BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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Church, Frank C.	Professor
eRA COMMONS USER NAME Frank_Church	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Louisiana State University, Baton Rouge	B.S.	1975	Microbiology
Louisiana State University, Baton Rouge	M.S.	1978	Microbiol./Enzymol.
North Carolina State University, Raleigh	Ph.D.	1982	Protein Chem./Biochem.
University of North Carolina, Chapel Hill	Postdoct.	1982-85	Biochem. Blood Coagul.

A. Positions and Honors

Positions and Employment

1974-1975 Undergraduate research assistant, Dept. Microbiology, LSU
1975-1978 Graduate research assistant, Depts. Food Sci., Microbiol., and Marine Sci., LSU
1978-1982 Graduate research assistant, Depts. Food Science and Biochemistry, NCSU
1982-1985 Postdoctoral Research Fellow, Department of Pathology
1985-1987 Research Assistant Professor of Pathology and Medicine
1985-2003 Member, Center for Thrombosis & Hemostasis
1987-1993 Assistant Professor of Pathology
1987-1995 Associate (Scientific) Director of the Clinical Coagulation Laboratory, UNC Hospitals
1989-1993 Assistant Professor of Medicine
1991-pres. Member, Program in Molecular Biology and Biotechnology
1994-1999 Associate Professor of Pathology and Laboratory Medicine, and Medicine (with tenure)
1996-pres. Member, Lineberger Comprehensive Cancer Center
1999-pres. Professor, Departments of Pathology and Laboratory Medicine, Pharmacology, and Medicine
2002-pres. Member, Carolina Cardiovascular Biology Center

Other Experience and Professional Memberships

1991-1997 The Journal of Biological Chemistry, Editorial Board Member
1992 "Opponent" in Ph.D. defense, Royal Inst. of Technology, Stockholm, Sweden
1994-2000 Co-Director SURE (Summer Undergraduate Research Experience) Program, UNC-CH
1996-2001 Director of Graduate Admissions, Dept. of Pathology and Lab. Medicine, UNC-CH
1996-pres. Course Organizer and Sole Lecturer for Biology/Pathology 134 "Biology of Blood Diseases"
1998-pres. Medical School Admissions Ad Hoc Committee Member
1999-pres. J. Thrombosis and Haemostasis, Editorial Advisory Board Member for Senior Editor H.R. Roberts
2001-pres. Course Director, Hematology-Oncology, Medicine, UNC-CH School of Medicine
2001-pres. Medical Student's Promotions Committee, UNC-CH School of Medicine
2001-pres. FAHA, Fellow of The American Heart Association
2000-2003 Executive Council Member for Thrombosis, American Heart Association
2000-2004 Chair, Plasma Coagulation Inhibitors, SSC, International on Society Thrombosis & Haemostasis
2001-2005 (Co-Chair/Chair 2003-2005) Mid-Atlantic American Heart Association Study Section 2
2002-pres. Director of Graduate Studies, Department of Pathology and Lab Medicine, UNC-CH
2003-pres. NIH, NHLBI, Hemostasis and Thrombosis Study Section (HT) Ad Hoc Reviewer
2005-pres. Executive Council Member of the Carolina Cardiovascular Biology Center, UNC-CH SOM

Honors

1982 Graduate Student Research Award National American Dairy Science Association
1989-1991 and 1995-1997 University Research Council Award Recipient
1990-1991 Junior Faculty Development Award Recipient

1990-1994 Jefferson-Pilot Medical Fellowship in Academic Medicine Recipient
1998 Patent No. 5,712,247 entitled “Use of Lactoferrin to Modulate and/or Neutralize Heparin Activity”
1999 Tanner Faculty Award for Excellence in Undergraduate Teaching, UNC-CH
2000 Teaching Excellence Award, Department of Pathology, UNC-CH School of Medicine
2000-pres. The University of North Carolina at Chapel Hill Academy of Distinguished Teaching Scholars
2001 Patent No. 6,207,419 entitled “Thrombin Inhibitory Agents”
2003 Teaching Excellence Award, Department of Pathology, UNC-CH School of Medicine
2004 Student Undergraduate Teaching And Staff Awards (SUTASA) Recipient, UNC-CH
2005 Tanner Faculty Award for Excellence in Undergraduate Teaching, UNC-CH

