

EXHIBIT

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JUN 24 1987

MARSHALL, OTOOLE



**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

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Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
06/0754290	11/30/84	LLR	710

HERKHOFF, MARSHALL & BICKNELL
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EXAMINER	
ART UNIT	PAPER NUMBER
	17

DATE MAILED: 06/24/87

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

This application has been examined Responsive to communication filed on 3/12/87 This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~from~~ from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- Notice of References Cited by Examiner, PTO-892.
- Notice re Patent Drawing, PTO-948.
- Notice of Art Cited by Applicant, PTO-1449
- Notice of Informal Patent Application, Form PTO-152
- Information on How to Effect Drawing Changes, PTO-1474
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Part II SUMMARY OF ACTION

1. Claims 1-13, 16, 37-57, 59, 60 and 73-103 are pending in the application.

Of the above, claims 1-13, 16, 37-57, 59 and 60 are withdrawn from consideration.

2. Claims _____ have been cancelled.

3. Claims _____ are allowed.

4. Claims 73-103 are rejected.

5. Claims _____ are objected to.

6. Claims _____ are subject to restriction or election requirement.

7. This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.

8. Allowable subject matter having been indicated, formal drawings are required in response to this Office action.

9. The corrected or substitute drawings have been received on _____. These drawings are acceptable; not acceptable (see explanation).

10. The proposed drawing correction and/or the proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been approved by the examiner. disapproved by the examiner (see explanation).

11. The proposed drawing correction, filed _____, has been approved. disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections **MUST** be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.

12. Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has been received not been received

been filed in parent application, serial no. _____; filed on _____

13. Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. Other

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AM 27 008492

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Serial NO. 675,298

2

Art Unit 127

The sequences on pages 38-40 designated as Table V; on pages 43-47 designated as Table VI; on page 50 as Table VII; on page 67 as Table IX; on page 69 as Table XI; on page 71 as Table XIII; on page 72 as Table XIV; on page 77 as Table XVI; on page 79 as Table XVIII; on page 81 as Table XX and on page 82 as Table XXI are not in fact Tables but drawings. As such they should be presented as official drawings and applicant is so required. In this regard it should be noted that Tables V VI submitted as part of an Exhibit are not official drawings since an exhibit is an improper way of presenting drawings. They should be submitted separately. Moreover, the designation on drawings that they are also Tables is improper and inaccurate. Note that in conforming to this requirement applicant should renumber the remaining Tables.

The previously approved citation of Documents A13, A15 and A16 has been withdrawn since those documents have not been submitted.

Claims 73-102 are rejected under 35 U.S.C. 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation of markush member (c) in claim 73

375

382

: Dial No. 675,298

3

Art Unit 127

is indefinite and unduly broad. It is not clear what is meant by the recitation "but for the degeneracy of the genetic code." Also the language "would hybridize ..." is permissive and thus not an absolute limitation. Further the Markush member (c), and the sequence of claim 77 and 96 appear to embrace substantially all known DNA sequences since the isolated DNA sequence is not designated as encoding for erythropoietin. One that encodes for a protein having "a" therapeutic activity of erythropoietin is not the same thing. In order to embrace the subject matter of that Markush member (c) a separate claim drawn to an isolated DNA sequence encoding an erythropoietin selected from the group consisting of human and monkey erythropoietin would be acceptable. The embodiments of claims 77 and 96 could properly be expressed as for example an isolated DNA sequence consisting of a DNA sequence encoding a polypeptide having the structure sufficiently duplicative of that of a naturally-occurring erythropoietin to allow possession of the biological properties of being able to cause bone marrow cells to increase hemoglobin synthesis and iron uptake and stimulate reticulocyte response. Claim 74 appears to read on naturally occurring erythropoietin producing cells. Claims 84, 86, 87, 89, 90 and 99 are redundant of claim 77 or claim 96 since the DNA sequence has no memory of its creation.

