

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 10/01/93

Project No. G-33-537_____ Center No. 10/11-6-P5164-1A0_

Project Director POWERS J C_____ School/Lab CHEMISTRY_____

Sponsor DHHS/PHS/NIH/NATL INSTITUTES OF HEALTH_____

Contract/Grant No. 1 F31 HL08813-01_____ Contract Entity GTRC

Prime Contract No. _____

Title INHIBITORS FOR COAGULATION PROTEASES_____

Effective Completion Date 930930 (Performance) 931230 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	N	_____
Final Report of Inventions and/or Subcontracts	N	_____
Government Property Inventory & Related Certificate	N	_____
Classified Material Certificate	N	_____
Release and Assignment	N	_____
Other _____	N	_____

CommentsEFFECTIVE DATE 9-30-92. CONTRACT VALUE \$11,452. _____
CONTINUED BY G-33-549. _____

Subproject Under Main Project No. _____

Continues Project No. _____

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Management	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	Y
Project File	Y
Other CARL BAXTER-FMD _____	Y
FRED CAIN-OOD _____	Y

DEPARTMENT OF HEALTH AND HUMAN SERVICES—PUBLIC HEALTH SERVICE

USE THIS LABEL TO RETURN APPLICATION
INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD CONTINUATION APPLICATION

Form approved through 10/31/94

221 OMB No. 0925-0002

633-5377

5 F31 HL08813-02 NATIONAL INSTITUTES OF HEALTH, NHLBI-DEA GRANTS OPERATIONS BRANCH WESTWOOD BUILDING, ROOM 4A09A BETHESDA, MARYLAND 20892	REVIEW GROUP SRC -7	TYPE 5	ACTIVITY F31	FELLOWSHIP NUMBER HL08813-02
	TOTAL AWARD PERIOD			
	From: 10/01/92		Through: 09/30/95	
REQUESTED BUDGET PERIOD				
From: 10/01/93		Through: 09/30/94		

To be verified by applicant. Check information in Items 1 through 6. If incorrect, furnish correct information in Item 11.

1. TITLE OF RESEARCH TRAINING PROPOSAL

INHIBITORS FOR COAGULATION PROTEASES

2a. APPLICANT (Name and address, street, city, state, zip code)

BROWN, AUDRA D
25694 GEORGIA TECH STATION
ATLANTA, GA 30332

4. SPONSORING INSTITUTION (Name and address, street, city, state, zip code)

GEORGIA TECH RESEARCH CORP
GEORGIA INST OF TECH
SCH OF CHEMISTRY
ATLANTA, GA 30332

5. ENTITY IDENTIFICATION NUMBER

1580603146A1

2b. SOCIAL SECURITY NUMBER

301-74-5813

2c. HIGHEST DEGREE(S)

BS

2d. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT

SCHOOL OF CHEMISTRY & BIOCHEM

2e. MAJOR SUBDIVISION

COLLEGE OF SCIENCES

3. NAME OF SPONSOR

POWERS, JAMES C

Complete the following (See instructions)

7. HUMAN SUBJECTS

7a. NO YES { OR Exemption # _____
 IRB Approval Date _____

7b. Assurance of Compliance # _____

8. VERTEBRATE ANIMALS

8a. NO Yes... IACUC Approval Date _____

8b. Animal Welfare Assurance # _____

9. TRAINING SITE(S) (Organizations and Addresses)

6. TITLE AND ADDRESS OF OFFICIAL SIGNING FOR SPONSORING INSTITUTION ~~XXXXXXX~~ **BUSINESS OFFICE**
Janis Goddard
CONTRACTING OFFICER
GEORGIA TECH RESEARCH CORP
GEORGIA INST OF TECHNOLOGY
ATLANTA, GA 30332-0420

BITNET/INTERNET ADDRESS

james.powers@chemistry.gatech.edu

10a. PERMANENT MAILING ADDRESS (Street, city, state, zip code)

