

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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

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Ex parte DANIEL TIM CURTIS,  
GEORGE ROSS FRANCIS,  
MICHAEL CHRISTOPHER ELLIS,  
DAVID ANDREW RUDDY,  
SHARMON MONIQUE NICOLL, and  
GARTH JOSEPH McGRATH

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Appeal No. 2006-1897  
Application No. 09/568,942

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ON BRIEF

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Before SCHEINER, GRIMES, and LEOVITZ, Administrative Patent Judges.

LEOVITZ, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to methods for identifying modulators of Notch or APP processing in *C. elegans*. The examiner has rejected the claims as lacking written description and enablement under 35 U.S.C. § 112, first paragraph, and as being indefinite under 35 U.S.C. § 112, second paragraph. We have jurisdiction under 35 U.S.C. § 134. We reverse.

### Background

“Alzheimer’s disease is a degenerative disorder of the [human] central nervous system which causes memory impairment and cognitive loss during mid to late life.” Specification, page 1, lines 10-15. The disease is associated with mutations in the amyloid precursor protein (APP) processing pathway which is expressed in brain cells. The pathway contains several different key proteins, including APP, presenilins, and gamma-secretase. Id., pages 1-2. The cells of *C. elegans*, an invertebrate organism, contain a signaling pathway that shares many similarities with the human APP processing pathway, including expression of orthologs of human presenilin. This pathway is known as the Notch signaling pathway. Id., page 3.

The application describes the discovery of presenilin enhancer (“pen”) genes, which encode products that are required for presenilin function in *C. elegans*. Id., page 4, lines 19-21. A cell-based assay is provided that uses mutant pen genes to identify modulators of the Notch pathway. Because of the similarity between the Notch and APP processing pathways, the application states that such modulators may be useful for studying Alzheimer’s disease and identifying pharmacological agents for its treatment. Id., page 6, lines 10-20.

### Discussion

Claims 147-174 are on appeal. We will focus on claim 147, the broadest claim on appeal, which reads as follows:

147. A method for specifically detecting a stress that alters a functional interaction of a presenilin enhancer (pen) polypeptide with Notch processing or with amyloid precursor protein (APP) processing in a *C.*

*C. elegans* cell in situ which provides a functional interaction of a pen polypeptide with Notch or APP processing, wherein the stress is a modulator of Notch or APP processing, wherein the pen polypeptide comprises a wild-type pen selected from the group consisting of *C. elegans* (SEQ ID NO:7) Pen-2 and *C. elegans* (SEQ ID NO:1) Pen-1, wherein said cell is stressed by a disruption of a pen gene function, said disruption sufficient to provide a sensitized Notch or APP processing pathway, the method comprising steps:

a) subjecting said cell to a putative modulator of Notch or APP processing; and

b) detecting a resultant change in Notch or APP processing in the cell, wherein said change identifies the putative modulator as a modulator of Notch or APP processing, and thereby detecting said stress,

wherein the disrupting is effected by (i) genomic disruption of the pen gene, (ii) RNAi-mediated interference with expression of the pen gene, or (iii) antisense RNA interference with expression of the pen gene, and wherein the disrupting provides non-natural or pathogenic expression of the pen gene.

1. Description requirement, 35 U.S.C. § 112, first paragraph

Claims 147-174 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification. There were two rejections under 35 U.S.C. § 112, first paragraph, set forth in the Answer, beginning on pages 4 and 8, respectively. The first rejection was characterized as a “new matter rejection,” a rejection made when claim amendments are alleged not to have support (written description) in the specification. This rejection overlapped with the issues raised in the second § 112, first paragraph, rejection described on page 8 of the Answer. Consequently, we treat them together.

The rejections of claims 147-174 were based on numerous instances in the claims where lack of written description was alleged. These included a lack of

description for: “disrupting a pen gene function” (id., pages 5 and 8); “functional interaction of a pen polypeptide with Notch processing or APP processing” (id., pages 5, 8, and 9); “detecting a change in Notch processing or APP processing ... to identify a modulator” (id., page 5); where the pen gene function is disrupted (Answer, page 5); pen gene (id., page 8); Notch processing (id., page 8); APP processing (id., pages 5 and 8); pen gene functions (id., pages 8 and 9); “sensitized” pathway (id., pages 9-10); and genus of polypeptides (id., pages 10-11).

“The ‘written description’ requirement [under 35 U.S.C. § 112, first paragraph] implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. ... The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.” Capon v. Eshhar, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005).

After reviewing the record before us, we find that the examiner erred in not applying the proper standard to assess compliance with the “written description” requirement. Rather than determine whether the application adequately described the method that was recited in the claims, the examiner improperly focused on whether the particular words utilized to claim the invention were recited and defined in the specification. For example, in response to Appellant’s arguments pointing to support in the specification for the claimed method, the examiner stated: “The specification at pp. 4 and 25-26 are not sufficiently directed to the terms of the claims.” Answer, page 6.