B. Selected peer-reviewed publications (16 from a total of over 95 papers)

1. Ciaccia, A. V., Willemze, A.J., and Church, F. C. (1997) Heparin promotes proteolytic inactivation by thrombin of a reactive site mutant (L444R) of heparin cofactor II. **J. Biol. Chem. 272:** 888-893.
2. Church, F.C., D.D. Cunningham, D. Ginsburg, M. Hoffman, D.M. Tollefsen, and S.R. Stone (Editors) (1997) "Chemistry and Biology of Serpins". Plenum Press, New York. 358 pages.
3. Bauman, S.J. and F.C. Church (1999) Enhancement of heparin cofactor II anticoagulant activity. **J. Biol. Chem. 274:** 34556-34565.
4. Shirk, R.A., N. Parthasarathy, J.D. San Antonio, F.C. Church, and W.D. Wagner (2000) Altered dermatan sulfate structure and reduced heparin cofactor II activity of biglycan and decorin from human atherosclerotic plaque. **J. Biol. Chem. 275:** 18085-18092.
5. Silverman G.A., P.I. Bird, R.W. Carrell, F.C. Church, P.B. Coughlin, P.G. Gettins, J.A. Irving, D.A. Lomas, C.J. Luke, R.W. Moyer, P.A. Pemberton, E. Remold-O'Donnell, G.S. Salvesen, J. Travis, and J.C. Whisstock (2001) The serpins are an expanding superfamily of structurally similar but functionally diverse proteins. **J. Biol. Chem.** 276: 33293-33296.
6. Oliver, J.A., D.M. Monroe, F.C. Church, H.R. Roberts, and M. Hoffman (2002) Activated protein C cleaves factor Va more efficiently on endothelium than on platelets. **Blood.** 100:539-546.
7. Baglin, T., R.W. Carrell, F.C. Church, C.T. Esmon and J.A. Huntington (2002) Crystal structures of native and thrombin-complexed heparin cofactor II reveal a multistep allosteric mechanism. **Proc. Natl. Acad. Sci. U.S.A. 99:** 11079-11084.
8. Mitchell, J.W. and F.C. Church (2002) Aspartic acid residues 72 and 75 and tyrosine-sulfate 73 of heparin cofactor II promote intramolecular interactions during glycosaminoglycan binding and thrombin inhibition. **J. Biol. Chem. 277**: 19823-19830.
9. Palmieri, D., J.-W. Lee, R.L. Juliano and F.C. Church (2002) Expression of plasminogen activator inhibitor-type 1 and 3 increase cell adhesion and motility of MDA-MB-435 cancer cells. **J. Biol. Chem. 277:** 40950-40957.
10. Glasscock, L.N., B. Gerlitz, S.T. Cooper, B.W. Grinnell, and F.C. Church (2003) Basic residues in the 37-loop of activated protein C modulate inhibition by protein C inhibitor but not by α_1-antitrypsin. **Biochim. Biophys. Acta**. **1649:** 106-117.
11. Whitley, B.R., D. Palmieri, C. Twerdi, and F.C. Church (2004) Expression of active plasminogen activator inhibitor-1 regulates cell migration and invasion in breast and gynecological cancer cells. **Exp. Cell Res. 296:** 151-162.
12. Fortenberry, Y.M., H.C. Whinna, H.R. Gentry, T. Myles, L.L.K. Leung, and F.C. Church (2004) Molecular mapping of the thrombin-heparin cofactor II complex. **J. Biol. Chem**. 279(41): 43237-44.
13. Hobson, J.P., S. Netzel-Arnett, R. Szabo, S.M. Réhault, F.C. Church, D.K. Strickland, D.A. Lawrence, T.M. Antalis, and T.H. Bugge (2004) Mouse *DESC1* is located within a cluster of seven *DESC1*-like genes and encodes a type II transmembrane serine protease that forms serpin inhibitory complexes. J. Biol. Chem. 279: 46981-94
14. Réhault, S.M., M. Zechmeister-Machhart, Y.M. Fortenberry, J. Malleier, N.M. Binz, S.T. Cooper, M., Geiger, M., and F.C. Church (2005) Characterization of recombinant human protein C inhibitor expressed in *Escherichia coli.* **Biochimica Biophysica Acta**. 1748: 57-65.
15. Whitley, B.R. and F.C. Church (2005) Regulation of wound-induced migration of MDA-MB-435 and SKOV-3 cancer cells by plasminogen activator inhibitor-1. **Int. J. Oncol.** 27:749-57.
16. Pike, R.N., Buckle, A.M., le Bonniec, B.F., and F.C. Church (2005) Control of the coagulation system by serpins: getting by with a little help from glycosaminoglycans. **FEBS J.** 272:4842-51

C. Research Support

Ongoing Research Support:

"Extravascular Thrombin Regulation by Heparin Cofactor II (HCII)"
Principal Investigator: F.C. Church, Ph.D.
Agency: National Institute of Heart, Lung and Blood Type: R01 (HL32656-17)
Period: 08/01/01-07/31/06 (competitive renewal submitted on 11/01/05)
The goals of this project are to define the physiological role of HCII as an extravascular thrombin inhibitor.

"RNA Aptamer-directed Anticoagulant Therapy"
Principal Investigator: Y.M. Fortenberry, Ph.D. (F.C. Church, Ph.D., Sponsor)
Agency: NIH, NHLBI, NRSA Postdoctoral Fellowship, F32 HL076108-01
Funding Period: 01/01/04-12/31/06
This project is to characterize new RNA aptamer-based anticoagulants.

