1994-1995
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Pieczenik

Serial No. 07/662,764:

Filed: February 28, 1991

For: METHOD AND MEANS FOR SORTING AND IDENTIFYING BIOLOGICAL INFORMATION

STATUS REQUEST FOR APPLICATION ON APPEAL

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Appellant respectfully requests an estimate of the time when the appeal in the above-identified application will be heard and/or decided. Response by return facsimile is requested.

It is believed that the present inquiry does not require the payment of any fee. If this is incorrect, however, please charge the required amount to Deposit Account 07-1969.

Respectfully submitted,

Donna M. Ferber
Reg. No. 53,876

GREENLEE, WINNER AND SULLIVAN, P.C.
5370 Manhattan Circle, Suite 201
Boulder, CO 80303
Telephone (303) 499-8080
Facsimile: (303) 499-8089
email: winner@greenwlaw.com

Attorney Docket No.: 4-89A
bmk: February 12, 1998

CERTIFICATE OF TRANSMISSION
I hereby certify that this correspondence is being transmitted by facsimile to the Patent and Trademark Office
No. 703-308-7952

12 February 1998 B. Kroge
Date B. Kroge

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00751
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: 

Pieczeniak 

Group Art Unit: 1204

Serial No. 07/662,764: 

Examiner: N. Vogel

Filed: February 28, 1991 

For: METHOD AND MEANS FOR SORTING 
AND IDENTIFYING BIOLOGICAL INFORMATION

STATUS REQUEST FOR APPLICATION ON APPEAL

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Appellant respectfully requests an estimate of the time when the appeal in the above-identified application will be heard and/or decided. Response by return facsimile is requested.

It is believed that the present inquiry does not require the payment of any fee. If this is incorrect, however, please charge the required amount to Deposit Account 07-1969.

Respectfully submitted,

[Signature]

Donna M. Ferber
Reg. No. 33,878

Pieczeniak and ICT v. Dyax 00 Civ. 0243 (IIB) 00752
RESPONSE TO STATUS INQUIRY

This is in response to the Status Inquiry filed on Feb 12, 1998, in Application No. 07/662,764. Appeal No. 96-1094 status of the application is indicated as follows:

( ) Your appeal was received on ______________ at the Board and it is currently awaiting review prior to docket assignment.

(x) Your appeal is currently assigned to the docket of an Administrative Patent Judge. There are ___56___ appeals ahead of your appeal on that judge's docket.

( ) Your appeal has been reviewed and is currently awaiting assignment of a hearing date.

If there are any questions regarding the status of this or any other application awaiting decision at the Board, please call one of the Program and Resources Administrators at (703) 308-9797.

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00753
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
Pieczenik  
: Group Art Unit: 1805
Serial No. 07/662,764  
: Examiner: N. Vogel
Filed: February 28, 1991  
: Appeal No. 96-1094
For:  
METHOD AND MEANS FOR SORTING  
AND IDENTIFYING BIOLOGICAL  
INFORMATION

ASSOCIATE POWER OF ATTORNEY  
UNDER 37 C.F.R. 1.34

Asst. Commissioner for Patents  
Washington, D.C. 20231

Sir:

Pursuant to 37 C.F.R. Section 1.34, and as a Principal Attorney of Record, I respectfully request that Joseph S. Littenberg, Registration No. 20,382; Marcus J. Millet, Registration No. 28,241; and Shawn P. Foley, Registration No. 33,071, of Lerner, David, Littenberg, Krumholz and Mentlik, 600 South Avenue West, Westfield, New Jersey 07090 be recognized as Associate Attorneys in the above-referenced application.

Respectfully submitted,

Donna M. Ferber  
Reg. No. 33,878

GREENLEE, WINNER AND SULLIVAN, P.C.  
5370 Manhattan Circle, Suite 201  
Boulder, CO 80303  
Telephone (303) 499-8080  
Facsimile: (303) 499-8089  
Email: winner@greenwin.com

Attorney Docket No. 4-89A  
bmk: March 16, 1998

CERTIFICATE OF MAILING
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C., 20231.

D. Ferber  
Date 3/16/98

Pieczenik and ICT v. Dyax    00 Civ. 0243 (HB)    00754
PLEASE ACKNOWLEDGE RECEIPT OF THE FOLLOWING:

Associate Power (1 pg)

Attorney docket 4-89A
07/662,764 Appeal No. 96-1094
dmt/bk
Mar 16 98
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.
If reconsideration by the examiner does not promptly result in the withdrawal of all pending rejections, the examiner must return this application to the jurisdiction of the board so that the appeal may be restored to its existing place in the order in which appeals are decided. A new appeal number will not be assigned nor will a new appeal fee be required in the event that the examiner returns this application to the jurisdiction of the board following reconsideration.

This application, by virtue of its "special" status, requires immediate action by the examiner. See MPEP § 708.01(d). The Board of Patent Appeals and Interferences must be informed promptly of any action affecting the appeal in this case, including reopening of prosecution, allowance and/or abandonment of the application.

REMANDED

BRUCE H. STONE, JR., Chief
Administrative Patent Judge

GARY V. HARKOM, Vice Chief
Administrative Patent Judge

WILLIAM F. SMITH
Administrative Patent Judge

-2-
TELECOPY/FACSIMILE TRANSMISSION

TO: Shawn Foley
FIRM: 
ATTORNEY'S DOCKET # OR SERIAL#: 07/662764
FAX/TELECOPIER NUMBER: (908) 654-7866
DATE: April 16, 1998

FROM: Examiner John S. Brusca, Ph.D.
ART UNIT 1636
FAX: (703) 305-7939
PHONE: (703) 308-4231
MAILING ADDRESS: John S. Brusca
Art Unit 1636
U.S. Patent and Trademark Office
Crystal Mall 1
7th Floor Receptionist
1911 S. Clark Street
Arlington, VA 22202
7th Floor Receptionist phone: (703) 308-0196

PAGES, INCLUDING COVER SHEET:

COMMENTS: Enclosed is a courtesy copy of interview summary of interview in Pieczenik (07/662764) of 4/15/98. This was not provided to you at the time of the interview by Office error. A copy is being mailed to the correspondence address of Greenlee and Associates. An Associate Power of Attorney has not been entered in the application as of today. Lorance Greenlee was contacted and gave permission to forward to you this copy of the interview summary. He informed me that an Associate Power of Attorney naming you has been filed in this application and that the correspondence address remains Greenlee and Associates. I will contact you with any questions regarding the application.

IF YOU HAVE NOT RECEIVED ALL THE PAGES OF THIS TRANSMISSION, PLEASE CONTACT THE EXAMINER AT THE TELEPHONE NUMBER LISTED ABOVE.

ALL FAX MACHINES RECEIVE TRANSMISSIONS 24 HOURS PER DAY, SEVEN DAYS PER WEEK.

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THE DOCUMENT(S) ACCOMPANYING THIS FACSIMILE TRANSMISSION CONTAIN(S) INFORMATION FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE WHICH IS CONFIDENTIAL AND/OR LEGALLY PRIVILEGED. THIS INFORMATION IS FOR THE USE OF THE INDIVIDUAL OR FIRM NAMED ON THIS SHEET. IF YOU ARE NOT THE INTENDED RECIPIENT, YOU ARE HEREBY NOTIFIED THAT ANY DISCLOSURE, COPYING, DISTRIBUTION, OR THE TAKING OF ANY ACTION IN RELIANCE ON THE CONTENTS OF THIS INFORMATION IS STRICTLY PROHIBITED. THE DOCUMENTS SHOULD BE RETURNED TO THE PATENT AND TRADEMARK OFFICE IMMEDIATELY. IF THIS FACSIMILE IS RECEIVED IN ERROR, PLEASE NOTIFY THE EXAMINER LISTED HEREON IMMEDIATELY.

Pieczenik and ICI v. Dyax 00 Civ. 0243 (HB) 00759
## Interview Summary

All participants (applicant, applicant's representative, PTO personnel):

1. **John S. Brusca** (PTO)
2. **George Elliott** (PTO)
3. **Shawn Foley**
4. **Joseph Littenberg**

**Date of interview:** 4/16/98

**Type:** □ Telephonic  ✔ Personal (copy is given to □ applicant  □ applicant's representative).

**Exhibit shown or demonstration conducted:** □ Yes  ✔ No. If yes, brief description:

---

**Agreement:** □ was reached.  ✔ was not reached.

**Claim(s) discussed:** 1, 3-6, 8, 11-15, and 17-21

**Identification of prior art discussed:**

**Goulian et al.**

**Description of the general nature of what was agreed to if an agreement was reached, or any other comments:**

Claim language was discussed which would overcome the outstanding rejections over prior art. The Applicants were informed that the rejection of claims under 35 U.S.C. § 112, first paragraph would be withdrawn. The Applicants agreed to file shortly an amendment addressing the remaining rejections of the pending claims.

---

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

---

1. ✔ It is not necessary for applicant to provide a separate record of the substance of the interview.

Unless the paragraph above has been checked to indicate to the contrary, A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a response to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW.

Since the Examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the interview unless box 1 above is also checked.

---

** Examiner Note:** You must sign and stamp this form unless it is an attachment to a signed Office action.

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Piecznik and ICT v. Dyax 00 Civ. 0243 (HDB) 00760
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: 
Pieczenik : Group Art Unit: 1805
Serial No. 07/662,764 : Examiner: N. Vogel
Filed: February 28, 1991 : Appeal No. 96-1094

For: METHOD AND MEANS FOR SORTING AND IDENTIFYING BIOLOGICAL INFORMATION

ASSOCIATE POWER OF ATTORNEY
UNDER 37 C.F.R. 1.34

Asst. Commissioner for Patents
Washington, D.C. 20231

Sir:

Pursuant to 37 C.F.R. Section 1.34, and as a Principal Attorney of Record, I respectfully request that Joseph S. Littenberg, Registration No. 20,382; Marcus J. Millet, Registration No. 28,241; and Shawn P. Foley, Registration No. 33,071, of Lerner, David, Littenberg, Krumholz and Mendlik, 600 South Avenue West, Westfield, New Jersey 07090 be recognized as Associate Attorneys in the above-referenced application.

Respectfully submitted,

[Signature]
Donna M. Ferber
Reg. No. 33,878

CERTIFICATE OF MAILING
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C., 20231

[Signature]
Date March 16, 1998

GREENLEE, WINNER AND SULLIVAN, P.C.
5370 Manhattan Circle, Suite 201
Boulder, CO 80303
Telephone (303) 499-8080
Facsimile: (303) 499-8089
Email: winner@greenwin.com

Attorney Docket No. 1-69
bank: March 16, 1998
Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks
**Interview Summary**

<table>
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<th>Applicant(s)</th>
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Examiner: John S. Brusca  
Group Art Unit: 1636

All participants (applicant, applicant's representative, PTO personnel):

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<td>(1)</td>
<td>John S. Brusca (PTU)</td>
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<td>(2)</td>
<td>George Elliott (PTO)</td>
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<td>Shawn Poley</td>
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<td>(4)</td>
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Date of Interview: 4/15/98

Type: □ Telephonic  ✗ Personal (copy is given to □ applicant □ applicant's representative).

Exhibit shown or demonstration conducted: □ Yes  ✗ No. If yes, brief description:

Agreement: □ was reached. ✗ was not reached.

Claim(s) discussed: 1, 3-6, 8, 11-15, and 17-21

Identification of prior art discussed:

Goulen et al.

Description of the general nature of what was agreed to if an agreement was reached, or any other comments:

Claim language was discussed which would overcome the outstanding rejections over prior art. The Applicants were informed that the rejection of claims under 35 U.S.C. § 112, first paragraph would be withdrawn. The Applicants agreed to file shortly an amendment addressing the remaining rejections of the pending claims.

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

1. ✗ It is not necessary for applicant to provide a separate record of the substance of the interview.

Unless the paragraph above has been checked to indicate to the contrary, A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW (See MPEP Section 713.04). If a response to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW.

2. □ Since the Examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the interview unless box 1 above is also checked.

Examiner Note: You must sign and stamp this form unless it is an attachment to a signed Office action.

JOHN S. BRUSCA  
PATENT EXAMINER  
ART UNIT 1636

Pieczenik and ICI v. Dyax  00 Civ. 0243 (HB)  00763
**FACSIMILE TRANSMITTAL SHEET**

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<td>Date:</td>
<td>May 18, 1998</td>
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<td>Fax Number</td>
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Number of Pages (Including Cover Page): 12

Client/Matter No: ICTECH/02

Original Being Mailed? No

Attached:

- Amendment Cover Sheet
- Amendment
- Copy of ASSOCIATE POWER OF ATTORNEY

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2) Busy
4) No facsimile connection

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Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00765
*** Transmission Result Report (May 18, 1998 1:15PM) ***

T T I
LERNER DAVID LITENBERG

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Reason for Error
1) Line busy or line fail
2) Busy
3) No answer
4) No facsimile connection

Pieczenik and ICT v. Dyax  00 Civ. 0243 (HB)  00766
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Transmitted herewith is an amendment in the above-identified application. The fee has been calculated as shown below.

CLAIMS AS AMENDED

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* If the entry in col. 2 is less than entry in col. 4 write "0" in col. 5.
** If the "highest number paid for" in this space is less than 20, write "20" in this space.
*** If the "highest number paid for" in this space is less than 3, write "3" in this space.

1. (a) ☒ A Verified Statement to establish small entity status under 37 C.F.R. 1.55 has been filed.
(b) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.55 is enclosed.
2. ☐ No additional fee is required.
3. ☒ Charge $41.00 to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.
4. ☒ Please charge any additional fees or credit overpayment to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

LEARNER, DAVID, LITTEenberg, KHOHOLZ & MENTLIK

Shawn P. Foley
Reg. No. 77,071

600 South Avenue West
Westfield, NJ 07090-1497
Telephone: (908) 654-5000
Facsimile: (908) 654-7866

F://D007/035A035/DL14352.DOC

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00767
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Pieczenik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and
Identifying Biological Information

AMENDMENT

Sir:

This is pursuant to the Remand of the above-captioned patent application from the Board of Appeals to the examination division for further consideration. In view of the indication by the Examiner that the finality of the Office action mailed February 24, 1994 has been withdrawn, this Amendment is being filed pursuant to Rule 115. In the event that any fees are occasioned by this Amendment, the Commissioner is authorized to charge Deposit Account No. 12-1059 accordingly.

A copy of the ASSOCIATE POWER OF ATTORNEY, mailed March 16, 1998, and naming the undersigned, is attached hereto. Applicant has been advised that as of even date herewith, this document has not been made of record. Accordingly, this Amendment is also being filed under Rule 34(a).

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent Office on the date shown below.

Shawn P. Foley, Reg.
Signature

May 18, 1998
Date
To: U.S.P.T.O
Attn: John S. Brusca
Fax No.: (703)305-7939
No. of Pages: 9
IN THE CLAIMS:

Cancel claim 1 and substitute new claim 29 therefore.

A population of oligonucleotides comprising double-stranded oligonucleotides, wherein each oligonucleotide in said population consists essentially of a coding region having a length of from about 4 to about 12 nucleotide triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues, and 5' and 3' flanking sequences that permit said oligonucleotides to be ligated into a vector,

and wherein the sum of said corresponding peptide sequences represents at least about 10% of all possible peptide sequences of said length.

(3)(amended). The oligonucleotide population of claim [1] 22 wherein the length of the coding region of each (sequence) oligonucleotide (comprising said selected length) is from 4 to 7 nucleotide triplets.

(4)(amended). The oligonucleotide population of claim [1] 23 wherein the population which is generated by random shearing of mammalian genetic material and size fractionation.

(5)(amended). The oligonucleotide population of claim [1] 24 wherein the population which is chemically synthesized from component nucleotides or codons.

(6)(amended). A population of recombinant vectors comprising:

substantially identical autonomously replicating nucleic acid sequences which nucleic acid sequences comprise a recombinant structural gene, each of the structural genes having inserted therein one member of an oligonucleotide population [into which insertions of nucleic acid sequences can be made, and

oligonucleotide inserts] wherein each member of said oligonucleotide population has [consisting essentially of a population of oligonucleotide inserts wherein each insert consists essentially of a sequence] a length from about 4 to about 12 nucleotide triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues, [in the order
Application No. 07/652,764

and identity of said triplets being random, and wherein each oligonucleotide insert has the same length, and

wherein each member of [the] said population of oligonucleotides [inserts] is [inserted in vitro into the structural gene of the replicating sequences to form a recombinant structural gene, and] contained in said recombinant vector population, and

wherein said recombinant structural genes are [vectors are capable of expressing] expressed upon transfer of said recombinant vectors [the recombinant structural genes when transferred] into [Escherichia coli] Escherichia coli host cells, and wherein expression of the recombinant structural genes yields polypeptides, each polypeptide comprising [a] said corresponding peptide sequence [encoded by the oligonucleotide insert and each comprising one length of from about 4 to about 12 L-amino acid residues encoded by the respective oligonucleotide inserts].

8. (amended). The vector population of claim 6 wherein each oligonucleotide insert has the same number of random sequences and wherein each random sequence comprises a single length from 4 to 7 nucleic acid triplets.

10. (amended). The vector population of claim 14 wherein the viral [replication] replicating sequence is lambda gt11.

19. (amended). The oligonucleotide population of claim 1 (amended) wherein each of said encoded corresponding peptide sequences [is capable of forming a] forms a binding pair with an antibody that has not been selected by immunization with said peptide sequence or said peptide sequence in conjugated form, said antibody being selected from the group consisting of all antibodies produced by lymphoid-derived antibody-producing cells, where the group [of all] contains antibodies [together is capable of binding to] that bind substantially all members of the discrete oligopeptide population encoded by [the] said oligonucleotide population of claim 1.

20. (amended). The vector population of claim 8 wherein each of the [generated] encoded corresponding [polypeptides] [is capable of forming] forms a binding pair with an antibody that has not been elicited by immunization with said peptide or said peptide in
Application No. 07/662,764

conjugated from said antibody being selected from the group consisting of all antibodies produced by lymphoid-derived antibody-producing cells, where the group of all antibodies together recognizes substantially all epitopic sequences.

Cancel claim 21, and substitute new claim 30 therefore.

30. A method of producing a population of epitopic peptide sequences, comprising the steps of:

- providing a population of recombinant E. coli cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising substantially identical autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene having inserted therein one member of an oligonucleotide population wherein each member of said oligonucleotide population having length from about 4 to about 12 nucleotide triplets that encodes a corresponding epitopic peptide sequence of from about 4 to about 12 L-amino acid residues, and wherein each member of said oligonucleotide population is contained in said recombinant vector population and wherein the sum of said corresponding epitopic peptide sequences represents substantially all possible peptide sequences of said length; and
- culturing said recombinant E. coli cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

Please add the following new claims.

31. A population of recombinant vectors comprising:

- substantially identical autonomously replicating nucleic acid sequences comprising a recombinant structural gene, each structural gene having inserted therein a member of an oligonucleotide population, wherein each member of said oligonucleotide population having length from about 4 to about 12 nucleotide triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues, and wherein the sum of corresponding peptide sequences encoded by said oligonucleotide population represents at least about 10% of all possible peptide sequences of said length,
Application No. 07/662,764

and wherein each member of said oligonucleotide population is contained in said recombinant vector population, and

wherein the recombinant structural genes are expressed upon transfer of said recombinant vectors into Escherichia coli host cells, and wherein expression of said recombinant structural genes yields polypeptides, each polypeptide comprising said corresponding peptide sequence.

