

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

APR 25 2023

Applicant's or agent's file reference
MONS:522WO

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US22/79380

International filing date (day/month/year)

07 November 2022 (07.11.2022)

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12 November 2021 (12.11.2021)

International Patent Classification (IPC) or both national classification and IPC

IPC - INV. C12N 15/82; A01H 1/06; A01H 5/08; C07K 14/415 (2023.01)

ADD.

CPC - INV. C12N 15/8218; A01H 1/06; A01H 5/08; C07K 14/415; C12N 15/8201; C12N 15/8241; Y02A 40/146

ADD.

Applicant MONSANTO TECHNOLOGY LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Date of completion of this opinion

10 April 2023 (10.04.2023)

Authorized officer

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Telephone No. 571-272-4300

**WRITTEN OPINION OF THE
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed.
☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(b)).

3. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

- a. ☐ forming part of the international application as filed.
b. ☒ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)),
☒ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

4. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established to the extent that a meaningful opinion could be formed without a WIPO Standard ST.26 compliant sequence listing.

5. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 7-30

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 7-30 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 7-30 are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 7-30

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing complying with WIPO Standard ST.26, and such listing was not available to the International Searching Authority in the form, language and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13^{ter}.1(a).

☐ See Supplemental Box for further details.

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest and, where applicable, the protest fee.
 - ☐ paid additional fees under protest but the applicable protest fee was not paid.
 - ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

-Please See Supplemental Page-

4. Consequently, this opinion has been established in respect of the following parts of the international application:

☐ all parts.

☒ the parts relating to claims Nos. Groups I+, Claims 1-6, 31-44, and SEQ ID NO: 30 (TFL1 gene polynucleotide sequence), SI

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	31-32, 43	YES
	Claims	1-6, 33-42, 44	NO
Inventive step (IS)	Claims	31-32	YES
	Claims	1-6, 33-44	NO
Industrial applicability (IA)	Claims	1-6, 31-44	YES
	Claims	NONE	NO

2. Citations and explanations:

Claims 1-6, 33-42, and 44 lack novelty under PCT Article 33(2) as being anticipated by US 2018/0092319 A1 to J.R. Simplot Company (hereinafter "Simplot").

As per claim 1, Simplot discloses a modified plant, plant seed, plant part, or plant cell (genetically modified plug plants; paragraph [0010]), comprising a modification that reduces the expression or activity of TFL1 (the reduced activity of TFL1 gene is induced by RNA interference, genome editing, or mutation of the endogenous TFL gene; paragraph [0008]), or a homolog thereof, as compared to the expression or activity of TFL1 or the homolog thereof in an otherwise identical plant, plant seed, plant part, or plant cell that lacks the modification (the genetically modified plug plant has reduced activity of a transcription factor encoded by a TFL1 gene compared to a non-genetically modified control plant; paragraphs [0008], [0012]).

As per claim 2, Simplot discloses the modified plant, plant seed, plant part, or plant cell of claim 1. Simplot further discloses wherein the modification is present in at least one allele of an endogenous TFL1 gene or homolog thereof (a TFL1 allele found in a plant species that has reduced activity when compared to the TFL1 allele in a control plant can be utilized to produce a plant with repressed TFL1 activity, by integrating the modified TFL1 allele having reduced activity into a desired plant (the modification is present in at least one allele of an endogenous TFL1 gene); paragraphs [0008], [0077], [0100]).

As per claim 3, Simplot discloses the modified plant, plant seed, plant part, or plant cell of claim 2. Simplot further discloses wherein the TFL1 gene or homolog thereof encodes a protein having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, or 100% sequence identity to SEQ ID NO:2 (a TFL1 gene sequence encoding for a protein having the sequence set forth in SEQ ID NO: 8, wherein SEQ ID NO: 2 of the instant PCT application is 83% identical to SEQ ID NO: 8 of the Simplot reference; paragraph [0022]).

As per claim 4, Simplot discloses the modified plant, plant seed, plant part, or plant cell of claims 2-3. Simplot further discloses wherein the modification is in a non-coding region of the TFL1 gene or homolog thereof (TFL1 gene expression is repressed by one or more mutations being introduced into the promoter, the intron, 5'-UTR, or 3'-UTR regions (non-coding region) of the target TFL1 gene; paragraphs [0008], [0077], [0106]).

