

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Church, Frank C.	POSITION TITLE Professor		
eRA COMMONS USER NAME Frank_Church			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	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. Thrombosis

**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, UNC-CH School of Medicine  
 2006-pres. Member, Program in Translational Medicine, UNC-CH School of Medicine  
 2007-pres. Member, Curriculum in Toxicology, UNC-CH

**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 426 (134) "Biology of Blood Diseases"  
 1998-pres. Medical School Admissions Ad Hoc Committee Member  
 1999-pres. J. Thrombosis and Haemostasis, Editorial Advisory Board Member  
 2001-pres. Course Director, "Hematology-Oncology", 2<sup>nd</sup> year course, UNC-CH School of Medicine  
 2001-pres. Medical Student's Promotions Committee, UNC-CH School of Medicine  
 2001-pres. Fellow of The American Heart Association (FAHA)  
 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  
 2002-2006 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. Course Director Path 713 (213), "Molecular and Cellular Pathophysiological Basis of Disease"

### **Other Experience and Professional Memberships (cont'd)**

2005-pres. Executive Council Member of the Carolina Cardiovascular Biology Center, UNC-CH SOM  
2006-2010 Vice-Chair/Chair Research Committee, Mid-Atlantic American Heart Association, AHA  
2006-2007 Member, Postdoctoral Research Awards Committee, Susan G. Komen for the Cure  
2007-2008 Member, MCBG-1 Grants Review Committee, Susan G. Komen for the Cure  
2007-2012 The Journal of Biological Chemistry, Editorial Board Member

### **Honors**

1982 Graduate Student Research Award National American Dairy Science Association  
1989, 1995 University Research Council Award Recipient, UNC-CH  
1990-1991 Junior Faculty Development Award Recipient, UNC-CH  
1990-1994 Jefferson-Pilot Medical Fellowship in Academic Medicine Recipient, UNC-CH  
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. Academy of Distinguished Teaching Scholars, The University of North Carolina at Chapel Hill  
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  
2005-07 "Coater" for White Coat Ceremony for 1<sup>st</sup> Year Medical Students, UNC-CH  
2006 "Star Heels" Award from the Office of Human Resources, UNC-CH  
2006 Joe Wheeler Grisham Award for Excellence in Teaching Graduate Students, UNC-CH  
2006 University Research Council Award Recipient, UNC-CH  
2007 Frank Porter Graham Honor Society, UNC-CH  
2007 Fellow, Academy of Educators, UNC-CH School of Medicine  
2007 Sophomore Basic Science Course Award, Hematology-Oncology, SOM, Course Director

### **B. Selected peer-reviewed publications (25 from a total of 100 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  $\alpha_1$ -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
17. Glasscock, L.N., S.M. Rehault, C.W. Gregory, Cooper, S.T., Jackson, T.P., Hoffman, M., and F.C. Church (2005) Protein C inhibitor (Plasminogen Activator Inhibitor-3) expression in the CWR22 prostate cancer xenograft. **Exp. Molec. Pathol.** **79**: 23-32.
18. Beaulieu, L.M. and F.C. Church (2006) Is protein C inhibitor antithrombotic and protective in pulmonary hypertension? **J. Thromb. Haemost.** **4**: 2327-2330.
19. Whitley, B.R., L.M. Beaulieu, J.C. Carter, and F.C. Church (2007) Phosphatidylinositol 3-kinase/Akt regulates the balance between plasminogen activator inhibitor-1 and urokinase to promote migration of SKOV-3 ovarian cancer cells. **Gynecol. Oncol.** Feb;104(2):470-9.
20. Beaulieu, L.M. and F.C. Church (2007) Activated Protein C promotes breast cancer cell migration through interactions with EPCR and PAR-1. **Exp. Cell Res.** Feb 15;313(4):677-87.
21. Church, F.C., R.N. Pike, D.M. Tollefsen, A.M. Buckle, A.V. Ciaccia, and S.T. Olson (2007) Regulation of hemostasis by heparin-binding Serpins. In "Molecular and cellular aspects of the serpinopathies and disorders of serpin activity", World Scientific Publishing Co. Chapter 22, 509-554.
22. Fortenberry, Y.M., H.C. Whinna, S.T. Cooper, T. Myles, L.L.K. Leung, and F.C. Church (2007) Essential thrombin residues for inhibition by protein C inhibitor with the cofactors heparin and thrombomodulin. **J. Thromb. Haemost.** **5**(7): 1486-1492.
23. Rau, J.C., L.M. Beaulieu, J.A. Huntington, and F.C. Church (2007) Serpins in thrombosis, hemostasis and fibrinolysis. **J. Thromb. Haemost.** **5** (Suppl. 1): 102-115.
24. Beaulieu, L.M., B.R. Whitley, T.F. Wiesner, D. Palmieri, S.M. Rehault, A. Elkahlon, and F.C. Church (2007) Breast cancer and metabolic syndrome linked through the plasminogen activator inhibitor-1 cycle. **BioEssays.** **29**(10):1029-38.
25. Gonzales, P.R., T.D. Walston, L.O. Camacho, D.M. Kielar, F.C. Church, A.R. Rezaie, and S.T. Cooper (2007) Mutation of the H-helix in antithrombin decreases heparin stimulation of protease inhibition. **Biochim Biophys Acta,** **1774**(11):1431-7.

