

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 John A. Williams		POSITION TITLE Professor, Molecular & Integrative Physiology	
eRA COMMONS USER NAME (credential, e.g., agency login) jawilliams		Professor, Internal Medicine	
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
Central Washington State College	B.A.	1963	Pre-Medicine
University of Washington, Seattle	M.D.	1968	Medicine
University of Washington, Seattle	Ph.D.	1968	Physiology & Biophysics
University of Utah	Postdoc	1969	Pharmacology

A. Positions and Honors

Positions and Employment:

- 1969-1971 Staff Associate, Clinical Endocrinology Branch
National Institute of Arthritis and Metabolic Disease, Bethesda, MD
- 1971-1972 Helen Hay Whitney Fellow, Department of Pharmacology
University of Cambridge, Cambridge, England
- 1973-1987 Assistant, Associate, & Professor of Physiology, University of California, San Francisco, CA
- 1979-1987 Co-Director, Cell Biology Laboratory
Mount Zion Hospital and Medical Center, San Francisco, CA
- 1983-1987 Professor of Internal Medicine, University of California, San Francisco, CA
- 1987-2008 Professor and Chair of Molecular & Integrative Physiology,
- 1987- Professor of Internal Medicine, University of Michigan, Ann Arbor, MI
- 2008- Professor of Molecular & Integrative Physiology

Awards and Other Professional Activities:

- 1968 M.D. with Highest Honors; Alpha Omega Alpha Medical Honorary
- 1985-1986 President, American Pancreatic Association
- 1985 Hoffman LaRoche Prize in Gastrointestinal Physiology
- 1985-1991 Editor, American Journal of Physiology: Gastrointestinal and Liver Physiology
- 1984-87 NIH GMA-2 Study Section
- 1991-1994 NIDDK Special Grants Review Committee C; Chair, 1994
- 1996-1999 Council, American Physiological Society
- 1997-2001 Associate Editor, Journal of Clinical Investigation
- 1998 Fellow, American Association for the Advancement of Science
- 1999 Ismar Boas Medal, German Gastroenterological Association
- 2001-2005 Editorial Committee and Section Editor, Annual Reviews of Physiology
- 2002-2005 President Elect, President, Past President, American Physiological Society
- 2002- Editorial Board, Gastroenterology
- 2002-2005 IUPS, National Organizing Committee
- 2004 American Association of Physicians
- 2004 Distinguished Faculty Achievement Award, University of Michigan
- 2005 VLW Go Lifetime Achievement Award, American Pancreatic Association
- 2008 Frank Brooks Memorial Lecture, American Pancreatic Association

B. RELEVANT PUBLICATIONS: (From a total of 278 original research papers and 78 chapters or reviews.)

1. Williams JA, M Korc, RL Dormer. Action of secretagogues on a new preparation of functionally intact isolated pancreatic acini. Am J Physiol 235:E517-524, 1978.

