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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
10 March 2016

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(54) Title: METHODS OF INCREASING CROP YIELD UNDER ABIOTIC STRESS

(57) Abstract: Methods and materials for increasing abiotic stress tolerance in plants are disclosed. For example, nucleic acids encoding abiotic stress tolerance-increasing polypeptides are disclosed as well as methods for using such nucleic acids to transform plant cells. Also disclosed are plants having increased tolerance to abiotic stress and methods of increasing plant yield under abiotic stress conditions.

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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12N 15/2 (2015.01)
CPC - C12N 15/8273 (2015.12)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A01H 5/00, 5/10; C07K 14/415; C12N 5/04, 5/10, 15/29, 15/82 (2015.01)
CPC - C07K 14/415; C12N 15/8261, 15/8273 (2015.12)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
US - 435/410, 419; 800/290, 298
CPC - C07K 14/415; C12N 15/8261, 15/8273 (2015.12) (keyworkd delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Patbase, Google Patent, PubMed

Search Terms Used: drought W3 stress osmotic W3 stress nitrogen W3 deficiency HMM score Panicum virgatum

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	WO 2010/068418 A2 (CERES, INC et al) 17 June 2010 (17.06.2010) entire document	1-3, 6-10, 13, 18-20 --- 4, 5, 11, 12
Y	WO 2011/021190 A1 (YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW UNIVERSITY OF JERUSALEM LTD et al) 24 February 2011 (24.02.2011) entire document	4, 11
Y	US 2013/0044919 A1 (BOARD OF TRUSTEES OF THE UNIVERSITY OF ARKANSAS et al) 21 February 2013 (21.02.2013) entire document	5, 12
A	BHASKARAN et al. "Accelerated Reactive Oxygen Scavenging System and Membrane Integrity of Two Panicum Species Varying in Salt Tolerance," Cell Biochemistry and Biophysics, 02 April 2013 (02.04.2013), Vol. 67, Iss. 3, Pgs. 885-892. entire document	1-13, 18-20
A	WO 2012/058223 A1 (CERES, INC et al) 03 May 2012 (03.05.2012) entire document	1-13, 18-20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 December 2015	14 JAN 2016
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 14, 15
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
See supplemental page

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-13, 18-20 to the extent that they read on SEQ ID NOs:1 and 2.

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Continued from Box No. III Observations where unity of invention is lacking

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 need to be paid.

Group I+: claims 1-13 and 16-21 are drawn to methods of increasing plant yield in a plant grown under drought stress, osmotic stress, or nitrogen deficiency; and methods of producing a plant with tolerance to drought stress, osmotic stress, or nitrogen deficiency.

The first invention of Group I+ is restricted to methods of increasing plant yield in a plant grown under drought stress, osmotic stress, or nitrogen deficiency; and methods of producing a plant with tolerance to drought stress, osmotic stress, or nitrogen deficiency, said methods comprising growing a plant comprising an exogenous nucleic acid, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide, wherein the polypeptide is selected to be SEQ ID NO:2, and the nucleotide sequence encoding the polypeptide is SEQ ID NO:1. It is believed that claims 1-13 and 18-20 read on this first named invention and thus these claims will be searched without fee to the extent that they read on SEQ ID NOs:1 and 2.

Applicant is invited to elect additional polypeptides with specified SEQ ID NO and/or corresponding nucleotide sequence encoding a polypeptide with specified SEQ ID NO to be searched in a specific combination by paying additional fee for each set of election. An exemplary election would be methods of increasing plant yield in a plant grown under drought stress, osmotic stress, or nitrogen deficiency; and methods of producing a plant with tolerance to drought stress, osmotic stress, or nitrogen deficiency, said methods comprising growing a plant comprising an exogenous nucleic acid, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide, wherein the polypeptide is selected to be SEQ ID NO:4, and the nucleotide sequence encoding the polypeptide is SEQ ID NO:3. Additional polypeptides and/or nucleotides will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on 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.