## C. Research Support

### Ongoing/Planned Research Support:

"p16<sup>INK4a</sup>, Senescence and Aging in Venous Thromboembolism";

Principal Investigator: F.C. Church, Ph.D.

Agency: NIH, National Institute of Aging and Heart, Lung and Blood; Type: R21 (1R21AG031068-01)

Period: 09/01/07-08/31/09;

This project is to study p16<sup>INK4a</sup> expression in venous thrombosis and thromboembolism in the elderly.

**“Breast Cancer and the Plasminogen Activator Inhibitor-1 Cycle”;**

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 research studies the link of adipokines from Metabolic Syndrome with breast cancer invasion.

**“Role of the Host Phosphoinositide 3-kinase Signaling Pathway in Promoting Breast Cancer Invasion and Metastasis”**

Principal Investigator: F.C. Church, Ph.D.; Agency: Susan G. Komen for the Cure

Type: Investigator-initiated Research Grant Proposal

Period: 03/01/08-02/29/11

This proposal ascribes novel activities to up-regulating host PI3K/Akt activities in breast cancer.

**“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: 05/01/05-04/30/08

This proposal ascribes novel activities to PAI-1 in tumor stromal adipocytes and to PPAR $\gamma$  ligands.

**“Protein C Pathway Signaling and Regulation in Blood Vessel Repair”**

Principal Investigator: F.C. Church, Ph.D.

Agency: NIH, National Institute of Heart, Lung and Blood; Type: R01 (1R01HL091908-01 pending)

Period: 04/01/08-03/31/13;

This project is to study the signaling mechanisms of APC-EPCR in the vasculature.

**“Engineering a Chimeric Serpin as a Preventative Therapeutic for Ischemic Stroke”**

Principal Investigator: J.C. Rau, B.S., M.A. (F.C. Church, Ph.D., Sponsor)

Agency: AHA, Mid-Atlantic Affiliate, Predoctoral Fellowship

Funding Period: 07/01/07-05/30/08

This project is to engineer a serpin as an effective inhibitor of ischemic stroke.

**“Grafting the Heparin-binding Site of Antithrombin on Bovine Pancreatic Polypeptide (bPP)”**

Principal Investigator: F.C. Church, Ph.D.;

Agency: UNC-CH; Type: University Research Council Grant;

Funding Period: 01/01/07-12/31/09

This is a protein-engineering project to design a model heparin-binding protein for structure-activity studies.

**“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 (HL32656-18)

Period: 08/01/01-07/31/06 (competitive renewal to be submitted on 11/01/07)

The goals of this project are to define the physiological role of HCII as an extravascular thrombin inhibitor.

**Completed Research Support:**

**“Role of the Protein C System in Blood Vessel Repair”**

Principal Investigator: L.M. Beaulieu, B.S. (F.C. Church, Ph.D., Sponsor)

Agency: NIH, Kirschstein-NRSA Predoctoral Fellowship, F31 NS054590-01A1

Funding Period: 08/01/06-07/31/07

This project is to determine the role of activated protein C and serpins in the pathophysiology of stroke.

**“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 HL076108-03;

Funding Period: 01/01/04-12/31/06

This project characterized new RNA aptamer-based anticoagulants.