

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 Khalil N. Bitar		POSITION TITLE Research Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) kbitar			
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
Universite De Provence, Marseilles, France	M.Sc.	1973	Neurophysiology
American University of Beirut, Lebanon	Ph.D.	1976	Physiology

A. POSITIONS AND HONORS

PROFESSIONAL EXPERIENCE

- 1973-74 Instructor in Physiology, Institute of Neurophysiology, Universite de Provence, Marseilles, France
- 1974-76 Instructor in Physiology, American University of Beirut, Lebanon
- 1976-78 Research Fellow, Division of Gastroenterology, Medical College of Virginia
- 1978-80 Instructor in Physiology, Department of Physiology and Research Associate, Department of Medicine, Medical College of Virginia
- 1980-84 Assistant Professor of Physiology, Medical College of Virginia, Richmond, Virginia
- 1985 Associate Professor of Physiology, Medical College of Virginia, Richmond, Virginia
- 1985-88 Associate Professor, Human Function, Physiology, Arabian Gulf University Bahrain
- 1989-92 Associate Research Scientist, University of Michigan Health System, Ann Arbor, Michigan
- 1990-00 Director of Gastroenterology Research, Department of Pediatrics, University of Michigan Health System, Ann Arbor, Michigan
- 1992-present Research Professor, Senior Research Scientist, Research Scientist, University of Michigan Health System, Ann Arbor, Michigan

HONORS AND AWARDS

- 2003 Research Scientist Achievement Award, University of Michigan
- 2006 Inducted as AGA Fellow, American Gastroenterological Association

B. SELECTED PEER-REVIEWED PUBLICATIONS - FROM MORE THAN 80 PUBLICATIONS

1. Bitar KN, Zhu XX. Expression of Bombesin Receptor Subtypes and Their Differential Regulation of Colonic Smooth Muscle Contraction. *Gastroenterology*, 105:1672-1680, 1993. PMID: 8253343
2. Yamada H, Strahler J, Welsh M, Bitar KN. Activation of MAP Kinase and Interaction with HSP27 Bombesin Induced Contraction of Gastrointestinal Smooth Muscle. *Am. J. Physiol.*, 269:G683-G691, 1995. PMID: 7491959
3. Hillemeier C, Rhim BY, Biancani P, Bitar KN. Protein Kinase C Mediates Spontaneous Tone in the Cat Lower Esophageal Sphincter. *J. Pharmacol. Exper. Therap.*, 277:144-149, 1996. PMID: 8613911
4. Sbrissa D, Yamada H, Hajra A, Bitar KN. Bombesin-Stimulated Ceramide Production and MAP Kinase Activation in Isolated Smooth Muscle Cells from Rabbit Colon. *Am. J. Physiol.*, 272:G1615-G1625, 1997. PMID: 9227500
5. Wang P, Bitar KN. Rho A Regulates Sustained Smooth Muscle Contraction through Cytoskeletal Reorganization of HSP27. *Am. J. Physiol.*, 275:G1454-G1462, 1998. PMID: 9843784
6. Xuehui S, Wang P, Ibitayo AI, Bitar KN. Differential Activation of Phosphoinositide 3-Kinase (PI3K) by Endothelin and Ceramide in Colonic Smooth Muscle Cells, *Am. J. Physiol.*, 276:G853-G861, 1999. PMID: 10198327