"Cooperation of Adipocytes with Breast Cancer Cells Promotes an Invasive Phenotype"
Principal Investigator: F.C. Church, Ph.D.
Agency: Susan G. Komen Breast Cancer Foundation
Type: Basic, Clinical and Translational Breast Cancer Grant (BCTR0503475)
Funding Period: 05/01/05-04/30/07
This proposal ascribes novel activities to PAI-1, to tumor stromal adipocytes, and to PPARγ ligands that could promote an invasive phenotype in breast cancer.

"Breast Cancer and the Plasminogen Activator Inhibitor-1 Cycle" [pending]
Principal Investigator: F.C. Church, Ph.D.
Agency: Susan G. Komen Breast Cancer Foundation
Type: Basic, Clinical and Translational Breast Cancer Grant BCTR45206
Funding Period: 05/01/06-04/30/09
This proposal is to test the role of adipocytokines from the Metabolic Syndrome and their influence on breast cancer and vascular endothelial cells, mediated through changes in PAI-1 expression.

"Regulation of Protein C System by Serpins" [pending]
Principal Investigator: F.C. Church, Ph.D.
Agency: American Heart Association, Mid-Atlantic Affiliate
Type: Grant-in-Aid
Funding Period: 07/01/06-06/31/08
This project is to determine the in vivo and in vitro relevance of regulating the protein C pathway of proteases by the serpins, protein C inhibitor and plasminogen activator inhibitor-1/vitronectin.

"Role of the Protein C System in Blood Vessel Repair"
Principal Investivator: L.M. Beaulieu, B.S. (F.C. Church, Ph.D., Sponsor)
Agency: Kirschstein-NRSA Predoctoral Fellowship, F31 NS054590-01
Funding Period: 04/01/06-03/31/07
This project is to determine the role of activated protein C and serpins in the pathophysiology of stroke.

"Heparin Cofactor II in the Aging Vasculature"
Principal Investivator: J.C. Rau, B.S., M.A. (F.C. Church, Ph.D., Sponsor)
Agency: Kirschstein-NRSA Individual Predoctoral Medical Scientist Fellowship, F30
Funding Period: 07/01/06-06/31/10
This project is to determine the role of heparin cofactor in atherosclerosis and in the aging population.

Completed Research Support:

"Glycosylphosphatidylinositol (GPI)-anchored Antithrombins"
Principal Investigator: H.C. Whinna, M.D./Ph.D. (F.C. Church, Ph.D., Sponsor)
Agency: National Institute of Heart, Lung and Blood Type: K08 (HL04063)
Period: 08/15/99-06/31/04
This project created and evaluated endothelial cell-GPI-anchored antithrombins in vitro and in vivo.

"Regulation of Protein C System by Protein C Inhibitor" (Project 3)
Principal Investigator: F.C. Church, Ph.D.
Agency: National Institute of Heart, Lung and Blood Type: P01 (HL06350) "Structure, Function, and Genetics of Coagulation Factors" D. Stafford, P.I. Period: 01/01/99-12/31/04
This project defined the protein elements of protein C inhibitor as it regulates thrombosis and tumor biology

"Plasminogen Activator Inhibitor-1 Confers a Survival Advantage to Cancer Cells"
Principal Investigator: Sophie Réhault, Ph.D. (F.C. Church, Ph.D., Sponsor)
Agency: Association pour la Recherche contre le cancer (ARC)
Funding Period: 01/01/02-12/31/02
We hypothesize that the expression of PAI-1 confers a survival advantage upon breast cancer cells by altering adhesive and proliferative characteristics.

"Regulatory Roles of Lactoferrin in Hemostasis"
Principal Investigator: H.-F. Wu, M.D. (F.C. Church, Ph.D., Sponsor)
Agency: National Institute of Heart, Lung and Blood Type: K08 (HL03279)
Period (original): 04/01/95-03/31/00 (Dr. Wu was receiving clinical training in Pathology at Columbia University and the Grant was reactivated 07/01 after an NIH-approved 3-year break at Ohio State University).
This project was to understand how the neutrophil-containing protein lactoferrin regulates hemostasis and DIC.

"Novel Differentiated Product of Endothelial Cells"
Principal Investigator: C.-J.S. Edgell, Ph.D.
Agency: National Institute of Heart, Lung and Blood
Type: R01 (HL55452) Period: 04/01/97-03/31/01, collaborator
This project characterized the novel endothelial cell proteoglycan testican.

"Role of Protein C Inhibitor in Hemostasis"
Principal Investigator: F.C. Church, Ph.D.
Agency: National American Heart Association, Grant-in-Aid 9750709N,
Funding Period: 01/01/98-12/31/00
This project involved the site-directed mutagenesis of protein C inhibitor.

"Molecular Mechanism of Thrombin Inhibition"
Principal Investigator: S.T. Cooper, Ph.D.)
Agency: National Institutes of Health, AREA Grant
Funding Period: 07/01/97-06/30/00, collaborator
This project prepared novel site-directed mutants of antithrombin expressed by baculovirus. These small grants are for investigators at small colleges with a relatively modest research budget.