



The Secretary, Senate Community Affairs Committee  
PO Box 6100, Parliament House  
Canberra ACT 2600

Supplement to Submission of American Patent and Health Law Professors on  
Australian Senate Community Affairs Committee Inquiry Into Gene Patents

This letter is to supplement our earlier response to the Senate Community Affairs Committee's Inquiry. Since that time, the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") decided an important case regarding the application of the obviousness (lack of inventive step) requirement to gene patents. In *re Kubin*, No.2008-1184 (Fed. Cir. Apr. 3, 2009). That case upheld the rejection by the U.S. Patent and Trademark Office (USPTO) of typical claims to gene sequences, as unpatentable because they were obvious. A copy of the decision is attached.

As we had indicated, the recent U.S. Supreme Court case *KSR International, Inc. v. Teleflex Corp.*, "calls into serious question the validity of many of the genetic sequence and other natural products or phenomena claims issued by the PTO." This is because the Federal Circuit and the USPTO for decades had been applying a much more limited test of obviousness than was authorized by the law and binding precedents. Recently, the Federal Circuit recognized that *KSR* had "unambiguously discredited" the Federal Circuit's earlier holdings that had rejected an "obvious to try" approach to finding gene patents obvious. *Kubin*, slip op. at 13. Given the correct approach, the Federal Circuit held the claims invalid; there was sufficient motivation for skilled persons to isolate the cDNA sequences, given prior art knowledge of the importance of the protein and a reasonable expectation of success in doing so given that the methods of DNA isolation were conventional. *Id.* at 13-17. "Therefore, the claimed invention is 'the product not of innovation but of ordinary skill and common sense.' *KSR*, 550 U.S. at 421." *Id.* at 16. Similar motivations should exist for isolating the sequences claimed by many issued patents, and the reasoning of *Kubin* (known methods, a reason to apply them, and expected success makes the result obvious) also should extend to other reasons for isolating genetic sequences than a known important protein. Thus, many if not most issued gene patents are likely invalid for obviousness.

/Joshua D. Sarnoff/ for

Joshua D. Sarnoff  
Practitioner-in-Residence  
Washington College of Law  
American University

Dr. Jonathan Kahn  
Associate Professor  
Hamline University  
School of Law

Lori B. Andrews  
Distinguished Professor of Law  
Chicago-Kent College of Law  
Illinois Institute of Technology

Attachment

# United States Court of Appeals for the Federal Circuit

2008-1184  
(Serial No. 09/667,859)

IN RE MAREK Z. KUBIN and RAYMOND G. GOODWIN

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences.

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DECIDED: April 3, 2009

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Before RADER, FRIEDMAN, and LINN, Circuit Judges.

RADER, Circuit Judge.

Marek Kubin and Raymond Goodwin (“appellants”) appeal from a decision of the Board of Patent Appeals and Interferences (the “Board”) rejecting the claims of U.S. Patent Application Serial No. 09/667,859 (“859 Application”) as obvious under 35 U.S.C. § 103(a) and invalid under 35 U.S.C. § 112 ¶ 1 for lack of written description. Ex parte Kubin, No. 2007-0819 (B.P.A.I. May 31, 2007) (“Board Decision”). Because the Board correctly determined that appellants’ claims are unpatentably obvious, this court affirms.

I.

This case presents a claim to a classic biotechnology invention – the isolation and sequencing of a human gene that encodes a particular domain of a protein. This court provided a primer on the basics of this technology in In re O’Farrell, 853 F.2d 894,

895-99 (Fed. Cir. 1988). Specifically, appellants claim DNA molecules (“polynucleotides”) encoding a protein (“polypeptide”) known as the Natural Killer Cell Activation Inducing Ligand (“NAIL”).

Natural Killer (“NK”) cells, thought to originate in the bone marrow, are a class of cytotoxic lymphocytes that play a major role in fighting tumors and viruses. NK cells express a number of surface molecules which, when stimulated, can activate cytotoxic mechanisms. NAIL is a specific receptor protein on the cell surface that plays a role in activating the NK cells.

