Pathways to Patents: Applying the Written Description Requirement Doctrine to Patents on Biological Pathways

Shengfeng Chen

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Pathways to Patents: Applying the Written Description Requirement Doctrine to Patents on Biological Pathways

by

SHENGFENG CHEN*

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* University of California, Hastings College of the Law, Juris Doctor Candidate 2008; Rutgers, the State University of New Jersey, New Brunswick, Ph.D., Chemistry, 2001. The author is grateful to Professor Margreth Barrett and Professor Robin Feldman for their insight and suggestions.
I. Introduction

In recent years, patenting biological functions has become the central topic of the debate over biotech patent policy. Courts have faced increasingly difficult questions such as research tool patents, and so-called “reach-through” claims. The concern over patenting biological functions reached its high-water mark when the Supreme Court granted certiorari in Labcorp v. Metabolite, where the disputed patent claimed a correlation between an elevated level of homocysteine and a deficiency in B vitamins in humans.

In Labcorp, the patent at issue involved methods for diagnosing vitamin B12 or folic acid deficiency. Simply put, it involved a biological function in the human body: when vitamin B12 or folic acid is deficient, a chemical called homocysteine cannot be properly metabolized; thus, the level of homocysteine increases in our body. Knowing this functional correlation, scientists can directly assay homocysteine to screen for vitamin B12 or folic acid deficiency. Metabolite, the licensee of the patent, sublicensed the patent to Labcorp. When an alternative method of homocysteine assay became available on the market, Labcorp switched to

1. The National Institutes of Health ("NIH") defines research tools as "tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones, and cloning tools (such as PCR), methods, laboratory equipment and machines." Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resource: Final Notice, 64 Fed. Reg. 72,090, 72,092 n.1 (Dec. 23, 1999).
4. Id. at 2924 (the claim in dispute reciting a method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of: assaying a body fluid for an elevated level of total homocysteine; and correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate).
6. Id.
7. Id.
8. Id. at 1359.
the alternative assay and discontinued royalty payments to Metabolite.\textsuperscript{9} Thereafter, Metabolite sued Labcorp, alleging that the use of the alternative assay infringed its patent.\textsuperscript{10} The Federal Circuit held that the patent was valid and that Labcorp willfully infringed the patent.\textsuperscript{11} Labcorp filed a petition for certiorari to the Supreme Court, contending that the patent claim was invalid as unpatentable subject matter.\textsuperscript{12} After hearing oral arguments, the Supreme Court dismissed the writ of certiorari as improvidently granted because the issue presented was not raised in the decision below.\textsuperscript{13}

Although the fundamental purpose of patent law is to promote progress,\textsuperscript{14} some judges and scholars worry that "too much patent protection can impede rather than 'promote the Progress of Science and useful Arts,' the constitutional objective of patent and copyright protection."\textsuperscript{15} This seems particularly a concern when it comes to claiming biological functionality. In biological and chemical arts, inventors have no difficulty in finding functional characteristics that cover a broad scope. For example, a drug functions in human cells by inhibiting specific protein targets,\textsuperscript{16} an antibody works by recognizing and binding to a specific region of the antigen,\textsuperscript{17} a polynucleotide probe detects a target generic material by hybridizing to a specific region of a genomic DNA.\textsuperscript{18}

The impact of claiming biological functionality is enormous. Many research tool and "reach-through" patents are the results of functional claiming. Due to their broad scope, the research tool patents potentially can cover prior art compounds. Even more significantly, the "reach-through" claims cast shadows on future development and downstream innovations involving the claimed biological functionality. On the other hand, an argument in favor of allowing functional claims is, "incentives may matter" to promote the upstream discoveries because they "may prove of great benefit to the human race."\textsuperscript{19}

\begin{itemize}
  \item \textsuperscript{9} Id.
  \item \textsuperscript{10} Id.
  \item \textsuperscript{11} Id. at 1358.
  \item \textsuperscript{12} \textit{Lab. Corp. of Am. Holdings}, 126 S. Ct. at 2925.
  \item \textsuperscript{13} Id. at 2921.
  \item \textsuperscript{14} U.S. CONST. art. I, § 8, cl. 8.
  \item \textsuperscript{15} \textit{Lab Corp. of Am. Holdings}, 126 S. Ct. at 2922 (Breyer, J., dissenting); see also, Rebecca S. Eisenberg & Michael A. Heller, \textit{Can Patents Deter Innovation? The Anticommons in Biomedical Research}, 280 SCIENCE 698 (1998).
  \item \textsuperscript{16} See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916 (Fed. Cir. 2004).
  \item \textsuperscript{17} See, e.g., Chiron Corp. v. Genentech, Inc., 363 F.3d 1247 (Fed. Cir. 2004).
  \item \textsuperscript{18} See, e.g., Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316 (Fed. Cir. 2002).
  \item \textsuperscript{19} \textit{Lab Corp. of Am. Holdings}, 126 S. Ct. at 2922 (Breyer, J., dissenting).
\end{itemize}
Courts and scholars have made various proposals to regulate the
research tool patents.\textsuperscript{20} Justice Breyer, in his dissenting opinion in the
Court's dismissal of \textit{Labcorp}, made it clear that he would have invalidated
the Metabolite patent on the ground of unpatentable subject matter.\textsuperscript{21}
Justice Breyer, however, recognized that "[t]he line between a patentable
'process' and an unpatentable 'principle' is not always clear."\textsuperscript{22} After all,
many patentable inventions rest upon the knowledge of natural phenomena,
and many process patents seek to make abstract intellectual concepts
workably concrete.\textsuperscript{23} In addition, the "complex relationship [between
patents and innovation] is industry-specific at each stage of the patent
process."\textsuperscript{24} Thus, for those cases at the boundary, the courts might be
reluctant to consider how broad or narrow the "natural phenomenon"
doctrine should be interpreted.

