



**Cynthia M. Smas**

**Associate Professor of Biochemistry and Cancer Biology**

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**EDUCATION AND TRAINING:**

B.A. Biology, Boston University, Boston, MA, 1980

M.S. Biological Sciences, University of Massachusetts, Lowell, MA, 1985

Thesis title: "Genome Organization of Bovine Herpes Virus"

D.Sc. Nutritional Biochemistry, Harvard University, School of Public Health - Division of Biological Sciences, Boston, MA, 1994

Dissertation title: "Studies on Pref-1, a Novel Inhibitory Regulator of Adipogenesis"

**PRE AND POSTDOCTORAL FELLOWSHIP TRAINING:**

1987 - 1994 Predoctoral (Graduate Student)

Harvard University

School of Public Health

Department of Nutritional Sciences/Division of Biological Sciences

Area of training: Nutritional Biochemistry; Molecular Biology of Obesity and Adipocytes

Supported by NIH National Research Service Award (NRSA), 1988-1992

1994 - 2000 Postdoctoral Research Fellow

University of California, Berkeley, CA

Division of Nutritional Sciences and Toxicology

Area of training: Molecular Biology of Obesity and Adipocytes

**EMPLOYMENT:**

2008 - pres Associate Professor (tenure-track), Department of Biochemistry and Cancer Biology, University of Toledo College of Medicine, Toledo, OH

2007 - 2009 Cancer Biology Track Vice-Director, Cancer Biology Graduate Program Track, University of Toledo College of Medicine, Toledo, OH

2003 - pres Adjunct Faculty, Department of Nutrition Sciences, Bowling Green State University, Bowling Green, OH (Volunteer)

2000 - 2008 Assistant Professor (tenure-track), Department of Biochemistry and Cancer Biology (formerly Department of Biochemistry and Molecular Biology), University of Toledo College of Medicine (formerly Medical College of Ohio), Toledo, OH

1985 - 1987 Research Assistant at Harvard Medical School, Howard Hughes Medical Institute and Department of Neurogenetics, Boston, MA

1983 - 1985 Graduate Teaching Assistant and Masters Degree Candidate at the University of Massachusetts, Department of Biological Sciences, Lowell, MA

1980 - 1983 Laboratory Technician/Teaching Laboratory Manager at University of Massachusetts,  
Department of Clinical Laboratory Sciences, Lowell, MA

**AWARDS AND COMMENDATIONS:**

Nominee - Deans Award for Junior Faculty Teaching Excellence  
University of Toledo College of Medicine  
2005

Nominee - Deans Award for Basic Science Faculty Teaching Excellence  
University of Toledo College of Medicine  
2006

Nominee - Deans Award for Basic Science Faculty Teaching Excellence  
University of Toledo College of Medicine  
2010

**EDITORIAL BOARDS:**

American Journal of Physiology – Endocrinology and Metabolism  
Formal appointment to a 3 yr editorial board term to commence July 2011  
Currently *ad hoc* editorial board member

Adipocyte  
Appointed editorial board member May 2011; first issue of this new journal  
publishes in January 2012.

**TEACHING (Course directorships, formal lectures and small group formats)**

**Medical Student Teaching**

Course Name: Cellular and Molecular Biology (Block I)

Course Name: First Year Integrated Pathophysiology (PBL)

Course Name: Clinical Decision Making I

5-Year Curriculum Medical Science Integration Course

University of Toledo College of Medicine MedStart (Undergraduate)  
Integrated Pathophysiology Block

**Graduate Student Teaching**

Course Director and Lecturer: Methods in Biomedical Sciences (Ph.D program core curriculum)

