## **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	POSITION TITLE
Ben M. Dunn	Distinguished Professor
eRA COMMONS USER NAME BENDUNN	

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
Univ. of Delaware (Newark, Del.) Univ. of California at Santa Barbara Lab. of Chemical Biology, NIH (Bethesda, Md.)	B.S. Ph.D. Postdoc.	1967 1971 1971-73	Chemistry Bioorganic Chemistry Protein Chem./Enzymol.

#### **Positions and Honors**

Staff Fellow, Laboratory of Chemical Biology, NIAMDD, 1973-1974.

<u>Assistant Professor</u> of Biochem. and Molec. Biol., Univ. of Florida, Sept. 1974-1980.

<u>Associate Professor</u> of Biochem. and Molec. Biol., Univ. of Florida, 1980-1986.

On leave, Jan. 1981 to Jan. 1982; Visiting Scholar at Univ. of Calif. Santa Cruz.

<u>Professor</u> of Biochemistry and Molecular Biology, University of Florida, 1986-1998.

<u>Distinguished Prof.</u> of Biochem. and Molec. Biol., Univ. of Florida, 1998-present.

Univ. of Florida Research Foundation Professor, 1999-2001.

#### Awards:

NIH Pre-doctoral Fellowship, 1968-1971; NIH Postdoctoral Fellowship, 1971-1973; NIH Research Career Development Award, 1977-1982; American Men and Women of Science; University of Wales Visiting Fellowship to Commemorate the 50<sup>th</sup> Anniversary of the British Council, July, 1985; Univ. Fl.Chapter of Sigma Xi, University of Florida Faculty Research Award, April 12, 1989; Univ. Fl. College of Medicine, Faculty Research Prize in Basic Science, 1994; Univ. Fl. Professorial Excellence Program Award, Dec.1996; Univ. Fl. Research Foundation Professorship, 1999-2001.

## Memberships:

American Chemical Society; American Society of Biological Chemists; Biophysical Society; The Protein Society; American Peptide Society (Councilor, 2002-06); International Proteolysis Society (Council Member, 2001-05; Secretary, 2001-03; President, 2003-05)

### Committees:

Organizing Committee: 7th Enzyme Mechanisms Conference (Jan. 1981) NIH Physiological Chemistry Study Section, Ad Hoc Review, March 19, 1981; Ad Hoc Review, Feb. 24, 1984.

NIH Bio-organic and Natural Products Chem. Study Section; Ad Hoc Rev., Feb. 1989.
NIH NIGMS Special Study Section (AIDS-Related Grants) Mar. 21-23, 1990.
NIH NIGMS Prog. Proj. Reverse Site Visit Panel, June 24-26, 1990.
NIH Biochem. Study Section, Ad Hoc, Oct. 1989; reg. member, Oct. 1990-June 1994.
NIH/NIAID Special Review Panel. Ad Hoc. Prog. 24/4/1000 prog. member, Oct. 1998.

NIH NIAID AAR3/ADDT Panel, Ad Hoc Rev., 3/1/1999; reg. member, Oct. 1999-June 2003; Chair, Nov. 2003 - July 2004. NSF Graduate Fellowship Review Panel – Biochem., Biophys., Molec. Biol.,

Feb. 12-14, 1985; Feb. 11-13, '86; Feb 9-13, '87; Feb. 8-11, '88; (Panel chair, 1987-

Lead Organizer: Aspartic Proteinase Conference, (Sept. 23-28, 1990);

Vice-Chair, Gordon Research Conf. on Proteolytic Enzymes and Their Inhibitors, June 1992; Chair, June 1994.

PHS 398/2590 (Rev. 05/01) Number pages consecutively at the bottom throughout the application. Do not use suffixes such as 3a, 3b. Program Advisor: 7th Aspartic Proteinase Conf., Gifu, Sept. 1993; Banff, Oct. 1996; 8<sup>th</sup> Aspartic Proteinase Conf., Madeira, Portugal, Sept. 1999. Organizer, 2<sup>nd</sup> Int'l. Conf. on Protease Inhibitors, Dec. 3-6, 1999, Gainesville, FL; Organizing Committee, Cold Spring Harbor Conference on Biology of Proteolysis, May 2001; 3rd International Proteolysis Society Meeting, Nov. 2003; Nagoya, Japan

#### **Editorial Duties:**

Editor-in-Chief, Protein and Peptide Letters, 1994-present. Co-Editor, Current Protocols in Protein Science, 1994-present; Co-Editor, Letters in Peptide Science, 1994-2005. Editorial Board, *Journal of Peptide Research*, 1996-1999. Editor-in-Chief, *Current Protein and Peptide Science*, 1999-present.

