

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.  
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Nigel Bunnett, Ph.D.		POSITION TITLE Professor of Surgery and Physiology, Vice Chair of Surgery, Director UCSF Center for the Neurobiology of Digestive Disease	
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
University of Leeds, England	B.Sc. First	1978	Animal Physiol.
University of Cambridge, England	Ph.D.	1981	Physiology
University of California, Los Angeles	Post-doc	1982-83	Physiology
University of Leeds, England	Post-doc	1983-85	Physiology
University of Leeds, England	B.Sc. First	1978	Animal Physiol.

**NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.**

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

1985 - 1986: Senior Scientific Officer, Physiology Division, Rowett Research Institute, Aberdeen, Scotland, UK.

1986 - 1987: Assistant Research Professor, Departments of Surgery and Biochemistry, University of Washington.

1987 - 1993: Assistant Professor, Departments of Surgery and Physiology, UCSF.

1993 - 1997: Associate Professor, Departments of Surgery and Physiology, UCSF.

1997 - present: Professor Departments of Surgery and Physiology.

2002 - present: Vice Chair of Surgery, Director UCSF Center for the Neurobiology of Digestive Disease.

**The University of Leeds:**

1. Crabtree Prize, July 1976.

2. Two prizes from the Flour Advisory Bureau, July 1977.

3. Seton prize, July 1978.

4. British Oil and Cake Prize, July 1978.

5. Medal for the Best Student in Agricultural Sciences, July 1978.

**The University of California, San Francisco:**

1. Nominated for award in "Excellence in Small Group Instruction", 1991, 1992.

2. Nominated for award in "Outstanding Lecture Series", 1992, 1994, 1996, 1997, 1998.

3. Nominated for Kaiser Award for "Excellence in Teaching", 1994, 2002.

4. Nominated for "Major Contribution to Teaching", 1994, 1996, 1997, 1998.

5. Recipient of award for "Major Contribution to Teaching", 1995.

**Other:**

1. Award for best paper in Journal of Gastroenterology, 1995

2. Editor: British Journal of Pharmacology

3. The Novartis Neurogastroenterology Award, 1999

4. Intestinal Disease Research Award, Calgary University, 2000

5. NIH Merit Award, 2000-2008

6. Grant from RW Johnson Focused Giving Program, 2000

7. Janssen Award for Research in Gastroenterology, 2001

8. Victor Mutt Medal for Research In Regulatory Peptides, 2002.

**B. Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation. (from ~160 papers and 30 chapters and reviews)

- Bowden, J. J., Garland, A. M., Baluk, P., Lefevre, P., Grady, E. F., Vigna, S. R., **Bunnett, N. W.** and McDonald, D. M. Direct observation of substance P-induced internalization of neurokinin 1 (NK1) receptors at sites of inflammation. Proc Natl Acad Sci U S A 91: 8964-8968, 1994.
- Bohm, S. K., Khitin, L. M., Grady, E. F., Aponte, G., Payan, D. G. and **Bunnett, N. W.** Mechanisms of desensitization and resensitization of proteinase-activated receptor-2. J Biol Chem 271: 22003-22016, 1996.
- Sternini, C., Spann, M., Anton, B., Keith, D. E., Jr., **Bunnett, N.**, von Zastrow, M., Evans, C., Brecha, N. Agonist-selective endocytosis of mu opioid receptor by neurons in vivo. Proc Natl Acad Sci U S A 93: 9241-9246, 1996.
- Bohm, S. K., Kong, W., Bromme, D., Smeekens, S. P., anderson, D. C., Connolly, A., Kahn, M., Nelken, N. A., Coughlin, S. R., Payan, D. G. and **Bunnett, N. W.** Molecular cloning, expression and potential functions of the human proteinase-activated receptor-2. Biochem J 314 ( Pt 3): 1009-1016, 1996.

