

## BIOGRAPHICAL SKETCH

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NAME James A. Wells		POSITION TITLE Professor	
eRA COMMONS USER NAME JAMESAWELLS			
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
University of California, Berkeley, CA	B.A.	1973	Biochemistry
Washington State University	Ph.D.	1979	Biochemistry
Washington State University	Postdoc	1979-1980	Chemistry
Stanford University Medical School	Postdoc	1980-1982	Biochemistry

### A. Positions and Honors.

#### Positions & Employment

- 1982-1986 Scientist, Genentech, Inc., Dept. of Protein Engineering  
1986-1989 Senior Scientist, Genentech, Inc., Dept. of Protein Engineering  
1989-1998 Staff Scientist, Genentech, Inc., Dept. of Protein Engineering  
1988-2005 Adjunct Assistant, Associate, and Full Professor, University of California, San Francisco, Dept of Pharmaceutical Chemistry  
1998-2005 President and Chief Scientific Officer, Sunesis Pharmaceuticals  
2005-present Harry Wm. and Diana V. Hind Professor in Pharmaceutical Sciences, University of California, San Francisco  
2005-present Director, Small Molecule Discovery Center, University of California, San Francisco

#### Other Experience and Professional Memberships

- 1994-2003 Organizer or Co-organizer of various scientific meetings (e.g., 2003 Keystone Drug Discovery Meeting; 2000 Protein Society meeting, 1999 ASBMB meeting, 1994 Peptides in Biology GRC)  
1989-present Editorial Board service on scientific journals (Proteins, Protein Engineering, Protein Science, Chemistry & Biology, Journal Molecular Biology, Trends in Biotechnology, PNAS)  
1994-1998 Member of the Executive Council of Protein Society  
2005-2007 Chair of NIH study section on Molecular Libraries Screening Centers Network (MLSCN)  
2005-present Member of the Executive Committee for QB3 at UCSF  
2006 Member UCSF Cancer Center  
2007-present Member of the Executive Council ASBMB

#### Honors (selected from a total of 18)

- 1979-1981 Damon M. Runyon - Walter Winchell Postdoctoral Fellowship  
1990 Pfizer Award (given by the American Chemical Society for achievements in enzyme chemistry)  
1998 Recipient of the Christian B. Anfinsen Award presented by the Protein Society  
1998 Recipient of the Vincent du Vigneaud Award given by the American Peptide Society  
1999 Elected Member to the National Academy of Sciences  
2003 Recipient of the Hans Neurath Award given by the Protein Society  
2006 Perlman Lecture Award of the ACS Biotechnology Division  
2006 Paul Janssen Prize in Adv. Biotech and Medicine  
2007: Fred Richards Distinguished Lecture, Yale University  
2008: Jane Darnell Distinguished Lecture, Rockefeller University