This Note argues that, where the patentable subject matter doctrine is
not easily applicable, the written description doctrine can provide a solution
to the issue of research tools. It is not necessary to draw an arbitrary line
between patentable subject matter and unpatentable scientific principle.
Part II of the Note explores the science and patenting of biological
pathways as an example of the problem presented by novel technologies to
the patent system. Part III of this Note examines the development of the
written description doctrine in the biotechnology patent cases. Part IV of
this Note proposes a new standard for functional claiming, and it illustrates
how the written description requirement applies to conform the scope of the
claims to the quid pro quo balancing of the patent system.

\textsuperscript{20.} See, e.g., Rochelle Dreyfuss, \textit{Biotechnology Patents Get Special Treatment: Protecting
the Public Domain of Science: Has the Time for an Experimental Use Defense Arrived?}, 46 \textit{ARIZ.}
L. REV. 457 (2004); David C. Hoffman, \textit{A Modest Proposal: Toward Improved Access to
Biotechnology Research Tools by Implementing a Broad Experimental Use Exception}, 89 \textit{CORNELL L. REV.}
993 (2004); Marlan D. Walker, \textit{The Patent Research Tool Problem After
\textsuperscript{21.} \textit{Lab. Corp. of Am. Holdings}, 126 S. Ct. at 2927 (Breyer, J., dissenting) ("[C]laim 13 is
invalid no matter how narrowly one reasonably interprets [the patentable subject matter]
doctrine.").
\textsuperscript{22.} \textit{Id.} at 2926 (citing Parker v. Flook, 437 U.S. 584, 585 (1978)).
\textsuperscript{23.} \textit{Id.} at 2926.
\textsuperscript{24.} \textit{Id.} at 2927 (citing Dan L. Burk & Mark A. Lemley, \textit{Policy Levers in Patent Law}, 89 \textit{VA. L. REV.}
1575, 1589 (2003)).
II. Patenting Biological Pathways

A. Biological Pathways in General and the NF-κB Pathway

A biological pathway is a group of cellular constituents wherein each constituent is under the influence of one or more other cellular constituents in the group. In the cell, there are many different kinds of enzymes that catalyze a variety of different reactions. The biological pathway refers to a specific sequence of events in which these reactions are carried out. For example, a reactant is converted to a product by an enzyme. In turn, the product of this enzyme becomes the reactant of a second enzyme in the biological pathway. Like a cascade, the sequence of reactions continues on until the final product is made through the series of steps in the pathway. The NF-κB pathway is one of such pathways in the human body.

Like any biological pathway, the NF-κB pathway is a complicated network for a number of reasons. First, NF-κB is not a single protein, but a family of closely related proteins that binds to a specific site of our genome. Second, NF-κB regulates numerous genes in our immune system, and consequently is implicated in many diseases. On the other hand, in the cascade of the NF-κB pathway, NF-κB proteins themselves are tightly controlled by several regulatory proteins. Lastly, within the general NF-κB pathway, there are multiple sub-pathways wherein NF-κB proteins can be activated via different activation mechanisms. These sub-


26. See Yixue Cao, Michael Karin, Florian R. Greten & Zhi-Wei Li, NF-κB in Cancer: From Innocent Bystander to Major Culprit, 2 NAT. REV. CANCER 301, 303 (2002) ("There are five mammalian reticuloendotheliosis family (REL)/nuclear factor of κB (NF-κB) proteins that belong to two groups: those that do not require proteolytic processing and those that do require proteolytic processing.").

27. See Bharat B. Aggarwal, Aladin M. Boriek, Ashok Kumar & Yasunari Takada, Nuclear Factor-κB: Its Role in Health and Disease, 82 J. MOL. MED. 434, 434 (2003) ("Nuclear factor-κB (NF-κB) transcription factors are a family of structurally related eukaryotic transcription factors that promote the expression of well over 150 genes involved in a variety of cellular processes.").

28. See id. ("The dysregulation of NF-κB is associated with many disease states such as AIDS, atherosclerosis, asthma, arthritis, cancer, diabetes, inflammatory bowel, disease, muscular dystrophy, stroke, and viral infections. Recent evidence also suggests that the dysfunction of NF-κB is a major mediator of some human genetic disorders.").

29. See Hideaki Kamata, Michael Karin & Jun-Li Luo, IKK/ NF-κB Signaling: Balancing Life and Death—A New Approach to Cancer Therapy, 115 J. CLIN. INVEST. 2625, 2625 (2005) ("Many stimuli activate NF-κB, mostly through IKK kinase-dependent (IKK-dependent) phosphorylation and subsequent degradation of IκB proteins. The liberated NF-κB dimmers enter the nucleus, where they regulate transcription of diverse genes encoding cytokines, growth factors, cell adhesion molecules, and pro- and antiapoptotic proteins.").

