

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PETER J. SIMS

Appeal 2007-0547
Application 10/403,340
Technology Center 1600

Decided: December 6, 2007

Before DONALD E. ADAMS, ERIC GRIMES, and LORA M. GREEN,
Administrative Patent Judges.

ADAMS, *Administrative Patent Judge.*

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 20-22 and 26; the only other pending claims (23-25) were withdrawn from consideration (Br. 2). We have jurisdiction under 35 U.S.C. § 6(b).

INTRODUCTION

The claims are directed to a compound. Claim 20 is illustrative:

20. A compound that specifically promotes the formation of the human C5b-9 complex selected from the group consisting of molecules

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structurally mimicking C9 amino acid residues 359 to 384 when they are in spatial orientation which promotes formation of the C5b-9 complex, wherein the compound is not human C9.

The Examiner relies on the following prior art references to show unpatentability:

Michael M. Frank et al., "Complement," Second Edition *Fundamental Immunology*, 679-701 (1989).

Dale L. Bodian et al., "Mutational Analysis of the Active Site and Antibody Epitopes of the Complement – inhibitory Glycoprotein, CD59," 185(3) *J. Exp. Med.*, 507-516 (1997).

The rejection as presented by the Examiner is as follows:

Claims 20-22 and 26 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Bodian.

We affirm.

DISCUSSION

The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Therefore, we limit our discussion to representative claim 20. Claim 21, 22 and 26 will stand or fall with claim 20.

Claim 20 is drawn to a compound. On February 10, 2005 the Examiner introduced a Restriction Requirement into the record. In addition to requiring an election of a patentably distinct group of invention, the Examiner required Appellant to elect a species of the claimed compound (Restriction Requirement 3). On March 7, 2005, Appellant responded by electing, without traverse, "[a]ntibody as the distinct species of the claimed

invention” (Election 2). Accordingly, we interpret the term compound to mean antibody.

According to claim 20, the antibody (1) specifically promotes the formation of the human C5b-9 complex and (2) is selected from the group consisting of molecules structurally mimicking C9 amino acid residues 359 to 384 when they are in a spatial orientation that promotes the formation of the C5b-9 complex.¹

Thus, claim 20 reads on an antibody that structurally mimics amino acid residues 359 to 384 of C9 when these C9 amino acid residues are in a spatial orientation that promotes the formation of C5b-9. As a result, the claimed antibody will specifically promote the formation of the human C5b-9 complex.

We direct attention to Appellant’s claim 21, which requires that the antibody of claim 20 binds “specifically to amino acids 42 to 58 of human CD59.” The Examiner reasons that “an antibody that binds specifically to amino acids 42-58 of human CD59 structurally mimics [amino] acid residues 359-384 of complement component C9 because they both specifically bind to the same region of CD59” (Answer 3). Stated differently, the Examiner construes claim 20 to read on, or encompass, an antibody that specifically binds to amino acids 42 to 58 of human CD59.

In this regard, the Examiner finds that Bodian teaches three monoclonal antibodies (HC2, 2/24, and A35) that specifically bind to the region of amino acids 42-58 of human CD59 (Answer 3-4). The Examiner

¹ Claim 20 also requires that the compound is not human C9, which in view of the species election, is superfluous to our review of the claim as it reads on an antibody.

reaches this conclusion by finding that Bodian teaches that single substitution mutations at amino acid positions within the region defined by amino acids 42-58 of human CD59, reduced the ability of each antibody to bind its target (*id.*). From this, the Examiner concludes that since each of the three monoclonal antibodies bind to the region of amino acids 42-58 of human CD59, each antibody structurally mimics amino acid residues 359-384 of C9 and will promote the formation of the human C5b-9 complex (Answer 4).²

In response Appellant argues that because Bodian does not state that the antibodies are structural mimics of C9, the Examiner's position which is based on the doctrine of inherent anticipation must fall (Br. 4; Reply Br. 3). Appellant develops his argument along two lines of reasoning:

1. The allosteric effect, wherein "mutations in a protein at one region can affect binding of antibodies that recognize complete[ly] different domains" (Br. 4); and
2. Even if Bodian's antibodies "did bind to one or more residues with the CD59 42-58 region, this fact alone does not mean that they must constitute a structural mimic of C9 sequences" (*id.* (emphasis removed)).

Accordingly, the issue before us is whether the evidence relied upon by the Examiner supports a finding that Bodian teaches an antibody that blocks CD59's ability to inhibit the formation of the C5b-9 complex; and if so, would a person of ordinary skill in the art understand Bodain to teach that such an antibody would mimic C9 amino acid residues 359 to 384 when

² The Examiner relies on Frank to provide background information (Answer 5). Accordingly, we do not include it in our discussion.

they are in a spatial orientation which promotes the formation of the C5b-9 complex?

Under the doctrine of inherency, if an element is not expressly disclosed in a prior art reference, the reference will still be deemed to anticipate a claim if the missing element “is necessarily present in the thing described in the reference.” *Cont'l Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). “Inherent anticipation requires that the missing descriptive material is ‘necessarily present,’ not merely probably or possibly present, in the prior art.” *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295 (Fed. Cir. 2002) (*quoting In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999)). Stated differently, “a bare suggestion or hope that requires significant experimentation for implementation or verification is not an invalidating ‘anticipation’ of that which is ultimately achieved.” *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1372 (Fed. Cir. 2007).

One aspect of Bodian’s study was to define the regions of the CD59 protein required for its complement-inhibitory activity (Bodian 508: col. 1, ll. 44-47). The antibodies used in Bodian’s study were obtained by purchase or gift (Bodian 508: bridging paragraph, cols. 1-2). The antibodies were chosen due to their varying capacity to block the protective effects of CD59 (Bodian 511: col. 1, ll. 6-8). Specifically, Bodian teaches that HC2 and 2/24 have strong CD59-blocking activity³, whereas A35 exhibits a weak CD59-blocking activity (Bodian 511: col. 1, ll. 10-12). Thus, the preponderance of

³ CD59-blocking activity refers to the ability of the antibody to block CD59’s ability to inhibit complement-mediated lysis of host cells (*see e.g.*, Bodian 510: col. 1, ll. 38-50).

the evidence relied upon by the Examiner supports a finding that Bodian teaches an antibody that blocks CD59's ability to inhibit the formation of the C5b-9 complex.

Therefore, the issue is whether a person of ordinary skill in the art would understand Bodain to teach an antibody that mimics C9 amino acid residues 359 to 384 when they are in a spatial orientation which promotes the formation of the C5b-9 complex? In this regard, we find that Bodian mapped the antibody epitopes by mutational analysis of CD59 (Bodian 511: col. 2, ll. 1-6; Table 1; and Fig. 4). Bodian provides NMR based structural diagrams of CD59 (Bodian 512: Figure 3). These diagrams identify the amino acid mutations Bodian made to CD59 and illustrate the location of these amino acids on CD59 (*id.*). Bodian teaches that a mutation of amino acid 40 “eliminates the complement-inhibitory function of CD59 and prevents the binding of all the function blocking anti-CD59 antibodies tested” (Bodian 513: col. 2, ll. 4-6; *cf.* 512: Figure 3). In addition, Bodian teaches that a mutation in amino acid 53, the amino acid adjacent to amino acid residue 40 in CD59’s three-dimensional structure (Bodian: Figure 3A), “inhibits the complement-inhibitory activity and reduces the binding of four^[4] of the six CD59-blocking antibodies, implicating this residue as part of the active site of CD59” (Bodian 514: col. 1, ll. 4-9). As the Examiner points out, the ability of monoclonal antibodies HC2, 2/24, and A35 to bind CD59 are all reduced by a mutation in amino acid 53 (Answer 3-4). Bodian also explains that

[s]ites of protein-protein interaction are often defined by regions of hydrophobic and irregular protein surface. In the

⁴ Antibodies A35, HC2, 2/24, and MEM43 (Bodian 511: Table 1).

NMR structures of human CD59 W40 lies at the base of a hydrophobic groove, formed by residues F23, C39, W40, and L54, which is lined on one side by a ridge of hydrophilic residues (K41, H44, R53 and R55; Fig. 3 D).

(Bodian 514, col. 1, ll. 51-57.) As illustrated by Bodian's figure 3A and discussed above, amino acid residues 40, 53 and 54 fall within the active site of CD59. The mutation of these amino acid residues directly affects the ability of monoclonal antibodies HC2, 2/24, and A35 to bind CD59; and block CD59's activity. According to Bodian, "the present data strongly suggest that there is a single active site [for C8 and C9] and that this site lies in the vicinity of W40" (Bodian 513: col. 2, ll. 1-3). In sum, the preponderance of the evidence on this record demonstrates that monoclonal antibodies HC2, 2/24, and A35 bind in a region defined by amino acid residues 42-58 of human CD59 and structurally mimic C9 amino acid residues 359 to 384 when they are in a spatial orientation which promotes the formation of the C5b-9 complex.

We recognize Appellant's arguments concerning the allosteric effect which "could be responsible for the loss of binding of Bodian's antibodies to" Bodian's CD59 mutants (Br. 4). This argument is not supported by the evidence of record; therefore we are not persuaded by this argument. If Appellant's argument had merit, then Bodian would not be able to map antibody epitopes by mutational analysis of CD59 (*see e.g.*, Bodian 511: col. 2, ll. 1-6; Table 1; and Fig. 4).

Further, while Bodian does not expressly teach that the HC2, 2/24, and A35 monoclonal antibodies are structural mimics of the C9 sequence, there is no evidence on this record that they are not. Instead, Bodian teaches that the C9 binding site on CD59 is at the same location that the HC2, 2/24,

and A35 antibodies recognize CD59 and inhibit its activity. Accordingly, we find that the preponderance of the evidence on this record supports the Examiner's finding that monoclonal antibodies HC2, 2/24, and A35 are structural mimics of C9 amino acid residues 359 to 384 when they are in spatial orientation which promotes formation of the C5b-9 complex. Accordingly, we are not persuaded by Appellant's assertion that

while the Examiner may be correct that the antibodies shown by Bodian do bind to the same regions of CD59 as C9, and may even be further correct that, in so doing they act as structural mimics of particular residues within C9, it is absolutely clear that the Examiner might also be incorrect.

(Br. 5.) The evidence on this record provides more than a bare suggestion that requires significant experimentation for implementation or verification. To the contrary, the evidence on this record supports the Examiner's conclusion that the prior art monoclonal antibodies bind the same site as C9, inhibit CD59 activity, and therefore would be expected to be a structural mimics of C9 amino acid residues 359 to 384 when they are in spatial orientation which promotes formation of the C5b-9 complex.

In our opinion the Examiner has provided the evidence necessary to shift the burden to Appellant. However, for the foregoing reasons, Appellant has failed to carry his burden. Accordingly, we affirm the rejection of claim 20 under 35 U.S.C. § 102(b) as being anticipated by Bodian. Claims 21, 22 and 26 fall together with claim 20.

CONCLUSION

In summary, we affirm the rejection of record.

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No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Ssc:

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