

## CURRICULUM VITAE

Name: Carl O. Pabo

Born: September 1, 1952

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Education:

Yale College New Haven, Connecticut B.S. ( <i>summa cum laude</i> ) Molecular Biophysics and Biochemistry	1974
Harvard University Cambridge, Massachusetts Ph.D., Biochemistry and Molecular Biology	1980

Positions:

Postdoctoral Fellow Department of Biochemistry and Molecular Biology Harvard University	1980–1982
Assistant Professor Department of Biophysics Johns Hopkins University School of Medicine	1982–1986
Associate Professor Department of Molecular Biology and Genetics and Department of Biophysics Johns Hopkins University School of Medicine	1986–1990
Associate Investigator Howard Hughes Medical Institute	1986–1991
Professor Department of Molecular Biology and Genetics and Department of Biophysics Johns Hopkins University School of Medicine	1990–1991
Professor Department of Biology Massachusetts Institute of Technology	1991–2001
Investigator Howard Hughes Medical Institute	1991–2001

Investigator Center for Cancer Research Massachusetts Institute of Technology	1999–2001
Senior Vice President and Chief Scientific Officer Sangamo BioSciences, Inc.	2001–2003
Chair, Scientific Advisory Board Sangamo BioSciences, Inc.	1998–2001; 2003–2008
Moore Distinguished Scholar California Institute of Technology	January 2004 – April 2004
Visiting Professor, Bio-X Program Stanford University	September 2004 – April 2005
Visiting Professor, Department of Systems Biology Harvard Medical School	June 2005 – July 2005
Miller Visiting Research Professor University of California at Berkeley	August 2005 – December 2005
Visiting Professor, Department of Systems Biology Harvard Medical School	February 2006 – May 2007
Founder and Research Director Protean Futures LLC	September 2007 – Present
Scientific Advisor NanoDimension	March 2008 – Present
Visiting Professor, Division of Biology and Biological Engineering California Institute of Technology	April 2017 – June 2017
Founder and President Humanity 2050, Inc. ( <a href="http://humanity2050.org">humanity2050.org</a> )	August 2017 – Present

Awards:

Elected to Phi Beta Kappa, 1973

NSF Predoctoral Fellowship, 1974–1977

Jane Coffin Childs Memorial Fund  
Postdoctoral Fellowship, 1980–1982

American Cancer Society Junior Faculty Research Award, 1983–1985

Protein Society Young Investigator Award, 1991

Pfizer Award in Enzyme Chemistry, 1992

Elected to American Academy of Arts and Sciences, 1993

Elected to National Academy of Sciences, 1998

Guggenheim Fellowship (“Theories of Thought”), 2005–2006

Teaching:

I have taught courses at Johns Hopkins, MIT, Caltech, and Stanford on biophysical chemistry, X-ray crystallography, protein design and engineering, evolution, theories of thought, and “The World in 2050.”

I have had extensive experience (both in academics and industry) as a mentor and advisor to young scientists.

Research:

I was born and have lived as an explorer: trying to understand everything I can about life, the world, the human condition, and prospects for the human future.

I started my career — building a solid foundation for all later work — by taking a strictly scientific stance, working on the structure and design of DNA-binding proteins, using X-ray crystallography to determine the atomic details of protein-DNA interactions, and then learning how to design novel DNA-binding proteins that bound so tightly and specifically that they were used (even before CRISPR) as tools for genome editing.

However, in much the way that Columbus and Magellan always wondered about the “world beyond the horizon,” I kept wondering about atomic/molecular systems (as with the human brain, and as with human societies) that were too complicated to usefully be described at an atomic/molecular level.

Seeing the chaos that filled the newspapers, seeing that scientific knowledge (by itself) cannot solve the fundamental problems facing the modern world, I felt impelled to see if I could find some better way to think about human thought and the human future, some better way to help address the most fundamental challenges now facing society. I thus resigned my tenured faculty position as a full professor at MIT and resigned my appointment as an Investigator with the Howard Hughes Medical Institute. I sailed on.

Since that time, I have developed a new way of describing and analyzing thought, using a physical frame of reference that encompasses both words and world. That is: I start by keeping everything grounded with reference to a flow of atomic, molecular events, avoiding any temptation to ever slip and start speaking of symbols, ideas, or thought as if they might exist in some separate, abstract, ethereal realm. (Thought is just one of the many things that complex assemblies of atoms and molecules can do; ideas are just one aspect of the way in which these atomic/molecular systems can be arranged and in which information can move.)

