

Change

Paper No. 53

**THIS OPINION WAS NOT WRITTEN FOR PUBLICATION**

The opinion in support of the decision being entered today  
(1) was not written for publication in a law journal and  
(2) is not binding precedent of the Board.

**UNITED STATES PATENT AND TRADEMARK OFFICE**

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

*Ex parte* ROBERTO CREA,  
ROY H.L. PANG, HERMANN OPPERMAN,  
PETER C. KECK, GABRIEL ALVARADO-URBINA  
GAY-MAY WU and CHARLES M. COHEN

**MAILED**  
**APR 24 1997**

BOARD OF  
PATENT APPEALS

Appeal No. 93-1823  
Application 07/799,769<sup>1</sup>

**ON BRIEF**

Before WILLIAM F. SMITH, GRON, and ELLIS, *Administrative Patent Judges.*

ELLIS, *Administrative Patent Judge.*

<sup>1</sup> Application for patent filed November 27, 1991. According to appellants, this application is a continuation of Application 07/562,454, filed August 2, 1990, which is a continuation of Application 06/845,541, filed March 28, 1986.

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*DECISION ON APPEAL*

This is an appeal from the final rejection of claims 6, 7, 10 through 13, 32, 33 and 35 through 39.<sup>2</sup> Claims 1 through 5, 8, 9, 14 through 31 and 34 are canceled.

The appealed claims are attached as an appendix to this decision.

As an initial matter, we note the similarity between subject matter claimed and the issues raised in this appeal and Appeal No. 97-0880. Accordingly, we have considered both appeals concurrently.

The claims were rejected in the Answer as follows:

I. Claims 6, 7, 10 through 13, 32, 33 and 35 through 37 stand rejected under 35 U.S.C. § 112, first paragraph, as being enabled only in accordance with pages 2 through 19 of the specification and Figures 1, 2 and 5.

II. Claims 6, 10, 33, 35 and 36 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as their invention.

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<sup>2</sup> Subsequent to the mailing of the Answer, claim 35 was canceled by the appellants and the only rejection encompassing claims 38 and 39 was canceled by the examiner. See Paper Nos. 48 and 50, respectively. Accordingly, claims 38 and 39 are now pending without rejection.

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III. Claims 6, 7, 10 through 13, 32, 33 and 35 through 39 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1, 2, 4, 12, and 17 of copending application 07/888,454.

In response to the Answer, the appellants filed a reply under 37 CFR § 1.193(b) with an accompanying amendment (Paper No. 47) which instructed the examiner to delete claim 35 and to amend the language of claim 33. A terminal disclaimer (Paper No. 49) was also submitted and entered into the file. Accordingly, the examiner withdrew (i) the provisional double patenting rejection set forth as Rejection III above, and (ii) the second paragraph rejection with respect to claims 33 and 35. See Paper No. 50. Therefore, the rejections now before us are Rejection I, *supra*, and a modified Rejection II which encompasses only claims 6, 10 and 36.

We have carefully studied the record in this case which includes, *inter alia*, the Brief (Paper No. 40), the Answer (Paper No. 43), the reply to the Answer (Paper Nos. 47, 48 and 49) and the examiner's letter to the appellants (Paper No. 50), and find ourselves in substantial agreement with the arguments advanced by

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the appellants. We **reverse** both rejections for the reasons set forth in the appellants' Brief, adding the following comments for clarification.

It is well established that claim analysis "should begin with the determination of whether the claims satisfy the requirements of the second paragraph," of 35 U.S.C. § 112. *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971).

*In Moore* the court stated:

[I]t should be realized that when the first paragraph speaks of "the invention", it can only be referring to that invention which the applicant wishes to have protected by the patent grant, i.e., the *claimed* invention. For this reason the claims must be analyzed first in order to determine exactly what subject matter they encompass. The subject matter there set out must be presumed, in the absence to evidence to the contrary, to be that "which the applicant regards as his invention" [emphasis in original].

This first inquiry therefore is merely to determine whether the claims do, in fact, set out and circumscribe a particular area with a reasonable degree of precision and particularity. It is here where the definiteness of the language employed must be analyzed--not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art [footnote and citation omitted].

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According to the examiner, claims 6, 10 and 36 are "indefinite in failing to identify the oligopeptide that links X and CF<sub>tPA</sub> which is defined by L. It is not known from the specification what the metes and bounds of amino acid sequences this encompasses." Answer, p. 5, last paragraph. We find this position untenable.

