

**BIOGRAPHICAL SKETCH**

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NAME Ernesto Freire	POSITION TITLE Henry Walters Professor, Biology and Biophysics		
eRA COMMONS USER NAME efreire1			
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
Univ. Peruana C. Heredia Medical School	B.Sc.	1972	Medicine/Biology
Univ. Peruana C. Heredia Medical School	M.Sc.	1973	Biochemistry
University of Virginia	Ph.D.	1977	Biophysics
University of Virginia	Postdoctoral	1977-1978	Biophysics

**A. Personal Statement**

Head of the leading biological thermodynamics and calorimetry laboratory in the world.

**B. Positions and Honors.****Positions and Employment**

- Visiting Assistant Professor of Biochemistry, University of Virginia, August 1978 - 1981
- Assistant Professor of Biochemistry, University of Tennessee, 1982-1986
- Assistant Professor of Biology and Biophysics, The Johns Hopkins University, 1986 - 1987
- Associate Professor of Biology and Biophysics, The Johns Hopkins University, 1987 - 1989
- Professor of Biology and Biophysics, The Johns Hopkins University, 1989 – present
- Henry Walters Professor of Biology, The Johns Hopkins University, 2001 – present
- Member, Johns Hopkins Malaria Research Institute, Johns Hopkins Bloomberg School of Public Health, 2001 - present
- Professor (joint appointment) Department of Biophysics and Biophysical Chemistry, The Johns Hopkins University School of Medicine, 2004- present

**Honors**

- Ford Foundation Fellowship, 1973 – 1976
- Fulbright Fellowship, 1973 – 1977
- Visiting Scientist, The Hebrew University, Jerusalem, Summer 1979
- Member, Center of Excellence, University of Tennessee, 1984 – 1986
- Phi Beta Kappa Certificate of Merit, 1985
- Stig Sunner Memorial Award for Outstanding Contributions to Thermochemistry and Thermodynamics. The Calorimetry Conference, 1988
- Johnson & Johnson Focused Giving Program Award 1993-1994
- Editorial Board, Proteins: Structure, Function and Genetics 1997 – present
- Dupont Educational Aid Grant 1998-1999
- Board of Directors. Institute of Biocomputation. University of Zaragoza, Spain 2003- present
- Microcal Prize for Outstanding Contributions to Experimental Thermodynamics, Budapest, Hungary, September 2004
- Miembro de Honor. Sociedad Española de Bioquímica y Biología Molecular. September 2005 – present
- Member of the Academy of Sciences of Latin America. September 2005- present

**C. Selected Publications Last Three Years (2008-2010)**

- Cremades N, Velazquez-Campoy A, Freire E, Sancho J. (2008) The flavodoxin from Helicobacter