Once I had this clear way of keeping ideas grounded in the physical world, I then developed a set of flow diagrams — using a few, simple symbols to help track the ways in which information (ideas) can move and change form. Although my model only needs about a half dozen such symbols, these can be combined to construct

complex flow diagrams, showing the overall flow of information that occurs as we speak; as we think; as we act; as we work with others in a democratic system.

I have a draft manuscript from 2018 (*Mind in the 21st Century: Human Thought for a Human Future*) that gives a broad overview of this new approach; yet — as described below — I'm most interested in using these ideas to address the pressing challenges of the human future, and I have developed a more focused way to proceed.

Humanity 2050:

I founded an institute — Humanity 2050 — that focuses on hyper-complex challenges of the modern age — challenges like global warming, environmental degradation, risks to the stability of our financial and social systems, risks posed by the rise of artificial intelligence, etc. We thus work to help ensure a livable human future for our children and grandchildren.

The strategies that we use at Humanity 2050 build on my model of thought and ideas from my draft manuscript on human thought and the human future, but we now boil this down to an approach — as described in white papers on our website — that involves the use of 1) “special focus teams” and 2) a new “algorithm for thought.” We thus offer a clear, “actionable” strategy for thought designed to help society develop better ways to address the challenges of the human future, and we are testing this approach with a first project that explores prospects for climate engineering (via the use of stratospheric aerosols) as a way to help cool the Earth and thus try avoiding the worst ravages of climate change. The potential risks, and potential rewards, are so great that there is a desperate need for our new tools for thought — helping society make an informed decision about one of the most fateful choices ever to confront our species.

Patents:

Listed on last two pages of CV (after publications).

## PUBLICATIONS

1. Pabo, C.O., Sauer, R.T., Sturtevant, J.M. & Ptashne, M. (1979) The  $\lambda$  Repressor Contains Two Domains. **Proc. Natl. Acad. Sci., USA** **76**, 1608-1612.
2. Sauer, R.T., Pabo, C.O., Meyer, B.J., Ptashne, M. & Backman, K.C. (1979) The Regulatory Functions of the  $\lambda$  Repressor Reside in the Amino-Terminal Domain. **Nature** **279**, 396-400.
3. Johnson, A.D., Pabo, C.O. & Sauer, R. T. (1980) Bacteriophage  $\lambda$  Repressor and Cro Protein: Interactions with Operator DNA. **Meth. Enz.** **65**, 839-856.
4. Ptashne, M., Jeffrey, A., Johnson, A.D., Mauer, R., Meyer, B.J., Pabo, C.O., Roberts, T.M. & Sauer, R.T. (1980) How the  $\lambda$  Repressor and Cro Work. **Cell** **19**, 1-11.
5. Pabo, C.O., Krovatin, W., Jeffrey, A. & Sauer, R.T. (1982) The N-Terminal Arms of  $\lambda$  Repressor Wrap Around the Operator DNA. **Nature** **298**, 441-443.
6. Pabo, C.O. & Lewis, M. (1982) The Operator-Binding Domain of  $\lambda$  Repressor: Structure and DNA Recognition. **Nature** **298**, 443-447.
7. Sauer, R.T., Yocum, R.R., Doolittle, R.F., Lewis, M. & Pabo, C.O. (1982) Homology Among DNA-Binding Proteins Suggests Use of a Conserved Super-Secondary Structure. **Nature** **298**, 447-451.
8. Ptashne, M., Johnson, A.D. & Pabo, C.O. (1982) A Genetic Switch in a Bacterial Virus. **Scientific American** **247**, 128-140.
9. Lewis, M., Jeffrey, A., Wang, J-H., Ladner, R.C., Ptashne, M. & Pabo, C.O. (1983) Structure of the Operator-Binding Domain of  $\lambda$  Repressor: Implications for DNA Recognition and Gene Regulation. **Cold Spring Harbor Symp. Quant. Biol.** **47**, 435-440.
10. Gussin, G., Johnson, A.D., Pabo, C.O. & Sauer, R.T. (1983) Repressor and Cro. **Lambda II** (J. Roberts, ed.) Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 93-121.
11. Ohlendorf, D.H., Anderson, W.F., Lewis, M., Pabo, C.O. & Matthews, B.W. (1983) Comparison of the Structures of Cro and  $\lambda$  Repressor Proteins from Bacteriophage  $\lambda$ . **J. Mol. Biol.** **169**, 757-769.
12. Sauer, R.T. & Pabo, C.O. (1983) Protein-DNA Recognition: The  $\lambda$  Repressor-Operator Complex. **American Society for Microbiology News** **49**, 131-136.
13. Pabo, C.O. (1983) Designing Proteins and Peptides. **Nature** **301**, 200.
14. Pabo, C.O., Jordan, S.R. & Frankel, A.D. (1983) Systematic Analysis of Possible Hydrogen Bonds Between Amino Acid Side Chains and B-Form DNA. **J. Biomolecular Structure and Dynamics** **1**, 1039-1049.
15. Sauer, R.T. & Pabo, C.O. (1984) How  $\lambda$  Repressor Binds Operator DNA. **Microbiology** **1984**.
16. Pabo, C.O. & Sauer, R.T. (1984) Protein-DNA Recognition. **Ann. Rev. Biochem.** **53**, 293-321.
17. Pabo, C.O. (1984) DNA-Protein Interactions. **Proceedings of the Robert A.**

