

## **David Cowburn**

### **Professional Biographical Information**

#### **Education:**

- 1965 B.Sc.Hon. 1962-65 Dept. of Biochemistry, University of Manchester Institute Science and Technology;
- 1970 Ph.D., Medical Research Council Biophysics Research Unit, King's College, University of London;

#### **Employment:**

- 2010- (Sept.) Professor, Biochemistry, Physiology and Biophysics, Albert Einstein College of Medicine, New York
- 2000-10 President & CEO; Director, Lab. Physical Biochemistry, New York Structural Biology Center
- 1973-2002 Assistant, Associate Professor, Head of Lab, Rockefeller University
- 1970-3 Research Associate, Department of Neurology; College of Physicians and Surgeons of Columbia University, New York.
- 1971-3 Research Fellow of the Interdisciplinary Research Training Program in the Biological Sciences in relation to Mental Health, College of Physicians and Surgeons of Columbia University, New York.
- 1970 Research Fellow of the European Molecular Biology Organization, Laboratory of Molecular Biophysics, Portsmouth Polytechnic, England
- 1969 Physics Teacher, London Education Authority Adult Classes (Part time)
- 1966-8 Demonstrator in Biochemistry, King's College

#### **Awards and distinctions:**

- State scholar, 1962-5.
- EMBO Fellow, 1970.
- Member, American Society of Biochemistry and Molecular Biology, 1978.
- Doctor of Science, University of London, 1981 (by examination).
- Adjunct Faculty, The Rockefeller University, 2003-; Mount Sinai School of Medicine, 2008-
- Fellow, New York Academy of Sciences, 2003.

**Patents issued:**

1. United States Patent 5,888,763 Hanafusa, et al. March 30, 1999 Peptides specific for the first Crk-SH3 domain. Licensed to Amgen.
2. United States Patent 6,171,804 Cowburn, et al. January 9, 2001 Method of determining interdomain orientation and changes of interdomain orientation on ligation.
3. United States Patent 6,391,649 Cowburn, et al. May 21, 2002 Method for the comparative quantitative analysis of proteins and other biological material by isotopic labeling and mass spectroscopy. Licensed by Invitrogen
4. United States Patent 6,642,059 Cowburn, et al. November 4, 2003 Method for the comparative quantitative analysis of proteins and other biological material by isotopic labeling and mass spectroscopy. Licensed by Invitrogen
5. World Patent WO9816638-A1; AU9674324-A Cowburn et al. 1998, Consolidated ligand comprising two ligands - for different binding domains on protein, used as diagnostic agent, for drug screening and therapeutically, has greater affinity and specificity than single ligands.

**Research Interests:**

Structure - function relationships in biological chemistry. Application of the above disciplines to understanding molecular contributions to physiological mechanisms in health and diseases of control of genetic expression, and of intracellular signal transduction. Development of magnetic resonance techniques in biomedical research.

**Publications: (Peer reviewed)**

127. Silvia Frutos, Michael Goger, Baldissera Giovani, David Cowburn and Tom W. Muir (2010) "Branched Intermediate Formation Stimulates Peptide Bond Cleavage in the *Mxe* GyrA Intein Protein Splicing Reaction", *Nat Chem Biol*
126. Ferrage, F., Shekhtman, D., Dutta, K., and Cowburn, D. (2010) "Structural Determination of Biomolecular Interfaces by Nuclear Magnetic Resonance of Proteins with Reduced Proton Density, *J. Biomol. NMR* **47** 41-54
125. Matthew P. Nicholas, Ertan Eryilmaz, Fabien Ferrage, David Cowburn, and Ranajeet Ghose (2010) "Nuclear Spin Resonance Relaxation in Isotropic and Anisotropic Media" *Prog. NMR Spectroscopy*
124. Bhattacharya, S., Dai, Z., Li, J., Baxter, S., Callaway, D.J., Cowburn, D., and Bu, Z. (2010). "A conformational switch in the sodium/ hydrogen exchange regulatory factor 1(NHERF1) controls autoinhibition and complex formation." *J Biol Chem.* **285** 9981-94