# B. Selected, peer-reviewed publications (in chronological order, from a total of 188)

- Wlodawer A, Gustchina A, Reshetnikova L, Lubkowski J, Zdanov A, Hui KY, Angleton EL, Farmerie WG, Goodenow MM, Bhatt D, Zhang L, Dunn BM. Structure of an inhibitor complex of the protease from feline immunodeficiency virus. Nature Structural Biology 1995;2480-488.
- Powell DJ, Bur D, Wlodawer A, Gustchina A, Payne SL, Dunn BM, Kay J. Expression, characterization and mutagenesis of the aspartic proteinase from equine infectious anaemia virus. Eur J Biochem 1996;241:664-674.
- Wilson SI, Phylip LH, Mills JS, Bur D, Gulnik S, Dunn BM, Kay J. Escape mutants of HIV-1 proteinase: enzymic efficiency and susceptibility to inhibition. Biochem Biophys Acta 1996;1339:113-125.
- Kervinen J, Lubkowski J, Zdanov A, Bhatt D, Dunn BM, Hui KY, Powell DJ, Kay J, Wlodawer A, Gustchina A. Toward a universal inhibitor of retroviral proteases: comparative analysis of the interactions of LP-130 complexed with proteases from HIV-1, FIV, and EIAV. Protein Science 1998;7:2314-2323.
- Dunn BM, Pennington MW, Frase DC, Nash K. Comparison of inhibitor binding to FIV and HIV proteases: structure-based drug design and the resistance problem. Biopolymers (Peptide Science) 1999;51:69-77.
- Perez EE, Rose SL, Peyser B, Lamers SL, Burkhardt B, Dunn BM, Hutson AD, Sleasman JW, and Goodenow MM. Human immunodeficiency virus type 1 protease genotype predicts immune and viral response to combination therapy with protease inhibitors (PIs) in PI-naive patients. J Infec Dis 2001;183:579-88.
- Dunn BM. Anatomy and pathology of HIV-1 peptidase. In: Hooper NM, ed. Essays in Biochemistry, Volume 38: Proteases in Biology and Medicine. London: Portland Press;2002;113-127.
- Goodenow MM, Bloom G, Rose SL, Pomeroy SM, O'Brien PO, Perez EE, Sleasman JW, Dunn BM. Naturally occurring amino acid polymorphisms in human immunodeficiency virus type 1 (HIV-1) Gag p7<sup>NC</sup> and the Ccleavage site impact Gag-Pol processing by HIV-1 protease. Virology 2002;292:137-149.
- Clemente JC. Hemraiani R. Blum LE. Goodenow MM. Dunn BM. Secondary mutations M36I and A71V in the human immunodeficiency virus type 1 protease can provide an advantage for the emergence of the primary mutation D30N. Biochemistry 2003;4251:15029-15035.
- Green TB, Ganesh O, Perry K, Smith L, Phylip LH, Logan TM, Hagen SJ, Dunn BM, Edison AS. IA3, an aspartic proteinase inhibitor from Saccharomyces cerevisiae, is intrinsically unstructured in solution. Biochemistry. 2004;43(14):4071-4081.
- Pettit SC, Everitt LE, Choudhury S, Dunn BM, Kaplan AH. Initial cleavage of the human immunodeficiency virus type 1 GagPol precursor by its activated protease occurs by an intramolecular mechanism. J Virol. 2004:78:8477-8485.
- Li T, Yowell CA, Beyer BB, Hung SH, Westling J, Lam MT, Dunn BM, Dame JB. Recombinant expression and enzymatic subsite characterization of Plasmepsin 4 from the four Plasmodium species infecting man. Mol Parasitol. 2004;135(1);101-109.
- Clemente JC, Moose RE, Hemrajani R, Whitford LRS, Govindasamy L, Reutzel R, McKenna R, Agbandje-McKenna M, Goodenow MM, Dunn BM. Comparing the accumulation of active- and nonactive-site mutations in the HIV-1 protease. Biochemistry. 2004;43(38):12141-12151.
- Madabushi A, Chakraborty S, Fisher SZ, Clemente JC, Yowell C, Agbandje-McKenna M, Dame JB, Dunn BM, McKenna R. Crystallization and preliminary X-ray analysis of the aspartic protease plasmepsin 4 from the malarial parasite *Plasmodium malariae*. Acta Cryst. 2005;F61:228-231.

