

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RICHARD A. BERG,
PAUL D. TOMAN and DONALD G. WALLACE

Appeal No. 1999-2231
Application No. 08/278,774

ON BRIEF

Before ADAMS, MILLS and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-3, 6-9, 14-16 and 18, which are all the claims pending in the application.

Claims 1 and 6 are illustrative of the subject matter on appeal and is reproduced below:

1. A recombinant procollagen polypeptide chain comprising a natural collagen polypeptide chain, a first natural procollagen C-terminal propeptide and a first non-natural site-specific proteolytic agent recognition site, wherein said first non-natural site-specific proteolytic agent recognition site is located between said collagen chain and said first propeptide.
6. A recombinant procollagen chain according to claim 1, further comprising a second propeptide and a second non-natural site-

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specific proteolytic agent recognition site, wherein said second non-natural site-specific proteolytic agent recognition site is located between said collagen chain and said second propeptide.

The references relied upon by the examiner are:

Olsen et al. (Olsen), "Purification and Characterization of a Peptide from the Carboxy-Terminal Region of Chick Tendon Procollagen Type I," Biochemistry, Vol. 16, No. 13, pp. 3030-3036 (1977)

Prockop et al. (Prockop), "The Biosynthesis of Collagen and its Disorders," New England Journal of Medicine, Vol. 301, No. 1, pp. 13-23 (1979)

Chu et al. (Chu), "Human pro α 1(I) collagen gene structure reveals evolutionary conservation of a pattern of introns and exons," Nature, Vol. 310, pp. 337-340 (1984)

Carter, "Site-Specific Proteolysis of Fusion Proteins," Protein Purification: From Molecular Mechanisms to Large-Scale Processes, Vol. 47, Chp. 13, pp. 181-193 (American Chemical Society 1990)

GROUND OF REJECTION¹

Claims 1-3, 6-9, 14-16 and 18 stand rejected under 35 U.S.C. § 103 as being unpatentable over Chu, Prockop and Olsen in view of Carter.

We affirm the rejection of claims 1-3, 8, 9, 14-16 and 18. We reverse the rejection of claims 6 and 7.

DISCUSSION

In reaching our decision in this appeal, we considered appellants' specification and claims, in addition to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer², and the for the examiner's reasoning in support of the rejections. We further

¹ We note the examiner withdrew the Final rejection of claim 14 under 35 U.S.C. § 112, first and second paragraph. Answer, page 3.

² Paper No. 29, mailed June 19, 1998. We note the Answer incorrectly notes that it is Paper No. 27. Paper No. 27, mailed May 19, 1998 represents a Notification of non-compliance with the requirements of 37 CFR § 1.192(c).

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reference appellants' Brief³, and appellants' Reply Brief⁴ for the appellants' arguments in favor of patentability. We note the examiner considered the Reply Brief, and entered it into the record.⁵

CLAIM GROUPING:

Appellants state (Brief, page 3) that "claims 1-3, 8-9, 14-16 and 18 shall stand as a group; claims 6-7 shall stand as a separate group...." The Brief contains separate arguments for each grouping. Accordingly, group I: claims 1-3, 8, 9, 14-16 and 18 stand or fall together, and group II: claims 6 and 7 stand or fall together. Therefore, with respect to group I, we limit our discussion to representative independent claim 1, claims 2-3, 8, 9, 14-16 and 18 will stand or fall together with claim 1. With respect to group II, we limit our discussion to representative claim 6, claim 7 will stand or fall together with claim 6. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

THE REJECTION UNDER 35 U.S.C. § 103:

The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). In meeting this burden we note that "the test for obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." In re Rosselet, 347 F.2d 847, 851, 146 USPQ 183, 186 (CCPA 1965).

³ Paper No. 28, received May 20, 1998.

⁴ Paper No. 31, received August 24, 1998.

⁵ Paper No. 32, mailed September 3, 1998.

According to the examiner (Answer, page 3) Chu and Prockop “teach the human pro α 1(I) procollagen and the N and C propeptides (see Fig. 3 in each).” The examiner relies on Olsen (Answer, page 3) to “teach the C-terminal propeptide of type I procollagen.” The examiner relies on Carter (Answer, page 3) to teach “that a gene can be fused so as to produce fusion proteins and that these fusion proteins can be specifically cleaved using various chemical and enzymatic means (see Table I).”

According to the examiner (Answer, page 3):

It would have been obvious to one of ordinary skill in the art to make a fusion protein that consisted of collagen and either the N or C-terminal propeptide, as taught in the primary references, using the methods taught in Carter, et. al. ... Whether or not a non-natural amino acid was used and which specific cleavage site and agent was used would have been obvious and well within the skill level of the ordinary artisan, absent unexpected results.

We note that appellants do not discuss Chu, Prockop or Olsen, beyond stating (Brief, page 4) that “[t]o the extent that these references are cited to show that procollagens, including their natural propeptide terminal portions are known in the art, Appellants concur.” Instead, appellants focus their argument on the teachings of Carter.

Claims 1-3, 8-9, 14-16 and 18:

According to appellants (Brief, page 4) “procollagens already have fused propeptides and cleavage sites that enhance proper expression: nowhere does Carter suggest or motivate replacing a native propeptide with a different

propeptide or replacing the proteolytic cleavage site of an existing propeptide with a non-native site.” In addition, appellants argue (Brief, page 5) that:

[o]ne would have to turn Carter on its head to fuse a collagen propeptide to a collagen protein and then call it an “affinity handle”. The whole point of Carter and affinity handles is to take a protein that doesn’t provide a good binding target and stick a convenient tag on it. If collagen propeptides provided affinity tags, there would be no point in making a fusion protein – a suitable handle is already there.

