

Ariel Fernández Curriculum Vitae

Born in Bahía Blanca, Argentina; DOB: April 8, 1957
Single, no dependents
American citizen

Current Positions

Karl F. Hasselmann Chair in Engineering
Professor of Bioengineering
Department of Bioengineering
Rice University, Houston, TX 77005
Phone: 713 348 3681; Fax: 713 348 3699; e-mail: arifer@rice.edu

Adjunct Professor of Computer Science, The University of Chicago

Adjunct Professor of Molecular Therapy, M. D. Anderson Cancer Center (UTMC)

Scientific Consultant, Eli Lilly and Company

Primary research foci

Molecular Therapeutics Engineering; Rational Drug Design; Molecular Biophysics; Chemical Physics; Bioinformatics; Clinical Kinomics

Websites

<http://bioe.rice.edu/FacultyDetail.cfm?RiceID=81397>
<http://www.owl.net.rice.edu/~arifer/>
<http://www.cs.uchicago.edu/people/ariel>

Education

- Ph. D., M. Sc., M. Phil., Yale University, 1981-1983 (fastest awarded Yale Ph. D.).
 - Sr. Research Scientist, Max-Planck-Institut fuer biophysikalische Chemie, Division of Nobel Laureate Manfred Eigen, Goettingen, Germany, 1986-1989.
 - Research Associate (1985-1987), Visiting Senior Research Scientist (1994-1996), Princeton University.
 - Licenciado en Matematica (1980), Quimico (1979), Universidad Nacional del Sur, Bahia Blanca, Argentina.
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Awards and Previous Appointments

- Camille and Henry Dreyfus Teacher-Scholar Awardee, 1991
 - Camille and Henry Dreyfus Distinguished New Faculty Awardee, 1989
 - John S. Guggenheim Memorial Foundation Fellow, 1995-1996
 - Consultant to U.S. Federal Government, NIH, Special Panel on Centers of Excellence in Systems Biology, 2003-
 - National Cancer Institute (NCI) Reviewer. NIH Study Section RFA-07-005 "Advanced Proteomic Platforms and Computational Sciences for NCI Clinical Proteomic Technologies Initiative", 2006-
 - Guest Professor, Institute for Protein Research, Osaka University, Japan, 2003
 - Visiting Senior Researcher, Max-Planck-Institut fuer Biochemie, Abteilung Robert Huber, Martinsried, Germany, 2000-
 - Visiting Senior Scientist, Institute for Nonlinear Science, University of California at San Diego, 1989
 - Managing Editor, Frontiers in Bioscience, Encyclopedia of Bioscience, 2006-
 - Editor, Journal of Biological Physics and Chemistry, Basel, Switzerland, 2000-
 - Fulbright Scholar, US Information Agency, 1999 and Fulbright Fellow, 1981
 - Alexander von Humboldt Foundation Awardee (1995)
 - Max Planck Society Scholar, Goettingen, Germany (1987-1989)
 - Feinberg Fellow, Israel, 1984-1985
 - Full Professor, Indiana University School of Informatics, 2003-2005.
 - Full Professor, Center for Computational Biology and Bioinformatics, Indiana University School of Medicine, 2003-2005.
 - Elected Fellow, American Institute for Medical and Biological Engineering, 2006
 - Full Professor and Principal Investigator, UNS and Natl. Res. Council of Argentina, 1994-2003
 - Medal "State of Buenos Aires" to the best graduate, Argentina, 1980
 - Deputy Governor, American Biographical Institute, 1998-
 - Co-organizer and Proceedings Editor of the Miami Bio/Technology Winter Symposium, Nature-sponsored, 1993.
 - Chair, "Resistance and Safety", Discovery on Target: Cambridge Healthtech Institute's Second Annual KINASE INHIBITORS; October 20-23, Boston, MA, USA.
 - Honorary Associate Member, Collegium Basilea, Institute for Advanced Study, Basel, Switzerland.
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Current grant support, PI: Ariel Fernandez

- NIH Grant Award 1R01 GM072614 from the National Institute of General Medical Sciences (NIGMS). Title: “Protein packing defects as functional markers and drug targets”. Total amount of award: \$1.6million (2005-2009).
 - John and Ann Doerr Fund for Computational Biomedicine (Program GC4R 2005). Amount of Award: \$180,000 (2006-2008).
 - Eli Lilly and Company, Unrestricted research funds (2004-)
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Recent Lectures

