLC.

KEY FINDINGS: Acetone extract of S. discolor (SDE) inhibited the growth and survival of cancer cells to varying degree, but the inhibition was found to be maximum in cervical cancer cell lines. There was no significant toxicity induced to normal cells. The cell death was mediated through apoptosis. There was increased mitochondrial membrane depolarization, expression of Bax, caspase-9, caspase-3 and cleaved-PARP indicating that SDE-induced caspase dependent apoptosis in HeLa cells. Moreover, SDE caused cell cycle arrest in G_2 phase in HeLa cells. Cytotoxicity guided fractionation of SDE led to the isolation of chrysin as the active principle responsible for the antiproliferative activity for cervical cancer cells. Interestingly, chrysin was the major phytochemical constituent present in S. discolor.

SIGNIFICANCE: S. discolor is an important anticancer plant and a new source of chrysin.

http://www.ncbi.nlm.nih.gov/pubmed/26541229

Anticancer plant 2

Nat Prod Res. 2015 Nov 5:1-6. [Epub ahead of print]

Cytotoxic oplopane sesquiterpenoids from Arnoglossum atriplicifolium.

Clement JA[1,2], Bleich RM[1], Campbell HE[1], Naylor K[1], Flood MJ[1], Kelly RM[3], Wu SB[4], Kennelly EJ[4], Schmitt JD[3].

Author information

Abstract

Pale Indian plantain (Arnoglossum atriplicifolium (L.) H. Rob.) is a plant with traditional medicinal usage among the Cherokee Native American tribe for treating cancer. Two oplopane sesquiterpenoids were isolated from an extract of A. atriplicifolium from Western North Carolina. The compounds were isolated by bioassay-guided fractionation using an MCF-7 breast tumour cell line assay. The known compound (1S,6R,7R,8R)-1-acetoxy-6,7-diangeloxy-8,10-epoxy-2-oxo-oplopa-3,14Z,11,12-dien-13-al (1) had an EC_{50} value of 9.0 μM against MCF-7 cells, while the new compound (1S,3R,6R,7R,8R,11S)-1-acetoxy-6,7-diangeloxy-8,10,11,13-bisepoxyoplopan-2-one (2) had an EC_{50} value of 96 μM. The compounds were characterised by 1D and 2D NMR spectroscopy and by comparison with literature values in the case for 1. Based on NOESY analysis, a correction of the relative configuration for 1 is presented. The presence of these compounds may help to explain the folk remedy usage of this plant as an anticancer agent.

http://www.ncbi.nlm.nih.gov/pubmed/26540019

Anticancer plant 3

Int J Mol Med. 2015 Oct 27. doi: 10.3892/ijmm.2015.2396. [Epub ahead of print]

Sulforaphane exerts anti-inflammatory effects against lipopolysaccharide-induced acute lung injury in mice through the Nrf2/ARE pathway.

Qi T[1], Xu F[2], Yan X[1], Li S[1], Li H[1].

Author information

Abstract

Sulforaphane (1-isothiocyanate-4-methyl sulfonyl butane) is a plant extract (obtained from cruciferous vegetables, such as broccoli and cabbage) and is known to exert anticancer, antioxidant and anti-inflammatory effects. It stimulates the generation of human or animal cells, which is beneficial to the body. The aim of the current study was to determine whether sulforaphane protects against lipopolysaccharide (LPS)–induced acute lung injury (ALI) through its anti-inflammatory effects, and to investigate the signaling pathways involved. For this purpose, male BALB/c mice were treated with sulforaphane (50 mg/kg) and 3 days later, ALI was induced by the administration of LPS (5 mg/kg) and we thus established the model of ALI. Our results revealed that sulforaphane significantly decreased lactate dehydrogenase (LDH) activity (as shown by LDH assay), the wet-to-dry ratio of the lungs and the serum levels of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) (measured by ELISA), as well as nuclear factor-κB protein expression in mice with LPS-induced ALI. Moreover, treatment with sulforaphane significantly inhibited prostaglandin E2 (PGE2) production, and cyclooxygenase-2 (COX-2), matrix metalloproteinase-9 (MMP-9) protein expression (as shown by western blot analysis), as well as inducible nitric oxide synthase (iNOS) activity in mice with LPS-induced ALI. Lastly, we noted that pre-treatment with sulforaphane activated the nuclear factor-E2-related factor 2 (Nrf2)/antioxidant response element (ARE) pathway in the mice with LPS-induced ALI. These findings demonstrate that sulforaphane exerts protective effects against LPS-induced ALI through the Nrf2/ARE pathway. Thus, sulforaphane may be a potential a candidate for use in the treatment of ALI.

http://www.ncbi.nlm.nih.gov/pubmed/26531002

Anticancer plant 4

Bakupari, tropical fruit

BMC Complement Altern Med. 2015 Oct 30;15(1):393. doi: 10.1186/s12906-015-0911-1.

Anticancer activity of 7-epiclusianone, a benzophenone from Garcinia brasiliensis, in glioblastoma.

Sales L[1], Pezuk JA[2], Borges KS[3], Brassesco MS[4], Scrideli CA[5], Tone LG[6], Santos MH[7], Ionta M[8], Oliveira JC[9].

Author information

Abstract

BACKGROUND: Glioblastoma is the most common tumor of the central nervous system and one of the hardest tumors to treat. Consequently, the search for novel therapeutic options is imperative. 7-epiclusianone, a tetraprenylated benzophenone isolated from the epicarp of the native plant Garcinia brasiliensis, exhibits a range of biological activities but its prospect anticancer activity is underexplored. Thus, the aim of the present study was to evaluate the influence of 7-epiclusianone on proliferation, clonogenic capacity, cell cycle progression and induction of apoptosis in two glioblastoma cell lines (U251MG and U138MG).

METHODS: Cell viability was measured by the MTS assay; for the clonogenic assay, colonies were stained with Giemsa and counted by direct visual inspection; For cell cycle analysis, cells were stained with propidium iodide and analyzed by cytometry; Cyclin A expression was determined by immunoblotting; Apoptotic cell death was determined by annexin V fluorescein isothiocyanate labeling and Caspase-3 activity in living cells.

RESULTS: Viability of both cell lines was drastically inhibited; moreover, the colony formation capacity was significantly reduced, demonstrating long-term effects even after removal of the drug. 7-epiclusianone treatment at low concentrations also altered cell cycle progression, decreased the S and G2/M populations and at higher concentrations increased the number of cells at sub-G1, in concordance with the increase of apoptotic cells.

CONCLUSION: The present study demonstrates for the first time the anticancer potential of 7-epiclusianone against glioblastoma cells, thus meriting its further investigation as a potential therapeutic agent.

http://www.ncbi.nlm.nih.gov/pubmed/26518729

Anticancer plant 5

Anticancer Res. 2015 Nov;35(11):5773-88.

Natural Products That Target Cancer Stem Cells.

Moselhy J[1], Srinivasan S[1], Ankem MK[1], Damodaran C[2].

Author information

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Abstract

The cancer stem cell model suggests that tumor initiation is governed by a small subset of distinct cells with stem-like character termed cancer stem cells (CSCs). CSCs possess properties of self-renewal and intrinsic survival mechanisms that contribute to resistance of tumors to most chemotherapeutic drugs. The failure to eradicate CSCs during the course of therapy is postulated to be the driving force for tumor recurrence and metastasis. Recent studies have focused on understanding the unique phenotypic properties of CSCs from various tumor types, as well as the signaling pathways that underlie self-renewal and drug resistance. Natural products (NPs) such as those derived from botanicals and food sources may modulate vital signaling pathways involved in the maintenance of CSC phenotype. The Wingless/Integrated (WNT), Hedgehog, Notch and PI3K/AKT/mTOR pathways have all been associated with quiescence and self-renewal of CSCs, as well as execution of CSC function including differentiation, multidrug resistance and metastasis. Recent studies evaluating NPs against CSC support the epidemiological evidence linking plant-based diets with reduced malignancy rates. This review covers the key aspects of NPs as modulators of CSC fate.

http://www.ncbi.nlm.nih.gov/pubmed/26503998

Anticancer plant 6

J Agric Food Chem. 2015 Nov 4;63(43):9504-12. doi: 10.1021/acs.jafc.5b03045. Epub 2015 Oct 21.

