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POTTER ANDERSON & CORROON LLP
ATTN: JANET E. REED, PH.D.
P.O. BOX 951
WILMINGTON, DE 19899-0951

EXAMINER	
GAMBEL, PHILLIP	

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JOHN D. LAMBRIS and MACIEJ M. MARKIEWSKI [1]

Appeal 2019-002574
Application 12/918,101
Technology Center 1600

Before ERIC B. GRIMES, RICHARD M. LEBOVITZ, and RACHEL H. TOWNSEND, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of treating an individual having a tumor, which have been rejected as lacking adequate written description and as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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[1] Appellant identifies the Real Party in Interest as the Trustees of the University of Pennsylvania. Appeal Br. 3. We use the word Appellant to refer to "applicant" as defined in 37 C.F.R. § 1.42(a).

STATEMENT OF THE CASE

The Specification states that the complement system is a "potential player in the response to cancer." Spec. 2. "Of the[] complement components, the C3 protein is considered to be central to the complement cascade. Enzymatic cleavage of C3 leads to the production of . . . [C3a] and C3b," and "C3b . . . is [] a main component of the C5 convertase, an enzyme complex that cleaves C5 to produce the anaphylatoxin C5a and C5b." *Id*.

The Specification discloses that "the complement system and particularly C5a contribute to mechanisms that promote the growth of malignant tumors." *Id*. at 10.

> One aspect of the invention features a method for treating an individual having a malignant tumor, the method comprising administering a therapeutically effective amount of a complement inhibitor to the individual, wherein the complement inhibitor reduces or prevents C5a receptor signaling in the tumor, thereby preventing, reducing or delaying growth of the tumor.

Id. at 3. "In [one] embodiment, formation of C5a is reduced or prevented through the use of a C3 inhibitor. Preferably, the C3 inhibitor is compstatin or a compstatin analog, derivative," etc. *Id*. at 12. Exemplary compstatin analogs have the sequences shown in SEQ ID NO: 2 and SEQ ID NO: 3. *Id*.

Claims 1, 9–11, 24, 29–32, and 34 are on appeal. Claim 1 is illustrative and reads as follows:

> 1. A method for treating an individual having a tumor, the method comprising the steps of:
>
> (1) providing an individual having a tumor;
>
> (2) administering to the individual a therapeutically effective amount of a complement inhibitor comprising a pharmaceutically acceptable carrier and at least one polypeptide

having an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:3;

(3) measuring the size of the tumor in the individual;

wherein the administering of the complement inhibitor results in a reduction in tumor size, or a delay or prevention of increase in tumor size, thereby treating the individual having the tumor.

Claim 29 is also independent and is directed to a "method of reducing or delaying growth or development of a tumor disposed within an individual," comprising the same active steps as claim 1.

The claims stand rejected as follows:

Claims 1, 9–11, 24, 29–32, and 34 under 35 U.S.C. § 112, first paragraph, as lacking adequate written description in the Specification (Final Action[2] 3) and

Claims 1, 9–11, 24, 29–32, and 34 under 35 U.S.C. § 103(a) as obvious based on Chiang,[3] Lambris '899,[4] Lambris '328,[5] Mass,[6] Ignatovich,[7] and Chelsky[8] (Final Action 7).

[2] Office Action mailed March 8, 2018.
[3] Chiang et al. (US 2005/0222027 A1, published Oct. 6, 2005).
[4] Lambris et al. (WO 99/13899, published Mar. 25, 1999).
[5] Lambris (WO 2004/026328 A1, published Apr. 1, 2004).
[6] Mass (US 7,993,834 B2, issued Aug. 9, 2011).
[7] Ignatovich et al. (US 2005/0271663 A1, published Dec. 8, 2005).
[8] Chelsky et al. (US 2007/0269434 A1, published Nov. 22, 2007).

OPINION

Written Description

The Examiner has rejected all of the claims on appeal on the basis that the Specification does not adequately describe the claimed method. The Examiner finds that

> the specification as filed does not appear to provide sufficient written description of applying the claimed series of steps, including measuring the size of the tumor in the individual are not readily apparent with respect to the claimed methods of treating an [sic] and methods of reducing or delaying growth or development of a tumor disposed with[in] an individual in treating humans as claimed as currently claimed [sic] (e.g., see Summary of the Invention, Description of the invention including pages 10–11 of the specification noted in applicant's remarks previously presented).

Final Action 6. *See also id*. ("[A]pplicant fails to provide written description of the current claims in the context of methods of treating a human individual having a tumor and combining steps (1) providing, (2) administering and (3) measuring tumor size in treating humans."); Ans. 8 ("[T]he specification as filed does not appear to provide sufficient written description of applying the claimed series of steps, *including measuring the size of the tumor in the individual*," emphasis in original).

As we understand it, the Examiner's position is that the Specification does not adequately describe a method of treating a human individual in the manner claimed, including a step of measuring the size of the tumor.

Appellant argues that, "when the teachings of the specification are fully considered, the skilled artisan would have no doubt that Appellants had possession of the measuring step at the time of filing." Appeal Br. 16.