25694 Georgia Tech Station
Atlanta, Georgia 30332

10b. APPLICANT'S TELEPHONE INFORMATION

	Area Code	Phone number & extension
OFFICE	404	894-4076
FAX	404	894-7452
HOME	404	953-1646
PERMANENT ADDRESS	404	953-1646

11. USE THIS SPACE FOR CORRECTIONS TO ITEMS 1 THROUGH 6. INDICATE THE NUMBER(S) WHERE ANSWERS APPLY.

12. APPLICANT CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, accurate, and complete to the best of my knowledge, and I agree to comply with Public Health Service terms and conditions if an award is issued as a result of this application. I certify that I have read the National Research Service Award Service Assurance, that I will abide by the Assurance if an award is made, and that the award will not support residency training. Willful provision of false information is a criminal offense (U.S. Code, Title 18, Section 1001). I am aware that any false, fictitious, or fraudulent statement may, in addition to other remedies available to the Government, subject me to civil penalties under the Program Fraud Civil Remedies Act of 1986 (45 CFR Part 79),

SIGNATURE

DATE 28 July 1993

**INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD
CONTINUATION APPLICATION**

FELLOWSHIP NUMBER

HL08813-02

13. APPLICANT SUMMARY OF ACTIVITIES (Do not exceed 3 pages.)

A. CHANGES

Since submission of the last application, have any significant changes occurred in the training program, particularly the research project, academic status, or time distribution of activities (i.e., percentage of time devoted to research project, course work, teaching, etc.)? If so, explain.

B. PROGRESS REPORT

Describe concisely the research performed and research training obtained during the past year. List all courses and publications.

C. RESEARCH TRAINING PLANS

Describe concisely the research and research training planned for the requested budget period, including any course work.

13. APPLICANT SUMMARY OF ACTIVITIES

A. CHANGES

Since submission of the last application, no significant changes have occurred in my training program. As stated in my original application, my time distribution was as follows: 20%, coursework; 5%, attending division and departmental seminars; 20%, preparation for the comprehensive exam; 45% research. The remaining 10%, originally planned for preparation of a seminar, was divided between coursework and research as necessary. The amount of time spent on research was divided as follows: 70%, the research project described in the original application; 30%, an additional research project involved with kinetic studies of neutrophil elastase.

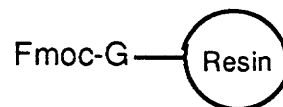
B. PROGRESS REPORT

Since October 1, 1992, the following peptide, a substrate for factor VIIa, has been made by solid phase peptide synthesis.

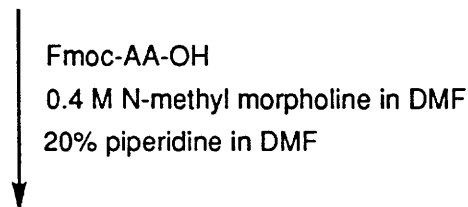
$$\begin{array}{cccccccccccccccc}
 P_{10} & & & & P_5 & & & & P_1 & P_{1'} & & & P_5' & & & & P_{10}' \\
 \text{Gln-Pro-Glu-Arg-Gly-Asn-Asn-Leu-Thr-Arg}^* \text{Ile-Val-Gly-Gly-Gln-Glu-Cys-Lys-Asn-Gly}
 \end{array}$$

scissile
bond

The reaction scheme for this synthesis is shown below:



