

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

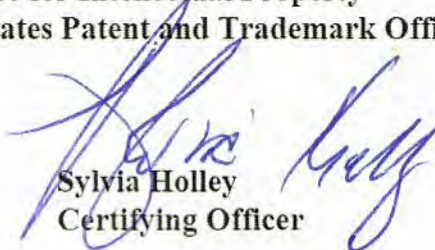
THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM  
THE RECORDS OF THIS OFFICE OF:

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.<sup>7</sup>** ..... **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<sup>+</sup> 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<sub>H</sub> and V<sub>L</sub> chains of a single chain monoclonal antibody to CD19, Fc represents at least part of a constant region of an IgG<sub>1</sub>, 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 E 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 GACACAGAGT CACCATCAGT TTAGGGCAA GTCAGGACAT TAGTAARTAT
CGGAGAGACC CTCTGTCTCA GTGGTAGTCA ACGTCCCGTT CAGTCTGTG 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 TCCTCAGGG TAGTCCAAAG TCACCGTCAC 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 TCCAACTTT 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 TGSTCCCGC 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 DCG 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
GACCCATCATT 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 ACCATCATCA AGGACRACTC AAGAGCCCT TTTTCTTAA AAATGAACAG TCTGCAAACT
TGGTAGTAGT TCCTGTGAG GTTCTCGGT TAAAAGAATT 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

.hingeF<sub>1</sub>

```

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

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

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

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

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

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

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

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

    Q V S L T L L V K G E Y P S D I A Y E W
1241 GAGTCTGAGT CAAAGGATGT GTTAAAGGCT TTTAAAGGCA GTTACTATCT CCTTAACTCT
    GTCCAGTCGG ACTGGACCGA CCAGTTTCCG AAGATAGGGT CCTCTAGCGG CCACCTCACG

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

    G S F F L V S K L T V D K S R W Q Q G N
1381 GGCTCCTCTC TCCTCTACAG CAAGCTCACG CTGGACAAGA CCAGSTGGCA GCAGGGGAC
    CCGAGGAAGA AGGAGATGTC GTTCGAGTGG CACCTGTTCT CGTCCACCGT CGTCCCTTG

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

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

    F I G L G I F F R V K F S R S A D A P A
1561 TTCATTGGGG TAGGCATCTT CTCAGAGTG AGTTCAGCA GGAGCGCAGR CCCCCCGG
    AAGTAACCCG ATCCGTAGAA GAAGTCTCAC TTCAGTGGT COTCGCTCT SCGGGGGGCG
    
```

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
174  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.