32. A method of producing a population of epitopic peptide sequences, comprising the steps of:

providing a population of recombinant E. coli cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising substantially identical autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene having inserted therein one member of an oligonucleotide population wherein each member of said oligonucleotide population has a length from about 4 to about 12 nucleotide triplets that encodes a corresponding epitopic peptide sequence of from about 4 to about 12 L-amino acid residues, and wherein each member of said oligonucleotide population is contained in said recombinant vector population and wherein the sum of said corresponding epitopic peptide sequences represents at least about 10% of all possible peptide sequences of said length; and

culturing said recombinant E. coli cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

33. A peptide population obtained from the process of claim 32 (35).

34. A population of peptides wherein each member of said population has a length of from about 4 to about 12 amino acid residues, and wherein said population contains at least about 10% of all possible peptide sequences of said length.

35. The peptide population of claim 34, wherein each member has a length of from 4 to 7 amino acid residues.

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00772
Application No. 07/162,764

36. The peptide population of claim 34, wherein each member has a length of 5 amino acid residues.

27. A population of binding pairs comprising:

a population of peptides, each member of said population having a length of from about 4 to about 12 amino acid residues, wherein said population represents at least about 10 percent of all possible peptide sequences of said length; wherein substantially every member of said peptide population is bound to an antibody.

38. A matrix comprising the population of binding pairs of claim 37.

39. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a length of from 1 to 7 nucleotide triplets and the encoded corresponding peptide sequences have a length of from 2 to 7 L-amino acid residues.

40. The recombinant vector population of claim 39, wherein each of said members of said oligonucleotide population has a length of 5 nucleotide triplets and the encoded corresponding peptide sequences have a length of 5 L-amino acid residues.

REMARKS

Examiner Elliott's efforts in having this application remanded from the Board of Appeals for further consideration, and the courtesies extended by Examiners Elliott and Brusca to Applicant and his representatives during the interview conducted on April 17 are greatly appreciated. As reflected in the Interview Summary Form, it was agreed that the objection to the specification and the rejection of claims 1, 3-5 and 19-21 under § 112, first paragraph, as nonenabling will be withdrawn on the basis of the arguments and evidence of record. Agreement was also reached that an amendment to claim 8 to delete language lacking antecedent basis in claim 1 would overcome the rejection under § 112, second paragraph. It was further agreed that an amendment to claim 1 further defining the oligonucleotides in terms of additional e.g., flanking, sequences permitting insertion into a vector, would serve to overcome the rejection of claims 1, 3-5 and 19 under § 102(b) over the Genentech publication.
Applicant has rewritten claims 1 and 21 as new claims 29 and 30. The recitation in claim 29, further defining each member of the oligonucleotide population as having "5' and 3'
flanking sequences that permit said oligonucleotides to be ligated into a vector," is supported by the disclosure in the paragraph bridging pages 16-17, and particularly page 17, lines 4-6. The term "random" has been deleted as surorousae. To the extent that it relates to the order and identity of the nucleotide triplets, randomness is covered by the phrase "wherein the sum of said corresponding peptide sequences represent at least about 10% of all possible peptide sequences of said length," to the extent that it relates it to the starting materials and/or process used to prepare the oligonucleotide population, it is an unnecessary limitation. Accordingly, dependent claim 5 has been amended to explicitly define the shearing as "random", support for which is set forth on page 7, line 1. Support for the newly added recitation "or codons" in claim 5 is set forth on page 15, lines 30-31. Claims 3-5 have also been amended to be more succinct and to establish proper dependency from claim 29. Claim 30 incorporates recitations of claims 1, 6 and 29, along with a "culturing" step, support for which is set forth on page 23, line 16. Claim 6 has been amended simply for even greater clarity. Claims 8, 15, 19 and 20 have also been amended for this purpose, as well as to maintain proper antecedent basis. New claims 31 and 32 differ from claims 6 and 30 respectively, in that they recite that the sum of corresponding peptide (or epitopic) peptide sequences represents "at least about 10%" of all possible sequences of the recited length. Support for the recitations of newly added claims 33-35 is set forth on page 7, lines 16-27. Claim 36 supported by the disclosure on page 7, lines 20-30. Claim 37 is supported by a disclosure in the paragraph bridging pages 8-9. Claim 38 is supported by the disclosure on page 9, lines 14-16. Claim 39 is supported by the disclosure on page 8, line 7, and claim 40 is supported by the disclosure on page 8, line 8.

Accordingly, no new matter has been added. Entry of the amendments is therefore requested.
In view of the indication by the Examiner that the rejection of claims 1, 3-5 and 19-21 under § 112, first paragraph, is withdrawn, its stands to reason that claim 6, 8, 11-15, 17, 18, 20, 30-32, 39 and 40 are allowable.

Claims 1, 3-5 and 19 stand rejected under § 102(b). The prior Examiner concluded that the Goulian et al., publication discloses a double-stranded oligonucleotide population, which as evidenced from the contents of Fig. 4 and Table II therein, meets the claim limitations.

Applicant submits that the invention defined by claims 29, 3-5 and 19 is not anticipated by the teachings of Goulian. This publication reports on the investigation of the optimal specificity of E. coli DNA polymerase I from the standpoints of primer length, nucleotide sequence, nucleotide sugar, enzyme and incubation conditions. To generate the single stranded primers used in the experiments, Goulian incubated calf thymus DNA with DNAase (obtained from Worthington Biochemical Corp.) and MgCl₂, followed by mixing with EDTA, KOH, heating (at 70° for 10 minutes) and then neutralising with HCl. The process yields single-stranded oligonucleotides, which as shown in Fig. 4 and Table II on page 2897, have lengths ranging from 1 to 15.1 nucleotides.

The Examiners and Applicant agree that there is no disclosure or suggestion in the Goulian publication of an oligonucleotide population having the rected coding region and 5' and 3' flanking sequences that permit ligation of the oligonucleotides into a vector. In view of the foregoing, reconsideration and withdrawal of the rejection are requested. Newly added claims 33-38 are not disclosed or suggested by the teachings of Goulian, so they are believed to be allowable as well.

Withdrawal of the rejection of claim 8 under § 112, second paragraph, as indefinite, is also requested in view of the amendment thereto.

Applicant submits that the present Amendment places the claims in condition for allowance. An early Notice to this effect is therefore solicited.
Application No. 07/662,764

Applicant wishes to bring to the Examiner's attention the grant of its corresponding European patent application. A copy of EP O 241 487 B1, granted April 22, 1998, along with a Supplemental Information Disclosure Statement containing the publications cited in said European Patent, are being submitted under separate cover.

The Examiner is encouraged to contact the undersigned if he has any questions.

Respectfully submitted,

LERNER, DAVID, LITTEMBERG, KREIFMAN & MENTZIK

SHAWN P. FOLEY
Reg. No. 33,071

600 South Avenue West
Westfield, New Jersey 07090
Telephone: (908) 654-5000
Facsimile: (908) 654-7066

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00776
Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents
Interview Summary

Application No. 07/662,764
Applicant(s) Pieczenik
Examiner John S. Brusca
Group Art Unit 1636

All participants (applicant, applicant's representative, PTO personnel):
(1) John O. Brusca
(2) 
(3) Shawn Foley
(4) 

Date of Interview 5/13/98

Type: ☒ Telephonic ☐ Personal (copy is given to ☐ applicant ☐ applicant's representative).

Exhibit shown or demonstration conducted: ☐ Yes ☒ No. If yes, brief description:

Agreement ☐ was reached. ☒ was not reached.

Claim(s) discussed: None

Identification of prior art discussed: none

Description of the general nature of what was agreed to if an agreement was reached, or any other comments:
The Applicants were informed that the finality of the last final rejection has been withdrawn, and any future amendments or filings will not be considered as after final submissions.

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

1. ☒ It is not necessary for applicant to provide a separate record of the substance of the interview.

Unless the paragraph above has been checked to indicate to the contrary, a FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a response to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW.

2. ☐ Since the Examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the interview unless box 1 above is also checked.

Examiner Note: You must sign and stamp this form unless it is an attachment to a signed Office action.

JOHN S. BRUSCA
PATENT EXAMINER
ART UNIT 1636

Pieczenik and ICT v. Dyax 00 Civ. 0243 (IID) 00778
May 27, 1998

Mr. David Chassen
600 W. 58th St., Ste. 9054
New York, NY 10019

Our Docket No.: 4-89A

Dear David:

Enclosed is a copy of an Interview Summary from the Patent and Trademark Office, dated May 18, 1998, for the above referenced matter.

Please do not hesitate to contact us with any questions or concerns regarding this matter.

Sincerely,

[Signature]
Donna M. Ferber, Ph.D.

DMF: gal

Enclosure

cc: Dr. George Piecznik (w/ encl.)
Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents
Interview Summary

All participants (applicant, applicant's representative, PTO personnel):

(1) John S. Drusca
(2) Shawn Foley
(3) 
(4) 

Date of Interview: 5/13/98

Type: ☑ Telephonic ☐ Personal (copy is given to ☑ applicant ☐ applicant's representative).

Exhibit shown or demonstration conducted: ☐ Yes ☑ No. If yes, brief description:

Agreement ☐ was reached. ☑ was not reached.

Claim(s) discussed: None

Identification of prior art discussed:
none

Description of the general nature of what was agreed to if an agreement was reached, or any other comments:
The Applicants were informed that the finality of the last final rejection has been withdrawn, and any future amendments or filings will not be considered as after final submissions.

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agrees would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

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Examiner Note: You must sign and stamp this form unless it is an attachment to a signed Office action.

JENNIFER S. DRUSCA
PATENT EXAMINER
ART UNIT 1636

Fax: 212-377-1592

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00782
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Pieczynik and ICT v Dyax  00 Civ. 0243 (HB)  00784
**LIST OF PRIOR ART (CITED) BY APPLICANT**

(Use several sheets if necessary)

| Filing Date: February 28, 1991 | Group 1536 |

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**EXAMINER**

[Signature]

**DATE CONSIDERED**

6/23/98

*EXAMINER: Initial if reference 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.*
LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK, LLP
600 South Avenue West
Westfield, New Jersey 07090

Telephone: (908) 654-5000
Facsimile: (908) 654-7866

FACSIMILE TRANSMITTAL SHEET

To: Examiner J. Brusca
Fax Number: 703-305-7939
Company: PTO

From: Marcus J. Millet, Esq.
Date: July 30, 1998

Number of Pages (Including Cover Page): 11

Client/Matter No. ICTECII/02

Original Being Mailed? No

To replace papers previously faxed.

Attached:

Amendment Cover Sheet
Supplemental Amendment

NOTICE: The information contained herein is intended only for the addressee identified above. It may be or may include material which is confidential, attorney-client privileged, attorney work product, copyrighted, and/or trade secret information. If you are not the intended recipient, or a person responsible for delivering this message to the intended recipient, you are hereby notified that the unauthorized use, disclosure, distribution or copying is strictly prohibited and may be in violation of court order or otherwise unlawful. If you have received this transmission in error, please immediately notify us at (908) 654-5000 (Collect, if necessary) and return this document to us by mail.

Picezenik and ICT v. Dyax 00 Civ. 0243 (HR) 00786
In re Patent Application of Pienzenik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

Assistant Commissioner for Patents
Washington, D.C.

Sir:

Transmitted herewith is an amendment in the above-identified application. The fee has been calculated as shown below.

CLAIMS AS AMENDED

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* If the entry in col. 2 is less than entry in col. 4 write "0" in col. 5.
** If the "highest number paid for" in this space is less than 20, write "20" in this space.
*** If the "highest number paid for" in this space is less than 3, write "3" in this space.

1. (a) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.19 and 1.27 has been filed.
   (b) ☐ A verified statement to establish small entity status under 37 C.F.R. 1.19 and 1.27 is enclosed.
2. ☐ No additional fee is required.
3. ☐ Charge $780.00 to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.
4. ☐ Please charge any additional fees or credit overpayment to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

Lerner, David, Littenberg, Krumholtz & Mentlik, LLP

Marcus J. Millet
Reg. No. 28,341

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Pienzenik and ICT v. Dyax 00 Civ. 0243 (HB) 00787
SUPPLEMENTAL AMENDMENT

Sir:

In the event that any fees are occasioned by this Supplemental Amendment, the Commissioner is authorized to charge Deposit Account No. 12-1095 accordingly.

Please amend the above-captioned patent application as follows.

IN THE CLAIMS:

6(twice amended). A population of recombinant vectors comprising:

[substantially identical] autonomously replicating nucleic acid sequences which nucleic acid sequences comprise a recombinant structural gene, each of the structural genes [having inserted therein] comprising an insert containing one member of an oligonucleotide population, [and]

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent Office on the date shown below.

[Signature]

July 30, 1998
Date

To: U.S.P.T.O

Attn: John S. Brusca

Fax No.: (703)305-7939

No. of Pages: 9
Application No. 07/661,764

[wherein each member of said] said population comprising oligonucleotides
[population has] having a coding region having a length from about 4 to about 12 nucleotide
triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid
residues, and

[wherein each member of said population of oligonucleotides is contained in said
recombinant vector population; and]

wherein said recombinant structural genes are expressed upon transfer of said
recombinant vectors into Escherichia coli host cells, and wherein expression of the recombinant
structural genes yields polypeptides, each polypeptide comprising said corresponding peptide
sequence.

In claim 8, line 3, insert "a coding region having" immediately after "has".

Cancel claims 17 and 18.

30(Amended). A population of oligonucleotides comprising double-stranded
oligonucleotides[, wherein each oligonucleotide in said population consists] that consist
essentially of a coding region having a length of from about 4 to about 12 nucleotide triplets that
encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues,
and 5' and 3' flanking sequences that permit said oligonucleotides to be ligated into a vector,

and wherein the sum of said corresponding peptide sequences represents at least

about 10% of all possible peptide sequences of said length.

In claim 30, line 8, insert "a coding region having" immediately after "has".

In claim 31, line 4, insert "a coding region having" immediately after "has".

In claim 39, line 2, insert "about" immediately before "4"; in line 3, insert "about-

immediately before "4".

In claim 40, line 2, insert "a coding region having" immediately after "has".

Please add the following claims.

Piozenik and ICT v. Dyax 00 Civ. 0243 (HB) 00789
41. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 4 nucleotide triplets and the encoded corresponding peptide sequence has a length of 4 amino acid residues.

42. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 6 nucleotide triplets and the encoded corresponding peptide sequence has a length of 6 amino acid residues.

43. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 7 nucleotide triplets and the encoded corresponding peptide sequence has a length of 7 amino acid residues.

44. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 8 nucleotide triplets and the encoded corresponding peptide sequence has a length of 8 amino acid residues.

45. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 9 nucleotide triplets and the encoded corresponding peptide sequence has a length of 9 amino acid residues.

46. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 10 nucleotide triplets and the encoded corresponding peptide sequence has a length of 10 amino acid residues.

47. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 11 nucleotide triplets and the encoded corresponding peptide sequence has a length of 11 amino acid residues.

48. The recombinant vector population of claim 6, wherein each of said members of said oligonucleotide population has a coding region having a length of 12 nucleotide triplets and the encoded corresponding peptide sequence has a length of 12 amino acid residues.

49. A population of oligonucleotides comprising double stranded oligonucleotides that consist essentially of a coding region having a length of from about 4 to about 12 nucleotide triplets encoding a peptide having a random sequence of from about 4 to
about 12 L-amino acid residues, and 5' and 3' flanking sequences that permit said oligonucleotide to be ligated into a vector.

30. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is from about 4 to 7 nucleotide triplets.

51. The oligonucleotide population of claim 50, which is generated by random shearing of mammalian genetic material and size fractionation.

32. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 4 nucleotide triplets.

33. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 5 nucleotide triplets.

34. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 6 nucleotide triplets.

35. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 7 nucleotide triplets.

36. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 8 nucleotide triplets.

37. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 9 nucleotide triplets.

38. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 10 nucleotide triplets.

39. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 11 nucleotide triplets.

40. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 12 nucleotide triplets.

41. The oligonucleotide population of claim 49, which is chemically synthesized from the component nucleotides or codons.
62. The oligonucleotide population of claim 49, wherein each of said corresponding peptide sequences forms a binding pair with an antibody.

63. A population of peptides wherein each member of said population has a random sequence of from about 4 to about 12 amino acid residues.

64. The peptide population of claim 63, wherein each member has a length of 4 amino acid residues.

65. The peptide population of claim 63, wherein each member has a length of 5 amino acid residues.

66. The peptide population of claim 63, wherein each member has a length of 6 amino acid residues.

67. The peptide population of claim 63, wherein each member has a length of 7 amino acid residues.

68. The peptide population of claim 63, wherein each member has a length of 8 amino acid residues.

69. The peptide population of claim 63, wherein each member has a length of 9 amino acid residues.

70. The peptide population of claim 63, wherein each member has a length of 10 amino acid residues.

71. The peptide population of claim 65, wherein each member has a length of 11 amino acid residues.

72. The peptide population of claim 65, wherein each member has a length of 12 amino acid residues.

73. A population of binding pairs comprising:

a population of peptides, each member of said population having a random sequence of from about 4 to about 12 amino acid residues, wherein substantially every member of said peptide population is bound to an antibody.
74. The population of claim 73, wherein each peptide has a length of 4 amino acid residues.

75. The population of claim 73, wherein each peptide has a length of 5 amino acid residues.

76. The population of claim 73, wherein each peptide has a length of 6 amino acid residues.

77. The population of claim 73, wherein each peptide has a length of 7 amino acid residues.

78. The population of claim 73, wherein each peptide has a length of 8 amino acid residues.

79. The population of claim 73, wherein each peptide has a length of 9 amino acid residues.

80. The population of claim 73, wherein each peptide has a length of 10 amino acid residues.

81. The population of claim 73, wherein each peptide has a length of 11 amino acid residues.

82. The population of claim 73, wherein each peptide has a length of 12 amino acid residues.

83. A matrix comprising the population of binding pairs of claim 73.

84. A method of producing a population of epitopic peptide sequences, comprising:

providing a population of recombinant E. coli cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene containing an insert comprising a member of an oligonucleotide population, said oligonucleotide population comprising oligonucleotides consisting essentially of coding regions having a length from about 4
Application No. 07/662,764

to about 12 nucleotide triplets encoding an epitopic peptide having a random sequence of from about 4 to about 12 L-amino acid residues; and

culturing said recombinant *E. coli* cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

85. The oligonucleotide population of claim 29, wherein the length of the coding region is 4 nucleotides.

86. The oligonucleotide population of claim 29, wherein the length of the coding region is 6 nucleotides.

87. The oligonucleotide population of claim 29, wherein the length of the coding region is 7 nucleotides.

88. The oligonucleotide population of claim 29, wherein the length of the coding region is 8 nucleotides.

89. The oligonucleotide population of claim 29, wherein the length of the coding region is 9 nucleotides.

90. The oligonucleotide population of claim 29, wherein the length of the coding region is 10 nucleotides.

91. The oligonucleotide population of claim 29, wherein the length of the coding region is 11 nucleotides.

92. The oligonucleotide population of claim 29, wherein the length of the coding region is 12 nucleotides.

93. The peptide population of claim 34, wherein each member has a length of 4 amino acid residues.

94. The peptide population of claim 34, wherein each member has a length of 6 amino acid residues.

95. The peptide population of claim 34, wherein each member has a length of 7 amino acid residues.
The peptide population of claim 34, wherein each member has a length of 8 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 9 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 10 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 11 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 12 amino acid residues.

