UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/333,830	12/21/2011	Samuel Sai Ming SUN	549072000900	7011

25225 7590 01/22/2019

MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER
WORLEY, CATHY KINGDON

ART UNIT	PAPER NUMBER
1662	

NOTIFICATION DATE	DELIVERY MODE
01/22/2019	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PatentDocket@mofo.com
EOfficeSD@mofo.com
pair_mofo@firsttofile.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SAMUEL SAI MING SUN and LI TIAN[1]

Appeal 2017-002121
Application 13/333,830
Technology Center 1600

Before TAWEN CHANG, JOHN E. SCHNEIDER, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

CHANG, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method to obtain a desired protein from plants, plant parts, or plant cells, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

STATEMENT OF THE CASE

The Specification states that purification of target proteins from plant samples is estimated to account for 80% of the production costs in large-

---

[1] Appellants identify the Real Party in Interest as The Chinese University of Hong Kong. (Appeal Br. 1.)

scale industrial production of recombinant therapeutic proteins by plant-based bioreactors. (Spec. ¶ 3.) The Specification teaches that "[t]raditional protein purification methods involve expression of target proteins as fusion to affinity tags," but these methods "suffer from the difficulty and high cost of scaling-up of the required affinity chromatography." (*Id.* ¶ 4.) The Specification also describes other purification strategies using fusion tags; however, the Specification states that proteolytic cleavage is often required to remove fusion tags, and the "additional cleavage step results in high cost due to the cost of protease and . . . an extra step in its removal, in addition to the potential occurrence of non-specific protein cleavage." (*Id.*)

According to the Specification, "development of a simple and cost-effective downstream recombinant protein purification system is thus highly desirable." (*Id.*) The Specification further describes "[t]he elastin-like polypeptide (ELP)-intein system [as] a simple and efficient method for purification of protein," wherein ELP proteins have the property of "temperature-sensitive phase transition" and inteins are "a kind of protein splicing element [that] catalyzes self-cleavage." (*Id.* ¶¶ 5–6.)

Claims 1, 42, 52, and 53 are on appeal. Claim 1 is illustrative and reproduced below:

> 1. A method to obtain a desired protein from plants, plant parts, or plant cells which method comprises
>
> (a) preparing an extract of proteins from said plants, plant parts or plant cells that stably produce said desired protein as a fusion protein from a recombinant expression system that produces said fusion protein, wherein said fusion protein comprises at either the N-terminus or C-terminus or both of the desired protein, an ELP-intein tag which tag comprises an elastin-like polypeptide (ELP) domain and an intein splicing element (intein) wherein the intein is between the N- and/or C-

terminus or both of the desired protein and the ELP domain; and

wherein any tag at the N-terminus of the desired protein is cleaved at the C-terminus of the intein and any tag at the C-terminus of the desired protein is cleaved at the N-terminus of the intein; and

wherein the codons of the recombinant expression system are optimized for expression in plants;

(b) optionally removing insoluble materials from said extract;

(c) aggregating the fusion proteins and separating them from the remainder of the extract;

(d) resolubilizing the fusion proteins into an aqueous solution;

optionally repeating steps (c) and (d);

(e) effecting cleavage of the fusion protein;

(f) separating the desired protein from the tag(s);

wherein the ELP domain contains at least 20 ELP units; and

wherein the fusion protein further includes one or more linker sequences between the desired

protein and intein and/or intein and ELP and/or among ELP units.

(Appeal Br. 10 (Claims App.).)

The Examiner rejects claim 1 under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Wood[2] and Yadav.[3] (Final Act. 10; Ans. 12.)[4]

---

[2] Wood et al., US 2006/0263855 A1, published Nov. 23, 2006.

[3] Yadav et al., US 2004/0172688 A1, published Sep. 2, 2004.

[4] Claim 1 was originally rejected as obvious over Wood, Yadav, and Natarajan et al., *Comparison of Protein Solubilization Methods Suitable for Proteomic Analysis of Soybean Seed Proteins*, 342 ANALYTICAL BIOCHEMISTRY 214 (2005). The Examiner modified the rejection in the Answer to remove Natarajan in light of the after-final amendments Appellants submitted on April 13, 2016. (Ans. 12.)