As pointed out by the appellants, and acknowledged by the examiner,<sup>3</sup> the nature of the oligopeptide linker is not critical. Brief, p. 17, last paragraph. The linker is not the linchpin of the appellants' invention, it merely refers to art-recognized means of joining two peptides together. Therefore, it is reasonable to conclude that one skilled in the art would have understood the claims to encompass the direct linkage of X and CF<sub>tPA</sub> by means of a peptide bond, or linkage by means of any oligopeptide which does not interfere with the biological activity of X and CF<sub>tPA</sub>. Moreover, any question in the examiner's mind as to a possible ambiguity associated with the term "oligopeptide linker" should have been readily resolved by looking to the specification. The specification states on p. 8, lines 18-27 that:

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<sup>3</sup> Answer, p. 14, para. 2.

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L taken together with X represents a bond, or L individually represents a peptide bond linking a polypeptide X to  $CF_{tPA}$  or L represents an oligopeptide linker of desired structure and function. It can be an amino acid sequence which provides a preferential site for cleavage. For example, L can be the cleavage site for Factor  $X_a$ . Incorporation of this site into the analogues provides for cleavage of X and  $CF_{tPA}$  at the site.

In our opinion, one of ordinary skill in this art would have reasonably understood the nature of the subject matter encompassed by the term "L" from these teachings.

Turning to the rejection under the first paragraph of § 112, we observe that the primary concern articulated by the examiner throughout the Answer is best summarized as: the specification fails satisfy the "how to make" aspect of the enablement requirement. It is the examiner's position that the claims should be limited to the working examples disclosed in the specification. We agree that the enablement section of 35 U.S.C. § 112, first paragraph, "requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). But, in order to determine whether the present claims are enabled we, and the examiner, must analyze the teachings of the specification, and make an inquiry into the knowledge of persons

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skilled in the art. In re Bowen, 492 F.2d 859, 861, 181 USPQ 48, 50 (CCPA 1974).

In this case, we find that there are two basic flaws underlying the examiner's reasoning. The first is the mistaken belief that "the claims encompass a prohibitive number of combinations of tPA analogues." Answer, p. 12, lines 24-25. According to the examiner the specification provides "no guidance as to which analogues would be expected to be operative and which would not." Answer, p. 12, lines 17-18. While we agree that the appellants have not disclosed every tPA amino acid sequence which possesses serine protease activity, or tested every region of Protein A to determine which have fibrin binding activity, they are not required to do so. *Compare Atlas Powder Co. v. E.I. Du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 414 (Fed. Cir. 1984); *In re Dinh-Nguyen*, 492 F.2d 856, 858-59, 181 USPQ 46, 48 (CCPA 1974) ("[i]t is not the function of the claims to specifically exclude either possible inoperative substances or ineffective reactant proportions"). Rather, the critical inquiry is- given the teachings of the specification would one skilled in the art have been enabled to make an analogue of tPA having the claimed characteristics.

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To that end we point out that the claims are directed to a fusion protein comprising two functional components; i.e., a catalytic fragment of tPA and a fibrin-binding domain of Protein A. The specification discloses that the catalytic fragment of human tPA encompasses amino acids 262-527. See, for example, specification, p. 2, line 28- p. 3, line 2; p. 5, lines 4-10. The specification also discloses that the B domain of Protein A has fibrin binding activity. Specification, p. 10, lines 8-18. Finally, the specification describes how to construct an analogue of tPA comprising polypeptides derived from the aforementioned regions. Specification, pp. 19-43; Fig. 5. Thus, unquestionably the specification would have enabled one skilled in the art to make an analogue of tPA having fibrinolytic and fibrin-binding activity as described in the claims. Moreover, if such person wished to make an analogue of tPA other than those disclosed by the appellants, but which possesses the same biological properties, she would only need to read the specification which discloses biological assays that readily enable one to determine whether a polypeptide has the relevant attributes. See specification, p. 35, lines 3-25 for the assay to detect the conversion of plasminogen into plasmin; pp. 36 and 43, for the fibrin binding

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assays. Since the examiner has not challenged the precision or reliability of either of these assays, it is reasonable to conclude that one skilled in this art, given the teachings of the assays, would have been able to readily determine which analogues within the scope of the claims would work and which would not.