REMARKS

Claims 6, 30, 31 and 40, drawn to recombinant vector populations, have been amended to be consistent with the recitation "coding region" now set forth in claim 29. Claims 17 and 18 have been canceled in light of concerns expressed by the Examiner that these claims may lack written description in Applicant's grandparent application. Although Applicant does not concede that such claims lack written description in the grandparent application, these claims have been cancelled to expedite prosecution of the present application. Such cancellation is without prejudice to Applicant's right to present these claims in a further continuing application. Claim 39 has been amended to avoid being duplicative with claim 8. Newly added independent claims 49, 63, 73 and 84 have been added at the invitation of the Examiner, pursuant to his indication that broader protection for Applicant's invention is obtainable in view of the paucity of prior art on oligonucleotide and peptide libraries. The newly added claims, directed to oligonucleotide, peptide and peptide/antibody populations, and methods for producing the peptide populations, do not require "10%" complexity. Instead, they recite that the populations contain (or encode, in the case of the oligonucleotide populations) peptides having random sequences of from about 4 to about 12 amino acid residues. Support for these recitations is set forth on page 8, lines 1-12 (which discloses the peptide populations displayed on vectors, without any limitation on
complexity).  Cases 15-16 (disclosing "random peptide sequences") and example IV beginning on page 38 (which illustrates the "randomness" of oligonucleotide and peptide sequences).  As shown in the literature, libraries of epitopic peptides do not require 10 percent complexity to be commercially useful. See, e.g., Devlin et al., Science 249:404-405 (1990) (disclosing a library of 2 x 10^7 15-residue peptide sequences); and Gould v. Quigg, 822 F.2d 1074, 1076 (Fed. Cir. 1987) (ruling that post filing date publications can be introduced as evidence of the level of ordinary skill in the art at the time of the application and that the invention claimed would have been operative.).  Most newly added dependent claims are directed to specific lengths of oligonucleotides and peptides, i.e., 4, 5, 6, 7, 8, 9, 10, 11 and 12, support for which is based on the originally disclosed range of "from about 4 to about 12." Accordingly, no new matter has been added.  Entry of the Amendment is therefore respectfully requested.

Applicant submits that all pending claims are in condition for allowance, and thus solicits and early Notice to this effect.  The Examiner is encouraged to contact the undersigned if he has any questions.

Respectfully submitted,

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KRUMHOLZ & MENTLIK, LLP

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Pieczenik and ICT v. Dyax  00 Civ. 0243 (HB)  00796
LERNER, DAVID, LITTENBERG, KRAMHOLZ & MENTLIK, LLP

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FACSIMILE TRANSMITTAL SHEET

To: Examiner J. Brusca
    Fax Number
    703-305-7939
    Company
    PTO

From: Shawn P. Foley, Esq.
Date: July 30, 1998

Number of Pages (Including Cover Page): 11

Client/Matter No: I C T E C H / 0 2

Original Being Mailed? No

Attached:

Amendment Cover Sheet
Supplemental Amendment

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In re Patent Application of
Pieczenik

Application No. 07/667,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

For: Method and Means for Sorting and Identifying Biological Information

Assistant Commissioner for Patents
Washington, D.C. 20233

Sir:

Transmitted herewith is an amendment in the above-identified application. The fee has been calculated as shown below:

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TOTAL ADDITIONAL FEE $ 780.00

1. (a) ☑ A Verified Statement to establish small entity status under 37 C.F.R. 1.19 and 1.27 has been filed.

(b) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.19 and 1.27 is enclosed.

2. ☑ No additional fee is required.

3. ☐ Charge $780.00 to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

4. ☑ Please charge any additional fees or credit overpayment to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

LENDER, DAVID, LITENBERG, KRUNHOLOZ & MENILIK, LLP

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F:DOC31184318J.01/35258.BOC

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00798
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Pieczenik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

Group Art Unit: 1636
Examiner: John S. Brusca
Date: July 30, 1998

Assistant Commissioner for Patents
Washington, D.C. 20231

SUPPLEMENTAL AMENDMENT

Sir:

In the event that any fees are occasioned by this Supplemental Amendment, the Commissioner is authorized to charge Deposit Account No. 12-1095 accordingly.

Please amend the above-captioned patent application as follows.

IN THE CLAIMS:

5(twice amended). A population of recombinant vectors comprising:

[substantially identical] autonomously replicating nucleic acid sequences which
nucleic acid sequences comprise a recombinant structural gene, each of the structural genes
[have inserted therein] comprising an insert containing one member of an oligonucleotide
population, [and]

CERTIFICATION OF FASCIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent Office on the date shown below.

Shawn P. Foley, Esp.

Signature

July 30, 1998
Date

To: U.S.P.T.O
Attn: John S. Brusca
Fax No.: (703)305-7919
No. of Pages: 9
wherein each member of said population comprising oligonucleotides having a coding region having a length from about 4 to about 12 nucleotide triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues, and

wherein each member of said population of oligonucleotides is contained in said recombinant vector population, and]

wherein said recombinant structural genes are expressed upon transfer of said recombinant vectors into Escherichia coli host cells, and wherein expression of the recombinant structural genes yields polypeptides, each polypeptide comprising said corresponding peptide sequence.

In claim 8, line 3, insert —a coding region having— immediately after "has".

Cancel claims 17 and 18.

20(Amended). A population of oligonucleotides comprising double-stranded oligonucleotides wherein each oligonucleotide in said population consists of a coding region having a length of from about 4 to about 12 nucleotide triplets that encodes a corresponding peptide sequence of from about 4 to about 12 L-amino acid residues, and 5' and 3' flanking sequences that permit said oligonucleotides to be ligated into a vector, and wherein the sum of said corresponding peptide sequences represents at least about 10% of all possible peptide sequences of said length.

In claim 30, line 8, insert —a coding region having— immediately after "has".

In claim 31, line 4, insert —a coding region having— immediately after "has".

In claim 39, line 2, insert —about— immediately before "4", in line 3, insert —about— immediately before "4".

In claim 40, line 2, insert —a coding region having— immediately after "has".

Please add the following claims.
The recombinant vector population of claim \( 4 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 4 nucleotide triplets and the encoded corresponding peptide sequence has a length of 4 amino acid residues.

The recombinant vector population of claim \( 5 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 6 nucleotide triplets and the encoded corresponding peptide sequence has a length of 6 amino acid residues.

The recombinant vector population of claim \( 6 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 7 nucleotide triplets and the encoded corresponding peptide sequence has a length of 7 amino acid residues.

The recombinant vector population of claim \( 7 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 8 nucleotide triplets and the encoded corresponding peptide sequence has a length of 8 amino acid residues.

The recombinant vector population of claim \( 8 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 9 nucleotide triplets and the encoded corresponding peptide sequence has a length of 9 amino acid residues.

The recombinant vector population of claim \( 9 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 10 nucleotide triplets and the encoded corresponding peptide sequence has a length of 10 amino acid residues.

The recombinant vector population of claim \( 10 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 11 nucleotide triplets and the encoded corresponding peptide sequence has a length of 11 amino acid residues.

The recombinant vector population of claim \( 11 \) wherein each of said members of said oligonucleotide population has a coding region having a length of 12 nucleotide triplets and the encoded corresponding peptide sequence has a length of 12 amino acid residues.

A population of oligonucleotides comprising double stranded oligonucleotides that consist essentially of a coding region having a length of from about 4 to about 12 nucleotide triplets encoding a peptide having a random sequence of from about 4 to
about 12 L-amino acid residues, and 5' and 3' flanking sequences that permit said oligonucleotide to be ligated into a vector.

50. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is from about 4 to 7 nucleotide triplets.

51. The oligonucleotide population of claim 50, which is generated by random shearing of mammalian genetic material and size fractionation.

52. The oligonucleotide population of claim 49 wherein the length of the coding region of each oligonucleotide is 4 nucleotide triplets.

53. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 5 nucleotide triplets.

54. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 6 nucleotide triplets.

55. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 7 nucleotide triplets.

56. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 8 nucleotide triplets.

57. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 9 nucleotide triplets.

58. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 10 nucleotide triplets.

59. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 11 nucleotide triplets.

60. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 12 nucleotide triplets.

61. The oligonucleotide population of claim 49, which is chemically synthesized from the component nucleotides or codons.
62. The oligonucleotide population of claim 49, wherein each of said corresponding peptide sequences forms a binding pair with an antibody.

A population of peptides wherein each member of said population has a random sequence of from about 4 to about 12 amino acid residues.

64. The peptide population of claim 63, wherein each member has a length of 4 amino acid residues.

66. The peptide population of claim 63, wherein each member has a length of 6 amino acid residues.

67. The peptide population of claim 63, wherein each member has a length of 7 amino acid residues.

68. The peptide population of claim 63, wherein each member has a length of 8 amino acid residues.

69. The peptide population of claim 63, wherein each member has a length of 9 amino acid residues.

70. The peptide population of claim 63, wherein each member has a length of 10 amino acid residues.

71. The peptide population of claim 63, wherein each member has a length of 11 amino acid residues.

72. The peptide population of claim 63, wherein each member has a length of 12 amino acid residues.

A population of binding pairs comprising:

a population of peptides, each member of said population having a random sequence of from about 4 to about 12 amino acid residues, wherein substantially every member of said peptide population is bound to an antibody.
74. The population of claim 73, wherein each peptide has a length of 4 amino acid residues.

75. The population of claim 73, wherein each peptide has a length of 5 amino acid residues.

76. The population of claim 73, wherein each peptide has a length of 6 amino acid residues.

77. The population of claim 73, wherein each peptide has a length of 7 amino acid residues.

78. The population of claim 73, wherein each peptide has a length of 8 amino acid residues.

79. The population of claim 73, wherein each peptide has a length of 9 amino acid residues.

80. The population of claim 73, wherein each peptide has a length of 10 amino acid residues.

81. The population of claim 73, wherein each peptide has a length of 11 amino acid residues.

82. The population of claim 73, wherein each peptide has a length of 12 amino acid residues.

83. A matrix comprising the population of binding pairs of claim 73.

84. A method of producing a population of epitopic peptide sequences, comprising:

providing a population of recombinant E. coli cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene containing an insert comprising a member of an oligonucleotide population, said oligonucleotide population comprising oligonucleotides consisting essentially of coding regions having a length from about 4...
to about 12 nucleotide triplets encoding an epitopic peptide having a random sequence of from about 4 to about 12 L-amino acid residues; and
culturing said recombinant E. coli cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

62 9/11,114 The oligonucleotide population of claim 29, wherein the length of the coding region is 4 nucleotides.

66 9/11,118 The oligonucleotide population of claim 29, wherein the length of the coding region is 6 nucleotides.

57 9/11,123 The oligonucleotide population of claim 29, wherein the length of the coding region is 7 nucleotides.

68 9/11,128 The oligonucleotide population of claim 29, wherein the length of the coding region is 8 nucleotides.

69 9/11,133 The oligonucleotide population of claim 29, wherein the length of the coding region is 9 nucleotides.

60 9/11,138 The oligonucleotide population of claim 29, wherein the length of the coding region is 10 nucleotides.

61 9/11,143 The oligonucleotide population of claim 29, wherein the length of the coding region is 11 nucleotides.

62 9/11,148 The oligonucleotide population of claim 29, wherein the length of the coding region is 12 nucleotides.

69 9/11,153 The peptide population of claim 34, wherein each member has a length of 4 amino acid residues.

94 9/11,158 The peptide population of claim 34, wherein each member has a length of 6 amino acid residues.

95 9/11,163 The peptide population of claim 34, wherein each member has a length of 7 amino acid residues.
The peptide population of claim 34, wherein each member has a length of 8 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 9 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 10 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 11 amino acid residues.

The peptide population of claim 34, wherein each member has a length of 12 amino acid residues.

**REMARKS**

Claims 6, 30, 31 and 40, drawn to recombinant vector populations, have been amended to be consistent with the recitation "coding region" now set forth in claim 29. Claims 17 and 18 have been canceled as allegedly lacking written description support in the grandparental application. Claim 39 has been amended to avoid being duplicative with claim 8. Newly added independent claims 49, 63, 73 and 84 have been added at the invitation of the Examiner, pursuant to his indication that broader protection for Applicant's invention is obtainable in view of the paucity of prior art on oligonucleotide and peptide libraries. The newly added claims, directed to oligonucleotide, peptide and peptide/antibody populations, and methods for producing the peptide populations, do not require "10%" complexity. Instead, they recite that the populations contain (or encode, in the case of the oligonucleotide populations) peptides having random sequences of from about 4 to about 12 amino acid residues. Support for these recitations is set forth on page 8, lines 1-12 (which discloses the peptide populations displayed on vectors, without any limitation on complexity), pages 15-16 (disclosing "random peptide sequences") and example IV beginning on page 38 (which illustrates the "randomness" of oligonucleotide and peptide sequences). As shown in the literature, libraries of epitopic peptides do not require 10 percent complexity to be commercially useful. See, e.g., Devlin et al., Science 249:404-405 (1990) (disclosing a library of
2 x 10^7 13-residue peptide sequences), and Gould v. Quigg, 826 F.2d 1019, 1019 (Fed. Cir. 1987) (ruling that post filing date publications can be introduced as evidence of the level of ordinary skill in the art at the time of the application and that the invention claimed would have been operative.). Most newly added dependent claims are directed to specific lengths of oligonucleotides and peptides, i.e., 4, 5, 6, 7, 8, 9, 10, 11 and 12, support for which is based on the originally disclosed range of "from about 4 to about 12." Accordingly, no new matter has been added. Entry of the Amendment is therefore respectfully requested.

Applicant submits that all pending claims are in condition for allowance, and thus solicits and early Notice to this effect. The Examiner is encouraged to contact the undersigned if he has any questions.

Respectfully submitted,

LEARNER, DAVID, LITTEMBERG, KRUMHOLZ & MENTLIK, LLP

SHAWN P. FOLEY
Reg. No. 33,071

600 South Avenue West
Westfield, New Jersey 07090
Telephone: (908) 654-5000
Facsimile: (908) 654-7866
May 29, 1998

VIA FEDERAL EXPRESS

Ms. Barbara Landon Kuebler
Landon & Stark Associates, Inc.
2011 Crystal Drive, Suite 310
One Crystal Park
Arlington, Virginia 22202-3709

Re: ICTECH 3.0-002 CIP CONT
Method and Means for Sorting
and Identifying Biological Information

Dear Barbara:

Please hand carry the enclosed documents to the Chemical Matrix receptionist.

The enclosed postcard should be stamped by someone at the Patent Office and returned to us. Thanks very much for your help.

Very truly yours,

LERNER, DAVID, LITENBERG, KRUMHOLZ & MENTLIK

SHAWN P. FOLEY

SPF/tf
Enclosures
CHANGE OF CORRESPONDENCE

Sir:

The following is provided as the new correspondence address under 37 C.F.R. § 1.33 in connection with this patent application:

Shawn P. Foley
Lerner, David, Littenberg, Krumholz & Mentlik
600 South Avenue West
Westfield, New Jersey 07090-1497

Any prior correspondence address for this patent is hereby revoked.

Various members of the Lerner, David firm, namely Joseph S. Littenberg (Reg. No. 20,832), Marcus J. Millet (Reg. No. 28,241) and Shawn P. Foley (Reg. No. 11,071) were granted Associate Power of Attorney filed with the Patent Office on March 16, 1998.

It is certified that the person whose signature appears below has the authority to change the correspondence address for this patent.

Dated: [Jan 27, 1997]

[Signature]

By: GEORGE PIECZENIK
Title: Inventor

Identity of Signatory: Inventor
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of
Pieczenik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and
Identifying Biological Information

Assistant Commissioner For Patents
Washington, D.C. 20231

HAND CARRY

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR § 1.97(a)

Sir:

Applicant respectfully requests that the references listed on the enclosed Form PTO-1449 be made of record and considered with respect to the above-referenced U.S. patent application. A copy of each reference is enclosed. Submission of the present Information Disclosure Statement should not be taken as an admission that the cited references are legally available prior art or that the same are pertinent or material.

Most of these publications were cited in Applicant's corresponding International Application No. PCT/US86/01796. A copy of the International Search Report is also enclosed. As shown in the Annex, there are no English equivalents of DD-A-143794 or DE-A-3300632. A courtesy copy of Applicant's corresponding European patent, EP 0 241,487 B1, which was granted on April 22, 1998, is also enclosed.

Please charge deposit account No. 12-1095 in the amount of $240.00 pursuant to 37 C.F.R. § 1.17(p). In the event that any additional fee is due in connection with the present request, the same should be charged to deposit account No. 12-1095.

Respectfully submitted,

LERNER, DAVID, LITDENBERG,
KRUMHOLZ & MENTLIK

SHAWN P. FOLEY
Reg. No. 33,071

600 South Avenue West
Westfield, New Jersey 07090
Telephone: (908) 654-5000
Fax: (908) 654-7877

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00810
LIST OF PRIOR ART LIED BY APPLICANT

(Fill several sheets if necessary)

U.S. PATENT DOCUMENTS

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OTHER PRIOR ART (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)

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EXAMINER:

DATE CONSIDERED:

*EXAMINER: Initial if reference considered. Whether or not citation is in compliance with MPEP 607. Draw line through citation if not in compliance and not considered. Include copy of this form with next communication to applicant.
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**Other Prior Art (Including Author, Title, Date, Permanent Pages, etc.)**

| AR |
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| AT |

**Examiner**

*Examiner:* Initial of reference 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.
Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

LDLK&M
AUG 10 1998
RECEIVED

Piecznik and ICT v. Dyax 00 Civ. 0243 (HB) 00814
**Interview Summary**

All participants (applicant, applicant's representative, PTO personnel):

(1) John S. Brusca  
(2) Shawn Foley  
(3) Marcus Millett  
(4)  

Date of Interview: 7/30/98

Type: ☒ Telephonic  ☐ Personal (copy is given to)  ☐ applicant  ☐ applicant's representative.

Exhibit shown or demonstration conducted: ☐ Yes  ☒ No. If yes, brief description:

Agreement ☐ was reached. ☒ was not reached.

Claim(s) discussed: 17 and 18

Identification of prior art discussed:

none

Description of the general nature of what was agreed to if an agreement was reached, or any other comments:

The Applicants were advised that priority for claims 17 and 18 would not be granted to parent applications 07/201368 and 06/770390 because the parent applications did not satisfy the requirements of 35 U.S.C. § 112, first paragraph. The Applicants maintained that the parent applications discussed above enabled the invention of claims 17 and 18, but that they would cancel claims 17 and 18 without prejudice for future prosecution solely to facilitate the allowance of the remaining claims in the instant application.

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

1. ☒ It is not necessary for applicant to provide a separate record of the substance of the interview.

Unless the paragraph above has been checked to indicate the contrary, A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a response to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW.

2. ☐ Since the Examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the interview unless box 1 above is also checked.

Examiner Note: You must sign and stamp this form unless it is an attachment to a signed Office action.

JOHN S. BRUSCA  
PATENT EXAMINER  
ART UNIT 1636

U.S. Patent and Trademark Office  
PTO-413 (Rev. 10-95)  
Interview Summary  
Paper No. 50

Piezenik and ICT v. Dyax 00 Civ. 0243 (HB) 00815
TELECOPY/FACSIMILE TRANSMISSION

TO: Shawn Foley
FIRM:
ATTORNEY’S DOCKET # OR SERIAL#: 07/662764
FAX/TELECOPIER NUMBER: (908) 054-7806
DATE: August 24, 1998

FROM: Examiner John S. Brusca, Ph.D.
ART UNIT 1636
FAX: (703) 305-7939
PHONE: (703) 308-4231
MAILING ADDRESS: John S. Brusca
Art Unit 1636
U.S. Patent and Trademark Office
Crystal Mall 1
7th Floor Receptionist
1911 S. Clark Street
Arlington, VA 22202
7th Floor Receptionist phone: (703) 308-0196

PAGES, INCLUDING COVER SHEET: 7

COMMENTS: courtesy copy of draft Examiner’s Amendment. Please note that the
application is not in compliance with the sequence rules due to peptide sequences on pages 43-
45. A revised Sequence Listing and CRF must be filed along with an amendment to insert SEQ
ID Nos. for the peptides in the specification before the application can be allowed.