123. Piserchio, A., Ghose, R., Cowburn, D. (2009) "Optimized Bacterial Expression and Purification of the c-Src Catalytic Domain for Solution NMR Studies" *J. Biomol. NMR*, **44** 87-93.
122. Ferrage, F., Cowburn, D., Ghose, R. (2009) "Accurate Sampling of High-Frequency Motions in Proteins by Steady-State  $^{15}\text{N}$ - $\{^1\text{H}\}$  Nuclear Overhauser Effect Measurements in the Presence of Cross-Correlated Relaxation" *J. Am. Chem. Soc.* **131**, 6048-9.
121. Pellecchia, M.; Bertini, I.; Cowburn, D.; Dalvit, C.; Giralt, E.; Jahnke, W.; James, T. L.; Homans, S. W.; Kessler, H.; Luchinat, C.; Meyer, B.; Oschkinat, H.; Peng, J.; Schwalbe, H.; Siegal, G., (2008) Perspectives on NMR in drug discovery: a technique comes of age. *Nat Rev Drug Discov* **7** 738-745.
120. Schwartz EC, Shekhtman A, Dutta K, Pratt MR, Cowburn D, Darst S, Muir TW. (2008) "A full-length group 1 bacterial  $\sigma$  factor adopts a compact structure incompatible with DNA binding." *Chem Biol.* **15** 1091-103.
119. Bhattachara S., Zhang H., Debnath A., Cowburn D. (2008) "Solution structure of a peptide inhibitor in complex with monomeric C-terminal domain of HIV-1 capsid", *J Biol Chem*, **283** 16274-8.
118. Xiong X, Cui P, Hossain S, Xu R, Warner B, Guo X, An X, Debnath A, Cowburn D, Kotula L. (2008) . Allosteric Inhibition of the nonMyristoylated c-Abl Tyrosine Kinase by Phosphopeptides Derived from Abi1/Hssh3bp1. *BBA Molecular Cell Research*, **1783**, 737-47.
117. Zhang H, Zhao Q, Bhattacharya S, Waheed A, Tong X, Hong A, Heck S, Curreli F, Goger M, Cowburn D, Freed E, Debnath A. (2008) A Cell-penetrating Helical Peptide as a Potential HIV-1 Inhibitor. *J Mol Biol*, **378**, 565-80.
116. Liu D, Xu R, Dutta K, Cowburn D. (2008) N-terminal cysteinyl proteins can be prepared using thrombin cleavage. *FEBS letts*, **382**, 1163-7.
115. Ferrage F, Piserchio A, Cowburn D, Ghose R. (2008) On the Measurement of  $^{15}\text{N}$ - $\{^1\text{H}\}$  Nuclear Overhauser Effects. *J Mag Res*, **192**, 302-13.
114. Valentine ER, Ferrage F, Massi F, Cowburn D, and Palmer AG (2007) 'Joint Composite Rotation Adiabatic-Sweep Isotope Filtration' *J. Biomol. NMR* **38**, 11-22.
113. Ferrage, F, Pelepussey P, Cowburn D, Bodenhausen G (2007) "Intra-residue dipolar cross-relaxation rates between  $^{13}\text{C}\alpha$  and  $^{13}\text{C}'$  as a measure of internal dynamics in proteins by NMR Spectroscopy" *J. Am. Chem. Soc.* **128** 11072-8
112. Ji, H., Shekthman, A., McDonnell, J., Ghose, R., Cowburn D. (2006) "NMR determination that an extended BH3 motif of pro-apoptotic BID is specifically bound to BCL-X<sub>L</sub>" *Magnetic Res. Chem.* **44** 101-6