As per claim 5, Simplot discloses the modified plant, plant seed, plant part, or plant cell of claim 4. Simplot further discloses wherein the non-coding region is selected from the group consisting of a promoter, an intron, a 5'-untranslated region, a 3'-untranslated region, and combinations of any thereof (TFL1 gene expression is repressed by one or more mutations being introduced into the promoter, the intron, 5'-UTR, or 3'-UTR regions (non-coding region) of the target TFL1 gene; paragraphs [0008], [0077], [0106]).

As per claim 6, Simplot discloses the modified plant, plant seed, plant part, or plant cell of claim 5. Simplot further discloses wherein the modification is in the promoter of the TFL1 gene or homolog thereof (TFL1 gene expression is repressed by one or more mutations being introduced into the promoter region of the target TFL1 gene; paragraphs [0008], [0077], [0106]).

As per claim 33, Simplot discloses a method for producing a plant comprising a modified TFL1 gene (methods for genetically enhancing (modified TFL1 gene) plant production, such as strawberry plant production; paragraphs [0005], [0008]), the method comprising: a. introducing a modification into at least one target site in an endogenous TFL1 gene or a homolog thereof of a plant cell (plants with modified endogenous TFL1 gene, wherein the modification is a target site; paragraphs [0006], [0007], [0008]); b. identifying and selecting one or more plant cells of step a. comprising said modification in said TFL1 gene or homolog thereof (identification and selection of genetically stable clones with the modified TFL1 gene; paragraphs [0006], [0007], [0008], [0119], [0143], [0146]); and c. regenerating at least one plant from at least one or more cells selected in step b (strawberry plants regenerated after transformation with TFL1 gene-modifying vectors; paragraphs [0023], [0143], [0146], [0150]).

As per claim 34, Simplot discloses the method of claim 33. Simplot further discloses wherein the target site is located in a non-coding region of an endogenous TFL1 gene or homolog thereof (TFL1 gene expression is repressed by one or more mutations being introduced into the promoter, the intron, 5'-UTR, or 3'-UTR regions (non-coding region) of the target TFL1 gene; paragraphs [0008], [0077], [0106]).

---Continued in Supplemental Box---

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

****-Continued From Box IV (ii): Lack of unity of invention-****

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups I+, Claims 1-6, 31-44, and SEQ ID NO: 30 (TFL1 gene polynucleotide sequence), SEQ ID NO: 13 (guide RNA sequence) are directed towards TFL1 gene and plants, and polynucleotides, guide RNAs, and methods associated therewith.

The TFL1 gene and plants, and polynucleotides, guide RNAs, and methods of Claims 1-6, 31-32 (each in-part), 33-44 are believed to encompass the first named invention of Groups I+ and are the claims that will be searched without fee to the extent that they encompass SEQ ID NO: 30 (first exemplary TFL1 gene polynucleotide sequence), SEQ ID NO: 13 (first exemplary guide RNA sequence). This first named invention of Group I+ has been selected to encompass the first species of each of the genera found in claims 31-32 based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines.

Applicant is invited to elect additional TFL1 gene polynucleotide sequence(s), guide RNA sequence(s) to be searched. Additional TFL1 gene polynucleotide sequence(s), guide RNA sequence(s) will be searched upon the payment of additional fees. Applicants must specify the searchable claims that encompass any additionally elected TFL1 gene polynucleotide sequence(s), guide RNA sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. Exemplary elections would be SEQ ID NO: 31 (TFL1 gene polynucleotide sequence), SEQ ID NO: 14 (guide RNA sequence).

Groups I+ were considered to share the technical features including: a modified plant, plant seed, plant part, or plant cell, comprising a modification that reduces the expression or activity of TFL1, or a homolog thereof, as compared to the expression or activity of TFL1 or the homolog thereof in an otherwise identical plant, plant seed, plant part, or plant cell that lacks the modification; a polynucleotide comprising a sequence; a guide RNA comprising a polynucleotide sequence; a method for producing a plant comprising a modified TFL1 gene, the method comprising: a. introducing a modification into at least one target site in an endogenous TFL1 gene or a homolog thereof of a plant cell; b. identifying and selecting one or more plant cells of step a. comprising said modification in said TFL1 gene or homolog thereof; and c. regenerating at least one plant from at least one or more cells selected in step b; a method for increasing the determinacy of a plant, comprising modifying at least one allele of an endogenous promoter of a TFL1 gene, such that TFL1 protein production is reduced as compared to the production of TFL1 protein production in an otherwise identical plant that lacks the modification; these shared technical features are previously disclosed by the publication entitled "Targeted deletion of floral development genes in Arabidopsis with CRISPR/Cas9 using the RNA endonuclease Csy4 processing system" by Liu, et al. (hereinafter "Liu").