2. Sankaran H, ID Goldfine, CW Deveney, KY Wong, JA Williams. Binding of cholecystokinin to high affinity receptors on isolated rat pancreatic acini. *J Biol Chem* 255:1849-1853, 1980.
3. Saito A, H Sankaran, ID Goldfine, JA Williams. Cholecystokinin receptors in the brain: Characterization and distribution. *Science* 208:1155-1156, 1980.
4. Logsdon CD, JA Williams. Pancreatic acinar cells in monolayer culture: Direct trophic effects of caerulein *in vitro*. *Am J Physiol* 250:G440-447, 1986.
5. Matozaki T, JA Williams. Multiple sources of 1,2-Diacylglycerol in isolated rat pancreatic acini stimulated by cholecystokinin: Involvement of phosphatidylinositol bisphosphate and phosphatidylcholine hydrolysis. *J Biol Chem* 264:14729-14734, 1989.
6. Groblewski GE, ACC Wagner, JA Williams. Cyclosporin A inhibits Ca^{2+} /calmodulin-dependent protein phosphatase and secretion in pancreatic acinar cells. *J Biol Chem* 269:15111-15117, 1994.
7. Yule DI, E Stuenkel, JA Williams. Intercellular calcium waves in rat pancreatic acini: mechanism of transmission. *Am J Physiol* 271:C1285-C1294, 1996.
8. Dabrowski A, T Grady, CD Logsdon, JA Williams. Jun kinases are rapidly activated by cholecystokinin in rat pancreas both *in vitro* and *in vivo*. *J Biol Chem* 271:5686-5690, 1996.
9. Dabrowski A, GE Groblewski, C Schaefer, K-L Guan, JA Williams. Cholecystokinin and EGF activate a MAPK cascade by different mechanisms in rat pancreatic acinar cells. *Am J Physiol* 273:C1472-C1479, 1997.
10. Ohnishi H, LC Samuelson, DI Yule, SA Ernst, JA Williams. Overexpression of Rab3D enhances regulated amylase secretion from pancreatic acini of transgenic mice. *J Clin Invest* 100:3044-3052, 1997.
11. Groblewski GE, M Yoshida, MJ Bragado, SA Ernst, J Leykam, JA Williams. Purification and characterization of a novel physiological substrate for calcineurin in mammalian cells. *J Biol Chem* 273:22738-22744, 1998.
12. Schäfer C, P Clapp, MJ Welsh, R Benndorf, JA Williams. Hsp27 expression regulates CCK-induced changes of the actin cytoskeleton in CHO-CCKA cells. *Am J Physiol* 277:C1032-C1043, 1999.
13. Bragado MJ, M Tashiro, JA Williams. Regulation of the initiation of pancreatic digestive enzyme protein synthesis by cholecystokinin in rat pancreas *in vivo*. *Gastroenterology* 119:1731-1739, 2000.
14. Williams JA. Intracellular signaling mechanisms activated by cholecystokinin-regulating synthesis and secretion of digestive enzymes in pancreatic acinar cells. *Ann Rev Physiol* 63:77-97, 2001.
15. Chen X, Edwards JAS, Logsdon CD, Ernst SA, Williams JA. Dominant negative Rab3D inhibits amylase release from mouse pancreatic acini. *J Biol Chem* 277:18002-18009, 2002.
16. Sans MD, MJ DiMagno, LG D'Alecy, JA Williams. Caerulein-induced acute pancreatitis inhibits protein synthesis through effects on eIF2B and eIF4F. *Am J Physiol* 285:G517-G528, 2003.
17. LePage S, Y Bi, JA Williams. The CCKA receptor activates RhoA through $G\alpha_{12/13}$ in NIH 3T3 cells. *Am J Physiol: Cell Physiology* 285:G1197-1206, 2003.
18. Chen X, SA Ernst, JA Williams. Dominant negative Rab3D mutants reduce GTP-bound endogenous Rab3D in pancreatic acini. *J Biol Chem* 278:50053-50060, 2003.
19. Sans MD, S-H Lee, LG D'Alecy, JA Williams. Feeding activates protein synthesis in mouse pancreas at the translational level without increase in mRNA. *Am J Physiol* 287:G667-G675, 2004.
20. Tashiro M, LC Samuelson, RA Liddle, JA Williams. Calcineurin mediates pancreatic growth in protease inhibitor-treated mice. *Am J Physiol* 286:G784-G790, 2004.
21. Kubisch C, DiMagno MJ, Tietz AB, Welsh MJ, Ernst SA, Brandt-Nedelev B, Diebold J, Wagner ACC, Göke B, Williams JA, Schäfer C. Overexpression of heat shock protein Hsp27 protects against cerulein-induced pancreatitis. *Gastroenterology* 127:275-286, 2004. PMID: 15236192
22. Li C, X Chen, JA Williams. Regulation of CCK-induced amylase release by protein kinase C delta in rat pancreatic acinar cells. *Am J Physiol* 287:G764-G771, 2004.
23. Bi Y, JA Williams. A role for Rho and Rac in secretagogue induced amylase release by pancreatic acini. *Am J Physiol* 289:C22-C32, 2005.
24. Chen X, AK Walker, JR Strahler, ES Simon, SL Tomanicek-Volk, BB Nelson, MC Hurley, SA Ernst, JA Williams, PC Andrews. Organellar proteomics: Analysis of pancreatic zymogen granule membranes. *Mol Cell Proteomics* 5:306-312, 2006 PMID: 16278343
25. Tashiro M, A Dabrowski, L Guo, MD Sans, JA Williams. Calcineurin dependent and independent signal transduction pathways activated as part of pancreatic growth. *Pancreas* 32:314-320, 2006.
26. Crozier SJ, MD Sans, L Guo, LG D'Alecy JA Williams. Activation of the mTOR signaling pathway is required for pancreatic growth in protease inhibitor-fed mice. *J Physiol* 573:775-786, 2006.