111. Mukherjee, M., Dutta, K., White, M.A., Cowburn, D., Fox, R.O. (2006) "NMR solution structure and backbone dynamics of domain III of the E protein of tick-borne Langat flavivirus, suggests a potential site for molecular recognition" *Protein Science* **15** 1342-1355.
110. Muliharan V., Dutta K., Cho J., Vila-Perello M., Raleigh DP., Cowburn D., Muir TW 'Solution Structure and Folding Characteristics of the C-Terminal SH3 Domain of c-Crk-II' *Biochemistry* **45** 8874-8884
109. Burz, D.S., Dutta, K., Cowburn, D., Shekhtman, A. (2006) Mapping structural interactions in proteins using NMR (STINT-NMR). *Nature Methods* **3**, 93-95
108. Romanelli, A., Shekhtman, A., Cowburn, D., and Muir, T. W. (2004). "Semisynthesis of a segmental isotopically labeled protein splicing precursor: NMR evidence for an unusual peptide bond at the N-extein-intein junction". *Proceedings of the National Academy of Sciences U S A* **101**, 6397-6402
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105. Shekhtman, A., Ghose, R., Goger, M., and Cowburn, D. (2002). "NMR structure determination and investigation using a reduced proton (REDPRO) labeling strategy for proteins". *FEBS Lett* **524**, 177-182
104. Camarero, J. A., Shekhtman, A., Campbell, E. A., Chlenov, M., Gruber, T. M., Bryant, D. A., Darst, S. A., Cowburn, D., and Muir, T. W. (2002). "Autoregulation of a bacterial sigma factor explored by using segmental isotopic labeling and NMR". *Proceedings of the National Academy of Sciences of the United States of America* **99**, 8536-8541.
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92. Fushman, David; Xu, Rong; Cowburn, David. (1999) "Direct determination of changes of interdomains orientation on ligation: use of the orientational dependence of  $^{15}\text{N}$  NMR relaxation in Abl SH(32)" *Biochemistry*, **38**, 10225-10230.
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88. Pfeiffer, Stephania; Fushman, David, and Cowburn, David (1999) "Impact of Cl<sup>-</sup> and Na<sup>+</sup> ions on simulated structure and dynamics of  $\beta$ ARK1 PH domain", *Proteins*, **35**, 206-19.
87. Xu, Rong; Ayers, Brenda; Cowburn, David; Muir, Tom W. (1999) "Chemical Ligation of Folded Recombinant Proteins: Segmental Isotopic Labeling of Domains for NMR Studies" *PNAS*, **96**, 388-393.
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84. Fushman, David; Cowburn, David. (1998) "Model-independent analysis of <sup>15</sup>N chemical shift anisotropy from NMR relaxation data. Ubiquitin as a test example." *J. Am. Chem. Soc.* **120**, 7109-7110.
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- R3. Karlin, A; Cowburn, D. "Molecular properties of membrane-bound and of solubilised and purified acetylcholine receptor identified by affinity labeling." (1974) *Neurochemistry of cholinergic receptors*. Ed. E. De Robertis and R. Schacht. Raven Press, New York .
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- R1. Cowburn D. "Equilibrium and kinetic studies of the conformation of proteins." (1970) Thesis University of London.

Numerous other anonymous publications as editorial correspondent of journals and as contributor to computer program libraries.

### **Theses**

- 1978 Alan J. Fischman. "The solution conformation of oxytocin." Ph. D.
- 1978 Dana Giulian, M.D. "Biochemical events within the visual system of the goldfish during neural regeneration." Ph. D.
- 1980 Alan K. Engel. "NMR studies of isotopic isomers of Dipalmitoyl Phosphatidyl Choline." Ph. D.
- 1993 Michael Overduin. "Solution structure of c-Abl SH2" Ph .D.

### **Reviewing, Consulting, Adjunct Positions**

I have been a reviewer for, consultant to, or have held adjunct, board, or editorial positions with the following agencies or journals:

National Institutes of Health; National Science Foundation; U.S. Department of Defense; U.S. Dept. of Energy; European Commission; Canadian Foundation for Innovation; U.S.-Israel Bi-national Science Foundation; New York State Health Department; State of Missouri; American Heart Association; American Cancer Society; Wellcome Trust; BBSRC; Petroleum Research Fund; Memorial Sloan-Kettering Cancer Center; New York Hospital/ Cornell University Medical College; New York University; Columbia University; Albert Einstein College of Medicine; Australian National University; City University of New York; Mount Sinai School of Medicine; Eastern Analytical Symposium; NMR Concepts; General Electric; Kodak; Lederle Laboratories; Technovon Corp.; Intermagnetics General Co.; Oxford University Press; Nature; Science; Cell; Proceedings of the National Academy of Science; New England Journal of Medicine; EMBO Journal; Journal of The American Chemical Society; Biochemistry; The

Journal of Biological Chemistry; Bioorganic Chemistry; The Journal of Magnetic Resonance; Journal of Experimental Medicine; Journal of Molecular Biology; Journal of Biomolecular Stereodynamics; Biopolymers; Molecular and Biochemical Parasitology; The Medical Letter; International Journal of Peptide and Protein Research; Canadian Journal of Chemistry; Steroids; Concepts in Magnetic Resonance; Magnetic Resonance in Medicine; Inorganic Chemistry; Open Cell Signaling Journal; PLOS Computational Biology.

### **Funded Grants Since 2000:**

- 1992- National Institutes of Health, "Structural Biology of Tyrosyl Kinases"
- 2000- National Institutes of Health, "Segmental labeling for protein NMR" (PI Tom Muir)
- 2000-03 DOD Breast Cancer, "Designed Mimics of BH3 motifs"
- 2000 -04 National Institutes of Health, "Myosin Binding Proteins" (PI Don Fischman)
- 2001-09 New York State Office of Science, Technology and Academic Research, "Strategically Targeted Academic Research Center"
- 2002 National Institutes of Health, "Research Facilities Construction"
- 2002-08 National Institutes of Health, "900 MHz NMR Spectrometer for Structural Biology"
- 2002-08 Department of the Army, "900 MHz NMR Spectrometer for Structural Biology"
- 2005-09 National Institutes of Health "Novel Receptors for vitamin A in the cytoplasm" (PI Ulrich Hammerling)
- 2008- National Institutes of Health, "Dynamic character of kinase domains" (PI Ranajeet Ghose)
- 2009- National Institutes of Health, "Rational design of HIV capsid inhibitors" (PI Asim Debnath)

### **Society Memberships.**

The American Society of Biochemistry and Molecular Biology; The American Chemical Society; American Association for the Advancement of Science, New York Academy of Science.

### **Selected Recent Lectures**

**2009** University of South Florida – Structural Biology using NMR

- Albert Einstein College of Medicine – Dynamic structures in protein – protein interactions.
- 2008** Duke University – Biochemistry Seminar  
New York University (Chemistry)  
Academy of American Medical Colleges – The New York Structural Biology Center  
U Colorado Cancer Center – Structural Biology in Cancer Drug Design  
Mid-Atlantic American Chemical Society – Developing a Dynamic Structural View of Protein
- 2007** U. Maryland – Symposium in Modern Applications of NMR  
U. Kansas – Symposium on protein interaction modeling
- 2006** XXII ICMRBS – Gottingen – Protein Interfaces  
Cleveland Center for Structural Biology – Frontiers of NMR Spectroscopy  
NHLBI, NIH – Forty years of NMR in Biological Systems
- 2005** Rockefeller U - NMR determination of protein structure, Biochem. Course  
IBM Almaden - The future of Structural Biology  
XXI ICMRBS, Hyderabad, India - Reduced proton density interface mapping
- 2004** Bionet Conference on Enabling Technologies, Durham, UK - Using NMR to study protein domain interactions  
Tokyo Metropolitan University - New methods of isotope labeling  
Yokohama U. - NMR studies of Csk  
ANZMAG 04 - What NMR can do in studying domain motions

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