The specification of the claimed invention recites an amino acid sequence of a NAIL polypeptide. The invention further isolates and sequences a polynucleotide that encodes a NAIL polypeptide. Moreover, the inventors trumpet their alleged discovery of a binding relationship between NAIL and a protein known as CD48. The NAIL-CD48 interaction has important biological consequences for NK cells, including an increase in cell cytotoxicity and in production of interferon. Representative claim 73 of appellants’ application claims the DNA that encodes the CD48-binding region of NAIL proteins:

73. An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22-221 of SEQ ID NO:2, wherein the polypeptide binds CD48.

In other words, appellants claim a genus of isolated polynucleotides encoding a protein that binds CD48 and is at least 80% identical to amino acids 22-221 of SEQ ID NO:2 – the disclosed amino acid sequence for the CD48-binding region of NAIL.

Appellants’ specification discloses nucleotide sequences for two polynucleotides falling within the scope of the claimed genus, namely SEQ ID NO:1 and SEQ ID NO:3. SEQ ID NO: 1 recites the specific coding sequence of NAIL, whereas SEQ ID NO: 3

recites the full NAIL gene, including upstream and downstream non-coding sequences. The specification also contemplates variants of NAIL that retain the same binding properties:

Variants include polypeptides that are substantially homologous to the native form, but which have an amino acid sequence different from that of the native form because of one or more deletions, insertions or substitutions. Particular embodiments include, but are not limited to, polypeptides that comprise from one to ten deletions, insertions or substitutions of amino acid residues, when compared to a native sequence.

A given amino acid may be replaced, for example, by a residue having similar physiochemical characteristics. Examples of such conservative substitutions include substitution of one aliphatic residue for another, such as Ile, Val, Leu, or Ala for one another; substitutions of one polar residue for another, such as between Lys and Arg, Glu and Asp, or Gln and Asn; or substitutions of one aromatic residue for another, such as Phe, Trp, or Tyr for one another. Other conservative substitutions, e.g., involving substitutions of entire regions having similar hydrophobicity characteristics, are well known.

'859 Application at 26. However, the specification does not indicate any example variants of NAIL that make these conservative amino acid substitutions.

## II.

The Board rejected appellants' claims as invalid under both § 103 and § 112. With regard to the § 112 rejection, the Board found the genus of nucleic acids of representative claim 73 unsupported by an adequate written description. First, the Board observed that although appellants had sequenced two nucleic acids falling within the scope of claim 73, they had not disclosed any variant species where amino acids 22-221 were different in any way from the disclosed SEQ ID NO:2 sequence. Thus, the Board concluded that appellants were not entitled to their genus claim of DNA molecules encoding proteins 80% identical to SEQ ID NO:2:

[Appellants] have not described what domains of those sequences are correlated with the required binding to CD48, and thus have not described which of NAIL's amino acids can be varied and still maintain binding. Thus . . . their Specification would not have shown possession of a sufficient number of sequences falling within their potentially large genus to establish possession of their claimed genus.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement.

Board Decision at 16-17.

Regarding obviousness, the Board rejected appellants' claims over the combined teachings of U.S. Patent No. 5,688,690 ("Valiante") and 2 Joseph Sambrook et al., Molecular Cloning: A Laboratory Manual 43-84 (2d ed. 1989) ("Sambrook"). The Board also considered, but found to be cumulative to Valiante and Sambrook, Porunelloor Mathew et al., Cloning and Characterization of the 2B4 Gene Encoding a Molecule Associated with Non-MHC-Restricted Killing Mediated by Activated Natural Killer Cells and T Cells, 151 J. Immunology 5328-37 (1993) ("Mathew").

Valiante discloses a receptor protein called "p38" that is found on the surface of human NK cells. Valiante teaches that the p38 receptor is present on virtually all human NK cells and "can serve as an activation marker for cytotoxic NK cells." '690 Patent col.3 ll.3-4; see also id. at col.5 ll.6-7 ("Stimulation of p38 results in activation of cytotoxicity"). Valiante also discloses and claims a monoclonal antibody specific for p38 called "mAB C1.7." The Board found (and appellants do not dispute) that Valiante's p38 protein is the same protein as NAIL. Board Decision at 4. A monoclonal antibody is an antibody that is mass produced in the laboratory from a single clone and that recognizes only one antigen. Monoclonal antibodies are useful as probes for specifically identifying and targeting a particular kind of cell.