Course Director and Instructor: Readings in Molecular and Cellular Biology

Systems Pathophysiology II

Advanced Topics in Cardiovascular & Metabolic Diseases

Molecular Basis of Disease

Grant Writing Workshop

## **MAJOR RESEARCH INTERESTS:**

### **Adipocyte Function and Obesity:**

Obesity is now at epidemic proportions and is closely linked to co-morbidities including heart disease and diabetes. There is no question that this is a significant health problem in this country. In order to better understand and treat obesity we are studying adipogenesis and preadipocyte/adipocyte function. We are identifying novel gene products that show adipose tissue specific expression patterns, hormonal regulation, and protein sequence elements indicative of important roles in preadipocyte or adipocyte function; we are characterizing their function in the pathogenesis of obesity. A particular interest here is novel secreted products of adipocytes, termed adipokines, in that their actions likely impact systemic physiology and as such have the potential to act as therapeutic targets in the fight against obesity and its co-morbidities. We are also interested in the proteins comprise and control the function of the adipocyte lipid droplet; we have published two manuscripts in the last few years on one such protein, Fat Specific Protein 27 (FSP27) also known as CIDE-C (Kim, J.Y., Lui, K., Zhou, S., Tillison, K., Wu, Y., and Smas, C.M. "Assessment of Fat Specific Protein 27 (FSP27) in the Adipocyte Lineage Suggests a Dual Role for FSP27 in Adipocyte Metabolism and Cell Death". *Am. J. Physiol. Endocrinol. Metab.*, 294:E654-E667, 2008 and Liu, K., Zhou, S., Kim, JY, Tillison, K., Majors, D., Rearick, D., Lee, JH, Fernandez-Boyanapalli, R.F., Barricklow, K., Houston, M.S., and Smas, C.M. "Functional Analysis of FSP27 Protein Regions for Lipid Droplet Localization, Caspase-Dependent Apoptosis, and Dimerization with CIDEA". *Am. J. Physiol. Endocrinol. Metab.*, 297:E1395-E13413, 2009.

To better study adipocytes, we have also invested effort in generation of new cell culture models. One of these ScAP23, was published in 2007 (Kim, J.Y., Wu, Y., and Smas, C.M. "Characterization of ScAP-23, a New Cell Line from Murine Subcutaneous Adipose Tissue, Identifies Genes for the Molecular Definition of Preadipocytes". *Physiol. Genomics*. 31:328-42, 2007). A manuscript on another novel cell culture model we developed, mBAP-9 (a model of brown adipocytes) is currently in preparation for publication (Kim, J.Y., Wu, Y., and Smas, C.M. "Novel Adipocyte-Enriched Genes Revealed by Characterization of mBAP-9, a New *in vitro* Brown Adipogenesis Model").

In addition, we aim to better understand the preadipocyte and the early stages of adipocyte lineage commitment, much of which still remains to be elucidated. In contrast to fat cells, studies of preadipocytes area largely un-mined research area. By better understanding this cell type we can potentially target obesity before its formation, at the preadipocyte stage. These studies of preadipocytes form the basis of our recently awarded NIH funding. Importantly, this recent funding was attained under the newly reorganized NIH grant format and the NIH grant peer review criteria which now stresses high impact research, defined by the NIH as the likelihood for the project to exert a sustained, powerful influence on the research field.

## **BIBLIOGRAPHY (Published works)**

### **Articles published in scientific journals - peer reviewed primary research articles**

1. Adler, G.K., Smas, C.M., and Majzoub, J.A. "Expression and Dexamethasone Regulation of the Human Corticotropin-Releasing Hormone Gene in a Mouse Anterior Pituitary Cell Line". *J. Biol. Chem.* 263:5846-5852, 1988.
2. Frim, D.M., Emanuel, R.L., Robinson, B.G., Smas, C.M., Adler, G.K., and Majzoub, J.A. "Characterization and Gestational Regulation of Corticotropin-Releasing Hormone Messenger RNA in Human Placenta". *J. Clin. Invest.* 82:287-292, 1988.
3. Gravallesse, E.M., Boothby, M.R., Smas, C.M., and Glimcher, L.H. "A Lipopolysaccharide-Induced DNA-binding Protein for a Class II Gene in B cells is Distinct from NF-kappa B". *Mol. Cell. Biol.* 9:3184-3192, 1989.
4. Adler, G.K., Smas, C.M., Fiandaca, M., Frim, D.M., and Majzoub, J.A. (1990). "Regulated Expression of the Human Corticotropin-Releasing Hormone Gene by Cyclic AMP". *Mol. Cell. Endocrinol.* 70:165-174.