5. Corvera, C. U., Dery, O., McConalogue, K., Bohm, S. K., Khitin, L. M., Caughey, G. H., Payan, D. G. and **Bunnett, N. W.** Mast cell tryptase regulates rat colonic myocytes through proteinase-activated receptor 2. J Clin Invest 100: 1383-1393, 1997.
6. Kong, W., McConalogue, K., Khitin, L. M., Hollenberg, M. D., Payan, D. G., Bohm, S. K. and **Bunnett, N. W.** Luminal trypsin may regulate enterocytes through proteinase-activated receptor 2. Proc Natl Acad Sci 94: 8884-8889, 1997.
7. Lu, B., Figini, M., Emanuelli, C., Geppetti, P., Grady, E. F., Gerard, N. P., Ansell, J., Payan, D. G., Gerard, C., **Bunnett, N.** The control of microvascular permeability and blood pressure by neutral endopeptidase. Nat Med 3: 904-907, 1997.
8. Bertog, M., Letz, B., Kong, W., Steinhoff, M., Higgins, M. A., Bielfeld-Ackermann, A., Fromter, E., **Bunnett, N. W.** and Korbmacher, C. Basolateral proteinase-activated receptor (PAR-2) induces chloride secretion in M-1 mouse renal cortical collecting duct cells. J Physiol 521 Pt 1: 3-17, 1999.
9. Sturiale, S., Barbara, G., Qiu, B., Figini, M., Geppetti, P., Gerard, N., Gerard, C., Grady, E. F., **Bunnett, N. W.** and Collins, S. M. Neutral endopeptidase (EC 3.4.24.11) terminates colitis by degrading substance P. Proc Natl Acad Sci U S A 96: 11653-11658, 1999.
10. Dery, O., Thoma, M. S., Wong, H., Grady, E. F. and **Bunnett, N. W.** Trafficking of proteinase-activated receptor-2 and beta-arrestin-1 tagged with green fluorescent protein. beta-Arrestin-dependent endocytosis of a proteinase receptor. J Biol Chem 274: 18524-18535, 1999.
11. Nguyen, T. D., Moody, M. W., Steinhoff, M., Okolo, C., Koh, D. S., **Bunnett, N. W.** Trypsin activates pancreatic duct epithelial cell ion channels through proteinase-activated receptor-2. J Clin Invest 103: 261-269, 1999.
12. DeFea, K. A., Vaughn, Z. D., O'Bryan, E. M., Nishijima, D., Dery, O. and **Bunnett, N. W.** The proliferative and antiapoptotic effects of substance P are facilitated by formation of a beta-arrestin-dependent scaffolding complex. Proc Natl Acad Sci U S A 97: 11086-11091, 2000.
13. DeFea, K. A., Zalevsky, J., Thoma, M. S., Dery, O., Mullins, R. D. and **Bunnett, N. W.** beta-arrestin-dependent endocytosis of proteinase-activated receptor 2 is required for intracellular targeting of activated ERK1/2. J Cell Biol 148: 1267-1281, 2000.
14. Steinhoff, M., Vergnolle, N., Young, S. H., Tognetto, M., Amadesi, S., Ennes, H. S., Trevisani, M., Hollenberg, M. D., Wallace, J. L., Caughey, G. H., Mitchell, S. E., Williams, L. M., Geppetti, P., Mayer, E. A., **Bunnett, N. W.** Agonists of proteinase-activated receptor 2 induce inflammation by a neurogenic mechanism. Nat Med 6: 151-158, 2000.
15. de Garavilla, L., Vergnolle, N., Young, S. H., Ennes, H., Steinhoff, M., Ossovskaya, V. S., D'Andrea, M. R., Mayer, E. A., Wallace, J. L., Hollenberg, M. D., andrade-Gordon, P., **Bunnett, N. W.** Agonists of PAR1 induce plasma extravasation by a neurogenic mechanism. Br J Pharmacol 133: 975-987, 2001.
16. Vergnolle, N., **Bunnett, N. W.**, Sharkey, K. A., Brussee, V., Compton, S. J., Grady, E. F., Cirino, G., Gerard, N., Basbaum, A. I., andrade-Gordon, P., Hollenberg, M. D. and Wallace, J. L. Proteinase-activated receptor-2 and hyperalgesia: A novel pain pathway. Nat Med 7: 821-826, 2001.
17. Cenac, N., Coelho, A. M., Nguyen, C., Compton, S., andrade-Gordon, P., MacNaughton, W. K., Wallace, J. L., Hollenberg, M. D., **Bunnett, N. W.**, Garcia-Villar, R., Bueno, L. and Vergnolle, N. Induction of intestinal inflammation in mouse by activation of proteinase-activated receptor-2. Am J Pathol 161: 1903-1915, 2002.
18. Schmidlin, F., Amadesi, S., Dabbagh, K., Lewis, D. E., Knott, P., **Bunnett, N. W.**, Gater, P. R., Geppetti, P., Bertrand, C. and Stevens, M. E. Protease-activated receptor 2 mediates eosinophil infiltration and hyperreactivity in allergic inflammation of the airway. J Immunol 169: 5315-5321, 2002.
19. Schmidlin, F., Dery, O., **Bunnett, N. W.** and Grady, E. F. Heterologous regulation of trafficking and signaling of G protein-coupled receptors: beta-arrestin-dependent interactions between neurokinin receptors. Proc Natl Acad Sci 99: 3324-3329, 2002.
20. Cuffe, J. E., Bertog, M., Velazquez-Rocha, S., Dery, O., **Bunnett, N.**, Korbmacher, C. Basolateral PAR-2 receptors mediate KCl secretion and inhibition of Na<sup>+</sup> absorption in mouse colon. J Physiol 539: 209-222, 2002.
21. Reed, D.E., Barajas-Lopez, C., Cottrell, G., Velazquez-Rocha, S., Dery, O., Grady, E.F., **Bunnett, N.W.** and Vanner, S.J. Mast cell tryptase and proteinase-activated receptor 2 induce hyperexcitability of guinea-pig submucosal neurons. J Physiol 547: 531-542, 2003.
22. Cenac, N., Garcia-Villar, R., Ferrier, L., Larauche, M., Vergnolle, N., **Bunnett, N.W.**, Coelho, A.M., Fioramonti, J. and Bueno, L. Proteinase-Activated Receptor-2-Induced Colonic Inflammation in Mice: Possible Involvement of Afferent Neurons, Nitric Oxide, and Paracellular Permeability. J Immunol 170: 4296-4300, 2003.
23. Roosterman, D., Schmidlin, F. and **Bunnett, N.W.** Rab5a and rab11a mediate agonist-induced trafficking of protease-activated receptor 2. Am J Physiol Cell Physiol 284: C1319-1329, 2003.
24. Kirkup, A.J., Jiang, W., **Bunnett, N.W.** and Grundy, D. Stimulation of the proteinase-activated receptor 2 excites jejunal afferent nerves in anaesthetized rats. J Physiol, 2003.
25. Cottrell, G., Amadesi, S., Grady, E.F. and **Bunnett, N.W.** Trypsin IV: A novel agonist of protease-activated receptors 2 and 4. J Biol Chem. In press, 2003.
26. Ossovasaka, V., **Bunnett, N.W.** Protease-activated receptors: contribution to physiology and disease. Ann Rev Physiol. In press, 2003.

