

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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

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

Ex parte ANDREW J. MURPHY,
Y. GOPI SHANKER, and
GEORGE D. YANCOPOULOS

Appeal No. 2007-0534
Application No. 10/463,016

ON BRIEF

Before MILLS, GRIMES, and LEBOVITZ, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1, 2, 5, 7-11, 15, 16, and 27-31.

Claim 1 is representative of the claims and reads as follows.

1. A method for identifying a compound capable of modulating activity of an active domain, comprising:

(a) generating a first fusion protein, wherein the first fusion protein comprises an anchor component and a variable component;

(b) generating a second fusion protein, wherein the second fusion protein comprises a docking domain and an active domain, wherein the anchor component of the first fusion protein and the docking domain of the second fusion protein are binding partners;

(c) contacting the first and second fusion proteins under conditions in which the anchor component and the docking domain bind wherein the binding affinity of the binding partners is at least 1 μ M and the binding of the docking domain and the anchor component brings the variable component and active domain into spatial proximity to allow modulation of the active domain; and

(d) determining an activity of the active domain in the presence relative to the absence of the first fusion protein, wherein an increase or decrease in the activity of the active domain in the presence relative to the absence of the first fusion protein indicates that the variable component of the first fusion protein is a modulator of the active domain.

The prior art cited by the examiner is:

Hamilton et al. (Hamilton)	6,780,599	Aug. 24, 2004
Silver et al. (Silver)	WO 01/55452	Aug. 2, 2001

Grounds of Rejection

Claims 1, 2, 5, 7-11, 15, 16, and 27-31 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement.

Claims 1, 2, 5, 7-11, 15, 16, and 27-31 stand rejected under 35 U.S.C. § 103(a) over Silver.

Claims 1, 2, 5, 7-11, 15, 16, and 27-31 stand rejected under 35 U.S.C. § 103(a) over Hamilton.

We reverse the written description rejection and affirm the obviousness rejections.

DISCUSSION

35 U.S.C. § 112, first paragraph

Claims 1, 2, 5, 7-11, 15, 16, and 27-31 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement.

The examiner contends that the specification fails to provide an adequate written description for a method of identifying a compound comprising steps that employ the numerous recited generic components. The examiner argues that the claims and the specification do not define structure for the "unnamed" first and second fusion proteins.

Answer, page 3. The examiner further argues that a "laundry list disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species." Answer, pages 3-4.

The appellants contend that the "function of the binding molecules is simply to bind to one another" and that there are "numerous pairs of binding molecules known in the art, of which several representative examples are provided in the specification." Brief, page 11. The Appellants conclude that "given the nature of the invention, the state of the art and the description provided by the specification of both a genus and numerous examples . . . the Examiner has not met.... [the] burden to show lack of description of an original claim." Brief, pages 11-12.

It is well settled that written description is a question of fact, judged from the

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perspective of one of ordinary skill in the art as of the relevant filing date. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111 (Fed. Cir. 1991). Falkner v. Inglis, 448 F.3d 1357, 1363, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). In Capon v. Eshhar, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005) the Federal Circuit stated, “[t]he ‘written description’ requirement 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. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. " Capon, 418 F.3d at 1357, 76 UPQ2d at 1084.

"Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science." Id.

Precedent illustrates that the determination of what 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. See, e.g., In re Wallach, 378 F.3d 1330, 1333-34 [71 USPQ2d 1939] (Fed. Cir. 2004) (an amino acid sequence supports “the entire genus of DNA sequences” that can encode the amino acid

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sequence because “the state of the art has developed” such that it is a routine matter to convert one to the other); University of Rochester, 358 F.3d at 925 (considering whether the patent disclosed the compounds necessary to practice the claimed method, given the state of technology); Singh v. Brake, 317 F.3d 1334, 1343, 65 USPQ2d 1641 (Fed. Cir. 2002) (affirming adequacy of disclosure by distinguishing precedent in which the selection of a particular species within the claimed genus had involved “highly unpredictable results”).

Id. at 1359, 76 USPQ2d at 1085. Furthermore, an actual reduction to practice is not required for written description. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 926, 69 USPQ2d 1886, 1094 (Fed. Cir. 2004).

In the present case, we agree with appellants that given such considerations as the state of the prior art, that the examiner has failed to set forth a prima facie case of lack of adequate written description for the pending claims. While the examiner is correct in that the claim scope, i.e., the fusion proteins, is broad, in our view the examiner has failed to give adequate weight to the state of the relevant prior art.