Physapubescin B Exhibits Potent Activity against Human Prostate Cancer In Vitro and In Vivo.

Ding W[1], Hu Z[1], Zhang Z[2], Ma Q[1], Tang H[2], Ma Z[1].

Author information

Abstract

The present data showed that a natural compound isolated from the plant Physalis pubescens L. (Solanaceae), physapubescin B, exhibited antitumor activity against prostate cancer in vitro and in vivo. Treating prostate cancer cells with physapubescin B resulted in the accumulation of cells in the G2/M phase, which was associated with reduced Cdc25C levels and increased levels of CyclinB1, P21 as well as p-Cdk1 (Tyr15). Additionally, reactive oxygen species (ROS) generation was increased in physapubescin B-treated PC-3 cells. Furthermore, the physapubescin B-induced decrease of Cdc25C protein expression together with the G2/M phase cell cycle arrest were significantly abrogated by antioxidant NAC and GSH. Our data also demonstrated that physapubescin B exhibited strong in vivo antitumor efficacy in human prostate cancer PC3 xenograft. In conclusion, our results provide clear evidence that physapubescin B exhibits antitumor activity both in vitro and in vivo and deserves further development as an anticancer agent.

http://www.ncbi.nlm.nih.gov/pubmed/26415552

Anticancer plant 7

Purification, structural characterization and anticancer activity of the novel polysaccharides from Rhynchosia minima root.

Jia X[1], Zhang C[1], Qiu J[1], Wang L[2], Bao J[1], Wang K[1], Zhang Y[1], Chen M[1], Wan J[1], Su H[1], Han J[2], He C[3].

Author information

Abstract

Three novel acidic polysaccharides termed PRM1, PRM3 and PRM5 were purified from Rhynchosia minima root using DEAE-52 cellulose and sephadex G-150 column chromatography. Their structures were characterized by ultraviolet (UV) and Fourier transform infrared (FTIR) spectrometry, gel permeation chromatography (GPC), gas chromatography-mass spectrometry (GC-MS), and differential scanning colorimeter (DSC) analysis. The uronic acid contents of PRM1, PRM3 and PRM5 were 30.7%, 12.7% and 47.7%, respectively. PRM1 (143.2 kDa), PRM3 (105.3 kDa) and PRM5 (162.1 kDa) were heteropolysaccharides because they were composed of arabinose, mannose, glucose and galactose. Their enthalpy values were 201.0, 111.0 and 206.8 J/g, respectively. PRM3 and PRM1 exhibited strong in vitro anticancer activity against lung cancer A549 and liver cancer HepG2 cells in a dose-dependent manner. These findings suggested that PRM1 and PRM3 could be potentially developed as natural anticancer agents.

Common names	**SENEGAL**: *ARABIC (Senegal)* mesran l'avar (JB) musran l'ehoir (JB) *BEDIK* gi-nyí go-kέr = bean of the monkey (FG&G) *FULA-PULAAR (Senegal)* ñébé lèlli (JB) *MANDING-BAMBARA* potro (JB) *WOLOF* mborosan (JB) sèb u kévèl (JB) **GUINEA**: *BASARI* a-tièɓɛn
Uses	(root-bark) Food: sweets, sweetmets (leaf, root) Medicines: generally healing (root) Medicines: laxatives, etc. (root) Medicines: diarrhoea, dysentery (root) Medicines: vermifuges (leaf-sap, root) Medicines: anus, haemorrhoids (root) Medicines: genital stimulants/depressants (leaf) Medicines: abortifacients, ecbolics Medicines: heart (seed) Phytochemistry: miscellaneously poisonous or repellent Agri-horticulture: fodder Agri-horticulture: composting, manuring
Description	A slender trailing or twining herb from a woody root-stock, widespread in the open savanna and drier parts of the Region, variable in three varieties (dealt with together here), from Senegal to N and S Nigeria, and more or less pan-tropical Africa, and tr

http://www.ncbi.nlm.nih.gov/pubmed/26256325

Anticancer plant 8

J Ethnopharmacol. 2015 Nov 4;174:644-58. doi: 10.1016/j.jep.2015.07.005. Epub 2015 Jul 10.

Cytotoxicity of 35 medicinal plants from Sudan towards sensitive and multidrug-resistant cancer cells.

Saeed ME[1], Abdelgadir H[2], Sugimoto Y[3], Khalid HE[2], Efferth T[4].

Author information

Abstract

BACKGROUND: Cancer is a complex disease with multiple genetic and epigenetic alterations. Since decades, the hallmark of cancer therapy is chemotherapy. Cytotoxic drugs erase rapidly dividing cells without sufficient differentiation between normal and cancerous cells resulting in severe side effects in normal tissues. Recently, strategies for cancer treatment focused on targeting specific proteins involved in tumor growth and progression. The present study was designed to investigate the cytotoxicity of 65 crude extracts from 35 Sudanese medicinal plants towards various cancer cell lines expressing molecular mechanisms of resistance towards classical chemotherapeutics (two ATP-binding cassette transporters, ABCB1 (P-glycoprotein) and ABCB5, tumor suppressor p53, epidermal growth factors receptor (EGFR). And the aim was to identify plant extracts and isolated compounds thereof with activity towards otherwise drug-resistant tumor cells.

METHODS: Cold maceration was performed to obtain crude extracts from the plants. The resazurin assay was used to determine cytotoxicity of the plant extracts. Microarray-based mRNA expression profiling, COMPARE, and hierarchical cluster analyses were applied to identify, which genes correlate with sensitivity or resistance to ambrosin, the main constituent of the most active extract Ambrosia maritima.

RESULTS: The results of the resazurin assay on different tumors showed that Lawsonia inermis, Trigonella foenum-graecum and Ambrosia maritma were the most active crude extracts. Ambrosin was selected as one active principle of A. maritima for microarray-based expression profiling. Genes from various functional groups (transcriptional regulators, signal transduction, membrane transporters, cytoskeleton organization, chaperones, immune system development and DNA repair) were significantly correlated with response of tumor cell lines to ambrosin.

CONCLUSION: The results revealed cytotoxicity and pharmacogenomics studies of Sudanese medicinal plants provide an attractive strategy for the development of novel cancer therapeutics with activity towards cell lines that resistance to established anticancer agents.

http://www.ncbi.nlm.nih.gov/pubmed/26165828

In planta transformation 1

Biotechnol Adv. 2015 Nov 1;33(6 Pt 2):1024-42. doi: 10.1016/j.biotechadv.2015.03.012. Epub 2015 Mar 25.

Transient plant transformation mediated by Agrobacterium tumefaciens: Principles, methods and applications.

Krenek P[1], Samajova O[2], Luptovciak I[3], Doskocilova A[4], Komis G[5], Samaj J[6].

Author information

Abstract

Agrobacterium tumefaciens is widely used as a versatile tool for development of stably transformed model plants and crops. However, the development of Agrobacterium based transient plant transformation methods attracted substantial attention in recent years. Transient transformation methods offer several applications advancing stable transformations such as rapid and scalable recombinant protein production and in planta functional genomics studies. Herein, we highlight Agrobacterium and plant genetics factors affecting transfer of T-DNA from Agrobacterium into the plant cell nucleus and subsequent transient transgene expression. We also review recent methods concerning Agrobacterium mediated transient transformation of model plants and crops and outline key physical, physiological and genetic factors leading to their successful establishment. Of interest are especially Agrobacterium based reverse genetics studies in economically important crops relying on use of RNA interference (RNAi) or virus-induced gene silencing (VIGS) technology. The applications of Agrobacterium based transient plant transformation technology in biotech industry are presented in thorough detail. These involve production of recombinant proteins (plantibodies, vaccines and therapeutics) and effectoromics-assisted breeding of late blight resistance in potato. In addition, we also discuss biotechnological potential of recombinant GFP technology and present own examples of successful Agrobacterium mediated transient plant transformations.

http://www.ncbi.nlm.nih.gov/pubmed/25819757

Molecular farming 1

Biomaterials. 2015 Nov;70:84-93. doi: 10.1016/j.biomaterials.2015.08.004. Epub 2015 Aug 5.

