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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte GERARD ZURAWSKI, ANNE-LAURE FLAMAR, and EYNAV KLECHEVSKY

Appeal 2019-003621
Application 14/887,151
Technology Center 1600

Before JEFFREY N. FREDMAN, DEBORAH KATZ, and JOHN G. NEW, *Administrative Patent Judges*.

KATZ, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellant[1] seeks our review, under 35 U.S.C. § 134(a), of the Examiner's decision to reject claims 39–47, 49–53, 59, and 60. (Appeal Brief filed July 2, 2018 ("Br.") 1–4.)[2]

We have jurisdiction under 35 U.S.C. § 6(b). We AFFIRM.

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the Real Party in Interest as Baylor Research Institute. (*See* Br. 1.)

[2] Claims 48, 61, and 62 are withdrawn.

INTRODUCTION

Appellant's Specification provides a method of assembling antibody-antigen complexes by simply mixing components. (Specification dated October 3, 2017 ("Spec.") ¶ 6.) The Specification discloses that cohesin and dockerin protein domains, which are derived from bacterial cellulosome, can be used to produce fusion proteins in mammalian cells because they form high affinity protein-protein complexes. (*Id.* ¶¶ 8–10.) The Specification exemplifies the use of cohesion-dockerin binding pairs in a modular rodent monoclonal antibody (rAb) carrier that includes at least a portion of an antibody linked to one half of a cohesin-dockerin binding pair and an antigen linked to the other half of the cohesin-dockerin binding pair. (*Id.* ¶ 12, Fig. 1.)

Appellant's claim 39 is representative of the subject matter on appeal and recites:

> A method of making a complex comprising
>
> combining an antigen-specific binding domain with one or more antigen carrier domain(s),
>
> wherein the antigen-specific binding domain comprises one of a cohesin or dockerin binding pair and
>
> the antigen carrier domain comprises a peptide antigen and the other of a cohesin dockerin binding pair.

(Br. 5.)

The Examiner rejected the claims as follows:

Claims Rejected	35 U.S.C. §	Basis	Final Office Action
39–43, 45–46, 49–51, 60	103(a)(pre-AIA)	Bayer[3] and Bozzacco[4]	4–9
44, 47, 52, 53	103(a)	Bayer, Bozzacco, Hawiger,[5] and Ninomiya[6]	9–13
59	103(a)	Bayer, Bozzacco, and Bates[7]	13–14

ANALYSIS

The Examiner finds that Bayer teaches the strong interaction between cohesion and dockerin forms an affinity complex. (Final Action dated December 12, 2017 ("Final Act.") 4, citing Bayer 384.) The Examiner finds that Bayer teaches hybrid biomolecules of dockerins or cohesins fused to protein A, antibodies, lectins, or DNA. (*Id.*, citing Bayer 384–385.) The Examiner finds "[f]or example, a dockerin-antibody hybrid can be mixed

[3] Bayer, E. A. et al., *The Cellulosome - A Treasure-trove for Biotechnology*, 12 Trends in Biotechnology 379–386 (1994).
[4] Bozzacco, L. et al., *DEC-205 Receptor on Dendritic Cells Mediates Presentation of HIV Gag Protein to CD8+ T cells in a Spectrum of Human MHC I Haplotypes*, 104 Proc. Nat'l Acad. Sci. 1289–1294 (2007).
[5] Hawiger et al., US 2004/0258668 A1, published December 23, 2004.
[6] Ninomiya, A. et al., *Intranasal Administration of A Synthetic Peptide Vaccine Encapsulated in Liposome Together With an anti-CD40 Antibody Induces Protective Immunity Against Influenza A Virus In Mice*, 20 Vaccine 3123–3129 (2002).
[7] Bates, E. E. M. et al., *APCs Express DCIR, a Novel C-Type Lectin Surface Receptor Containing an Immunoreceptor Tyrosine-Based Inhibitory Motif*, 163 J. Immunol. 1973–1983 (1999).

with cohesin-lectin hybrid in order to couple to a desired antigen or glycoprotein." (*Id.*, citing Bayer 385.) The Examiner finds further that Bayer teaches advantages using a cohesion-dockerin affinity complex to provide numerous advantages, for example that the 1:1 binding ratio of dockerin to cohesin enables better control of the coupling component and that multi-component complexes can contain a series of different cohesins complexing with multiple dockerins. (Final Act. 4–5, citing Bayer 385.)

Because Bayer does not teach a peptide antigen, the Examiner cites Bozzacco for its teaching to link a monoclonal antibody that binds to a human receptor with a viral antigen to improve presentation of the antigen and increase vaccine efficacy. (Final Act. 5, citing Bozzacco 1292.) More specifically, the Examiner finds Bozzacco teaches a monoclonal antibody that binds to dendritic cell receptor DEC-205 fused to an HIV antigen gag p24 peptide. (*Id.*) The Examiner finds one of ordinary skill in the art would have been motivated modify Bayer's hybrid biomolecule complex with Bozzacco's antibody-antigen pair by attaching an anti-DEC-205 antibody to cohesin or dockerin and a viral peptide antigen to the complementary dockerin or cohesin in order to delivery viral antigens to dendritic cells. (Final Act. 5–6.) The reason to do so would be to take advantage of the flexibility and high affinity of dockerin-cohesin 1:1 binding complex. (*Id.* at 6.)