**Welch Foundation Conferences on Chemical Research XXVII Stereospecificity in Chemistry and Biochemistry**, Robert A. Welch Foundation, Houston, TX, 222-255.

18. Lewis, M., Wang, J. & Pabo, C.O. (1985) Structure of the Operator Binding Domain of  $\lambda$  Repressor. **Biological Macromolecules and Assemblies, Volume 2** (Drs. Journak & McPherson, eds.) John Wiley and Sons, Inc., New York, 266-287.
19. Jordan, S.R., Pabo, C.O., Vershon, A.K. & Sauer, R.T. (1985) Crystallization of the Arc Repressor. **J. Mol. Biol.** **185**, 445-446.
20. Jordan, S.R., Whitcombe, T.V., Berg, J.M. & Pabo, C.O. (1985) Systematic Variation in DNA Length Yields Highly Ordered Repressor-Operator Co-Crystals. **Science** **230**, 1383-1385.
21. Pabo, C.O. & Suchanek, E.G. (1986) Computer-Aided Model-Building Strategies for Protein Design. **Biochemistry** **25**, 5987-5991.
22. Sauer, R.T., Hehir, K., Stearman, R.S., Weiss, M.A., Jeitler-Nilsson, A., Suchanek, E.G. & Pabo, C.O. (1986) An Engineered Intersubunit Disulfide Enhances the Stability and DNA Binding of the N-Terminal Domain of  $\lambda$  Repressor. **Biochemistry** **25**, 5992-5998.
23. Weiss, M.A., Pabo, C.O., Karplus, M. & Sauer, R.T. (1986) Dimerization of the Operator-Binding Domain of Phage  $\lambda$  Repressor. **Biochemistry** **26**, 897-904.
24. Pabo, C.O. (1987) Introductory chapter for **Protein Engineering** (D. L. Oxender & C. F. Fox, eds.) Alan R. Liss, Inc., New York, xv-xvii.
25. Berg, J.M., Jordan, S.R. & Pabo, C.O. (1987) The Structure and Function of Bacteriophage  $\lambda$  Repressor. **DNA: Protein Interactions and Gene Regulation** (E.B. Thompson & J. Papaconstantinou, eds.) University of Texas Press, Austin, 1-12.
26. Pabo, C.O. (1987) New Generation Databases for Molecular Biology. **Nature** **327**, 467.
27. Frankel, A.D., Berg, J.M. & Pabo, C.O. (1987) Metal-Dependent Folding of a Single Zinc Finger from Transcription Factor IIIA. **Proc. Natl. Acad. Sci., USA** **84**, 4841-4845.
28. Frankel, A.D., Bredt, D.S. & Pabo, C.O. (1988) Tat Protein from Human Immunodeficiency Virus Forms a Metal-Linked Dimer. **Science** **240**, 70-73.
29. Frankel, A.D. & Pabo, C.O. (1988) Fingering Too Many Proteins. **Cell** **53**, 675.
30. Frankel, A.D., Chen, L., Cotter, R.J. & Pabo C.O. (1988) Dimerization of the Tat Protein from HIV: A Cysteine-Rich Peptide Mimics the Normal Metal-Linked Dimer Interface. **Proc. Natl. Acad. Sci., USA** **85**, 6297-6300.
31. Stearman, R.S., Frankel, A.D., Freire, E., Liu, B. & Pabo, C.O. (1988) Combining Thermostable Mutations Increases the Stability of  $\lambda$  Repressor. **Biochemistry** **27**, 7571-7574.
32. Jordan, S.R. & Pabo, C.O. (1988) Structure of the  $\lambda$  Complex at 2.5 Å Resolution: Detailed View of the Repressor-Operator Interactions. **Science** **242**, 893-899.

