

PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1
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EPAS ID: PAT3903067

SUBMISSION TYPE:	CORRECTIVE ASSIGNMENT	
NATURE OF CONVEYANCE:	Corrective Assignment to correct the CONFIRMATORY LICENSE FILED 3/10/2015 NO. 503211145. TYPO ON APPLICATION NUMBER 13655143 SHOULD HAVE BEEN FOR 13655142. previously recorded on Reel 035167 Frame 0166. Assignor(s) hereby confirms the UNIVERSITY OF CALIFORNIA, SAN FRANCISCO TO US ARMY SECRETARY OF THE ARMY.	
RESUBMIT DOCUMENT ID:	503814767	
CONVEYING PARTY DATA		
	Name	Execution Date
	UNIVERSITY OF CALIFORNIA, SAN FRANCISCO	02/12/2015
RECEIVING PARTY DATA		
Name:	U.S. ARMY, SECRETARY OF THE ARMY	
Street Address:	810 SCHREIDER STREET	
Internal Address:	USAMRMC-JA - DAMD17-02-1-0029	
City:	FORT DETRICK	
State/Country:	MARYLAND	
Postal Code:	21702-5012	
PROPERTY NUMBERS Total: 1		
	Property Type	Number
	Application Number:	13655142
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NAME OF SUBMITTER:	JANET P. WEHRENBURG	
SIGNATURE:	/Janet P. Wehrenberg/	
DATE SIGNED:	06/06/2016	
Total Attachments: 11		
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PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1

Stylesheet Version v1.2

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PATENT**REEL: 038811 FRAME: 0719**

CORRESPONDENCE DATA**Fax Number:** (301)619-5034**Email:** JANET.P.WEhrenberg.CTR@MAIL.MIL*Correspondence will be sent to the e-mail address first; if that is unsuccessful, it will be sent using a fax number, if provided; if that is unsuccessful, it will be sent via US Mail.***Correspondent Name:** US ARMY, SECRETARY OF THE ARMY**Address Line 1:** 810 SCHREIDER STREET**Address Line 2:** USAMRMC-JA - DAMD17-02-1-0029**Address Line 4:** FORT DETRICK, MARYLAND 21702-5012**NAME OF SUBMITTER:**

JANET P. WEHRENBURG

Signature:

/JANET P. WEHRENBURG/

Date:

05/06/2016

This document serves as an Oath/Declaration (37 CFR 1.63).

Total Attachments: 1

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RECEIPT INFORMATION**EPAS ID:** PAT3861415**Receipt Date:** 05/06/2016[Return to home page](#)[| HOME](#) | [INDEX](#) | [SEARCH](#) | [eBUSINESS](#) | [CONTACT US](#) | [PRIVACY STATEMENT](#)

FEDERAL REPORTING FORM

Reported by: The Regents of the University of California
UCSF Office of Technology Management
185 Berry Street, Suite 4603
San Francisco, CA 94107
Tel.: 415-353-4472
Fax: 415-348-1579

SENT VIA FACSIMILE TO:
Div. of Extramural Inventions &
Technology Resources
301-480-0272
6 Page(s)

NIH Docket No.

UCSF Case No. SF2006-007

Federal Agency: DOD Grant No(s). DAMD17-02-1-0029; W81XWH-04-1-0745

Invention Title: R2Fas-L: a VEGF-activated Fas Ligand

Inventor(s): 1. Timothy P. Quinn 4.
2. 5.
3. 6.

Inventor(s) is a VA or USDA Employee: ☐ yes ☐ no

Comments: This disclosure form has not yet received an NIH sponsor number. Please provide government sponsor number (i.e. 0577508-05-XXXX). Edison will not accept this grant number.

NEW CASES: Part 1

	Date	Initials
A disclosure which appears to have arisen under the above funding agreement is enclosed.	07/18/2005	MS
UCSF elects to retain title in accordance with the terms of Public Law 98-620.		

APPLICATION FILED: Part 2

A 111A application has been filed, copy enclosed.	
USSN: Filing Date: UCSF Case No.:	
A license to the Government is also enclosed.	