IF YOU HAVE NOT RECEIVED ALL THE PAGES OF THIS TRANSMISSION, PLEASE CONTACT THE
EXAMINER AT THE TELEPHONE NUMBER LISTED ABOVE.
ALL FAX MACHINES RECEIVE TRANSMISSIONS 24 HOURS PER DAY, SEVEN DAYS PER WEEK.
IN COMPLIANCE WITH 10CFR 1.21, THE FILING DATE ACCORDED EACH OFFICIAL FAX TRANSMISSION
WILL BE DETERMINED BY THE FAX MACHINE DATE STAMP FOUND ON THE LAST PAGE OF THE
TRANSMISSION, UNLESS THAT DATE IS A SATURDAY, SUNDAY, OR FEDERAL HOLIDAY WITHIN THE
DISTRICT OF COLUMBIA, IN WHICH CASE THE OFFICIAL DATE OF RECEIPT WILL BE THE NEXT
BUSINESS DAY.

THE DOCUMENT(S) ACCOMPANYING THIS FACSIMILE TRANSMISSION CONTAIN(S) INFORMATION
FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE WHICH IS CONFIDENTIAL AND/OR
LEGALLY PRIVILEGED. THIS INFORMATION IS FOR THE USE OF THE INDIVIDUAL OR FIRM NAMED ON
THIS SHEET. IF YOU ARE NOT THE INTENDED RECIPIENT, YOU ARE HEREBY NOTIFIED THAT ANY
DISCLOSURE, COPYING, DISTRIBUTION, OR THE TAKING OF ANY ACTION IN RELIANCE ON THE
CONTENTS OF THIS INFORMATION IS STRICTLY PROHIBITED. THE DOCUMENTS SHOULD BE
RETURNED TO THE PATENT AND TRADEMARK OFFICE IMMEDIATELY. IF THIS FACSIMILE IS
RECEIVED IN ERROR, PLEASE NOTIFY THE EXAMINER LISTED HEREON IMMEDIATELY.
DETAILED ACTION

1. Applicant’s request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Examiner’s Amendment

An examiner’s amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner’s amendment was given in a telephone interview with Shawn Foley on .

2. The application has been amended as follows:

Claim 6 is amended as follows:

6 (three times amended). A population of recombinant vectors comprising:

autonomously replicating nucleic acid sequences which nucleic acid sequences comprise a recombinant structural gene, each of the structural genes comprising an insert containing one member of an oligonucleotide population, said oligonucleotide population comprising oligonucleotides [having] comprising a coding region [having] consisting of a length from about 4 to about 12 nucleotide triplets [that encodes a] , said oligonucleotide population
encoding a plurality of random corresponding peptide sequences of from about 4 to about 12
L-amino acid residues, and
wherein said recombinant structural genes are expressed upon transfer of said
recombinant vectors into *Escherichia coli* host cells, and wherein expression of the
recombinant structural genes yields polypeptides, each polypeptide comprising one of said
plurality of random corresponding peptide sequences.

In claim 29, lines 2-3, the phrase “that consist essentially” has been deleted and --
consisting-- has been substituted therefor.

In claim 29, line 7, the phrase “of said length” has been deleted.

In claim 4, line 1, the term “29” has been deleted and --3-- has been substituted
therefor.

In claim 5, line 2, the term “the” has been deleted.

Claim 49 has been amended as follows:

49 (once amended). A population of oligonucleotides comprising double stranded
oligonucleotides that [consist essentially of] *comprise* a coding region having a length of from
about 4 to about 12 nucleotide triplets, said coding regions encoding a plurality of peptides
having a random sequence of from about 4 to about 12 L-amino acid residues, [and] said
oligonucleotides comprising 5' and 3' flanking sequences that permit said oligonucleotides to be ligated into a vector.

In claim 61, line 2, the term “the” has been deleted.

Claim 63 has been amended as follows:

63 (once amended). A population of peptides consisting of random sequences of from about 4 to about 12 amino acid residues.

Claim 73 has been amended as follows:

73 (once amended). A population of binding pairs comprising:

a population of peptides consisting of random sequences [each member of said population having a random sequence] of from about 4 to about 12 amino acid residues, wherein substantially every member of said peptide population is bound to an antibody.

Claim 84 has been amended as follows:

84 (once amended). A method of producing a population of epitopic peptide sequences comprising:
providing a population of recombinant \textit{E.} \textit{coli} cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene containing an insert comprising a member of an oligonucleotide population, said oligonucleotide population comprising oligonucleotides [consisting essentially of coding regions having] comprising a coding region consisting of a length from about 4 to about 12 nucleotide triplets, said oligonucleotide population encoding a plurality of epitopic peptides consisting of random sequences [encoding an epitopic peptide having a random sequence] of from about 4 to about 12 L-amino acid residues; and
culturing said recombinant \textit{E.} \textit{coli} cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

The claims have been reordered so that independent claims are immediately followed by their dependent claims.

\textit{Reasons for Allowance}

The following is an examiner's statement of reasons for allowance:
The rejection of claims under 35 U.S.C. § 102(b) over Goulian et al. is withdrawn because the nucleic acid fragments of Goulian et al. do not comprise 5' and 3' flanking
Application/Control Number: 07/662764
Art Unit: 1636

sequences that permit ligation to a vector because the DNase treatment of Goulian et al.
produces protruding 3’ and 5’ ends of random sequences.

The rejection of claims under 35 U.S.C. § 103 over Lupski et al. in view of Goulian et
al. is withdrawn because of the deficiencies in the Goulian et al. reference described above.

The rejection of claims under 35 U.S.C. § 112, first paragraph is withdrawn because
one of skill in the art would be able to select those members of the claimed populations of
vectors, oligonucleotides, or peptides which were of interest.

The rejection of claims under 35 U.S.C. § 112, second paragraph are withdrawn in
view of the Amendment filed 7/30/98 and the Examiner’s Amendment detailed above.

The terms “having”, “has”, and “have” in the claims are considered to be closed and
equivalent to the terms “consisting of” and “consists of”.

Any comments considered necessary by applicant must be submitted no later than the
payment of the issue fee and, to avoid processing delays, should preferably accompany the
issue fee. Such submissions should be clearly labeled “Comments on Statement of Reasons for
Allowance.”

Conclusion

Are essential to the claimed invention and must be obtainable by a repeatable method set
forth in the specification or otherwise be readily available to the public. If the strains are not so
obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the
strains. The specification does not disclose a repeatable process for obtaining the \( ? \) and it is not apparent that the \( ? \) are readily available to the public. (state why) The requirements for description and enablement may be met by depositing the strains in a recognized depository. The Applicant's attention is directed to the enclosed attachment providing suggestions for deposit of biological material.
August 31, 1998

VIA FEDERAL EXPRESS

Ms. Barbara Landon Kuebler
Landon & Stark Associates, Inc.
2011 Crystal Drive, Suite 310
One Crystal Park
Arlington, Virginia 22202-3709

Re: ICTECH 3.0-002 CIP CONT
Method and Means for Sorting
and Identifying Biological Information

Dear Barbara:

Please hand carry the enclosed documents to the Chemical Matrix receptionist.

The enclosed postcard should be stamped by someone at the Patent Office and
returned to us. Thanks very much for your help.

Very truly yours,

LERNER, DAVID, LITENBERG,
KRUMHOLZ & MENTLIK, LLP

SHAWN P. FOLEY

SPF/af
Enclosure

F:\DOCS\SCP\00146936.DOC

Pioceznik and ICT v. Dyax 00 Civ. 0243 (HB) 00823
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Pieczenik

Application no. 03/092,697

Filed: February 28, 1991

For: Method and Means for Sorting

Identifying Microbiological

Assistant Commissioner for Patents

Washington, D.C. 20231

Sirs:

Transmitted herewith is an amendment in the above-identified application. The fee has been calculated as shown below.

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** If the "highest number paid for" in this space is less than 20, write "20" in this space.
*** If the "highest number paid for" in this space is less than 3, write "3" in this space.

1. (a) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.19 and 1.27 has been filed.

(b) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.19 and 1.27 is enclosed.

2. ☐ No additional fee is required.

3. ☐ Charge $0.00 to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

4. ☐ Please charge any additional fees or credit overpayment to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

LERNER, DAVID, LITTENBERG, KRAMHOLZ & MENTLIK, LLP

Shawn P. Foley
Reg. No. 33,071

600 South Avenue West
Westfield, NJ 07090-1497
Telephone: (908) 654-9000
Facsimile: (908) 654-7866

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00824
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE PATENT APPLICATION OF
Pieczenik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

DATE: August 31, 1998

HAND CARRY

AMENDMENT

Sir:

This is in response to the Examiner's request to supply a Sequence Listing. A Sequence Listing was filed on June 13, 1991. Not all of the sequences set forth in the specification were included. In addition, Applicant has since discovered two minor errors in corresponding hexapeptide sequences. Accordingly, the following substitute Sequence Listing is being provided herewith, along with appropriate amendments introducing the proper sequence designation numbers in the specification.

Please amend the above-captioned patent application as follows.

IN THE SPECIFICATION

On page 39, line 25, insert -SEQ ID NO:1- immediately after "GATCCCTNnAA";

on page 40, line 21, change "About" to "about";

on page 42, end of line 7, insert -SEQ ID NO:2-; at the end of line 8, insert -SEQ ID NO:3-; at the end of line 9, insert -SEQ ID NO:4-; at the end of line 10, insert -SEQ ID NO:5-; at the end of line 11, insert -SEQ ID NO:6-; at the end of line 12, insert -SEQ ID NO:7-; at the end of line 13, insert -SEQ ID NO:8-; at the end of line 14, insert -SEQ ID NO:9-; at the end of line 15, insert -SEQ ID NO:10-; at the end of line 16, insert -SEQ ID NO:11-; at the end of line 17, insert -SEQ ID NO:12-; at the end of line 18, insert -SEQ ID NO:13-;
Application No. 07/604,764

NO:13--; at the end of line 19, insert --SEQ ID NO:14--; at the end of line 20, insert --SEQ ID NO:15--; on page 43, at the end of line 6, insert --SEQ ID NO:16--; at the end of line 5, (i.e., "LYS"), insert --SEQ ID NO:17--; at the end of line 12, insert --SEQ ID NO:18--; at the end of line 13, (i.e., "... SIQ"), insert --SEQ ID NO:19--; at the end of line 16, insert --SEQ ID NO:20--; on line 17, change "F" to --E--, and at the end of line 17, insert --SEQ ID NO:21--; at the end of line 20, insert --SEQ ID NO:22--; at the end of line 21 (i.e., "... PKQ"), insert --SEQ ID NO:23--; at the end of line 24, insert --SEQ ID NO:24--; at the end of line 25 (i.e., "... QRO"), insert --SEQ ID NO:25--; at the end of line 31, insert --SEQ ID NO:26--; at the end of line 32 (i.e., "... ALK"), insert --SEQ ID NO:27--; at the end of line 38, insert --SEQ ID NO:28--; at the end of line 39 (i.e., "... ALQ"), insert --SEQ ID NO:29--; at the end of line 44, insert --SEQ ID NO:30--; at the end of line 49 (i.e., "... VOG"), insert --SEQ ID NO:31--; on page 44, at the end of line 3, insert --SEQ ID NO:32--; at the end of line 11, insert --SEQ ID NO:34--; at the end of line 12, insert --SEQ ID NO:35--; at the end of line 17, insert --SEQ ID NO:36--; at the end of line 18, insert --SEQ ID NO:37--; at the end of line 24, insert --SEQ ID NO:38--; at the end of line 25, change "T" to --T--, at the end of said line, insert --SEQ ID NO:39--; at the end of line 30, insert --SEQ ID NO:40--; at the end of line 31, insert --SEQ ID NO:41--; at the end of line 34, insert --SEQ ID NO:42--; at the end of line 33, insert --SEQ ID NO:43--; on page 45, line 11, insert --SEQ ID NO:44--; immediately after "Tyr", and insert the following pages 49a-49b.

Pieczenik and ICT v. Dyax
00 Civ. 0243 (HB)
00826
TELECOPY/FACSIMILE TRANSMISSION

TO: Shawn Pote
FIRM:  
ATTORNEY’S DOCKET # OR SERIAL#: 07/662764  
FAX/TELECOPIER NUMBER: (000) 654-7866  
DATE: August 24, 1998

FROM: Examiner John S. Brusca, Ph D.  
ART UNIT 1636  
FAX: (703) 305-7939  
PHONE: (703) 308-4231

MAILING ADDRESS: John S. Brusca  
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U.S. Patent and Trademark Office  
Crystal Mall 1  
7th Floor Receptionist  
1911 S. Clark Street  
Arlington, VA 22202  
7th Floor Receptionist phone: (703) 308-0196

PAGES. INCLUDING COVER SHEET: 7

COMMENTS: courtesy copy of draft Examiner’s Amendment. Please note that the application is not in compliance with the sequence rules due to peptide sequences on pages 43-45. A revised Sequence Listing and CRF must be filed along with an amendment to insert SEQ ID No. for the peptides in the specification before the application can be allowed.

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Pieczenik and ICT v. Dyax 00 Civ 0243 (HR) 00827
DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.332. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Shawn Foley on 8.

2. The application has been amended as follows:

Claim 6 is amended as follows:

6 (three times amended). A population of recombinant vectors comprising:

autonomously replicating nucleic acid sequences which nucleic acid sequences comprise a recombinant structural gene, each of the structural genes comprising an insert containing one member of an oligonucleotide population, said oligonucleotide population comprising oligonucleotides [having] comprising a coding region [having] consisting of a length from about 2 to about 12 nucleotide triplets [that encodes a] said oligonucleotide population
Encoding a plurality of random corresponding peptide sequences of from about 4 to about 12 L-amino acid residues, and

wherein said recombinant structural genes are expressed upon transfer of said recombinant vectors into *Escherichia coli* host cells, and wherein expression of the recombinant structural genes yields polypeptides, each polypeptide comprising one of said plurality of random corresponding peptide sequences.

In claim 29, lines 2-3, the phrase “that consist essentially” has been deleted and --consisting-- has been substituted therefor.

In claim 29, line 7, the phrase “of said length” has been deleted.

In claim 4, line 1, the term “29” has been deleted and --3-- has been substituted therefor.

In claim 5, line 2, the term “the” has been deleted.

Claim 49 has been amended as follows:

49 (amended). A population of oligonucleotides comprising double stranded oligonucleotides that [consist essentially of] comprise a coding region having a length of from about 4 to about 12 nucleotide triplets, said coding regions encoding a plurality of peptides having a random sequence of from about 4 to about 12 L-amino acid residues, [and] said
Application/Control Number: 07/662764

Art Unit: 1636

oligonucleotides comprising 5' and 3' flanking sequences that permit said oligonucleotides to be ligated into a vector.

In claim 61, line 2, the term “the” has been deleted.

Claim 63 has been amended as follows:

63 (once amended). A population of peptides consisting of random sequences of from about 4 to about 12 amino acid residues.

Claim 73 has been amended as follows:

73 (once amended). A population of binding pairs comprising:

a population of peptides consisting of random sequences [each member of said population having a random sequence] of from about 4 to about 12 amino acid residues, wherein substantially every member of said peptide population is bound to an antibody.

Claim 84 has been amended as follows:

84 (once amended). A method of producing a population of epitopic peptide sequences comprising:
providing a population of recombinant [*E.* *Escherichia coli*] cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene containing an insert comprising a member of an oligonucleotide population, said oligonucleotide population comprising oligonucleotides [consisting essentially of coding regions having] comprising a coding region consisting of a length from about 4 to about 12 nucleotide triplets, said oligonucleotide population encoding a plurality of epitopic peptides consisting of random sequences [encoding an epitopic peptide having a random sequence] of from about 4 to about 12 L-amino acid residues; and
culturing said recombinant [*E.* *Escherichia coli*] cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

The claims have been reordered so that independent claims are immediately followed by their dependent claims.

*Reasons for Allowance*

The following is an examiner's statement of reasons for allowance:

The rejection of claims under 35 U.S.C. § 102(b) over Goulian et al. is withdrawn because the nucleic acid fragments of Goulian et al. do not comprise 5' and 3' flanking

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB)
sequences that permit ligation to a vector because the DNase treatment of Goulian et al. produces protruding 3' and 5' ends of random sequences.

The rejection of claims under 35 U.S.C. § 103 over Lupski et al. in view of Goulian et al. is withdrawn because of the deficiencies in the Goulian et al. reference described above.

The rejection of claims under 35 U.S.C. § 112, first paragraph is withdrawn because one of skill in the art would be able to select those members of the claimed populations of vectors, oligonucleotides, or peptides which were of interest.

The rejection of claims under 35 U.S.C. § 112, second paragraph are withdrawn in view of the Amendment filed 7/30/98 and the Examiner's Amendment detailed above.

The terms "having", "has", and "have" in the claims are considered to be closed and equivalent to the terms "consisting of" and "consists of".

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

...
strains. The specification does not disclose a repeatable process for obtaining the ? and it is not apparent that the ? are readily available to the public. (state why) The requirements for description and enablement may be met by depositing the strains in a recognized depository. The Applicant's attention is directed to the enclosed attachment providing suggestions for deposit of biological material.
TELECOPY/FACSIMILE TRANSMISSION

TO: Traci French  
FIRM:  
ATTORNEY'S DOCKET # OR SERIAL #: 07/662764  
FAX/TELECOPIER NUMBER: (908) 654-7866  
DATE: August 26, 1998

FROM: Examiner John S. Brusca, Ph.D.  
ART UNIT 1636  
FAX: (703) 305-7939  
PHONE: (703) 308-4231

MAILING ADDRESS: John S. Brusca  
Art Unit 1636  
U.S. Patent and Trademark Office  
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7th Floor Receptionist  
1911 S. Clark Street  
Arlington, VA 22202  
7th Floor Receptionist phone: (703) 308-0196

PAGES, INCLUDING COVER SHEET: 3

COMMENTS: Courtesy copy of Rule 63 Declaration

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Pieczenik and ICT v. Dyax  00 Civ. 0243 (HB)  00834
DECLARATION FOR PATENT APPLICATION

As the above named inventor, I hereby declare that:

My residence, post office address and citizenship is as stated below my name;

I believe that I am the original, first and sole inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled

METHOD AND MEANS FOR SORTING AND IDENTIFYING BIOLOGICAL INFORMATION, the specification of which

was attached hereto.

was filed on _______________ as Application Serial No. _______________ and was amended on _______________ (if applicable)

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor’s certificate listed below and have also identified below any foreign application(s) for patent or inventor’s certificate having a filing date before that of the application on which priority is claimed;

Prior Foreign Application(s)

<table>
<thead>
<tr>
<th>Country</th>
<th>Application No.</th>
<th>Date of Filing (day, month, year)</th>
<th>Date of Issue (day, month, year)</th>
<th>Priority Claimed Under 35 U.S.C. 119</th>
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<td>Yes — No</td>
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<tr>
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<td></td>
<td>Yes — No</td>
</tr>
</tbody>
</table>

N/A

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application;

<table>
<thead>
<tr>
<th>Application Serial Number</th>
<th>Date of Filing (day, month, year)</th>
<th>Status — Patented, Pending, Abandoned</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/770, 390</td>
<td>August 28, 1985</td>
<td>Abandoned</td>
</tr>
<tr>
<td>07/201, 358</td>
<td>May 26, 1988</td>
<td>Pending</td>
</tr>
</tbody>
</table>

And I hereby appoint, both jointly and severally, as my attorneys with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected herewith the following attorneys, their registration numbers being listed after their names:

Lorance L. Greenlee, Reg. No. 27,324; Sally A. Sullivan, Reg. No. 32,064; Ellen P. Winner, Reg. No. 28,547; Diane H. McCleary, Reg. No. 33,960; Donna M. Ferber, Reg. No. 33,878; Margaret M. Wall, Reg. No. 33,482; and Jennie M. Caruthers, Reg. No. 34,464.