The examiner's second problem is based on a misunderstanding of the meaning of "undue experimentation." The examiner is apparently of the opinion that since the only disclosed means of determining which additional polypeptides are encompassed by the claim requires performing an assay, the experimentation is "undue."<sup>4</sup> We disagree. To perform an assay which is fully disclosed, as is true in the present case, *may* require a considerable amount of experimentation depending on the number of

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<sup>4</sup> We direct attention to the holding of the court in *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) that:

The first paragraph of 35 U.S.C. § 112 requires, *inter alia*, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without "undue experimentation." *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). That *some* experimentation may be required is not fatal; the issue is whether the amount of experimentation required is "undue." *Id.* at 736-37, 8 U.S.P.Q.2d at 1404 (emphasis in original).

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routine in nature, and not "undue." That is, one skilled in the art would have been able to readily perform the assays disclosed in the specification without needing further inventive skill or ingenuity (such as the development of new assays or protocols), and determine which polypeptides possess the claimed biological properties. *Fields v. Conover*, 443 F.2d 1386, 1390-91, 170 USPQ 276, 279 (CCPA 1971).

Accordingly, Rejections I and II are reversed.

**REVERSED**

  
WILLIAM F. SMITH

Administrative Patent Judge



TEDDY S. GRON

Administrative Patent Judge



JOAN ELLIS

Administrative Patent Judge

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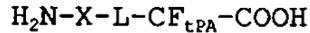
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**APPENDIX**

6. An analogue of tissue plasminogen activator (tPA)  
of the formula: \_\_\_\_\_



wherein  $\text{CF}_{\text{tPA}}$  represents a catalytic fragment of tPA;

X represents a fibrin binding domain of protein A  
present in single or multiple units; and

L represents a peptide bond linkage between X and  $\text{CF}_{\text{tPA}}$   
or an oligopeptide linking X and  $\text{CF}_{\text{tPA}}$ , wherein said analogue  
possesses fibrinolytic and fibrin-binding activities.

7. A tPA analogue of Claim 6, wherein X is the B domain of  
protein A.

10. An analogue of tissue plasminogen activator (tPA) of  
the formula:



wherein  $\text{CF}_{\text{tPA}}$  represents a catalytic fragment of tPA;

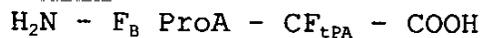
$\text{F}_{\text{BProA}}$  represents the B domain of protein A;

L represents a peptide bond or an oligopeptide linker  
linking  $\text{F}_{\text{BProA}}$  and  $\text{CF}_{\text{tPA}}$ ; and

n is an integer from 1 to 5, wherein said analogue  
possesses fibrinolytic and fibrin-binding activities.

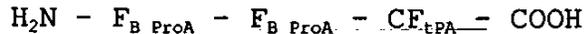
11. An analogue of Claim 10, wherein  $\text{CF}_{\text{tPA}}$  is the catalytic  
fragment spanning amino acid residues 262-527 of tPA as shown in  
Figure 1 or a fragment having substantially equivalent  
thrombolytic activity.

12. A tPA analogue of Claim 10, having the formula:



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13. A tPA analogue of Claim 10, having the formula:

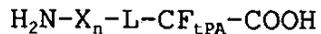


32. An analogue of tissue plasminogen activator (tPA) comprising a domain of protein A that binds fibrin linked through its carboxy terminus to the amino terminus of a catalytic fragment of tPA, wherein said analogue possesses fibrinolytic and fibrin-binding activities.

33. An analogue of tissue plasminogen activator of Claim 32, wherein the domain of protein A that binds fibrin is the B domain of protein A or multiple units thereof.

35. An analogue of tissue plasminogen activator of Claim 34, wherein the prokaryotic fibrin binding polypeptide is the B domain of protein A.

36. An analogue of tissue plasminogen activator (tPA) of the formula:



wherein  $\text{CF}_{\text{tPA}}$  is the catalytic fragment spanning amino acid residues 262-527 of tPA as depicted in Figure 1

X represents a fibrin binding domain of protein A;

L represents a peptide bond or an oligopeptide linker separating X and  $\text{CF}_{\text{tPA}}$ ;

and

n is an integer from 1 to 5.

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37. An analogue of tissue plasminogen activator (tPA), comprising a catalytic fragment of human tPA linked at its amino terminus directly to the B domain of protein A or multiple units thereof.

38. An analogue of Claim 37, wherein the catalytic fragment of human tPA comprises amino acid residues 262-527 of tPA as shown in Figure 1.

39. An analogue of tissue plasminogen activator (tPA), comprising a catalytic fragment of human tPA spanning amino acid residues 262-527 of tPA as shown in Figure 1 linked at its amino terminus directly to a B domain of protein A.