

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

THE JOHNS HOPKINS UNIVERSITY,
Petitioner,

v.

BIOCON LIMITED,
Patent Owner.

Case IPR2016-00175
Patent 8,815,247 B2

Before LORA M. GREEN, DEBORAH KATZ,
and GRACE KARAFFA OBERMANN, *Administrative Patent Judges*.

OBERMANN, *Administrative Patent Judge*.

DECISION
Denying *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Petitioner filed a Petition requesting an *inter partes* review of claim 1 of U.S. Patent No. 8,815,247 B2 (Ex. 1001, “the ’247 patent”). Paper 2 (“Pet.”). Patent Owner filed a Preliminary Response. Paper 7 (“Prelim. Resp.”). Applying the standard set forth in 35 U.S.C. § 314, which requires a showing of a reasonable likelihood that Petitioner would prevail at trial with respect to at least one challenged claim, we deny the Petition and decline to institute a trial.

A. *Related Proceedings*

According to Petitioner, “there are no related matters.” Pet. 1.¹

B. *The ’247 Patent (Ex. 1001)*

The ’247 patent is titled “Targeting/Immunomodulatory Fusion Proteins.” Ex. 1001, Title. The ’247 patent concludes with a single claim directed to a chimeric fusion protein comprising at least one targeting moiety and at least one immunomodulating moiety linked by an amino acid spacer. *Id.* at 69:39–41 (claim 1). The targeting moiety targets a cancer cell and the immunomodulating moiety counteracts immune tolerance. *Id.* The amino acid spacer is selected from two specific amino acid sequences set forth in the specification and identified in the claim as SEQ ID NO: 3 and SEQ ID NO: 11. *Id.* at 69:42–43; 70:38–39 (claim 1); *see id.* at col. 29 (identifying the specific amino acid sequence that is SEQ ID NO: 3); col. 39 (identifying the specific amino acid sequence that is SEQ ID NO: 11).

¹ The body of the Petition includes no page numbers. We cite to page numbers beginning with “1” on the page after the Table of Exhibits.

Claim 1 specifies that “one targeting moiety is an antibody selected from Anti-EGFR1 (heavy chain SEQ ID NO: 5 and light chain SEQ ID NO: 6).” *Id.* at 70:40–42 (claim 1). The specific amino acid sequences of those specified heavy and light chains are set forth in the specification. *Id.* at col 31–32 (amino acid sequence of SEQ ID NO: 5); col. 33 (amino acid sequence of SEQ ID NO: 6). Claim 1 also specifies that “the immunomodulating moiety is SEQ ID NO: 4,” another amino acid sequence set forth in the specification. *Id.* at 69:65; 70:38 (claim 1); col. 29 (identifying the specific amino acid sequence that is SEQ ID NO: 4).

The central dispute in this case surrounds a further limitation in claim 1, which requires that the immunomodulating moiety (identified as SEQ ID NO: 4) “is attached via the amino acid spacer” (selected from SEQ ID NO: 3 and SEQ ID NO: 11) “*to the C-terminus of SEQ ID NO 5 or SEQ ID NO: 6.*” *Id.* at 70:42–44 (claim 1) (emphasis added). Critical to our analysis, the ’247 patent specification discloses that the amino acid residue at the C-terminus of SEQ ID NO: 5 is glycine (“Gly” or “G”), while the C-terminus of the anti-EGFR1 heavy chain in the prior art has an extra amino acid, lysine (“Lys” or “K”), to which the spacer is fused. *Id.* at col. 31.

C. Illustrative Claim

Claim 1, the only challenged claim, is reproduced below with the claim language at issue highlighted:

1. A chimeric fusion protein comprising at least one targeting moiety to target a cancer cell and at least one immunomodulating moiety that counteracts immune tolerance, wherein the targeting moiety and the immunomodulating moiety are linked by an amino acid spacer of sufficient length of amino acid residues so that both moieties can successfully bind to their individual target, wherein the immunomodulating moiety is SEQ ID NO: 4, wherein the amino acid spacer is selected from SEQ ID NO: 3 or SEQ ID NO: 11; and *wherein one targeting moiety is an antibody selected from Anti-EGFR1 (heavy chain SEQ ID NO: 5 and light chain SEQ ID NO: 6); wherein SEQ ID NO: 4 is attached via the amino acid spacer to the C-terminus of SEQ ID NO 5 or SEQ ID NO: 6.*

D. The Asserted Prior Art Reference

Petitioner challenges the patentability of claim 1 based on the disclosure of Bedi, *et al.*, U.S. Patent No. 8,993,524 B2, which issued on March 31, 2015 (Ex. 1003, “Bedi”).

E. The Asserted Grounds of Unpatentability

The Petition asserts the following grounds of unpatentability:

Claim	Basis	References
1	§ 102(b)	Bedi
1	§ 103(a)	Bedi

II. ANALYSIS

As an initial matter, Patent Owner contends that Bedi does not qualify as prior art under 35 U.S.C. § 102(b) or § 102(e). Prelim. Resp. 10–14. Petitioner contends that Bedi “is § 102(b) prior art to the ’247 patent.”