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00835
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signature ___________________________ Date ______

Full Name of Sole Inventor ____________

Family Name ____________ First Given Name ______

Second Given Name ______

Residence ______

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Citizenship United States of America

Post Office Address ______

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Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00836
REMARKS

The amendments to the specification have been made to comply with the requirements set forth in 37 C.F.R. § 1.821 et seq. On page 43, the phenylalanine ("F") residue has been changed to "E" because the codon "GAG" encodes E, and the isoleucine ("I") residue in the amino acid sequence on page 44, line 25, on page 44 has been changed to "T" because the codon "ACT" encodes T. No new matter has been added. Accordingly, Applicant respectfully requests entry of the Amendment.

Respectfully submitted,

LERMER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK, LLP

SHAWN P. FOLEY
Reg. No. 33,071

600 South Avenue West
Westfield, New Jersey 07090
Telephone: (908) 654-6000
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Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00837
SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Pieczenik, George

(ii) TITLE OF INVENTION: METHOD AND MEANS FOR SORTING AND IDENTIFYING BIOLOGICAL INFORMATION

(iii) NUMBER OF SEQUENCES: 44

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: LERNER, DAVID, LITTMANBERG, KRUMHOLZ & MENTILIK
(B) STREET: 600 South, Avenue West
(C) CITY: Westfield
(D) STATE: New Jersey
(E) COUNTRY: USA
(F) ZIP: 07090

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: Patentin Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER: US 07/662,764
(B) FILING DATE: 28-FEB-1991
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: US 07/201,358
(B) FILING DATE: 26-MAY-1988

(viii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: US 06/770,390
(B) FILING DATE: 28-AUG-1985

(ix) ATTORNEY/AGENT INFORMATION:
(A) NAME: Foley, Shawn P.
(B) REGISTRATION NUMBER: 33,071
(C) REFERENCE/DOCKET NUMBER: ICTECH/0002

(x) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: 908-654-5000
(B) TELEFAX: 908-654-7060

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "oligonucleotide"

49a
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
GATCCTNNN NNNNNNNNN NNA

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:
CTTACCAGC WUAIQVAA A

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:
CTTATGCAAG ACTCGATACA

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:
CTTGCGGGGT CAGAGGCGA A

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

49b
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(MOLECULAR TYPE: DNA (genomic))

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CTTCGATAT TTCCGAAGCA A

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

CTTACATCC TCCAACGGCA A

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CTTCCATCC TCCACTGCA A

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CTTACCCGA GGGCGTCCA A

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:9:

CTTCCTAGAT TCGTGGCGAA A

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:10:

CTTAGGTGC TCGACGCGCA A

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:11:

CTTCAGGACA AAGTACATCA A

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

CTTGA\text{AATAT} \text{AAGCG} \text{CCA} \text{GAG} \text{A}

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

CTTGG\text{TTTCC} \text{TACTCCG} \text{G} \text{A}

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

CTTCT\text{TATCA} \text{TAAACAACA} \text{A}

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

CTTGACCGGG \text{ATAAGG} \text{AAA} \text{A}

49e
(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(vi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

TCITTTACAG TCCGGCTCGGT AAGATCCCTA TGAGATCTT ACC GAG CGG ACT GGT

Thr Glu Arg Thr Gly

1 5

AAA GA

Lys

60

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Thr Glu Arg Thr Gly Lys

1 5

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(iii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(vi) SEQUENCE DESCRIPTION: SEQ ID NO:18:
(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xvi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:
Met Gln Asp Ser Ile Gln

1 5

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iia) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(xvi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:
TCTTGTACG CTGACCCCGC AAGATCTCA TGAGGATCTT GCG GGG TCA GAG GGC

Ala Gly Ser Glu Gly

1 5

GAA GA
Glu

60

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xvi) SEQUENCE DESCRIPTION: SEQ ID NO: 21.
Ala Gly Ser Glu Gly Glu
1 5

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

TCTTGCTTGAAGATCCTAGAGGATCTTCAATA TTT CCG AAG
Cln Ile Phe Pro Lys
1 5

CAA GA
Gln

60

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Gln Ile Phe Pro Lys Gln
1 5

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

49h
TCTTGCGGGT GGAGGATGT AAGATCCTCA TGAGGATCTT AAC ATC CTC CAA CGG
Asn Ile Leu Gln Arg
1 5

CAA GA
Gln

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:
Asn Ile Leu Gln Arg Gln
1 5

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:
TCTTGAGGTTCAGGGATGG AAGATCCTCA TGAGGATCTT CCA TCG CTG AAA CTC
Pro Ser Leu Lys Leu
1 5

AAA GA
Lys

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

491
Pro Ser Leu Lys Leu Lys
1 5

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 40..57

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

CATGGAGCC CCGCTACCTT AAGATCTCT CAGATGTT ACC CCC CCC CTC
Thr Pro Arg Ala Leu
1 5

CAA GA
Gln

59

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(iii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Thr Pro Arg Ala Leu Gln
1 5

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

TCTTGCCCA CGAATTCTAG AAGAYUTTYC TGAAYATU TCTA GAA TTC GTG GCC
Leu Glu Phe Val Gly

1 5

AAA GA
Lys

60

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

Leu Glu Phe Val Gly Lys

1 5

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDINESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:32:

TCTTGCTGT CGAGCAGCT AAGATCTCA TGAGATCTT AGC GTG CTC GAC AGG
Ser Val Leu Asp Arg

55

CAA GA
Gln

60

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

49k

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00848
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Ser Val Leu Asp Arg Gln
1  5

(ii) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:35:

TCTTGATGTA CTTTGCTTG AAGATCTCA TGAGGATCTT CAA GAC AAA GTA CAT

Gln Asp Lys Val His
1  5

CAAs Gln
Gln

60

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Gln Asp Lys Val His Gln
1  5

(2) INFORMATION FOR SEQ ID NO:36.

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

TCTTCTGCTT GATATACTTC AAGATCCCTCA TGAGGATCTT GAA GTA TAT CAA GCA 55
Glu Val Tyr Gln Ala
1 5

GAA GA
Glu
60

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Glu Val Tyr Gln Ala Glu
1  5

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(iii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58

(x) SEQUENCE DESCRIPTION: SEQ ID NO:38:

TCTTGGGGAG TAAAGAAAAC AAGATCCCTCA TGAGGATCTT GTT TTC CTT ACT CCC 55
Val Phe Leu Thr Pro
1  5

GAA GA
Glu
60

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Val Phe Leu Thr Pro Glu
1 5

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: rnc
(B) LOCATION: 41..58

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

TCTTTGTTGG TTATGTATAG AAGATCCTCA TGAGGATCTT CTA TAC ATA ACC AAC 55
Leu Tyr Ile Thr Asn
1 5
AAA GA
Lys

60

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

Leu Tyr Ile Thr Asn Lys
1 5

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41..58
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

TCCTTTCCCTA TATCCGCTC AAGATCCTCA TGAGGATCTT GAC GCC GAT ATA GGA
Asp Ala Asp Ile Gly
1 5

AAG A
Lys

59

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
   (A) LENGTH: 6 amino acids
   (B) TYPE: amino acid
   (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Asp Ala Asp Ile Gly Lys
1 5

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
   (A) LENGTH: 16 amino acids
   (B) TYPE: amino acid
   (C) STRANDEDNESS:
   (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Asp Asp Glu Val Asp Val Asp Gly Thr Val Glu Glu Asp Leu Gly Tyr
1 5 10 15

490

Pieczenik and ICT v. Dyax  00 Civ. 0243 (HB)  00852
To: Examiner J. Brusca
From: Shawn P. Foley, Esq.
Date: September 4, 1998

Number of Pages (Including Cover Page): 8
Client/Matter No: ICTECH/02

Attached:
Amendment Cover Sheet
Amendment

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Pieczenik

Application No. 07/622,764

Filed: February 20, 1991

For: Method and Means for Sorting and Identifying Biological Information

Examiner: John S. Bruce

Date: September 4, 1998

Assistant Commissioner for Patents
Washington, D.C. 20231

Sirs:

Transmitted herewith is an amendment in the above-identified application. The fee has been calculated as shown below.

CLAIMS AS AMENDED

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* If the entry in col. 3 is less than entry in col. 4 write "0" in col. 5.
** If the "highest number paid for" in this space is less than 20, write "20" in this space.
*** If the "highest number paid for" in this space is less than 3, write "3" in this space.

1. (a) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.9 and 1.27 has been filed.
   (b) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.9 and 1.27 has been filed.

2. ☐ No additional fee is required.

3. ☒ Charge $20.00 to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

4. ☒ Please charge any additional fees or credit overpayment to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

LERNER, DAVID, LITTEMBERG, KERSHOLM & RENTMEIJER, LLP

Shawn P. Foley
Reg. No. 33,071

600 South Avenue West
Westfield, NJ 07090-1497
Telephone: (908) 654-0000
Facsimile: (908) 654-7866

F:	000854

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00854
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Pieczenik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

Group Art Unit: 1536
Examiner: John S. Brusca

Date: September 4, 1998

AMENDMENT

Sir:

The Commissioner is authorized to charge Deposit Account No. 12-1095 for the fees occasioned by this Amendment.

Please amend the above-captioned patent application as follows.

IN THE CLAIMS:

(3) (amended). The oligonucleotide population of claim [29] wherein the population is generated by shearing of mammalian genetic material and size fractionation.

(4) (amended). The oligonucleotide population of claim [29] wherein the population is chemically synthesized from [the] component nucleotides.

(6) (thrice amended). A population of recombinant vectors comprising:

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent Office on the date shown below.

[Signature]

September 4, 1998

Date

To: U.S.P.T.O.

Fax: (202)393-7429

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00855
autonomously replicating nucleic acid sequences which nucleic acid sequences
comprise a recombinant structural gene, each of the structural genes comprising an insert
containing one member of an oligonucleotide population,
said oligonucleotide population comprising oligonucleotides [having] comprising a
coding region [having] consisting of a length from about 4 to about 12 nucleotide triplets (that
amongst a) said oligonucleotide population encoding a plurality of corresponding random
peptide sequences of from about 4 to about 12 L-amino acid residues, and

wherein said recombinant structural genes are expressed upon transfer of said
recombinant vectors into Escherichia coli host cells, and wherein expression of the recombinant
structural genes yields polypeptides, each polypeptide comprising one of said plurality of
corresponding random peptide sequences.

(28) (Amended). A population of oligonucleotides comprising double-stranded
oligonucleotides [that consist essentially of] comprising coding regions [having] consisting of a
length of from about 4 to about 12 nucleotide triplets, said coding regions encoding a plurality of
[that amongst a corresponding] peptide sequences of from about 4 to about 12 L-amino acid
residues, said oligonucleotides also comprising [and] 5’ and 3’ flanking sequences that permit said
oligonucleotides to be ligated into a vector,

and wherein the sum of said [corresponding] peptide sequences represents at least

about 10% of all possible peptide sequences of said length.

(49) (amended). A population of oligonucleotides comprising double stranded
oligonucleotides that [consist essentially of] comprise [a] coding regions [having] consisting of a
length of from about 4 to about 12 nucleotide triplets said coding regions encoding a plurality of
peptide [having a] consisting of random sequences of from about 4 to about 12 L-amino acid
residues, [and] said oligonucleotides comprising 5’ and 3’ flanking sequences that permit said
oligonucleotide to be ligated into a vector.

(61) (amended). The oligonucleotide population of claim 49, which is chemically
synthesized from [the] component nucleotides or codons.
(10) Application No. 97/562, r/64

(11) 33 (amended) A peptide population [of] comprising peptides consisting of random sequences [wherein each member of said population has a random sequence] of from about 4 to about 12 amino acid residues.

(14) 33 (amended). A population of binding pairs comprising:

a peptide population [of] comprising peptides[, ] consisting of random sequences [such member of said population having a random sequence] of from about 4 to about 12 amino acid residues, wherein substantially every member of said peptide population is bound to an antibody.

(16) 34 (amended). A method of producing a population of epitopic peptide sequences, comprising:

providing a population of recombinant [E.] Escherichia coli cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising autonomously replicating nucleic acid sequences, said nucleic acid sequences comprising a recombinant structural gene, each structural gene containing an insert comprising a member of an oligonucleotide population, said oligonucleotide population comprising oligonucleotides [consisting essentially of coding regions having] comprising a coding region consisting of a length from about 4 to about 12 nucleotide triplets, said oligonucleotide population encoding a plurality of epitopic peptides consisting of random sequences [encoding an epitopic peptide having a random sequence] of from about 4 to about 12 L-amino acid residues, and

culturing said recombinant [E.] Escherichia coli cells to allow expression of said recombinant structural genes such that said epitopic peptide sequences are accessible to antibody recognition.

(18) 35 (amended). The oligonucleotide population of claim 29, wherein the length of the coding region is 4 nucleotide(s) triplets.

(19) 36 (amended). The oligonucleotide population of claim 29, wherein the length of the coding region is 6 nucleotide(s) triplets.
The oligonucleotide population of claim 29, wherein the length of the coding region is 7 nucleotide(s) triplets.

88 (amended). The oligonucleotide population of claim 29, wherein the length of the coding region is 8 nucleotide(s) triplets.

89 (amended). The oligonucleotide population of claim 29, wherein the length of the coding region is 9 nucleotide(s) triplets.

90 (amended). The oligonucleotide population of claim 29, wherein the length of the coding region is 10 nucleotide(s) triplets.

91 (amended). The oligonucleotide population of claim 29, wherein the length of the coding region is 11 nucleotide(s) triplets.

92 (amended). The oligonucleotide population of claim 29, wherein the length of the coding region is 12 nucleotide(s) triplets.

Please add the following claims.

101. The oligonucleotide population of claim 49, wherein a number of the encoded plurality of peptides has sufficient conformational similarity with an antibody binding site of a test species such that an antibody that binds to the antibody binding site of the test species also binds a peptide of the encoded plurality of peptides.

102. The peptide population of claim 61, comprising a number of peptide sequences of said length having sufficient conformational similarity with an antibody binding site of a test species such that an antibody that binds the antibody binding site of the test species also binds a member of said peptide population.

103. The oligonucleotide population of claim 73, wherein said population of peptides comprises a number of peptides of said length having sufficient conformational similarity with an antibody binding site of a test species such that an antibody that binds to the antibody binding site of the test species also binds a member of said peptide population.

104. The method of claim 84, wherein said oligonucleotide population encodes a number of peptide sequences of said length having sufficient conformational similarity with an
antibody binding site of a test species such that an antibody that binds to the antibody binding site of the test species also binds a peptide of the encoded plurality of peptides.

105. The oligonucleotide population of claim 49, which encodes substantially all possible peptide sequences of said length.

106. The peptide population of claim 61, comprising substantially all peptide sequences of said length.

107. The binding pair population of claim 73, wherein said population of peptides comprises substantially all peptides of said length.

108. The method of claim 84, wherein the oligonucleotide population encodes substantially all peptides of said length.

REMARKS

The Examiner's fastidious efforts and scrutiny of all pending claims is greatly appreciated. The present amendments have been made pursuant to discussions with the Examiner regarding his desire to use transitional language consistent with current PTO policy. Otherwise, claims 85-92 have been amended to correct minor errors. Support for the recitations set forth in claims 101-104 flow from claim 27, and the recitations of claims 105-108 are supported by the disclosures on page 8, lines 12-15, and claim 21. Accordingly, no new matter has been added. Entry of the Amendment is therefore respectfully requested.

In accordance with the requirement set forth in 37 C.F.R. § 1.821(f), Applicant submits that the paper copy and the computer readable form of the Sequence Listing filed on September 1, 1998 are the same.
Applicant submits that the present Amendment serves to place all pending claims in condition for allowance. An early Notice to this effect is therefore solicited. The Examiner is encouraged to contact the undersigned if he has any remaining questions.

Respectfully submitted,

LENNERT, DAVID, LITFENBERG,
KRUMHOLZ & MENTLIK, LLP

Shawn P. Foley
Reg. No. 33,071

600 South Avenue West
Westfield, New Jersey 07090
Telephone: (908) 654-5000
Facsimile: (908) 654-7866
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Piecznik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

Group Art Unit: 1536
Examiner: John S. Brusca
Date: September 4, 1998

HAND CARRY

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

It is respectfully requested that the references listed on the enclosed Form PTO-1449 be made of record and considered with respect to the above-referenced U.S. patent application. Each cited reference was of record in the corresponding Israeli application. A copy of each reference is enclosed. Submission of the present Information Disclosure Statement should not be taken as an admission that the cited references are legally available prior art or that the same are pertinent or material. Please charge Deposit Account No. 12-1095 in the amount of $240.00 pursuant to 37 C.F.R. § 1.17(p).

Respectfully submitted,

LERNER, DAVID, LITZENBERG, KRUMHOLZ & MENTLIK, LLP

SHAWN P. FOLEY
Reg. No. 33,071

600 South Avenue West
Westfield, New Jersey 07090
Telephone: (908) 654-3000
Facsimile: (908) 654-7866
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EXAMINER: Initial if reference considered, whether or not citation is in accordance with MPEP 609; Draw line through citation if not in accordance and not considered. Include copy of this form with next communication to applicant.
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LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK, LLP

600 South Avenue West
Westfield, New Jersey 07090

Telephone: (908) 654-5000
Facsimile: (908) 654-7866

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To: Jennifer

Fax Number 703-892-4510

Company Landon & Stark

From: Shawn P. Foley, Esq.

Date: September 4, 1998

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Per our conversation, please hand carry the attached Supplemental IDS, PTO-1449 and the cited references that you obtained for me. I have also attached a copy of a postcard. Please have someone at the PTO stamp it. Please send me copies of the references and the original of the stamped postcard.

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Application No. 07/662,764

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Two pages of PTO 1449
One copy of each cited reference

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**FOREIGN PATENT DOCUMENTS**

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**OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)**

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EXAMINER: [Signature]

DATE CONSIDERED: 9/21/98

*EXAM-220-G-2H: Not to be considered whether or not citation is in conformity with MPEP 609. Draw line through citation if not in conformity and not considered. Include copy of this form with next communication to applicant.*
**LIST OF PRIOR ART CITED BY APPLICANT**

(Use several sheets if necessary)

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*EXAMINER: Initial if reference considered, whether or not citation is in accordance with MPEP 601. Draw line through citation if not in accordance and not considered. Include copy of this form with next communication to applicant.

Pleczentik and ICT v. Dyax 00 Civ. 0243 (HB) 00868
TO: Shawn Foley
FIRM: ATTORNEY'S DOCKET # OR SERIAL#: 07/662764
FAX/TELECOPIER NUMBER: (908) 654-7866
DATE: September 25, 1998

FROM: Examiner John S. Brusca, Ph.D.
ART UNIT 1636
FAX: (703) 305-7099
PHONE: (703) 308-4231

MAILING ADDRESS: John S. Brusca
Art Unit 1636
U.S. Patent and Trademark Office
Crystal Mall 1
7th Floor Receptionist
1911 S. Clark Street
Arlington, VA 22202
7th Floor Receptionist phone: (703) 308-0196

PAGES, INCLUDING COVER SHEET:

COMMENTS: courtesy copy of notice of allowability

IF YOU HAVE NOT RECEIVED ALL THE PAGES OF THIS TRANSMISSION, PLEASE CONTACT THE EXAMINER AT THE TELEPHONE NUMBER LISTED ABOVE.
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IN COMPLIANCE WITH 37 CFR 1.106 (2), THE FILING DATE ACCORDED EACH OFFICIAL FAX TRANSMISSION WILL BE DETERMINED BY THE FAX MACHINE DATE STAMP FOUND ON THE LAST PAGE OF THE TRANSMISSION, UNLESS THAT DATE IS A SATURDAY, SUNDAY, OR FEDERAL HOLIDAY WITHIN THE DISTRICT OF COLUMBIA, IN WHICH CASE THE OFFICIAL DATE OF RECEIPT WILL BE THE NEXT BUSINESS DAY.