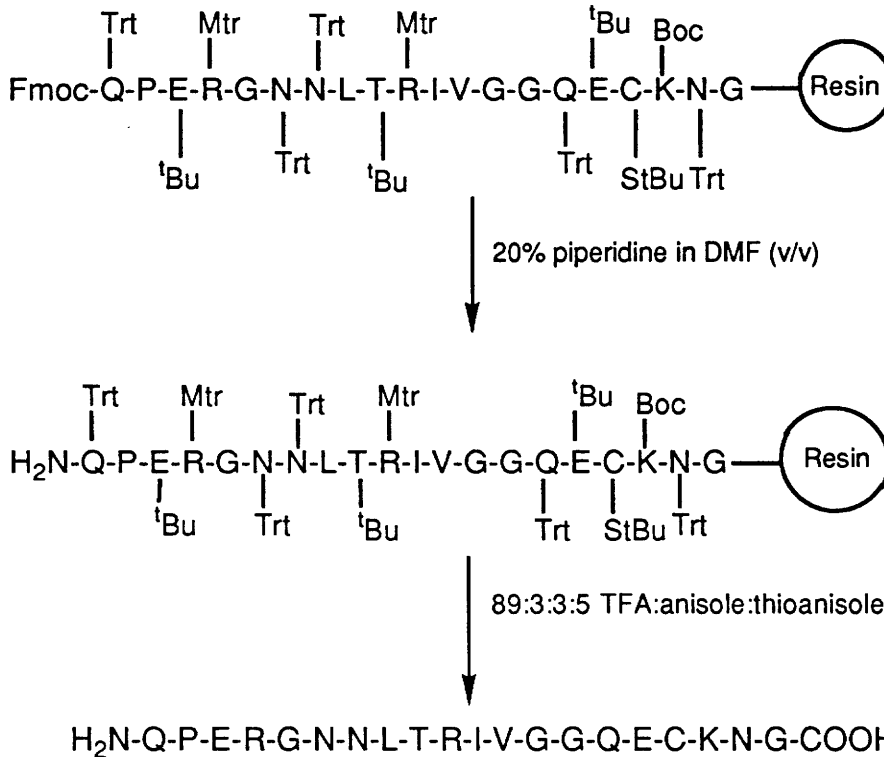
Resin = 1% Cross-linked Divinylbenzene-Styrene
p-Alkoxybenzyl Alcohol Linker
0.3-0.5 mmol/g, 200-400 mesh



INDIVIDUAL NRSA APPLICATION
CONTINUATION PAGE

NAME OF APPLICANT (Last, first, middle initial)

Brown, Audra D.



The abbreviations that stem from the amino acids in this peptide represent the protecting groups on each residue. They are defined as follows: Trt, triphenylmethyl; Mtr, 4-methoxy-2,3,6-trimethylbenzylsulfonyl; *t*Bu, *tert*-butyl; Boc, *tert*-butyloxycarbonyl; StBu, *tert*-butylsulfonyl.

The synthesis was done using a Rainin PS3 Peptide Synthesizer that was purchased by the School of Chemistry and Biochemistry in the Spring of 1992. Fmoc chemistry was used to accomplish the synthesis. The Fmoc-amino acids were obtained from BACHEM California, and the common chemicals were obtained from either Aldrich or Sigma. Cleavage of the peptide from the resin was accomplished using 89% TFA, 5% 1,2-ethanedithiol, 3% anisole, and 3% thioanisole. Purification of this peptide by reverse phase HPLC has proven to be very difficult, and optimal conditions for purification as well as cleavage from the resin are currently being sought.

The next phase of the project involves synthesis of a truncated sequence such that it has 12, 14, 16, 18 and 20 amino acid residues. These substrates of different lengths will be used to assess the importance of various residues of the peptide in reaction with factor VIIa. In addition, the fluorescent-quench substrates will be synthesized. Methods for the synthesis of the amino acids containing the fluorescent group and the quenching group are currently being researched in the literature. These substrates will be synthesized by the end of the calendar year 1993.

**INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD
CONTINUATION APPLICATION**

(To be completed by sponsor—follow instructions)

FELLOWSHIP NUMBER

HL08813-02

14. SUPPLEMENTATION OF FELLOW: NO YES — If "yes," specify the amount(s) and dates on which supplementation occurred, and the source of the funds.

15. COMMENTS OF SPONSOR *(Use additional page, if necessary)*

- A. Evaluate the quality of the training (including academic work) and research progress made by the fellow during the past year. Include performance on cumulative and qualifying examinations, if applicable.
- B. Human subjects and vertebrate animals *(see instructions)*.