30. See id. (There are at least two known NF-κB activation pathways, the classical pathway and the alternative pathway. The classical pathway is normally triggered in response to microbial
pathways involve different cellular constituents, and regulate different downstream genes. In sum, "NF-κ[β] acts at the crossroads of many signaling pathways." 31

Such biological pathways are perfect candidates for functional claiming. Usually a patent may be granted if the patentee discovered a compound(s) or a class of the compounds that are effective in treating a certain disease. When the compound for treating a disease is not known, the disclosure will not meet the written description requirement, unless it relies on functional descriptions. 32 There is little difficulty in finding such functional descriptions in a biological pathway. By describing the regulatory proteins that control NF-κβ, one can characterize the activity of NF-κβ proteins because they are tightly controlled by those regulatory proteins. In turn, by describing the NF-κβ proteins, one can characterize the activity of genes and proteins of the immune systems controlled by NF-κβ. The potential functional claiming does not stop here. By simply describing the NF-κβ proteins, one can essentially characterize the method of treating any disease related to the NF-κβ pathway.

B. The NF-κβ Patent

The patentability of biological functionality remains unsolved after *Labcorp*. The core issue continues to be a major concern to the biotechnology and pharmaceutical industry, and continues to be the subject of patent litigation.

On June 25, 2002, the United States Patent and Trademark Office granted a patent on the NF-κβ pathway, 33 which claims various methods of treating human disease by regulating the NF-κβ activity, based on the functionality of the NF-κβ pathway. 34 On the same day, Ariad Pharmaceuticals, Inc., the exclusive licensee, filed a suit against Eli Lilly & Company, “alleging that Lilly’s sales and marketing of Évista and Xigris..."
constitute infringement of 20 claims of the '516 patent.\textsuperscript{35} The jury awarded $65 million damages to Ariad.\textsuperscript{36}

With 203 claims, the 516 patent covers methods of reducing the naturally occurring NF-κβ activity in cells affecting gene expression, for example:

Claim 1. A method of inhibiting expression, in a eukaryotic cell, of a gene whose transcription is regulated by NF-κβ, the method comprising reducing NF-κβ activity in the cell such that the expression of said gene is inhibited.

Claim 203. A method of inhibiting expression, in a mammalian cell, of a gene whose transcriptional activity is activated by binding of NF-κβ to said gene, comprising introducing a nucleic acid decoy molecule into the cell in an amount sufficient to inhibit expression of the gene, which decoy includes a NF-κβ binding site that binds NF-κβ.\textsuperscript{37}

Since the NF-κβ pathway controls "the expression of well over 150 genes involved in a variety of cellular processes,"\textsuperscript{38} the broad patent claims could cover a wide range of drugs for treating various disease.\textsuperscript{39} In fact, the patented method covers compounds known and patented before the discovery of the NF-κβ pathway. Eli Lilly's osteoporosis and severe sepsis drugs Evista and Xigris, both patented before Ariad's patent, were alleged to infringe on Ariad's patent because "these drugs treat [diseases] by inhibiting NF-κβ activity" at the molecular level.\textsuperscript{40} Allowing such biological pathway patents could potentially remove even known materials from the public domain.\textsuperscript{41}

Relying on functional description, functional claiming of the biological pathway could be classified into three categories. Under the first scenario, a general method of modulating the pathway for treating diseases is broadly claimed without claiming or disclosing any drug. An example of this type of claim is claim 1 of Ariad's patent (supra). The second scenario involves a method of modulating the pathway by introducing a class of drugs, without disclosing any embodiment of the class. Claim 203 of Ariad's patent (supra) is a good example of this type of claim, wherein a
class of nucleic acid decoy is claimed without disclosing any specific drug. In the third scenario, a method of modulating the pathway is disclosed and claimed, as well as some specific embodiments that are useable for treating diseases. As far as patenting the biological pathway is concerned, all three categories of patent claims can constitute research tools.

Some scholars have suggested that realities will limit any tendency that patentee may have to limit access to or charge exorbitant licensing fees on its patented biological pathway methods. First, Ariad has to license such methods broadly because it could not possibly support all of the feasible related research on its own. This ensures “a wide range of nonrivalrous research . . . using the patented methods.” Second, clinical application of these methods would be complicated and unpredictable due to the “intricate network of NF-κB interactions.” This, in combination with “the cost and uncertainty of biotech research and development” in general, will diminish the value of the patent and “mitigate [its] potential negative impacts.”

These arguments have some merit, particularly in an individual case like the NF-κB pathway. We still have difficulty, however, when dealing with this problem broadly, for example, where the clinical application is not as unpredictable or where the involved proteins have become the active drug targets.

On the other hand, one may argue that a biological pathway, as a natural phenomenon, is not patentable subject matter. However, the patentable subject matter doctrine poses a low bar to patentability. The Federal Circuit has held that a process is a patentable subject matter if it produces “a useful, concrete and tangible result.” A method of treating diseases, or a method of inhibiting gene expression, passes muster under 35 U.S.C. 101. The mere involvement in a biological pathway does not render a specific drug or a method of using that drug unpatentable subject


43. Id. at 1026.

44. Id.

45. Id.

46. Id.


49. Section 101 of the Patent Act provides that “[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.” 35 U.S.C. § 101 (2008).
matter per se. In fact, all drugs modulate some biological pathways in order to function in the human body. Thus, the courts would be hard-pressed to announce the across-the-board unpatentability of such methods, particularly where specific compounds have been disclosed.