Valiante teaches that “[t]he DNA and protein sequences for the receptor p38 may be obtained by resort to conventional methodologies known to one of skill in the art.” ‘690 Patent col.7 ll.49-51.

For example, the receptor may be isolated by immunoprecipitation using the mAb C1.7. Alternatively, the receptor may be obtained by prokaryotic expression cloning, using the lambda phage gtlI, which is described in detail in Sambrook et al, *Molecular Cloning, A Laboratory Manual*, 2d edit., Cold Spring Harbor, N.Y. (1989), pp. 2.43-2.84, incorporated by reference herein.

Additionally, as described in Example 12 below, the DNA sequence encoding the receptor can be obtained by the “panning” technique of screening a human NK cell library by eukaryotic expression cloning, of which several are known. Briefly, plasmids are constructed containing random sequences of a human NK cell library which are obtained by restriction digestion. Such libraries may be made by conventional techniques or may be available commercially.

Suitable cells, preferably mammalian cells, such as COS-1 cells, are transfected with the plasmids and the mAb C1.7 antibody employed to identify transfectants containing the receptor after repeated rounds of panning. The receptor insert in these cells is then identified and sequenced by conventional techniques, such as overlapping deletion fragments [Sambrook et al. cited above]. Other known techniques may also be employed to sequence the receptor and/or the mAb C1.7.

Id. at col.7 l.51-col.8 l.7. Example 12 of Valiante’s patent further describes a five-step cloning protocol for “isolating and identifying the p38 receptor.” Id. at col.18 l.6-col.19 l.28. Valiante discloses neither the amino acid sequence of p38 recognized by mAb C1.7 nor the polynucleotide sequence that encodes p38. Sambrook, incorporated by reference (as cited above) in Valiante, describes methods for molecular cloning. Sambrook does not discuss how to clone any particular gene, but provides detailed instructions on cloning materials and techniques.

The Mathew reference discloses a cell surface receptor protein called 2B4 “expressed on all NK . . . cells.” Mathew at 5328. Mathew discloses that 2B4 is

involved in activating mouse NK cells, and further teaches the “chromosomal mapping, cloning, expression, and molecular characterization of the 2B4 gene.” Id. at 5329. Further, Mathew teaches a monoclonal antibody, mAb 2B4, specific to 2B4, and a detailed cloning protocol for obtaining the sequence of the gene that codes for the 2B4 protein. Id. at 5328-330. The Board found that Mathew’s signaling molecule 2B4 is the murine (mouse) version of Valiante’s p38. Board Decision at 5. The Board viewed Mathew’s teachings to be “cumulative to the teachings in Valiante and Sambrook and merely . . . exemplary of how routine skill in the art can be utilized to clone and sequence the cDNA of a similar polypeptide.” Id.

The Board found as a factual matter that appellants used conventional techniques “such as those outlined in Sambrook” to isolate and sequence the gene that codes for NAIL. Id. The Board also found that appellants’ claimed DNA sequence is “isolated from a cDNA library . . . using the commercial monoclonal antibody C1.7 . . . disclosed by Valiante.” Id. With regard to the amino acid sequence referred to as SEQ ID NO:2, the Board found that

Valiante’s disclosure of the polypeptide p38, and a detailed method of isolating its DNA, including disclosure of a specific probe to do so, i.e., mAb C1.7, established Valiante’s possession of p38’s amino acid sequence and provided a reasonable expectation of success in obtaining a polynucleotide encoding p38, a polynucleotide within the scope of Appellants’ claim 73. (See Valiante, col.7, l.48 to col.8, l.7.)

Id. at 6. Because of NAIL’s important role in the human immune response, the Board further found that “one of ordinary skill in the art would have recognized the value of isolating NAIL cDNA, and would have been motivated to apply conventional methodologies, such as those disclosed in Sambrook and utilized in Valiante, to do so.” Id. at 6-7.

Based on these factual findings, the Board turned to the legal question of obviousness under § 103. Invoking the Supreme Court's decision in KSR International Co. v. Teleflex Inc., 550 U.S. 398 (2007), the Board concluded that appellants' claim was "the product not of innovation but of ordinary skill and common sense,' leading us to conclude NAIL cDNA is not patentable as it would have been obvious to isolate it." Board Decision at 9 (citing KSR, 550 U.S. at 421).