The specification, page 2, describes that the first fusion protein includes an anchor component and a variable component and the second fusion protein includes a docking member (which docks with the anchor component of the first fusion protein) and a target domain (which is modulated by, and binds to the variable component of the first fusion protein.) According to the specification, “the method of the invention may be used to identify an activator or inhibitor of the target active domain.” Id.

The specification provides broad and general examples of the types of molecules which may be used as the anchor component and variable component. For example, it

is stated that "[t]he anchor component may be a protein, peptide, or a molecule capable of binding to the docking domain. The anchor component may be ... any ligand, agonist, antagonist, antibody or peptide that binds the docking domain." Specification, page 3. It is also stated that the variable component "may be a small molecule; a peptide agonist, antagonist, inhibitor, or activator; or any portion of a protein to be tested for affecting activity of the active target and/or inducing a physiological change." Id.

Anchor and docking binding partners may include "(i) a small molecule and a single-chain or multi-chain antibody immunospecific for the small molecule, (ii) fluorescein and an anti-fluorescein single-chain or multi-chain antibody; (iii) dinitrophenyl (DNP), or a DNP derivative and an anti-DNP single chain or multi-chain antibody; (iv) novobiocin or a novobiocin derivative and a novobiocin binding domain of gyrase B; (v) biotin, or a biotin derivative and avidin, streptavidin or neutravidin; (vi) FK506, or an FK506 derivative, and FKBP." Specification, page 7. The specification also provides additional examples at ¶¶ 7 and 40. Moreover, the examiner has not argued that those skilled in the art would not know or be able to determine which binding pairs have binding affinity of at least 1 μ M. In sum, the specification describes generally the type of docking and anchor partners which can be used, and then provides specific examples to guide the choice. The specification further provides specific examples of a fusion protein having a docking domain which is a human Fc receptor and an active domain of MCR4 (melanocortin receptor 4). This fusion peptide binds to a fusion protein comprising an Fc anchor domain and an HFRW, a low affinity agonist for MCR4.

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Specification, pages 9-10 and 12.

Similarly, the prior art cited in the present case in both instances uses broad terminology to describe protein-protein interactions. See, e.g., Hamilton, claim 1; Silver claim 1.

In view of the existing knowledge in the particular field, the extent and content of the prior art cited in this case, the maturity of the science or technology of protein-protein interactions, and the predictability of the aspect at issue, in our view the claimed invention is adequately described in the specification when read in view of the eyes of one of ordinary skill in the art.

The rejection of the claims for lack of written description is reversed.

35 U.S.C. § 103(a)

Claims 1, 2, 5, 7-11, 15, 16, and 27-31 stand rejected under 35 U.S.C. § 103(a) over Silver.

According to the examiner, Silver's method involves using DNA encoding a protein of interest tagged with one member of a fluorescent protein pair and DNA sequences encoding a plurality of proteins to be screened, wherein the screening proteins are tagged to the other member of the fluorescent pair. Answer, page 6. When the proteins are located physically within an appropriate distance of one another fluorescence resonance energy transfer (FRET) occurs between the fluorescent protein pair. Abstract, Answer, page 6.

The examiner acknowledges that Silver does not expressly disclose the spatial proximity between the target domain and the variable component, as claimed. Id. However, the examiner concludes "such [a] determination would have been obvious in view of the teachings of Silver that the proteins are located physically within an appropriate distance of one another such that FRET occurs" and that one "would be motivated to determine such spatial proximity since. . . Silver taught this would indicate [a] definite interaction (modulation, as claimed) of the proteins." Id. at 6-7.

In response, Appellants contend that the method of Silver does not function in a manner equivalent to the claimed method. Brief, page 14. Appellants argue that in the claimed method, the known binding partners force a test protein (variable component) into proximity with the protein of interest (active domain) to determine whether the test protein modulates the activity of the protein of interest. They assert the modulation event is detected by means independent of the binding partners.

In contrast, Appellants argue that in the Silver method, "the binding of a test protein with a protein [of] interest forces a fluorescent protein pair into proximity generating a signal indicating that the interaction has occurred." Thus, Appellants argue Silver is the reverse of the claimed method. Brief, pages 14-15.