The Examiner rejects claims 42 and 52 under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Wood, Yadav, Vierstra,[5] and Sun.[6] (Final Act. 13; Ans. 13.)[7]

The Examiner rejects claim 53 under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Wood, Yadav, Vierstra, Sun, and Ooi.[8] (Final Act. 20; Ans. 13.)[9]

I.

Issue

The Examiner has rejected claim 1 as obvious over Wood and Yadav. The Examiner has rejected claims 42 and 52 as obvious over Wood, Yadav,

---

[5] Vierstra et al., US 6,455,759 B1, issued Sep. 24, 2002.
[6] Sun et al., US 2004/0268431 A1, published Dec. 30, 2004.
[7] Claims 52 and 53 were added in the April 13, 2016 after-final amendments. However, the Examiner rejected them "for the same grounds that were applied to the previously rejected claims 42 and 49, respectively, with the modification that the rejection of claim 53 no longer requires the reference of Huang et al., [US 7,417,178 B2, issued Aug. 26, 2008,] which was required by cancelled claim 49." (Ans. 13.)
[8] Linda S.M. Ooi et al., *Purification and Characterization of Non-Specific Lipid Transfer Proteins from the Leaves of* Pandanus amaryllifolius *(Pandanaceae)*, 27 PEPTIDES 626 (2006).
[9] The Examiner stated in the Answer that claim 53, which was added in the Apr. 13, 2016 after-final amendment, is "rejected for the same ground[] that [was] applied to previously rejected claim[] . . . 49 . . . ; with the modification that the rejection of claim 53 no longer requires the reference of Huang et al. which was required by cancelled claim 49." (Ans. 13.) Claim 49 was rejected as obvious over Wood, Yadav, Huang, and Ooi. (Final Act. 20.) However, since claim 53 depends from claim 42, which was rejected over Wood, Yadav, Vierstra, and Sun, we understand the rejection of claim 53 to be over Wood, Yadav, Vierstra, Sun, and Ooi. Appellants appear to share this understanding. (Reply Br. 4.)

Vierstra, and Sun. The same issue is dispositive as to these rejections; we therefore discuss the rejections together.

The Examiner finds that Wood discloses almost all of the limitations of claim 1 and specifically suggests plant cells as potential hosts for expression of its fusion protein, but does not exemplify expression of a fusion protein in a plant, plant part, or plant cell, as required by claim 1. (Final Act. 8.) However, the Examiner finds that Yadav teaches transgenic plants expressing fusion proteins comprising inteins, as well as expression vectors modified to contain plant optimized codons and operable in plant cells to express a fusion protein. (*Id.* at 8–9.) The Examiner concludes that,

> [a]t the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to follow the suggestion of Wood et al to use plant cells as host cells, and it would have been obvious to use a plant expression system such as the 35S/NOS system taught by Yadav et al. Given the success of Wood et al in producing ELP-intein-protein fusions and utilizing this system to produce, cleave, and purify the protein of interest, and give[n] the success of Yadav et al in producing intein-protein fusions in a plant system, one would have had a reasonable expectation of success in moving the system of Wood et al into a plant system.

(*Id.* at 9.)

Appellants concede that "Wood discloses the same process steps as set forth in claim 1" and "exemplifies this [process] in prokaryotes." (Appeal Br. 5.) Appellants also do not dispute that Wood "speculates" that "[its] process could also be applied to proteins from plants." (*Id.*) Appellants contend, however, that "production [of recombinant fusion proteins] in plants is so unpredictable that the artisan would simply dismiss [Wood's suggestion] as aggressive patent drafting." (*Id.*)

Appellants do not advance any additional arguments with respect to the rejection of claims 42 and 52 over Wood, Yadav, Vierstra, and Sun in the Appeal Brief.[10] (Appeal Br. 8.) Therefore, the issue with respect to both rejections is whether a skilled artisan would have had a reasonable expectation of success in using Wood's method of expressing fusion proteins in plants, plant parts, or plant cells.

Analysis

We agree with the Examiner that claim 1 is obvious over Wood and Yadav. Only those arguments made by Appellants in the briefs have been considered; arguments not so presented are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2015); *see also Ex parte Borden*, 93 USPQ2d 1473, 1474 (BPAI 2010) (informative) ("Any bases for asserting error, whether factual or legal, that are not raised in the principal brief are waived.").