The written description requirement, on the other hand, may be a more appropriate means for assessing the patentability of biological pathway patents because the written description limits the patent scope based on the disclosure of the invention. To satisfy the written description requirement, an invention involving a chemical genus requires a precise definition, such as by structure, formula, or the chemical name of the claimed subject matter sufficient to distinguish it from other materials, or "functional characteristics when coupled with a known or disclosed correlation between function and structure." Thus, the patenting of the biological pathway can rely on functional characteristics coupled with correlation to satisfy the written description requirement. However, as will be discussed in Part III, the Federal Circuit has not developed a consistent body of law in this area.

III. Development of Written Description Requirement in Biotechnology Area

A. Regents of Univ. of Cal. v. Eli Lilly & Co — The Scope of the Claims Limited to the Disclosed Embodiments of the Invention

Regents of Univ. of Cal. v. Eli Lilly & Co, limited the scope of the claims to the disclosed embodiments of the invention. In Eli Lilly, the inventors at University of California discovered the rat cDNA sequences for PI and PPI insulin. However, the human, vertebrate and mammalian cDNA were not discovered at the time of the application, and thus were not disclosed. In their application, the inventors broadly claimed not only the cDNA sequences for rat insulin, but also the human, vertebrate and mammalian PI and PPI. The court invalidated those claims of the undisclosed cDNA sequences, reasoning that "a generic statement" of cDNA sequences "does not distinguish the claimed genus from others,

50. *Eli Lilly & Co.*, 119 F.3d at 1568.
52. *Eli Lilly*, 119 F.3d at 1562-1563. PI and PPI stand for preproinsulin and proinsulin, respectively.
53. *Id.* at 1568.
54. *Id.*
except by function." Such generic statements, without more, are not adequate written descriptions of the genus.

The Lilly court thus adopted a rigorous written description requirement standard, and rejected the patentability of broad functional claiming. Under Lilly, a definition by function "does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." "[T]he written description of an invention involving a chemical genus . . . requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials."

**B. Enzo Biochem, Inc. v. Gen-Probe Inc. — Functional Claiming May Satisfy the Written Description Requirement**

*Enzo Biochem, Inc. v. Gen-Probe Inc.*, by contrast, allowed claims having a broader scope than what was set out in the disclosed embodiments. In *Enzo*, the patentee discovered three nucleic acid probes and deposited them at the American Type Culture Collection, together with six strains of Neisseria gonorrhoea and of Neisseria meningitidis. The patentee sought to claim the three deposited probes even though the sequences of these probes were not determined. In addition, the patentee claimed a genus of "nucleic acid probes that selectively hybridize to the genetic material of . . . Neisseria gonorrhoeae" over that of Neisseria meningitides. The Federal Circuit, in its first decision, applied Lilly’s test and invalidated the genus claim for failure to meet the written description requirement.

A mere three months later, the Federal Circuit vacated its first decision and held that "it is not correct . . . that all functional descriptions

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55. *Id.*
56. *Id.*
57. *Id.*
58. *Id.* at 1562-1563.
60. *Id.* at 1321.
62. *Enzo Biochem, Inc.*, 296 F.3d at 1320; see also, Wenrong Huang, *Enzo's Written Description Requirement: Can It an Effective Check Against Overly Broad Biotechnology Claims?*, 16 ALB. L.J. SCI. & TECH. 1, 17 (2006) (explaining that the genus comprises numerous possible probes. "[E]ntirely different DNA sequences [can] display similar selectivity, but . . . bind to other parts of the N. gonorrhoeae DNA . . . [i]t’s like a blind person discovering the tail of an elephant.").
63. *Enzo Biochem, Inc.*, 285 F.3d at 1015 (The first *Enzo* court further invalidated the claims to three deposited probes because a publicly accessible depository does not provide "such descriptive means ... that fully set forth the claimed invention.").
of genetic material fail to meet the written description requirement. The *Enzo* II court held that even if the patentee did not disclose any structural features commonly possessed by members of the genus, the application could satisfy the written description requirement "if one of skill in the art would find the generically claimed sequences described on the basis of *Enzo*’s disclosure of the hybridization function and an accessible structure. . . ." Thus, under the *Enzo* II decision, "functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics," may satisfy the written description requirement.

The *Enzo* II decision has been criticized for "relax[ing] the requirement of *Eli Lilly* and open[ing] a door for overly broad claims." However, a distinction can be made between *Enzo* and *Eli Lilly*. In *Enzo*, "the claimed nucleotide sequences preferentially bind to the genomic DNA of the deposited strains of [Neisseria] gonorrhoeae and have a complementary structural relationship with that DNA . . . ." By contrast, this "complementary structural relationship" is absent in *Eli Lilly*. There, the patentee defined the claimed cDNA sequences by "the mere name ‘cDNA’" or "the name of the protein." Thus, one can distinguish *Enzo* from *Eli Lilly* by examining the presence or absence of a correlation between the function and structure.