Low cost industrial production of coagulation factor IX bioencapsulated in lettuce cells for oral tolerance induction in hemophilia B.

Su J[1], Zhu L[2], Sherman A[2], Wang X[2], Lin S[1], Kamesh A[1], Norikane JH[3], Streatfield SJ[3], Herzog RW[4], Daniell H[5].

Author information

Abstract

Antibodies (inhibitors) developed by hemophilia B patients against coagulation factor IX (FIX) are challenging to eliminate because of anaphylaxis or nephrotic syndrome after continued infusion. To address this urgent unmet medical need, FIX fused with a transmucosal carrier (CTB) was produced in a commercial lettuce (Simpson Elite) cultivar using species specific chloroplast vectors regulated by endogenous psbA sequences. CTB-FIX (~1 mg/g) in lyophilized cells was stable with proper folding, disulfide bonds and pentamer assembly when stored ~2 years at ambient temperature. Feeding lettuce cells to hemophilia B mice delivered CTB-FIX efficiently to the gut immune system, induced LAP(+) regulatory T cells and suppressed inhibitor/IgE formation and anaphylaxis against FIX. Lyophilized cells enabled 10-fold dose escalation studies and successful induction of oral tolerance was observed in all tested doses. Induction of tolerance in such a broad dose range should enable oral delivery to patients of different age groups and diverse genetic background. Using Fraunhofer cGMP hydroponic system, ~870 kg fresh or 43.5 kg dry weight can be harvested per 1000 ft(2) per annum yielding 24,000-36,000 doses for 20-kg pediatric patients, enabling first commercial development of an oral drug, addressing prohibitively expensive purification, cold storage/transportation and short shelf life of current protein drugs.

http://www.ncbi.nlm.nih.gov/pubmed/26302233

Molecular farming 2

Biotechnol Lett. 2015 Nov;37(11):2147-50. doi: 10.1007/s10529-015-1908-z. Epub 2015 Jul 7.

Molecular pharming's foot in the FDA's door: Protalix's trailblazing story.

Mor TS[1].

Author information

Abstract

OBJECTIVES: This short commentary examines the factors that led to Food and Drug Administration's approval of the first plant-derived biologic.

RESULTS: In 2012, the first plant-derived protein pharmaceutical (biologic) was approved for commercial use in humans. The product, a recombinant form of human β-glucocerebrosidase marketed as ELELYSO, was developed by Protalix Biotherapeutics (Carmiel, Israel). The foresight to select this particular therapeutic product for development, flawless production pipeline, and serendipity seem to provide the key in explaining how ELELYSO became the first plant-derived biologic to achieve approval by Food and Drug Administration.

CONCLUSIONS: While the circumstances that enabled Protalix and its scientists to become the first to arrive at this historic milestone are perhaps unique, it is anticipated that more biologics will follow suit in winning regulatory endorsement.

KEYWORDS: Ebola; FDA-approval; Gaucher's disease; Molecular pharming; Plant-derived biologics

http://www.ncbi.nlm.nih.gov/pubmed/26149580

Cytochrome p450 1

Sci Rep. 2015 Oct 23;5:15581. doi: 10.1038/srep15581.

Silencing NADPH-cytochrome P450 reductase results in reduced acaricide resistance in Tetranychus cinnabarinus (Boisduval).

Shi L[1], Zhang J[1], Shen G[1], Xu Z[1], Wei P[1], Zhang Y[1], Xu Q[2], He L[1].

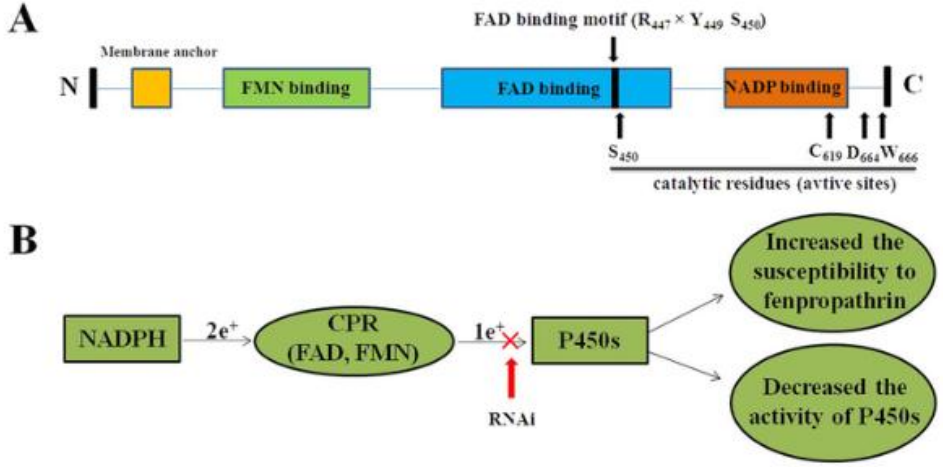
Author information

Abstract

Cytochrome P450 monooxygenases (P450s) are involved in metabolic resistance to insecticides and require NADPH cytochrome P450 reductase (CPR) to transfer electrons when they catalyze oxidation reactions. The carmine spider mite, Tetranychus cinnabarinus is an important pest mite of crop and vegetable plants worldwide, and its resistance to acaricides has quickly developed. However, the role of CPR on the formation of acaricide-resistance in T. cinnabarinus is still unclear. In this study, a full-length cDNA encoding CPR was cloned and characterized from T. cinnabarinus (designated TcCPR). TcCPR expression was detectable in all developmental stages of T. cinnabarinus, but it's much lower in eggs. TcCPR was up-regulated and more inducible with fenpropathrin treatment in the fenpropathrin-resistant (FeR) strain compared with the susceptible SS strain. Feeding of double-strand RNA was effective in silencing the transcription of TcCPR in T. cinnabarinus, which resulted in decreasing the activity of P450s and increasing the susceptibility to fenpropathrin in the FeR strain but not in the susceptible strain. The current results provide first evidence that the down-regulation of TcCPR contributed to an increase of the susceptibility to fenpropathrin in resistant mites. TcCPR could be considered as a novel target for the development of new pesticides.

Acaricides are pesticides that kill members of the arachnid subclass Acari, which includes ticks and mites

http://www.ncbi.nlm.nih.gov/pubmed/26493678



(A) Schematic drawing of TcCPR; (B) The role of TcCPR on P450 activities and acaricide resistance in *Tetranychus cinnabarinus*.

Cytochrome p450 1

Planta. 2015 Nov;242(5):1175-86. doi: 10.1007/s00425-015-2355-8. Epub 2015 Jun 24.

Biochemical characterization of allene oxide synthases from the liverwort Marchantia polymorpha and green microalgae Klebsormidium flaccidum provides insight into the evolutionary divergence of the plant CYP74 family.

Koeduka T[1], Ishizaki K[2], Mwenda CM[3], Hori K[4], Sasaki-Sekimoto Y[5], Ohta H[4,5], Kohchi T[6], Matsui K[7,8].

Author information

Abstract

MAIN CONCLUSION: Allene oxide synthases (AOSs) were isolated from liverworts and charophytes. These AOSs exhibited enzymatic properties similar to those of angiosperms but formed a distinct phylogenetic clade. Allene oxide synthase (AOS) and hydroperoxide lyase (HPL) mediate the formation of precursors of jasmonates and carbon-six volatiles, respectively. AOS and HPL utilize fatty acid hydroperoxides and belong to the plant cytochrome P450 74 (CYP74) family that mediates plant defense against herbivores, pathogens, or abiotic stresses. Although members of the CYP74 family have been reported in mosses and other species, the evolution and function of multiple CYP74 genes in plants remain elusive. Here, we show that the liverwort Marchantia polymorpha belongs to a basal group in the evolution of land plants; has two closely related proteins (59 % identity), MpAOS1 and MpAOS2, that are similar to moss PpAOS1 (49 and 47 % identity, respectively); and exhibits AOS activity but not HPL activity. We also found that the green microalgae Klebsormidium flaccidum, consist of multicellular and non-branching filaments, contains an enzyme, KfAOS, that is similar to PpAOS1 (37 % identity), and converts 13-hydroperoxide of linolenic acid to 12-oxo-phytodienoic acid in a coupled reaction with allene oxide cyclase. Phylogenetic analysis showed two evolutionarily distinct clusters. One cluster comprised AOS and HPL from charophytic algae, liverworts, and mosses, including MpAOSs and KfAOS. The other cluster was formed by angiosperm CYP74. Our results suggest that plant CYP74 enzymes with AOS, HPL, and divinyl ether synthase activities have arisen multiple times and in the two different clades, which occurred prior to the divergence of the flowering plant lineage.

http://www.ncbi.nlm.nih.gov/pubmed/26105654

Cytochrome p450 2

Protoplasma. 2015 Nov;252(6):1421-37. doi: 10.1007/s00709-015-0766-9. Epub 2015 Feb 17.