Pet. 9. Even if we accept Petitioner's contention that Bedi qualifies as prior art, for reasons that follow, we deny the Petition for failure to show sufficiently that the subject matter of claim 1 is anticipated by, or obvious over, the disclosure of Bedi.

A. Anticipation by Bedi

To establish anticipation, each and every element in a claim, "arranged or combined in the same way as recited in the claim," must be found in a single prior art reference. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008). Claim 1 requires a chimeric fusion protein comprising an "immunomodulating moiety" that "is SEQ ID NO: 4." Ex. 1001, 69:45, 70:38. Claim 1 specifies that "SEQ ID NO: 4 is attached via the amino acid spacer to the C-terminus of SEQ ID NO 5 or SEQ ID NO: 6." *Id.* at 70:42–44. In claim 1, "the amino acid spacer is selected from SEQ ID NO: 3 or SEQ ID NO: 11." *Id.* at 70:38–39.

Petitioner argues that Bedi's Figure 3 depicts a fusion protein that anticipates claim 1. Pet. 19. Figure 3 illustrates the "[a]nti-EGFR1 heavy chain + TGF β -R11 ECD fusion amino acid sequence." Figure 3 also depicts the "[a]nti-EGFR1 light chain amino acid sequence." The parties agree that Figure 3 depicts a "heavy chain" fusion protein that includes an immunomodulating moiety, corresponding to SEQ ID NO: 4, attached to an amino acid spacer, corresponding to SEQ ID NO: 3. *Compare* Pet. 9–19 with Prelim. Resp. 15–19. The Petition lacks a supported analysis, however, sufficient to show how Figure 3 anticipates a fusion protein wherein "SEQ ID NO: 4 is attached via the amino acid spacer to the C-terminus of SEQ ID NO 5 or SEQ ID NO 6." Ex. 1001, 70:43–44 (emphasis added); Pet. 18–19.

Petitioner contends that Figure 3 depicts “[t]he identical fusion construct” of claim 1, but does not explain adequately how or why an ordinary artisan, reading Bedi, would have understood that the spacer attaches to a heavy chain sequence at the amino acid specified in claim 1. Pet. 19. Furthermore, Figure 3 depicts a fusion protein wherein the immunomodulating moiety is attached via the spacer to the C-terminus of the illustrated heavy chain, not the light chain, sequence. Ex. 1003, Fig. 3.

The Petition refers to the amino acid spacer as “a “linker” or “linker sequence.” Pet. 4, 12. The Petition acknowledges that the “heavy chain sequence in Bedi” differs from claim 1 “in the addition of a C-terminal lysine (K) prior to the linker sequence.” *Id.* at 17. Both parties agree that Bedi’s amino acid spacer sequence is attached to a carboxyl group on a lysine residue at the terminus of the heavy chain; whereas in claim 1, the amino acid spacer sequence is attached to a carboxyl group on a glycine residue, when the heavy chain (SEQ ID NO. 5) is selected for the fusion protein. *Id.* at 17; Prelim. Resp. 16–17.

The Petition fails to explain how, in spite of that difference, the “heavy chain” fusion protein depicted in Bedi’s Figure 3 anticipates claim 1. Pet. 17, 19. On that point, the Petition states that Bedi’s Figure 3 depicts a “construct comprising” the requisite components of the invention, but does not explain why Bedi’s disclosure of a lysine residue, on the C-terminus of the heavy chain sequence, teaches the specific fusion protein recited in claim 1. *Id.* at 19; *see id.* at 17 (admitting that Bedi’s heavy chain sequence includes a lysine residue, and that the addition of that residue distinguishes Bedi’s fusion protein from the fusion protein of claim 1); Prelim. Resp. 16–19. We agree with Patent Owner that the Petition does not address

adequately the differences between the “heavy chain” fusion protein depicted in Bedi’s Figure 3 and the claimed invention. *Id.* at 18.

Nor does the Petition address adequately how Bedi’s Figure 3 depicts a fusion protein wherein the immunomodulating moiety “is attached via the amino acid spacer to the C-terminus of” the light chain sequence, specified in claim 1 as SEQ ID NO: 6. Ex. 1001, 70:43–44. We agree with Petitioner that Bedi depicts the same light chain sequence (identified as SEQ ID NO: 71 in Figure 3) as SEQ ID NO: 6 in claim 1. Ex. 1003, Fig. 3. The Petition, however, lacks supported analysis explaining how or why a person of ordinary skill in the art would understand Bedi to disclose in Figure 3 a fusion protein in which the immunomodulating moiety is attached via the amino acid spacer to the “light chain” sequence identified as SEQ ID NO: 71 in Bedi. Pet. 19 (arguing, without any evidentiary support, that Figure 3 depicts “attaching to anti-EGFR1 heavy or light chain (SEQ ID NO: 2 or 71, respectively)”). That attachment is not depicted in Figure 3, and the Petition directs us to no disclosure supporting the view that an ordinary artisan would have understood Figure 3 to illustrate an alternative fusion protein in which the immunomodulating moiety is attached via the amino acid spacer sequence to the C-terminus of the light chain sequence.

