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POTTER ANDERSON & CORROON LLP ATTN: JANET E. REED, PH.D. P.O. BOX 951 WILMINGTON, DE 19899-0951			ROBINSON, KEITH O NEAL	
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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* JULIAN M. CHAKY, MOLLY RYAN-MAHMUTAGIC,  
EDWIN JOSUE MENDEZ, SALLY ANNE SANTIAGO-PARTON,  
JOSHUA M. SHENDELMAN, JOHN B. WOODWARD,  
and YANWEN XIONG

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Appeal 2015-001609  
Application 13/339,548  
Technology Center 1600

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Before ERIC B. GRIMES, RICHARD M. LEBOVITZ, and  
KRISTI L. R. SAWERT, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal involves claims directed to a method for identifying improved resistance to one or more aphid biotypes comprising a step of detecting a marker or SNP in a soybean plant or germplasm. The Examiner finally rejected the claims as obvious under 35 U.S.C. § 103(a). We have jurisdiction under 35 U.S.C. § 134. The obviousness rejection is affirmed.

STATEMENT OF CASE

Appellants appeal from the Examiner's rejection of claims 1–3 and 8–22 under 35 U.S.C. § 103(a) (pre-AIA) as obvious in view of

Hill et al. (U.S. Publ. Pat. App. No. 2006/0015964 A1, publ. Jan 19, 2006) (“Hill ’964”) and Hill et al. (*A New Soybean Aphid (Hemiptera: Aphididae) Biotype Identified*, 103 J. Econ. Entomol. 509–515 (2010)) (“Hill (2010)”). Final. Rej. 4.

Claim 1, the only independent claim on appeal, reads as follows:

1. A method of identifying a first soybean plant or germplasm that displays improved resistance to one or more soybean aphid biotypes, the improved resistance comprising one or more of improved antibiosis resistance and improved antixenosis resistance, the method comprising detecting in the first soybean plant or germplasm, or a part thereof, at least one Rag haplotype that is associated with the improved soybean aphid resistance, the at least one Rag haplotype comprising marker loci selected from the group consisting of:

(a) one or more marker loci selected from the group consisting of S14181-1-Q1, S13871-1-Q1, S14161-1-Q10, S09515-1-Q1, S14151-1-Q1, S14151-2-Q4, S07164-1-Q12, S14182-1-Q1, S00812-1-A, and S02780-1-A;

(b) one or more marker loci selected from the group consisting of S01190-1-A, S14761-001-Q001, S14771-001-Q001, S07165-1-Q3, S14778-001-Q001, and S01164-1-Q1;

(c) one or more marker loci selected from the group consisting of S13662-1-Q3/Q6, S13663-1-Q1, S11411-1-Q1, S13664-1-Q1/Q002, S13672-1-Q1/Q2/Q3, S13674-1-Q1/Q007, and S13675-2-Q1;

(d) one or more SNP loci located at physical positions 5516385, 5516818, 5598980, 5602544, 5605203, 5605275, 5608106, 5630404, 6754454, and 6671535 on LG-M of the soybean genome;

(e) one or more SNP loci located at physical positions 28187733, 28829625, 28837383, 29097652, 29678319, and 29825175 on LG-F of the soybean genome; and

(f) one or more SNP loci located at physical positions 5140274, 5919650, 5960726, 6066531, 6231641, 6524877, and 6542422 on LG-J of the soybean genome.

## REJECTION

Claim 1, the only independent claim on appeal, is directed to a method of identifying a first soybean plant or germplasm that displays improved resistance to one or more soybean aphid biotypes. The method involves detecting a “Rag haplotype” comprising detecting marker loci selected from a list of marker loci and SNPs (single nucleotide polymorphisms).