Liu discloses a modified plant, plant seed, plant part, or plant cell, comprising a modification that reduces the expression or activity of TFL1, or a homolog thereof, as compared to the expression or activity of TFL1 or the homolog thereof in an otherwise identical plant, plant seed, plant part, or plant cell that lacks the modification (Arabidopsis seeds transformed (a modified plant seed) with Cas9-sgRNA-expressing vector to induce targeted deletion in the TFL1 gene resulting in loss of function in TFL1 expression (modification that reduces the expression or activity of TFL1, as compared to the expression or activity of TFL1 in an otherwise identical plant seed that lacks the modification); abstract; page 8, 1st column, 2nd paragraph and 2nd column, 2nd and 3rd paragraphs); a polynucleotide comprising a sequence (TFL1 genomic sequence; page 2, 2nd column, 2nd paragraph); a guide RNA comprising a polynucleotide sequence (Cas9-sgRNA-expressing vector, wherein the guide RNA would intrinsically comprise a specific polynucleotide sequence; page 8, 2nd column, 3rd paragraph); a method for producing a plant comprising a modified TFL1 gene, the method comprising: a. introducing a modification into at least one target site in an endogenous TFL1 gene or a homolog thereof of a plant cell; b. identifying and selecting one or more plant cells of step a. comprising said modification in said TFL1 gene or homolog thereof; and c. regenerating at least one plant from at least one or more cells selected in step b (Arabidopsis seeds transformed (method for producing) with Cas9-sgRNA-expressing vector to induce targeted deletion in the TFL1 gene (introducing a modification into at least one target site in an endogenous TFL1 gene) resulting in loss of function in TFL1 expression, followed by germination of the seeds and harvesting (identifying and selecting one or more plant cells of step a. comprising said modification in said TFL1 gene, and regenerating at least one plant from at least one or more cells selected in step b), which would intrinsically result in a plant comprising a modified TFL1 gene; abstract; page 8, 1st column, 2nd paragraph and 2nd column, 2nd and 3rd paragraphs; page 9, 1st column, 1st paragraph); a method for increasing the determinacy of a plant, comprising modifying at least one allele of a TFL1 gene, such that TFL1 protein production is reduced as compared to the production of TFL1 protein production in an otherwise identical plant that lacks the modification (Arabidopsis seeds transformed with Cas9-sgRNA-expressing vector to induce targeted deletion in the TFL1 gene (modifying at least one allele of a TFL1 gene) resulting in loss of function in TFL1 expression (TFL1 protein production is reduced as compared to the production of TFL1 protein production in an otherwise identical plant that lacks the modification), which caused a change from indeterminate to determinate inflorescences (method for increasing the determinacy of a plant); abstract; page 8, 1st column, 2nd paragraph and 2nd column, 2nd and 3rd paragraphs). In a separate, distinct embodiment, Liu discloses modifying at least one allele of an endogenous promoter of a gene (the targeted deletion between exon 1 and exon 2 of SVP gene significantly decreased mRNA transcription, indicating that this sequence may include promoter fragments of SVP (modifying at least one allele of an endogenous promoter of a gene); page 8, 1st column, 2nd paragraph). It would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the method, as previously disclosed by Liu, for the integration of modifying at least one allele of an endogenous promoter of a gene based on the teachings of the alternative embodiment of Liu, as this modification would provide the capability of increasing the determinacy of a plant by modifying at least one allele of an endogenous promoter of a TFL1 gene, such that TFL1 protein production is reduced as compared to the production of TFL1 protein production in an otherwise identical plant that lacks the modification, thereby providing a plant with an improved agronomical trait, such as being less prone to stem lodging.

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Liu reference, unity of invention is lacking.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

****-Continued From Box V. 2: Citations and Explanations-****

As per claim 35, Simplot discloses the method of claim 34. Simplot further discloses wherein the non-coding region is selected from the group consisting of a promoter, an intron, a 5'-untranslated region, a 3'-untranslated region, and combinations of any thereof (TFL1 gene expression is repressed by one or more mutations being introduced into the promoter, the intron, 5'-UTR, or 3'-UTR regions (non-coding region) of the target TFL1 gene; paragraphs [0008], [0077], [0106]).