There is no requirement that the claimed invention be described in the identical wording that was used in the specification, as long as there is sufficient disclosure to show one of skill in this art that the inventor “invented what is claimed.” See, e.g., Union Oil Co. of California v. Atlantic Richfield Co., 208 F.3d 989, 1000, 54 USPQ2d 1227, 1235 (Fed. Cir. 2000); Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

Claim 147 is directed to a cell-based assay performed in a “C. elegans cell in situ which provides a functional interaction of a pen polypeptide with Notch or APP processing,” where the “cell is stressed by a disruption of a pen gene function.” The claim has two steps involving a) subjecting the cell to a modulator of Notch or APP processing (also described as a “stress” in the claim); and b) detecting a change in Notch or APP processing in the cell which is caused by the modulator. After carefully studying the specification, we are persuaded that it reasonably conveys possession of the claimed method, including all of its limitations, to the skilled worker.

As discussed by Appellant, an example of the claimed method is illustrated on pages 24-25 of the specification. Brief, Page 6, lines, 2-8. Table 4 shows the results of an assay where two C. elegans mutants, each having a pen gene mutation (“disruption of a pen gene function”) (Pen-1 (ep140) and Pen-2 (ep220)), were used as the genetic background to screen “putative modulators” (“subjecting sad cell to a putative modulator”) for their effect on the egg laying phenotype (“detecting a resultant change in Notch processing”). The structural basis of the pen mutants utilized in the screen was described in the specification, e.g., on page 23, lines 1-5; lines 25-27. The pen genes were found to enhance a phenotype associated with presenilins, indicating that they

interact in the cell with presenilins. (“The above phenotypic comparison demonstrates that a reduction in pen-1+ or pen-2+ activity, in combination with a loss of sel-12+ activity, results in a loss of presenilin pathway function comparable to the effects of eliminating the two redundant presenilins encoded by sel-12 and hop-1.”) Specification, Page 20, line 12-Page 21, line 10.

The many objections set forth in the Answer faulting the specification for not explaining how the Notch processing pathway worked suggest that the examiner ignored the advanced state of scientific knowledge as described in the specification and the prior art. This must be taken into account when determining compliance with § 112, first paragraph. Capon v. Eshhar, 418 F.3d at 1357, 76 USPQ2d at 1084. According to Appellant’s patent application and the accompanying prior art, the key components of the Notch processing pathway were known prior to the application’s filing date. For example, the *C. elegans* orthologs of presenilin had been identified as sel-12, hop-1, and spe-4. Specification, page 3, lines 5-15. Notch orthologs, lin-12 and glp-1, had also been found in *C. elegans*. Id., page 3, lines 16-17; page 4, line 4. The application states that a “functional link” had been already been established between presenilin (e.g., sel-12) and Notch (e.g., lin-12). Id., page 3, lines 15-30. See, also Levitan and Greenwald, Development, 125: 3599-3606 (1998) (of record). Moreover, the egg-laying defect utilized in the application for “detecting a resultant change in Notch ... processing in the cell” (step b of claim 147) had been recognized as a phenotype associated with the Notch pathway. Baumeister et al., Genes and Function, 1:149-159 (1997) (of record).

We find that the phrase “functional interaction of a pen polypeptide with Notch processing” would be understood by the skilled worker (e.g., a scientist skilled in genetic technology). Appellant identified the pen genes in a genetic experiment that subjected presenilin mutants (*sel-12*) to mutagenesis, and then looked for new mutations that made the *sel-12* egg-laying defect worse. Specification, page 19, line 15-page 22, line 12. *Sel-12* had already been functionally linked to Notch (*lin-12*). See above. The experiments described in the application indicate that *pen* acts together with *sel-12*, which itself is a member of the Notch processing pathway. Thus, the skilled worker would understand that *pen* and *sel-12* act with each other in producing the Notch processing phenotype (e.g., egg-laying defect). Furthermore, the experiments involving *aph-2* RNAi were described as demonstrating “a functional interaction ... with presenilins and *pen-1* and *pen-2*.” *Id.*, page 26, lines 10-20. The precise nature of the “interaction” is not defined because it occurred in a cell and was determined on the basis of phenotypic observations, i.e., egg-laying defect.

The “*pen* gene function” is also described in the application, e.g., on Page 20, lines 15-25, where it was stated to interact genetically with *sel-12* and *hop-1*. Several of the *pen* mutations were classified as “loss-of-function” because the activity of the gene was completely knocked out. *Id.*, page 20, lines 14-25. In this context, we are persuaded that the phrase “disruption of the *pen* gene function” is supported by the written description, and that the skilled worker would understand it. A “sensitized” pathway is also described in the specification as a partial loss of function. *Id.*, Page 19, lines 15-20; Page 21, lines 11-12.

The objection to the specification as lacking a description of the pen-1 gene is unfounded. Answer, Page 8. GenBank entries containing genomic sequences are disclosed in the specification for both the pen-1 and pen-2 genes. Specification, Page 23, lines 6 and 31, respectively. When the prior art contains known sequence information, it is not necessary that it be disclosed in the specification. Capon v. Eshhar, 418 F.3d at 1357-1358, 76 USPQ2d at 1084-1085. (See also Falkner v. Inglis, 448 F.3d 1357, 1367, 79 USPQ2d 1001, 1008 (Fed. Cir. 2006). “Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here ‘essential genes’), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences.” ). The further statement in the Answer (pages 10-11) that the disclosure of SEQ ID NO: 1 is insufficient to support the scope of the genus is not understood since the claim refers two specific sequences, not a genus.

