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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* NEAL VAIL[1]

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Appeal 2018-004434
Application 13/786,067
Technology Center 1600

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Before ULRIKE W. JENKS, TIMOTHY G. MAJORS, and MICHAEL A. VALEK, *Administrative Patent Judges*.

VALEK, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a composition for promoting cell interaction, which have been rejected as directed to patent-ineligible subject matter and as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

STATEMENT OF THE CASE

Claims 1, 13, 15, 17–25, 27–29, 31, 33, and 34 are on appeal, and can be found in the Claims Appendix of the Appeal Brief. The only independent claim is claim 1. It reads as follows:

> 1. A composition for promoting cell interaction comprising a polycation and a polyanion, wherein at least one of the

[1] Appellant identifies the real party in interest as KCI Licensing, Inc. App. Br. 1.

> polycation and the polyanion comprises an engineered protein, wherein the engineered protein comprises one or more sequences each independently selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, and SEQ ID NO: 26.

App. Br. 17. According to the Specification, "[i]n various embodiments, the engineered protein is a collagen" and the claimed SEQ IDs are "biological functioning motifs" found in collagen and described in Russell,[2] which the Specification incorporates by reference. Spec. ¶¶ 62, 87.

Appellant seeks review of the following grounds of rejection[3] made by Examiner:

I. Claims 1, 13, 15, 17–25, 27–29, 31, 33, and 34 under 35 U.S.C. § 101 as directed to patent-ineligible subject matter.

II. Claims 1, 13, 15, 17–25, 27–29, 31, 33, and 34 under 35 U.S.C. § 103(a) as obvious over Stewart[4] and Russell.

As Appellant does not argue any of the dependent claims separately for either rejection, we focus our analysis on claim 1, and claims 13, 15, 17–25, 27–29, 31, 33, and 34 stand or fall with claim 1. 37 C.F.R. § 41.37(c)(1)(iv).

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[2] Brooke H. Russell et al., US 2011/0288274 A1, published Nov. 24, 2011 ("Russell").

[3] Examiner has withdrawn the section 112 rejections. Ans. 18. Thus, only the patent eligibility and obviousness rejections remain before us.

[4] Russell J. Stewart et al., US 2010/0120923 A1, published May 13, 2010 ("Stewart").

ANALYSIS

*I. Subject Matter Eligibility*

An invention is patent-eligible if it claims a "new and useful process, machine, manufacture, or composition of matter." 35 U.S.C. § 101. However, the Supreme Court has long interpreted 35 U.S.C. § 101 to include implicit judicial exceptions: "[l]aws of nature, natural phenomena, and abstract ideas" are not patentable. *E.g.*, *Alice Corp. v. CLS Bank Int'l*, 573 U.S. 208, 216 (2014).

In determining whether a claim falls within an excluded category, we are guided by the Supreme Court's two-step framework, described in *Mayo* and *Alice*. *Id.* at 217–18 (citing *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 75–77 (2012)). In step one, we ask whether the claims are directed to an exception to patent eligibility, such as an abstract idea or law of nature. *Alice Corp. Pty. V. CLS Bank Int'l*, 134 S.Ct. 2347, 2355 (2014). In step two, we examine the elements of the claims to determine whether they contain an inventive concept sufficient to transform the claimed judicial exception into a patent-eligible application. *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66, 71–72 (2012) (quoting *Alice*, 134 S.Ct. at 2355).

"When a law of nature or natural phenomenon is claimed as a physical product," as Examiner determined here, "the courts have often referred to the exception as a 'product of nature.'" MPEP § 2106.04(b); *see, e.g.*, *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116–17 (2013) ("*Myriad*") (analyzing whether isolated DNA was a patent ineligible "product of nature"). The product of nature exception to patent eligibility includes both naturally occurring products and "naturally occurring products

that lack markedly different characteristics" from their natural counterpart. *Id.* If it is determined that the claim is drawn, in whole or in part, to a nature-based product that lacks markedly different characteristics from its natural counterpart then the product of nature exception applies and we move on to step two of the analysis. MPEP § 2106.04(c).