As per claim 36, Simplot discloses the method of claim 36. Simplot further discloses wherein the non-coding region is a promoter (TFL1 gene expression is repressed by one or more mutations being introduced into the promoter region of the target TFL1 gene; paragraphs [0008], [0077], [0106]).

As per claim 37, Simplot discloses the method of claim 33. Simplot further discloses wherein the modification is facilitated by the presence of at least one site-specific genome modification enzyme in said plant cell (DNA nucleases are utilized to introduce mutations into an endogenous gene of the plant; paragraph [0103]).

As per claim 38, Simplot discloses the method of claim 37. Simplot further discloses wherein the site-specific genome modification enzyme is selected from the group consisting of: an RNA-guided nuclease, a zinc-finger nuclease, a meganuclease, a TALE-nuclease, a recombinase, a transposase, and combinations of any thereof (the site-specific genome modification enzyme is Cas9 enzyme (RNA-guided nuclease), a zinc-finger nuclease, a TALEN, or a recombinase; paragraph [0103]).

As per claim 39, Simplot discloses the method of claim 38. Simplot further discloses wherein the site-specific genome modification enzyme is an RNA-guided nuclease comprising a Cas nuclease, a CpfI nuclease, or a variant of either thereof (the site-specific genome modification enzyme is Cas9 enzyme (RNA-guided Cas nuclease); paragraph [0103]).

As per claim 40, Simplot discloses the method of claim 37. Simplot further discloses wherein the site-specific genome modification enzyme creates at least one strand break at the target site (DNA nucleases are utilized to introduce mutations into an endogenous gene of the plant, which intrinsically create at least one strand break at the target site; paragraph [0103]).

As per claim 41, Simplot discloses the method of claim 33. Simplot further wherein the modification is selected from the group consisting of a substitution, an insertion, an inversion, a deletion, a duplication, and a combination thereof (mutation of the endogenous TFL1 gene is by insertional mutagenesis, or insertions, deletions, translocations; paragraphs [0008], [0119]).

As per claim 42, Simplot discloses the method of claim 41. Simplot further discloses wherein the modification is a deletion (mutation of the endogenous TFL1 gene is by deletion; paragraphs [0008], [0119]).

As per claim 44, Simplot discloses a method for increasing the determinacy of a plant (method for reducing the amount of time necessary from the beginning of plug plant growth to the final product of a desired strawberry fruit, and increasing yield, thereby indicating increased determinacy of the plant; paragraphs [0017], [0019]), comprising modifying at least one allele of an endogenous promoter of a TFL1 gene (modifying an endogenous TFL1 allele to have reduced activity in a desired plant, wherein TFL1 gene expression is repressed by one or more mutations being introduced into the promoter region of the target TFL1 gene; paragraphs [0008], [0077], [0100], [0106]), such that TFL1 protein production is reduced as compared to the production of TFL1 protein production in an otherwise identical plant that lacks the modification (a TFL1 allele found in a plant species that has reduced activity when compared to the TFL1 allele in a control plant can be utilized to produce a plant with repressed TFL1 activity, by integrating the modified TFL1 allele having reduced activity into a desired plant; paragraphs [0008], [0077], [0100]).

Claim 43 lacks an inventive step under PCT Article 33(3) as being obvious over Simplot, in view of US 2006/0070141 A1 to Nielsen, et al. (hereinafter "Nielsen").

As per claim 43, Simplot discloses the method of claim 42. Simplot does not disclose wherein the deletion comprises a region of at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least 85, at least 90, at least 95, at least 100, at least 125, or at least 150 consecutive nucleotides. Nielsen discloses wherein the deletion comprises a region of at least 100 consecutive nucleotides (a 100 bp deletion in the promoter of TFL1 gene from a transgenic line; paragraphs [0111], [0159]). It would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the method, as previously disclosed by Simplot, for the integration of wherein the deletion comprises a region of at least 100 consecutive nucleotides, as previously disclosed by Nielsen, for the benefit of providing a well-defined mutagenesis approach at a target site for modifying the TFL1 gene and repressing its activity and expression, thereby improving the method for generating genetically modified plants with increased determinacy and increased yield.