33. Frankel, A.D. & Pabo, C.O. (1988) Cellular Uptake of the Tat Protein from Human Immunodeficiency Virus. **Cell** **55**, 1189-1193.
34. Sauer, R.T., Jordan, S.R. & Pabo, C.O. (1990)  $\lambda$  Repressor: A Model System for Understanding Protein-DNA Interactions and Protein Stability. **Adv. Prot. Chem.** **40**, 1-61.
35. Bowie, J.U., Clarke, N.D., Pabo, C.O. & Sauer, R.T. (1990) Identification of Protein Folds: Matching Hydrophobicity Patterns of Sequence Sets with Solvent Accessibility Patterns of Known Structures. **Proteins** **7**, 257-264.
36. Pabo, C.O., Aggarwal, A.K., Jordan, S.R., Beamer, L.J., Obeysekare, U. & Harrison, S.C. (1990) Conserved Residues Make Similar Contacts in Two Repressor-Operator Complexes. **Science** **247**, 1210-1213.
37. Liu, B., Kissinger, C.R., Pabo, C.O., Martin-Blanco, E. & Kornberg, T.B (1990) Crystallization and Preliminary X-ray Diffraction Studies of the Engrailed Homeodomain and of an Engrailed Homeodomain/DNA Complex. **Biochem. and Biophys. Res. Comm.** **171**, 257-259.
38. Kissinger, C.R., Liu, B., Martin-Blanco, E., Kornberg, T.B. & Pabo, C.O. (1990) Crystal Structure of an Engrailed Homeodomain/DNA Complex at 2.8 Å Resolution: A Framework for Understanding Homeodomain/DNA Interactions. **Cell** **63**, 579-590.
39. Wolberger, C., Pabo, C.O., Vershon, A.K. & Johnson, A.D. (1991) Crystallization and Preliminary X-ray Diffraction Studies of a MAT $\alpha$ 2-DNA Complex. **J. Mol. Biol.** **217**, 11-13.
40. Pavletich, N.P. & Pabo, C.O. (1991) Zinc Finger-DNA Recognition: Crystal Structure of a Zif268-DNA Complex at 2.1 Å. **Science** **252**, 809-817.
41. Wolberger, C. Vershon, A.K., Liu, B., Johnson, A.D. & Pabo, C.O. (1991) Crystal Structure of a MAT $\alpha$ 2 Homeodomain-Operator Complex Suggests a General Model for Homeodomain-DNA Interactions. **Cell** **67**, 517-528.
42. Clarke, N.D., Beamer, L.J., Goldberg, H.R., Berkower, C. & Pabo, C.O. (1991) The DNA Binding Arm of  $\lambda$  Repressor: Critical Contacts from a Flexible Region. **Science** **254**, 267-270.
43. Godley, L., Pfeifer, J., Steinhauer, D., Ely, B., Shaw, G., Kaufmann, R., Suchanek, E., Pabo, C., Skehel, J.J., Wiley, D.C. & Wharton, S. (1992) Introduction of Intersubunit Disulfide Bonds In the Membrane-Distal Region of the Influenza Hemagglutinin Abolishes Membrane Fusion Activity. **Cell** **68**, 635-645.
44. Pabo, C.O. & Sauer, R.T. (1992) Transcription Factors: Structural Families and Principles of DNA Recognition. **Annu. Rev. Biochem.** **61**, 1053-1095.
45. Beamer, L.J. & Pabo, C.O. (1992) Refined 1.8 Å Crystal Structure of the  $\lambda$  Repressor Operator Complex. **J. Mol. Biol.** **227**, 177-196.
46. Pavletich, N.P. & Pabo, C.O. (1993) Crystal Structure of a Five Finger GLI-DNA Complex: New Perspectives on Zinc Fingers. **Science** **261**, 1701-1707.
47. Pavletich, N.P., Chambers, K.A. & Pabo, C.O. (1993) The DNA-Binding Domain of p53 Contains the Four Conserved Regions and the Major Mutation Hot Spots. **Genes & Development** **7**, 2556-2564.