The inventions listed in Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The Groups I+ formulas do not share a significant structural element conferring tolerance to drought stress, osmotic stress, or nitrogen deficiency, requiring the selection of alternatives for the polypeptides, where "a polypeptide having at least 80% sequence identity to an amino acid sequence set forth in SEQ ID NO: 2, 4, 6, 8, 9, 10, 11, 13, 15, 44, 46, 48, 49, 74, 75, 76, 77, 104, 105, 107, 128, 130, 131, 149, 151, 153, 172, 174, 176, 194, 195, 196, 16, 17, 18, 20, 21, 22, 24, 25, 27, 29, 31, 33, 34, 35, 37, 39, 41, 42, 51, 52, 53, 54, 55, 56, 57, 58, 59, 61, 63, 64, 66, 68, 69, 70, 71, 72, 79, 81, 82, 84, 85, 86, 88, 89, 91, 93, 95, 96, 98, 99, 100, 102, 103, 108, 109, 111, 113, 115, 116, 117, 118, 120, 122, 123, 124, 126, 133, 154, 178, 197, 135, 155, 179, 198, 137, 138, 139, 140, 141, 142, 156, 157, 158, 159, 160, 162, 181, 182, 183, 184, 186, 187, 199, 200, 201, 202, 203, 205, 213, 214, 216, 218, 219, 220, 221, 222, 223, 225, 227, 235, 236, 237, 238, 239, 240, 242, 244, 246, 247, 249, 259, 261, 262, 263, 265, 266, 267, 269, 271, 273, 275, 284, 285, 286, 287, 289, 291, 292, 294, 296, 298, 299, 143, 144, 145, 146, 147, 163, 165, 167, 169, 171, 189, 190, 191, 192, 193, 206, 207, 209, 211, 212, 229, 230, 231, 232, 233, 250, 251, 253, 255, 257, 276, 278, 280, 282, 283, 300, 301, 302, 304, 306, 308, 309, 311, 312, 314, 315, 317, 319, 320, 322, 323, 324, 326, 328, 330, 332, 333, 334, 335, 337, 338, 339, 340, 341, 342, 344, 345, 347, 348, 350, 352, 353, 354, 355, 356, 357, 358, 359, 360, 362, 364, 365, 366, 367, 368, 370, 372, 374, 375, 376, 377, 378, 379, 381, 382, 383, 384, 385, 386, 387, 388, 390, 391, 392, 394, 395, 396, 397, 399, 401, and 403, or a truncation of said polypeptide" and "the amino acid sequences depicted in any one of Figures 1-7".

The Groups I+ share the technical features of a method of increasing plant yield in a plant grown under drought stress, osmotic stress, or nitrogen deficiency, said method comprising growing a plant comprising an exogenous nucleic acid under drought stress, osmotic stress, or nitrogen deficiency, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, wherein the HMM bit score of the amino acid sequence of said polypeptide is greater than about 65, and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid; a method of increasing plant yield in a plant grown under drought stress, osmotic stress, or nitrogen deficiency, said method comprising growing a plant comprising an exogenous nucleic acid under drought stress, osmotic stress, or nitrogen deficiency, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid; a method of producing a plant with tolerance to drought stress, osmotic stress, or nitrogen deficiency, said method comprising (a) expressing in a plurality of plants an exogenous nucleic acid comprising a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, wherein the HMM bit score of the amino acid sequence of said polypeptide is greater than about 65, and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid, and (b) selecting from said plurality a plant that has increased tolerance to drought stress, osmotic stress, or nitrogen deficiency; a method of producing a plant with tolerance to drought stress, osmotic stress, or nitrogen deficiency, said method comprising (a) expressing in a plurality of plants an exogenous nucleic acid comprising a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid, and (b) selecting from said plurality a plant that has increased tolerance to drought stress, osmotic stress, or nitrogen deficiency; and a plant cell containing a modified endogenous nucleic acid, said nucleic acid comprising a nucleotide sequence encoding a polypeptide, wherein the HMM bit score of the amino acid sequence of said polypeptide is greater than about 65, and wherein a plant produced from said plant cell has a difference in tolerance to drought stress, osmotic stress, or nitrogen deficiency as compared to the corresponding composition of a control plant where said nucleic acid has not been modified. However, these shared technical features do not represent a contribution over the prior art.

Specifically, WO 2012/058223 A1 to Ceres, Inc. et al. discloses a method of increasing plant yield in a plant grown under drought stress, osmotic stress, or nitrogen deficiency (methods and materials related to modulating biomass composition, e.g., sucrose content or conversion efficiency, in plants ...methods and materials for increasing ...sucrose content and conversion efficiency in plants Pg. 21,