The examiner, however, responds and argues that the claims do not recite a distinguishing feature over the methods of Silver and that each of the methods employ similar method steps. Answer, page 17.

We agree with the examiner that the present claims do not distinguish from prior art methods of detecting protein-protein interactions. We are not persuaded by Appellants' arguments.

To begin, considering claim 1, Appellants define what is meant by "modulation" of the target or active domain in the specification on pages 7-8. "Modulation" is said to include "signal transduction, signal transduction inhibition, second messenger production, ... channel dilation, ion gate open/closure, a cellular response, a chemical reaction, inhibition of a chemical reaction, an enzyme interaction, inhibition of an enzyme reaction or any other measurable or detectable response." Id. Therefore, "modulation" as broadly interpreted, and consistent with the specification, would encompass any type of protein/protein interaction, including energy transfer between two proteins as described in Silver. In addition, the specification, page 8, discloses that FRET can be used to determine modulation.

In addition, the claimed method steps and components of the prior art are similar. Appellants argue that the method of Silver is the reverse of the claimed method. We disagree. The claims essentially recite a method including steps of (1) preparing two fusion proteins and (2) contacting them together such that binding occurs. Then an activity of the active domain is determined.

While Appellants argue Silver discloses a reverse order of steps, the claims only require that the first and second fusion proteins are contacted and that binding occurs with no specific order of binding recited. Further, since "modulation" is defined so

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broadly in the specification as to encompass just about any protein/protein interaction, the claim requirement of modulation of the active domain by the variable component is met readily by any protein/protein binding or antigen antibody interaction.

In Silver, when the putative target interacts with the protein of interest FRET (fluorescence resonance energy transfer) occurs between a complementary pair of fluorescent tags attached to the two fusion proteins. Thus, two fusion protein partners are prepared and contacted with one another such that binding occurs and a measurable modulation (FRET) is exhibited.

Appellants have not shown and do not allege that either of the protein/protein interactions in Silver (or Hamilton) do not result in a binding affinity of the binding partners of at least 1 μ M.

In view the above, the rejection of the claims for obviousness over Silver is affirmed.

35 U.S.C. § 103(a)

Claims 1, 2, 5, 7-11, 15, 16, and 27-31 stand rejected under 35 U.S.C. § 103(a) over Hamilton.

Hamilton describes a method of identifying a polypeptide that interacts with a known polypeptide comprising a known peptide sequence linked to a first green fluorescent protein (GFP) fragment, producing a second fusion protein comprising a test

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polypeptide linked to a second GFP fragment, allowing the first fusion protein to associate with the second fusion protein to form a complex mediated by non-covalent association of the known polypeptide and test polypeptide and detecting whether association between the first and second GFP fragments occurs. Answer, page 7; Hamilton, col. 6, ll 45-65.

The examiner argues it would have been obvious that the protein-protein interaction in Hamilton is the same as the claimed modulation effect because the protein-protein interactions result in a modifying effect of one protein by the other protein. Answer, page 8.

Appellants again argue that in Hamilton (and Silver) it is critically important that the interaction of the test and known polypeptide occurs first and subsequently triggers signal generation from the detection system, in the case of Hamilton, the two GFP fragments. Appellants assert that if the reverse occurred, and the GFP fragments associated themselves, they would generate a signal whether or not the test peptide and known peptide had an affinity for one another. Brief, page 17. Appellants argue that in the claimed method the anchor component and docking domain bring the variable component and active domain into spatial proximity to allow modulation of the active domain.

As discussed above, the claims do not require a specific order of fusion protein partner binding, as they merely require contact and binding of the fusion proteins. In view of the above, appellants have failed to indicate a difference between the claimed

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method and the prior art methods of detecting protein/protein interactions.

The rejection of the claims for obviousness over Hamilton is affirmed.

CONCLUSION

The rejection of claims 1, 2, 5, 7-11, 15, 16, and 27-31 under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement is reversed.

The rejection of claims 1, 2, 5, 7-11, 15, 16, and 27-31 under 35 U.S.C. § 103(a) over Silver is affirmed.

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The rejection of claims 1, 2, 5, 7-11, 15, 16, and 27-31 under 35 U.S.C. § 103(a)
over Hamilton is affirmed.

AFFIRMED

Demetra J. Mills
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

Richard M. Lebovitz
Administrative Patent Judge

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REGENERON PHARMACEUTICALS, INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN NY 10591