

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

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*Ex parte* ANDREW P. MILLER, PING HU, MARK EDWARD CURRAN,  
MARC RUTTER, and JIAN-YING WANG

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Appeal 2008-3323  
Application 10/121,746  
Technology Center 1600

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Decided: June 27, 2008

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Before DONALD E. ADAMS, DEMETRA J. MILLS, and ERIC GRIMES,  
*Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

**DECISION ON APPEAL**

This is an appeal under 35 U.S.C. § 134 involving claims to nucleic acids encoding a subunit of a voltage-gated potassium channel. The Examiner has rejected the claims as lacking utility, nonenabled, and lacking adequate description in the Specification. We have jurisdiction under

35 U.S.C. § 6(b). We affirm the rejections for lack of utility and nonenablement but reverse the written description rejection.

#### BACKGROUND

“The potassium channel gene family is believed to be the largest and most diverse ion channel family” (Spec. 1). “Four human conditions, episodic ataxia with myokymia, long QT syndrome, epilepsy and Bartter’s syndrome have been shown to be caused by defective K<sup>+</sup> ion channels” (*id.*).

“The K<sup>+</sup> channel superfamily can be broadly classified into groups, based upon the number of transmembrane domain (TMD) segments in the mature protein” (*id.* at 1-2). “The 6TMD, or Shaker-like channels, presently comprise the largest subset of known K<sup>+</sup> channels” (*id.* at 2). Voltage-gated K<sup>+</sup> channels are composed of four  $\alpha$  subunits, each of which has six transmembrane domains (*id.* at 6: 29-32).

The Specification discloses several nucleic acids encoding putative K<sup>+</sup> channel subunits (*see, e.g., id.* at 8-9). One of them is designated K<sup>+</sup>Hnov9 and has the sequence shown in SEQ ID NO: 7 (*id.* at 8). K<sup>+</sup>Hnov9 is disclosed to encode a voltage-gated K<sup>+</sup> channel and to be encoded by a gene on chromosome 8 (*id.*). The Specification discloses K<sup>+</sup>Hnov9 is expressed in brain, cerebellum, kidney, pancreas, and testis, among other tissues (*id.* at 37).

The Specification states that the disclosed nucleic acids

find use in identifying homologous or related genes; in producing compositions that modulate the expression or function of its encoded proteins; for gene therapy; mapping functional regions of the proteins; and in studying associated physiological pathways. In addition, modulation of the gene activity *in vivo* is used for prophylactic and therapeutic

purposes, such as treatment of potassium channel defects, identification of cell type based on expression, and the like.

(*Id.* at 5.)

## DISCUSSION

### 1. CLAIMS

Claims 15-20 are pending and on appeal. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R.

§ 41.37(c)(1)(vii). Claim 15 (the only independent claim) reads as follows:

Claim 15: An isolated nucleic acid encoding a polypeptide comprising a subunit of a voltage-gated potassium channel, the nucleic acid having at least 90% sequence identity to SEQ ID NO: 7.

### 2. UTILITY

Claims 15-20 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility (Ans. 3, 8). The Examiner does not dispute that SEQ ID NO: 7 encodes a subunit of a voltage-gated K<sup>+</sup> channel, but finds that “its identification as such is not sufficient to establish either a well-known, or a specific and substantial utility” (*id.* at 4). The Examiner reasons that the “art teaches that voltage-gated potassium channels serve a wide range of functions, including regulation of the resting membrane potential, and control of the shape, duration, and frequency of action potentials” (*id.* at 4-5) but the Specification “does not disclose a specific biological role for the K<sup>+</sup>Hnov9 protein or its significance to a particular disease, disorder, or physiological process which one would manipulate for a desired physiological or clinical effect” (*id.* at 4).

We agree with the Examiner that the Specification does not disclose a utility for the claimed nucleic acids that satisfies 35 U.S.C. § 101. Section

101 requires a utility that is both substantial and specific. *In re Fisher*, 421 F.3d 1365, 1371 (Fed. Cir. 2005). A substantial utility is one that “show[s] that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the ‘substantial’ utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public.” *Id.* A specific utility is “a use which is not so vague as to be meaningless.” *Id.* In other words, “in addition to providing a ‘substantial’ utility, an asserted use must also show that th[e] claimed invention can be used to provide a well-defined and particular benefit to the public.” *Id.*

The Specification states that K<sup>+</sup>Hnov9 is useful for gene therapy and that “modulation of the gene activity *in vivo* is used for prophylactic and therapeutic purposes, such as treatment of potassium channel defects” (Spec. 5). However, the Specification does not identify any specific disorder that can be treated or prevented by modulating the activity of the K<sup>+</sup>Hnov9 gene.