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Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00869
Notice of Allowability

Application No. 07/662,764
Applicant(s) Pieczenik
Examiner John S. Brusca
Group Art Unit 1638

All claims being allowable, PROSECUTION ON THE MERITS IS (UN MARKED) CLOSED IN this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

☐ This communication is responsive to the amendments filed 5/18/98, 7/30/98, 9/1/98, and 9/4/98.

☐ The allowed claim(s) is/are 3-6, 8, 11-15, 19, 20, and 29-108.

☐ The drawings filed on ______________________ are acceptable.

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been 
received.
☐ received in Application No. (Series Code/Serial Number) ____________________.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received:


A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

☐ Applicant MUST submit NEW FORMAL DRAWINGS

☐ because the originally filed drawings were declared by applicant to be informal.

☐ including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. ____________.

☐ including changes required by the proposed drawing correction filed on ________________, which has been approved by the examiner.

☐ including changes required by the attached Examiner's Amendment/Comment.

Identifying Indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/ SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

☐ Notice of References Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 49, 54.
☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152
☐ Interview Summary, PTO-413
☒ Examiner's Amendment/Comment

☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
☒ Examiner's Statement of Reasons for Allowance

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00870
NOTICE OF ALLOWANCE AND ISSUE FEE DUE

HM11/0928

SHAWN PL FOLEY
LERNER, DAVID, LITENBERG, KRUMHOLZ &
MENTLIK
600 SOUTH AVENUE WEST
WESTFIELD, NJ 07090-1497

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First Name: PIECZENIK, GEORGE

TITLE OF INVENTION: METHOD AND MEANS FOR SORTING AND IDENTIFYING BIOLOGICAL INFORMATION

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THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED.

THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.

HOW TO RESPOND TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.
   If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
   A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
   B. If the status is the same, pay the FEE DUE shown above.

II. Part B-Issue Fee Transmittal should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B Issue Fee Transmittal should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section 4b of Part B-Issue Fee Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give application number and batch number. Please refer all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issued on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (REV. 10-96) Approved for use through 06/30/99. (0651-0033)

YOUR COPY
**MAKING INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE. Blocks 1 through 4 should be completed when applicable. All further correspondence including the issue fee receipt, the patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated below or directed elsewhere in Block 1, by (a) specifying a new correspondence address, and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

**CURRENT CORRESPONDENCE ADDRESS** (Note: Legibly mark-up with any corrections or use Block 1):

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**Filing Name:**

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**METHOD AND MEANS FOR SORTING AND IDENTIFYING BIOLOGICAL INFORMATION**

**ATTY'S DOCKET NO.**

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1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.366). Use of PTO form(s) is recommended, but not mandatory.

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" indication form PTO/SB/47) attached.

2. For printing on the patent front page, list:
   (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the names of a single firm (having as a member a registered attorney or agent) and the names of up to 3 registered patent attorneys or agents. If no name is listed, no name will be placed.

☐ LERNER, DAVID, LITTMENBERG
☐ KRUMHOLZ & MENTLIK

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type):

     (A) NAME OF ASSIGNEE

     (B) RESIDENCE: CITY & STATE OR COUNTRY

     Please check the appropriate assignee category indicated below (will not be printed on the patent)

     ☐ individual ☐ corporation or other private group entity ☐ government

4. The following fees are enclosed (make check payable to Commissioner of Patents and Trademarks):

   ☐ Issue Fee
   ☐ Advance Order - # of Copies

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5. The following fees or deficiency in these fees should be charged to:

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   ☐ Issue Fee
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**The Commissioner of Patents and Trademarks is requested to apply the fee(s) in the amount(s) identified above**

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**NOTE:** The issue fee will not be accepted from anyone other than the applicant, a registered attorney or agent, or the assignee or other party in interest as shown by the records of the Patent and Trademark Office.

**Burdens Hour Statement:** This form is estimated to take 0.2 hours to complete. Time will vary depending on the needs of the individual case. Any comments on the amount of time required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES ON COMPLETED FORM TO THIS ADDRESS. SEND FEES AND THIS FORM TO: Box Issue Fee, Assistant Commissioner for Patents, Washington D.C. 20231

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Notice of Allowability

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

☒ This communication is responsive to the amendments filed 5/18/98, 7/30/98, 9/1/98, and 9/4/98.

☒ The allowed claim(s) is/are 3-6, 8, 11-15, 19, 20, and 29-108.

☐ The drawings filed on ________________ are acceptable.

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.

☐ received in Application No. (Series Code/Serial Number) ____________________.

☐ received in this national stage application from the International Bureau IPC Rule 17.2(a).

*Certified copies not received: ____________________.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

☐ Applicant MUST submit NEW FORMAL DRAWINGS

☐ because the originally filed drawings were declared by applicant to be informal.

☐ including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. ________________.

☐ including changes required by the proposed drawing correction filed on ________________, which has been approved by the examiner.

☐ including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/ SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 49, 54

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☐ Interview Summary, PTO-413

☒ Examiner's Amendment/Comment

☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material

☒ Examiner's Statement of Reasons for Allowance

U. S. Patent and Trademark Office
PTO-37 (Rev. 9-95) Notice of Allowability Part of Paper No. 55

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00873
DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Shawn Foley on 9/21/98.

2. The application has been amended as follows:

In claim 101, line 2, "antibody binding site" has been deleted and --epitope-- has been substituted therefor.

In claim 101, line 3, "antibody binding site" has been deleted and --epitope-- has been substituted therefor.

In claim 102, line 2, "antibody binding site" has been deleted and --epitope-- has been substituted therefor.

In claim 102, line 3, "antibody binding site" has been deleted and --epitope-- has been substituted therefor.
In claim 103, line 3, "antibody binding site" has been deleted and --epitope-- has been substituted therefor.

In claim 103, bridging lines 3 and 4, "antibody binding site" has been deleted and --epitope-- has been substituted therefor.

In claim 104, line 3, at each of the two occurrences of the phrase "antibody binding site" has been deleted and --epitope-- has been substituted therefor.

The claims have been reordered so that independent claims are followed by their dependent claims.

Reasons for Allowance

3. The following is an examiner's statement of reasons for allowance:

The rejection of claims under 35 U.S.C. § 102(b) over Goulion et al. is withdrawn because the nucleic acid fragments of Goulion et al. do not comprise 5' and 3' flanking sequences that permit ligation to a vector because the DNase treatment of Goulion et al. produces protruding 3' and 5' ends of random sequences.

The rejection of claims under 35 U.S.C. § 103 over Lupschi et al. in view of Goulion et al. is withdrawn because of the deficiencies in the Goulion et al. reference described above.

The rejection of claims under 35 U.S.C. § 112, first paragraph is withdrawn because one of skill in the art would be able to select those members of the claimed populations of vectors, oligonucleotides, or peptides which were of interest.
The rejection of claims under 35 U.S.C. § 112, second paragraph are withdrawn in view of the Amendment filed 7/30/98 and the Examiner’s Amendment detailed above.

The terms “having”, “has”, and “have” in the claims are considered to be closed and equivalent to the terms “consisting of” and “consists of”.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

4. Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. For routine submissions the FAX number is (703) 308-4242. For FAX transmissions in cases in which the Examiner has been notified by phone to expect the transmission, the FAX number is (703) 305-7939. In such cases please call the Examiner at (703) 308-4231 at the time of transmission to expedite delivery of the FAX. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6 (d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant’s representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.
Application/Control Number: 07/662764
Art Unit: 1636

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca, Ph.D. whose telephone number is (703) 308-4231. The examiner can normally be reached on Monday through Friday from 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, Ph.D., can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

John S. Brusca, Ph.D.  
Examiner

George C. Elliott, Ph.D.  
Supervisory Patent Examiner  
Technology Center 1600

Plecznik and ICT v. Dyax  00 Civ. 0243 (HB)  00877
To:       Examiner J. Brusca  
Fax Number   703-305-7939  
Company:     PTO  

From:    Shawn P. Foley, Esq.  
Date:      October 13, 1998  

Number of Pages (Including Cover Page): 4  
Client/Matter No: ICTECH/02  
Original Being Mailed? No  

Attached:  
Amendment Cover Sheet  
Amendment under 37 C.F.R § 1.312(a)  

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Pieczenik and ICT v. Dyax  00 Civ. 0243 (HB)  00878
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Pienkenik

Application No. 07/662,764

Filed: February 28, 1991

For: Method and Means for Sorting and Identifying Biological Information

Claim 1 of 11 is amended. The fee has been calculated as shown below.

| CLAIMS | HIGHEST NUMBER OF EXTRA ADJUS TOTAL |  |  |  |  |  |  |  |
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| (1)    | (2)                                 | (3) | (4) | (5) | (6) | (7) |    |
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| TOTAL  | 111      | MINUS| 92    |    |    |    | 209.00 |
| INDEPENDENT | 11    | MINUS| 11    |    |    |    | 0.00   |

FEE FOR FIRST PRESENTATION OF
MULTIPLE DEFENDANT CLAIMS
$135 = $ 135.00

TOTAL ADDITIONAL FEE $344.00

* If the entry in col. 1 is less than entry in col. 4 write "C" in col. 5.
** If the "highest number paid for" in this space is less than 20, write "20" in this space.
*** If the "highest number paid for" in this space is less than 3, write "3" in this space.

1. (a) ☒ A Verified Statement to establish small entity status under 37 C.F.R. 1.27 has been filed.
(b) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.27 and 1.55 is enclosed.
2. ☐ No additional fee is required.
3. ☒ Charge $344.00 to Deposit Account No. 10-1095. A duplicate copy of this sheet is enclosed.
4. ☒ Please charge any additional fees or credit overpayment to Deposit Account No. 10-1095. A duplicate copy of this sheet is enclosed.

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Pienkenik and ICT v. Dyax 00 Civ. 0243 (HB) 00879
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Pieczenik
Application No. 07/662,764
Filed: February 28, 1991
For: Method and Means for Sorting and Identifying Biological Information

Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT UNDER 37 C.F.R § 1.312(a)

Sir:

This is in response to the Notice of Allowability, mailed September 28, 1998. The Commissioner is authorized to charge Deposit Account No. 12-1095 for the fees occasioned by this Amendment.

Please amend the above-captioned application as follows.

IN THE CLAIMS:

In claim 40, line 1, insert —or 31— immediately after "6".

In claim 41, line 1, insert —or 31— immediately after "6".

In claim 42, line 1, insert —or 31— immediately after "6".

In claim 43, line 1, insert —or 31— immediately after "6".

In claim 44, line 1, insert —or 31— immediately after "6".

CERTIFICATION OF POSSIBLE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent Office on the date shown below.

Sharon P. Falty, Req.
Signature

October 13, 1998
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Attn: John S. Brusca

FAX No.: (703) 308-3022

No. of Pages: 2

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00880
In claim 45, line 1, insert "or 31- immediately after "6".
In claim 46, line 1, insert "or 31- immediately after "6".
In claim 47, line 1, insert "or 31- immediately after "6".
In claim 48, line 1, insert "or 31- immediately after "6".
In claim 53, line 1, insert "29 or- immediately before "claim".
In claim 19, line 1, insert "51 or- immediately after "claim".
In claim 75, line 1, insert "37 or- immediately after "claim".
In claim 76, line 1, insert "17 or- immediately after "claim".
In claim 77, line 1, insert "37 or- immediately after "claim".
In claim 78, line 1, insert "37 or- immediately after "claim".
In claim 79, line 1, insert "37 or- immediately after "claim".
In claim 80, line 1, insert "37 or- immediately after "claim".
In claim 81, line 1, insert "37 or- immediately after "claim".
In claim 82, line 1, insert "37 or- immediately after "claim".

REMARKS

The present Amendment simply creates multiple dependencies in claims that define the lengths of the oligonucleotides and peptides. Accordingly, no new matter is being added.

Entry of the Amendment is respectfully requested.

Respectfully submitted,

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P/DOC199730.114484.DOC

2

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**Reason for Error**

1. Manual error
2. No answer
3. Fax transmission connection

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Pieczenik and ICT v. Dyax  00 Civ. 0243 (HB)  00882
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FACSIMILE TRANSMITTAL SHEET

To: Examiner J. Brusca
Fax Number: 703-305-7939
Company: PTO

From: Shawn P. Foley, Esq.
Date: October 21, 1998

Number of Pages (Including Cover Page): 4
Client/Matter No: ICTECH/02
Original Being Mailed? No

Attached:
Amendment Cover Sheet
Amendment under 37 C.F.R § 1.512(a)

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Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00883
In re: Patent Application of

Pieczenik

Application No. 07/662,764

Filed: February 28, 1991

For: Method and Means for Sorting and Identifying Biological Information

Date: October 21, 1998

Assistant Commissioner for Patents
Washington, D.C. 20231

Transmitted herewith is an amendment in the above-identified application. The fee has been calculated as shown below.

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FEE FOR FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM(S)

$135 = $135.00

TOTAL ADDITIONAL FEE FOR THIS AMENDMENT...

* If the entry in col. 3 is less than entry in col. 4 write "0" in col. 5.
** If the "highest number paid for" in this space is less than 20, write "20" in this space.
*** If the "highest number paid for" in this space is less than 1, write "1" in this space.

1. (a) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.9 and 1.27 has been filed.

(b) ☐ A Verified Statement to establish small entity status under 37 C.F.R. 1.9 and 1.27 is enclosed.

2. ☐ No additional fee is required.

3. ☐ Charge $135.00 to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

* ☐ Please charge any additional fees or credit overpayment to Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.

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Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00884
AMENDMENT UNDER 37 C.F.R § 1.312(a)

Sir:

This is in response to the Notice of Allowability, mailed September 28, 1998. The Commissioner is authorized to charge Deposit Account No. 12-1095 for the fees occasioned by this Amendment.

Please amend the above-captioned application as follows.

IN THE CLAIMS:

In claim 40, line 1, insert —or 31— immediately after "6".

In claim 41, line 1, insert —or 31— immediately after "6".

In claim 42, line 1, insert —or 31— immediately after "6".

In claim 43, line 1, insert —or 31— immediately after "6".

In claim 44, line 1, insert —or 31— immediately after "6".

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent Office on the date shown below.

Shawn P. Foley, Esq.

[Signature]

October 21, 1998
Date

To: U.S.P.T.O

[Address]

Fax No.: [Number]

No. of Pages: 2
In claim 45, line 1, insert "or 31-- immediately after "5". 
In claim 46, line 1, insert "or 31-- immediately after "5". 
In claim 47, line 1, insert "or 31-- immediately after "5". 
In claim 48, line 1, insert "or 31-- immediately after "5". 
In claim 53, line 1, insert "29 or-- immediately after "claim". 
In claim 71, line 1, change "35" to "03--. 
In claim 72, line 1, change "65" to "63--. 
In claim 74, line 1, insert "37 or-- immediately after "claim". 
In claim 75, line 1, insert "37 or-- immediately after "claim". 
In claim 76, line 1, insert "37 or-- immediately after "claim". 
In claim 77, line 1, insert "37 or-- immediately after "claim". 
In claim 78, line 1, insert "37 or-- immediately after "claim". 
In claim 79, line 1, insert "37 or-- immediately after "claim". 
In claim 80, line 1, insert "37 or-- immediately after "claim". 
In claim 81, line 1, insert "37 or-- immediately after "claim". 
In claim 82, line 1, insert "37 or-- immediately after "claim".

REMARKS
The present Amendment simply creates multiple dependencies in claims that define the lengths of the oligonucleotides and peptides. Accordingly, no new matter is being added. Entry of the Amendment is respectfully requested.

Respectfully submitted,

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Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00886
Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks
☐ The petition filed on ________________ under 37 CFR 1.312(b) is granted. The paper has been forwarded to the examiner for consideration on the merits.

☑ The amendment filed on 10/21/08 under 37 CFR 1.312 has been considered, and has been:
☑ entered.
☐ entered as directed to matters of form not affecting the scope of the invention (Order 3311).
☐ disapproved. See explanation below.
☐ entered in part. See explanation below.

George C. Elliott, Ph.D.
Supervisory Patent Examiner
Technology Center 1600
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APPLICANT(S)  GEORGE PIECZENIK, NEW YORK NEW YORK

Pieczenik and ICT v. Dyax  00 Civ. 0243 (HB)  00889
METHOD AND MEANS FOR SORTING AND IDENTIFYING BIOLOGICAL INFORMATION

Inventor: George Piecznik

Appl. No.: 662,764
Filed: Feb. 28, 1991

Related U.S. Application Data

Continuation-in-part of Ser. No. 201,358, May 26, 1988, abandoned, which is a continuation of Ser. No. 770,790, Aug. 28, 1985, abandoned.

Int. Cl. 8 C12P 21/02; C12N 15/11; C12N 15/53; A61K 38/04

Field of Search 435/91, 435/91.1, 435/92, 435/20, 330/237; 330/228; 330/239; 330/230, 330/237.5, 536/231

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4,618,758 10/1985 Burke 435/6
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A1 0 048 118 1/1984 European Pat. Off.
A 145794 9/1980 Germany.
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206871 8/1981 United Kingdom.
2113661 10/1987 United Kingdom........ C12N 1500
WO 84/02022 8/1984 WIPO
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WO 85/03725 8/1985 WIPO.
WO 86/00991 2/1986 WIPO
WO 86/01487 11/1986 WIPO
90/1570 12/1990 WIPO

OTHER PUBLICATIONS


Wells et al. (1985), Gene, vol. 34, pp. 313-324.

Primary Examiner—George C. Elliot
Assistant Examiner—John S. Brusca
Attorney, Agent, or Firm—Lerner, David, Littenberg, Kurz, Hyman & Metallik

ABSTRACT

In one aspect, the invention discloses a matrix comprising a discrete population of random oligopeptides of the same length, the length being selected from about 4 to about 12 L-amino acid residues, the population comprising at least 10% of all amino acid sequences of the selected length; and a heterogeneous population of antibodies comprising antibodies capable of binding to substantially every member of the oligopeptide population.

93 Claims, No Drawings
Dame, J. B. et al., Science 225:593 (1984), sequenced the CS gene of Pneumocystis carinii and discovered 41 tandem repeats of a tetrapeptide, with some minor variations. Using synthetic peptides of 4, 7, 11, and 15 amino acid residues of the predominant repeating amino acid sequence, Dame et al. then conducted competitive binding assays to determine what length of peptide would inhibit the binding of the CS protein with a monoclonal antibody specific to that protein. Dame et al. found that the synthetic 4 amino acid sequence did not significantly inhibit binding, but the 7, 11 and 15 amino acid sequences did inhibit binding. These results suggest that this monoclonal antibody to the CS protein recognizes a 5 to 7 amino acid sequence comprising the repeating tetrapeptide.

The known crystal structures of the Fab fragment and lysosome show that there are two contact points on the lysosome molecule for the antibody combining site, and each contact point spans over about five amino acids. Earlier work on antibody binding to carbohydrate antigens and glycosidase cleavage protection experiments show that 5-6 sugar residues are protected from glycosidase cleavage. Studies with antibody binding to haptens also suggest that antibody sites are small. Peptide competition experiments, also called epitope mapping experiments, show that oligopeptides 4 to 5 amino acids in length can specifically compete for antibody binding.

In addition, linear sequences which differ in only one amino acid, can compete for antibody binding with varying degrees of specificity (see, e.g., Geyser et al. (1986) in Synthetic Peptides as Antigens; Ciba Foundation Symposium 119, R. Porter and J. Wheelan, Eds. (New York, Wiley) pp. 130-149).

While five amino acids is a representative length of peptide sequence which can bind with differential specificity to an antibody, five amino acid residues is not necessarily the size of an immunogenic peptide. Generally, when an oligopeptide is the desired immunogen, it is first conjugated to a larger carrier molecule. The actual operational relationship between the immunizing entity and the binding entity can only be resolved when an in vivo immunization-dependent antibody synthesis system is developed.