7. Ibitayo AI, Sladick J, Tuteja S, Louis-Jacques O, Yamada H, Groblewski G, Welsh M, Bitar KN. HSP27 in signal transduction and association with contractile proteins in smooth muscle cells. *Am. J. Physiol.* 277:G445-G454, 1999. PMID: 10444459
8. Bitar KN, Ibitayo AI, Patil SB. HSP27 modulates agonist-induced association of translocated RhoA and PKC- α in muscle cells of the colon. *J. Appl Physiol* 92:41-49, 2002. PMID: 11744641
9. Bitar KN. HSP27 phosphorylation and interaction with actin-myosin in smooth muscle contraction. *Am. J. Physiol* 282:G894-G903, 2002. PMID: 11960785
10. Bitar KN. Aging and neural control of the GI tract V. Aging and gastrointestinal smooth muscle. From signal transduction to contractile proteins. *Am. J. Physiol.* 284:G1-G7, 2003. PMID: 12488230
11. Bitar KN. Overview of GI Smooth Muscle Function: From Signaling to Contractile Proteins. *Am. J. Med.* 115(3A):15S-23S, 2003. PMID: 12928070
12. Patil SB, Pawar MD, Bitar KN. Phosphorylated HSP27 essential for acetylcholine-induced association of RhoA with PKC α . *Am. J. Physiol. Gastrointest. Liver Physiol.* 286(4):G635-44, 2004. PMID: 14592945
13. Xin X, Hou YT, Li L, Schmiedlin-Ren P, Christman GM, Cheng HL, Bitar KN, Zimmermann EM. IGF-I increases IGFBP-5 and collagen alpha1(I) mRNAs by the MAPK pathway in rat intestinal smooth muscle cells. *Am. J. Physiol. Gastrointest Liver Physiol.* 286(5):G777-83, 2004. PMID: 15068962
14. Patil SB, Pawar MD, Bitar KN. Direct association and translocation of PKC α with calponin. *Am. J. Physiol Gastrointest Liver Physiol.* 286(6):G954-63, 2004. PMID: 14726309
15. Somara S, Bitar KN. Tropomyosin interacts with phosphorylated HSP27 upon agonist induced contraction in smooth muscle. *Am. J. Physiol. Cell Physiol.* 286(6):C1290-301, 2004. PMID: 14749215
16. Patil SB, Tsunoda Y, Pawar MD, Bitar KN. Translocation and association of ROCK II with RhoA and HSP27 during contraction of rabbit colon smooth muscle cells. *Biochem Biophys Res Commun.* 319(1):95-102, 2004. PMID: 15158447
17. Bitar KN, Patil S. Aging and gastrointestinal smooth muscle. *Mech Ageing Dev.* 125: 907-910, 2004. PMID: 15563937
18. Somara S, Pang H, Bitar KN. Agonist-Induced Association of Tropomyosin with Protein Kinase C α in colonic smooth muscle. *Am J Physiol, Gastrointest Liver Physiol.* 288(2):G268-G276, 2005. PMID: 15486343
19. Hecker L, Baar K, Dennis R, Bitar KN. Development of a 3-Dimensional Physiological Model of the Internal Anal Sphincter Bioengineered *in-vitro* from Isolated Smooth Muscle Cell. *Am J Physiol, Gastrointest Liver Physiol.* 289 (2):G188-96, 2005. PMID: 15774939
20. Bitar KN. Aging and GI Smooth Muscle - Fecal Incontinence: Is Bioengineering an Option? *Exp Gerontol.* 40 (8-9):643-649, 2005. PMID: 15970414
21. Pang H, Bitar KN. Direct association of RhoA with Specific Domains of PKC α ., *Am. J. Physiol, Cell Physiol.* 289 (4):C982-93, 2005. PMID: 15930143
22. Patil SB, Bitar KN. RhoA and PKC α mediated phosphorylation of MYPT and its association with HSP27 in colonic smooth muscle cells. *Am. J. Physiol, Gastrointest Liver Physiol.* 290: G83-G95, 2006. PMID: 16179599
23. Somara S and Bitar, KN. Phosphorylated HSP27 modulates the association of phosphorylated caldesmon with tropomyosin in colonic smooth muscle. *Am J Physiol; Gastrointest Liver Physiol.* *Am J Physiol Gastrointest Liver Physiol* 291: G630-G639, 2006. PMID16627824
24. Goldsmith AM, Bentley JK, Zhou L, Jia Y, Bitar KN, Fingar DC, and Hershenson MB. TGF β Induces Airway Smooth Muscle Hypertrophy: Role of Translational Control. *Am J Respir Cell Mol Biol,* 2006. 34(2): p. 247-54. PMID: 16239645
25. Somara S, Bitar KN. Phosphorylated HSP27 modulates the association of phosphorylated caldesmon with tropomyosin in colonic smooth muscle. *Am J Physiol; Gastrointest Liver Physiol.* 291: G630-G639, 2006. PMID: 16627824
26. Somara S, Gilmont RR, Martens JR and Bitar KN. Ectopic Expression of Caveolin-1 Restores Physiological Contractile Response of Aged Colonic Smooth Muscle Accepted for publication, *Am J Physiol; [in press] Gastrointest Liver Physiol.* 2007. PMID: 17431219
27. Huebner M, Margulies RU, Fenner DE, Ashton-Miller JA, Bitar KN, DeLancey JO. Age effects on internal anal sphincter thickness and diameter in nulliparous females. *Dis Colon Rectum.* 2007 Sep;50(9):1405-11. PMID: 17665265