386

383

Dial No. 675,298

4

Art Unit 127

Claim 100 absent the designation "isolated" reads on naturally occurring mutant erythropoietin sequences.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless-

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

397

384

Serial No. 675,298

5

Art Unit 127

Claims 73-79, 81, 84, 85, 88 and 91-99 are rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Talmadge et al who disclose the expression of a mammalian protein using recombinant DNA transformed microorganisms. In view of the rejections under 35 USC 112 supra, the claims are deemed to embrace the recombinant materials disclosed by Talmadge et al.

Claims 73-103 are rejected under 35 U.S.C. 103 as being unpatentable over any of Goldwasser et al (US 4,558,005) of record, Weiss et al (PNAS Vol. 79) of record and Egrie (US 4,558,006) taken in view of either Young et al or Broome et al and in further view of Ullrich et al or Martial et al. Goldwasser, Weiss et al and Egrie teach the preparation of a monoclonal antibody to human erythropoietin. Young et al and Broome et al teach a process of isolating genes using antibody probes. More specifically, Young et al teach isolating unknown foreign antigenic proteins encoded by antigen producing clones of a lambda gt11 recombinant cDNA library by using antibody probes. The foreign gene is inserted into the galactosidase gene of the lambda phage so as to result in a fused protein. Ullrich et al and Martial teach a basic process for isolating mRNA and converting it into a cDNA library for use in cloning and expressing mammalian genes. It would be obvious to prepare erythropoietin as a fused peptide by extracting

398

385

Patent No. 675,298

6

Art Unit 127

the messenger RNA for erythropoietin from kidney cells known to be rich therein and converting that mRNA to a cDNA library in the manner taught by Ullrich et al or Martial. If desired, substituting the lambda gt 11 phage library vector of Young et al for its advantages would be an obvious choice. It would further be obvious to use the Young et al or Broome et al gene isolating technique together with erythropoietin antibody of the primary references as a probe for isolating a clone producing erythropoietin. At best only routine genetic engineering techniques would be involved.

ATanenholtz/klc

703/557-3920

6-18-87

Alvin E. Tanenholtz
ALVIN E. TANENHOLTZ
PRIMARY EXAMINER
ART UNIT 127

379

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Sheet 2 of 11

Form PTO-1449 (REV. 2-82)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO. 7183	SERIAL NO. 675,298	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)				APPLICANT FU-KUEN LIN		
				FILING DATE Nov. 30, 1984	GROUP 127	
U.S. PATENT DOCUMENTS						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
<i>JMY</i>	A12 4 4 6 5 6 2 4	8/14/84	Chiba, et al.			
<i>JMY</i>	A13 4 6 3 7 2 4		Esrie (not enclosed)	See, B5		
<i>JMY</i>	A14 4 8 3 4 5 1	4/15/83	Alton, et al. (not enclosed)	See, B11		
<i>JMY</i>	A15 4 8 7 7 5 3		Bitter (not enclosed)	See, B9		
<i>JMY</i>	A16 6 3 6 7 2 7		Morris (not enclosed)	See, B12		
<i>JMY</i>	A17 4 4 6 8 4 6 6	8/28/84	Cohen et al.			
<i>JMY</i>	A18 4 5 0 3 1 5 1	3/5/85	Paddock			
<i>JMY</i>	A19 4 4 4 2 2 0 5	4/10/84	Hamer et al.			
<i>JMY</i>	A20 4 4 1 1 9 9 4	10/25/83	Gilbert et al.			
<i>JMY</i>	A21 4 3 3 8 3 9 7	7/6/82	Gilbert et al.			
<i>JMY</i>	A22 4 5 6 8 4 8 8	2/4/86	Lee-Huang			
FOREIGN PATENT DOCUMENTS						
	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
<i>JMY</i>	B6 0 1 1 7 0 5 8	8/29/84	European Patent Office			
<i>JMY</i>	B7 0 1 1 7 0 5 9	8/29/84	European Patent Office			
<i>JMY</i>	B8 0 1 1 7 0 6 0	8/2/84	European Patent Office			
<i>JMY</i>	B9 0 1 2 3 2 9 4	4/19/84	European Patent Office			
<i>JMY</i>	B10 2 0 8 5 8 8 7	5/6/82	United Kingdom			
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)						
<i>JMY</i>	C4	Baron, et al., Cell, 28, pp. 395-404 (1982)				
<i>JMY</i>	C5	Beaucage, et al., Tetrahedron Letters, 22, pp. 1859-1862 (1981)				
<i>JMY</i>	C6	Billat, et al., Expt.Hematol., 10(1) 133-140 (1982)				
EXAMINER <i>Joanne M. Gasser</i>			DATE CONSIDERED <i>June 2, 1986</i>			
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.						

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Sheet 1 of 1

Form PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		ATTY. DOCKET NO. 7183		SERIAL NO. 675,29R	
		APPLICANT FU-KUEN LIN			
		FILING DATE November 30, 1984		GROUP 127	
U.S. PATENT DOCUMENTS					
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS					
	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS TRANSLATION YES NO
<i>NA</i>	B15/85	01/9/85	PCT	—	—
<i>MC</i>	B16/86	03/5/86	PCT	—	—
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)					
<i>MC</i>	C 135	Lin, et al., <u>Exp.Hematol.</u> , 12, 357 (1984)			
<i>MC</i>	C 136	Lee-Huang, <u>Blood</u> , 56, 627-624 (1980)			
EXAMINER		DATE CONSIDERED			
<i>Tarenta</i>		5/1/87			
*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 509; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					

302

390

TO SEPARATE. TOP AND BOTTOM EDGES, SNAP-APART AND HARD CARBON

FORM PTO-892 (REV. 3-78)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		SERIAL NO. 675298	GROUP ART UNIT 127	ATTACHMENT TO PAPER NUMBER 18	
NOTICE OF REFERENCES CITED				APPLICANT(S) <i>Lin</i>			
				U.S. PATENT DOCUMENTS			
	DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE	
A	4558006	12/10/85	Egrie	435	70	2/4/83	
B							
C							
D							
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F							
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FOREIGN PATENT DOCUMENTS							
	DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	Pgs. SHTS. DWG
L							
M							
N							
O							
P							
Q							
OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)							
R	Young et al PNAS vol 80 pp 1194-1198 March 1983						
S	Broome et al PNAS vol 75 pp 2746-2749 June 1978						
T	Ullrich et al Science vol 196 pp 1313-1319 June 17 1977						
U	Mantel et al Science vol 205 pp 602-606 Aug. 10 1979						
EXAMINER <i>Tanenhat</i>		DATE 6/17/87					
A copy of the references is not being furnished with this office action. (See Manual of Patent Examining Procedure, section 707.05 (a).)						380 388	

TO SEPARATELY HOLD TOP AND BOTTOM EDGES, SNAP-APART AND CARD CARBON

FORM PTO-892 (REV. 3-78)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE			SERIAL NO. 675298	GROUP/UNIT 22	ATTACHMENT TO PAPER NUMBER	
NOTICE OF REFERENCES CITED					APPLICANT(S) Lin			
U.S. PATENT DOCUMENTS								
*	DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE		
A								
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FOREIGN PATENT DOCUMENTS								
*	DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG.	PP. SPEC.
L								
M								
N								
O								
P								
Q								
OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)								
	R	Bennetzen et al 1982 "Codon Selection in Yeast" J. Biol Chem 257(6) 3026-31						
	S	Lewin Genes 8th John Wiley & Sons p 307						
	T							
	U							
EXAMINER Jeanne M. Giesse				DATE 6/2/86				
* A copy of this reference is not being furnished with this office action. (See Manual of Patent Examining Procedure, section 707.05 (a).)								

389

381