C. The "Full Characterization" Requirement

Subsequent to *Enzo* II, the Federal Circuit has developed further requirements for functional claiming, and held that applicants cannot "define the unknown [structures] by . . . another unknown," when relying on the functional characteristics coupled with a known or disclosed correlation between function and structure. In *Noelle v. Lederman*, the applicant discovered a "mouse" form of a monoclonal antibody that specifically binds to a CD40CR antigen. As the patentees in *Eli Lilly*, the

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64. *Enzo Biochem, Inc.*, 296 F.3d at 1324.
65. *Id.* at 1328.
66. *Id.* at 1324.
67. Huang, supra note 62, at 13. (2006); see also, Paula K. Davis, *Questioning the Requirement for Written Description: Enzo Biochem v. Gen-Probe and Overly Broad Patent Cases*, 37 IND. L. REV. 467, 490-491 (2004) ("The [Enzo’s genus] claims are not limited to specific metes and bounds but instead describe an unknown but potentially astronomical number of compounds of unknown sequences and structures, yielding overly broad claims.").
68. *Enzo Biochem, Inc.*, 296 F.3d at 1328.
71. *Id.* at 1345-1346; Antibody is a Y-shaped protein on the surface of B cells that is secreted into the blood or lymph in response to an antigenic stimulus, such as a bacterium, virus,
applicant sought to claim more than the scope of the disclosure—the "human" form of the antibodies and the "genus" form of the antibodies. As in Eli Lilly, the Federal Circuit held that the applicant "failed to disclose the structural elements of human CD40CR antibody or antigen . . . ," and thus did not provide a sufficient written description of the claimed "genus" or "human" form of antibodies. However, unlike in Eli Lilly, the Federal Circuit held that it would have allowed functional claiming if the applicants had disclosed a "fully characterized antigen." Here, the binding affinity to the antigens alone could not sufficiently describe the "human" form of antibody. Therefore, "[i]f Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed his antibody by simply stating its binding affinity for the 'fully characterized' antigen."

The Federal Circuit further articulated the "full characterization" requirement in In re Wallach: if the functional "characterization contributes little . . . to the description" of the claimed genus, the written description requirement is not met, even if there is "disclosure of a partial structure." There, the applicants sought to claim a genus of genes encoding for a protein, even though 95 percent of the amino acid sequence was not determined at the time of the application. The Federal Circuit rejected the applicants' argument that the written description was satisfied because they "were in possession of the protein" and the sequences of the protein were merely "an inherent property of the protein." Physical possession does not amount to knowledge of the sequence.

Following Enzo II, the Wallach court did not reject patentability by functional claiming, but held that "functional description can be sufficient only if there is also a structure-function relationship known to those of
ordinary skill in the art." Disclosure of a complete amino acid sequence may suffice for written description of the genus of the DNA molecules encoding for the protein because, analogous to the case of the nucleotide hybridization in Enzo, "such a well-known relationship exists between a nucleic acid molecule's structure and its function in encoding a particular amino acid sequence . . ." However, a mere partial sequence cannot describe the structures of the genus. There is no evidence of "any known or disclosed correlation between the combination of a partial structure of a protein, the protein’s biological activity, and the protein’s molecular weight, . . . and the structure of the DNA encoding the protein . . .”

D. No-compound, No-patent — Univ. of Rochester v. G.D. Searle & Co.

In Univ. of Rochester v. G.D. Searle & Co., the Federal Circuit seemed to have returned to Eli Lilly's holding, limiting the scope of the claims to the disclosed embodiments of the invention. In Rochester, the University discovered the existence and separate functions of two distinct cyclooxygenases, “COX-1” and “COX-2.” The University “hypothesized that it would be possible to reduce inflammation without gastrointestinal side effects if a method could be found for selectively inhibiting the activity of COX-2 . . . without inhibiting COX-1 activity.” The University “developed a screening assay for use in determining whether a particular drug displayed such selectivity,” but failed to disclose or identify even a single selective compound. The claims to assay methods were allowed and issued in a prior patent. The University further sought to patent a method of selectively inhibiting COX-2 activity in a human host by administering a non-steroidal compound that selectively inhibits COX-2 activity to a human host in need of such treatment. The Federal Circuit ruled that this method claim was invalid for lack of written description, because the application did not disclose any COX-2 selective compound.

80. Id. at 1335.
81. Id. (explaining that given the amino acid sequence, one can determine the chemical structure of all nucleic acid molecules that can serve the function of encoding that sequence).
82. Id.
83. Id.
85. Id. at 917.
86. Id. at 918.
87. Id.
88. Id. at 928.
89. Id.
90. Id. at 918.
"Without such disclosure, the claimed methods cannot be said to have been described."\textsuperscript{91}

However, the Rochester court did not close the door for functional claiming in pharmaceutical patents, and has left many questions unanswered. In rejecting Rochester's written description requirement arguments, the court seemed to suggest that functional claiming was not available because the genus was described by a "vague functional description."\textsuperscript{92} An ordinarily skilled artisan would not be able to "identify any compound based on this vague functional description as 'a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product.'" Conversely, if the functional description was not vague, the court would be willing to consider the functional claiming.