- “Curbing the Cardiotoxicity of Kinase Inhibitors: The Methyl that Saved the Heart”, *Discovery on Target 2007*, Cambridge Healthtech Institute Fifth Annual, “Developing inhibitors for Promising Drug Targets”, World Trade Center, Boston, MA, October 15-18 (2007).
 - “7th International Workshop on Pharmacodynamics of Anticancer Agents”, organized by the University of Chicago, Guanacaste, Costa Rica, September 16-20 (2007).
 - “Re-engineering of Imatinib to Decrease Cardiac Risk: Translational Ideas in Drug Discovery”, *World Pharmaceutical Congress*, Cambridge Healthtech Institute Second Annual “Cardiotoxicity and Drug Safety”, Philadelphia, PA, May 12-13 (2008).
 - “Curbing side effects in anticancer drugs”, in “Science for Health with a Human Face”, *International Symposium* (4 Nobel laureates in attendance), Madrid, Spain, November 4-7 (2008).
 - “Translational ideas in drug discovery”, Guest lecturer, *Genomics Research Center, Academia Sinica*, Taipei, Taiwan, June 14-21 (2008).
 - Lecturer and Chair, “Resistance and Safety”. Lecture title: “Translational ideas to curb side effects in anticancer kinase-targeting therapy: Reducing cardiotoxicity through inhibitor redesign”. *Discovery on Target: Cambridge Healthtech Institute’s Second Annual KINASE INHIBITORS*; October 20-23, Boston, MA, USA.
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Critiques on recent work

- *Nature* **432**, 688 (2004)
News and Views article on: Despa, F., Fernandez, A. and Berry, R.S. Dielectric modulation of biological water. *Phys. Rev. Lett.* **93**, 228104 (2004)
- *Journal of Clinical Investigation* **117**, 3650-3653 (2007)
Commissioned Editorial Commentary by George Demetri on: Fernández, A. *et al.* An anticancer C-Kit kinase inhibitor is re-engineered to make it

more active and less cardiotoxic. *Journal of Clinical Investigation* **117**, 4044-4054 (2007)

- *Nature Reviews Drug Discovery* **7**, 120-121 (2008)
Research Highlights, “Anticancer drugs: Redesigning kinase inhibitors”, on: Fernández, A. et al. An anticancer C-Kit kinase inhibitor is re-engineered to make it more active and less cardiotoxic. *Journal of Clinical Investigation* **117**, 4044-4054 (2007)
- *Chemical & Engineering News (ACS)* **86**, number 09, p.31 (2008)
Science & Technology Concentrates: “Drug Design Strategy Aims for Disorder”, on: Crespo, A. and Fernández, A. Induced disorder in protein-ligand complexes as a drug-design strategy”. *Molecular Pharmaceutics* (ACS), published online February 16, 2008.

Critique Excerpts

The research by Fernández and collaborators (cf. *Journal of Clinical Investigation* **117**, 4044-4054 (2007)) has been auspiciously received by key researchers in cancer therapy and is being perceived as a conceptual and technical breakthrough. Thus, Harvard Medical School Professor *George Demetri*, director of the Center for Sarcoma and Bone Oncology at Dana-Farber Cancer Institute, wrote:

“The approach used here by Fernández et al. holds great promise to allow more customized development of rationally designed therapeutic agents.”
“...with tools such as those described by Fernández et al., the future certainly looks bright for constructing ever-better agents that can be combined safely and effectively to manage, and eventually cure, many forms of human cancer.”

(from Demetri’s Commentary, *Journal of Clinical Investigation* **117**, 3650-3653, 2007).

Thomas Force, Wilson Professor of Medicine at Thomas Jefferson University, who first characterized and reported imatinib cardiotoxicity in his 2006 *Nature Medicine* article, said:

“...this knowledge could potentially steer drug development away from targets and pathways that would lead to toxicity, but would leave tumor cell killing intact. Fernández and co-workers, in this really remarkable piece of work, have proven that this is indeed possible. Their findings will hopefully encourage drug makers to pursue a similar approach of “rational drug re-design” (and drug design) in the development of new anti-cancer agents...”

<http://www.media.rice.edu/media/NewsBot.asp?MODE=VIEW&ID=10334&SnID=1798653505>

<http://www.medicalnewstoday.com/articles/90646.php>

In “Chemistry World” (Royal Society of Chemistry, UK), Force added:

“The biggest message of this paper is that a cardiotoxic cause can be identified and steered away from. There are hundreds of agents in development that could benefit from this research.”

<http://www.rsc.org/chemistryworld/News/2007/December/03120703.asp>

The research by Fernández also received coverage from the popular press (*Reuters*):

<http://www.reuters.com/article/healthNews/idUSN0341290220071203>

Finally, the Fernández' contribution was highlighted in *Nature Reviews Drug Discovery* **7**, 120-121 (February 2008). (Research Highlights, “Anticancer drugs: Redesigning kinase inhibitors”). Thus, *Nature Reviews* editor Sarah Crunkhorn wrote:

“In summary, WBZ_4 [the drug designed by the Fernandez team] could have potential as a novel therapy for *GISTs* [gastro-intestinal stromal tumors], and the approach demonstrated in the study might also be applied to engineer the specificity of other kinase inhibitors with the aim of creating safer and more effective drugs.”