Examiner's analysis follows the Supreme Court's two-step framework as well as the guidance concerning the product of nature exception in MPEP § 2106.04(b)-(c). Examiner starts by determining that the product of nature exception is implicated because the claims recite a composition comprising a polycation and polyanion "wherein either . . . is simply a derivative/fragment of a natural peptide [and] is not found to be significant/markedly different in structure from naturally occurring products." Non-Final Act. 4. In doing so, Examiner explains that the term "engineered" does not distinguish the claimed proteins from their natural counterparts because "[a] protein can be 'engineered' that has not resulted in a markedly/significant difference from that of a naturally occurring protein." *Id.* at 5. Then, analogizing Appellant's claims to claim 1 of Nature-Based Product Example 6 in the USPTO's Subject Matter Eligibility Guidance,[5] Examiner determines that the claimed combination of a polycation and polyanion was not eligible because "the mixture does not have markedly different characteristics from what occurs in nature" and the claims do not recite "additional features that could add significantly more to the exception." *Id.* at 7–9; Ans. 8.

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[5] This example, originally published in December 2014, has been renumbered as Example 14 in current index of subject matter eligibility examples. Index of Eligibility Examples, available at https://www.uspto.gov/sites/default/files/documents/ieg-example-index.pdf.

Appellant disputes Examiner's subject matter eligibility rejection in three respects. First, Appellant contends that the product of nature exception does not apply because claim 1 requires an "engineered" protein. App. Br. 6-7. Second, Appellant argues that the composition as a whole, which comprises a polycation and a polyanion, is significantly different than what is found in nature because it is "the combination of the two components that forms the coacervate and promotes cell interaction." *Id.* at 7. Third, Appellant urges that even if the judicial exception does apply, the claimed compositions "amount to significantly more than the judicial exception" because the "polycation and the polyanion by themselves do not possess the beneficial properties of being able to form a coacervate . . . to promote cell interaction." *Id.* at 8; *see also* Reply 3.

**USPTO Guidance Step 2A, Prong 1**

We are unpersuaded by Appellant's arguments and agree with Examiner that claim 1 is directed to the product of nature exception. Claim 1 is broadly directed to a "composition . . . comprising a polycation and a polyanion, wherein at least one of the polycation and the polyanion comprises an engineered protein" comprising one or more of the peptide sequences in SEQ ID NO: 1 to SEQ ID NO: 26. Appellant does not dispute, and Examiner cites evidence demonstrating, that several of the recited sequences in SEQ ID NO: 1 to SEQ ID NO: 26 are present in naturally-occurring collagen proteins. Non-Final Act. 8 (quoting Haynie ¶111,[6] which teaches that SEQ ID NOS: 1-3 are "recognition sequences in collagen for collagen-binding integrins."); *see also* Russell ¶ 7 (teaching that SEQ ID

[6] Donald T. Haynie, US 2007/0077276 A1, published Apr. 5, 2007 ("Haynie").

NO: 1 and 2 are "type I collagen derived sequences"). Thus, as written, the "polycation" and "polyanion" in claim 1 encompass proteins with the same amino sequence as their naturally-occurring counterparts, that is, naturally-occurring collagen proteins and fragments thereof.

We are not persuaded by Appellant's argument that the product of nature exception does not apply because the term "engineered protein" limits the claims to "proteins that comprise engineered sequences (*i.e.*, not naturally occurring)." *Id.* at 7. Examiner determined otherwise, explaining that "engineered . . . also encompasses making any naturally occurring protein, rather than isolating such from nature." Non-Final Act. 6. The Specification supports Examiner's interpretation, not Appellant's. It states that an "engineered protein" can be produced by "chemical synthesis" or by "recombination biology, directed evolution, or combination thereof." Spec ¶ 60. This suggests that the term encompasses proteins "engineered" by chemically synthesizing an otherwise naturally-occurring protein. Indeed, the Specification teaches that "[i]n various embodiments, the engineered protein is a collagen, *including* a recombinant collagen." Spec ¶¶ 62, 87 (emphasis added). Thus, while the term certainly includes proteins whose amino acid sequence has been altered by recombinant techniques, the broadest reasonable interpretation of "engineered protein" is not so limited.