Appellants appeal the Board's decisions both as to obviousness and written description. This court has jurisdiction under 28 U.S.C. § 1295(a)(4) and 35 U.S.C. § 141.

### III.

This court reviews the Board's factual findings for lack of substantial evidence, and its legal conclusions without deference. In re Gartside, 203 F.3d 1305, 1315 (Fed. Cir. 2000).

Obviousness is a question of law based on underlying findings of fact. An analysis of obviousness must be based on several factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviousness, if any. See Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966). The teachings of a prior art reference are underlying factual questions in the obviousness inquiry. See Para-Ordnance Mfg., Inc. v. SGS Imp. Int'l, Inc., 73 F.3d 1085, 1088 (Fed. Cir. 1995).



A.

As a factual matter, the Board concluded that appellants' methodology of isolating NAIL DNA was essentially the same as the methodologies and teachings of Valiante and Sambrook. Appellants charge that the record does not contain substantial evidence to support this Board conclusion.

This emphasis on similarities or differences in methods of deriving the NAIL DNA misses the main point of this obviousness question. Of note, the record nowhere suggests that the technique in Valiante's Example 12 for isolating NAIL (p38) DNA, even if slightly different than the technique disclosed in the claimed invention, would not yield the same polynucleotide claimed in claim 73. Stated directly, the record shows repeatedly that Valiante's Example 12 produces for any person of ordinary skill in this art the claimed polynucleotide.

More to the point, however, any putative difference in Valiante's/Sambrook's and appellants' processes does not directly address the obviousness of representative claim 73, which claims a genus of polynucleotides. The difference between Valiante's and the application's techniques might be directly relevant to obviousness in this case if Kubin and Goodwin had claimed a method of DNA cloning or isolation. But they did not. Appellants claim a gene sequence. Accordingly, the obviousness inquiry requires this court to review the Board's decision that the claimed sequence, not appellants' unclaimed cloning technique, is obvious in light of the abundant prior art.

In any event, this court determines that the Board had substantial evidence to conclude that appellants used conventional techniques, as taught in Valiante and Sambrook, to isolate a gene sequence for NAIL. In particular, appellants' arguments

that Valiante and Sambrook are deficient because they do not provide “any guidance for the preparation of cell culture that will serve as a useful source of mRNA for the preparation of a cDNA library,” Appellants’ Br. 34, are diminished by appellants’ own disclosure:

A “nucleotide sequence” refers to a polynucleotide molecule in the form of a separate fragment or as a component of a larger nucleic acid construct. The nucleic acid molecule has been derived from DNA or RNA isolated at least once in substantially pure form and in a quantity or concentration enabling identification, manipulation, and recovery of its component nucleotide sequences by standard biochemical methods (such as those outlined in Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989)).

'859 Application at 16-17 (emphasis added). Thus, Kubin and Goodwin cannot represent to the public that their claimed gene sequence can be derived and isolated by “standard biochemical methods” discussed in a well-known manual on cloning techniques, while at the same time discounting the relevance of that very manual to the obviousness of their claims. For this reason as well, substantial evidence supports the Board’s factual finding that “[a]ppellants employed conventional methods, ‘such as those outlined in Sambrook,’ to isolate a cDNA encoding NAIL and determine the cDNA’s full nucleotide sequence (SEQ NOS: 1 & 3).” Board Decision at 5.

In a similar vein, this court reviews the Board’s reference to the teachings of Mathew and the connection between Mathew’s 2B4 and Valiante’s p38 proteins. As an initial point, the Board referenced Mathew only as cumulative of Sambrook and Valiante. Therefore, the Board’s obviousness analysis does not explicitly rely on Mathew at all. Instead the Board observed that Mathew is “exemplary of how routine skill in the art can be utilized to clone and sequence the cDNA of a similar polypeptide.” Id. In that connection, the record shows that a researcher of ordinary skill in this art

would have recognized that both Valiante and Mathew are indisputably focused on regulation of NK cells – Mathew with regard to mice and Valiante with regard to humans. Like Valiante’s Example 12, Mathew discusses a detailed protocol for identifying, isolating, and cloning cDNA encoding 2B4, which was later discovered to be the murine equivalent of Valiante’s p38 and appellants’ NAIL protein. Moreover, Mathew expressly states that his genomic DNA blot analysis “identified a human homologue of the 2B4 gene.” Mathew at 5333. In sum, substantial evidence supports the Board’s conclusion that Mathew reinforces the relative ease of deriving the claimed sequence following the teachings of the prior art.