5. Smas, C.M., and Sul, H.S. "Pref-1, a Protein Containing EGF-like Repeats, Inhibits Adipocyte Differentiation". *Cell* 73:725-734, 1993.
6. Smas, C.M., Green, D., and Sul, H.S. "Structural Characterization and Alternate Splicing of the Gene Encoding the Preadipocyte EGF-like Protein Pref-1". *Biochemistry* 33:9257-9265, 1994.
7. Smas, C.M., Chen, L., and Sul, H.S. "Cleavage of Membrane-Associated Pref-1 Generates a Soluble Inhibitor of Adipocyte Differentiation". *Mol. Cell. Biol.* 17:977-988, 1997.
8. Smas, C.M., Kachinskas, D., Liu, C., Xie, X., Dircks, L.K., and Sul, H.S. "Transcriptional Control of the Pref-1 Gene in 3T3-L1 Adipocyte Differentiation". Sequence Requirement for Differentiation-Dependent Suppression. *J. Biol. Chem.* 273:31751-31758, 1998.
9. Smas, C.M., Chen, L., Zhao, L., Latasa, M.J., and Sul, H.S. "Transcriptional Repression of Preadipocyte Factor-1 by Glucocorticoids Promotes 3T3-L1 Adipocyte Differentiation". *J. Biol. Chem.* 274:12632-12641, 1999.
10. Moon<sup>#</sup>, Y.S., Smas<sup>#</sup>, C. M., Lee<sup>#</sup>, K., Villena, J. A., Kim, K.H., Yun E.J., and Sul, H.S. "Mice Lacking Paternally Expressed Pref-1/Dlk1 Display Growth Retardation and Accelerated Adiposity". *Mol. Cell. Biol.* 22:5585-92, 2002. (<sup>#</sup>: equal first co-authorship)
11. Kim, J.Y., Tillison, K. and Smas, C.M. "Cloning, Expression and Differentiation- Dependent Regulation of SMAF1 in Adipogenesis". *Biochem. Biophys. Res. Commun.* 326:36-44, 2005.
12. Kim, J.Y., Tillison, K., Lee, J.H., Rearick, D.A., and Smas, C.M. "The Adipose Tissue Triglyceride Lipase ATGL/PNPLA2 is Downregulated by Insulin and TNF $\alpha$  in 3T3-L1 Adipocytes and is a Target for Transactivation by PPAR $\gamma$ ". *American J. Phys. Endo. Metabol.*, 291:E115-E127, 2006.
13. Kim, J.Y., Tillison, K.S., Zhou, S. Wu, Y., and Smas, C.M. "The Major Facilitator Superfamily Member Slc37a2 is a Novel Macrophage-Specific Gene Selectively Expressed in obese White Adipose Tissue". *Am. J. Physiol. Endocrinol. Metab.*, 293: E110—E120, 2007.
14. Kim, J.Y., Tillison, K.S., Zhou, S. Lee, J.H., and Smas, C.M. "Differentiation-Dependent Expression of Adhfe1 in Adipogenesis". *Arch. Biochem. Biophys.* 464:100-111, 2007.
15. Kim, J.Y., Wu, Y., and Smas, C.M. "Characterization of ScAP-23, a New Cell Line from Murine Subcutaneous Adipose Tissue, Identifies Genes for the Molecular Definition of Preadipocytes". *Physiol. Genomics.* 31:328-42, 2007.
16. Kim, J.Y., Lui, K., Zhou, S., Tillison, K., Wu, Y., and Smas, C.M. "Assessment of Fat Specific Protein 27 (FSP27) in the Adipocyte Lineage Suggests a Dual Role for FSP27 in Adipocyte Metabolism and Cell Death". *Am. J. Physiol. Endocrinol. Metab.*, 294:E654-E667, 2008.
17. \*Wu, Y., and Smas, C.M. "Wdm1-like, a New Adipokine with a Role in MMP-2 Activation". *Am. J. Physiol. Endocrinol. Metab.*, 295:E205-15, 2008.
18. \*Wu, Y., Kim, J.Y., Zhou, S., and Smas, C.M. "Differential Screening Identifies Transcripts with Depot-Dependent Expression in White Adipose Tissues". *BMC Genomics*, 9:397, 2008.
19. Wu, Y., and Smas, C.M. "Expression and Regulation of Transcript for the Novel Transmembrane Protein Tmem182 in the Adipocyte and Muscle Lineage". *BMC Res. Notes* 1: 85, 2008.
20. \*Liu, K., Zhou, S., Kim, JY, Tillison, K., Majors, D., Rearick, D., Lee, JH, Fernandez-Boyanapalli, R.F., Barricklow, K., Houston, M.S., and Smas, C.M. "Functional Analysis of FSP27 Protein Regions for Lipid

Droplet Localization, Caspase-Dependent Apoptosis, and Dimerization with CIDEA". *Am. J. Physiol. Endocrinol. Metab.*, 297:E1395-E13413, 2009.