IV. Applying the Written Description Requirement Doctrine to Patents on Biological Pathways

A. Scholastic Responses to the Federal Circuit's Written Description Jurisprudence in Biotechnology Inventions

Thus far, the Federal Circuit precedents regarding the written description requirement have been confusing. In Eli Lilly, the court limited the scope of the claims to disclosed embodiments of the invention.\textsuperscript{93} The Enzo II decision allowed claims having scope broader than what was set out in the disclosure.\textsuperscript{94} In Rochester, the court took a no-drug, no-patent approach.\textsuperscript{95} These conflicting decisions have "foster[ed] further confusion in what is already a confusing area of our precedent."\textsuperscript{96}

Commentators have criticized the need for a separate written description requirement.\textsuperscript{97} Some commentators have advocated that an

\textsuperscript{91} Id. at 927.  
\textsuperscript{92} Id. at 928.  
\textsuperscript{93} Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1559 (Fed. Cir. 1997).  
\textsuperscript{94} Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316 (Fed. Cir. 2002).  
\textsuperscript{95} G.D. Searle & Co., 358 F.3d at 926.  
\textsuperscript{97} See, e.g., Robin Feldman, The Inventor's Contribution, 2005 UCLA J.L. & Tech. 6 (2005) (critiquing the need for a separate written description requirement). See also, Stephen J. Burdick, Moba v. Diamond Automation, Inc.: Questioning the Separate Written Description Requirement, 19 Berkeley Tech. L.J. 133 (2004) (arguing that the effects of the separate written description requirement is redundant with enablement and new matter requirements, and that the separate written description requirement should be eliminated entirely); Dan L. Burk & Mark A. Lemley, Biotechnology's Uncertainty Principle, 54 CASE W. RES. L. REV. 691 (2004); Mark D. Janis, On Courts Herding Cats: Contending with the "Written Description" Requirement (And
optimal biotechnology patent policy should require "a fairly low disclosure requirement" coupled with "a fairly high obviousness threshold, and argued that a variety of policy levers (such as utility and abstract ideas doctrines) might be employed to prevent unnecessary upstream patents that threaten to hold up downstream innovation. The proposed policy, however, might still result in overreaching upstream patents, particularly for inventions that do meet utility and abstract ideas standards, such as patenting on biological pathways.

Other commentators recognized that issues addressed in the separate written description doctrine properly reside in the disclosure inquiry and reflect legitimate concerns, but argued that a separate written description doctrine is unnecessary. In particular, it has been strongly argued that the issues addressed in the separate written description doctrine can be resolved by harmonizing disclosure with other doctrines of patent law and by properly applying traditional disclosure doctrines. Under this proposal, information that could have been known should be reachable only if it does not require undue experimentation, and information that could not have been known at the time of the application should be beyond the reach of the invention. The same rationale and analysis, however, are equally applicable to the separate written description requirement in priority cases, a requirement that has been firmly established for decades. If courts were to adopt this approach, they will have to abandon the separate written description requirement all together, whether in priority cases or in original claims cases. Alternatively, if we are going to keep the written description requirement, a better standard for meeting the written description requirement is needed because of the above concerns.

Other Unruly Patent Disclosure Doctrines), 2 Wash. U. J.L. & Pol'y 55 (arguing that the distinction between the written description and enablement requirements is artificial).

98. See, e.g., Burk & Lemley, supra note 97, at 737 (explaining that biotechnology is properly described in part by the anti-commons theory and in part by prospect theory, and that a rational patent policy should seek to minimize the anti-commons problems and give inventors control to induce them to walk the uncertain path towards commercial development).

99. See, e.g., Feldman, supra note 97, at 135. See also, Burdick, supra note 97.

100. Feldman, supra note 97, at 134.

101. Id.


103. Feldman, supra note 97, at 24. (noting that the written description inquiries in priority cases and in original claims cases concern the same issue, and the difference between two inquiries is just a matter of timing).

104. In cases involving priority issues, the U.S. Patent and Trademark Office and the court have to determine which of two inventors could properly claim to be the first to invent. See, e.g., In re Baker, 559 F.2d 588 (C.C.P.A. 1977) (noting that a separate written description requirement is "a statutory requirement duly recognized by the courts").
B. Proposal: A New Standard for Meeting the Written Description Requirement

1. A "Common Feature" Test

Recognizing the need for certainty for inventors, practitioners, and the courts, this Note proposes a "common feature" test that resolves this issue, replaces the "possession of the invention" test, or "complementary structural relationship" test, and avoids many uncertainties under the precedents.

Under the "common feature" test, there are two conditions for describing a genus by functional characterization: (1) a "fully characterized" defining material; and (2) a defining correlation sufficient to identify a "common feature" of the structures. Under this approach, functional claiming would not meet the written description requirement in two instances. First, a genus could not be defined by "another unknown [material]," nor could it be defined if the functional "characterization contributes little . . . to the description" of the claimed genus. Second, the genus could not be defined by a mere "vague functional description."

However, the "common feature" test would not completely preclude the patentability of functional claiming. Under this approach, functional claiming could meet the written description requirement in two scenarios, provided that the defining material itself is fully characterized. First, the defining correlation is of a "complementary structural relationship," or "known to those of ordinary skill in the art." Second, absent such a complementary or well-known correlation, the written description requirement would be met if the defining correlation would sufficiently identify a common feature of the structures of the genus.

The inquiry under the common feature test would not focus on whether or not any specific working examples were disclosed. Some working examples would be helpful for establishing such a common feature. However, even with no compound, the written description requirement would be met if the defining correlation, coupled with ordinary

105. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1564 (Fed. Cir. 1991) ("[T]he applicant must ... convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.").
106. Enzo Biochem, Inc., 296 F.3d at 1328.
108. Id.
111. Enzo Biochem, Inc., 296 F.3d at 1328.
112. Wallach, 378 F.3d at 1335.
skill in the art, would reveal a common feature of the genus. By taking this approach, the test avoids a hard-and-fast no-compound, no-patent rule. The next part of the Note uses three hypothetical claims to illustrate how this test can be apply to functional claiming of biological pathways.