This court notes that Mathew contains some data that “suggests that [the] 2B4 gene is not expressed in humans.” *Id.* This part of the record, however, does not undermine the Board’s correct conclusion that Mathew does not “teach away” from combining its teachings with Valiante. “A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.” In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994). According to Mathew, “[i]t appears . . . that the 2B4 gene is somewhat conserved during evolution.” Mathew at 5335. Mathew’s quasi-agnostic stance toward the existence of a human homologue of the 2B4 gene cannot fairly be seen as dissuading one of ordinary skill in the art from combining Mathew’s teachings with those of Valiante. Rather, Mathew’s disclosure, in light of Valiante’s teachings regarding the p38 protein and its role in NK cell activation, would have aroused a skilled artisan’s curiosity to isolate the gene coding for p38. Thus, the record supplies ample evidence

to support the Board's finding that Mathew "exemplifies how the cDNA encoding 2B4, the mouse version of Valiante's p38 expressed on all NK cells, can be isolated and sequenced." Board Decision at 10.

This court also observes that the Board had no obligation to predicate its obviousness finding on factual findings regarding a prior art teaching of NAIL's binding to the CD48 protein. Even if no prior art of record explicitly discusses the "wherein the polypeptide binds CD48" aspect of claim 73, the Kubin-Goodwin application itself instructs that CD48 binding is not an additional requirement imposed by the claims on the NAIL protein, but rather a property necessarily present in NAIL. See, e.g., '859 Application at 1, 8 (describing CD48 as NAIL's "counterstructure"). Because this court sustains, under substantial evidence review, the Board's finding that Valiante's p38 is the same protein as appellant's NAIL, Valiante's teaching to obtain cDNA encoding p38 also necessarily teaches one to obtain cDNA of NAIL that exhibits the CD48 binding property. See, e.g., Gen. Elec. Co. v. Jewel Incandescent Lamp Co., 326 U.S. 242, 249 (1945) ("It is not invention to perceive that the product which others had discovered had qualities they failed to detect."); In re Wiseman, 596 F.2d 1019, 1023 (CCPA 1979) (rejecting the notion that "a structure suggested by the prior art, and, hence, potentially in the possession of the public, is patentable . . . because it also possesses an inherent, but hitherto unknown, function which [patentees] claim to have discovered. This is not the law. A patent on such a structure would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art.").

B.

The instant case also requires this court to consider the Board's application of this court's early assessment of obviousness in the context of classical biotechnological inventions, specifically In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995). In Deuel, this court reversed the Board's conclusion that a prior art reference teaching a method of gene cloning, together with a reference disclosing a partial amino acid sequence of a protein, rendered DNA molecules encoding the protein obvious. Id. at 1559. In reversing the Board, this court in Deuel held that "knowledge of a protein does not give one a conception of a particular DNA encoding it." Id. Further, this court stated that "obvious to try" is an inappropriate test for obviousness.

[T]he existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs. . . . "Obvious to try" has long been held not to constitute obviousness. A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out.

Id. (internal citations omitted) (emphases added). Thus, this court must examine Deuel's effect on the Board's conclusion that Valiante's teaching of the NAIL protein, combined with Valiante's/Sambrook's teaching of a method to isolate the gene sequence that codes for NAIL, renders claim 73 obvious.

With regard to Deuel, the Board addressed directly its application in this case. In particular, the Board observed that the Supreme Court in KSR cast doubts on this court's application of the "obvious to try" doctrine:

To the extent Deuel is considered relevant to this case, we note the Supreme Court recently cast doubt on the viability of Deuel to the extent the Federal Circuit rejected an "obvious to try" test. See KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, \_\_\_, 82 U.S.P.Q. 2d 1385, 1394, 1396

(2007) (citing Deuel, 51, F.3d at 1559). Under KSR, it's now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated.