Selected Recent Publications (308 total)

1. Fernández, A., Kostov, K., and Berry, R.S.: “From residue matching patterns to protein folding topographies: general model and bovine pancreatic trypsin inhibitor”, *Proc. Natl. Acad. Sci., USA* **96**, 12991-12996 (1999).
2. Fernández, A., Colubri, A., and Berry, R.S.: “Topology to geometry in protein folding: beta-lactoglobulin”, *Proc. Natl. Acad. Sci., USA* **97**, 14062-14066 (2000).
3. Fernández, A., Sosnick, T.R., and Colubri, A.: “Dynamics of hydrogen-bond desolvation in folding proteins”, *J. Mol. Biol.* **321**, 659-675 (2002).
4. Fernández, A. and Scheraga, H.A.: “Insufficiently dehydrated hydrogen bonds as determinants for protein interactions”, *Proc. Natl. Acad. Sci., USA* **100**, 113-118 (2003).
5. Fernández, A. and Berry, R.S.: “Proteins with hydrogen-bond packing defects are highly interactive with lipid bilayers: implications for amyloidogenesis”, *Proc. Natl. Acad. Sci., USA* **100**, 2391-2396 (2003).
6. Fernández, A. and Scott, R.: “Adherence of packing defects in soluble proteins”, *Phys. Rev. Lett.* **91**, 018102 (2003).
7. Fernández, A., Kardos, J., Scott, R., Goto, Y., and Berry, R.S.: “Structural defects and the diagnosis of amyloidogenic propensity”, *Proc. Natl. Acad. Sci., USA* **100**, 6446-6451 (2003).
8. Fernández, A.: “Functionality of wrapping defects in soluble proteins: what cannot be kept dry must be conserved”, *J. Mol. Biol.* **337**, 477-483 (2004).
9. Fernández, A., Scott, R. and Berry, R.S.: “The nonconserved wrapping of conserved protein folds reveals a trend towards increasing connectivity in proteomic networks”, *Proc. Natl. Acad. Sci., USA* **101**, 2823-2827 (2004).

10. Fernández, A., Rogale, K., Scott, R., and Scheraga, H.A.: "Inhibitor design by wrapping packing defects in HIV-1 proteins", Proc. Natl. Acad. Sci., USA 101, 11640-11645 (2004).
 11. Fernández, A. and Berry, R.S.: "Molecular dimension explored in evolution to promote proteomic complexity", Proc. Natl. Acad. Sci., USA 101, 13460-13465 (2004).
 12. Fernández, A.: "Keeping dry and crossing membranes", Nature Biotechnology 22, 1081-1084 (2004).
 13. Despa, F., Fernández, A. and Berry, R.S.: "Dielectric modulation of biological water", Phys. Rev. Lett. 93, 228104 (2004); featured in Nature (News and Views) 432, 688 (2004).
 14. Fernández, A.: "Incomplete protein packing as a selectivity filter in drug design", Structure 13, 1829-1836 (2005)
 15. Chen, J., Zhang, X. and Fernández, A.: "Molecular basis for specificity in the druggable kinome: sequence-based analysis", Bioinformatics 23, 563-572 (2007).
 16. Dunker, A. K. and Fernández, A.: "Engineering a productive enzyme confinement", Trends in Biotechnology 25, 189-191 (2007).
 17. Fernández, A. et al.: "Rational drug redesign to overcome drug resistance in cancer therapy: *imatinib* moving target", Cancer Research 67, 4028-4033, Priority Report (2007). (Cover featured)
 18. Pietrosevoli, N., Crespo, A. and Fernández, A.: "Dehydration propensity of order-disorder intermediate regions in soluble proteins", Journal of Proteome Research 6, 3519-3526 (2007)
 19. Liang, H., Rogale-Plazonic, K., Chen, J., Li, W.-H. and Fernández, A.: "Protein under-wrapping causes dosage sensitivity and decreases gene duplicability", PLoS Genetics 4, e11 (2008).
 20. Fernández, A. et al.: "An anticancer C-Kit kinase inhibitor is re-engineered to make it more active and less cardiotoxic", Journal of Clinical Investigation 117, 4044-4054 (2007) (Editorial-commissioned Commentary, Press Releases, etc).
 21. Crespo, A. and Fernández, A.: "Kinase packing defects as drug targets", Drug Discovery Today 12, 917-923 (2007).
 22. Zhang, X., Crespo, A. and Fernández, A.: "Turning promiscuous kinase inhibitors into safer drugs". Trends in Biotechnology 26, 295-301 (2008).
 23. Jianping Chen, Han Liang and Ariel Fernández: "Protein structure protection commits gene expression patterns". Genome Biology 9, R107 (2008).
 24. Fernández, A. and Crespo, A.: "Protein wrapping: a marker for association, aggregation and molecular targeted therapy". Chemical Society Reviews (Royal Society of Chemistry, UK) 37, 2373-2382, Tutorial Review (2008).
 25. Fernández, A., Bazan, S. and Chen, J.: "Taming the induced folding of drug-targeted kinases". Trends in Pharmacological Sciences, in press (2009).
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