48. Rebar, E.J. & Pabo, C.O. (1994) Zinc Finger Phage: Affinity Selection of Fingers with New DNA-Binding Specificities. **Science** **263**, 671-673.
49. Raumann, B.E., Rould, M.A., Pabo, C.O. & Sauer, R.T. (1994) DNA Recognition by  $\beta$ -sheets in the Arc Repressor-Operator Crystal Structure. **Nature** **367**, 754-757.
50. Klemm, J.D., Rould, M.A., Aurora, R., Herr, W. & Pabo, C.O. (1994) Crystal Structure of the Oct-1 POU Domain Bound to an Octamer Site: DNA Recognition with Tethered DNA-Binding Modules. **Cell** **77**, 21-32.
51. Ma, P.C.M., Rould, M.A., Weintraub, H. & Pabo, C.O. (1994) Crystal Structure of MyoD bHLH Domain-DNA Complex: Perspectives on DNA Recognition and Implications for Transcriptional Activation. **Cell** **77**, 451-459.
52. Nekludova, L. & Pabo, C.O. (1994) Distinctive DNA Conformation with Enlarged Major Groove Is Found in Zn Finger-DNA and Other Protein-DNA Complexes. **Proc. Natl. Acad. Sci., USA**, **91**, 6948-6952.
53. Clarke, N.D., Kissinger, C.R., Desjarlais, J., Gilliland, G.L., & Pabo, C.O. (1994) Structural Studies of the Engrailed Homeodomain. **Prot. Sci.** **3**, 1779-1787.
54. Pomerantz, J.L., Sharp, P.A., & Pabo, C.O. (1995) Structure-Based Design of Transcription Factors. **Science** **267**, 93-96.
55. Xu, W., Rould, M.A., Jun, S., Desplan, C., & Pabo, C.O. (1995) Crystal Structure of a Paired Domain-DNA Complex at 2.5 Å Resolution Reveals Structural Basis for Pax Developmental Mutations. **Cell** **80**, 639-650.
56. Pomerantz, J.L., Pabo, C.O., & Sharp, P.A. (1995) Analysis of Homeodomain Function by Structure-Based Design of a Transcription Factor. **Proc. Natl. Acad. Sci., USA** **92**, 9752-9756.
57. Klemm, J.D. & Pabo, C.O. (1996) Oct-1 POU Domain-DNA Interactions: Cooperative Binding of Isolated Subdomains and Effects of Covalent Linkage. **Genes & Development** **10**, 27-36.
58. Rebar, E.J., Greisman, H.A., & Pabo, C.O. (1996) Phage Display Methods for Selecting Zinc Finger Proteins with Novel DNA-Binding Specificities. **Methods In Enzymology** **267**, 129-149.
59. Elrod-Erickson, M., Rould, M.A., Nekludova, L., & Pabo, C.O. (1996) Zif268 Protein-DNA Complex Refined at 1.6 Å: A Model System for Understanding Zinc Finger-DNA Interactions. **Structure** **4**, 1171-1180.
60. Greisman, H.A. & Pabo, C.O. (1997) A General Strategy for Selecting High-Affinity Zinc Finger Proteins for Diverse DNA Target Sites. **Science** **275**, 657-661.
61. Kim, J.-S., Kim, J., Cepek, K.L., Sharp, P.A., & Pabo, C.O. (1997) Design of TATA Box-Binding Protein/Zinc Finger Fusions for Targeted Regulation of Gene Expression. **Proc. Natl. Acad. Sci., USA** **94**, 3616-3620.



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64. Pomerantz, J.L., Wolfe, S.A., & Pabo, C.O. (1998) Structure-Based Design of a Dimeric Zinc Finger Protein. **Biochemistry** **37**, 965-970.
65. Kim, J.-S. & Pabo, C.O. (1998) Getting a Handhold on DNA: Design of Poly-Zinc Finger Proteins with Femtomolar Dissociation Constants. **Proc. Natl. Acad. Sci. USA** **95**, 2812-2817.
66. Elrod-Erickson, M., Benson, T.E., & Pabo, C.O. (1998) High-Resolution Structures of Variant Zif268-DNA Complexes: Implications for Understanding Zinc Finger-DNA Recognition. **Structure** **6**, 451-464.
67. Fraenkel, E. & Pabo, C.O. (1998) Comparison of X-ray and NMR Structures for the Antennapedia Homeodomain-DNA Complex. **Nature Struct. Bio.** **5**, 692-697.
68. Fraenkel, E., Rould, M.A., Chambers, K.A., & Pabo, C.O. (1998) Engrailed Homeodomain-DNA Complex at 2.2 Å Resolution: A Detailed View of the Interface and Comparison with Other Engrailed Structures. **J. Mol. Biol.** **284**, 351-361.
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71. Xu, H.E., Rould, M.A., Xu, W., Epstein, J.A., Maas, R.L., & Pabo, C.O. (1999) Crystal Structure of the Human Pax6 Paired Domain-DNA Complex Reveals Specific Roles for the Linker Region and Carboxy-terminal Subdomain in DNA Binding. **Genes & Development** **13**, 1263-1275.
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- Vascular Endothelial Growth Factor A in Glioblastoma Cells Using Engineered Zinc Finger Transcription Factors. **Cancer Res.** **63**, 8968-8976.
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## PATENTS

### Protein Translocation

Frankel, A., Pabo, C.O., Barsoum, J.G., Fawell, S.E., Pepinsky, and Blake, R. (inventors for the first six patents listed below):

**Nucleic Acids Encoding and Methods of Making Tat-derived Transport Polypeptides** (US patent #5,652,122; issued in 1997)

**Nucleic Acid Conjugates of Tat-derived Transport Polypeptides** (US patent #5,670,617; issued in 1997)

**Fusion Protein Comprising Tat-derived Transport Moiety** (US patent #5,674,980; issued in 1997)

**Tat-derived Transport Polypeptide Conjugates** (US patent #5,747,641; issued in 1998)

**Tat-derived Transport Polypeptides and Fusion Proteins** (US patent #5,804,604; issued in 1998)

**Tat-derived Transport Polypeptides** (US patent #6,316,003; issued in 2001)

Design of DNA-Binding Proteins

Rebar, E.J. and Pabo, C.O. --- **Zinc Finger Proteins with High Affinity New DNA Binding Specificities** (US patent #5,789,538; issued in 1998)

Pomerantz, J.L., Sharp, P.A., and Pabo, C.O. --- **Chimeric DNA-Binding Proteins** (US patent #6,326,166; issued in 2001; US patent #7,008,780; issued in 2006; US patent #7,485,441; issued in 2009; and US patent #7,763,446; issued in 2010)

Greisman, H.A. and Pabo, C.O. --- **General Strategy for Selecting High-Affinity Zinc Finger Proteins for Diverse DNA Target Sites** (US patent #6,410,248; issued in 2002)

Kim, J-S. and Pabo, C.O. --- **Poly Zinc Finger Proteins with Improved Linkers** (US patent #6,479,626; issued in 2002; US patent #6,903,185; issued in 2005; US patent #7,595,376; issued in 2009; and US patent #7,928,195; issued in 2011)

Kim, J-S. and Pabo, C.O. --- **Nucleic Acid Encoding Poly-Zinc Finger Proteins with Improved Linkers** (US patent #7,153,949; issued in 2006)

Joung, J.K., Miller, J., and Pabo, C.O. --- **Methods and Compositions for Interaction Trap Assays** (US patent #7,029,847; issued in 2006; US patent #7,297,491; issued in 2007; and US patent #7,393,318; issued in 2008)

Miller, J., Guofu, L., Pabo, C.O., and Collingwood, T. --- **Simultaneous Modulation of Multiple Genes** (US patent #7,361,635; issued in 2008 and US patent #7,939,327; issued in 2011)

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Wang, B.S. and Pabo, C.O. --- **Dimerizing Peptides** (US patent #7,943,731; issued in 2011)