28. Deng H, Dokshin GA, Lei J, Goldsmith AM, Bitar KN, Fingar DC, Hershenson MB, Bentley JK. Inhibition of glycogen synthase kinase-3beta is sufficient for airway smooth muscle hypertrophy. *J Biol Chem.* 2008 Apr 11;283(15):10198-207. Epub 2008 Feb 5. PMID: 18252708
29. Gilmont RR, Somara S, Bitar KN. VIP induces PKA-mediated rapid and sustained phosphorylation of HSP20. *Biochem Biophys Res Commun.* 2008 Oct 31;375(4):552-6. Epub 2008 Aug 24. PMID: 18725196
30. Bentley JK, Deng H, Linn MJ, Lei J, Dokshin GA, Fingar DC, Bitar KN, Henderson Jr WR, Hershenson MB. Airway smooth muscle hyperplasia and hypertrophy correlate with glycogen synthase kinase-3{beta} phosphorylation in a mouse model of asthma. *Am J Physiol Lung Cell Mol Physiol.* 2008 Nov 14. PMID: 19011050
31. Somara S, Bitar KN. Direct association of calponin with specific domains of PKC-alpha. *Am J Physiol Gastrointest Liver Physiol.* 2008 Dec; 295(6):G1246-54. Epub 2008 Oct 23. PMID: 18948438
32. Somara S, Gilmont R, Dennis R and Bitar KN Bioengineered Internal Anal Sphincter Derived from Isolated Human Internal Anal Sphincter Smooth Muscle Cells *Gastroenterology.* March 2009 {Epub ahead of print} PMID 19328796
33. Raghavan S, Lam MT, Foster L, Gilmont RR, Somara S, Takayama S and Bitar KN. Bioengineered three-dimensional physiological model of colonic longitudinal smooth muscle in vitro. *Submitted for publication. AJP GI. Tissue Engineering.*
34. Deng H, Hershenson MB, Lei J, Bitar KN, Fingar DC, Solway J, Bentley JK. p70 Ribosomal S6 Kinase is Required for Airway Smooth Muscle Cell Size Enlargement but not Increased Contactile Protein Expression. *Am J Respir Cell Mol Biol.* 2009 Jul 31. PMID: 19648476
35. Somara S and Bitar KN. Age-related Decline in Myosin Phosphatase-Mediated Maintenance of Myosin Light Chain Phosphorylation can be restored by Phosphorylated HSP27 in Colonic Smooth Muscle. *Submitted for publication. Am J Physiol Gastrointest Liver Physiol*
36. Somara S, Gilmont RR, Bitar KN. Role of thin-filament regulatory proteins in relaxation of colonic smooth muscle contraction. *Am J Physiol Gastrointest Liver Physiol.* 2009 Sep 3. [Epub ahead of print] PMID: 19729493

C. Research Support

Ongoing Research Support

Supplemental Bitar (PI)
NIH/NIDDK

10/01/09-09/30/2011

Restoration of Fecal Continence in Aging IAS s

The goal is to restore the motor function in aging Internal Anal Sphincter. The new biomedical engineering techniques will be used.

Role: Principal Investigator

1 R01 HL079339-01A1 Hershenson (PI)
NIH

07/01/06-06/30/11

Mechanisms of Airway Smooth Muscle Hypertrophy

The major goal of this project is to determine the roles of translational and cell cycle control in the development of human airway smooth muscle hypertrophy, examine the signaling pathways regulating cap-independent protein synthesis in human airway smooth muscle

Role: Co-PI

1R01 DK071614-02 Bitar (PI)
NIH/NIDDK

02/01/08-1/31/13

Restoration of Fecal Continence in Aging IAS

The major goals of this project are to restore the motor function in aging Internal Anal Sphincter. The new biomedical engineering techniques will be used.

Role: Principle Investigator

DK42876-15 Bitar (PI)
NIH/NIDDK

05/01/09-04/30/12

Myogenic Control Mechanisms of Circular Muscle of the Rectosigmoid Colon

The major goals of this project are to study the signal transduction pathways mediating PKC sustained smooth muscle contraction of the rectosigmoid colon.

Role: Principle Investigator

2 R01 DK071614 Bitar (PI)

9/15/09-8/31/10

NIH/NIDDK – Administrative Supplement

Restoration of Fecal Continence in Aging IAS

The goal is to restore the motor function in aging Internal Anal Sphincter. The new biomedical engineering techniques will be used.

Role: Principle Investigator

Completed Research Support

SCOR P50 HD044406 (DeLancey)

09/25/02-08/31/07

NIH

Office of Research of Women's Health, Specialized Center of Research (SCOR) on Sex and Gender Factors affecting Women's Health

Birth, muscle injury and pelvic floor dysfunction

The major goals of this project are to seek to improve care for women who suffer from urinary incontinence and pelvic organ prolapse that arise as consequences of vaginal birth and to gain insights that can be used to better treat and prevent these common and debilitating conditions.

Role: Co-Investigator

1 R21 DK075413-01A1 (Teitelbaum)

04/01/07-03/31/09

NIH/NIDDK

Enterogenesis with the Use of an Implanted Mechanotransduction Device

The major goal of this project are to seek the lengthening of the small intestine - and provide substantially more bowel to enhance adaptation in Short bowel syndrome (SBS)

Role: Co-Investigator