14. The fellow was given a supplement of \$295/month from a Miles, Inc. grant to carry out kinetic studies with human leukocyte elastase. The amount is the difference between the normal stipend of \$13,000/year for chemistry graduate students and the amount provided by the NIH fellowship.

15A. Audra Brown has been getting excellent grades in her recent courses. At the end of the spring quarter of 1993, she took the comprehensive exam in biochemistry. Her performance was marginal and the Biochemistry division agreed that she be given an oral exam at the time of her proposition (the second part of the comprehensive exam) sometime within the next year.

Audra's research progress to date has been satisfactory, but quite slow. She works in the laboratory, is enthusiastic and interested in her research problem. I believe she needs to learn to budget her time more effectively, focus on research, and learn to ignore distractions which take her away from research. She has started the synthesis of a peptide inhibitor, but has yet to purify the peptide. She needs to obtain a command of the techniques for peptide synthesis.



Audra has the stated goal of obtaining an academic position once she completes her Ph.D. degree. I agree that she is one of the few students each year with this potential. However she is still not performing at this level. She hasn't yet made the work commitment to reach for this goal, but I believe that she will do so shortly.

15B. No human subjects or vertebrate animals are involved in this research.

Provide the number of subjects enrolled in the study to date according to the following categories (see Page 6 for definitions).

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	TOTAL
Female							
Male							
Unknown							
TOTAL							

16. CERTIFICATION. We, the undersigned, certify that: (a) the information herein, including involvement of Human Research Subjects, Recombinant DNA Research, and Vertebrate Animals, are true, accurate, and complete to the best of our knowledge; (b) if this application results in an award, appropriate training, adequate facilities, and supervision will be provided; and (c) we will comply with the Public Health Service terms and conditions of award. A willfully false certification is a criminal offense (U.S. Code Title 18, Section 1001). We are aware that any false, fictitious, or fraudulent statement may, in addition to other remedies available to the Government, subject us to civil penalties under the Program Fraud Civil Remedies Act of 1986 (45 CFR Part 79).

SIGNATURE	TYPED NAME	OFFICE TELEPHONE	DATE
	James C. Powers	(404) 894-4038	7/27/93
	Loren M. Tolbert	(404) 894-4002	7/29/93
OFFICIAL SIGNING FOR SPONSORING INSTITUTION	Janis L. Goddard	404/894-4817	7/30/93

**INDIVIDUAL NRSA CONTINUATION APPLICATION
CHECKLIST**

Applicant completes Section I. Sponsor completes Section II.

FELLOWSHIP NUMBER

HL08813-02

Section I—Applicant

ASSURANCES/CERTIFICATIONS

The following assurances/certifications are made by checking the appropriate boxes and are verified by your signature in Item 12 on the FACE PAGE of the application. Descriptions of individual assurances/certifications begin on page 2 of the application instructions.

- A. Debarment and Suspension No Yes (*Attach explanation*)
B. Delinquent Federal Debt No Yes (*Attach explanation*)

Section II—Sponsoring Institution

The following assurances/certifications are made by checking the appropriate boxes and verified by the signature of the Official Signing for Sponsoring Institution in Item 16. Descriptions of sponsoring institution assurances/certifications begin on page 7 of the application instructions.

- A. Human Subjects (*Complete Item 7 on the Face Page*) Full IRB Review Expedited Review

Use of Human Subjects: Change No Change Since Previous Submission

- B. Vertebrate Animals (*Complete Item 8 on the Face Page*)

Use of Vertebrate Animals: Change No Change Since Previous Submission

- C. Debarment and Suspension No Yes (*Attach explanation*)

- D. Misconduct in Science (Form PHS 6315) Filed Not Filed

If filed, date of Initial Assurance or latest Annual Report. 1/14/92

- E. Civil Rights (Form HHS 441) Filed Not Filed

- F. Handicapped Individuals (Form HHS 641) Filed Not Filed

- G. Sex Discrimination (Form HHS 639A) Filed Not Filed

- H. Age Discrimination (Form HHS 680) Filed Not Filed