- pylori: structural determinants of thermostability and FMN cofactor binding. *Biochemistry*. 2008 47 627-639 PMID: 18095659
- Bower, E., Bacha, U.M., Kawasaki, Y. and Freire, E. Inhibition of HIV-2 Protease by HIV-1 Protease Inhibitors in Clinical Use (2008) *Chem. Biol. Drug. Design* 71 298-305 PMID: 18312292
  - Hosahudya Gopi, M.Umashankara, Vanessa Pirrone, Judith LaLonde, Navid Madani, Ferit Tuzer, Sabine Baxter, Isaac Zentne, Simon Cocklin, Navneet Jawanda, Shendra R. Miller, Arne Schön, Jeffrey C. Klein, Ernesto Freire, Fred C. Krebs, Amos B. Smith III, Joseph Sodroski and Irwin Chaiken (2008) Structural Determinants for Affinity Enhancement of a Dual Antagonist Peptide Entry Inhibitor of Human Immunodeficiency Virus Type-1 *J. Medicinal Chem.* 51 2638-2647 PMID: 18402432
  - Bacha, U., Barrila, J., Gabelli, S.B., Kiso, Y. Amzel, L.M. Freire, E. (2008) Development of Broad-Spectrum Halomethyl Ketone Inhibitors Against Coronavirus Main Protease 3CLpro *Chem. Biol. Drug. Design* 72, 34-49 PMID: 18611220
  - Freire, E. (2008) Do Enthalpy and Entropy Distinguish First in Class From Best in Class? *Drug Discovery Today* 13, 869-874 PMID: 18703160
  - Navid Madani, Arne Schon, Amy M. Princiotta, Judith M. LaLonde, Joel R. Courter, Takahiro Soeta, Danny Ng, Liping Wang, Evan T. Brower, Shi-Hua Xiang, Young Do Kwon, Chih-chin Huang, Richard Wyatt, Peter D. Kwong, Ernesto Freire, Amos B. Smith III and Joseph Sodroski (2008) Small-Molecule CD4 Mimics Interact with a Highly Conserved Pocket on HIV-1 gp120. *Structure* 11, 1689-1701 PMID: 19000821
  - Hidaka, K., Kimura, T., Ruben, A. J., Uemura, T., Kamiya, M., Kiso, A., Okamoto, T., Tsuchiya, Y., Hayashi, Y., Freire, E. and Kiso, Y. (2008) Antimalarial activity enhancement in hydroxymethylcarbonyl (HMC) isostere-based dipeptidomimetics targeting malarial aspartic protease plasmepsin. *Bioorganic and Medicinal Chemistry*, 16, 10049-10060 PMID: 18952439
  - Freire, E. A Thermodynamic Platform for Drug Discovery and Optimization (2008) in *Towards Drugs of the Future*, pages 13-22 Kruse, C.G. and Timmerman, H. Eds.
  - Freire, E. ITC: Affinity is not everything (2009) *European Pharmaceutical Review* 14, 44-47
  - Brower, E. T., Schon, A., Klein, J. C., and Freire, E. Binding Thermodynamics of the N-Terminal Peptide of the CCR5 Coreceptor to HIV-1 Envelope Glycoprotein gp120 (2009) *Biochemistry* 48, 779-785 PMID: 19170639
  - Kassa A, Madani N, Schön A, Haim H, Finzi A, Xiang SH, Wang L, Princiotta A, Pancera M, Courter J, Smith AB 3rd, Freire E, Kwong PD, Sodroski J. (2009) Transitions to and from the CD4-bound conformation are modulated by a single-residue change in the human immunodeficiency virus type 1 gp120 inner domain. *J. Virol.* 2009 83, 8364-8378 PMID: 19535453
  - Regnier T, Sarma D, Hidaka K, Bacha U, Freire E, Hayashi Y, Kiso Y. (2009) New developments for the design, synthesis and biological evaluation of potent SARS-CoV 3CL(pro) inhibitors. *Bioorg Med Chem Lett.* 19, 2722-2727 PMID: 19362479
  - Chunlong Ma, Alexei Polishchuk, Yuki Ohigashi, Amanda Stouffer, Arne Schön, Emma Magavern, James D. Lear, Ernesto Freire, Robert A. Lamb, William F. DeGrado, and Lawrence H. Pinto Identification of the Functional Core of the Influenza A Virus A/M2 Proton-Selective Ion Channel (2009) *Proceedings of the National Academy of Sciences* 106:12283-12288 PMID: 19590009
  - Ernesto Freire A thermodynamic approach to the optimization of drug candidates (2009) *Chem Biol Drug Design* 74, 468-47 PMID: 19793186
  - E. Freire, A. Schon and A. Velazquez-Campoy (2009) Isothermal Titration Calorimetry: General Formalism Using Binding Polynomials. *Methods Enzymol.* 455, 127-155 PMID: 19289205
  - E. Freire, Y. Kawasaki, A. Velazquez-Campoy and A. Schön (2010) Characterization of Ligand Binding by Calorimetry; in *Biophysical approaches for determining ligand binding to biomolecular targets: detection, measurement and modeling*, Alberto Podjarny, Annick Dejaegere and Bruno Kieffer Editors, RSC Publishing

- Ruben, A. J., Kiso, Y. and Freire, E. (2010) The Plasmeprin Family as Antimalarial Drug Targets In Press
- Yuko Kawasaki, Eduardo E. Chufan, Virginie Lafont, Koushi Hidaka, Yoshiaki Kiso, L. Mario Amzel, and Ernesto Freire (2010) How Much Binding Affinity Can be Gained by Filling a Cavity? Chem. Biol. Drug Design 75, 143-151 PMID: 20028396
- Ladbury, J. E., Klebe, G. and Freire, E. (2010) Adding calorimetric data to decision making in lead discovery: a hot tip. Nature Review Drug Discovery, 9, 23-27 PMID: 19960014
- H. S. Lee, M. Contarino, M. Umashankara, A. Schon, E. Freire, A. B. Smith III, I. Chaiken and L. S. Penn (2010) Use of the quartz crystal microbalance to monitor ligand-induced conformational rearrangements in HIV-1 envelope protein gp120. Anal. Bioanal. Chem. 396, 1143-1152. PMID: 20016882
- E.T. Brower, A. Schon and E. Freire (2010) Naturally Occurring Variability in the Envelope Glycoprotein of HIV-1 and the Development of Cell Entry Inhibitors. Biochemistry 49, 2359–2367 PMID: 20166763
- J. Barrila, S. Gabelli, U. Bacha, L. M. Amzel and E. Freire (2010) Mutation of Asn28 Disrupts the Dimerization and Enzymatic Activity of SARS 3CL<sup>pro</sup>. Biochemistry In Press