PATENT ISSUED: Part 3

A soft copy of the issued patent is enclosed.	
US Patent No.: Date Issued: UCSF Case No.:	

LICENSED AS A TANGIBLE RESEARCH PROPERTY: Part 4

A license to the Government is enclosed.	
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TECHNOLOGY DISCLOSURE FORM**UCSF OFFICE OF TECHNOLOGY MANAGEMENT**Case No: *SF2006-007*Licensing Officer: *JRH***1. TITLE OF INVENTION: R2FasL: a VEGF-activated Fas Ligand**

2. DESCRIPTION OF INVENTION: VEGF is a secreted, dimeric angiogenic factor that stimulates tumor angiogenesis. VEGF normally binds to and activates its receptors: VEGFR-1, VEGFR-2, and Neuropilin-1. VEGF is overexpressed by many human cancers, and consequently many agents that inhibit VEGF activity are being investigated as cancer therapies (e.g. anti-VEGF antibody from Genentech). I have investigated a completely different approach, designed not to inhibit VEGF, but to reverse its activity from an angiogenic factor into a cell death factor. The concept is to make VEGF that is overexpressed by a tumor act as a death factor against the tumor itself or its blood vessels. In essence, to turn the tumor's weapon, overexpressed VEGF, against the tumor itself.

Fas ligand (FasL) is a cell death factor that induces apoptosis by binding to, clustering, and thereby activating the transmembrane Fas apoptosis receptor. The key feature is that Fas receptor clustering by FasL is required for Fas receptor activation. Both FasL and Fas are produced as trimeric proteins.

I generated a soluble chimeric protein (R2FasL) that combines VEGF-binding extracellular domains from VEGFR-2 with the trimerization domain and Fas-binding domain from FasL. The chimeric protein was designed such that VEGF dimers would bring together R2FasL trimers into clusters, which could then bind to, cluster, and activate Fas receptor. In vitro experiments showed that in the absence of VEGF, the R2FasL protein had minimal or no apoptotic activity on Jurkat cells (a T cell line that is sensitive to Fas apoptotic signaling). In the presence of VEGF, R2FasL stimulated rapid apoptosis, demonstrating that the R2FasL protein converts VEGF into a cell death factor.

3. IDENTIFY THE PRODUCTS OR SERVICES A COMPANY MIGHT DEVELOP USING THIS TECHNOLOGY

This technology might be used to create:

- A. An anti-cancer agent for tumors that overexpress VEGF.
- B. An anti-angiogenic agent for use in diseases characterized by pathologic angiogenesis, such as cancer, rheumatoid arthritis, or proliferative retinopathy.
- C. An agent that would convert other growth factors into death factors, by replacing the VEGFR-2 domain in R2FasL with the ligand binding domain for a different growth factor (e.g. PDGF).

4. EXPLAIN HOW THE INVENTION IS TECHNICALLY DISTINCT FROM AND SUPERIOR TO THE STATE OF THE ART AND WHAT COMPETITIVE ADVANTAGE IT AFFORDS A LICENSEE

R2FasL is different from the many agents being developed that target VEGF or its receptors. All of those agents (neutralizing antibodies, soluble VEGF receptors, RNA aptamers, RNAi, ribozymes, antisense, small molecule kinase inhibitors) are designed to inhibit the expression or activity of VEGF or its receptors. In contrast, R2FasL uses exploits VEGF overexpression to generate apoptotic activity.

5. LIST ANY RELEVANT COMPETING INVENTIONS AND PATENTS (to search see: <http://www.uspto.gov/patft/index.html> and <http://pctgazette.wipo.int/>)

The patents or patent applications that I found that describe FasL fusion proteins or FasL variants include:

Baekkeskov	6,451,759
Chu	6,544,523
Chu	20040126859
Nagata	6,348,334
Nishi	6,235,878
Queen	6,046,310
Ramer	6,001,962
Tohma	20040053249
Wallach	20050013816

To my reading, these patents did not appear to describe FasL fusion proteins similar to R2FasL.