C. Three Scenarios of Functional Claiming On Biological Pathways

As discussed briefly in Part II. 2, supra, there could be three categories of functional claiming of biological pathways. The first kind would claim a general method of modulating the pathway without claiming or disclosing any drug. The second would claim a method of modulating the pathway using a genus of drugs, without specific examples of the claimed genus. The third would claim a method of modulating pathways using a genus of drugs, accompanied with some examples of specific drugs. To summarize, these three categories of functional claiming can be formulated as the following:

Hypothetical claim 1: A method of modulating X pathway by reducing the activity of protein X in the cell.

Hypothetical claim 2: A method of modulating X pathway by inhibiting protein X with a genus of inhibitors Y.

The specification does not disclose any working example of inhibitors Y.

Hypothetical claim 3: A method of modulating X pathway by inhibiting protein X with a genus of inhibitors Y.

The specification discloses some working examples of inhibitors Y.

The details of the disclosure and the scope of the claims correspond well to the process of research and development in biotechnology inventions. At the early stage, a pathway is discovered, important players such as the key enzymes in the pathway are revealed, and the relationship between this pathway and diseases is elucidated. As the research goes on, researchers conceive that a certain class of compounds will potentially inhibit the key enzyme and thus could constitute an effective treatment for diseases. Nonetheless, as is typical for the biotechnology and pharmaceutical industry, no compound is possible prior to a time-consuming and expensive process. If he or she is lucky, a researcher may eventually discover some effective compounds.

Essentially, discoveries of pathways, at the early stage, are “upstream discoveries that may be useful in a variety of different future research paths or for the development of a variety of commercial products.”113 Does this

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kind of discovery, being remote from any commercial development, merit the award of a patent and exclusion rights?

D. Application of the Proposal to the Biological Pathway Patents

Hypothetical claim 2 closely resembles the selective inhibitor method claimed in Rochester. In Rochester, the claim was directed to "[a] method for selectively inhibiting [enzyme] activity [by] administering a non-steroidal compound . . . ,” without disclosing a single non-steroidal compound.114 Essentially, the University claimed a method of inhibiting the enzyme with a genus of non-steroidal compounds, without disclosing any species. Here, as in Rochester, hypothetical claim 2 does not disclose any specific compound. Thus, under Rochester’s no-compound, no-patent rule, a method of modulating X pathway by inhibiting protein X with a genus of inhibitors Y would not meet the standard.

Hypothetical claim 1 claims an even broader scope than the selective inhibitor method claimed in Rochester. By not claiming any genus of compounds in its language, this type of claim in effect covers any genus of compound that modulates the pathway. Thus, the method claim is analogous to “a cure for cancer by utilizing a substance that attacks and destroys cancer cells while leaving healthy cells alone.”115 Such a claim is “more theoretical than real,” “such a ‘cure’ is illusory . . . .”116 Hypothetical claim 1 would not pass muster under Rochester either.

The fate of hypothetical claim 3 under current written description precedents is uncertain. Unlike hypothetical claim 2, hypothetical claim 3 is supported by some working examples. Should the scope of the claims be limited to the disclosed embodiments? If functional claiming is to be allowed, would this disclosure of working examples overcome the “vague functional description” rejection in Rochester?117 The Rochester court left little guidance in determining how many examples are necessary to render the functional description not vague.

Under the “common feature” test, hypothetical claim 1 also fails to satisfy the written description requirement because the defining correlation does not identify the common feature of the structures. First, a biological pathway often has multiple defining materials,118 and each defining material may define a different class of inhibitors. Second, a complex

116. Id.
117. G.D. Searle & Co., 358 F.3d at 928.
118. See supra Part II. NF-κβ is a family of five related proteins.
biological pathway usually comprises multiple sub-pathways.\textsuperscript{119} The correlation defined by each sub-pathway is dissimilar to the others, resulting in a different class of inhibitors. Third, because the defining material may be controlled by other cellular constituents,\textsuperscript{120} the inhibition of the defining material could be accomplished indirectly by regulating those cellular constituents. The correlation defined by indirect inhibition would differ significantly from the correlation defined by direct inhibition. Due to these variables, it is unlikely that the defining correlation would be of a “complementary structural relationship,”\textsuperscript{121} or “known to those of ordinary skill in the art.”\textsuperscript{122} Further, it is unlikely that there is any common feature among the large variety of inhibitors defined by the multiple correlations.

Hypothetical claim 2, by focusing on one genus of inhibitors, eliminates many variables seen in hypothetical claim 1. There still might be multiple defining materials. But claim 2 is unlikely to involve multiple sub-pathways, and possibly involves only one inhibition mechanism, either direct or indirect.\textsuperscript{123} The “common feature” test would yield a different result from that under the current precedents.

In most cases, the inhibition correlation does not identify a common feature of the structures. The selective COX-2 inhibition method litigated in \textit{Rochester}, for example, comprises a variety of inhibitors that are dissimilar to each other.\textsuperscript{124} Some selective COX-2 inhibitors are composed of three six-member rings (Etoricoxib) or two six-member rings (Nimesulide, Lumiracoxib), some others are composed of two six-member rings plus one five-member ring (Celecoxib, Rofecoxib, Valdecoxib, Deracoxib, Parecoxib).\textsuperscript{125} Without some working examples in each of these classes of inhibitors, an ordinary person skilled in the art has no way to identify a common feature among all selective inhibitors.