## B. Selected publications (in chronological order from a total of 140)

42. Abrahamsen, L., Tom, J., Burnier, J., Butcher, K., Kossiakoff, A.A., Wells, J.A., (1991) *Biochemistry* 30, 4151-4159. "Engineering Subtilisin and its substrates for efficient ligation of peptide bonds in aqueous solution."
44. Bass, S.H., Mulkerrin, M.G., and Wells, J.A. (1991) *Proc. Natl. Acad. Sci. USA*, 88, 4498-4502. "A systematic mutational analysis of hormone-binding determinants in the human growth hormone receptor."
47. Carter, P.C., Abrahamsen, L., and Wells, J.A. (1991) *Biochemistry* 30, 6142-6148. "Probing the mechanism and Improving the Rate of Substrate-assisted Catalysis in Subtilisin BPN'."
48. Cunningham, B.C., Mulkerrin, M.G., and Wells, J.A. (1991) *Science* 253, 545-548, "Dimerization of Human Growth Hormone by Zinc."
49. Lowman, H.B., Bass, S., Simpson, N., Wells, J.A. (1991) *Biochemistry* 30, 10832-10838 "Engineering a Hormone for Improved Receptor binding Affinity by Monovalent Phage Display."
50. Cunningham, B.C., Ultsch, M., DeVos, A.M., Mulkerrin, M.G., Clauser, K.R., Wells, J.A. (1991) *Science* 254, 821-825. "Dimerization of the Extracellular Domain of the Human Growth Hormone Receptor by a Single Hormone Molecule."
55. Fuh, G. Cunningham, B.C., Fukunaga, R., Nagata, S., Goeddel, D.V., and Wells, J.A. (1992) *Science*, 256, 1677-1680. "Rational Design of Potent Antagonists to the Human Growth Hormone Receptor."
60. Matthews, D.J. and Wells, J.A. (1993) *Science* 260, 1113-1117. "Substrate Phage: Selection of Protease Substrates by Monovalent Phage Display."
75. Jackson, D.Y., Burnier, J., Quan, C., Stanley, M., Tom, J. and Wells, J.A. (1994) *Science* 266, 243-247. "A Designed Peptide Ligase for Total Synthesis of Ribonuclease A with Unnatural Catalytic Residues."
76. Chang, T.K., Jackson, D.Y., Burnier, J.P. and Wells, J.A. (1994) *Proc. Natl. Acad. Sci. USA* 91, 12544-12548. "Subtiligase: a Tool for Semi-synthesis of Proteins."
79. Jackson, D.Y., Burnier, J.P. and Wells, J.A. (1995) *J. Am. Chem. Soc.* 117, 819-820. "Enzymatic Cyclization of Linear Peptide Esters Using Subtiligase."
81. Clackson, T. and Wells, J.A. (1995) *Science* 267, 383-386. "A Hot Spot of Binding Energy in a Hormone-Receptor Interface".
86. Li, B., Tom, J.Y.K., Oare, D., Yen, R., Fairbrother, W., Wells, J.A., and Cunningham, B.C. (1995) *Science* 270, 1657-1660. "Minimization of a Polypeptide Hormone".
88. Braisted, A. and Wells, J.A. (1996) *Proc. Natl. Acad. Sci. USA* 93, 5688-5692. "Minimization of a Binding Domain of Protein A".
94. Ballinger, M.D., Tom, J. and Wells, J.A. (1996) *Biochemistry* 35, 13579-13585. "Furilisin: a Variant of Subtilisin BPN' Engineered for Cleaving Tribasic Substrates".
95. Atwell, S.A., Ridgway, J.B.B., Wells, J.A. and Carter, P.J. (1997) *J.Mol.Biol.* 270, 26-35. "Stable Heterodimers from Remodeling the Domain Interface of a Homodimer using a Phage Display Library".
96. Baca, M., Presta, L.G., O'Connor, S. and Wells, J.A. (1997) *J. Biol. Chem.* 272, 10678-10684. "Antibody Humanization Using Monovalent Phage Display".
97. Ballinger, M. and Wells, J.A. (1998) *Handbook of Proteases*, Academic Press, Eds. Barrett, A., Rawlings, N.D. and Woessner, J.F., pp 289-294. "Subtilisin".
98. Braisted, A., Judice, K. and Wells, J.A. (1997) *Methods in Enzymology* Vol. 289 (in press) "Assembly of Proteins with Subtiligase".
99. Scheidig, A., Hynes, T. Pellitier, L., Wells, J.A. and Kossiakoff, A.A. (1997) *Protein Science* 6, 1806-1824. "Crystal Structures of Bovine Chymotrypsin and Trypsin Complexed to the Inhibitor Domain of Alzheimer's Amyloid  $\beta$ -Protein Precursor (APPI) and Basic Pancreatic Trypsin Inhibitor (BPTI): Engineering of Inhibitors with Altered Specificities".
100. Pearce, K.H., Potts, B.J., Presta, L.G., Bald, L.N., Fendly, B.M. and Wells, J.A. (1997). *J. Biol. Chem.* 272, 20595-20602. "Mutational Analysis of Thrombopoietin for Identification of Receptor and Neutralizing Antibody Sites".
101. Muller, Y.A., Li, B., Christinger, H.W., Wells, J.A., Cunningham, B.C. and De Vos, A.M. (1997) *Proc. Natl. Acad. Sci. USA* 94, 7192-7197. "Vascular Endothelial Growth Factor: Crystal Structure and Functional Mapping of the Kinase Domain Receptor Binding Site".
102. Ellman, J., Stoddard, B., and Wells, J.A. (1997) *Proc. Natl. Acad. Sci. USA* 94, 2779-2782. "Combinatorial Thinking in Chemistry and Biology".
103. Baca, M., Scanlan, T.S., Stephenson, R.C. and Wells, J.A. (1997) *Proc. Natl. Acad. Sci. USA* 94, 10063-10068. "Phage Display of a Catalytic Antibody to Optimize Affinity for Transition-State Analog Binding".