“[D]ifferences between the prior art reference and a claimed invention, however slight, invoke the question of obviousness, not anticipation.” *Net MoneyIN, Inc.*, 545 F.3d at 1371. On this record, we determine that the Petition does not direct us to information sufficient to show that Bedi anticipates claim 1.

B. Obviousness over Bedi

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The Petition asserts that the subject matter of claim 1 would have been obvious over the disclosure of Bedi and, specifically, the fusion protein depicted in Figure 3. Pet. 20–29.

The obviousness challenge rests on the disclosure of Bedi, in view of two background references (Ex. 1007; Ex. 1008). *Id.* at 20. The Petition is not supported by testimonial evidence, for example, a declaration directed to the understanding of a person of ordinary skill in the art. *Id.* at 20–29. We approach the Petition mindful that attorney argument cannot take the place of evidence lacking in the record. *See, e.g., In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997); *In re De Blauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984).

Petitioner's obviousness challenge is interlaced with unsupported factual contentions. Pet. 20–29. The Petition rests on bare argument to establish how two asserted background references (Ex. 1007 and Ex. 1008) would have informed the understanding of an ordinary artisan's reading of Bedi. Pet. 24–27. A lack of evidence also undermines Petitioner's attempt to explain why "[o]ne of skill in the art would have been motivated to take the teachings of Bedi and apply them to constructing a fusion protein" according to claim 1 (*id.* at 27), "wherein SEQ ID NO: 4 is attached via the amino acid spacer to the C-terminus of SEQ ID NO 5 or SEQ ID NO: 6." Ex. 1001, 70:42–44. The Petition, moreover, directs us to no support for the argument that "one of ordinary skill in the art would appreciate that the

Fox3+CD25+CD4 Tregs described in (Ex. 1007 and 1008) will inherently express EGFR under inflammatory conditions, and that EGFR-positive Treg cells are more immunosuppressive than EGFR-negative Treg cells.” Pet. 27. Compounding that evidentiary deficit, the Petition advances bare attorney argument that “one so skilled would be motivated to use the EGFR targeting moiety of Bedi, to target the most immunosuppressive Treg populations set forth in Bedi and” a background reference. *Id.*

We agree with Patent Owner that “[a]ssertions regarding elements that were known in the art or what was common sense to a person of ordinary skill must be supported by documentary or testimonial evidence.” Prelim. Resp. 21. Even though “the Board has subject matter expertise,” we are not free to “accept general conclusions about what is ‘basic knowledge’ or ‘common sense’ as a replacement for documentary evidence for core factual findings in a determination of obviousness.” *Id.* (quoting *K/S HIMPP v. Hear-Wear Techs., LLC*, 751 F.3d 1362, 1365–66 (Fed. Cir. 2014)). For example, without supporting evidence, we are not free to accept that one of ordinary skill in the art would have found it obvious to construct a fusion protein linked at the Gly amino acid instead of the Lys amino acid of Bedi SEQ ID NO: 2. Nor are we free to accept, without supporting evidence, that one of ordinary skill in the art would have found it obvious to fuse the immunomodulatory moiety and linker to the anti-EGFR1 light chain (SEQ ID NO: 71) that is disclosed in Figure 3 of Bedi.

The essence of Petitioner’s obviousness challenge is that, “[r]egarding the impact of the teachings of Bedi, one of skill in the art would have looked to Bedi as a roadmap for producing targeted immunomodulatory fusion proteins, such as the fusion protein of claim 1.” *Id.* at 21. That ultimate

assumption, regarding the impact of Bedi upon the understanding of an ordinary artisan, is not supported adequately in the Petition by documentary or testimonial evidence. See Prelim. Resp. 20–22. Accordingly, we determine that the information presented in the Petition does not show sufficiently that a person of ordinary skill in the art would have been led to modify Bedi by fusing SEQ ID NO: 104 (which corresponds to the specified spacer SEQ ID NO: 3) to the C-terminal glycine instead of the C-terminal lysine of SEQ ID NO: 2 to attain the fusion protein of claim 1. Pet. 26–29; Ex. 1003, Figs. 3, 7. Furthermore, the information presented in the Petition does not show sufficiently that an ordinary artisan would have been led to modify Bedi by fusing the SEQ ID NO: 104 linker and the SEQ ID NO: 87 immunomodulatory moiety, depicted in Figure 3, to the SEQ ID NO: 71 anti-EGFR1 light chain also depicted in Figure 3. Pet. 28; Ex. 1003, Fig. 3.

III. CONCLUSION

Taking account of the information presented in the Petition and Preliminary Response, we determine that the Petition fails to show that there is a reasonable likelihood that Petitioner would prevail at trial with respect to claim 1 of the '247 patent.

IV. ORDER

It is

ORDERED that the Petition is *denied* and no trial is instituted.

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