\textsuperscript{119} See supra Part II. (There are multiple sub-pathways wherein NF-κβ proteins can be activated via different activation mechanisms).
\textsuperscript{120} See supra Part II. (NF-κβ proteins themselves are tightly controlled by several regulatory proteins).
\textsuperscript{121} \textit{Enzo Biochem, Inc.}, 296 F.3d at 1328.
\textsuperscript{122} \textit{In re Wallach}, 378 F.3d 1330, 1335 (Fed. Cir. 2004).
\textsuperscript{123} One of the most common means to inhibit an enzymatic activity is to block a binding pocket or an “active site” of the enzyme—the region of an enzyme at which a chemical reaction occurs, and to render it incapable of functioning in the cell. For example, HIV transcriptase inhibitor and protease inhibitor function by binding to and inhibiting the active sites of HIV transcriptase and protease.
\textsuperscript{125} Id.
In some cases, however, the inhibition correlation may identify a common feature. For example, claim 203 of Ariad's patent claims a method of inhibiting NF-κβ protein by using a nucleic acid decoy molecule. Because NF-κβ protein binds to a specific site of our genome, a nucleic acid decoy inhibitor works by "directly targeting the DNA-binding activity of individual NF-κβ proteins..." The design of the nucleic acid decoy imitates the sequences in the genome to which NF-κβ protein binds, which contain a portion consensus among all binding sequences. As a result, the designed decoy molecules are similar to each other, all containing the consensus sequence. Thus, the inhibition correlation does identify a common feature of the decoy structures—the consensus sequence of the binding sites. In this case, even without any working example, a person ordinary skilled in the art could envision the structure of the genus based on the common feature identified. The written description requirement would be satisfied under the proposed test. This approach avoids the arbitrary outcome resulting from the no-compound, no-patent rule.

Under the "common feature" test, the fate of hypothetical claim 3 is more predictable and certain. In cases like the selective COX-2 inhibition method, working examples in each class of inhibitors are needed in order to identity a common feature. In cases like the NF-κβ decoy method, working examples, though not needed, would certainly help the patentee's argument in fulfilling her disclosure requirement. In other cases, the written description requirement could be met if a sufficient number of working examples would reveal a common feature. For example, there would be pathways where the defining correlation does not itself identify a common feature, in the absence of specific embodiments. With a number of working examples, it becomes clear to an ordinary artisan that the correlation necessarily requires all inhibitors to possess a common structure motif. Then, under the "common feature" test, the written description requirement should be satisfied.

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126. See supra Part II.
127. See Cao, Greten, Karin & Li, supra note 26, at 303.
E. Application of the “Common Feature” Test to Existing Patentable Inventions

Some may argue that, by adding a “common feature” requirement, this new test would negatively affect the patentability of inventions that currently would be patented. But the “common feature” test merely makes the existing written description doctrine more workable in a muddy area of the patent law. It would not affect the status of currently existing patents.

For example, “as long as an applicant has disclosed a ‘fully characterized antigen, . . . the applicant can then claim an antibody by its binding affinity to that described antigen.” The U.S. Patent and Trademark Office routinely allows the antibody patents by functional description of an antigen. Because an antigen may sometimes contain a large number of epitopes, the number of antibodies that can be made from an antigen may correspondingly be a large figure.

The “common feature” test would produce a consistent result with the current practice. Under this approach, the written description for even a large number of antibodies would be satisfied if an ordinary person skilled in the art could identify a “common feature,” common structural motif, or a substantial portion of the consensus structures among the genus. Because antibody art is “well developed and mature,” it is known that antibodies only exist in five limited classes, all with “well-defined structural characteristics . . . .” An ordinary artisan would readily recognize a common structural motif among the spectrum of antibodies specific to an antigen. Thus, the written description requirement is also met under the “common feature” test. The new test would not affect the validity of the existing patents, and is congruous with the previous court decisions in these cases.

V. Conclusion

This Note proposes a new test to determine whether, and under which circumstances, functional claiming may satisfy the written description requirement. By excluding unwarranted functional claiming patents, the proposed approach preserves the purpose of the written description requirement: to “ensure that the scope of the [patent] does not overreach the scope of the inventor’s contribution to the field of art as described in

130. Noelle v. Lederman, 355 F.3d 1343, 1349 (Fed. Cir. 2004). The disclosure still needs to satisfy other patentability requirements, such as enablement requirement, in order to be patentable. Id.
131. An epitope is the localized region on the surface of an antigen that is capable of eliciting an immune response and of combining with a specific antibody to counter that response.
the patent specification."' The "common feature" test would not deny functional claiming in all cases. Rather, the proposed test would only ensure that the scope of the claims conforms to the *quid pro quo* balancing of the patent system.\(^{134}\)

The proposed approach would provide a workable written description doctrine, and reconcile the confusing, conflicting precedents on this issue.\(^{135}\) Apart from enhancing the certainty in conforming to the patent law, this test would also avoid the drawing of an arbitrary "line between a patentable 'process' and an unpatentable 'principle.'"\(^{136}\) The approach would provide sufficient incentive for pioneering inventions, preserve room for the future, and thus promote progress and advance the purposes of Patent law.


\(^{134}\) See, e.g., Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1330 (Fed. Cir. 2002) ("The public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.").

\(^{135}\) See supra Part III (discussing the development of written description requirement in biotechnology area).