**SUMMARY OF THE INVENTION**

In one aspect the invention features a discrete population of oligonucleotides, each comprising the same length of from about 4 to about 12 nucleotide coding triplets in random order. Each oligonucleotide encodes a corresponding oligopeptide of from about 4 to about 12 L-amino acid residues, and the entire population represents at least about 10% of all oligopeptide sequences of the selected length. In preferred embodiments, each member of the oligonucleotide population has a single copy of the random sequence of nucleotide triplets, the oligonucleotide sequence has between 4 and 7 triplets, and the oligonucleotide population can be generated by random shearing of mammalian genetic material or is chemically synthesized from the component nucleotides.

It is particularly preferred that each oligonucleotide sequence comprises four to nine triplets. The oligonucleotide population may also be composed of members, each of which contains the same number of tandem repeats of each peptide coding sequence, where the number of tandem repeats is from two to about fifty. It is particularly preferred that the oligonucleotide population be sufficiently redundant so that each of all possible encoded oligopeptide sequences is present at least 10 times on average.

In a second aspect the invention features a discrete population of oligopeptides each of random amino acid sequence of the same length, of about 4 to about 12 L-amino acid residues, and the population makes up at least 10% of all peptide sequences of the predetermined length. In preferred embodiments each member of the population has a single copy of the peptide sequence, the oligopeptide sequence has between 4 and 7 L-amino acid residues and the population can be generated by shearing of proteins, by chemical synthesis from the component L-amino acids, or by the translation of the oligonucleotides of random coding sequences.

It is particularly preferred that there be five amino acid residues in each oligopeptide. It is particularly preferred that the population of oligopeptides is sufficiently large so that each sequence is represented at least 10 times on average.

The peptide population can also be composed of member peptides, each of which contains the same number of tandem repeats of the amino acid sequence, where the number of repeats is from two to about fifty.

In a third aspect, the invention features a discrete recombinant vector population of summarized identical autonomously replicating nucleic acid sequences including a structural gene and a population of oligonucleotide inserts therein, each insert containing a uniform length selected from between about 4 and about 12 nucleotide coding triplets, preferably between 4 and 7, and most preferably five. Each insert is recombinantly inserted in frame into the structural gene of one of the nucleotide sequences, and preferably the oligonucleotide population encodes all oligopeptide sequences of the predetermined length. Preferably the recombinant vector population is redundant, i.e., contains a sufficient number of random oligonucleotide members so that all possible members are represented at least once. It is particularly preferred that the population is sufficiently redundant so that the population contains at least 10 copies of oligonucleotides encoding each possible peptide sequence, on average. In preferred embodiments each member of the insert population has a single copy of the sequence of nucleotide triplets, and the insert has coding triplets; the replicating sequence can be a plasmid such as pBR322, a virus such as λgt11 or vaccinia, or a filamentous bacteriophage, such as fd or M13. The recombinant vector population can also be made up of individual vectors each containing the same number tandem repeats of an oligonucleotide sequence as defined above. The number of tandem repeats can be from two to about fifty in number.

The recombinant vector population can also be made up of individual vectors each containing the same number tandem repeats of an oligonucleotide sequence as defined above. The number of tandem repeats can be from two to about fifty in number.

In a fourth aspect, the invention features a discrete heterogeneous population of oligonucleotides comprising member antibodies capable of binding to substantially all members of the discrete oligopeptide population featured in the second aspect of the invention, above.

In a fifth aspect, the invention features a discrete population of binding pairs that includes the discrete population of peptide sequences all of the same length selected from about 4 to about 12 L-amino acid residues and the heterogeneous population of antibodies capable of binding to substantially all the peptide sequences, where substantially every member of the peptide population is bound to a corresponding antibody.

In a sixth aspect, the invention features a matrix including a discrete population of random peptide sequences and a heterogeneous population of antibodies.
present having the ability to produce antibodies specific for that antigen. Since there is a finite number of linear peptide sequences of the length that is recognized by antibodies, it can be expected that each mammal has the capability to produce antibodies that will recognize most, if not all of these sequences. Thus, the spleen of a mouse or another inbred strain can serve as an appropriate source for a full range of antibodies. The spleen can be harvested from a laboratory animal, and, using standard techniques, the individual cells are fused to myeloma cells and hybridoma strains are developed.

Depending on the desired characteristics of the resulting hybridoma population, either specifically stimulated animals can be used, or animals that have not been specifically challenged with the antigenic material of interest can be used.

If antigenically stimulated animals are used, then a higher proportion of the resulting hybridomas will produce antibodies specific to the antigen used. If, on the other hand, unchallenged animals are used, then it can be expected that the antibodies retrieved from the resulting population of hybridomas will represent a broader range of the antibodies that the animals are capable of producing. The predominant antibodies produced by a mature animal raised under standard laboratory conditions will reflect and be limited by its individual exposure history. If spleens are harvested from several (at least about 10) unchallenged mature animals and combined together, and the spleen cells fused to myeloma cells, then the resulting discrete population of hybridomas will produce a more complete range of antibodies than would hybridomas from any single individual. Antibodies produced by the hybridomas derived from the spleen cells of mature animals that were raised asexually or from fetal or neonatal animals that were raised asexually or from fetal or neonatal animals will not reflect any exposure history and can be expected to represent a random sample of the full range of antibodies that the animals are capable of producing.

Since this procedure does not require antigenic stimulation of donor animals before harvesting the spleens, it is now possible to develop antibodies derived from human cells. Normal spleen cells can be collected from one or a number of human donors and the harvested cells fused to myeloma cells and cultured as described above. Alternatively, a library of human antibodies can be developed over time by obtaining cell cultures from, e.g., a large number of myeloma patients, each patient having a distinctive tumor.


Production of Peptide Sequences

Numerous methods are available for the production of the desired population of peptide sequences. For certain embodiments of the invention these peptide sequences can be produced directly either by randomly shearing proteins and then recovering by electrophoresis the peptide sequences of the appropriate length or by synthesizing the desired random peptide sequences from the component amino acids.

Alternatively, these peptides can be produced through genetic engineering techniques. Peptides produced according to this general method can be used without further purification.

A population of nucleotide sequences of the correct length to encode random peptide sequences of the desired length is generated. This can be accomplished either by random cleavage of biological genetic material followed by electrophoresis to recover those nucleotide sequences that were cut or sheared to the desired length, or by chemical synthesis from the appropriate nucleotides in solution.

Depending on the desired characteristics of the resulting population of nucleotide sequences and ultimately, of the peptide sequences to be produced, different techniques are used to obtain the population of nucleotides. If a random population of nucleotide sequences is desired, then the nucleotides can be synthesized by adding the four nucleotides with equal frequency at each position of the growing nucleotide chain. If it is desired that the nucleotide triplets more closely reflect the distribution of naturally occurring triplets, then the frequency of each nucleotide employed at the first, second, or third position of each triplet can be manipulated to approximate the frequencies at which each nucleotide residue appears at each position in nature, as suggested in Crick F. H. C., et al. (1976) Science 194:580–597. Any of several sources of genetic material can be selected to obtain by shearing nucleotide sequences of the desired length, e.g., cellular DNA or cDNA. cDNA, of course, would provide a closer representation of the naturally occurring coding sequences. Alternatively, chemically synthesized oligonucleotides of random sequence may be used.

When the desired population of nucleotide sequences has been obtained, the population can then be treated to facilitate the insertion of each sequence into a vector and to facilitate the subsequent recovery of the desired peptide sequence from the culture of host cells incorporating the engineered vector. For example, using known techniques, AUG sequences can be ligated to each end of each member of the population of nucleotide sequences. When each nucleotide sequence is translated, the desired peptide sequence will be flanked by methionine residues. The translated protein can then be treated with cyanogen bromide, which cleaves the peptide from the DNA at methionine sites, to excise the desired peptide sequence from the protein. The excised peptide can then be purified by electrophoresis. Preferably, a restriction endonuclease recognition site can be ligated to each end of each member of the population of nucleotide sequences and then the population of nucleotide sequence can be treated with the endonuclease recognizing the ligated sequence to produce "sticky ends" which facilitate the insertion of the nucleotide sequence at the restriction site in a vector recognized by the endonuclease. When the population of nucleotide sequences is chemically synthesized, flanking restriction sites may be designed into the oligonucleotide nucleotide sequence, as understood in the art.

Each nucleotide sequence is then inserted into an appropriate vector. The ratio of nucleotide sequences to vectors can be controlled to ensure that, on the average, no more than one nucleotide sequence is inserted into any vector. The nucleotide sequence must be inserted at a location in the vector where it will be translated in phase when the vector is transferred into an appropriate host cell, and where it will not interfere with the replication of the vector under experimental conditions employed, i.e., the nucleotide sequence must be inserted into a non-essential region of the vector. Finally, if the vector is to incorporate foreign DNA into a non-essential region of a vector, Smith (1985) Science 228:1315–1317 describes the insertion of heterologous coding sequences into the unique...
labeled with an appropriate label, such as a fluorescent compound, an enzyme, or a radioactive tracer, as known in the art. The peptide sequence itself can serve as a sensitive biological tag where it occurs on the surface of a protein, virus or modified host cell.

When the antibodies are immobilized, the peptide sequences or polypeptides comprising those peptide sequences are then contacted with the antibodies under appropriate conditions and for a sufficient amount of time so that each immobilized antibody binds to the peptide sequence to which it is specific. Where the peptide sequences are immobilized, the antibodies are then contacted with the peptide sequences so that each immobilized peptide sequence is recognized and bound by an antibody specific for that particular sequence. Each complex of peptide sequence and its bound antibody can be termed a binding pair. In some cases, the antibodies or peptide sequences themselves are immobilized on the substrate; in other cases the cell cultures producing the antibodies or the mounted yeast cells expressing the peptides are immunoassayed.

Binding pairs are created in a single step, taking advantage of the natural affinity of antibodies for the peptide sequences to which they are specific. If a sample of antibodies is contacted with a population of immobilized antibodies, then the antibodies will self-sort and each will bind to its corresponding antibody. Similarly, if a sample of antibodies is contacted with a population of immobilized peptides, then the antibodies will self-sort and each will bind to its cognate peptide. The sorting will occur spontaneously, and there is no prior knowledge as to the functional characteristics of any of the individual antibodies or peptides.

A matrix where the antibodies are immobilized on the substrate will be designated an antibody-immobilized matrix, or AIM. Where each immobilized antibody forms a binding pair with a corresponding peptide sequence, the matrix will be designated P-AIM. Similarly, a matrix where the peptide sequences are immobilized on the substrate will be designated an antibody-immobilized matrix, or AIM. Where each immobilized peptide sequence forms a binding pair with a corresponding antibody, the matrix will be designated P-AIM.

Generally, the method of the invention involves contacting a test species with an intact P-AIM or an intact A-PIM, the specific characteristics of the matrix depending on the nature of the information sought as the skilled artisan will readily understand. Considering the large number of different hybridomas, recombinant vectors and genetically modified host cells that are available in the practice of the invention, the antibodies or peptide sequences can be immobilized very densely on the substrate. Areas of competitive binding are identified when the test species is contacted with the matrix.

Recombinant vectors or modified host cells can mediate from these areas of competitive binding can then be retrieved, repeated less densely, and the competitive binding step with the test species repeated in order to specifically identify the individual colony producing the antibody or amino acid sequence where pairing was disturbed.

Screening an Antibody or Test Species of Interest

A P-AIM is used both to identify and obtain antibody clones that are specific to a test species of interest and to identify the specific peptide sequence recognized by an antibody of interest. The test species can be, for example, a virus, a bacteriophage, a virus coat protein, a surface protein of a viral or bacterial pathogen, a protein on the surface of a malignant cell, an enzyme, or a peptide having the sequence of a natural peptide of a protein of interest. The test species need not contain peptides, but may be, e.g., a drop or carbohydrate having a three-dimensional structure that is closely approximated by a peptide sequence.

The test species is contacted with a P-AIM in a competitive binding assay with each of the complexed binding pairs. Each binding pair occupies a unique site on the matrix. Where there have been labeled, any pairings disturbed by the presence of the test species can be identified.

A particularly sensitive labeling technique is obtained where the peptide sequences bound to the immobilized antibodies are on the surface of a protein or vector. After the P-AIM is created and the binding pairs are established, the P-AIM is thoroughly washed to remove any unbound peptide sequences. The test species is then contacted with the P-AIM. Any peptide sequences that are displaced from their corresponding antibodies by the presence of the test species can be directly titered off the P-AIM. The matrix is then washed again, and each clone producing an antibody that binds to a test species is identified and cultured to provide a source of the antibody.

Where the test species is an antigen, its binding can be detected directly. Each clone producing an antibody that binds to a test species is identified and cultured to provide a source of the antibody. Each culture producing a peptide sequence displaced by the presence of an antibody of interest is identified and cultured to provide a source of that peptide sequence.

A PIM is used both to identify the specific sequences on a test protein or polypeptide that can be recognized by antibodies and to identify the specific peptide sequences recognized by an antibody of interest. Each clone or peptide in a PIM represents the expression or presence of at least $10^3$--$10^5$ copies of the individual peptide sequence so that detection of labeled antibody binding or of the displacement of bound labeled antibody is readily accomplished using techniques known to the art. The procedure for screening on a PIM is analogous to the procedure, above, for screening on an AIM. The test protein or polypeptide sequence, or the test antibody, is contacted with an intact P-IM in a competitive binding assay with each of the antibody-peptide sequence pairs. The pairings disturbed by the presence of the test protein or polypeptide or test antibody are noted, and the clones producing the amino acid sequence to which pairing was disturbed are identified and cultured. By this method, not only is it possible to determine the amino acid sequence recognized by the antibody, but it is now possible as well to identify a nucleic acid sequence encoding this amino acid sequence as the oligonucleotide insert in the vector contained in the clone that produces the recognized amino acid sequence.

**EXAMPLE 1**

Production of Hybridoma Cell Lines

Several C57Bl/10 mice are each immunized intraperitoneally with 100 micromgrams of human insulin precipitated in alum, mixed with 2×10⁷ killed Bordetella pertussis organisms as adjuvant. A second injection of 100-200 micrograms of insulin in saline is given a month later.

Three days after the second injection the spleens are removed aseptically and transferred into a sterile bacteriological-type plastic petri dish containing 10 ml of GKN solution. GKN solution contains, per 1 liter of distilled water: 8 g NaCl, 0.4 g KCl, 1.77 g Na₂HPO₄·2H₂O, 0.69 g NaH₂PO₄, 0.05 g NaHCO₃, 0.5 g glucose, and 0.01 g penicillin. The cells are teased from the capsule with a spatula. Clumps of cells

Pieczenik and IC1 v. Dyax

00 Civ. 0243 (HB)
pol(A)+ RNA, first and second strand cDNA is synthesized using avian myeloblastosis virus reverse transcriptase. The double linker method of Kozak and Miroshin (1981) Gene 13:145 can be employed. The double stranded cDNA, with intact hairpin loops at the ends corresponding to the 5' ends of the pol(A)+ RNA, are filled in with the Klenow fragment of E. coli DNA polymerase I, (available, e.g., from Boehringer Mannheim or New England BioLabs). The filled in cDNA is then ligated to [32P] labeled Sal I octanucleotide linkers (available from Collaborative Research, Waltham, Mass.). The cDNA with Sal I linkers attached to the end corresponding to the 3' end of the pol(A)+ RNA is then treated with nuclease S1 to destroy the hairpin loop and again is filled in with the Klenow fragment of E. coli DNA polymerase I, EcoRI octanucleotide linkers (Collaborative Research) are ligated to the cDNA. The DNA is digested to completion with both EcoRI and Sal I. A Sepharose 4B column equilibrated with 10 mM Tris-HCl (pH 7.6) containing 1 mM EDTA and 300 mM NaCl is used to isolate and purify those cDNA fragments containing oligonucleotide II sequences. 15 nucleotides in length, which are then flanked by the octanucleotide linkers.

The plasmid vector pUC8, described in Viriza et al. (1982) gene 19:259, is digested to completion with EcoRI and Sal I and extracted twice with a 1:1 (v:v) mixture of phenol and chloroform. The 2.9 kilobase fragment is separated from the oligonucleotide fragment on a Sepharose 4B column equilibrated at set forth above. Fragments containing the large fragment are pooled and precipitated with ethanol. The cDNA is ligated to the vector at a weight ratio of vector to cDNA of 1000:1. Approximately 1 nanogram of cDNA is ligated to 1 microgram of the plasmid vector.

Conventional techniques are employed to transform E. coli strain DH-1 with the engineered pUC8 vector. The transformed bacterial cells are plated onto 82 mm nitrocellulose filters (Millipore Filter 0.45 μm) overlaid on ampicillin plates to give about 1,000 colonies per filter. Colonies are replica plated onto nitrocellulose sheets (available from Schleicher & Schuell) and the replicas are regrown on selective plates for antibiotic and hybridization screening and on glycerol plates for long-term storage at -70°C.

Antibody Production and Immunological Screening

Each plate is immunologically screened to identify colonies where the plasmid contains a 15 base pair oligonucleotide insert encoding a peptide sequence corresponding to a portion of the chicken tropomyosin gene. Monoclonal antibodies for use in the screening are developed as follows.

Spleen cells are harvested from donor mice that have been antigenically stimulated with chicken tropomyosin. Alternatively, spleen cells can be harvested from mice that have not been antigenically stimulated. The spleen cells are fused with myeloma cells to produce hybridoma clones. The monoclonal antibody produced by each hybridoma line is purified from the culture supernatant and concentrated by affinity chromatography on a protein A sepharose column.

Antibodies are screened for reactivity with chicken tropomyosin and with the parental bacterial strain, DH-1, preferably containing unmodified pUC8. Those antibodies reactive with the tropomyosin and unreactive with DH-1 (pUC8) are selected for use in screening the transformed bacterial colonies.

To prepare the bacterial colonies for screening, cells are lysed by suspending the nitrocellulose filters for fifteen minutes in an atmosphere saturated with CHCl3 vapor. Each filter is then placed in an individual Petri dish in 10 ml of 50 mM Tris-Cl (pH 7.2), 120 mM NaCl, 5 mM MgCl2 containing 3% (v/v/vol) bovine serum albumin. 1 microgram of DNase, and 40 micrograms of lysozyme per milliliter.

Each filter is incubated gently overnight at room temperature, and then rinsed in saline (50 mM Tris-Cl, pH 7.5) 150 mM NaCl). Each filter is incubated with a dilute saline solution of a monoclonal antibody selected from those antibodies exhibiting reactivity with tropomyosin but not with DH-1 (pUC8). The filters then are washed five times with saline at room temperature, for one half to one hour per wash. The filters then are incubated with 5×10⁶ cpm of 125I-labeled goat anti-mouse IgG at a specific activity of about 10⁶ cpm/microgram diluted in 10 ml of saline containing 3% bovine serum albumin. The goat anti-mouse IgG can be an affinity purified fraction. The labeling is accomplished according to the chloramine-T procedure of Burnside & (1978) Methods Enzymol 50-57. After one hour of incubation the filters are washed again in saline, with five or six changes, at room temperature, dried, and autoradiographed 24-72 hours, preferably using Dupont Cronex Lightning Plus x-ray enhancing screens. In the immunological cross reactions, a filter is stained homogeneously with which defined amounts of various purified proteins are spotted. The tissue serves as a further control for the specificity of the immunological detection of the antigens. Quantities of less than 1 nanogram of purified protein can be detected in these assays.

This procedure permits the identification and characterization of the specific five amino acid epitopic sequence of the tropomyosin protein that is identified by a particular monoclonal antibody. As this immunological reactivity process is repeated with different monoclonal antibodies, several distinct antigenic sites on the tropomyosin protein are identified. The 15 nucleotide sequence of cDNA that encodes each antigenic site is preserved in the cDNA derived library, and a source of antibody that recognizes each site is preserved in the separate hybridoma lines.

Use

The invention is useful to produce antibodies that recognize and bind to particular test species, and to determine either (1) the specific peptide sequence on a protein, enzyme, or peptide that an antibody recognizes or (2) an amino acid sequence with a configuration very close to the structure of a non-peptide or a discontinuous epitopic test species recognized by an antibody. The invention is also useful to determine the nucleotide sequence or sequences corresponding to the codon degeneracy, encoding the amino acid sequence that is recognized by an antibody.

To identify a peptide sequence that closely approximates an antibody binding site on an antigen, either an A-PAM or a P-ADM can be used. If an A-PAM is used, then the test species is first contacted with the intact A-PAM. Any antibodies bound to immobilized peptide sequences that have an affinity for the test species will be "removed off" the matrix to bind to the test species. The peptide sequence immobilized at a site where antibodies are "competed off" has a conformational similarity to the site on the test species where the antibodies are now bound. If a P-ADM is used, then the test species is first contacted with the intact P-ADM. The test species displaces any peptide sequences that have a sufficient conformational similarity to an antibody recognition site on the test species that an antibody capable of binding to the peptide sequence is also capable of binding to the test species. Displaced peptide sequences can then be filtered off the matrix and identified. It is not necessary that the test species be proteinaceous or derived from peptides. It can be, for example, a carbohydrate or a non-peptide drug. It can be expected that the peptide sequence can be closely approximated by the conformation...
nucleotide sequences, each 15 nucleotides in length, can encode the population of random peptide sequences that five amino acids in length.

Because the genetic code is degenerate, i.e., there are 61 codons coding for 20 amino acids; each amino acid, on the average, has 61/20 or 3.05 synonymous codons. In terms of the genetic universe, there are 0.5 to the power 3 possible nucleotide sequences coding for the 3.2 million possible epitopes. Therefore, there are 8.44,596,301 possible nucleotide sequences coding for 3,200,000 possible peptide sequences. This means that there are 263,94, synonymous codings for each pentapeptide sequence. This high degree of synonymous degeneracy allows us one way of evaluating whether one has generated the universe of possible pentameric epitopes. Generating 3-5 synonymous representations of the coding for the pentapeptide universe statistically suggests an almost complete representation of each member of the pentameric universe. That is, if the nucleotide distribution generated is equimolar and random, one would expect that if one randomly generated 3-5 synonymous codings for any particular pentapeptide sequence, one would have had a statistically good chance of having generated any other pentapeptide sequence in the population of 3.2 million possible pentamers.

A discrete population comprising a random distribution of nucleotide sequences (15 mers) and thereby at least one copy of each of the sequences encoding all possible peptide was chemically synthesized as oligonucleotides of the formula GATCCCTN_{x}AA SEQ ID NO: 1 where N is G, A, T or C. The 15 base random sequences are the coding sequence for the peptide epitope universe, 4^{15} or 4, 294, 967, 290 different molecules were synthesized at an average of 243 codings per pentapeptide sequence, this represents a population with about five-fold redundancy. About 1 microgram of DNA was recovered and 10^{-6} recombinant plasmid was produced. The TT and AA bases at the 5' and 3' ends, respectively, will allow the sequence to base pair with itself in phase on both strands if GAT is in the sense phase. In addition, the oligonucleotide, after hybridizing to a complementary oligonucleotide, can be ligated into a BamHI site without regenerating a BamHI site so that a BamHI selection against parental molecules lacking inserts can be performed.

One test of the randomness of the chemical synthesis is that half of the approximately 4.2x10^7 oligonucleotides should be able to form duplexes with the other half. The oligonucleotides were purified on a Sep Pak\textsuperscript{TM} (Millipore, Waters Chromatography, Milford, Mass.) column, lyophilized and reconstituted in ligation buffer heated at 100\textdegree C for 5 min and brought to room temperature slowly and incubated overnight. The duplex oligonucleotides were then ligated into f1 RF DNA which had been previously digested with BamHI and purified after agarose gel electrophoresis.

A distribution with a Chi-square of 2.57 and 3 degrees of freedom can be gotten randomly 50% of the time. Therefore, our observed distribution does not differ significantly from our expected (and synthesized) global base composition.

### Table 1

<table>
<thead>
<tr>
<th>Ligation Reaction</th>
<th>Encoding Strand Composition</th>
<th>Phage Strand (+) Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>30 \pm 120 = 18.6%</td>
<td>= A</td>
</tr>
<tr>
<td>C</td>
<td>26 \pm 120 = 26.7%</td>
<td>= G</td>
</tr>
<tr>
<td>G</td>
<td>30 \pm 120 = 25.2%</td>
<td>= C</td>
</tr>
<tr>
<td>A</td>
<td>30 \pm 120 = 25.9%</td>
<td>= T</td>
</tr>
<tr>
<td>T</td>
<td>25 \pm 22.6 = 6.4 \pm 40.95%</td>
<td>1.54</td>
</tr>
<tr>
<td>C</td>
<td>25 \pm 26.7 = -1.1 \pm 1.7</td>
<td>1.39 \pm 25 = 18</td>
</tr>
<tr>
<td>G</td>
<td>25 \pm 25.2 = -0.2 \pm 0.2</td>
<td>0.45 \pm 24 = 0.14</td>
</tr>
<tr>
<td>A</td>
<td>25 \pm 29.5 = -4.3 \pm 30.7</td>
<td>0.01 \pm 35 = 0.25</td>
</tr>
</tbody>
</table>

A distribution with a Chi-square of 2.57 and 3 degrees of freedom can be gotten randomly 50% of the time. Therefore, our observed distribution does not differ significantly from our expected (and synthesized) global base composition.

### Table 2

<table>
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<th>Encoding Strand Composition</th>
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<td>25 \pm 29.5 = -4.3 \pm 30.7</td>
<td>0.01 \pm 35 = 0.25</td>
</tr>
</tbody>
</table>
7.4. The reaction was carried out in the dark at 4°C for 2 hr. Excess reagents were removed by dialysis at 4°C (against 3 l water for 4 hr, against 3 l PBS overnight). Peptide conjugates were stored in 50% glycerol in PBS (vol/vol) at -20°C.

Rabbit antisera were produced by injecting 5 mg peptide-protein conjugate in 2 ml 50% Freund's adjuvant, with 10 days until an antibody response was detected using standard techniques.


Defining the Endoplasmic Epitope

Peptides were chemically synthesized, each of which was a contiguous five amino acid sequence from the 21st to 25th amino acid sequence of endoplasm. These peptides were immobilized to a solid support in individual spots. Polyclonal antisera (as described above) were allowed to bind to the immobilized peptides. Detection of the bound antibody revealed that only the peptide containing amino acids 2-6 of endoplasm bound antibody molecules.

Recombinant phage with the chemically synthesized 15 bp oligonucleotide encoding the known epitope (amino acids 2-6) of endoplasm in BamHI-compatible ends are prepared by inserting the coding sequence into BamHI-cut φ1 RF.

Recombinant phage are propagated in liquid culture and partially purified from cell-free supernatants by three cycles of polyethylene glycol-salt precipitation and resuspension. The final supernatant is spun at high speed (about 100,000xG) to pellet the phage. The gelatinous phage pellet (containing about 10^10-10^12 phage) is resuspended in about 50 microliters 0.2% Ponceau S in 6% acetic acid. Glycerol and tracking dye are added to make the sample sufficiently dense for gel loading. The resuspended phage mixture is then loaded onto an SDS-polyacrylamide gel and electrophoresed (Laemmli et al. (1970) supra).

After electrophoresis, the proteins in the SDS-polyacrylamide gel are transferred to nitrocellulose using standard techniques. The nitrocellulose blot is then soaked briefly in 0.2% Ponceau S in 6% acetic acid to visualize protein bands. The pIII band is relatively sharply resolved. Then the stained blot is rinsed in water or PBS to remove the stain. Western blotting is carried out essentially as described in McCaffrey et al. (1990) Nature 348:552-554, with the use of Cadbury's brand of skim milk powder.

The inventors note that treatment of the phage in 6% acetic acid prior to electrophoreses is crucial for obtaining successful electrophoregrams and Western blots. With the acetic pretreatment, recombinant phage carrying only one copy of an oligopeptide epitope can be successfully detected by Western blotting.

For topological mapping, an oligonucleotide complimentary to a sequence encoding amino acids 2-6 of endoplasm as a tandem repeat of two copies, is chemically synthesized, e.g., using automated DNA synthesis (Model 380B, Applied Biosystems, Inc., Foster City, Calif.). After synthesis and purification, the two strands of the oligonucleotide are allowed to self anneal, appropriate linkers are added, and then inserted into randomized linear φ1 RF molecules as previously described (U.S. Pat. Nos. 4,528,266 and 4,359,553 which are incorporated by reference herein).

The recombinant φ1 DNA molecules are then transferred into competent E. coli cells, and plated. Plaques which result from recombinant phage are identified using conventional hybridization techniques.

Plaques are also screened with the endoplasmic-specific antibody described above and labeled second antibody. The immunological screening was carried out essentially as described in McCaffrey et al. (1990) except that the nitrocellulose containing the "lifted" plaques was first treated with 0.2% Ponceau S in 6% acetic acid for 3-4 minutes, followed by rinsing in water until destained. As before, Cadbury's brand of skim milk powder is used. Immunostaining and unsealed plaques were used as a control in the immunological screen. Recombinant φ1 expressing the endoplasmic epitope comprising the peptide sequence are identified by the screen.

For best results when using the BamHI site within the pIII gene for epitope analysis, one should use either a tandem repeat of at least two copies of each peptide sequence encoded, or a single copy of a random peptide target sequence should be flanked with a short oligopeptide sequence, e.g., about three amino acids on either side. This extra peptide sequence associated with the epitope improves the accessibility of the epitope to antibody for binding. Similarly, the Ponceau S-acetic acid pretreatment of proteins to be blotted allows one to detect epitopes whose coding oligonucleotides are incorporated at the BamHI site within the gene encoding pIII of φ1. In topological mapping or in immunological screening of plaque lifts on nitrocellulose, the acid treatment is also key to successful results.

Other Embodiments

Other embodiments are also within the scope of the appended claims.
CTTCAAGATAT TTTCCGAAAAGCA A

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:6:

CTTAAACATCC TCTCAAACGCA A

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CTTCCCATGCG TCTAAACTCA A

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CTTACACCGAA GCGGCTCCCA A

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:9:

CTTCTTAAATT TCGTGTGGCA A

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:10:

CTTACGCTGCG TCGACACGCA A

(2) INFORMATION FOR SEQ ID NO:11:

(xii) SEQUENCE DESCRIPTION: SEQ ID NO:11:
(D) TOPOLOGY: linear

(i) MOLECULE TYPE: DNA (genomic)

(ii) FEATURES:
(A) NAME/KEY: CDS
(B) LOCATION: 41-58

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:16:

TCTTACCAAG TCCTCGTGGT AGAATCTCTCA TGAGATCTG ACC GAO CGG ACT GGT

Thr Gln Arg Thr Gly

AAA GA

60

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 amino acids
(B) TYPE: protein
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i) MOLECULE TYPE: protein

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Thr Gln Arg Thr Gly Lys

1 5

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 amino acids
(B) TYPE: protein
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i) MOLECULE TYPE: DNA (genomic)

(ii) FEATURES:
(A) NAME/KEY: CDS
(B) LOCATION: 41-58

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:18:

TCTTGTACG AGTCTGCTGAGA ATCTCTCTCA TGAGATCTG ATG CCA GAG TCG ATA

Met Gln Asp Ser Ile

CAA GA

60

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 amino acids
(B) TYPE: protein
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i) MOLECULE TYPE: protein

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:19:

Met Gln Asp Ser Ile Gln

1 5

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 amino acids
(B) TYPE: protein
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

Picecznik and ICT v. Dyax 00 Civ. 0243 (HB) 00906
(1) INFORMATION FOR SEQ ID NO:25:

(1) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(1) MOLECULE TYPE: protein

(1) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Asp Ile Leu Gln Arg Gln

1 5

(2) INFORMATION FOR SEQ ID NO:26:

(1) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 base pairs
(B) TYPE: nucleic acid
(C) STRAND: sense
(D) TOPOLOGY: linear

(1) MOLECULE TYPE: DNA (genomic)

(1) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41-58

(1) SEQUENCE DESCRIPTION: SEQ ID NO:26:

TCTYCCCTT GGAAGATTT TACATCTCA GAAATGCCTC TGAAGATCT T CCA TCG CTC AAA CTC

Pro Ser Leu Lys Leu

1 5

AAA GAA

1 5

(2) INFORMATION FOR SEQ ID NO:27:

(1) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 base pairs
(B) TYPE: nucleic acid
(D) TOPOLOGY: linear

(1) MOLECULE TYPE: protein

(1) SEQUENCE DESCRIPTION: SEQ ID NO:27:

Pro Ser Leu Lys Leu Lys

1 5

(2) INFORMATION FOR SEQ ID NO:28:

(1) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 base pairs
(B) TYPE: nucleic acid
(C) STRAND: sense
(D) TOPOLOGY: linear

(1) MOLECULE TYPE: DNA (genomic)

(1) FEATURE:

Piecznik and ICT v. Dyax 00 Civ. 0243 (HIB) 00908
(1) SEQUENCE DESCRIPTION: SEQ ID NO:32:
TCTGCTCTG CCAACACCT AAGATCCTA TGAAGATCTT AAG GCT CTC GAC AGG
55
Ser Val Leu Asp Arg

CAA GAA
G1a

(2) INFORMATION FOR SEQ ID NO:32:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: protein
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) SEQUENCE DESCRIPTION: SEQ ID NO:32:
Ser Val Leu Asp Arg G1a

(2) INFORMATION FOR SEQ ID NO:34:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: protein
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41-53

(iii) SEQUENCE DESCRIPTION: SEQ ID NO:34:
TCTGATGTAA CTGGCTCTG AAGATCCTA TGAAGATCTT CAA GAC AAA GTC CAT
55
Gla Asp Lys Val His

CAA GAA
G1a

(2) INFORMATION FOR SEQ ID NO:35:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: protein
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41-53

(iii) SEQUENCE DESCRIPTION: SEQ ID NO:35:
Gla Asp Lys Val His G1a

(2) INFORMATION FOR SEQ ID NO:36:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: protein
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i) MOLECULE TYPE: DNA (genomic)

(ii) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 41-53

(iii) SEQUENCE DESCRIPTION: SEQ ID NO:36:

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Picezenik and ICT v. Dyax 00 Civ. 0243 (HB) 00910
(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: protein
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Asp Asp Glu Val Asp Val Asp Gly Thr Val Glu Glu Asp Lys Gly Tyr

1  2  3  4  5  6  7  8  9 10 11 12 13

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: protein
(D) TOPOLOGY: linear

(iii) MOLECULE TYPE: protein

(iii) SEQUENCE DESCRIPTION: SEQ ID NO:46:

Asp Asp Glu Val Asp Val Asp Gly Thr Val Glu Glu Asp Lys Gly Tyr

1  2  3  4  5  6  7  8  9 10 11 12 13

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00912
curing said recombinant E. coli cells to allow expression of said recombinant structural gene such that said epitoic peptide sequences are accessible to antibody recognition.

35. A peptide population obtained from the process of claim 34.

36. A population of peptides wherein each member of said population has a length of from about 4 to about 12 amino acid residues, and wherein said population contains at least about 10% of all possible peptide sequences of said length.

37. The peptide population of claim 36, wherein each member has a length of from 4 to 7 amino acid residues.

38. The peptide population of claim 36, wherein each member has a length of 5 amino acid residues.

39. The peptide population of claim 36, wherein each member has a length of 4 amino acid residues.

40. The peptide population of claim 36, wherein each member has a length of 3 amino acid residues.

41. The peptide population of claim 36, wherein each member has a length of 2 amino acid residues.

42. The peptide population of claim 36, wherein each member has a length of 1 amino acid residues.

43. The peptide population of claim 36, wherein each member has a length of 0 amino acid residues.

44. A matrix comprising the population of binding pairs of claim 47.

45. A population of oligonucleotides comprising double stranded oligonucleotides that comprise coding regions consisting of a length of from about 4 to about 12 nucleotides, wherein said population comprises coding regions of said length, wherein substantially every member of said peptide population is bound to an antibody.

46. A method of producing a population of epitoic peptide sequences, comprising the steps of: providing a population of recombinant E. coli cells, each of said cells containing at least one member of a recombinant vector population, each member of said vector population comprising a DNA sequence that autonomously replicates a corresponding sequence comprising a recombinant structural gene, wherein each member of said oligonucleotide sequence contains a length from about 4 to about 12 nucleotide sequences that are coding regions encoding a plurality of peptides consisting of random sequences of from about 4 to about 12 L-amino acid residues, said oligonucleotides comprising 5' and 3' flanking sequences that permit said oligonucleotide to be ligated into a vector.

50. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is from about 4 to 7 nucleotide triplets.

51. The oligonucleotide population of claim 49, wherein the length of the coding region of each oligonucleotide is 6 nucleotide triplets.
March 31, 1999

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Attention: Publishing Division
Certificate of Correction Branch

Re: Certificate of Correction
U.S. Patent No. 5,866,363
Inventors: Pieczenik
Our File: ICTECH 3.0-002 CIP CONT
Title: Method and Means for Sorting and Identifying Biological Information

Dear Sir:

Enclosed herewith is an original and one copy of a Certificate of Correction with respect to the above-identified U.S. Patent.

The corrections indicated should be made as the application as originally titled does not contain such errors. There is no requirement for payment of a fee since the errors were made by the Patent Office.

We look forward to early return of the copy of the Certificate of Correction duly certified.

Respectfully submitted,

LERNER, DAVID, LITTEBENG,
KRUMHOLZ & MENTLIK, LLP

/acid
Enclosures

175952.1.DOC

Pieczenik and ICT v. Dyax 00 Civ. 0243 (HB) 00942
UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 5,866,363
DATED : February 2, 1999
INVENTOR(S) : Pieczenik

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 1, lines 6, 7, after "application" insert --.--

Column 12, line 65, "NaHPO₄·2H₂O" should read -- NaHPO₄·2H₂O--

Column 12, line 66, "Na₂H₂PO₄·H₂O" should read -- Na₂H₂PO₄·H₂O --

Column 21, item 5), at the end of line 1 delete --SEQ ID NO:24--

Column 21, item 5), at the end of line 2 insert --SEQ ID NO:24--

Column 21, item 5), at the end of line 3 insert --SEQ ID NO:25--

Column 21, item 6), at the end of line 1 delete --SEQ ID NO:26--

Column 21, item 6), at the end of line 2 insert --SEQ ID NO:26--

Column 21, item 6), at the end of line 3 insert --SEQ ID NO:27--

Column 21, item 7), at the end of line 1 delete --SEQ ID NO:28--

Column 21, item 7), at the end of line 2 insert --SEQ ID NO:28--

Column 21, item 7), at the end of line 3 insert --SEQ ID NO:29--

Column 21, item 8), at the end of line 1 delete --SEQ ID NO:30--

Column 21, item 8), at the end of line 2 insert --SEQ ID NO:30--

MAILING ADDRESS OF SENDER:

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Pieczenik and ICT v. Dyaax 00 Civ. 0243 (IID) 00943

PATENT NO. 5,866,363

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 5,866,363
DATED : February 2, 1999
INVENTOR(S) : Pieczenik

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 21, item 9), at the end of line 1 delete --SEQ ID NO:32--

Column 21, item 9), at the end of line 2 insert --SEQ ID NO:32--

Column 21, item 9), at the end of line 3 insert --SEQ ID NO:33--

Column 45, line 45, after "from" insert --about--

Column 47, line 43, after "1" insert --or 24--.