- Beyer BB, Johnson JV, Chung AY, Li T, Madabushi A, Agbandje-McKenna M, McKenna R, Dame JB, **Dunn BM**. Active-site specificity of digestive aspartic peptidases from the four species of *Plasmodium* that infect humans using chromogenic combinatorial peptide libraries. Biochemistry 2005;44:1768-1779.
- Goldfarb NE, Lam MT, Bose AK, Patel AM, Duckworth AJ, **Dunn BM**. Electrostatic switches that mediate the pH-dependent conformational change of "short" recombinant human pseudocathepsin D. Biochemistry 2005;44(48):15725-15733.
- Khan JA, **Dunn BM**, Tong L. Crystal structure of human Taspase1, a crucial protease regulating the function of MLL. Structure 2005 13(10):1443-1452.
- Ersmark K, Nervall M, Hamelink E, Janka LK, Clemente JC, **Dunn BM**, Blackman MJ, Samuelsson B, Aqvist J, Hallberg A. Synthesis of malarial plasmepsin inhibitors and prediction of binding modes by molecular dynamics simulations. Journal Medicinal Chemistry 2005;48(19):6090-6106.
- Oyama H, Fujisawa T, Suzuki T, **Dunn BM**, Wlodawer A, Oda K. Catalytic residues and substrate specificity of recombinant human tripeptidyl peptidase I (CLN2) Journal of Biochemistry 2005;138;(2):127-134.
- Pettit SC, Clemente JC, Jeung JA, **Dunn BM**, Kaplan AH. Ordered processing of the human immunodeficiency virus type 1 Gagpol precursor is influenced by the context of the embedded viral protease. Journal Virology 2005;79(16):10601-10607.
- Castanheira P, Samyn B, Sergeant K, Clemente JC, **Dunn BM**, Pires E, Van Beeumen J, Faro C. Activation, proteolytic processing, and peptide specificity of recombinant cardosin A. Journal Biological Chemistry 2005; 280(13):13047-13054.
- Dell'Agli, M; Parapini, S; Galli, G; Vaiana, N; Taramelli, D; Sparatore, A; Liu, P; **Dunn, BM**; Bosisio, E; Romeo, S, High antiplasmodial activity of novel plasmepsins I and II inhibitors, JOURNAL OF MEDICINAL CHEMISTRY, 49 (25): 7440-7449 DEC 14 2006
- Gutierrez-de-Teran, H; Nervall, M; **Dunn, BM**; Clemente, JC; Aqvist, J, Computational analysis of plasmepsin IV bound to an allophenylnorstatine inhibitor, FEBS LETTERS, 580 (25): 5910-5916 OCT 30 2006
- Okubo, A; Li, M; Ashida, M; Oyama, H; Gustchina, A; Oda, K; **Dunn, BM**; Wlodawer, A; Nakayama, T, Processing, catalytic activity and crystal structures of kumamolisin-As with an engineered active site, FEBS JOURNAL, 273 (11): 2563-2576 JUN 2006
- Clemente, JC; Coman, RM; Thiaville, MM; Janka, LK; Jeung, JA; Nukoolkarn, S; Govindasamy, L; Agbandje-McKenna, M; McKenna, R; Leelamanit, W; Goodenow, MM; **Dunn, BM**, Analysis of HIV-1CRF\_01 A/E protease inhibitor resistance: Structural determinants for maintaining sensitivity and developing resistance to atazanavir, BIOCHEMISTRY, 45 (17): 5468-5477 MAY 2 2006
- Ersmark, K; Nervall, M; Gutierrez-de-Teran, H; Hamelink, E; Janka, LK; Clemente, JC; **Dunn, BM**; Gogoll, A; Samuelsson, B; Aqvist, J; Hallberg, A, Macrocyclic inhibitors of the malarial aspartic proteases plasmepsin I, II, and IV, BIOORGANIC & MEDICINAL CHEMISTRY, 14 (7): 2197-2208 APR 1 2006
- Clemente, JC; Govindasamy, L; Madabushi, A; Fisher, SZ; Moose, RE; Yowell, CA; Hidaka, K; Kimura, T; Hayashi, Y; Kiso, Y; Agbandje-McKenna, M; Dame, JB; **Dunn, BM**; McKenna, R, Structure of the aspartic protease plasmepsin 4 from the malarial parasite Plasmodium malariae bound to an allophenylnorstatine-based inhibitor, ACTA CRYSTALLOGRAPHICA SECTION D-BIOLOGICAL CRYSTALLOGRAPHY, 62: 246-252 Part 3 MAR 2006.

# C. Research Support

Ongoing:

R01 AI-28571 (Dunn) NIH/NIAID 3/1/2006 - 2/28/2010

"Human Immunodeficiency Virus Proteinase"

The major goals of this project are to understand the role of variability in the amino-acid sequence of HIV PR and its cleavage junctions in the function of the protease during viral replication. Merit Award.

1-R01-GM66681 (Andrew H. Kaplan, PI)

7/1/2002 - 6/30/2007

NIH

"HIV Protease Activation and Viral Replication"

The major goals of this project are to define the role of individual amino acids in dimer formation, viral replication, and gag/pol polyprotein processing, with an aim of identifying targets for therapeutic intervention.

0313579 (Dr. Linda Walling, PI)

9/1/2003 - 8/31/2006

National Science Foundation

"Collaborative Research: A Functional Genomics Approach to N-Terminal Modifying Enzymes" The goal of this project is to characterize the enzymatic properties of a family of mono-, di-, and triaminopeptidases from a plant.

## **Completed During the Last Three Years:**

R01 Al-49063-03 (Dunn; Co-Pl, Arthur S. Edison)

1/1/2001 - 12/31/2003

NIH

"Novel Inhibitors of Fungal Aspartic Proteinases"

The major goal of this project is to address the need for new concepts in drug design against opportunistic infections in HIV positive patients, with a focus on IA-3 and yeast proteinase A.

R01 AI-28571 (Dunn)

7/1/2000 - 2/28/2006

NIH/NIAID

"Human Immunodeficiency Virus Proteinase", years 11-16

The major goals of this project are to understand the role of variability in the amino-acid sequence of HIV PR and its cleavage junctions in the function of the protease during viral replication.