Moreover, even if we agreed with Appellant's claim construction, the test is not whether the claim is directed to a product that is structurally identical to one found in nature. To avoid the product of nature exception, the claimed product must exhibit characteristics that are "markedly different" from its natural counterpart. MPEP § 2106.04(c). This is true even if the structure of the claimed product differs somewhat from its natural

counterpart. *See, e.g.*, *Myriad*, 133 S. Ct. at 2116–17 (isolated gene not patent eligible even though it differed from the structure of the gene in the natural chromosome because it lacked connective covalent bonds at the ends). Appellant does not contend that the "engineered sequences" it says are required by claim 1 result in a polycation or polyanion protein with markedly different characteristics from their natural counterparts. *See* App. Br. 7.

To the contrary, the only characteristic recited in claim 1—that these proteins comprise one or more sequences at least some of which are naturally-occurring—suggests that the claimed proteins need *not* have markedly different characteristics from their natural counterparts. According to Russell, which Appellant's Specification incorporates by reference, the "collagen derived sequences" in SEQ ID NO: 1 and SEQ ID NO: 2 are significant because they "bind with high affinity" to particular integrins (*i.e.*, cell surface receptors) "involved in cell-cell and cell-substrate adhesion." Russell ¶¶ 6–7. In other words, they are pre-existing sequences that have been identified because they have the same function as naturally-occurring collagen, *i.e.*, promoting cell interaction, as that recited for the claimed composition. In this sense, claim 1 is similar to the composition claims for DNA primers, which our reviewing court has repeatedly held to be patent ineligible. *See Roche Molecular Sys. Inc. v. CEPHEID*, 905 F.3d 1363, 1370–71 (Fed. Cir. 2018) (DNA primers identified because they bind to certain naturally-occurring "position-specific signature nucleotides" held ineligible because patentee only identified the "pre-existing" sequence; "it did not create them."); *In re BRCA1– and BRCA2–Based Hereditary Cancer Test Patent Litigation*, 774 F.3d 755, (Fed. Cir. 2014) ("A DNA structure

with a function similar to that found in nature can only be patent eligible as a composition of matter if it has a unique structure, different from anything found in nature."). It may be the case that a protein containing one of the claimed peptide sequences, but possessing markedly different characteristics can be engineered. Claim 1, however, is not limited to such proteins.

**USPTO Guidance Step 2A, Prong 2**

We are also unpersuaded by Appellant's argument that the claimed composition as a whole avoids the product of nature exception because it requires both a polycation and a polyanion. As explained above, claim 1 is broadly drafted such that either or both of the claimed composition's components may be a naturally-occurring collagen protein or protein fragment. In the absence of some markedly different characteristic resulting from their combination, a mixture comprising two products of nature is not patent eligible. *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948) (claims to a combination of different naturally-occurring bacteria held ineligible where the combination "produces no new bacteria, no change in the . . . bacteria, and no enlargement of the range of their utility.").

Appellant contends that "the presently claimed compositions are distinguishable from the mixture of bacteria in *Funk Brothers*" because the claimed combination of a polycation and polyanion "forms the coacervate and promotes cell interaction." Reply Br. 3. That argument is not persuasive for two reasons. First, Appellant's claims do not require the formation of a coacervate. Nor is such a requirement inherent in claim 1's recitation of a "composition for promoting cell interaction comprising a polycation and a polyanion." To the contrary, the Specification distinguishes between "polyionic compositions," like that in claim 1, and the

"coacervates" such compositions may or may not form "depending" on various other unclaimed parameters. Spec. ¶ 1. Second, Appellant offers no evidence that the mixture of a naturally-occurring polycation and polyanion in the claimed composition functions differently with respect to promoting cell interaction than do those components individually. Rather, the Specification states that in various embodiments it is polycation or polyanion alone as opposed to the composition of the two that promotes cell interaction. Spec. ¶ 47.

Accordingly, given their broadest reasonable interpretation, there is nothing in the claims that demonstrates that either the claimed "composition" or its individual polycation and polyanion components have any markedly different property from their naturally-occurring counterparts. *See In re Roslin Institute (Edingurgh)*, 750 F.3d 1333, 1338 (Fed. Cir. 2014) (holding that alleged differences in mitochondrial DNA of cloned sheep did not distinguish them from natural sheep for patent eligibility analysis because those differences were not claimed); *see also* MPEP § 2106.04(c). For this reason, we determine that claim 1 does not integrate the judicial exception into a practical application. *See* USPTO's January 7, 2019 Memorandum, *2019 Revised Patent Subject Matter Eligibility Guidance,* 84 Fed. Reg. 50–57, 54 n. 20 (2019) (noting that MPEP 2106.04(b) and (c) continue to guide the analysis for the product of nature exception).

**USPTO Guidance Step 2B**

Proceeding to the second step of the Supreme Court's analysis (and the related Step 2B as provided in the Office's Guidance), we determine that claim 1 does not add significantly more beyond the claimed products of nature themselves. As explained above, claim 1 is directed to a composition

that comprises a polycation and a polyanion both of which may be naturally-occurring proteins or protein fragments. There are no other requirements, much less additional limitations requiring the composition's components to be complexed or combined with other components that distinguish them from their naturally-occurring counterparts. To the contrary, the only structural requirement is that claimed proteins must contain peptide sequences at least some of which Examiner has shown are identical to those in naturally-occurring collagen proteins. Non-Final Act. 8 (quoting Haynie ¶ 111); *see also* Russell ¶ 7. As such, claim 1 does not add anything beyond the product of nature itself. Appellant's argument regarding the coacervate and its allegedly beneficial properties fails because, as explained above, claim 1 does not recite a coacervate and is not limited to the formation of such.

Appellant has not argued any of the dependent claims separately, nor otherwise suggested that any limitation in those claims is pertinent to the subject matter eligibility analysis. Accordingly, we conclude that claims 1, 13, 15, 17–25, 27–29, 31, 33, and 34 are directed to patent-ineligible subject matter.

*II. Obviousness*

Claims 1, 13, 15, 17–25, 27–29, 31, 33, and 34 were rejected as obvious over the combination of Stewart and Russell. Examiner finds that Stewart teaches all of the claim limitations, including that the engineered protein may be a known collagen. Non-Final Act. 11–12; 13–16. Examiner points to Russell "as evidence that presently elected collagen peptide SEQ ID NO: 1 was a known collagen peptide to a person having ordinary skill in the art." Ans. 18. According to Examiner, the skilled artisan would

"appreciate[] that the known collagen peptide of . . . SEQ ID NO: 1 taught by Russell was open for selection . . . and in fact was one of three (3) preferred peptides guided to in Russell." *Id.* (citing Russell ¶ 44).

Appellant argues that Stewart teaches collagen hydrosolate, rather than collagen. App. Br. 9–10. Thus, urges Appellant, "there [is] no teaching or suggestion in Stewart that would motivate persons of ordinary skill in the art to employ a collagen, such as that disclosed in Russell, as either a polycation or polyanion in its adhesive complex coacervates." *Id.* at 10. Appellant further contends that Stewart teaches away from the use of collagens in its coacervates because "Stewart teaches that collagens need to be chemically modified in order to be able to form coacervates." *Id.*

The issue with respect to this rejection is: Does the preponderance of evidence of record support Examiner's conclusion that the cited prior art renders obvious the claimed compositions?

We begin our analysis with findings of fact regarding the teachings in Stewart and Russell.

FF1. Stewart teaches "adhesive complex coacervates" that are "composed of a mixture of one or more polycations and one or more polyanions." Stewart, Abstract. These "adhesive complex coacervates have numerous biological applications" including as "bioadhesives." *Id.*

FF2. In one embodiment, Stewart teaches a coacervate "created using a low MW (3-5 kda) non-gelling collagen hydrosolate as the polycation." Stewart ¶ 105. Stewart teaches that the collagen hydrosolate was aminated with ethylenediamine, which "shifted the pI from 5.4 to 10.4" and allowed the "aminated collagen [to] form[] dense coacervates at 25°C over a broad range of compositions." *Id.*

FF3. Russell teaches collagen proteins containing certain peptide sequences, including the "type I collagen derived sequences" GFOGER, GLOGER and GASGER. Russell ¶ 7. GFOGER, GLOGER and GASGER are the amino acid sequences in SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 of Appellant's claims.

FF4. Russell teaches that "[p]ost-translational modification of collagen to include hydroxyproline residues is important to stabilize the triple helical conformation of collagen." Russell ¶ 43. In addition, Russell teaches other "biologically active sequences" in SEQ ID NO: 4 to 12 that include unhydroxylated proline and "support adherence . . . regardless of the lack of hydroxyproline." *Id.* ¶ 44. Russell's SEQ ID NO: 4 to 12 are the same sequences as those in SEQ ID NO: 4 to 12 of Appellant's claims.

We are unpersuaded by Appellant's arguments and agree that the obviousness rejection is supported by a preponderance of the evidence. Short of describing the particular collagen-derived peptide sequences in SEQ ID NO: 1 or others of the claimed SEQ IDs, Stewart teaches all of the limitations of claim 1. Stewart teaches collagen hydrolysate as a preferred polycation embodiment to form its coacervates. As Appellant acknowledges, "collagen hydrolysate" is a form of collagen "produced from the hydrolysis of collagen." App. Br. 10. A skilled artisan would recognize that the hydrolysate is another common form of the same thing. Indeed, after aminating collagen hydrolysate with ethylenediamine, Stewart refers to the product as an "aminated collagen." FF2.

We disagree with Appellant's argument that Stewart's teaching that its collagen needed to be aminated before a coacervate could be formed constitutes a teaching away from using collagen as a polycation. To teach

away, a reference generally must "criticize, discredit, or otherwise discourage the solution claimed." *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). Stewart does none of this. Rather, it provides a specific procedure for using a collagen protein as a polycation in conjunction with a polyanion to form a coacervate complex and teaches that it works "over a broad range of compositions." *Id.*

We also find that Examiner has articulated a sufficient rationale to combine Stewart with collagen proteins that include the biologically active sequences, *i.e.*, the claimed SEQ ID NOs, taught in Russell. As explained above, Stewart teaches collagen as a preferred embodiment for forming a coacervate. Russell teaches that SEQ ID NO: 1 and SEQ ID NO: 2 is derived from naturally-occurring collagen and discloses collagen proteins comprising the other claimed SEQ ID NOs. It would be obvious for the skilled artisan to select a collagen protein comprising those sequences to form a coacervate as taught in Stewart, particularly in light of Russell's teaching that the hydroxyproline in SEQ ID NO: 1 and SEQ ID NO: 2 is "important" to stabilize the protein's structure. FF4. Appellant points out that Russell teaches that the proline residues in SEQ ID NO: 4 to SEQ ID NO: 12 are sufficient to support adherence even when they do not undergo posttranslational modification to hydroxyproline. App. Br. 11. But that teaching merely provides additional support for Examiner's rationale to combine the references because Appellant's claims encompass SEQ ID NO: 4 to SEQ ID NO: 12 just as they do SEQ ID NO: 1.[7]

[7] Examiner's rejection focuses on SEQ ID NO: 1 because Appellant elected that sequence earlier in prosecution. *See* Non-Final Act 2. However, claim 1 encompasses proteins comprising any of the peptide sequences in

Examiner also finds that Stewart teaches each of the limitations added by the appealed dependent claims. Non-Final Act. 14–16. We agree with Examiner's findings in that regard and incorporate them here. Appellant does not dispute any of those findings on appeal. Accordingly, the obviousness rejection is affirmed as to all of the appealed claims.

## SUMMARY

We affirm the rejection of claims 1, 13, 15, 17–25, 27–29, 31, 33, and 34 under 35 U.S.C. § 101 as being directed to patent ineligible subject matter.

We affirm the rejection of claims 1, 13, 15, 17–25, 27–29, 31, 33, and 34 under 35 U.S.C. § 103 over Stewart and Russell.

## TIME PERIOD FOR RESPONSE

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

SEQ ID NO: 1 to SEQ ID NO: 26. As the Specification explains (Spec ¶¶ 62, 87) those sequences are incorporated from Russell, which teaches the same SEQ ID NOs. *See* Russell 12–18 (listing sequences).