Claims 31 and 32 meet the criteria set out in PCT Article 33(2)-(3).

Claim 31 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a polynucleotide comprising a sequence of SEQ ID NO: 30.

The publication entitled "Glycine max GmTFL1b gene for terminal flower 1b, complete cds" by Liu, et al. (hereinafter "Liu"), discloses a gene sequence comprising a sequence having similarity with SEQ ID NO: 30 (Glycine max GmTFL1b gene sequence which is 4216 nt in length and comprises a nucleotide sequence having about 96% identity to SEQ ID NO: 30 of the instant PCT application; pgs. 1-2). Liu does not disclose a polynucleotide comprising a sequence of SEQ ID NO: 30.

****-Continued Within the Next Supplemental Box-****

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

----Continued from previous Supplemental Box----

US 10517242 B1 to Syngenta Participations AG (hereinafter "Syngenta") discloses a nucleotide sequence having similarity with SEQ ID NO: 30 (a marker sequence comprising SEQ ID NO: 6, wherein SEQ ID NO: 30 of the instant PCT application is about 25% identical to SEQ ID NO: 6 of the Syngenta reference; column 2, lines 39-41). Syngenta does not disclose a polynucleotide comprising a sequence of SEQ ID NO: 30.

The publication entitled "Glycine max cultivar Changshanidou Dt1 (Dt1) gene, complete cds" to Tian, et al. (hereinafter "Tian") discloses a gene sequence having similarity with SEQ ID NO: 30 (Glycine max Dt1 gene sequence which is 2341 nt in length and comprises a nucleotide sequence having about 28% identity with SEQ ID NO: 30 of the instant PCT application; pgs. 1-2). Tian does not disclose a polynucleotide comprising a sequence of SEQ ID NO: 30.

Liu, Syngenta, and Tian, either alone or in combination, fail to disclose a polynucleotide comprising a sequence of SEQ ID NO: 30. While Liu, Syngenta, and Tian disclose a sequence similar to SEQ ID NO: 30, they do not disclose a polynucleotide comprising a sequence of SEQ ID NO: 30. Thus, it would not have been obvious to a person of ordinary skill in the art, at the time of invention, to have implemented the polynucleotide of claim 31 because the references of record fail to disclose all the elements.

Claim 32 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a guide RNA comprising a polynucleotide sequence of SEQ ID NO: 13.

The publication entitled "PREDICTED: Sorghum bicolor probable receptor-like protein kinase At5g18500 (LOC8060368), mRNA" by National Center for Biotechnology Information (hereinafter "NCBI") discloses a nucleotide sequence comprising a sequence having similarity with SEQ ID NO: 13 (Sorghum bicolor probable receptor-like protein kinase gene that is 2330 nt long and comprises a sequence having about 86% identity with SEQ ID NO: 13 of the instant PCT application; pages 1-2). NCBI does not disclose a guide RNA comprising a polynucleotide sequence of SEQ ID NO: 13.

Syngenta discloses a nucleotide sequence having similarity with SEQ ID NO: 13 (a marker sequence comprising SEQ ID NO: 6, wherein SEQ ID NO: 13 of the instant PCT application is about 96% identical to a sequence comprised in SEQ ID NO: 6 of the Syngenta reference; column 2, lines 39-41). Syngenta does not disclose a guide RNA comprising a polynucleotide sequence of SEQ ID NO: 13.

Tian discloses a nucleotide sequence comprising the nucleotide sequence of SEQ ID NO: 13 (Glycine max Dt1 gene sequence which is : 2341 nt in length and comprises a nucleotide sequence having about 100% identity with SEQ ID NO: 13 of the instant PCT application; pgs. 1-2). Tian does not specifically disclose a guide RNA comprising a polynucleotide sequence of SEQ ID NO: 13.

NCBI, Syngenta, and Tian, either alone or in combination, fail to disclose a polynucleotide sequence of SEQ ID NO:13. While Syngenta and Tian disclose sequences comprising a nucleotide having the sequence set forth in SEQ ID NO: 13, they do not disclose a guide RNA comprising a polynucleotide sequence of SEQ ID NO:13. Thus, it would not have been obvious to a person of ordinary skill in the art, at the time of invention, to have implemented the guide RNA of claim 32 because the references of record fail to disclose all the elements.

Claims 1-6 and 31-44 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.