As discussed above, Appellants concede that "Wood discloses the same process steps as set forth in claim 1" and "exemplifies this [process] in prokaryotes." (Appeal Br. 5.) Wood also states that

> [o]ne advantage of [its] invention is that it can be used with many different types of host cells. For instance, it is envisioned that the purification system can be used with a prokaryotic cell or a eukaryotic cell. Preferably, the host cell is a bacterial cell, a fungal cell, a mammalian cell, an

[10] In the Reply Brief, Appellants do make additional arguments specifically directed to claims 42 and 52. These arguments are waived, however, because they were not presented in the opening brief, thereby denying the Board the benefit of the Examiner's response, and no showing of good cause was made by Appellants to explain why the late argument should be considered by the Board. *See* 37 C.F.R. § 41.41(b)(2); *Cf. Optivus Technology, Inc. v. Ion Beam Applications S.A.*, 469 F.3d 978, 989 (Fed. Cir. 2006) (argument raised for the first time in the Reply Brief that could have been raised in the opening brief is waived).

> insect cell, a yeast cell, or ***a plant cell***. In one embodiment, the host cell is a bacterial cell, such as *E. coli*. More particularly, it is envisioned that the invention can be used successfully in mammalian cells.

(Wood ¶ 57 (emphasis added).)

Appellants contend that claim 1 is not obvious over Wood and Yadav because "it [would not have been] predictable that fusion proteins [comprising] intein and at least 20 ELP units could be produced recombinantly in plants and extracted in sufficient quantity to subject them to the macroscopic scale purification process set forth in claim 1." (Appeal Br. 4.)

We are not persuaded. As an initial matter, as the Examiner points out, Claim 1 does not require any particular quantity of proteins to be produced and extracted. (Interview Summary (Apr. 22, 2016).) Appellants contend that "there is no disagreement that the steps set forth in claim 1 are done on a macroscopic scale and therefore sufficient fusion proteins must be produced to permit application of these steps." (Appeal Br. 4; *see also id.* at 5.) We are not persuaded, however, because claim 1 also does not contain limitations regarding the scale of the process. "[W]hile it is true that claims are to be interpreted *in light of* the specification . . . , it does not follow that limitations from the specification may be read into the claims. . . . [T]he claims define the invention." *Sjolund v. Musland*, 847 F.2d 1573, 1581–82 (Fed. Cir. 1988).

Assuming for the sake of argument that "there is no disagreement that the steps set forth in claim 1 are done on a macroscopic scale and therefore sufficient protein must be produced to permit application of these steps" (Appeal Br. 4), we nevertheless agree with the Examiner that a skilled

artisan would have had a reason to produce Wood's recombinant protein in a plant cell, as required by claim 1, with a reasonable expectation of success, in light of Wood's explicit disclosure that its invention may be used with many different types of host cells including plant cells and Yadav's disclosure of transgenic plants expressing fusion proteins comprising inteins and plant optimized codons. (Wood ¶ 57; Yadav Abstract, ¶ 19.)

Appellants contend that there is no documentation in support of the Examiner's position that "it is a routine matter to produce large amounts of recombinant proteins in plants in view of successes in the art in producing, for example, pharmaceuticals." (Appeal Br. 4, 7.)

We are not persuaded. The Examiner points to prior art references that disclose production of significant amounts of recombinant proteins in plants. (Ans. 13–14; *see also e.g.,* Sun Abstract (describing a "plant production method . . . [having] promising potential to mass-produce some of the most expensive biopharmaceuticals of restricted availability in a much cheaper way"); Huang 6:40–43 (describing "a mature, transgenic monocot seed that yields, by extracting ground seed with an aqueous medium, a total soluble protein fraction containing at least 3% by total protein weight of a human milk protein" and further describing an embodiment wherein "the total soluble protein fraction contains at least 20% by total protein weight of the human milk protein").) Moreover, the Specification itself states that

> [u]sing transgenic plants for large-scale production of pharmaceutical proteins has been demonstrated as an attractive system with the advantages of low cost, high yield, easy harvest and reduced health risks in comparison to traditional microbial and mammalian bioreactors, and many valuable recombinant therapeutic proteins have been expressed in transgenic plants as proof-of-concept and feasibility demonstrations.