In response, the examiner argues (Answer, page 4) that:

[a]pplicants do not argue that putting two (or three) well known sequences together with a “non-natural site-specific proteolytic agent recognition site” between them would not have been obvious over the prior art but rather [they] argue that there would be no motivation to do so. As stated in the final rejection this construct could be made to purify the collagen with an affinity handle. This is taught in Carter, first paragraph. For instance, an antibody could be made to particular procollagen, the construct of the instant claims could be put on an affinity column containing this antibody bound to a solid matrix, the contaminating proteins washed out and then the site-specific cleavage means could be employed to cleave the collagen molecule, thereby facilitating purification. This same procedure could also have been done batch-wise, not using a column.

The examiner further argues (Answer, bridging paragraph, pages 5-6) that:

[o]ne could make a cleavage site that could be readily and easily cleaved using a site-specific cleavage means instead of using the cleavage means used in the processing of natural collagen, [sic]. This process[ing of natural collagen] uses enzymes thought to be expressed only in cells that naturally produce collagen. In addition, the use of the construct in a purification scheme involving solubility discussed supra has not been addressed by applicants.

As set forth in In re Soderquist, 326 F.2d 1016, 1018, 140 USPQ 387, 389 (CCPA 1964)

It is not necessary in a combination rejection that the structure of one reference be substituted bodily in that of the reference with

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which it is combined. In re Billingsley, 47 CCPA 1108, 279 F.2d 689, 126 USPQ 370; In re Mason, 44 CCPA 727, 240 F.2d 362, 112 USPQ 328. Rather, the question is whether what applicant has done would be obvious from the references in combination.

In our opinion, on the record before us, the examiner has provided sufficient evidence to support a conclusion that the claimed subject matter would have been prima facie obvious within the meaning of 35 U.S.C. § 103.

We note appellants' emphasis (Brief, page 5) that “[a]ll the pending claims require (1) a C-terminal propeptide, whereas the affinity handles of Carter are all N-terminal fusions....” In response to this position, the examiner explains (Answer, page 5) that the claims “only require that the ‘first non-natural site-specific proteolytic agent recognition site is located between said collagen chain and said first propeptide’, not that the affinity handle be a C-fusion.” We note that appellants withdrew their remarks regarding this issue in the Reply Brief.

Accordingly, we affirm the rejection of claim 1 under 35 U.S.C. § 103 as being unpatentable over Chu, Prockop and Olsen in view of Carter. As discussed supra claims 2, 3, 8, 9, 14-16 and 18 fall together with claim 1.

Claims 6 and 7:

According to appellants (Brief, page 5):

[c]laims 6 and 7 further limit claim 1 to require a second propeptide and a second non-natural site-specific proteolytic agent recognition site located between the collagen chain and the second propeptide. As there is no suggestion whatsoever in the cited art of using a second recognition site and a second propeptide, the rejection of claims 6 and 7 under 35 U.S.C. [sic] [§] 103 is improper.

Initially, we note that the examiner failed to address these limitations in his statement of the rejection (Answer, page 3). Further, while explaining how the combination of Chu, Prockop and Olsen in view of Carter meet the limitations of claims 1, 2, 3, 8, 9, 14-16 and 18, the examiner states (Answer, page 5) that “[t]he same is true of claims 6 and 7 where the C-terminal propeptide and the second propeptide could be located at either end of the collagen, or the two propeptides could both [be] located at one end of the collagen [chain].” The examiner, however, fails to identify a suggestion in the art to prepare such a construct.

As discussed above, we agree with the examiner that, in view of the combination of prior art relied upon it would have been prima facie obvious at the time the invention was made to prepare a collagen chain fusion that is substantially the same as the native procollagen molecule but for the presence of a “non-native” site-specific proteolytic agent recognition site located between the collagen chain and the propeptide, as set forth in claims 1, 2, 3, 8, 9, 14-16 and 18. We agree with the examiner that, in view of the combination of prior art relied upon a person of ordinary skill in the art would recognize that such a

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construction would facilitate purification (Answer, page 4), and allow the use of alternative means, as taught by Carter, for cleaving the propeptide from the collagen chain, than those “enzymes though to be expressed only in cells that naturally produce collagen” (Answer, page 5).

In contrast, we can not agree with the examiner’s position that, in view of the combination of prior art relied upon a person of ordinary skill in the art would recognize that “the second propeptide could be located at either end of the collagen, or the two propeptides could be located at one end of the collagen” (Answer, page 5). While a person of ordinary skill in the art may possess the requisite knowledge and ability to make the modifications suggested by the examiner, the modifications are not obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 211 USPQ 1125, 1127 (Fed. Cir. 1984). Here we see no reason, and the examiner failed to identify the reason in the art, to suggest that a person of ordinary skill in the art would modify the references to include a second propeptide and a second non-natural site-specific proteolytic agent recognition site.

The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On these circumstances, we are constrained to reach the conclusion that the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness. Accordingly, we reverse the rejection of claim 6 under 35 U.S.C. § 103 as being unpatentable over Chu, Prockop and Olsen in view of Carter. As discussed supra claim 7 stands together with claim 6.

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

AFFIRMED-IN-PART

DONALD E. ADAMS)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
DEMETRA J. MILLS)	
Administrative Patent Judge)	APPEALS AND
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)	INTERFERENCES
)	
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