104. Atwell, S., Ultsch, M., De Vos, A.M. and Wells, J.A. (1997) *Science* 278, 1124-1127 "Structural Plasticity in a Remodeled Protein-Protein Interface"
105. Cunningham, B.C. and Wells, J.A. (1997) *Current Opinion in Structural Biology* 7, 457-462. "Minimized Proteins".
106. Starovasnik, M., Braisted, A. and Wells J.A. (1997) *Proc. Natl. Acad. Sci. USA* 94, 10080-10085. "Structural Mimicry of a Native Protein by a Minimized Binding Domain".
107. Wiesmann, C., Fuh, G., Christinger, H.W., Eigenbrot, C., Wells, J.A., De Vos, A.M. (1997) *Cell* 91, 695-704. "Crystal Structure at 1.7Å resolution of VEGF in Complex with Domain 2 of the Flt-1 Receptor".
108. Fuh, G., Li, B., Crowley, C., Cunningham, B.C. and Wells, J.A. (1998) *J. Biol. Chem.* 273, 11197-11204. "Requirements for Binding and Signaling of the Kinase Domain Receptor for Vascular Endothelial Growth Factor".
109. Jones, J.T., Ballinger, M.D., Piscanne, P.I., Lofgren, J.A., Fitzpatrick, V.D., Fairbrother, W.J., Wells, J.A. and Sliwkowski, M.X. (1998) *J. Biol. Chem.* 273, 11667-11674. "Binding Interaction of the Heregulin-EGF-domain with ErbB3 and ErbB4 Receptors Assessed by Alanine-Scanning Mutagenesis".
110. Ballinger, M.D., Jones, J.T., Lofgren, J.A., Fairbrother, W.J., Akita, R.W., Sliwkowski, M.X. and Wells, J.A. (1998) *J. Biol. Chem.* 273, 11675-11684. "Selection of Heregulin Variants Having Higher Affinity for the ErbB3 Receptor by Monovalent Phage Display".
111. Pearce, K.H. and Wells, J.A. (1998) in *Human Growth Hormone: Basic and Clinical Research*. Human Growth Hormone: Basic and Clinical Research. Humana Press, Inc pp131-143 "Activation of the Human Growth Hormone Receptor: Structure and Function of the Ligand-Receptor Complex".
112. Clackson, T., Ultsch, M., Wells, J.A. and De Vos, A.A. (1998) *J. Mol. Biol.* 277, 1111-1128. "Structural and Functional Analysis of the 1:1 Growth Hormone:Receptor Complex Reveals the Molecular Basis for Receptor Affinity".
113. Ballinger, M.D. and Wells, J.A. (1998) *Nature Struct. Biol.* 5, 938-940. "Will Any Dimer Do?" News and Views.
114. Erlanson, D.A. and Wells, J.A. (1998) *Tet. Lett.*, 39, 6799-6802. "Facile Synthesis of Cyclic Peptides Containing Di-, Tri-, Tetra- and Pentasulfides".
115. Fairbrother, W.J., Christinger, H.W., Cochran, A.G., Fuh, G., Keenan, C.J., Quan, C., Schriver, S.K., Tom, J.Y.K., Wells, J.A. and Cunningham, B.C. (1998) *Biochemistry* 37, 17754-17764. "Novel Peptides Selected to Bind Vascular Endothelial Growth Factor Target the Receptor-Binding Site".
116. Arkin, M.R. and Wells, J.A. (1998) *J. Mol. Biol.* 284, 1083-1094. "Probing the Importance of Second Sphere Residues in an Esterolytic Antibody by Phage Display".
117. Pearce, K.H., Cunningham, B.C., Fuh, G., Teeri, T. and Wells, J.A. (1999) *Biochemistry* 38, 81-89. "Growth Hormone Binding Affinity for Its Receptor Surpasses the Requirements for Cellular Activity".
118. Atwell, S. and Wells, J.A. (1999) *Proc. Natl. Acad. Sci USA* 96, 9497-9502. "Selection for Improved Subtiligases by Phage Display".
119. Sidhu, S.S., Lowman, H.B., Cunningham, B.C. and Wells, J.A. (2000) *Methods in Enzymology*, Vol. 328. 333-363. "Phage Display for Selection of Novel Binding Peptides".
120. Sidhu, S.S., Weiss, G.A. and Wells, J.A. (2000) *J. Mol. Biol.* 296, 487-495. "High Copy Display of Large Proteins on M13 Phage for Functional Selections".
121. DeLano, W.L., Ultsch, M.H., De Vos, A.M. and Wells, J.A. (2000) *Science* 287, 1279-1283. "Convergent Solutions to Binding at a Protein-Protein Interface".
122. Weiss, G.A., Wells, J.A. and Sidhu, S.S. (2000) *Protein Science* 9, 647-654. "Mutational Analysis of the Major Coat Protein of M13 Identifies Residues that Control Protein Display"
123. Erlanson, D.A., Braisted, A.C., Raphael, D.R., Randal, M., Stroud, R.M., Gordon, E.M. and Wells, J.A. (2000) *Proc. Natl. Acad. Sci. USA* 97, 9367-9372. "Site-Directed Ligand Discovery".
124. Arkin, M.R., Randal, M., DeLano, W., Hyde, J., Loung, T.N., Oslob, J.D., Raphael, D.R., Taylor, L., Wang, J., McDowell, R.S., Wells, J.A., Braisted, A.C. (2003) *Proc. Natl. Acad. Sci USA* 100, 1603-1608. "Binding of Small Molecules to an Adaptive Protein:Protein Interface".
125. Nguyen, J. and Wells, J.A. (2003) *Proc. Natl. Acad. Sci USA*, 100, 7533-7538. "Direct Activation of the Apoptosis Machinery as a Mechanism to target Cancer Cells".
126. Thanos, C.D., Randal, M., and Wells, J.A. (2003) *J. Am. Chem. Soc.*, 125, 15280-15281. "Potent Small-molecule Binding to a Dynamic Hot-spot on IL-2".
127. Stroud, R.M. and Wells, J.A. (2004) *Science STKE*, 2004, re7. "Mechanistic Diversity of Cytokine Signaling Across Cell Membranes"