Board Decision at 8. Insofar as Deuel implies the obviousness inquiry cannot consider that the combination of the claim's constituent elements was "obvious to try," the Supreme Court in KSR unambiguously discredited that holding. In fact, the Supreme Court expressly invoked Deuel as a source of the discredited "obvious to try" doctrine. The KSR Court reviewed this court's rejection, based on Deuel, of evidence showing that a particular combination of prior art elements was obvious because it would have been obvious to one of ordinary skill in the art to attempt such a combination:

The only declaration offered by KSR—a declaration by its Vice President of Design Engineering, Larry Willemsen—did not go to the ultimate issue of motivation to combine prior art, i.e. whether one of ordinary skill in the art would have been motivated to attach an electronic control to the support bracket of the assembly disclosed by Asano. Mr. Willemsen did state that an electronic control "could have been" mounted on the support bracket of a pedal assembly. (Willemsen Decl. at P33, 36, 39.) Such testimony is not sufficient to support a finding of obviousness, however. See, e.g., In re Deuel, 51 F.3d 1552, 1559 (Fed. Cir. 1995) ("'Obvious to try' has long been held not to constitute obviousness.").

Teleflex, Inc. v. KSR Int'l Co., 119 F. App'x 282, 289 (Fed. Cir. 2005). The Supreme Court repudiated as "error" the Deuel restriction on the ability of a skilled artisan to combine elements within the scope of the prior art:

The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR, 550 U.S. at 421 (internal citation omitted) (emphasis added).

The Supreme Court's admonition against a formalistic approach to obviousness in this context actually resurrects this court's own wisdom in In re O'Farrell, which predates the Deuel decision by some seven years. This court in O'Farrell cautioned that "obvious to try" is an incantation whose meaning is often misunderstood:

It is true that this court and its predecessors have repeatedly emphasized that "obvious to try" is not the standard under § 103. However, the meaning of this maxim is sometimes lost. Any invention that would in fact have been obvious under § 103 would also have been, in a sense, obvious to try. The question is: when is an invention that was obvious to try nevertheless nonobvious?

In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988). To differentiate between proper and improper applications of "obvious to try," this court outlined two classes of situations where "obvious to try" is erroneously equated with obviousness under § 103. In the first class of cases,

what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

Id. In such circumstances, where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness. The inverse of this proposition is succinctly encapsulated by the Supreme Court's statement in KSR that where a skilled artisan merely pursues "known options" from a "finite number of identified, predictable solutions," obviousness under § 103 arises. 550 U.S. at 421.

The second class of O'Farrell's impermissible "obvious to try" situations occurs where

what was “obvious to try” was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

853 F.2d at 903. Again, KSR affirmed the logical inverse of this statement by stating that § 103 bars patentability unless “the improvement is more than the predictable use of prior art elements according to their established functions.” 550 U.S. at 417.

This court in O’Farrell found the patentee’s claims obvious because the Board’s rejection of the patentee’s claims had not presented either of the two common “obvious to try” pitfalls. Specifically, this court observed that an obviousness finding was appropriate where the prior art “contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful.” 853 F.2d at 902 (emphasis added). Responding to concerns about uncertainty in the prior art influencing the purported success of the claimed combination, this court stated: “[o]bviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success.” Id. at 903-04 (emphasis added). The Supreme Court in KSR reinvigorated this perceptive analysis.

KSR and O’Farrell directly implicate the instant case. Appellants’ claim 73 recites a genus of isolated nucleic acid molecules encoding the NAIL protein. As found by the Board, the Valiante reference discloses the very protein of appellants’ interest – “p38” as per Valiante. Board Decision at 4. Valiante discloses a monoclonal antibody mAb C1.7 that is specific for p38/NAIL, and further teaches a five-step protocol for cloning nucleic acid molecules encoding p38/NAIL using mAb C1.7. Id. In fact, while stating that “[t]he DNA and protein sequences for the receptor p38 may be obtained by