(Spec. ¶ 3.)

In the Reply Brief, Appellants contend that the prior art "shows that high level heterologous protein production in plants is actually a problem" and teaches that "in order to achieve high levels of expression, the conditions must be manipulated in ways that are specific to each protein and to each type of plant." (Reply Br. 2–3.) Appellants cite Patel[11] and Streatfield[12] in support of their argument.

We are not persuaded. Appellants concedes that Patel "suggests using the ELP unit in multiple copies to enhance expression." (Reply Br. 3.) However, Appellants argue that Patel does not mention "coupling [ELP units] to the basic protein to be produced with an intein sequence" and further argue that, while Patel teaches enhancing expression with an 11.3 kD ELP tag, it teaches doing so "only in conjunction with an ER retention signal." (*Id.*) However, the fact that all of the limitations in a claim are not described in a single reference does not suffice to render the claim non-obvious. Likewise, while Patel does state that "it is clear that the 11.3 kDa ELP tag in conjunction with an ER retention signal[] was instrumental in increasing the accumulation of three quite different target proteins in tobacco leaves" (Patel 248, left column), claim 1 does not preclude inclusion of an ER retention signal.

Appellants also argue that Streatfield "makes it clear that . . . obtaining practical amounts of recombinant proteins in plants is not

---

[11] Patel et al., *Elastin-Like Polypeptide Fusions Enhance the Accumulation of Recombinant Proteins in Tobacco Leaves*, 16 TRANSGENIC RESEARCH 239 (2007).
[12] Stephen J. Streatfield, Review Article, 5 PLANT BIOTECHNOLOGY J. 2 (2007).

straightforward, but requires manipulation of conditions that are unique to individual situations." (Reply Br. 3.) We are not persuaded. Streatfield teaches that "[s]trategies have been developed to increase the levels of recombinant proteins for plant production systems" and that "[t]he type of system used for protein production specifies the range of approaches that can be applied." (Streatfield 4, left column.) Appellants have pointed to no specific teachings in Streatfield that suggests a skilled artisan would not have a reasonable expectation of success in adapting known strategies for increasing recombinant protein levels in plants to produce the recombinant protein described in Wood. In this regard, we emphasize that "obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success": "[E]xpectation of success need only be reasonable, not absolute." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007).

Appellants contend that, while Wood provides "a speculation that it would be possible to apply [its] process to recombinant plant-produced fusion proteins," the production of fusion proteins in plants is "so unpredictable that the artisan would simply dismiss [Wood's suggestion] as aggressive patent drafting." (Appeal Br. 5.) We are not persuaded. As discussed, Appellants provide no persuasive evidence to support their contention that a skilled artisan would not have had a reasonable expectation of success of applying Wood's process to recombinant plant-produced fusion proteins to arrive at the claimed invention. "Attorneys' argument is no substitute for evidence." *Johnston v. IVAC Corp.*, 885 F.2d 1574, 1581 (Fed. Cir. 1989).

Appellants argue that the Examiner's inclusion of Yadav indicates that the Examiner agrees that Wood's suggestion of applying its process to recombinant plant-produced fusion proteins is insufficient to establish a prima facie case of obviousness as to claim 1. (Appeal Br. 5, 7; Reply Br. 2.) We are not persuaded. Appellants cite no authority, and we are aware of none, that the Examiner's citation of a combination of art in a § 103 rejection may or should be treated as a concession that a subset of the combination is insufficient to invalidate the claim(s) at issue. Indeed, the predecessor to our reviewing court has suggested the opposite, in holding that the Board may rely on less than all of the references relied upon by the Examiner. *In re Bush*, 296 F.2d 491, 496 (CCPA 1961).