Appellant argues that there is no reason "to modify the complex of Bozzacco to employ the cohesin and dockerin molecules described in Bayer, and one would not have a reasonable expectation of success for performing the methods described in Bozzacco with such modifications." (Br. 2.)

Appellant further argues that the Examiner's proposed modification would change the principle of operation of the references. (*Id.*)

Appellant contends that Bozzacco teaches a fusion protein of an antibody covalently attached to an HIV antigen. (Br. 2, citing Bozzacco 1293.) Appellant argues there is no reason to modify Bozzacco's fusion protein with Bayer's non-covalent affinity complex. (*Id.*) Appellant argues that covalent bonds are metastable and typically require a catalyst to break the bond. (*Id.* at 3, citing Mathews.[8]) Appellant further argues that Bozzacco requires internalization of the fusion protein for effective cross-presentation, and that there is no evidence that a molecular complex would function similarly to a covalent bond attachment. (*Id.* at 2–3.) Appellant contends that "although the claims are not drawn to a method of antigen presentation, the proposed modifications to the complex of Bozzacco cannot render the complex unsatisfactory and/or change the principle of operation of the complex for use in the methods described in Bozzacco." (*Id.* at 3.)

We are not persuaded by Appellant's arguments that there would not have been a reason to combine the prior art. Appellant argues against modifying Bozzacco's antibody-antigen fusion protein with Bayer's cohesin-dockerin affinity complex. However, the Examiner's rejection modifies Bayer's dockerin-antibody cohesin-hybrid affinity complex with Bozzacco's specific DEC-205 antibody and HIV peptide antigen. Therefore, Appellant does not address the Examiner's rejection.

[8] Mathews C., and Van Hold, K., *Biochemistry*, The Benjamin/Cummings Publishing Company at 25 (1996), submitted October 3, 2017.

Bayer teaches hybrid biomolecules including fusion proteins incorporating cohesin and dockerin. (Bayer 384–385.) Bayer teaches a dockerin-antibody hybrid can be mixed with a cohesin-hybrid (e.g., lectin, toxin, protein) to couple a desired antigen. *Id.* The Examiner cites Bozzacco for identifying a specific peptide antigen to be combined with a specific antibody in a cohesin-dockerin affinity system in order to deliver viral antigens to dendritic cells. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). Because the Examiner articulated a reason from the prior art to combine the references, we are not persuaded that the Examiner erred.

We are not persuaded by Appellant's arguments there would not have been a reasonable expectation of success in the claimed method. (*See* Br. 3.) Obviousness does not require absolute predictability of success. . . . [A]ll that is required is a reasonable expectation of success. *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006). The combined prior art cited by the Examiner provides more than a general approach in a promising field of experimentation; the prior art provides specific guidance as to the particular form of the claimed invention and how to achieve it. (*See id.*) In particular, Bayer teaches the specific advantages of using a cohesin-dockerin affinity complex, as well as specific examples of fusion proteins, including dockerin-antibody and cohesin-antigen that would have been obvious to combine with Bozzacco's preferred antibody and peptide antigen. Moreover, the modification does not change the operation of Bayer, it merely selects a specific antigen as taught by Bozzacco. Although the

affinity complex may function differently from a covalent bond, "a given course of action often has simultaneous advantages and disadvantages, and this does not necessarily obviate motivation to combine." (*Id.*) Because the prior art establishes a reasonable expectation of success in modifying Bayer with the specific antibody and peptide antigen of Bozzacco, we are not persuaded that the Examiner erred.

Accordingly, we affirm the Examiner's rejection of claim 39. Appellant does not present separate arguments against the rejection of claims 41–43. Appellant argues that the Examiner erred in rejecting claims 44, 47, 52, 53, and 59 for the same reasons argued against the rejection of claim 39. (*See* Br. 4.) Because, as discussed above, we are not persuaded by Appellant's arguments we affirm the Examiner's rejections of all of Appellant's pending claims as being obvious under 35 U.S.C. § 103(a).

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	References/ Basis	Affirmed	Reversed
39–43, 45–46, 49–51, 60	103(a)	Bayer and Bozzacco	39–43, 45–46, 49–51, 60	
44, 47, 52, 53	103(a)	Bayer, Bozzacco, Hawiger, and Ninomiya	44, 47, 52, 53	
59	103(a)	Bayer, Bozzacco, and Bates	59	
Overall Outcome			39–47, 49–53, 59, 60	

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

AFFIRMED