resort to conventional methodologies known to one of skill in the art,” ‘690 Patent at col.7 ll.49-51, Valiante cites to the very same cloning manual, Sambrook, cited by Kubin and Goodwin for their proposition that the gene sequence is identified and recovered “by standard biochemical methods.” ‘859 Application at 16. Moreover, the record strongly reinforces (and appellants apparently find no room to dispute) the Board’s factual finding that one of ordinary skill would have been motivated to isolate NAIL cDNA, given Valiante’s teaching that p38 is “expressed by virtually all human NK cells and thus plays a role in the immune response.” Board Decision at 6. The record shows that the prior art teaches a protein of interest, a motivation to isolate the gene coding for that protein, and illustrative instructions to use a monoclonal antibody specific to the protein for cloning this gene. Therefore, the claimed invention is “the product not of innovation but of ordinary skill and common sense.” KSR, 550 U.S. at 421. Or stated in the familiar terms of this court’s longstanding case law, the record shows that a skilled artisan would have had a resoundingly “reasonable expectation of success” in deriving the claimed invention in light of the teachings of the prior art. See O’Farrell, 853 F.2d at 904.

This court also declines to cabin KSR to the “predictable arts” (as opposed to the “unpredictable art” of biotechnology). In fact, this record shows that one of skill in this advanced art would find these claimed “results” profoundly “predictable.” The record shows the well-known and reliable nature of the cloning and sequencing techniques in the prior art, not to mention the readily knowable and obtainable structure of an identified protein. Therefore this court cannot deem irrelevant the ease and predictability of cloning the gene that codes for that protein. This court cannot, in the

face of KSR, cling to formalistic rules for obviousness, customize its legal tests for specific scientific fields in ways that deem entire classes of prior art teachings irrelevant, or discount the significant abilities of artisans of ordinary skill in an advanced area of art. See In re Durden, 763 F.2d 1406, 1411 (Fed. Cir. 1985) (“Our function is to apply, in each case, § 103 as written to the facts of disputed issues, not to generalize or make rules for other cases which are unforeseeable.”). As this court’s predecessor stated in In re Papesch, “[t]he problem of ‘obviousness’ under section 103 in determining the patentability of new and useful chemical compounds . . . is not really a problem in chemistry or pharmacology or in any other related field of science such as biology, biochemistry, pharmacodynamics, ecology, or others yet to be conceived. It is a problem of patent law.” 315 F.2d 381, 386 (CCPA 1963).

The record in this case shows that Valiante did not explicitly supply an amino acid sequence for NAIL or a polynucleotide sequence for the NAIL gene. In that sense, Kubin and Goodwin’s disclosure represents some minor advance in the art. But “[g]ranted patent protection to advances that would occur in the ordinary course without real innovation retards progress.” KSR, 550 U.S. at 419. “Were it otherwise patents might stifle, rather than promote, the progress of useful arts.” Id. at 427. In light of the concrete, specific teachings of Sambrook and Valiante, artisans in this field, as found by the Board in its expertise, had every motivation to seek and every reasonable expectation of success in achieving the sequence of the claimed invention. In that sense, the claimed invention was reasonably expected in light of the prior art and “obvious to try.” See Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 520 F.3d 1358, 1364 (Fed. Cir. 2008) (“KSR posits a situation with a finite, and in the context of the art,

small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness.”). These references, which together teach a protein identical to NAIL, a commercially available monoclonal antibody specific for NAIL, and explicit instructions for obtaining the DNA sequence for NAIL, are not analogous to prior art that gives “no direction as to which of many possible choices is likely to be successful” or “only general guidance as to the particular form of the claimed invention or how to achieve it.” O’Farrell, 853 F.2d at 903. As the Board found, the prior art here provides a “reasonable expectation of success” for obtaining a polynucleotide within the scope of claim 73, Board Decision at 6, which, “[f]or obviousness under § 103 [is] all that is required.” O’Farrell, 853 F.2d at 903. Thus, this court affirms the Board’s conclusion as to obviousness.

#### IV.

For the reasons stated above, the Board did not err in finding appellants’ claims obvious as a matter of law. Thus, this court need not address appellants’ contention that the Board erred in finding its claims invalid under § 112 ¶ 1. Accordingly, this court affirms the decision of the Board.

AFFIRMED

COSTS

Each party shall bear its own costs.