Light and auxin responsive cytochrome P450s from Withania somnifera Dunal: cloning, expression and molecular modelling of two pairs of homologue genes with differential regulation.

Srivastava S[1,2], Sangwan RS[3,4], Tripathi S[1], Mishra B[1], Narnoliya LK[1], Misra LN[1], Sangwan NS[5,6].

Author information

Abstract

Cytochrome P450s (CYPs) catalyse a wide variety of oxygenation/hydroxylation reactions that facilitate diverse metabolic functions in plants. Specific CYP families are essential for the biosynthesis of species-specialized metabolites. Therefore, we investigated the role of different CYPs related to secondary metabolism in Withania somnifera, a medicinally important plant of the Indian subcontinent. In this study, complete complementary DNAs (cDNAs) of four different CYP genes were isolated and christened as WSCYP93Id, WSCYP93Sm, WSCYP734B and WSCYP734R. These cDNAs encoded polypeptides comprising of 498, 496, 522 and 550 amino acid residues with their deduced molecular mass of 56.7, 56.9, 59.4 and 62.2 kDa, respectively. Phylogenetic study and molecular modelling analysis of the four cloned WSCYPs revealed their categorization into two CYP families (CYP83B1 and CYP734A1) belonging to CYP71 and CYP72 clans, respectively. BLASTp searches showed similarity of 75 and 56 %, respectively, between the two CYP members of CYP83B1 and CYP734A1 with major variances exhibited in their N-terminal regions. The two pairs of homologues exhibited differential expression profiles in the leaf tissues of selected chemotypes of W. somnifera as well as in response to treatments such as methyl jasmonate, wounding, light and auxin. Light and auxin regulated two pairs of WSCYP homologues in a developing seedling in an interesting differential manner. Their lesser resemblance and homology with other CYP sequences suggested these genes to be more specialized and distinct ones. The results on chemotype-specific expression patterns of the four genes strongly suggested their key/specialized involvement of the CYPs in the biosynthesis of chemotype-specific metabolites, though their further biochemical characterization would reveal the specificity in more detail. It is revealed that WSCYP93Id and WSCYP93Sm may be broadly involved in the oxygenation reactions in the plant and, thereby, control various pathways involving such metabolic reactions in the plant. As a representative experimental validation of this notion, WSCYP93Id was heterologouly expressed in Escherichia coli and catalytic capabilities of the recombinant WSCYP93Id protein were evaluated using withanolides as substrates. Optimized assays with some major withanolides (withanone, withaferin A and withanolide A) involving spectrophotometric as well as high-pressure liquid chromatography (HPLC)-based evaluation (product detection) of the reactions showed conversion of withaferin A to a hydroxylated product. The genes belonging to other CYP group are possibly involved in some specialised synthesis such as that of brassinosteroids.

ashwagandha, Indian ginseng, poison gooseberry, or winter cherry, is a plant in the Solanaceae or nightshade family.

http://www.ncbi.nlm.nih.gov/pubmed/25687294

Herbal drug 1

Curr Comput Aided Drug Des. 2015 Nov 5. [Epub ahead of print]

Interaction studies of Withania somnifera's key metabolite Withaferin A with different receptors associated with cardiovascular disease.

Ravindran R, Sharma N, Roy S[1], Thakur AR, Subhadra G, Sriram K, Devi J, Rajkumar J.

Author information

Full text unavailable

Abstract

Withania somnifera commonly known as Ashwagandha in India is used in many herbal formulations to treat various cardiovascular diseases. The key metabolite of this plant, Withaferin A was analyzed for its molecular mechanism through docking studies on different targets of cardiovascular disease Six receptor proteins associated with cardiovascular disease were selected and interaction studies were performed with Withaferin A using AutoDock Vina. CORINA was used to model the small molecules and HBAT to compute the hydrogen bonding. Among the six targets, β1-adrenergic receptors,HMG-CoA and Angiotensinogen-converting enzyme showed significant interaction with Withaferin A. Pharmacophore modeling was done using PharmaGist to understand the pharmacophoric potential of withaferin A. Clustering of withaferin with different existing drug molecules for cardiovascular disease was performed with ChemMine based on structural similarity and physicochemical properties. The ability of natural active component, Withaferin A to interact with different receptors associated with cardiovascular disease was elucidated with various modeling techniques. These studies conclusively revealed Withaferin A as a potent lead compound against multiple targets associated with cardiovascular disease.

http://www.ncbi.nlm.nih.gov/pubmed/26548552

Herbal drug 2

J Ethnopharmacol. 2015 Nov 3. pii: S0378-8741(15)30199-9. doi: 10.1016/j.jep.2015.10.040. [Epub ahead of print]

Network pharmacology-based prediction of the active ingredients and potential targets of Mahuang Fuzi Xixin decoction for application to allergic rhinitis.

Tang F[1], Tang Q[1], Tian Y[2], Fan Q[3], Huang Y[1], Tan X[4].

Author information

Abstract

ETHNOPHARMACOLOGICAL RELEVANCE: Certain herbal formulae from Traditional Chinese Medicine (TCM) are effective for treating and preventing diseases in clinical practice. Mahuang fuzi Xixin Decoction (MFXD) is a TCM that is used to treat allergic rhinitis (AR); however, the active ingredients and potential targets of its action against AR remain unclear. Therefore, further investigation is required.

METHODS: A network pharmacology approach comprising drug-likeness evaluation, oral bioavailability prediction, multiple drug target prediction, and network analysis has been used in this study.

RESULTS: The comprehensive systematic approach was successfully to indentify 41 bioactive ingredients in MFXD, while 37 potential targets hit by these ingredients related to AR. Moreover, wherein four predicted ingredients possess anti-inflammatory effects were found by this technique.

CONCLUSIONS: Our works successfully predict the active ingredients and potential targets of MFXD for application to allergic rhinitis and helps to illustrate mechanism of action on a systematic level. This study not only provides new insights into the chemical basis and pharmacology of MFXD but also demonstrates a feasible method for discovering potential drugs from herbal medicine.

http://www.ncbi.nlm.nih.gov/pubmed/26545458

Herbal drug 3

J Toxicol Environ Health A. 2015 Oct 29:1-11. [Epub ahead of print]

Negligible Pharmacokinetic Interaction of Red Ginseng and Losartan, an Antihypertensive Agent, in Sprague-Dawley Rats.

Ryu SH[1,2], Kim YS[3,4], Jang HJ[1], Kim KB[1].