**C. Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

#### **Proteinase-activated Receptors in the Peripheral Nervous System**

Principal Investigator: Nigel Bunnett

Agency: NIH/NIDDK

Type RO1 (DK57840, years 01-05)

Period: 07/01/00-06/30/05

To determine how proteases from regulate spinal primary afferent and enteric neurons and thereby induce inflammation and pain.

#### **Regulation of Cellular Responses to Neuropeptides**

Principal Investigator: Nigel Bunnett

Agency: NIH/NIDDK

Type: RO1 (DK39957, years 13-18)

Period: 07/01/00 - 06/30/08. Merit Award

To examine the pathway, mechanism and importance of endocytosis and trafficking of the substance P receptor to mitogenic signaling, desensitization and resensitization.

#### **Regulation of Signaling by Cell-surface Proteolysis**

Principal Investigator: Nigel Bunnett

Agency: NIH/NIDDK

Type: R01 (DK43207, years 04-08)

Period: 6/1/97-4/30/03. Renewal submitted 11/01/03

To investigate the mechanisms by which proteases regulate cellular functions by cleaving and activating proteinase-activated receptors.

#### **Training Grant in Gastrointestinal Surgery**

Principal Investigator: Nigel Bunnett

Agency: NIH/NIDDK

Type: T32 (years 10-15)

Period: 6/01/04-5/31/09

To provide surgery residents with two years of research training in basic gastrointestinal research.

#### **Proteinase-activated Receptors and Inflammation**

Principal Investigator: Nigel Bunnett

Agency: R.W. Johnson Focused Giving Program

Period: 2000-2003

To evaluate the role of proteases and their receptors in inflammation and pain

#### **Neurogenic Mechanisms of Intestinal Inflammation**

Principal Investigator: Eileen Grady

Co-investigator: Nigel Bunnett

Agency: NIH/NIDDK

Type: R01 (DK52388, years 04-09).

Period: 6/1/02-4/30/07

To investigate signaling by substance P, calcitonin gene related peptide and their receptors in intestinal inflammation.

#### **Neural Regulation of Pancreatic Function**

Principal Investigator: Kimberley Kirkwood

Co-investigator: Nigel Bunnett

Agency NIH/NIDDK

Type: R29 (DK46285, years 01-05)

Period: 08/1/98 - 04/30/03

To examine the role of sensory nerves, tachykinins and neurokinin receptors in pancreatic inflammation.