128. Arkin, M.R. and Wells, J.A. (2004) *Nature Rev. Drug Disc.* 3, 301-317. "Small Molecule Inhibitors of Protein-Protein Interactions: Progressing Towards the Dream"
129. Erlanson, D.A., Wells, J.A. and Braisted, A.B. (2004) *Annu. Rev. Biophys. Biomol Struct.* "TETHERING: Fragment-based Drug Discovery". 33, 199-233.
130. Hardy, J.A., Lam, J., Nguyen, J.T., O'Brien, T and Wells, J.A. (2004) *Proc. Natl. Acad. Sci. USA* "Discovery of an Allosteric Site in Caspases". 101, 12461-12466.
131. Hardy, J.A. and Wells, J.A. (2004) *Current Opinion in Structural Biology* 14, 706-715. "Searching for New Allosteric Sites in Enzymes"
132. Buck, E., Bourne, H. and Wells, J.A. (2005) *J. Biol. Chem* 280, 4009-4012. "Site-specific Disulfide Capture of Agonist and Antagonist Peptides to the C5a Receptor"
133. Buck, E. and Wells, J.A. (2005) *Proc. Natl. Acad. Sci. USA* 102, 2719-2724. "Disulfide Trapping to Localize Small Molecule Agonists and Antagonists for the Complement 5a Receptor"
134. Scheer, J., Wells, J.A. and Romanowski, M. (2006) *Protein Expression and Purification* 41, 148-153. "Malonate-assisted Purification of Human Caspases"
135. Scheer, J.M., Romanowski, M.J., and Wells, J.A. (2006) *Proc. Natl. Acad. Sci. USA* 103, 7595-7600. "A Common Allosteric Site and Mechanism in Caspases"
136. Thanos, C.T., Delano, W.D. and Wells, J.A. (2006) *Proc. Natl. Acad. Sci. USA* 103, 15422-15427. "Hot spot Mimicry of a Cytokine Receptor by a Small Molecule" (Covered in *Nature* (2006) 443,886 *Research Highlites*; also selected for coverage in *Faculty of 1000 Biology*: <http://www.f1000biology.com/article/id/1097485/evaluation>)
137. Wells, J.A., and McClendon, C.L. (2007) *Nature* 450, 1001-1009. "Reaching for high-hanging fruit in drug discovery at protein-protein interfaces". (Selected for *Faculty of 1000 Biology*: <http://www.f1000biology.com/article/id/1115699>).
138. Datta, D., Scheer, J.M., Romanowski, M.J. and Wells, J.A. (2008) *J. Mol Biol*, 381, 1157-1167 "An Allosteric Circuit in Caspase-1".
139. Yoshihara, H.A.I., Mahrus, S. & Wells, J.A. (2008). *Bioorganic Med. Chem. Lett.* in Press. N-Terminal Tags for Labeling Protein N-termini with Subtiligase for Proteomics.
140. Mahrus, M., Trinidad, J.C, Barkan, D.T., Sali, A., Burlingame, A.L., Wells, J.A. (2008) *Cell*, 134, in press. "Global Sequencing of Proteolytic Cleavage Sites in Apoptosis by Specific Labeling of Protein N Termini".