Appellants argue that Yadav "falls short of establishing predictability for the fusion proteins of the present claims," because Yadav's fusion proteins do not contain ELP units. (Appeal Br. 6.) Appellants argue that, because the "at least 20 ELP units" required by claim 1 would add to the fusion protein "a 100-amino acid 'tail' . . . contain[ing] 20 prolines," and because proline is "instrumental in determining protein conformation and stability," a skilled artisan "would not consider it predictable that plants would be a successful host for producing recombinant proteins to be subjected to the purification procedure of claim 1." (*Id.*)

We are not persuaded. As already discussed, arguments from attorneys cannot take the place of evidence, *Johnston*, 885 F.2d at 1581 (Fed. Cir. 1989), and Appellants cite insufficient persuasive evidence that supports their attorneys' arguments. In addition, Appellants attack Yadav individually. However, "[n]on-obviousness cannot be established by attacking references individually where the rejection is based upon the

teachings of a combination of references. . . . [The reference] must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole." *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986).

Finally, citing to paragraphs 8–13, Appellants argue that the disclosures in the Specification supports their contention regarding the lack of reasonable expectation of success. (Appeal Br. 6, 7.)

We are not persuaded. Paragraphs 8–11 state that, while the prior art discloses "application of ELP or intein in the alternative in transgenic plants," Appellants are "not aware of any report on the use of ELP and intein in combination in transgenic plants." (Spec. ¶¶ 8–11.) However, as already discussed, the mere fact that all of the limitations of a claim are not found in a single prior art reference does not suffice to show that the claim is non-obvious. Neither have Appellants argued or provided evidence of the existence of any secondary considerations of non-obviousness, such as failure of others.

Paragraphs 12 and 13 describe difficulties that may be encountered and/or have been encountered by Appellants in practicing the claimed invention. (Spec. ¶¶ 12–13.) However, the Specification suggests that such difficulties may be overcome simply by "routine optimization" of extraction and purification conditions and procedures. (*Id.* (stating that "[r]outine optimization of extraction and purification procedures . . . may be needed to purify target proteins from plant samples by the ELP-intein system" after describing potential issues in practicing the claimed method).) Thus, we are not persuaded that the Specification supports Appellants' attorney argument

that a skilled artisan would not have had reasonable expectation of success in combining Wood and Yadav to arrive at the claimed invention.[13]

Accordingly, we affirm the Examiner's rejection of claim 1. Claims 42 and 52, which are not separately argued, fall with claim 1. 37 C.F.R. § 41.37(c)(1)(iv).

II.

Issue

The Examiner has rejected claim 53 as obvious under Wood, Yadav, Vierstra, Sun, and Ooi. Claim 53 depends from claim 42, which is reproduced below:

> 42. The method of claim 1:
>
> (i) wherein the plants, plant parts or plant cells are tobacco and the expression system comprises in the 5' to 3' orientation: a 35S promoter, a sequence encoding ubiquitin, a sequence encoding a phaseolin signal peptide, a sequence encoding a desired protein, a sequence encoding an intein, a

[13] In the Appeal Brief, Appellants mention certain other limitations of claim 1 – in particular that "the fusion protein further includ[ing] one or more linker sequences between the desired protein and intein and/or intein and ELP and/or among ELP units," and that "codons be optimized for expression in plants." (Appeal Br. 7.) Appellants do not dispute that those limitations are disclosed in either Wood or Yadav and argue only that "Wood is directed to production of . . . proteins in bacteria" and that Yadav does not teach plant-optimized codon "with the view of providing successful production of the [claimed] fusion protein as opposed to simply the intein/desired protein fusion." (*Id.*) We are not persuaded for the reasons already discussed: Based on the record before us, we agree with the Examiner that a skilled artisan would have had reason to combine Wood and Yadav to arrive at the claimed invention, with a reasonable expectation of success, and Appellants' arguments, which amount to an attempt to establish non-obviousness by attacking the references individually, accordingly fail. *In re Merck & Co.*, 800 F.2d at 1097.

> linker sequence, a sequence encoding at least 20 ELP repeats and a NOS terminator sequence; or
>
> (ii) wherein the plants, plant parts or plant cells are rice and the expression system comprises in the 5' to 3' orientation a glutelin promoter, a sequence encoding a phaseolin signal peptide, a sequence encoding at least 20 ELP repeats, a linker sequence, a sequence encoding an intein, a sequence encoding a desired protein and a NOS terminator sequence.

(Appeal Br. 10–11 (Claims App.).) Claim 53 claims "[t]he method of claim 42 wherein in (ii) the desired protein is *Pandanus lectin* protein." (*Id.* at 11 (Claims App.).)