Claims 151, 165, and 174

Claims 151, 165, and 174 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking written description. These claims were stated to be “newly directed” to a putative modulator which is an aph-2 RNAi, and that the “experimentation [in the specification] is not set forth specifically with respect to recitation of the claims.” Answer, Page 7.

We do not agree with the examiner. On pages 24-25 of the application, an example is disclosed where mutant pen-1 and pen-2 genetic backgrounds (“said cell is

stressed by a disruption of a pen gene function”) was challenged with the aph-2 RNAi (“subjecting said cell to a putative modulator”). As we explained above, this example shows possession of the claimed invention. The glp-1 sterility is used as a read-out for “detecting a resultant change in Notch or APP processing.” Specification, page 26; page 4. The application expressly describes this result as demonstrating a “functional interaction of aph-2 with presenilins and pen-1 and pen-2.” *Id.*, page 26. The examiner failed to establish a lack of written description of the subject matter recited in these claims.

2. Enablement requirement, 35 U.S.C. § 112, first paragraph

In setting forth the grounds of the rejection, the examiner stated there were various deficiencies in the application, including that “the specification fails to disclose the functional significance of the [pen-1] peptide inside the cells and fails to note it’s [sic] relationship or interaction with Notch ... and fails to note specific stresses that alter functional interaction of Pen-1 with Notch processing ...” Answer, Page 14.

“To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. In re Wright, 999 F.2d at 1562, 27 USPQ2d at 1513 (Fed. Cir. 1993).

We do not find that the examiner has set forth a reasonable scientific basis to doubt the enablement provided in the application. For example, the relevance to the claimed invention of the unpredictability of protein chemistry as described on pages 13-14 of the Answer was not articulated. The alleged failure to “disclose the functional significance of the [pen] peptide inside the cell and... to note [its] relationship or interaction with Notch processing” does not provide a scientific reason to doubt that the enablement of the invention. The application describes how to obtain pen mutants (“disruption of a pen gene function”) that interact with Notch processing to produce a phenotype, and then how to identify modulators of this pathway. See, discussion above. The fact that Appellants have not spelled out the molecular interaction between the pen peptide and presenilin (sel-12) is insufficient to cast reasonable doubt, especially when the claimed method apparently worked as shown in Table 4 of the specification. The examiner did not explain how the lack of a precise molecular picture of the pathway would lead the skilled person to doubt that other pen gene disruptions and modulators would also not work.

The examiner also stated that while the “specification notes particular embodiments of the invention ... none of the embodiments appear to meet all of the limitations of the claims as now recited.” Answer, page 15. Despite this strong language, the examiner did not point out specifically what limitations were not met. In general, while the examiner alleged many insufficiencies, she did not adequately explain how these impacted compliance with the statutory requirements.

Furthermore, the examiner stated that the only exemplifications of pen gene disruption were the particular mutants disclosed in the application, but the application

did not provide examples where RNAi or anti-sense were used to disrupt pen gene function. Working examples are not required to comply with § 112, first paragraph. In re Borkowski, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Methods of conducting RNA mediated interference were known in the prior art (specification, page 22, lines 20-21), as well as being described in the specification. Specification, pages 26-27. Anti-sense technology was also established in the art. Crook, Antisense & Nucleic Acid Drug Dev., 8:115-122 (1998) (of record and listed in PTO-892). In view of the knowledge of those skilled in the art, the examiner has not adequately explained why undue experimentation would be required to carry out the full scope of the claims.

### 3. Indefiniteness, 35 U.S.C. §112, second paragraph

Claims 147-174 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

The examiner stated that “the claims appear to conflict with the requirements of the base claim in genetic disruption of pen. In particular, Appellants have specified that the disrupting mechanism is a disrupting of ‘pen gene function’ yet the cell is required to provide pen polypeptide.” Answer, Page 18.

This confusion is not justified. The application makes clear that *C. elegans* has two pen genes, pen-1 and pen-2. Specification, page 4, lines 19-20. It is also stated that *C. elegans* can have “a reduction in pen-1+ or pen-2+ activity.” Id., Page 21, lines 7-12. Thus, it would be understood that at least one of the pen genes could be disrupted, while the other is not. This is expressly shown in the example on Page 25 of

genotype pen-1 (ep140) [pen-1 is disrupted, but pen-2 is not] and genotype pen-2(ep220) [pen-2 is disrupted, but pen-1 is not]. The rejection is reversed.

Summary

The rejections of claims 147-174 under 35 U.S.C. § 112, first and second paragraphs, are reversed.

REVERSED

Toni R. Scheiner	)	
Administrative Patent Judge	)	
	)	
	)	
	)	BOARD OF PATENT
Eric Grimes	)	
Administrative Patent Judge	)	APPEALS AND
	)	
	)	INTERFERENCES
	)	
Richard M. Lebovitz	)	
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