6. NEXT STEPS REQUIRED TO VALIDATE THE INVENTION

The R2FasL protein has been shown in vitro to induce apoptosis in Jurkat cells in a VEGF-dependent manner, demonstrating that R2FasL acts as a VEGF-dependent Fas ligand. The next steps involve examining other cancer cell lines and endothelial cell lines in vitro to determine if R2FasL induces apoptosis in those cells when VEGF is present. Ultimately, an in vivo test using a mouse tumor model will be required to assess in vivo function.

7. INVENTORS (please indicate the following)

Name: Timothy P. Quinn
SS#: 585-50-6904
Citizenship: USA
Position: Asst. Adj. Prof.
Dept: Pediatrics
Wk. Address: Box 1245, Laurel Heights, UCSF

Wk. Phone: 502-5196
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 Email: tpquinn@itsa.ucsf.edu
 Hm. Address: 565 Eureka Street, San Francisco, CA 94114
 Hm. Phone: 415-285-3750

8. FUNDING SOURCE(S) Give the full applicable contract or grant number(s) used for your research in development of this invention (please include industry sponsored research, non-profit funding, governmental funding, applicable fellowships, etc.).

<u>Funding Source/Sponsor</u>	<u>Contract or Grant Number</u>	<u>Principal Investigator/ Supervisor or Fellow to whom awarded</u>
Prostate Cancer Research Program, Department of Defense	DAMD17-02-1-0029	Timothy P. Quinn, M.D.
Breast Cancer Research Program, Department of Defense	W81XWH-04-1-0745 BC032859	Timothy P. Quinn, M.D.

9. EVENTS

A. Initial Idea

Date: 20 Apr 2005

References and Comments: Idea conceived while at American Association for Cancer Research meeting in Anaheim, April 2005.

B. First description of complete invention, oral or written (conception)*

Date: 20 April 2005

References and Comments: Diagram of Idea drawn out 20 April 2005.

C. First successful demonstration, if any (first actual reduction to practice)*

Date: 8 July 2005

References and Comments: First demonstration that R2FasL protein kills Jurkat cells in vitro in a VEGF-dependent manner.

D. First publication, abstract, theses, webpostings, etc. containing full description of invention (establishment of publication bar)*

Date: None

References and Comments:

E. External oral disclosures (including seminars, group meetings, etc.)

Date: None

References and Comments:

F. Impending publications or oral disclosures. (NOTE - please alert the OTM well in advance of any public disclosures to allow enough time for the OTM to make informed decisions regarding possible patent protection; public disclosure can negatively impact the OTM's ability to obtain foreign patent protection).

Date: 15 August 2005

References and Comments: A high school student (Eric Liu) is working on R2FasL as part of the UCSF Dept. of Pediatrics High School Summer Internship Program in Biomedical and Health Sciences. As part of the program, he and the other students in the program will give presentations to their families and mentors on 15 August 2005.

10. THIS INVENTION USED DATA OR MATERIALS INVOLVING:

- ☒ (X) Material Transfer Agreement - "MTA" (non-UC material)
- ☐ () A subscription to the Celera Database
- ☐ () Affymetrix microarrays
- ☐ () Cre/lox technology

11. COMPANIES THAT COULD BE INTERESTED: (NOTE - if any inventor has a financial interest in a company that might be interested, DO NOT identify that company here; contact the OTM Director to discuss next steps).

Biotechnology or pharmaceutical companies working on anti-angiogenesis or cancer therapies (e.g. Genentech, Chiron, Regeneron, Amgen, etc.)

12. I HEREBY ASSIGN ALL RIGHT, TITLE, AND INTEREST, INCLUDING BUT NOT LIMITED TO COPYRIGHT AND COPYRIGHT RIGHTS, PATENT RIGHTS AND PROPERTY RIGHTS, IN THE INVENTION DISCLOSED HEREIN TO THE REGENTS OF THE UNIVERSITY OF CALIFORNIA.

Inventor's Signature: 

Date: 13 July 2005

12. INVENTION UNDERSTOOD BY

Witness' SignatureTM: 

Date: 13, July 2005

Witness' SignatureTM: 

Date: 13, July 2005

REVIEWED BY

OTM Licensing Officer:

Date:

* see instructions

** please have PI sign if PI is not an inventor; a suitable witness is someone who has a reasonable understanding of the invention but is not an inventor and has no vested interest in the invention.