The Examiner finds that the combination of Wood, Yadav, Viestra, and Sun suggests all of the limitations of claim 53, except that the combination does not teach a *Pandanus* lectin protein. (Final Act. 14–16 (discussing claim 42), 21–22 (discussing cancelled claim 49), Ans. 13 (claim 53 rejected on same ground as cancelled claim 49).) The Examiner finds, however, that Ooi teaches the purification and characterization of a *Pandanus* lectin protein. (Final Act. 22.) The Examiner concludes that it would have been obvious to a skilled artisan to obtain a *Pandanus* lectin protein as taught by Ooi using the method suggested by Wood, Yadav, Viestra, and Sun, because this would be "an obvious combination of known elements that produced predictable results." (*Id.* at 22.)

Appellants contend that claim 53 is patentable for the same reasons as discussed above with respect to claim 1, and further contend that claim 53 is patentable for the additional reason that "Ooi does not suggest recombinant production of *Pandanus* lectin." (Appeal Br. 9.)

The issue with respect to this rejection is whether it would have been obvious to a skilled artisan to produce a *Pandanus* lectin protein using the method suggested by the combination of Wood, Yadav, Viestra, and Sun.

Analysis

We agree with the Examiner that claim 53 is obvious over Wood, Yadav, Vierstra, Sun, and Ooi. Only those arguments made by Appellants in the briefs have been considered; arguments not so presented are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2015); *see also Ex parte Borden*, 93 USPQ2d at 1474.

As to Appellants' contention that claim 53 is patentable for the same reasons as discussed above with respect to claim 1, we are not persuaded for the reasons already discussed with respect to claim 1.

Appellants further contend that

> [c]laim 53 is patentable for the additional reason that there is no evidence in the art that *Pandanus* lectin is a candidate for recombinant production in plants. As is apparent from the document itself, *Pandanus* lectin is not produced recombinantly as a foreign protein in plants, but rather from its native source, *Pandanus amaryllifolius*. Ooi does not provide incentive to produce *Pandanus* lectin recombinantly in plants, and claim 53 is patentable for this additional reason.

(Appeal Br. 8.)

We are not persuaded. Again, "[n]on-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." *In re Merck & Co.*, 800 F.2d at 1097. As the Examiner points out, the other references cited in the rejection suggest the desirability of plants as a system for producing recombinant proteins. (Ans. 16; *see also e.g.*, Wood ¶ 57 (stating that an advantage of its inventive purification system is that it can be used with many different types of host cells, including preferably a plant cell); Yadav ¶ 11 (stating that "[p]lants are increasingly being looked to as platforms for

the production of materials foreign to plant systems"); Vierstra 1:18–23 (stating that "it has now become common practice to create . . . transgenic plants"); Sun ¶ 5 (stating that "[t]he commercial potential of using transgenic plants as production systems is very high due to the unique and outstanding characteristics of the plants").) This suggestion, combined with Ooi's suggestion of *Pandanus* lectin[14] as a protein of interest (*see e.g.,* Ooi 626–627 (identifying proteins as non-specific lipid transfer proteins and suggesting possible biological functions and potential application)), provides a reason for a skilled artisan to combine Ooi with Wood, Yadav, and Vierstra to arrive at the claimed invention, in the absence of evidence to the contrary.[15]

Accordingly, we affirm the Examiner's rejection of claim 53.

SUMMARY

For the reasons above, we affirm the Examiner's decision rejecting claims 1, 42, 52, and 53.

---

[14] In their Reply Brief, Appellants argue for the first time that Ooi does not disclose *Pandanus* lectin at all. (Reply Br. 5.) While we acknowledge that Ooi describes the proteins it purifies as "lectin-like" rather than lectins (Ooi 630, right column), no showing of good cause was made by Appellants to explain why this argument was not presented in the opening brief, thereby denying the Board the benefit of the Examiner's response. Accordingly, we decline to consider this argument, which is waived. *See* 37 C.F.R. § 41.41(b)(2); *Cf. Optivus Technology*, 469 F.3d at 989.

[15] For instance, Appellants have not suggested that using the method described in Wood to purify a recombinant *Pandanus* lectin from a plant host cell produces unexpected results.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED