

8224038



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

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

March 14, 2022

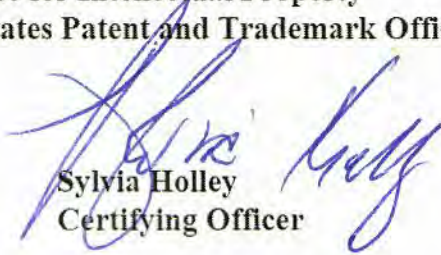
**THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM
THE RECORDS OF THIS OFFICE OF:**

Pre-Grant Publication Number: 2004/0126363

Pre-Grant Publication Date: July 1, 2004

**By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office**




Sylvia Holley
Certifying Officer



(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2004/0126363 A1**
Jensen et al. (43) **Pub. Date: Jul. 1, 2004**

(54) **CD19-SPECIFIC REDIRECTED IMMUNE CELLS**

Publication Classification

(76) Inventors: **Michael C. Jensen**, Pasadena, CA (US); **Stephen Forman**, San Marino, CA (US); **Andrew Raubitschek**, San Marino, CA (US)

(51) **Int. Cl.⁷** **A61K 48/00**; C12N 5/08
(52) **U.S. Cl.** **424/93.21**; 424/93.7; 435/372

Correspondence Address:
ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005 (US)

(57) **ABSTRACT**

(21) Appl. No.: **10/416,011**

Genetically engineered, CD19-specific redirected immune cells expressing a cell surface protein having an extracellular domain comprising a receptor which is specific for CD19, an intracellular signaling domain, and a transmembrane domain. Use of such cells for cellular immunotherapy of CD19⁺ malignancies and for abrogating any untoward B cell function. In one embodiment, the immune cell is a T cell and the cell surface protein is a single chain scFvFc:ζ receptor where scFv designates the V_H and V_L chains of a single chain monoclonal antibody to CD19, Fc represents at least part of a constant region of an IgG₁, and ζ represents the intracellular signaling domain of the zeta chain of human CD3. The extracellular domain scFvFc and the intracellular domain ζ are linked by a transmembrane domain such as the transmembrane domain of CD4. A method of making a redirected T cell expressing a chimeric T cell receptor by electroporation using naked DNA encoding the receptor.

(22) PCT Filed: **Nov. 7, 2001**

(86) PCT No.: **PCT/US01/42997**

Related U.S. Application Data

(60) Provisional application No. 60/246,117, filed on Nov. 7, 2000.

XbaI (hGMCSF signal peptide-)
 ----- M L L L V T S L L L C E L P

1 ATCTCTAGAG CGCCACCAT GCTTCTCCTG GTGACAAGCC TTCTGCTCTG TGAGTTACCA
 TAGAGATCTC GCGGGTGGTA CGAAGAGGAC CACTGTTCGG AAGACGAGAC ACTCAATGGT

(V₁-)
 H P A F L L I P D I Q M T Q T T S S L S
 51 CACCCAGCAT TCCTCCTGAT CCCAGACATC CAGATGACAC AGACTACATC CTCCTGTCT
 GTSGGTCGTA AGGAGGACTA GGGTCTGTAG GTCTACTGTG TCTGATCTAG GAGGGACAGA

A S L G D R V T I S C R A S Q D I S K Y
 121 GCCTCTCTGG GLLACAGAGT CACCATCAGT TLLAGGGCAA GTCAGGACAT TAGTAARTAT
 CGGAGAGACC CTCTGTCTCA STGGTAGTCA ACGTCCCGTT CAGTCTGTGA ATCATTTATA

L N W Y Q Q K P D G T V K L L I Y H T S
 181 TTAATTGGT ATCAGCAGAA ACCAGATGGA ACTGTAAAC TCCTGATCTA CCTACATCA
 AATTAACCA TAGTCGTCTT TGGTCTACCT TGACAATTTG AGGACTAGAT GGTATGTAGT

R L H S G V P S R F S G S G S G T D Y S
 241 AGATTACT CAGGAGTCCC ATCAAGGTTG AGIGGCAGTG GGTCTGGAAC AGATTATTCT
 TCTAATGGA GTCTCAGGG TAGTTCAGG TCACCGTAC CCAGACCTTG TCTAATAAGA

L T I S N L E Q E D I A T Y F C Q Q G N
 301 CTCACCATTA GCAACCTGGA GCAAGAAGAT ATTGCCACTT ACTTTTGCCA ACAGGGTAAT
 GAGTGGTAAT CGTTGGACCT CGTTCTTCTA TAACGGTGAA TGAAAACGGT TGTCCCATTA

(Whitlow linker-)
 T L P Y T F S G G T K L E I T G S T S G
 361 ACGCTCCGT ACACGTTCGG AGGGGGGACT AAGTTGGAAA TAACAGGCTC CACCTCTGA
 TGCGAAGGCA TGTGCAAGCC TCCCCCTGA TCCACCTTT ATTGTCCGAG GTGGAGACCT

(V₂-)
 S S K F S S G E S S T K G E V K L Q E S
 421 TCCGGCAATC CCGGATCTGG CGAGGGATCC ACCAAGGGCG AGGTGAAACT GCAGGAGTCA
 AGGCCSTTGG GGCCTAGACC GCTCCCTAGG TGSTTCCCGC TCCACTTTGA CGTCTCAGT

G P G L V A P S Q S L S V T C T V S G V
 481 GGACCTGGCC TGGTGGCGCC CTCACAGAGC CTGTCCGTCA CATGCACTGT CTCAGGGGTC
 CCTGGACCGG ACCACCGCGG GAGTGTCTCG GACAGSCAGT GTACGTGACA GAGTCCCCAG

S L P D Y G V S W I R Q P P R K G L E W
 541 TCATTA LGG ACTATGSGT AAGCTGGATT CGCCAGCCTC CACGAAAGGG TCTGGAGTGG
 AGTAATGGGC TGATACCACA TTCGACCTAA GCGGTGGGAG GTGCTTTCCC AGACCTCACC

L G V I W G S E T T Y Y N S A L K S R L
 601 CTGGGAGTAA TATGGGGTAG TGAACCACA TACTATAATT CAGCTCTCAA ATCCAGACTG
 GACCCCTATT ATACCCCATC ACTTTGGTGT ATGATATTAA GTCGAGAGTT TAGGTCTGAC

T I I K D N S K S Q T F D K M N S L Q T
 661 ACCATCATLA AGGACRACTC JAAGAGCCCT TTTTCTTAA AAATGAACAG TCTGCAAACT
 TGGTAGTAGT TCCTGTGAG GTTCTCGGT JAAAAGAATT TTTACTTGTC AGACGTTTGA

D D T A I Y Y C A K H Y Y Y G G S Y A M
 721 GATGACACAG CCATTTACTA CTGTGCCAAA CATTATTACT ACGGTGGTAG CTATGCTATG
 CTACTGTGTC GGTAATGAT SACACGGTTT GTAATAATGA TGCCACCATC GATACGATAC

FIGURE 1A

.hingeF₁

781 D Y W G Q G T S V T V S S Y E P K S S D
 GACTACTGGG GTCAAGGAC CTCAGTCACC CTCCTCTCAG TAGAACCCAA ATCTTCTGAC
 CTSATGACCC CAGTTCTCTG GAGTCAGTGG CAGAGGAGTC ATCTTGGGTT TAGAAGACTG

841 K T H T C P F C P A P E L C G G P S Y F
 AAAACTCACA GGTGCCACCC GTGCCAGCA CCTGAACCTC TGGGGGGACC CTCAGTCTTC
 TTTTGASTGT GCACGGGTGG CACGGGTGGT GGACTTGAGG ACCCCCTGG CAGTCAGAAG

901 L T F P K P K D T L M T S R T P E V I F
 CTCTTCCCGG CAARAACCAA GGACACCGTC AGCATCTCCG TGACCCCTGA GGTCAATGG
 GAGAAGGGGG GTTTTGGGTT CCTGTGGGAG TACTAGAGGG CCTGGGGACT CCAGTGTAGG

961 V V V D V S H E D P E V K F N W Y V D G
 GTGGTGGTGG ACGTGAGCCA CGAAGACCCT GAGGTCAAGT TCAACTGGTA TGTGGACGGC
 CACCACCACC TGCCTCGGT GCTTCTGGGA CTCCAGTTCA AGTTGACCAT GCACCTGCCG

1021 V E V H N A K T K P R E E Q Y N S T Y R
 GTGGAGGTGC ATAATGCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCGT
 CACCTCCACG TATTACGGTT CTGTTTCGGC GCCCTCCTCG TCATGTTGTC GTGCATGGCA

1081 J V S V L T V L H Q D W L N G K E Y K C
 GTGGTCAGCG TCCTCACCCT CCTGCACCAG GACTGGCTGA ATGGCAAGGA GTACAAGTGC
 CACCAGTCGC AGGAGTGGCA GGACGTGGTC CTGACCGACT TACCGTTCCT CATGTTCCAG

1141 K V S N K A L P A P I E K T I S K A K G
 AAGGTCTCCA ACAAAGCCCT CCCAGCCCCC ATCGAGAAAA CCATCTCCA AGCCAAAGGG
 TTCAGAGGT TGTTCGGGA GGGTCGGGGG TAGCTCTTTT GGTAGAGGTT TCGGTTCCCG

1201 Q P R E P Q V Y T L P P S R D E L T K N
 CAGCCCGGAG AACCAAGGCT GTACACCGTC CCACCATCAC GAGATGAGCT GACCAAGGAC
 CTGGGGGCTG TTGCTGTCCA CATGTGGGAC GTTGTGAGTG CCTTACTGSA GTGGTCTCTG

1241 Q V S L T L L V K G E Y P S D P A Y E W
 GAGTCTGAGT GAAAGGATGT GTTAAAGGCT TTTAAAGGCA GTTAAATGCT GGTGATGAGT
 GTCCAGTCGG ACTGGACCGA CCAGTTTCCG AAGATAGGGT CCTGTAGCGG CCACCTGACG

1321 E S N G Q P E N N Y K T T P P V L D S D
 GAGAGCAATG GGCAGCCCGA GAACAACCTAC AAGACCACGC CTCCTGTGCT GGACTCCGAC
 CTCTCGTTAC CCGTCGGCCT CTTGTTGATG TTCTGGTGGC GAGGGCACGA CCTGAGGCTG

1381 G S F F L V S K L T V D K S R W Q Q G N
 GGCTCCTCTC TCCTGTACAG CAAGCTCACG GTGGACAAGA GCAGGTGGCA GCAGGGGAC
 CCGAGGAAGA AGGAGATGTC GTTCGAGTGG CACCTGTTCT CGTCCACCGT CGTCCCTTG

1441 Y F S C S Y M H E A L H N H Y T Q K S L
 CTCTTCTCAT GCTCCGTGAT GCATGAGGCT CTGCACAACC ACTACACGCA GAAGAGCCIC
 CAGAAGAGTA CGAGGCACTA CGTACTCCGA GAGGTGTTGG TGATGTGCGT CTCTCTGGAG

1501 S L S F G K M A L I V L S G V A G L L L
 TCCCTGTCTC CCGGAAAAT GGCCCTGATT GTGCTGGGGG GCGTGGCCGG CCTCCTGCTT
 AGGGACAGAG GCGCCCTTTA CCGGGACTAA CAGGACCCCG CCGAGCCGGC GGAGGACGAA

1561 F I G L G I F F R V K F S R S A D A P A
 TTCATTGGGG TAGGCATCTT CTTCAGAGTG AAGTTCAGCA GGAGCGCAGR CCCCCCGCG
 AAGTAACCCG ATCCGTAGAA GAAGTCTCAC TTCAAGTGGT CCGCGCGTCT CCGGGGGCGG

FIGURE 1B

```

      Y Q Q   G Q N Q   L Y N   E L N   L G R R   E E Y
1621 TACCAGCAGG GCCAGAACCA GCTCTATAAC GAGCTCAATC TAGGACGAAG AGAGGAGTAC
      ATGGTTCGTC CGGTCTTGGT CGAGATATTG CTCGAGTTAG ATCCTGCTTC TCTCCTCATG

      D V L   D K R R   G R D   P E M   G G K P   R R K
1681 GATGTTTTGG ACAAGAGACG TGGCCGGGAC CCTGAGATGG GGGGAAAGCC GAGAAGGAAG
      CTACAAAACC TGTTCTCTGC ACCGGCCCTG GGACTCTACC CCCCTTTCGG CTCTTCCTTC

      N P Q   E G L Y   N E L   Q K D   K M A E   A Y D
1741 AACCCCTCAGG AAGGCCTGTA CAATGAACTG CAGAAAGATA AGATGGCCGA GGCCTACAGT
      TTGGGAGTCC TCCCGGACAT GTTACTTGAC GTCTTTCTAT TCTACCGCCT CCGGATGTCA

      E I G   M K G E   R R R   G K G   H D G L   Y Q G
1801 GAGATTGGGA TGAAAGGCGA GCGCCGGAGG GGCAAGGGGC ACGATGGCCT TTACCAGGGT
      CTCTAACCCCT ACTTTCGCT CGCGGCCTCC CCGTTCOCCG TGCTACCGGA AATGGTCCCA

      L S T   A T K D   T Y D   A L H   M Q A L   P P R
1861 CTCAGTACAG CCACCAAGGA CACCTACGAC GCCCTTCACA TGCAGGCCCT GCCCCCTCGC
      GAGTCATGTC GGTGGTTCCT GTGGATGCTG CGGGAAGTGT ACGTCCGGGA CGGGGGAGCG

      Not I
      ~~~~~
1921 TAAGCGGCCG C
      ATTCGCCGGC G

```

FIGURE 1C

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.