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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte MEI CHEN and DAVID WOODLEY

Appeal 2018-007648
Application 13/657,594[1]
Technology Center 1600

Before DONALD E. ADAMS, RYAN H. FLAX, and
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method for treating healing of a wound of a subject having epidermolysis bullosa, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF THE CASE

Dystrophic Epidermolysis Bullosa (DEB) "is an incurable genetic disease caused by a gene defect in the gene that encodes for type VII

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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 the University of Southern California. (Appeal Br. 3.)

collagen." (Spec. 2.) Type VII collagen is "a protein that serves to anchor the epidermis onto the dermis." (*Id.*) Those who suffer from Dystrophic Epidermolysis Bullosa have "skin fragility, blistering, and repeated wounding and healing of their skin wounds" and they suffer from chronic wounds. (*Id.*) Patients with severe Dystrophic Epidermolysis Bullosa "have widespread lesions and multiple wounds spanning large areas of trauma-prone sites such as the sacrum, hips, feet, mouth, scalp, lower back and hands." (*Id.* at 5.) Appellant's invention is directed at a method for treating skin wounds in those who have Dystrophic Epidermolysis Bullosa. (See *id.* at 6 ("Accordingly, it is an object of the present invention to provide effective methods and therapeutic agents for treating DEB that avoids the problems of other methods in the art.").)

Claims 7–9, 11, 13, 15–18, 20–23, and 25 are on appeal. Claim 7 is representative and reads as follows:

> 7. A method for treating or accelerating healing of a wound in the skin of a subject having epidermolysis bullosa, comprising:
>
> intravenously administering to the subject having epidermolysis bullosa and the skin wound an effective amount of a pharmaceutical composition comprising recombinant human collagen type VII protein comprising an alpha chain having a collagenous triple-helical segment.

(Appeal Br. 23.)

The following grounds of rejection by the Examiner are before us on review:

Claims 7–9, 11, 13, 15–18, 20–23, and 25 under 35 U.S.C. § 103(a) as unpatentable over Woodley,[2] Simpson,[3] and Wilkes.[4, 5]

DISCUSSION

The Examiner finds that Woodley teaches intradermal administration of a liquid pharmaceutical composition comprising human recombinant collagen type VII in a mouse model representative of dystrophic epidermolysis bullosa and that sub-epidermal blistering was corrected and type VII collagen expression was restored. (Final Action 6.) The Examiner finds that Woodley teaches that

> "we did not observe the injected human type VII collagen distributed diffusely throughout the dermis of either mouse skin or regenerated DEB skin". "Rather it was localized to the basement membrane zone (BMZ) between the dermis and epidermis."

(Ans. 14.)

The Examiner recognizes that Woodley does not teach intravenous administration but asserts that such administration would have been obvious to one of ordinary skill in the art in light of Simpson and Wilkes. (Final

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[2] David T. Woodley et al., *Injection of recombinant human type VII collagen restores collagen function in dystrophic epidermolysis bullosa*, 10(7) Nature Medicine, 693–95 (July 2004).
[3] Simpson et al., US 2004/0037813 A1, published Feb. 26, 2004.
[4] Wilkes et al., US 7,939,281 B2, issued May 10, 2011.
[5] The Examiner had also provisionally rejected claims 7–9 11, 13, and 15 for obviousness-type double patenting over claims 1 and 10 of U.S. Application No. 13/946,847. The '847 application went abandoned on June 7, 2019, and thus the rejection is moot.

Action 6–7.) In this regard, the Examiner finds that Simpson teaches use of electroprocessed collagen where the collagen type can include type VII collagen and in recombinant form and that Simpson "teach[es] administering [the collagen] intravenously." (*Id.* at 6.) The Examiner finds that Wilkes teaches intravenously administering "recombinant collagen such as collagen type V" to human subjects "who suffer from a disease or disorder that involves autoimmunity to collagen" and that "preferably a collagen compound will prevent or diminish the onset of acute or chronic pathology," i.e., suppress the autoimmune response. (*Id.* at 7–8.)

The Examiner further contends that one of ordinary skill in the art would have been motivated to modify the Woodley intradermal delivery with intravenous delivery and expect success because "Woodley fails to teach that intradermally administered collagen type VII can migrate to other wound areas on the body" (*id.* at 8) and one would want "to get a systemic effect, thus treating multiple blisters all over the body rather than intradermally injecting collagen type VII at every localized blister site" (Ans. 13–14).

We do not agree with the Examiner's conclusion of obviousness. The Examiner has not pointed to evidence in the references applied in the rejection that would support a reasonable expectation of success that intravenously administered recombinant collagen type VII would be able to treat or accelerate healing of a wound in the skin of a subject having epidermolysis bullosa. (*See, e.g.*, Appeal Br. 11, 13–14; Reply Br. 5.) There is no dispute that Woodley teaches the suitability of collagen type VII in wound healing for epidermolysis bullosa. However, that alone does not provide an expectation that collagen type VII, however delivered to a

patient, would be capable of assisting in wound healing. And the Examiner failed to establish an evidentiary basis on this record to support a conclusion that Simpson and Wilkes provide any reasonable expectation that intravenous delivery of collagen type VII would result in wound healing in the skin (*see generally* Ans. 5 (discussing Simpson's disclosure)). While we agree with the Examiner that Simpson teaches formation and use of electroprocessed collagen and indicates its use for wound healing, in that context, Simpson teaches direct application to the wound site as well as providing additional materials onto or into the wound site, stating:

> Electroprocessed collagen can also be delivered directly to a desired location. For example, an electroprocessed material can be produced directly onto a skin wound, with or without substances such as molecules or cells. Additional cells or materials can then be aerosolized onto or into the wound site.

(Simpson ¶ 198.) Simpson teaches that cells may produce substances to aid in healing. (*Id.* ¶ 110.) Other substances such as fibrin and laminin are described for use with the collagen as well as other "regulatory elements that may be needed to promote activities such as healing, regeneration, and cell differentiation." (*Id.* ¶ 138.)

Simpson does mention intravenous administration "of the compositions of the present invention, or of formulations comprising such compositions and other materials" in a list of in vivo administration methods. (*Id.* ¶ 272.) But we note that Simpson teaches numerous uses for electroprocessed collagen, such as manufacture of engineered organs in a mold, induction of differentiation of cells in vitro or in vivo, tissue scaffolding (*id.* ¶¶ 11–12, 228–244), and as a delivery vehicle (*id.* ¶¶ 252, 268). Simpson's mention of the possibility of intravenous administration alone may provide one of ordinary skill in the art with some expectation of

success for use of electroprocessed collagen as a delivery vehicle, but the Examiner failed to establish an evidentiary basis to support a conclusion that Simpson makes obvious the intravenous administration of collagen type VII protein comprising an alpha chain having a collagenous triple-helical segment to treat or accelerate healing of a wound in the skin of a subject having epidermolysis bullosa, as required by Appellant's claimed invention.

Furthermore, while Wilkes teaches using intravenous injection of type V collagen that may be recombinantly obtained, the therapy that this collagen is used for is immunosuppressive therapy of a patient with pulmonary disease or, as the Examiner asserts, to prevent or diminish the onset of acute or chronic pathology in the subject." (*See* Ans. 6; *see also* Wilkes claim 1, *see also id*. at col. 42 (Example 10, using type V collagen to suppress alloimmune response to organ transplant).) That has nothing to do with promoting wound healing (Appeal Br. 15), and thus, it does not provide a reasonable expectation that collagen type VII would be able to provide wound healing even if it was reasonable to believe from Wilkes that any collagen type could be administered intravenously without causing adverse effects to the patient (*see* Ans. 16–17 ("the Wilkes reference was used because it teaches that various type of collagen can be administered intravenously")).

While it may be true that one of ordinary skill in the art would have ideally desired to achieve a systemic effect (Ans. 13) with collagen type VII, that desire does not establish that one of ordinary skill in the art would have had a reasonable expectation that intravenous administration would obtain a wound healing effect in the skin by systemically administering a recombinant human collagen type VII protein within the scope of

Appellant's claimed invention. (Appeal Br. 13–14, 19.) That is especially true where Woodley teaches that intradermal administration to skin tissue that was in effect wounded shows activity *locally* in the basement membrane zone of the wounded skin. (*See* Woodley Abs. and 694–95 ("We did not observe the injected human type VII collagen distributed diffusely throughout the dermis of either mouse skin or regenerated RDEB skin. Rather, it was localized to the BMZ between the dermis and epidermis.").)

Thus, we reverse the Examiner's rejection of independent claim 7, and dependent claims 8, 9, 11, 13, 15–18, 20–23, and 25 under 35 U.S.C. § 103(a) as unpatentable over Woodley, Simpson, and Wilkes.

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
7–9, 11, 13, 15–18, 20–23, 25	103(a)	Woodley, Simpson, Wilkes		7–9, 11, 13, 15–18, 20–23, 25

REVERSED