### C. Research Support

RO1 AI070292-01A1

NIH/NIAID

2/1/07 – 1/31/12

"Site-specific Allosteric Inhibitors for Inflammatory Caspases": The major goal of this project is to utilize an integrative chemical biology approach to characterize the allosteric circuitry of inflammatory caspases and to develop selective small molecule allosteric inhibitors to probe the roles of these caspases in cellular inflammation."

Role: Principal Investigator

RO1 GM081051

NIH/NIGMS

4/1/07 - 3/31/12

"Global analysis of Proteolysis in Apoptosis": The long term goal of the proposed work is to elucidate the process leading to programmed cell death by applying a new and general method we have developed for global proteomic profiling of proteolysis ("degradomics").

Role: Principal Investigator

Hartwell Foundation Individual Biomedical Research Award

5/1/07 – 4/30/10

"Novel Drug Targets for Leukemias": Use of global profiling of proteolysis in a leukemia cell line and RNAi analysis to identify and validate new drug targets.

Role: Principal Investigator

CHDI Foundation, Inc., Collaboration Research Award

10/1/07-1/1/10

"Identification of Caspase-2 and Caspase-6 Inhibitors for Huntington's Disease Research"

Role: Principal Investigator (with Dr. Michelle Arkin and Dr. Adam Renslo)

Sandler New Technologies Award

4/1/08 – 4/14/10

“Fragment-based Discovery Technology for Small Molecule Discovery”: The goal is to initiate a fragment discovery center as part of the Small Molecule Discovery Center (SMDC) at UCSF.

Role: Principal Investigator (with Dr. Michelle Arkin)

Rogers Foundation Research Award

1/1/09 – 12/30/09

“Apoptotic Biomarkers for Hematologic Cancers”

Role: Principal Investigator

RO1 CA136779

NIH/NCI

12/5/08 - 11/30/13

“Direct Chemical Activators of Caspases”: The long term goal of this proposal is to gain a fundamental understanding of the terminal process in cell death mediated by executioner caspases-3, -6, and -7

Role: Principal Investigator

S10 Shared Instrumentation Grant

NIH?NCRR

1/1/09 - 12/31/09

“High-throughput SPR Instrument for Small Molecule Discovery” at the SMDC

Role: Principal Investigator (with Dr. Michelle Arkin)