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Lns. 25-28; such transgenic plants can be used to provide yield stability at a lower input cost and/or under environmentally stressful conditions such as drought, Pg. 100, Lns. 5-7), said method comprising growing a plant comprising an exogenous nucleic acid under drought stress, osmotic stress, or nitrogen deficiency, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, wherein the HMM bit score of the amino acid sequence of said polypeptide is greater than about 65 (the method includes growing a plant cell comprising an exogenous nucleic acid. The exogenous nucleic acid includes a regulatory region operably linked to a nucleotide sequence encoding a polypeptide, where the HMM bit score of the amino acid sequence of the polypeptide is greater than about 65, Pg. 4, Lns. 3-7; under environmentally stressful conditions such as drought, Pg. 100, Lns. 6-7), and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid (plant produced from the plant cell has a difference in biomass composition compared to the corresponding composition of a control plant that does not comprise the nucleic acid. The difference in biomass composition in the plant can be a difference in the sucrose content or conversion efficiency, Pg. 4, Lns. 8-11); a method of increasing plant yield in a plant grown under drought stress, osmotic stress, or nitrogen deficiency (methods and materials related to modulating biomass composition, e.g., sucrose content or conversion efficiency, in plants ...methods and materials for increasing ...sucrose content and conversion efficiency in plants Pg. 21, Lns. 25-28; such transgenic plants can be used to provide yield stability at a lower input cost and/or under environmentally stressful conditions such as drought, Pg. 100, Lns. 5-7), said method comprising growing a plant comprising an exogenous nucleic acid under drought stress, osmotic stress, or nitrogen deficiency, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide (method of producing a plant that includes growing a plant cell comprising an exogenous nucleic acid. The exogenous nucleic acid comprises a regulatory region operably linked to a nucleotide sequence encoding a polypeptide, Pg. 4, Lns. 12-15; under environmentally stressful conditions such as drought, Pg. 100, Lns. 6-7), and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid (plant produced from the plant cell has a difference in biomass composition compared to the corresponding composition of a control plant that does not comprise the nucleic acid. The difference in biomass composition in the plant can be a difference in the sucrose content or conversion efficiency, Pg. 4, Lns. 8-11); a method of producing a plant with tolerance to drought stress, osmotic stress, or nitrogen deficiency (a method of producing a plant, Pg. 4, Ln. 3), said method comprising (a) expressing in a plurality of plants an exogenous nucleic acid comprising a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, wherein the HMM bit score of the amino acid sequence of said polypeptide is greater than about 65 (a plant cell comprising an exogenous nucleic acid. The exogenous nucleic acid includes a regulatory region operably linked to a nucleotide sequence encoding a polypeptide, where the HMM bit score of the amino acid sequence of the polypeptide is greater than about 65, Pg. 4, Lns. 3-7; expression of polypeptides and/or polynucleotides, Pg. 86, Ln. 7), and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid (plant produced from the plant cell has a difference in biomass composition compared to the corresponding composition of a control plant that does not comprise the nucleic acid. The difference in biomass composition in the plant can be a difference in the sucrose content or conversion efficiency, Pg. 4, Lns. 8-11), and (b) selecting from said plurality a plant that has increased tolerance to drought stress, osmotic stress, or nitrogen deficiency (a population of transgenic plants can be screened and/or selected for those members of the population that have a trait or phenotype conferred by expression of the trans gene, Pg. 85, Lns. 27-29; a modified plant can contain a transgene for other traits, such as ...tolerance, Pg. 96, Lns. 8-9; environmentally stressful conditions such as drought, Pg. 100, Lns. 6-7); a method of producing a plant with tolerance to drought stress, osmotic stress, or nitrogen deficiency (a method of producing a plant, Pg. 4, Ln. 3), said method comprising (a) expressing in a plurality of plants an exogenous nucleic acid comprising a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide, said exogenous nucleic acid comprising a regulatory region operably linked to a nucleotide sequence encoding a polypeptide or a truncation of said polypeptide (a plant cell comprising an exogenous nucleic acid. The exogenous nucleic acid comprises a regulatory region operably linked to a nucleotide sequence encoding a polypeptide, Pg. 4, Lns. 12-15; expression of polypeptides and/or polynucleotides, Pg. 86, Ln. 7), and wherein yield of said plant is increased as compared to the corresponding yield of a control plant that does not comprise said nucleic acid (plant produced from the plant cell has a difference in biomass composition compared to the corresponding composition of a control plant that does not comprise the nucleic acid. The difference in biomass composition in the plant can be a difference in the sucrose content or conversion efficiency, Pg. 4, Lns. 8-11), and (b) selecting from said plurality a plant that has increased tolerance to drought stress, osmotic stress, or nitrogen deficiency (a population of transgenic plants can be screened and/or selected for those members of the population that have a trait or phenotype conferred by expression of the trans gene, Pg. 85, Lns. 27-29; a modified plant can contain a transgene for other traits, such as ... tolerance, Pg. 96, Lns. 8-9; environmentally stressful conditions such as drought, Pg. 100, Lns. 6-7); and a plant cell containing a modified endogenous nucleic acid (this document also features plant cells and plants in which an endogenous biomass composition-modulating nucleic acid described herein has been modified, Pg. 93, Lns. 3-4), said nucleic acid comprising a nucleotide sequence encoding a polypeptide, wherein the HMM bit score of the amino acid sequence of said polypeptide is greater than about 65 (the endogenous nucleic acid encodes a polypeptide, and wherein the HMM bit score of the amino acid sequence of the polypeptide is greater than about 65, Pg. 6, Lns. 16-17), and wherein a plant produced from said plant cell has a difference in tolerance to drought stress, osmotic stress, or nitrogen deficiency as compared to the corresponding composition of a control plant where said nucleic acid has not been modified (the biomass composition of such plants is altered relative to the corresponding composition of a control plant in which the endogenous nucleic acid is not modified. Such plants are referred to herein as modified plants and may be used to produce, for example, increased amounts of a biomass component, e.g., sucrose, Pg. 93, Lns. 6-10; under environmentally stressful conditions such as drought, Pg. 100, Lns. 6-7).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☒ forming part of the international application as filed:

      ☒ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☒ furnished subsequent to the international filing date for the purposes of international search only:

      ☒ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☒ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

SEQ ID NOs: 1, 2, 6, 8, 13, 15, 20, 22, 24, 25, and 61 were searched.