The Specification states that “[f]our human conditions . . . have been shown to be caused by defective K<sup>+</sup> ion channels” (*id.* at 1). Specific disorders are caused by defects in specific proteins, however, and the potassium channel family is described as “very diverse” (*id.*) and divided into several different groups (*id.* at 1-2). The Specification does not assert that every K<sup>+</sup> channel is involved in each of the four disorders caused by defective K<sup>+</sup> channels, nor does it assert that a defective voltage-gated K<sup>+</sup> channel causes any of them.

Where the Specification provides further details of disease-related K<sup>+</sup> channels, in fact, those details make clear that K<sup>+</sup>Hnov9 is not the culprit.

The Specification states that the gene responsible for a myotonia is located on chromosome 1, the genes associated with a disease called type II PHA are located on chromosomes 1 and 17 (Spec. 4), and the genes associated with long QT syndrome are located on chromosomes 11 and 7 (*id.* at 17). The  $K^+Hnov9$  gene is located on chromosome 8 (*id.* at 8).

The Specification also states that the disease of the weaver mouse and a hypoglycemia of infants are associated with  $K^+$  channels, but one is a G-protein-coupled  $K^+$  channel and the other is an ATP-sensitive  $K^+$  channel; neither is described as a voltage-gated  $K^+$  channel (*id.* at 17). Thus, the Specification does not describe a single, specific disorder that is caused by a defect in any voltage-gated  $K^+$  channel, let alone in  $K^+Hnov9$  specifically.

We agree with the Examiner that the Specification's vague statement that modulation of  $K^+Hnov9$  gene activity *in vivo* is useful when used "for prophylactic and therapeutic purposes, such as treatment of potassium channel defects" (Spec. 5) does not provide a specific and substantial utility for the claimed nucleic acids.

Appellants argue that they "disclose a 'disease condition,' i.e., altered cell resting potential and excitability, that correlates with a 'biological activity,' i.e., the opening and closing of the claimed voltage-gated potassium channels" (App. Br. 7). Appellants argue that this disclosure, combined with the tissue-specific expression of  $K^+Hnov9$  and the Specification's statement that  $K^+Hnov9$  modulators can be used for treating "epilepsy, hypertension, or other central nervous system disorders," provides a "specific utility, e.g.,  $K^+Hnov9$  channels can mediate cell resting potential and excitability in certain tissues such as brain and kidney" (*id.*).

Similarly, Appellants also argue that

there is a real-world use of the present invention in the modulation of cell excitability through modulation of the  $K^+Hnov9$  channel activity, as well as in the identification of compounds that modulate  $K^+Hnov9$  channels and thus can be useful as therapeutic agents for treating diseases related to altered cell excitability in relevant tissues, such as epilepsy and hypertension.

(*Id.*)

These arguments do not persuade us that the Examiner's rejection should be reversed. First, Appellants have not pointed to any evidence of record to support their position that "altered cell resting potential and excitability" is a disease condition that can be treated using the claimed nucleic acids or any related product.

Second, the evidence of record does not support the position that  $K^+Hnov9$  modulators can be used to treat epilepsy, hypertension, or "other central nervous system disorders." As discussed above, neither the Specification nor any evidence cited by Appellants shows that inhibition or activation of  $K^+Hnov9$ , or voltage-gated  $K^+$  channels generally, would reasonably be expected to provide therapeutic benefit in any of these disorders.

Finally, the fact that  $K^+Hnov9$  might mediate cell resting potential and excitability in tissues in which it is expressed does not indicate a specific utility, only the predicted biological function of the protein. The Specification does not tie that predicted function to any specific and substantial utility for the claimed nucleic acids.

Appellants place great emphasis on the declaration submitted under 37 C.F.R. § 1.132 by Dr. Ken McCormack (received Dec. 8, 2005).

Appellants argue that the McCormack Declaration “further support[s] the contention that the asserted utility of this invention is specific, substantial, and credible” (App. Br. 9) and that the Examiner has not provided an adequate basis to rebut the declaratory evidence (*id.* at 9-13).

We have considered the McCormack Declaration but we find that Dr. McCormack’s conclusions are not adequately supported by the evidence of record, and the declaration therefore does not persuade us that the rejections are in error. *See In re American Acad. of Science Tech Ctr.*, 367 F.3d 1359, 1368 (Fed. Cir. 2004): “The Board has broad discretion as to the weight to give to declarations offered in the course of prosecution. *See Velandier v. Garner*, 348 F.3d 1359, 1371 (Fed. Cir. 2003) (“[A]ccord[ing] little weight to broad conclusory statements [in expert testimony before the Board] that it determined were unsupported by corroborating references [was] within the discretion of the trier of fact to give each item of evidence such weight as it feels appropriate.’)” (alterations in original).

Dr. McCormack states that a person of skill in the art would believe that K<sup>+</sup>Hnov9 channels “can serve as therapeutic targets for treatment of conditions related to aberrant cell excitability in the brain, cerebellum, or kidney, *e.g.*, epilepsy, other central nervous system disorders, or renal disorders” (McCormack Decl., ¶ 8). Dr. McCormack bases this conclusion on “the ability of K<sup>+</sup>Hnov9 in modulating cell excitability and the tissue-specific expression pattern of K<sup>+</sup>Hnov9 channels” (*id.*). Dr. McCormack also states that activators and inhibitors of K<sup>+</sup>Hnov9 can be routinely identified and “may be used as therapeutic agents for treating conditions caused by or related to abnormalities in vision or male fertility” (*id.*).

We do not find Dr. McCormack's conclusions to be supported by the evidence. First, Dr. McCormack's statement that  $K^+$ Hnov9 is likely to be a therapeutic target for unspecified disorders of the CNS or kidney that are "related to aberrant cell excitability" is too generic to provide a basis for patentable utility without some disclosure of *which* CNS or renal disorders fall into that category. The same is true of his statement that activators and inhibitors of  $K^+$ Hnov9 may be useful in treating "conditions caused by or related to abnormalities in vision or male fertility." Appellants have pointed to nothing in the record that would elucidate more specifically what disorders would be considered treatable by activation or inhibition of  $K^+$ Hnov9.

In addition, neither Dr. McCormack nor any other evidence of record provides an adequate basis to conclude that  $K^+$ Hnov9 would be useful in treating epilepsy based on its predicted function ("modulating cell excitability") and its expression in certain tissues. Although the Specification states the epilepsy has "been shown to be caused by defective  $K^+$  ion channels," (Spec. 1), it also states that "the  $K^+$  channel family is very diverse" (*id.*). Appellants have pointed to no evidence of record to show that any *voltage-gated*  $K^+$  channel, let alone  $K^+$ Hnov9 itself, is a therapeutic target for treating any disorder, let alone epilepsy.

Dr. McCormack also states that the Specification "teaches how to screen for compounds capable of modulating the  $K^+$ Hnov9 channel activity. . . . Upon reading this disclosure, a skilled artisan would be able to readily screen candidate compounds and identify activators or inhibitors of a  $K^+$ Hnov9 channel, without the need to carry out extensive additional research." (McCormack Decl., ¶ 9.)

The issue with respect to utility, however, is not whether a skilled artisan could identify inhibitors or activators of  $K^+$ Hnov9 without undue experimentation, but whether the Specification discloses a specific and substantial utility for such modulators once they are identified. For the reasons discussed above, we conclude that it does not. Appellants have not identified any specific and substantial application for such modulators. It would appear that their only use, once identified, would be as a subject of research themselves to determine if in fact they have any real-world value. That use does not satisfy § 101. *Cf. In re Kirk*, 376 F.2d 936, 942 (CPA 1967)(“[T]he sum and substance of the affidavit appears to be that one of ordinary skill in the art would know ‘how to use’ the compounds to find out in the first instance whether the compounds are – or are not – in fact useful or possess useful properties, and to ascertain what those properties are.”).

Finally, Dr. McCormack asserts that “targeting of a  $K^+$ Hnov9 channel . . . is an appropriate strategy for treating neurological disorders (*e.g.*, epilepsy) or renal disorders, whether or not such abnormality is directly caused by altered  $K^+$ Hnov9 channel activity” (McCormack Decl. ¶ 10). Dr. McCormack states that calcium channel blockers are used to relax the vasculature and treat hypertension, regardless of the illness actually causing the hypertension: “Relaxing the vasculature to reduce blood pressure is useful and effective, even if the original cause of the hypertension is not directly related to vascular tone” (*id.*). According to Dr. McCormack, “the use of  $K^+$ Hnov9 as a therapeutic target for treating” neurological disorders or renal disorders is analogous to treating hypertension with calcium channel blockers (*id.*).

Dr. McCormack cites no evidence to support the assertion that calcium channel blockers are useful in treating hypertension regardless of the underlying cause, but we will assume for present purposes the statement is accurate. Even so, we do not agree that K<sup>+</sup>Hnov9 would be expected to have uses analogous to the use of calcium channel blockers to treat hypertension.

A symptom of a disease may be predictably treated using a compound, based on a known property of the compound, even if the treatment does nothing to cure the underlying disorder. According to Dr. McCormack, calcium channel blockers are one example of such compounds: they have the property of relaxing the vasculature, so administering a calcium channel blocker causes a patient's blood vessels to open wider, and blood pressure predictably decreases.

But Dr. McCormack has not pointed to any similar property of the K<sup>+</sup>Hnov9 potassium channel blocker, or voltage-gated K<sup>+</sup> channels in general, that would lead someone skilled in the art to conclude that K<sup>+</sup>Hnov9 inhibitors or activators would be expected to have some property that would be recognized as providing a real-world use. All the Specification discloses about K<sup>+</sup>Hnov9 is that it is a voltage-gated K<sup>+</sup> channel expressed in certain tissues. Even combined with the prior art disclosures that are of record, that does not provide a specific and substantial utility for the claimed nucleic acids.

We have considered Appellants' other arguments regarding utility (based on the USPTO's Utility Examination Guidelines and on a related application that was allowed; App. Br. 14-15) but conclude that they lack

merit. The facts of the instant case are different from the example in the Utility Guidelines that Appellants cite, and the allowed application claimed nucleic acids encoding a different protein from the one claimed here.

We affirm the rejections of claim 15 under 35 U.S.C. §§ 101 and 112, first paragraph, on the basis that the Specification does not disclose a specific and substantial utility for the claimed nucleic acids. Claims 16-20 fall with claim 15.

### 3. ENABLEMENT

Claims 15 and 18-20 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that they are not enabled throughout their full scope even if they are found to have utility (Ans. 8). We have already concluded that the Specification does not disclose a utility for the claimed nucleic acids that satisfies the requirements of 35 U.S.C. § 101 and 112, first paragraph. Therefore, the Specification necessarily fails to teach how to use the claimed invention throughout its full scope. Appellants' arguments relating to scope of enablement (App. Br. 16-22) do not persuade us that the Specification discloses a patentable utility for the claimed invention. The rejection is affirmed.

### 4. WRITTEN DESCRIPTION

Claims 15 and 18-20 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the Specification does not adequately describe the claimed genus of nucleic acids (Ans. 11). In essence, the Examiner's position is that the rejected claims encompass nucleic acids having as little as 90% sequence identity to SEQ ID NO: 7 and encoding proteins that retain

the function of K<sup>+</sup>Hnov9, but the Specification's description does not show possession of the claimed genus of nucleic acids (Ans. 11-13).

Appellants argue that voltage-gated potassium channels have been extensively studied and characterized: “[T]here exists in the art an abundance of detailed knowledge of the family of voltage-gated potassium channels, such as specific structural features including both overall sequence homology and arrangement of various well defined functional domains . . . , as well as the presence of certain signature motifs (*e.g.*, the GYGD sequence in the K<sup>+</sup> selective pore region.” (App. Br. 25.) Appellants conclude that the state of the art supports their position that a skilled artisan would conclude that the Specification shows possession of the claimed nucleic acids (*id.*).

We will reverse this rejection. The written description requirement is satisfied if the Specification conveys with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. *See Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000).

The “written description requirement can be met by ‘show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.’” *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) (emphasis omitted, alterations in original).

“[W]hat is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.” *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

Here, the Examiner has accepted that the evidence of record shows that K<sup>+</sup>Hnov9 is a voltage-gated K<sup>+</sup> channel. (Ans. 4.) The evidence also shows that voltage-gated K<sup>+</sup> channels are a very well-characterized family of proteins. The Specification states that  $\alpha$  subunits of voltage-gated K<sup>+</sup> channels “share a six-transmembrane domain structure (S1-S6), with one highly positively charged domain (S4) and a pore region situated between S5 and S6” (Spec. 6-7). The Specification also states that there were at least twenty-three voltage-gated K<sup>+</sup> channel  $\alpha$  subunits known at the time the application was filed (*id.* at 7).

The scientific papers cited by the Examiner in support of the utility rejection also show that voltage-gated K<sup>+</sup> channels were well-characterized at the time this application was filed. Castellano<sup>1</sup> states that the “best known K<sup>+</sup> channels are the voltage-gated” (Castellano 4652). Castellano confirms that “[a]ll  $\alpha$ -subunits share a common general design: a central core with six putative transmembrane segments, flanked by hydrophilic N- and C-terminal domains of variable length, facing the cytosol” (*id.*), and that the domains

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<sup>1</sup> Antonio Castellano et al., *Identification and Functional Characterization of a K<sup>+</sup> channel  $\alpha$ -Subunit with Regulatory Properties Specific to Brain*, 17 *JOURNAL OF NEUROSCIENCE* 4652 (1997).

can be identified based on their sequences (*id.* at 4653, Fig. 1). Castellano also states that the N-terminal region is known to be “important for subunit recognition and assembly” (*id.* at 4660).

Like Castellano, Hugnot<sup>2</sup> teaches identification of the transmembrane segments and pore-forming region based on their sequence (Hugnot 3323, Fig. 1). Hugnot also teaches that certain amino acids in the transmembrane, pore, and C-terminal domain are “very conserved” (*id.* at 3328, right-hand col.).

Ottschytsch<sup>3</sup> discloses that each voltage-gated K<sup>+</sup> channel  $\alpha$ -subunit “contains six transmembrane domains (S1-S6) and a pore loop containing the GYG-motif, the signature sequence for potassium selectivity. The fourth transmembrane domain (S4) contains positively charged residues and is the major part of the voltage sensor.” (Ottschytsch 7986.) Ottschytsch states that “26 genes have been described encoding for different Kv  $\alpha$ -subunits” (*id.*). Ottschytsch also reports that each of the three new subunits that it discloses lacks the second proline of a conserved “P-X-P” motif, which Ottschytsch characterizes as a “major structural difference” (*id.* at 7990, right-hand col.).

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<sup>2</sup> Jean-Philippe Hugnot et al., *Kv8.1, a new neuronal potassium channel subunit with specific inhibitory properties towards Shab and Shaw channels*, 15 *EMBO JOURNAL* 3322 (1996).

<sup>3</sup> N. Ottschytsch et al., *Obligatory heterotetramerization of three previously uncharacterized Kv channel  $\alpha$ -subunits identified in the human genome*, 99 *PROC. NATL. ACAD. SCI. USA* 7986 (2002). Ottschytsch was published two months after the filing date of the instant application but its disclosure regarding the state of the art is evidence of the knowledge of the skilled artisan at the time this application was filed.

We find that the Specification's disclosure would have been recognized as showing possession of the claimed nucleic acids by those of ordinary skill in the art. The evidence of record shows that voltage-gated  $K^+$  channels were known to have a conserved structure, and that those skilled in the art recognized what parts of their structure were important to their function. The evidence shows that those skilled in the art were able to identify the different domains, including the pore-forming region, of new  $\alpha$ -subunits based on their sequence, that a "GYG-motif" was recognized as the signature sequence for  $K^+$  selectivity, that the S4 domain was known to be positively charged, and that certain amino acid positions in the different domains were known to be very conserved.

In our view, the evidence shows that those skilled in the art recognized a correlation between the structure and function of voltage-gated  $K^+$  channel  $\alpha$ -subunits. The well-characterized structure of the family of proteins to which  $K^+$ Hnov9 belongs would have led those of ordinary skill in the art to reasonably expect that particular amino acid variations either would or would not significantly affect function. For example, a conservative substitution in a functional domain, or a substitution outside a functional domain would be expected to preserve function, while a nonconservative substitution in a functional domain would be expected to disrupt function.

We find that the Specification's disclosure, combined with the knowledge of those of skill in the art, would have been recognized by persons of skill in the art as showing possession of the nucleic acids of

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claims 15 and 18-20. We therefore reverse the rejection for lack of adequate written description.

#### SUMMARY

We reverse the rejection of claims 15 and 18-20 based on the written description requirement of 35 U.S.C. § 112, first paragraph, but affirm the rejection of claims 15-20 under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of patentable utility.

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

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