21. Charkrabarti, P., English, T., Shi, J., Smas, C.M., and Kandror, K. "The mTOR Complex 1 Suppresses Lipolysis, Stimulates Lipogenesis and Promotes Fat Storage". *Diabetes*, 59:775-781, 2010.
22. \*Wu, Y., Zhou, S., and Smas, C.M. "Downregulated Expression of the Secreted Glycoprotein Follistatin-like 1 (Fstl1) is a Robust Hallmark of Preadipocyte to Adipocyte Conversion". *Mech. Dev.*, 127:183-202, 2010.
23. Wang, Y, Zhao, L., Smas, C.M., and Sul, H.S. "Pref-1 Interacts with Fibronectin to Inhibit Adipocyte Differentiation". *Mol. Cell. Biol.*, 30:3480-3492, 2010.
24. \*Lee, J.H., Zhou, S., and Smas, C.M. "Identification of RANBP16 and RANBP17 as Novel Interaction Partners for the bHLH Transcription Factor E12". *J. Cell. Biochem*, 11:195-206, 2010.

### **Articles published in scientific journals – peer reviewed review articles**

1. Sul, H.S., Smas, C.M., and Moustaid, N. "Positive and Negative Regulators of Adipocyte Differentiation". *J. Nutr. Biochem.* 4:554-562, 1993.
2. Smas, C.M., and Sul, H.S. "Control of Adipocyte Differentiation". *Biochem. J.* 309:697-710, 1995.
3. Smas, C.M., and Sul, H.S. "Characterization of Pref-1 and its Inhibitory Role in Adipocyte Differentiation". *Int. J. Obesity* 20:S65-S72, 1996.
4. Smas, C.M., and Sul, H.S. "Molecular Mechanisms of Adipocyte Differentiation and Inhibitory Action of Pref-1". *Crit. Rev. Eukaryotic Gene Expr.* 7:281-298, 1997.
5. Sul, H.S., Smas, C.M., Wang, D., Chen, L., and Fong, S. "Regulation of Fat Synthesis and Adipose Differentiation". *Prog. Nucleic Acid Res. and Mol. Biol.* 60:317-345, 1998.
6. Gregoire, F.M., Smas, C.M., and Sul, H.S. "Understanding Adipocyte Differentiation". *Physiol. Rev.* 78:783-809, 1998.
7. Sul, H.S., Smas, C.M., Mei, B., and Zhou, L. "Function of Pref-1 as an Inhibitor of Adipocyte Differentiation". *Int. J. Obes.* 24 Suppl 4:S15-9, 2000.
8. Wolf, G., and Smas, C.M. "Retinoic Acid Induces the Degradation of the Leukemogenic Protein Encoded by the Promyelocytic Leukemia Gene Fused to the Retinoic Acid Receptor Alpha Gene". *Nutr. Rev.* 58:211-214, 2000.

### **Chapters in books**

1. Sul, H.S., Moustaid, N., Sakamoto, K., Smas, C.M., Gekakis, N., and Jerkins, A. "Nutritional and Hormonal Regulation of Genes Encoding Enzymes Involved in Fat Synthesis". Book chapter in: *Nutrition and Gene Expression*,. Berdanier, J.L. and Hargrove, C.D. (eds.). CRC Press, Inc., Boca Raton, FL, 1993, pages 207-226.
2. Sul, H.S., Smas, C.M., Chen, L., Mei, B., and Zhao, L. "Pref-1, an Inhibitor of Adipogenesis". Book chapter in: *27th Steenbock Symposium: Adipocyte Biology and Hormone Signaling*, University of Wisconsin Press, WI, 2000, pages 185 - 199.
3. Smas, C.M. and Sul, H. S. "Control of Adipocyte Differentiation." Book chapter in: *Biochemical Journal Reviews*, Portland Press Ltd London, 1995, pages: 113-126.

## Published abstracts, preliminary communications, panel discussions

### Abstracts:

1. Adler, G.K, Smas C. M. and Majzoub, J. A. Expression and Dexamethasone Regulation of the Human Corticotropin-Releasing Hormone Gene in a Mouse Anterior Pituitary Cell Line Clin. Res. 35(3):A582, 1989.
2. Gravellese, E.M., Boothby, M.R., Smas C. and Glimcher, L. A Lipopolysaccharide-induced DNA-Binding Protein for Class-II Antigen Expression in B-Cells. Clin. Res. 37(2):A556, 1989.
3. Smas C.M. and Sul H.S. "cDNA Cloning of a Novel EGF-like Protein, Pref-1, which Inhibits Adipocyte Differentiation of 3T3-L1 cells". Presented at: *The 32<sup>nd</sup> Annual Meeting of the American Society for Cell Biology*; Denver CO November 15 - 19, 1992. Mol. Biol. Cell. 3:A237 1002, 1992.
4. Smas, C.M. and Sul H.S. "Pref-1, A Novel Member of the EGF-like Family of Proteins, Inhibits Adipocyte Differentiation". Presented at: *Keystone Symposium on the Adipose Cell*, January 14 - 21 1994; Park City UT. J. Cell. Biochem. 165 S18A, 1994.
5. Sul, H.S. Moustaid, N. Smas, C. Yet, SF, Beyer, R.S. and Jerkins, A. "Regulation of Gene Expression during Fat Synthesis and Adipocyte Differentiation". Presented at: *Keystone Symposium on the Adipose Cell*, January 14 - 21, 1994; Park City UT. J. Cell. Biochem. 153: S18A, 1994.
6. Smas, C.M. and Sul, H.S. "Pref-1, A Novel Member of the EGF-like Family of Proteins, Inhibits Adipocyte Differentiation." Presented at: 34th Annual Meeting of the American Society for Cell Biology, December 10 - 14, 1994 San Francisco, California, USA Mol. Biol. Cell. 5(SUPPL): 355A, 1994.
7. Smas, C.M. and Sul, H.S. "Pref-1, A Novel Member of the EGF-like Family of Proteins, Inhibits Adipocyte Differentiation." J. Cell. Biochem. Suppl. 18:165, 1994.
8. Moustaid, N. Smas, C. and Sul, H. S." Regulation of Gene Expression during Fat Synthesis and Adipocyte Differentiation". J. Cell. Biochem. Suppl. 18A:153, 1994.
9. Sul, H.S and Smas, C.M. "Pref-1, A Novel Member of the EGF-like Family of Proteins, Inhibits Adipocyte Differentiation." Presented at: International Symposium on Cellular and Molecular Biology of Adipose Cell Development and Growth, August 17 - 19, 1994 Ottawa, Ontario, Canada. Int. J. Obesity 20(S3):S123,1996.
10. Fong, S.Y., Smas, C.M. and Sul H.S. Regulation of pref-1 expression in 3T3-L1 cells. Presented at American Society for Biochemistry and Molecular Biology Annual Meeting, June 2 - 6, 1996; New Orleans LA. FASEB J. 10(6):1430,1996.
11. Smas, C.M. Chen, L. Zhao, L., Latasa, M.J., and Sul, H.S. "Transcriptional Repression of Preadipocyte Factor-1 by Glucocorticoids Promotes 3T3-L1 Adipocyte Differentiation", Presented at American Society for Biochemistry and Molecular Biology Annual Meeting, May 16-20, 1999; San Francisco CA. FASEB J. 13(7):A1460, 1999.
12. Kim, J. Y., Tillison, K.S. Lee, J. and Smas, C.M. "Characterization of mTTS\* a Novel Adipocyte-Enriched Insulin Target Gene". Presented at Federation of American Societies for Experimental Biology (FASEB) Annual Meeting, April 17 - 22, 2004; Washington D. C. FASEB J. 18(5) A877, 2004 (\*note: mTTS is identical with ATGL/PNPLA2).
13. Serneels, K. Kim J.Y., Tillison, K., Smas, C.M and Houston, M.S. "Apoptotic Activity of Fat-Specific Protein 27". Presented at Federation of American Societies for Experimental Biology (FASEB) Annual Meeting, April 17 - 22, 2004; Washington D. C. FASEB J. 18(5) A876, 2004.

14. Kim, JY; Tillison, KS; Smas, CM Cloning, "Expression and Differentiation-dependent Regulation of SMAF1 in Adipogenesis", FASEB JOURNAL 19(4) A72-A72, 2005.
15. Okeke, J., Zuniga, K., Meserve, L, Hentges D., Smas, C.M., and Houston, S. "Ellagic Acid Decreases Proliferation and IGFBP-2 in LNCaP Human Prostate Cancer Cells". Federation of American Societies for Experimental Biology (FASEB), American Society of Nutrition, 2007 Meeting, April 28 - May 2, Washington D. C. FASEB J. 21(5) A359, 2007.
16. Liu, K., Zhou, S. Tillison, K. and Smas C.M. "Dual Functions of FSP27/CIDEA in Lipid Droplet Formation and Apoptosis" 49<sup>th</sup> Annual Meeting of the American Society for Cell Biology, San Diego, CA, December 5 - 9, 2009.
17. Liu, K. Zhou, S. Kim, J.Y., Tillison, K., Majors, D. Fernandez-Boyanapalli, R.F. and Smas, C.M. "Functional Analysis of FSP27 Protein regions for Lipid Droplet Localization, Caspase-Dependent Apoptosis, and Dimerization with CIDEA", Abstract at Keystone Symposium on Adipocyte Biology, Keystone CO, January 24 - 29, 2010.