“Rag” is the notation for three different soybean aphid resistance genes that had been mapped to the soybean genome prior to the filing date of the application. Spec. 3:17–19. The three known aphid resistance genes are Rag1, Rag2, and Rag3. *Id.* at 3:20–29. The Specification explains that soybean resistance to aphids is important because soybean is a major cash crop and aphids are a widely distributed soybean pest that can cause severe damage and loss of soybean crops. *Id.* at 1:16 to 2:28. Hill ’964 teaches that aphid Rag resistance genes can be introduced by selective breeding into soybean plants to create inbred soybean plant lines that are resistant to aphids. Hill ’964 ¶ 17.

The Examiner rejected the claims as obvious in view of Hill ’964 and Hill (2010). The Examiner found that Hill ’964 identified Rag markers associated with resistance to soybean aphids. Final Rej. 7. The Examiner acknowledged that Hill ’964 does not describe the Rag markers recited in the claims, but found that the skilled worker would have been motivated to find other Rag markers in view of Hill ’964’s teaching (*id.*) that “[o]ther markers of linkage group M may also be used to identify the presence or absence of the gene.” Hill ’964 ¶ 12. The Examiner relied on Hill (2010) in rejecting claim 3 which specifies that the improved soybean aphid resistance

comprises improved resistance to at least two of soybean aphid biotypes 1, 2, 3, and X.

Appellants contend “it would not have been reasonable to expect that the skilled artisan would successfully arrive at the *specific and novel* markers recited in Applicants’ claims. This is because the markers recited in Applicants’ claims are *novel* markers that are not taught or even suggested by Hill 2006 or Hill 2010.” Appeal Br. 10–11. Appellants further argue that “Genetic screening can be unpredictable. In many cases, genetic screening efforts only fortuitously yield genetic loci that contribute to specific phenotypes or functions.” Reply Br. 6.

#### DISCUSSION

The Specification describes genetic markers that can be used to identify and select soybean plants with improved antibiosis and/or antixenosis resistance to one or more biotypes of soybean aphid. Spec. 5:5–13. “Antibiosis (non-choice) is the plant’s ability to reduce the survival, reproduction, and fecundity of the insect. Antixenosis (choice) is the plant’s ability to deter the insect from feeding or identifying the plant as a food source.” *Id.* at 3:13–16. A “biotype” is defined in the Specification as a “subspecies of soybean aphid that shares certain genetic traits or a specified genotype.” *Id.* at 3:8–9. Aphids can be characterized as a single biotype based on their resistance to a plant’s antibiosis or antixenosis effects.

The genetic markers to select aphid resistant soybean strains are recited in the rejected claims. While the Specification does not disclose how these markers were specifically identified, it does not appear to have been disputed that the markers are derived from the three different soybean aphid

resistance genes (Rag1, Rag2, and Rag3) which had previously been mapped to specific locations in the soybean genome. *Id.* at 3:17–29; 12:27 to 13:7; 30:20 to 32:12.

Hill '964 describes a method of identifying markers associated with soybean aphid resistance genes Rag1 and Rag2. Hill '964 ¶¶ 11, 12; Example 3 (¶¶ 85–86); Example 4 (¶¶ 87–90). The Examiner acknowledges that the claimed markers identified by the inventors for the known aphid resistance genes are novel, but found it would have been obvious to have identified them utilizing Hill '964's method. Final Rej. 7.

We agree with the Examiner's determination that the claims would have been obvious to one of ordinary skill in the art at the time of the invention based on the cited publications.

The claims in this appeal are directed to novel nucleic acid sequences; specifically, markers and SNPs that co-segregate with the *known* soybean aphid resistance genes Rag1, Rag2, and Rag3. The starting materials used to obtain these sequences appear to have been available. For example, numerous soybean germplasms from which to obtain the marker sequences were known at the time of the invention. *See* Hill '964, 52 (Table 1); Hill (2010), Table 1; *see* also Spec. 50:17–18 (disclosing the use of “Thirty five hundred soybean plant introductions (PIs) . . . obtained from the USDA Soybean Germplasm Collection.”). . The soybean aphid resistance linkage groups from which the markers were obtained were also known as established by admissions in the Specification and by Hill '964. Spec. 3:17–29; 5:15 to 12:9 (indicating that the claimed markers and sequences are present in soybean genomic regions known to contain the Rag genes). For example, the Specification discloses that a variety of the claimed sequences

reside in chromosomal linkage group LG-M. *Id.* at 5:17–18; 5:24–8:10. Hill '964 identified LG-M as the region in which Rag1 and Rag2 reside. Hill '964 ¶¶ 11, 20.