Author information

Abstract

Red ginseng (RG) is one of the top selling herbal medicines in Korea, but is not recommended in hypertensive patients. In this study, the pharmacokinetic (PK) interaction between RG and losartan, an antihypertensive drug, was examined. RG was orally administered for 2 wk to male Sprague-Dawley (S-D) rats at either control (0), 0.5, 1, or 2 g/kg/d for 2 wk. After the last administration of RG and 30 min later, all animals were treated with 10 mg/kg losartan by oral route. In addition, some S-D rats were administered RG orally for 21 d at 2 g/kg followed by losartan intravenously (iv) at 10 mg/kg/d. Post losartan administration, plasma samples were collected at 5, 15, and 30 min and 1, 1.5, 2, 3, 6, 12, and 24 h. Plasma concentrations of losartan and E-3174, the active metabolite of losartan, were analyzed by a high-pressure liquid chromatography-tandem mass spectrometer system (LC-MS/MS). Oral losartan administration showed dose-dependent pharmacokinetics (PK) increase with time to maximum plasma, but this was not significant between different groups. There was no significant change in t_{max} with E-3174 PK. With iv losartan, pharmacokinetics showed elevation of area under the plasma concentration-time curve from time zero extrapolated to infinitity. There was not a significant change in AUC_{inf} with E-3174 PK. Therefore, RG appeared to interfere with biotransformation of losartan, as RG exerted no marked effect on E-3174 PK in S-D rats. Data demonstrated that oral or iv treatment with losartan in rats pretreated with RG for 2 wk showed that losartan PK was affected but E-3174 PK remained unchanged among different dose groups. These results suggested that RG induces negligible influence on losartan and E-3174 PK in rats.

http://www.ncbi.nlm.nih.gov/pubmed/26514876

Herbal drug 4

J Ethnopharmacol. 2015 Nov 4;174:561-8. doi: 10.1016/j.jep.2015.03.005. Epub 2015 Mar 12.

Medicinal plants used as excipients in the history in Ghanaian herbal medicine.

Freiesleben SH[1], Soelberg J[2], Jäger AK[3].

Author information

Abstract

ETHNOPHARMACOLOGICAL RELEVANCE: The present study was carried out to investigate the traditional use, pharmacology and active compounds of four plants commonly used as excipients in herbal medicine in Ghana.

MATERIALS AND METHODS: A comprehensive literature search was conducted to gain knowledge about the traditional use, pharmacology and active compounds of the four plant excipients. The broth dilution antibacterial assay and the DPPH radical scavenging antioxidant assay were used to evaluate the antibacterial and antioxidant activity of the plants, respectively. Ethanol, warm water and cold water extracts were prepared from the dried seeds/fruits of Aframomum melegueta, Piper guineense, Xylopia aethiopica and Monodora myristica, and tested in the assays.

RESULTS: A. melegueta and P. guineense seemed to act as pharmacoenhancers, since they have been shown to inhibit specific CYP-enzymes. A. melegueta could act as an antioxidant to preserve herbal preparations. None of the plant excipients had antibacterial activity against the bacteria tested in this study. Compounds with an aromatic or pungent smell had been identified in all the plant excipients. An explanation for the use of the plants as excipients could rely on their taste properties.

CONCLUSION: The present study suggests that there may be more than one simple explanation for the use of these four plants as excipients. Plausible explanations have been proven to be: (1) a way to increase the effect of the medicine, (2) a way to make the medicine more palatable or (3) a way to preserve the activity of the medicinal preparation over time.

An **excipient** is a natural or synthetic substance formulated alongside the active ingredient of a medication, [:1] included for the purpose of long-term stabilization, bulking up solid formulations that contain potent active ingredients

Natural product plant 1

roble

BMC Res Notes. 2015 Oct 30;8(1):621. doi: 10.1186/s13104-015-1618-6.

In vitro antioxidant and free radical scavenging activity of different parts of Tabebuia pallida growing in Bangladesh.

Rahman MM[1], Islam MB[2], Biswas M[3], Khurshid Alam AH[4].

Author information

Abstract

BACKGROUND: In humans, many diseases are associated with the accumulation of free radicals. Antioxidants can scavenge free radicals and minimize their impact. Therefore, the search for naturally occurring antioxidants of plant origin is imperative. Here, we aimed to investigate the antioxidant and free radical scavenging properties of methanolic extracts from Tabebuia pallida (T. pallida) stem bark (TPSB), root bark (TPRB), leaves (TPL), and flowers (TPF).

METHODS: The antioxidant and free radical scavenging activity were determined by several standard methods using spectrophotomer. Total phenolic and flavonoid contents were estimated using Folin-Ciocalteu reagent and aluminum chloride colorimetric assay methods, respectively.

RESULTS: Among the extracts, TPL showed the highest total antioxidant capacity followed by TPRB, TPF, and TPSB. Based on DPPH and hydroxyl radical scavenging activity, TPL showed strong scavenging activity (91.05 ± 1.10 and 62.00 ± 0.57) with IC50 of 9.20 ± 0.28 and 46.00 ± 2.84 μg/mL, respectively when compared with standard BHT (IC50 of 7.00 ± 0.25 μg/mL) and CA (75.00 ± 0.14 μg/mL). These results suggest that TPL had the highest radical scavenging activity among the extractives that closely resembled the standard's. In lipid peroxidation inhibition assay, TPL exhibited the most potent inhibitory activity (83.18 ± 2.12 %) with IC50 of 12.00 ± 2.12 μg/mL, which closely resembled standard CA (IC50 of 10.50 ± 0.28 μg/mL). Also, the reducing capacity on ferrous ion was in the following order: TPL > TPRB > TF > TPSB. The phenolic and flavonoid contents of TPL were higher than other extractives. A positive correlation (p value <0.001) was observed between phenolic content and free radical (DPPH(·) and (·)OH) scavenging efficiencies and lipid peroxidation inhibition activity.

CONCLUSION: Methanolic extract of T. pallida leaf is a potential source of natural antioxidants and serves as an effective free radical scavenger and/or inhibitor. Hence, T. pallida might be a good plant-based pharmaceutical product for several diseases caused by free radicals.

http://www.ncbi.nlm.nih.gov/pubmed/26518275

Natural product plant 2

Phalsa or **Falsa**

Med Chem. 2015 Oct 30. [Epub ahead of print]

Antioxidant, Antimicrobial Activity and Medicinal Properties of Grewia asiatica L.

Shukla R, Sharma DC, Baig MH, Bano S, Roy S, Provazník I, Kamal MA[1].

Author information

Abstract

Since ancient time, India is a well known subcontinent for medicinal plants where diversity of plants is known for the treatment of many human disorders. Grewia asiatica is a dicot shrub belonging to the Grewioideae family and well known for its medicinally important fruit commonly called Falsa. G. asiatica, a seasonal summer plant is distributed in the forest of central India, south India, also available in northern plains and western Himalaya up to the height of 3000 ft. Fruits of G. asiatica are traditionally used as a cooling agent, refreshing drink, anti-inflammatory agent and for the treatment of some urological disorders. Recent advancement of Falsa researches concluded its antimicrobial and anti-diabetic activity. Since ancient time medicinal plants are traditionally used for the treatment of different diseases G. asiatica fruit is the edible and tasty part of the plant, now considered as a valuable source of unique natural product for development of medicines which are used in different disease conditions like anti-diabetic, anti-inflammatory, anti-cancerous and anti-microbial. Now a days, G. asiatica is being used in different Ayurvedic formulation for the cure of different types of diseases. Different pharmacological investigations reveal the presence of phenols, saponnins, flavonoids and tannins compound in the fruits. Present review highlights the phytopharmacological and different traditional use of G. asiatica which is mention in ancient Ayurvedic texts. This review stimulates the researchers and scientists for further work on G. asiatica.

http://www.ncbi.nlm.nih.gov/pubmed/26516779

Natural product plant 3

Pharm Biol. 2015 Oct 29:1-7. [Epub ahead of print]

Effects of methanol extracts from roots, leaves, and fruits of the Lebanese strawberry tree (Arbutus andrachne) on cardiac function together with their antioxidant activity.

Abidi E[1], Habib J[2], Yassine A[2], Chahine N[3], Mahjoub T[4], Elkak A[1].

Author information

Abstract

CONTEXT: Several plant-derived natural products have been used in clinical phase for applications in neurological, cardiovascular, and inflammatory diseases. Arbutus andrachne L. (Ericacea) is an evergreen shrub native to the Mediterranean region. Traditionally, the fruits and leaves of Arbutus tree are well known and used as antiseptics, diuretics, blood tonic, and laxatives.

OBJECTIVE: Data regarding the biological effects of compounds derived from the Lebanese Arbutus andrachne are not available. In the present work, we studied the antioxidant activity of methanol extracts of leaves, fruits, and roots of the plant against electrolysis; together with their effects on the cardiodynamics of isolated perfused rabbit hearts.

MATERIALS AND METHODS: In vitro electrolysis of the different root, leaves, and fruits methanol extracts was evaluated by the amount of free radicals that has been reduced by increasing the concentration of root extracts ranging from 0.5 to 2 mg after 1, 2, 3, and 4 min. Left ventricular pressure (LVP), heart rate (HR), and coronary flow (CR) were investigated in isolated rabbit heart after administration of 0.5, 1, 2, and 2 mg of each methanol extracts plotted against time (0, 0.5, 1.5, 5, and 10 min), according to the Langendorff method. Lipid peroxidation study was performed by the colorimetric method on myocard tissue after incubation with 500 µl of the different methanol extracts. The amount of MDA was determined at 500 nm absorbance after 5 min incubation.

RESULTS: Among the different methanol extracts, the roots showed the highest in vitro antioxidant activity, particularly observed at concentration of 2 mg which completely inhibits free radical generation after 4 min. LVP decreases by 32% at the dose of 2 mg of root extracts after 5 min. No significant effect was observed by the three tested extracts on the heart rate. The three methanol extracts did not show any significant effect on the coronary flow. Moreover, the roots show an increase in the coronary flow at a concentration of 1 and 2 mg/ml during 1 min. Electrolysis on heart tissue treated with the roots extracts shows a decrease in the MDA level from 70.51 ± 6.71 to 48.58 ± 4.15 nmole/g of tissue.

DISCUSSION AND CONCLUSION: Methanol extracts of the roots possess antihypertensive effect that may result from its ability to decrease the LVP together with its protective role by inhibiting free radical generation and significantly decreasing the MDA level of heart tissue.

http://www.ncbi.nlm.nih.gov/pubmed/26511200

Natural product plant 4

J Ethnopharmacol. 2015 Nov 4;174:403-9. doi: 10.1016/j.jep.2015.08.030. Epub 2015 Aug 28.

Gastroprotective effect of diligustilide isolated from roots of Ligusticum porteri coulter & rose (Apiaceae) on ethanol-induced lesions in rats.

Velázquez-Moyado JA[1], Martínez-González A[1], Linares E[2], Bye R[2], Mata R[1], Navarrete A[3].

Author information

Abstract

ETHNOPHARMACOLOGICAL RELEVANCE: The rhizome of Ligusticum porteri Coulter& Rose (LP) has been traditionally used by the ethnic group Raramuri in the North of México for treatment of diabetes, tuberculosis, stomachaches, diarrhea and ritual healing ceremonies. It is use as antiulcer remedy has been extended to all Mexico.

AIM OF THE STUDY: To evaluate the gastroprotective activity of LP organic extracts and the major natural product diligustilide (DLG),using as experimental model the inhibition of the ethanol-induced lesions in rats.

MATERIALS AND METHODS: Gastric ulcers were induced by intragastric instillation of absolute ethanol (1mL). We tested the gastroprotective activi of the organic extracts of LP and the pure compound DLG. The ulcer index (UI) was determined to measure the activity. In order to elucidate the actio mechanism of DLG the animals were treated with l-NAME, N-ethylmalemide, Forskolin, 2',5'-dideoxyadenosine, Indomethacin, Glibenclameide, Diazoxide, NaHS and DL-Propargylglycine. The pylorus-ligated rat model was used to measure gastric secretion.

RESULTS: The oral administration of organic extracts of Ligusticum porteri showed gastroprotective effect at 30mg/Kg on ethanol induced gastric lesions; hexane and dichloromethane extracts were the most active. DLG was the major compound in the hexane extract. This compound at 10mg/kg prevented significantly the gastric injuries induced by ethanol. The alkylation of endogenous non-protein-SH groups with N-ethylmaleimide abolished the gastroprotective effect of DLG and blocking the formation of endogenous prostaglandins by the pretreatment with indomethacin attenuated the gastroprotective effect of DLG.

CONCLUSION: The gastroprotective activity demonstrated in this study tends to support the ethnomedical use of Ligusticum porteri roots. DLG, isolated as major compound of this medicinal plant has a clear gastroprotective effect on the ethanol-induced gastric lesions. The results suggest that the antiulcer activity of DLG depends on the participation of the endogenous non-protein -SH groups and prostaglandins.

Ligusticum porteri, known as Osha or oshá, is a perennial herb found in parts of the Rocky Mountains and northern Mexico, especially in the southwestern United States.

http://www.ncbi.nlm.nih.gov/pubmed/26320689

Setaria 1

Plant Physiol. 2015 Nov;169(3):1850-61. doi: 10.1104/pp.15.00586. Epub 2015 Sep 15.

Temperature Responses of C4 Photosynthesis: Biochemical Analysis of Rubisco, Phosphoenolpyruvate Carboxylase, and Carbonic Anhydrase in Setaria viridis.

Boyd RA[1], Gandin A[1], Cousins AB[2].

Author information

Repeated

Abstract

The photosynthetic assimilation of CO2 in C4 plants is potentially limited by the enzymatic rates of Rubisco, phosphoenolpyruvate carboxylase (PEPc), and carbonic anhydrase (CA). Therefore, the activity and kinetic properties of these enzymes are needed to accurately parameterize C4 biochemical models of leaf CO2 exchange in response to changes in CO2 availability and temperature. There are currently no published temperature responses of both Rubisco carboxylation and oxygenation kinetics from a C4 plant, nor are there known measurements of the temperature dependency of the PEPc Michaelis-Menten constant for its substrate HCO3 (-), and there is little information on the temperature response of plant CA activity. Here, we used membrane inlet mass spectrometry to measure the temperature responses of Rubisco carboxylation and oxygenation kinetics, PEPc carboxylation kinetics, and the activity and first-order rate constant for the CA hydration reaction from 10°C to 40°C using crude leaf extracts from the C4 plant Setaria viridis. The temperature dependencies of Rubisco, PEPc, and CA kinetic parameters are provided. These findings describe a new method for the investigation of PEPc kinetics, suggest an HCO3 (-) limitation imposed by CA, and show similarities between the Rubisco temperature responses of previously measured C3 species and the C4 plant S. viridis.

Patent Trend (KIPRIS)

- Brassinosteroids
- CRISPR-Cas9
- Herbicide resistant
- Totipotency
- Herbal drug
- Natural product

Totipotency 1

[27] 메타크릴레이트화된 젤라틴을 포함하는, 심근세포분화 유도용 세포 지지체(Scaffold for inducing myocardiocyte differentiation compring methacrylated gelatin)

출원인 : 부산대학교 산학협력단 | 출원번호 : 1020140165408 | 출원일자 : 2014.11.25
공개일자 : | 등록일자 : 2015.10.15 | IPC : A61L 27/22 | C12N 5/071 | C12…

[28] 배아 줄기 세포 및 배-유도 세포의 유도(DERIVATION OF EMBRYONIC STEM CELL AND EMBRYO-DERIVED CELL)

출원인 : 오카타 세라퓨틱스, 인크. | 출원번호 : 1020087029539 | 출원일자 : 2008.12.03
공개일자 : 2009.04.20 | 등록일자 : 2015.11.09 | IPC : C12N 5/0735 | A61K 35/48 | C12…

[29] 태반 줄기세포를 이용한 염증 질환의 치료(TREATMENT OF INFLAMMATORY DISEASES USING PLACENTAL STEM CELLS)

출원인 : 안트로제네시스 코포레이션 | 출원번호 : 1020097018749 | 출원일자 : 2009.09.08
공개일자 : 2009.10.20 | 등록일자 : 2015.11.09 | IPC : A61P 17/00 | A61P 37/00 | A61K…

배아 줄기 세포 및 배-유도 세포의 유도(DERIVATION OF EMBRYONIC STEM CELL AND EMBRYO-DERIVED CELL)

(19) 대한민국특허청(KR)
(12) 공개특허공보(A)

(11) 공개번호 10-2009-0038393
(43) 공개일자 2009년04월20일

(51) Int. Cl.
C12N 5/06 (2006.01) *C12N 5/02* (2006.01)
A61K 35/45 (2006.01)
(21) 출원번호 10-2008-7029539
(22) 출원일자 2008년12월03일
심사청구일자 없음
번역문제출일자 2008년12월03일
(86) 국제출원번호 PCT/US2007/010985
국제출원일자 2007년05월03일
(87) 국제공개번호 WO 2007/130664
국제공개일자 2007년11월15일
(30) 우선권주장
60/797,449 2006년05월03일 미국(US)
(뒷면에 계속)

(71) 출원인
어드밴스드 셀 테크놀로지, 인코포레이티드
미국 매사추세츠 01605 우스터 바이오텍 브이 플레이션 스트리트 381
(72) 발명자
청, 영
미국, 메사추세츠 01545, 슈루즈버리, 아버 드라이브 9234
랜자, 로버트
미국, 메사추세츠 01510, 클린턴, 사우스 메도우 로드 35
클리만스카야, 이리나 브이.
미국, 메사추세츠 01568, 업톤, 머캐닉 스트리트 75
(74) 대리인
강명구

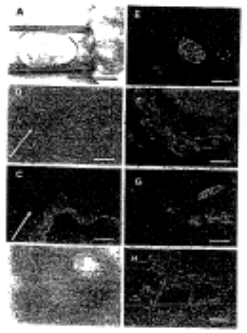
전체 청구항 수 : 총 81 항

(54) 배아 줄기 세포 및 배-유도 세포의 유도

(57) 요 약

본 발명은 배의 부득이한 파괴없이 배로부터 배아 줄기 세포 및 배-유도된 세포를 생산하는 신규한 방법을 제공한다. 본 발명은 또한 배의 파괴없이 유도된 세포 및 세포주를 제공하고, 치료 및 연구 목적으로 이들 세포를 이용하는 것에 관계한다. 또한 IVF와 같은 생식 요법과 연계하여 배의 착상전에 자가 줄기 세포를 확립하고 보관하는 신규한 방법을 제공한다.

대 표 도 - 도1



태반 줄기세포를 이용한 염증 질환의 치료(TREATMENT OF INFLAMMATORY DISEASES USING PLACENTAL STEM CELLS)

(19) 대한민국특허청(KR)
(12) 공개특허공보(A)

(11) 공개번호 10-2009-0109575
(43) 공개일자 2009년10월20일

(51) Int. Cl.
A61K 35/50 (2006.01) *A61P 17/00* (2006.01)
A61P 37/00 (2006.01)
(21) 출원번호 10-2009-7018749
(22) 출원일자 2008년02월12일
심사청구일자 없음
(55) 번역문제출일자 2009년09월08일
(56) 국제출원번호 PCT/US2008/001831
(57) 국제공개번호 WO 2008/100498
국제공개일자 2008년08월21일
(30) 우선권주장
60/901,067 2007년02월12일 미국(US)

(71) 출원인
안트로제네시스 코포레이션
미국 뉴저지주 07927 세다 놀스 호스힐 로드 45
(72) 발명자
에덴져, 제임스, 더블유.
미국, 뉴저지 07716, 벨포드, 273 레오나르드빌레 로드
하리리, 로버트, 제이.
미국, 뉴저지 07932, 플로르함 파크, 5 헤리타지 로드
(뒷면에 계속)
(74) 대리인
특허법인필앤온지

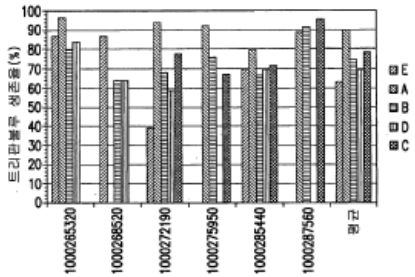
전체 청구항 수 : 총 18 항

(54) 태반 줄기세포를 이용한 염증 질환의 치료

(57) 요 약

본 명세서에서는 태반 줄기세포 또는 제대(umbilical cord) 줄기세포를 이용하여 면역 관련 질병, 장애 또는 상태가 있는 개체를 치료하는 방법을 제공하는데, 예를 들어 면역 관련 질병, 장애 또는 상태는 염증성 장자병, 이식 대 숙주병, 다발성 경화증, 류마티스성 관절염, 건선, 홍반성 루푸스, 당뇨병, 균상 식육종(Alibert-Bazin 증후군) 또는 피부 경화증이 있다.

대 표 도 - 도1



Herbal drug

[12] 발효율피 추출물을 유효성분으로 포함하는 항비만 조성물 및 이의 제조 방법(Fermented Castanea crenata inner shell extracts for anti-obesity and manufacturing method thereof)

출원인 : 고려대학교 산학협력단 | 출원번호 : 1020140000434 | 출원일자 : 2014.01.02
공개일자 : 2015.07.13 | 등록일자 : 2015.10.26 | IPC : A61P 3/00 | A61K 36/49 | A61P…

[13] 인슐린 민감성 강화제 및 항당뇨병제로서의 식물 추출물(HERBAL EXTRACT AS SENSITIVITY ENHANCER TOWARD INSULIN AND ANTIDIABETES)

출원인 : 피티. 덱사 메디카 | 출원번호 : 1020117002793 | 출원일자 : 2011.02.07
공개일자 : 2011.05.26 | 등록일자 : 2015.11.03 | IPC : A61P 5/50 | A61K 36/54 | A61P…

(19) 대한민국특허청(KR)
(12) 등록특허공보(B1)

(45) 공고일자 2015년11월02일
(11) 등록번호 10-1564826
(24) 등록일자 2015년10월26일

(51) 국제특허분류(Int. Cl.)
A61K 36/49 (2006.01) *A61P 3/00* (2006.01)
A61P 3/04 (2006.01)
(21) 출원번호 10-2014-0000434
(22) 출원일자 2014년01월02일
심사청구일자 2014년01월02일
(65) 공개번호 10-2015-0080963
(43) 공개일자 2015년07월13일
(56) 선행기술조사문헌
KR1020070052348 A
KR1020050045666 A
KR1020060090189 A

(73) 특허권자
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서울특별시 성북구 안암로 145, 고려대학교 (안암동5가)
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임원철
세종 조치원읍 돌마루1길 10-8, 301호 (형제빌딩)
(뒷면에 계속)
(74) 대리인
특허법인다나

전체 청구항 수 : 총 6 항 심사관 : 윤동준

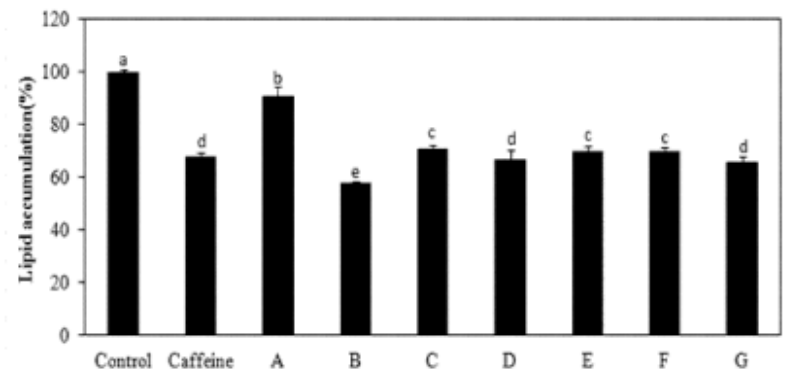
(54) 발명의 명칭 **발효율피 추출물을 유효성분으로 포함하는 항비만 조성물 및 이의 제조 방법**

(57) 요 약

본 발명은 비만의 예방, 개선 및 치료용 조성물에 관한 것이다.

본 발명에 따른 율피 효소 분해액의 발효물은 우수한 3T3-L1 지방전구세포주의 세포분화 억제 활성 및 지방세포 분화에 관여하는 상위 전사인자인 PPAR-γ, C/EBP-α, SREBP-1c 유전자 발현의 높은 저해를 나타내는 바, 비만의 예방, 개선 및 치료를 위해 유용하게 사용될 수 있다.

대 표 도 - 도1



(19) 대한민국특허청(KR)
(12) 등록특허공보(B1)

(45) 공고일자 2015년11월09일
(11) 등록번호 10-1567486
(24) 등록일자 2015년11월03일

(51) 국제특허분류(Int. Cl.)
A61K 36/64 (2006.01) *A61K 36/185* (2006.01)
A61P 3/10 (2006.01) *A61P 5/50* (2006.01)
(21) 출원번호 10-2011-7002793
(22) 출원일자(국제) 2009년08월04일
심사청구일자 2013년09월12일
(85) 번역문제출일자 2011년02월07일
(86) 국제출원번호 PCT/IB2009/053370
(87) 국제공개번호 WO 2010/023672
국제공개일자 2010년03월04일
(30) 우선권주장
P00200800564 2008년08월27일 인도네시아(ID)
(56) 선행기술조사문헌
WO2006127779 A2*
WO2005069310 A1*
*는 심사관에 의하여 인용된 문헌

(73) 특허권자
피디. 멕사 메디카
인도네시아 팔렘방 케가마탄 일리르 디무르 II 빌루라한 6 일리르 갈란 센더럴 발방 우모요 넘버 138
(72) 발명자
트한드라위나파 레이몬드 할.
인도네시아 12720 자카르타 셀라탄 케가마탄 담팡 프라파탄 케루라한 페라 담팡 알디001/알더블유012 제이엘. 방가 8 에이/22
시남벨라 제임스 앰
인도네시아 17148 베카시 베카시 셀라탄 베카푼 자야 본둑 베카푼 인다 블록 씨3 넘버07
(외9명 생략)
(74) 대리인
유미특허법인

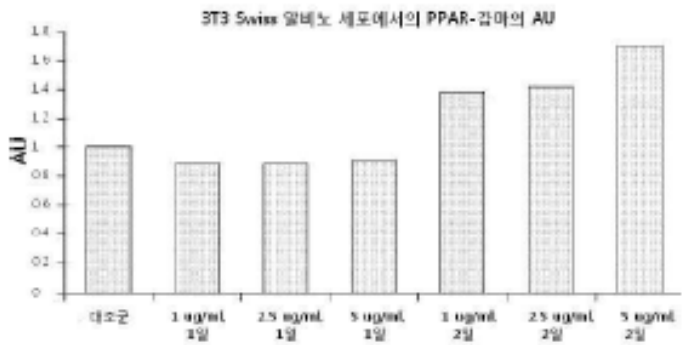
전체 청구항 수 : 총 7 항 심사관 : 강덕희

(54) 발명의 명칭 **인슐린 민감성 강화제 및 항당뇨병제로서의 식물 추출물**

(57) 요 약

부처꽃과 식물 및 녹나무과 식물로부터 유래된 식물 추출물 조성물 및 이의 인슐린 내성 강화제, 증후군 X 정상화, 당뇨병 전기 및 2형 당뇨병 치료, 특히 인슐린 신호 경로에서 활성자로서, 포도당 수송 시스템에서 조절자로서, 아디포넥틴 분비의 조절자로서, 및 인슐린 내성의 억제자로서의 용도. 부처꽃과 식물의 예로 라게르스트로에미아 스페키오사(*Lagerstroemia speciosa*)를 선택하였고, 녹나무과 식물의 예로 신나모멈 버마니(*Cinnamomum burmannii*)를 선택하였다. 이러한 식물 추출물 조성물은 상승적으로 작용하여 각 추출물을 단독 사용한 경우에 발현되는 약리학적 효과를 증강시킨다.

대 표 도 - 도1



Natural product plant

[66] 식물의 니코틴 알칼로이드 수준의 감소(Reducing levels of nicotinic alkaloids in plants)

출원인 : 22엔디 센츄리 리미티드, 엘엘씨 출원번호 : 1020137031265 출원일자 : 2013.11.25
공개일자 : 2013.12.05 등록일자 : 2015.10.22 IPC : A01H 5/00 | C12P 7/06

[67] 해상 구조물의 증발가스 처리 시스템(SYSTEM FOR TREATING BOIL-OFF GAS OF A MARINE STRUCTURE)

출원인 : 대우조선해양 주식회사 출원번호 : 1020140034689 출원일자 : 2014.03.25
공개일자 : 2014.06.19 등록일자 : 2015.10.30 IPC : F17C 9/00 | B63H 21/38 | F02M…

(19) 대한민국특허청(KR)
(12) 등록특허공보(B1)

(45) 공고일자 2015년10월28일
(11) 등록번호 10-1563998
(24) 등록일자 2015년10월22일

(51) 국제특허분류(Int. Cl.)
A01H 5/00 (2006.01) *C12P 7/08* (2006.01)
(21) 출원번호 10-2013-7031385(분할)
(22) 출원일자(국제) 2006년02월28일
심사청구일자 2013년12월23일
(85) 번역문제출일자 2013년11월25일
(65) 공개번호 10-2013-0133102
(43) 공개일자 2013년12월06일
(62) 원출원 특허 10-2013-7008698
원출원일자(국제) 2006년02월28일
심사청구일자 2013년04월11일
(86) 국제출원번호 PCT/IB2006/001741
(87) 국제공개번호 WO 2006/109197
국제공개일자 2006년10월19일
(30) 우선권주장
60/658,536 2005년02월28일 미국(US)
(56) 선행기술조사문헌
The Plant Cell, 6권, 페이지 723-735(1994년 5월)
NCBI의 database accession no.D28605.1(2003.01.10.)

(73) 특허권자
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(72) 발명자
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일본 나라켄 이코마시 다카야마쵸 8916-5 다이가쿠슈쿠샤 비-305
카토 아키라
일본 나라켄 나라시 사쿄 2-3-1 도레루스쿠에아 다카노하라 3-205
(74) 대리인
리엘특허법인

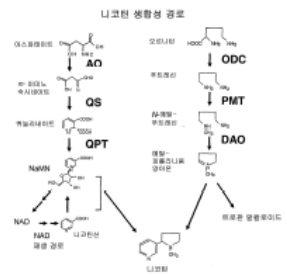
전체 청구항 수 : 총 10 항 심사관 : 이형곤

(54) 발명의 명칭 식물의 니코틴 알칼로이드 수준의 감소

(57) 요 약

두 개의 유전자인 A622와 NBB1은 식물에서 니코틴 알칼로이드의 감소를 달성하는데 영향을 줄 수 있다. 특히, A622와 NBB1 중 하나 또는 두 개 모두의 억제는 담배 식물에서 니코틴을 감소시키는데 사용될 수 있다.

대 표 도 - 도1



(19) 대한민국특허청(KR)
(12) 등록특허공보(B1)

(45) 공고일자 2015년11월05일
(11) 등록번호 10-1566267
(24) 등록일자 2015년10월30일

(51) 국제특허분류(Int. Cl.)
B63B 35/18 (2006.01) *B63H 21/38* (2006.01)
F02M 21/02 (2006.01) *F17C 9/00* (2006.01)
(21) 출원번호 10-2014-0034889(분할)
(22) 출원일자 2014년03월25일
심사청구일자 2014년03월25일
(65) 공개번호 10-2014-0076849
(43) 공개일자 2014년06월19일
(62) 원출원 특허 10-2013-0116089
원출원일자 2013년09월30일
심사청구일자 2013년11월28일
(30) 우선권주장
1020120143522 2012년12월11일 대한민국(KR)
(56) 선행기술조사문헌
JP2006348752 A
KR100854902 B1
KR1020120107851 A

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(뒷면에 계속)
(74) 대리인
특허법인에이아이피

전체 청구항 수 : 총 11 항 심사관 : 김성수

(54) 발명의 명칭 **해상 구조물의 증발가스 처리 시스템**

(57) 요 약

본 발명은 저장탱크에서 배출된 증발가스를 가압한 후 대부분은 선박의 고압 천연가스 분사 엔진의 연료로 사용하고 나머지 일부는 저장탱크로부터 새롭게 배출되는 증발가스의 냉열로 액화시켜 저장탱크로 복귀시킴으로써, 증발가스를 효율적으로 사용할 수 있도록 하는 해상 구조물의 증발가스 처리 시스템에 관한 것이다.

(뒷면에 계속)

대 표 도