27. Sans MD, M Tashiro, N Vogel, SR Kimball, LG D'Alecy, JA Williams. Leucine activates pancreatic translational machinery through mTOR independent of CCK and insulin. *J Nutrition*, 136:1792-1799 2006.
28. Kubisch, C.H., Sans, M.D., Ernst, S.A., Williams J.A., Logsdon, C.D. (2006). Early activation of endoplasmic reticulum stress is associated with arginine induced acute pancreatitis. *Am J Physiol* 291:G238-G245. PMID: 16574987
29. Williams JA, Yule DI. Stimulus-secretion coupling in pancreatic acinar cells. In: *Physiology of the Gastrointestinal Tract, Fourth Edition*, LR Johnson, Editor, New York, Academic Press 2006, pp 1337-1369.
30. Guo L, MD Sans, GT Gurda, SH Lee, SA Ernst, JA Williams. Induction of early response genes in trypsin inhibitor-induced pancreatic growth. *Am J Physiol* 292:G667-G677, 2007.
31. Gurda GT, L Guo, SH Lee, JD Molckentin, JA Williams. Cholecystokinin (CCK) activates pancreatic calcineurin-NFAT signaling in vitro and in vivo. *Mol Biol of the Cell*, 19:198-206, 2008. PMCID: PMC2174201
32. Sans MD, Crozier SJ, Williams JA. Regulation of pancreatic protein synthesis and growth. Chapter 11 In: *The Pancreas: A Clinical and Surgical Text, 2nd Ed.*, H Beger, Editor, Oxford, Blackwell, 2008.
33. Crozier SJ, MD Sans, CH Lang, LG D'Alecy, SA Ernst, JA Williams. CCK-induced pancreatic growth is not limited by mitogenic capacity in mice. *Am J Physiol* 294:G1148-G1157, 2008.
34. Sabbatini ME, X Chen, SA Ernst, JA Williams. Rap activation plays a regulatory role in pancreatic amylase secretion. *J Biol Chem*, 283:23884-23894, 2008. PMCID: PMC2527106
35. Chen X, Ulintz PJ, Simon ES, Williams JA and Andrews PC. Global topology analysis of pancreatic zymogen granule membrane proteins. *Mol Cell Proteomics*, 7:2323-2336, 2008 PMCID: PMC2596344
36. Williams JA. Receptor-mediated signal transduction pathways and the regulation of pancreatic acinar cell function. *Curr Opinion in Gastroenterology* 24:573-579, 2008.
37. Williams JA, Chen X, Sabbatini ME. Small G proteins as key regulators of pancreatic digestive enzyme secretion. *Am J Physiol: Endocrine Physiol.* 296:E405-E414, 2009.
38. Crozier SJ, LG D'Alecy, SA Ernst, LE Ginsberg, and JA Williams. Molecular mechanisms of pancreatic dysfunction induced by protein malnutrition. *Gastroenterology*, 137:1093-1101, 2009.
39. Lee SH, MJ Wishart, and JA Williams. Identification of phosphorylation sites on CRHSP-24. *Biochem Biophys Res Commun.* 385:413-417,2009.

Research Support (Current)

R37 DK 41122 (JA Williams, PI) 12/01/05-11/30/10
NIH

Calcium and Pancreas Stimulus-Secretion Coupling

This research on pancreatic secretion is focused on understanding the role of Ca²⁺ as an intracellular messenger controlling digestive enzyme secretion. It evaluates the Ca²⁺ activated phosphatase, calcineurin, the small G protein Rab3D and SNARE proteins in the mechanisms of Ca²⁺ activated exocytosis.

R01 DK 59578 (JA Williams, PI) 12/01/2009 to 11/30/2013
NIH

Dietary Regulation of Pancreatic Digestive Enzymes

The overall goal is to understand the regulation by GI hormones and dietary constituents, particularly amino acids of pancreatic digestive enzyme synthesis and pancreatic growth, both of which serve to ensure an adequate supply of digestive enzymes. Pancreatic protein synthesis and the activation state of translation initiation factors are being studied.

F32 DK 077423 (JA WILLIAMS, PI) 05/01/2007 - 04/30/2010
NIH

Mechanisms Of Protein Malnutrition-Induced Exocrine Pancreas Dysfunction

NRSA Postdoctoral Fellowship for Stephen J Crozier. The research is directed at the effect of dietary protein deficiency on pancreatic exocrine function.

P30 DK 34933 (C Owyang, PI)

12/01/05-11/30/10

NIH

Digestive Disease Research Core Center

The major goals: Core center providing funds for research cores, pilot projects and enrichment. Dr. Williams serves as Director of the Cell Biology Core which provides facilities and advice to center researchers working with fluorescent probes. Dr. Williams is also the Associate Director of the Center.

NIH P60 DK 20572 (W. Herman, PI)

12/01/07-11/30/12

Michigan Diabetes Research and Training Center

Major Goals: Core Center providing funds for research cores, pilot projects and enrichment. Dr. Williams is Director of the Morphology and Image Analysis Core. He receives 10% salary from the grant but receives no direct support for his own research. The core includes facilities to Center researchers working with fluorescent probe to measure Ca^{2+} , pH, etc. and provides standard confocal and electron microscopy facilities for Center researchers.

T32 GM 08322 (JA Williams, PI)

07/01/05-06/30/10

NIH

Systems and Integrative Biology Training Grant; No salary or research support to Dr. Williams. This is a predoctoral training grant currently providing support to 9 trainees.