Hill '964 provides evidence that techniques used to isolate markers from the linkage groups comprising the known soybean resistance genes were conventional and routine, as were the methods to use the markers to identify aphid resistant plants. Hill '964 ¶¶ 11, 12; Example 3 (¶¶ 85–86); Example 4 (¶¶ 87–90). Thus, the markers recited in the claims are a product of using known materials and conventional technology which had successfully been applied to obtain different markers for the same known Rag genes within the same identified linkage groups.

Appellants' argument that the sequences and positions of the markers recited in the rejected claims were unknown and not suggested by the cited Hill '964 and Hill (2010) does not persuade us that the Examiner made reversible error in determining that the claims are obvious. A novel nucleotide sequence is not necessarily non-obvious to one of ordinary skill in the art. *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009). In this case, the claimed markers were identified from linkage groups known to co-segregate with the aphid resistance genes. As found by the Examiner, Hill '964 expressly teaches that that “[o]ther markers of linkage group M may also be used to identify the presence or absence of the [aphid resistance] gene.” Hill '964 ¶ 12; Final Rej. 7. Appellants have not directed us to evidence in this record that the methods and materials utilized to identify the recited markers departed from the conventional materials and technology described in Hill '964 and as available prior to the application filing date.

Appellants contend that “a person of ordinary skill in the art would not have a reasonable expectation of success to arrive at the invention as claimed, given the often unpredictable nature of genetic screening.” Reply Br. 6–7. However, Appellants have not provided evidence of unpredictability. An argument made by counsel in a brief does not substitute for evidence lacking in the record. *Estee Lauder Inc. v. L’Oréal, S.A.*, 129 F.3d 588, 595 (Fed. Cir. 1997). On the other hand, Hill ’964 describes using the technique to identify markers. Consequently, a preponderance of the evidence does not support Appellants’ argument that it would have been unpredictable to have obtained the markers recited in the rejected claims.

Appellants argue that “[w]ithout recognizing the usefulness of the markers, as the markers were unknown, a person of ordinary skill in the art would not have a reasonable expectation of success to arrive at Appellants’ invention as claimed.” Reply Br. 7. This argument does not persuade us that the Examiner erred. Markers for the aphid resistance genes were known to be useful to identify soybean plants’ resistance to aphids. *See generally* Hill ’964. While the specific marker sequences recited in the claims were unknown, they are derived from the known aphid resistance genes and linkage groups, and it would have been obvious to have identified the markers utilizing Hill ’964’s method for its expected success. It was not unexpected, based on Hill ’964, that markers for soybean aphid resistance genes could be routinely identified. We have not been directed to evidence that would counter the teaching in Hill ’964 of the successful identification of marker sequences utilizing its technology.

In the Reply Brief, Appellants assert that “[a]s the presently claimed methods use markers outside of the paragraph [0012] region on LG-M, and

Hill [’964] does not actually teach or suggest using such markers, Appellants[’] use here should be nonobvious over the cited art.” Reply Br. 7. However, Appellants did not direct us to evidence that the markers are outside the region of LG-M defined by Hill ’964. Nonetheless, even if they did, the recited markers are present in the linkage groups disclosed by Hill ’964 to contain the known Rag genes. Appellants did not establish that it was surprising that useful markers would reside outside the specific genomic regions described in Hill ’964.

#### Claim 2

Claim 2, depends from claim 1, and further recites “wherein the improved soybean aphid resistance comprises both improved antibiosis resistance and improved antixenosis resistance.”