Appellant argues that the Specification "explicitly stated that an aspect of the invention is to treat an individual (which includes an animal or a human) having a tumor with complement inhibitor, wherein the complement inhibitor prevents, reduces, or delays growth of the tumor (see specification at page 3, second full paragraph)." *Id*. at 17.

Appellant also argues that the Specification's Example 3 describes measuring tumor size in mice and "the skilled artisan would immediately understand that any appropriate tumor measurement technique is suitable for use with the claimed method." *Id*. at 18. Appellant reasons that the

> disclosure of measuring a mouse tumor with a caliper reasonably conveys to the skilled artisan that Appellants had possession of a method of treating a tumor that includes any appropriate technique for tumor measuring because the particular selection of the tumor measuring technique is not important and will not materially change the effect the compstatin analog would have on treatment.

Id. at 19.

We agree with Appellant that a person of ordinary skill in the art would recognize the Specification as showing that Appellant was in possession of the claimed method at the time the application was filed. To satisfy 35 U.S.C. § 112, first paragraph, the "description must 'clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'" *Ariad Pharms., Inc. v. Eli Lilly & Co*., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (alteration in original).

"In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing

date." *Id*. "Requiring a written description of the invention limits patent protection to those who actually perform the difficult work of 'invention'—that is, conceive of the complete and final invention with all its claimed limitations—and disclose the fruits of that effort to the public." *Id*. at 1353.

Here, the Specification states that

> [o]ne aspect of the invention features a method for treating an individual having a malignant tumor, the method comprising administering a therapeutically effective amount of a complement inhibitor to the individual, wherein the complement inhibitor reduces or prevents C5a receptor signaling in the tumor, thereby preventing, reducing or delaying growth of the tumor. The methods of the invention may be applied to any individual, including humans and animals. In one embodiment, the individual is human.

Spec. 3. The Specification thus describes a method of treating a human individual to prevent, reduce, or delay growth of a tumor. The Specification also describes polypeptides comprising the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 3 as C3 inhibitors for use in the disclosed method. *Id*. at 12.

The Specification describes an experiment in which the size of tumors was measured during the course of treatment with a C5a receptor antagonist. *Id*. at 17. The Specification also describes an experiment in which tumor volumes were measured after tumor cell inoculation of C3-deficient mice. *Id*. at 24. The Specification thus describes methods in which complement was inhibited in an individual (either via administration of a C5a receptor antagonist or via innate deficiency in C3) and the size of tumors was measured.

It is true that the working examples were carried out using mice, not humans, but a specification need not exemplify every aspect of a claimed invention in order to show possession to those skilled in the art. *See Ariad*, 598 F.3d at 1352 ("[T]he written description requirement does not demand either examples or an actual reduction to practice."). Here, we conclude that those skilled in the art would recognize from the Specification's description that Appellant was in possession of the claimed method as of the effective filing date of the claimed invention.

We therefore reverse the rejection of claims 1, 9–11, 24, 29–32, and 34 under 35 U.S.C. § 112, first paragraph, based on lack of adequate written description.

Obviousness

The Examiner has rejected all of the claims on appeal as obvious based on Chiang, Lambris '899, Lambris '328, Mass, Ignatovich, and Chelsky. The Examiner finds that

> Chiang et al. teach compositions and methods for treating pain, including cancer-related pain, where cancer-related pain results from tumor growth compression of adjacent tissues as well as the injury caused by cancer treatments such as chemotherapy . . . by modulating the expression or activity of one or more components of the complement pathway including compstatin . . . via various modes and dosages of administration.

Final Action 15. The Examiner finds that Chiang "differs from the claimed invention by not exemplifying the treatment of a patient with malignant tumor with compstatin and by not describing all of the compstatin analogs encompassed by the claimed invention." *Id*.

The Examiner finds that Lambris '899 discloses "inhibiting complement activation and complement-mediated tissue injury in diseases involving complement-mediated damage with complement-inhibiting compounds of compstatin and its analogs specific for C3 activation." *Id*. The Examiner finds that Lambris '328 "teaches that compstatin inhibits the cleavage of C3 to C3a and C3b by C3 convertase, as well as compstatin analogs." *Id*.

The Examiner finds that "Mass teaches that therapeutically effective amounts for cancer therapy and efficacy can be measured by assessing the time for disease progression, survival, tumor size and response rates." *Id*. at 14. The Examiner finds that Ignatovich teaches that "treatment is considered effective if one or more symptoms is reduced . . . including . . . monitoring physical manifestations (e.g. inflammation, tumor size)." *Id*. at 11. The Examiner finds that Chelsky teaches that a "therapeutically effect[ive] amount of agent can be determined by monitoring an amelioration or improvement in disease symptoms to delay onset of [sic] slow progression of the disease, for example without limitation, a reduction in tumor size." *Id*.

The Examiner concludes that it would have been obvious

> to provide compstatin and compstatin analogs as taught by the prior art for inhibiting complement formation and activation in the context of treating individuals having a malignant tumor, where the individuals experiencing the pain associated with the malignant tumor itself and/or the treatment of said malignant tumor targeting / inhibiting complement activation via C3, as taught by the prior art at the time the invention was made, given the teachings of the applicability of compstatin and compstatin analogs to inhibit such cancer-related pain.

Id. at 15. The Examiner reasons that "the patients having cancer-related pain . . . would be the same patients having malignant tumors being administered the same active agent (compstatin and compstatin analogs) . . . in both the instant claims and the prior art reference." *Id*. at 16.

Appellant argues that "Chiang teaches compositions and methods for treating pain by 'modulating the expression of one or more components of the complement pathway.' . . . While the pain thus treated can be caused by cancer or by cancer treatments, Chiang nowhere suggests the use of complement inhibitors to treat the cancer instead of the pain." Appeal Br. 27. "[W]ithout a connection between complement inhibition and tumor growth itself, there would be no reason to believe that the complement inhibitors (e.g., compstatin analogs) would actually reduce the size of the tumor and, therefore, no obvious reason to measure the tumor size." *Id*. That is, "under Chiang's teaching, when an individual is being evaluated for the effectiveness of a treatment, that evaluation is solely based on the level of pain. Therefore, Chiang provides no suggestion that would motivate the skilled artisan to add a step relating to measuring tumor size." *Id*. at 29.

Appellant argues that the Lambris references "do not remediate the deficiencies of Chiang because these references make no mention of measuring indicators of tumor growth and development and fail to recognize the link between complement inhibition and tumor growth and development." *Id*. Appellant also argues that "Mass fails to recognize the link between complement inhibition and tumor growth and development," and "neither Ignatovich nor Chelsky has anything to do with complement activation in relation to cancer." *Id*. at 30. Appellant concludes that

> there is nothing in the secondary references that recognizes, or would enable the skilled artisan to recognize, the connection between complement inhibition with compstatin analogs and the reduction or delay in tumor growth and/or development. As such, there is nothing in any of the references cited by the examiner, either alone or in combination, that would suggest identifying an individual having a tumor, administering a compstatin analog, and measuring tumor size in a method of treating the individual having the tumor.

Id. at 30–31.

We agree with Appellant. Chiang states that its "invention is in the field of therapeutic agents for pain treatment." Chiang ¶ 2. Chiang "provides compositions and methods for treating pain that act through the modulation of a component of the complement pathway." *Id*. The complement component can be a complement inhibitor, including compstatin. *Id*. ¶¶ 102, 122. And the pain treated using Chiang's method can be cancer pain. *Id*. ¶¶ 127, 128. But the Examiner has not pointed to any teaching in Chiang indicating that its method is effective in treating cancer itself, as opposed to alleviating pain resulting from cancer, and thus the Examiner has not identified a reason in Chiang that would lead a skilled artisan to measure tumor size.

Lambris '899 discloses "peptides and peptidomimetics capable of binding the C3 protein and inhibiting complement activation." Lambris '899 1:10–12. Lambris '899 states that "[c]omplement-mediated tissue injury has been reported in a wide variety of diseases, including autoimmune diseases . . . [,] adult respiratory distress syndrome, stroke, heart attack," etc. *Id*. at 1:22–29.

Lambris ’328 also discloses “peptides and peptidomimetics capable of binding the C3 protein and inhibiting complement activation.” Lambris ’328 ¶ 3. Lambris ’328 states that “[c]omplement is implicated in several disease states, including various autoimmune diseases, and has been found to contribute to other clinical conditions such as adult respiratory syndrome, heart attack,” etc. *Id*. ¶ 5.

The complement-associated diseases and conditions listed in the Lambris references do not include cancer. The Examiner has not identified any disclosure in either of the Lambris references of treating cancer using a complement inhibitor. The Examiner cites Mass, Ignatovich, and Chelsky only for the disclosure that the efficacy of cancer therapy can be determined by, for example, measuring the change in tumor size. *See* Mass 8:17–26; Ignatovich ¶ 658; Chelsky ¶ 422. Again, however, the Examiner has not identified any disclosure in any of these references that would suggest using a complement inhibitor to treat cancer.

In short, the Examiner has not identified any teaching in the cited references that would have led a skilled artisan to expect that administering a complement inhibitor would be effective in treating cancer. Therefore, the Examiner has not shown that a person of ordinary skill in the art would have had a reason to combine (a) a step of administering one of the complement inhibitors encompassed by the claims to an individual having a tumor, and (b) a step of measuring the size of the tumor in the individual.

Because the rejection under 35 U.S.C. § 103(a) is not supported by a preponderance of the evidence, we reverse it.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Basis	Affirmed	Reversed
1, 9–11, 24, 29–32, 34	112, ¶ 1	Written description		1, 9–11, 24, 29–32, 34
1, 9–11, 24, 29–32, 34	103(a)	Chiang, Lambris '899, Lambris '328, Mass, Ignatovich, Chelsky		1, 9–11, 24, 29–32, 34
Overall Outcome				1, 9–11, 24, 29–32, 34

REVERSED