The Examiner states that neither of the cited publications describe improved antibiosis and antixenosis resistance. Final Rej. 9. However, the Examiner found it would have been obvious “that having both improved antibiosis resistance and improved antixenosis resistance would allow a soybean plant to have greater resistance to soybean aphid . . . as opposed to only having one or the other.” *Id.* The Examiner further found that Hill (2010) teaches both antibiosis and antixenosis screening of soybean for aphid resistance, providing a reason to have identified plants with both. Ans. 9.

Appellants contend that Hill (2010) “does not teach or suggest experiments to measure antibiosis, which concerns an insect’s increased mortality, shortened longevity or decreased reproduction capacity in response to a resistant plant.” Reply Br. 9–10. Rather, Appellants argue that

Hill (2010) “teaches two kinds of choice tests conducted by the authors, indicating that antixenosis, which concerns an insect’s non-preference for a resistant plant compared to a non-resistant plant, is the focus of their experiments.” *Id.* at 9.

This argument does not convince us that the Examiner erred.

Hill (2010)’s experiments were designed to characterize a new soybean aphid biotype. Hill (2010) 509, Abstract & 510, col. 2, ll. 2–6. Thus, even if Hill (2010)’s experiments only looked at antixenosis, the reason is that the tests were performed to identify the aphid as a new biotype.

Choice and nonchoice tests conducted in this study characterized the colonization of a soybean aphid isolate, collected from the overwintering host *Frangula alnus* P. Mill in Springfield Fen, IN, on different aphid resistant soybean genotypes. This isolate readily colonized plants with the *Rag2* resistance gene, distinguishing it from the two biotypes previously characterized and indicating that it represented a new biotype named biotype 3.

*Id.*, Abstract.

Nonetheless, we note that Hill (2010) report in Experiment 3 that the results “indicated that LD05-16611 had antibiosis-type resistance.” *Id.* at 513. Thus, contrary to Appellants’ argument, Hill (2010) looked at both antibiosis and antixenosis.

Hill (2010) stated that the identification of a new aphid biotype indicated that “there is high variability in virulence in soybean aphid populations present in North America, posing a significant challenge to soybean breeders developing soybean aphid resistant cultivars.” *Id.* at 514, col. 2 (first full paragraph). Because of this finding, Hill (2010) further stated that the known *Rag* aphid resistance genes might not be sufficient to

provide long-term resistance to aphids. *Id.* Consequently, Hill (2010) suggested identifying new aphid resistance genes. *Id.* Hill (2010) specifically discusses “[r]esistance gene stacking” as “a method used by breeders to improve the durability of plant disease resistance,” in which a plant is bred and selected to have more than one resistance gene, such as *Rag1*, *Rag2*, etc. *Id.* Based on this disclosure, the skilled worker would have had reason to have selected plants with more than one type of aphid resistance in an effort to “stack” plants with more than one resistance gene — as determined by the Examiner. Hill (2010) specifically mentions antibiosis:

Resistance in ‘Dowling’ had strong antibiosis that limited aphid colonization on plants in nonchoice tests. Detailed analysis of the effects of antibiosis on aphid biology indicated that the resistance in Dowling significantly reduced aphid survival, longevity, fecundity, and nymphal development . . . . The aphid resistance in Dowling was shown to be controlled by a single dominant gene named *Rag1*.

*Id.* at 510, col. 1, ll. 2–10.

Hill (2010) also characterizes plants with antibiosis and antixenosis phenotypes:

However, colonization on soybean genotypes with *Rag1* was significantly lower than on Williams 82 or on genotypes with *Rag2* in nonchoice tests (Fig. 1, Tables 4 and 5). These results seemed to indicate that some soybean genotypes with *Rag1* expressed antibiosis-type resistance with little, if any, antixenosis-type resistance.

*Id.* at 514, col. 2, ll. 3–9.

In sum, the preponderance of the evidence supports the Examiner’s determination that claim 2 would have been obvious to one of ordinary skill in the art.

Claims 11–14

Claims 11–14 recite specific sequences as the haplotype markers (SEQ ID NOS). Appellants contend that these sequences are not disclosed or suggested by Hill '964 and Hill (2010). Appeal Br. 13. While the sequences had not been identified in the cited publication as Rag haplotypes associated with improved aphid resistance, the sequences are an obvious result of applying the conventional technique described in Hill '964 to known starting materials. Consequently, we conclude that the claims are obvious for the same reasons discussed above for claim 1.

Claim 20

Claim 20 depends on claim 1, from claims 18 and 19, and further recites that the first soybean plant of claim 1 is crossed with a “second soybean plant or germplasm compris[ing] an exotic soybean strain or an elite soybean strain.” The Examiner found that Hill '964 teaches high yield parents which “read” on elite strains and that such crosses are conventional. Final Rej. 8; Ans. 11–12.

Appellants contend that “[a] person of ordinary skill in the art would understand that some elite strains do not display high yield.” Appeal Br. 13.

This argument is not persuasive. As found by the Examiner (Ans. 11), Hill '964 teaches:

The information disclosed herein regarding RAG loci is used to aid in the selection of breeding plants, lines and populations containing *Aphis glycines* resistance for use in introgression of this trait into elite soybean germplasm, or germplasm of proven genetic superiority suitable for variety release.

Hill '964, ¶ 13.

Claims 21 and 22

Claims 21 and 22 depend ultimately from claim 1, and recite that the first soybean plant or germplasm is selected from a specific list of soybean varieties identified by PI (“plant introduction,” Spec. 50:17) numbers. The claims require detecting “at least one Rag haplotype that is associated with the improved soybean aphid resistance, the at least one Rag haplotype” in one of the listed PI’s.

The Examiner determined that “it would have been obvious to one of ordinary skill in the art to select soybean PIs because it is known that PIs are sources for disease and pest resistant genes.” Final Rej. 8. The Examiner also found that Hill ’964 “provides evidence that there are many PIs that possess resistance to soybean aphids as shown in Table 1.” Ans. 12.

Appellants contend that the skilled worker would not have been able to predict that the specific PIs recited in the claims would have resistance to one or more soybean aphid biotypes. Appeal Br. 13–14.

As found by the Examiner, Hill ’964 teaches a list of PIs that are sources of resistance to soybean aphid. Hill ’964, ¶¶ 50–53. Hill ’964 teaches that screening using its markers can be performed on any of the parental lines disclosed by Hill ’964 or known in the art. *Id.* at ¶¶ 74, 75. Hill (2010) also teaches PIs that are resistant to the aphid. Hill (2010) 511 (Table 1), 512 (Table 2), 513 (Tables 3 and 4). The germplasms for the PIs are available from the USDA Soybean Germplasm Collection, Urbana, IL. *Id.* at 511 (footnote to Table 1). Consequently, as found by the Examiner, it would have been obvious to one of ordinary skill in the art to have selected a known PI for screening with markers. While the Examiner did not establish that the specific PI lines were known to be resistant to aphids or to possess

one of the specifically claimed markers, it would have been obvious to have screened for one based on the success of Hill '964 in doing so, and Hill '964's disclosure that screening can be performed on other parental lines.

Because the conventional technology of identifying aphid resistance and screening for resistance markers – as taught in Hill (2010) (characterizing aphid resistance in various soybean varieties) and Hill '964 – has been applied to known and available soybean lines, it would have been reasonably expected that other varieties would be routinely selected using these known methods. While the identification of these markers in the recited PIs may be new, Appellants have not provided evidence that it was unpredictable that they could be identified.

#### SUMMARY

Because Appellants did not identify a reversible error in the Examiner's rejection, we affirm the rejection of claims 1, 11–14, 20, 21, and 22 as obvious. Claims 2, 3, and 8–10, and 15–19 fall with claim 1 because separate reasons for their patentability were not provided. 37 C.F.R. § 41.37(c)(1)(iv).

#### TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED