

LYNNE REGAN

Professor of Molecular Biophysics & Biochemistry and Chemistry

EDUCATION

- 1977-1981 Oxford University B.A. (First Class Honors) Biochemistry
Distinction in Chemical Pharmacology
- 1981-1987 M.I.T., Department of Biology, Ph.D.

HONORS AND AWARDS

- 1977-1978 The Nuffield Exhibition in Biochemistry
- 1978-1981 The Nuffield Scholarship in Biochemistry
- 1981 The Gibbs Prize: Top First Class Honor, Degree in Biochemistry, Oxford University
The Hurry Prize: Top First Class Honors Degree, St. Hugh's College
- 1981-1983 Fulbright-Hayes Scholarship
- 1989-1990 The British Ramsay Fellowship in Chemistry
- 1992-1994 Shannon Award, NIH
- 1992-1997 National Young Investigator Award, NSF
- 1995 Camille Dreyfus Teacher-Scholar
- 1996 Margaret O. Dayhoff Award, Biophysical Society: Most promising young woman in biophysics
- 1998 Burroughs Wellcome Travel Award for sabbatical research in U.K.
- 1998 Wadsworth Center's Dickerman Award: Exceptional creativity in basic scientific research
- 2000 Eli Lilly Distinguished Lecturer, Colorado State University
- 2001 Distinguished Lecturer, Scripps Research Institute
- 2002 Distinguished CABR Lecturer, Center for Advanced Biomolecular Research, Departments of chemistry & Biochemistry, Texas A&M
- 2004 Keynote speaker, Undergraduate Science Research Symposium, Haverford College
- 2005 Guggenheim Fellowship

PROFESSIONAL EXPERIENCE

- 1987-1989 Visiting Scientist with Dr. W. F. DeGrado, CR&D, E. I. du Pont de Nemours & Co. Wilmington DE
- 1989-1990 Visitor, Structural Studies Division, The Laboratory of Molecular Biology, MRC, Cambridge, U.K.
- 1990-present Assistant, Associate, Professor (since 1998) of Molecular Biophysics and Biochemistry, Yale University
- 2000-present Professor of Chemistry, Yale University

SELECTED PROFESSIONAL ACTIVITIES

Reviewer of grants for many national and international research councils and private organizations. Council or committee member for Protein Society, Peptide Society, American Chemical Society. Conference organizer: Gordon Research Conference, Proteins, 2001 & 2003; Protein Society Annual Symposium 2004. Editorial Board of several journals. Scientific Advisory Board of COBRE University of

Delaware. Creator and executor of demonstrations to engage elementary school students in the excitement of science. Mentor and co-mentor of undergraduate researchers, from Yale, other institutions, high school and under-represented minorities (STARS program at Yale)
Executive committee of Proteomics & Genomics at Yale University; Head of Functional Genomics.

PUBLICATIONS

Jasin M., Regan L., & Schimmel P. (1983) "Modular arrangement of functional domains along the sequence of an aminoacyl tRNA synthetase" **Nature** 306:441-7.

Jasin M., Regan L., & Schimmel P. (1984) "Dispensable pieces of an aminoacyl tRNA synthetase which activate the catalytic site" **Cell** 36:1089-95.

Schimmel P., Jasin M., & Regan L. (1984) "Size polymorphism and the structure of aminoacyl-tRNA synthetases" **Fed. Proc.** 43:2987-90.

Jasin M., Regan L., & Schimmel P. (1985) "Two mutations in the dispensable part of alanine tRNA synthetase which affect the catalytic activity" **J. Biol. Chem.** 260:2226-30.

Regan L, Dignam J.D. & Schimmel P. (1986) "A bacterial and silkworm aminoacyl-tRNA synthetase have a common epitope which maps to the catalytic domain of each" **J. Biol. Chem.** 261:5241-4.

Regan L., Bowie J. & Schimmel, P. (1987) "Polypeptide sequences essential for RNA recognition by an enzyme" **Science** 235:1651-1653.

DeGrado W.F., Regan L., & Ho S.P. (1987) "The design of a four-helix bundle protein" **Cold Spring Harb. Symp. Quant. Biol.** 52:521-6

Regan L., Buxbaum L., Hill K. & Schimmel P. (1988) "Rationale for engineering an enzyme by introducing a mutation that compensates for a deletion" **J. Biol. Chem.** 263:18598-600.

Regan L. & Degrado W. F. (1988) "Characterization of a helical protein designed from first principles" **Science** 241:976-978.

Regan L. & Clarke N.D (1990) "A tetrahedral Zn(II)-binding site introduced into a designed protein" **Biochemistry** 29:10878-10883.

Marqusee S. & Regan L. (1991) "Deconstructing protein structure" **Curr. Biol.** 1:207-8

Regan L. (1991) "Protein design" **Curr. Opin. Biotechnol.** 2:544-50.

Regan L. (1993) "What determines where alpha-helices begin and end?" **Proc. Natl.**

Acad. Sci. U S A. 90:10907-8.

Regan L. (1993) "The design of metal-binding sites in proteins" **Annu. Rev. Biophys. Biomol. Struct.** 22:257-87

Munson M., O'Brien R., Sturtevant J. M. & Regan L. (1994) "Redesigning the hydrophobic core of a four-helix bundle protein" **Protein Science** 3:2015-2022.

Smith C. K., Withka J. M. & Regan L. (1994) "A thermodynamic scale for the β -sheet forming tendencies of the amino acids" **Biochemistry** 33:5510-5517.20)

Regan L. (1994) "Protein structure. Born to be beta" **Curr. Biol.** 4:656-8

Munson M., Predki P.F., & Regan L. (1994) "ColE1-compatible vectors for high-level expression of cloned DNAs from the T7 promoter" **Gene** 144:59-62.

Regan L., Rockwell A., Wasserman Z. & DeGrado W. (1994) "Disulfide crosslinks to probe the structure and flexibility of a designed four-helix bundle protein" **Protein Sci.** 3:2419-27.

Predki P. F., **Nayak L. M., Gottlieb M. B.** & Regan L. (1995) "Dissecting RNA-protein interactions: RNA-RNA recognition by Rop" **Cell** 80:41-50.

Predki P.F. & Regan L. (1995) "Redesigning the topology of a four-helix-bundle protein: monomeric Rop" **Biochemistry** 34:9834-9.

Smith C.K. & Regan L. (1995) "Guidelines for protein design: the energetics of β -sheet sidechain interactions" **Science** 270:980-982.

Klemba M., Gardner K. H., Marino S., Clarke N. D. & Regan, L. (1995) "Novel Metal Binding Proteins by Design" **Nature Structural Biology** 2:368-373.

Regan L. (1995) "Protein design: Novel metal-binding sites" **Trends Biochem. Sci.** 20:280-5

Munson M., Balasubramanian S., Fleming K. G., Nagi A. D., O'Brien R., Sturtevant J. M. & Regan L. (1996) "What makes a protein a protein? Hydrophobic core designs that specify stability and structural properties" **Protein Science** 5:1584-1593.

Predki P.F., **Agrawal V.**, Brunger A.T. & Regan L. (1996) "Amino-acid substitutions in a surface turn modulate protein stability" **Nat Struct Biol.** 3:54-8.

Smith CK, Bu Z, Anderson KS, Sturtevant JM, Engelman DM, Regan L. (1996) "Surface point mutations that significantly alter the structure and stability of a protein's denatured state" **Protein Sci.** 5:2009-19.

Dalal, S. Balasubramanian, S., and Regan, L. (1997) "Protein Alchemy: Changing beta-sheet into alpha-helix" **Nature Struct. Biol.** 4:548-552.

Munson M, Anderson KS & Regan L. (1997) "Speeding up protein folding: mutations that increase the rate at which Rop folds and unfolds by over four orders of magnitude" **Fold Des.** 2:77-8

Nagi AD & Regan L. (1997) "An inverse correlation between loop length and stability in a four-helix-bundle protein" **Fold Des.** 2:67-75.

Regan L. (1997) "Helix is a helix is a helix?" **Proc Natl Acad Sci U S A.** 94:2796-7.

Dalal S, Balasubramanian S, & Regan L. (1997) "Transmuting alpha helices and beta sheets" **Fold Des.** 2:71-9.

Farinas, E. & Regan, L. (1998) "*De novo* design of a rubredoxin-like Fe site" **Protein Science** 7:1939-1946.

Merkel, J.S. & Regan, L. (1998) "Aromatic rescue of glycine residues in beta-sheets" **Folding and Design** 3:449-455.

Regan L, Wells J. (1998) "Engineering and design. Recent adventures in molecular design" **Curr Opin Struct Biol.** 8:441-2.

Regan L. (1998) "Proteins to order?" **Structure** 6:1-4

Prodromou C., Siligardi G., O'Brien R., Woolfson D. N., Regan L., Panaretou, B., Ladbury J. E., Piper P. W. & Pearl L. H. (1999) "Regulation of Hsp90 ATPase activity by tetratricopeptide repeat (TPR)-domain co-chaperones" **EMBO Journal** 18:754-62.

Merkel J. S. Sturtevant J. M. & Regan L. (1999) "Sidechain interactions in parallel beta-sheets: the energetics of cross-strand pairings" **Structure** 7:1333-1343.

Marino S. F. & Regan L. (1999) "Secondary ligands enhance affinity at a designed metal-binding site" **Chem Biol.** 6:649-55.

Nagi AD, Anderson KS & Regan L. (1999) "Using loop length variants to dissect the folding pathway of a four-helix-bundle protein" **J. Mol Biol.** 286:257-65.

Regan L. (1999) "Protein redesign" **Curr Opin Struct Biol.** 9:494-9

Ma Y., Cunningham M.E., Wang X., Ghosh I., Regan L. & Longley B.J. (1999) "Inhibition of spontaneous receptor phosphorylation by residues in a putative alpha-helix in the KIT intracellular juxtamembrane region" **J. Biol Chem.** 274:13399-402.

Lurio L.B., Lumma D., Sandy A.R., Borthwick M.A., Falu P., Mochrie, S.G.J., Pelletier J.-F., Sutton M., Regan L., Malik A. & Stephenson G.B. (2000) "Absence of scaling for

the intermediate scattering function of a hard-sphere suspension: static and dynamic X-ray scattering from concentrated polystyrene latex spheres" **Phys. Rev. Lett.** 84:785-8.

Ghosh I., Hamilton A.D., & Regan L. (2000) "Antiparallel leucine zipper-directed protein reassembly: application to the green fluorescent protein" **Journal of the American Chemical Society** 122:5658-9.

Willis M.A., Bishop B., Regan L., & Brunger A.T. (2000) "Dramatic structural and thermodynamic consequences of repacking a protein's hydrophobic core" **Structure, Folding and Design** 8:1319-28.

Merkel J. S. and Regan L. (2000) "Modulating protein folding rates in vivo and in vitro by side-chain interactions between the parallel beta strands of green fluorescent protein" **J. Biol. Chem.** 275:29200-29206.

Balasubramanian S., **Schneider T.**, Gerstein M. & Regan, L. (2000) "Proteomics of *Mycoplasma genitalium*: identification and characterization of unannotated and atypical proteins in a small model genome" **Nucleic Acids Res.** 28:3075-82.

Dalal S. & Regan L. (2000) "Understanding the sequence determinants of conformational switching using protein design" **Protein Sci.** 9:1651-9.

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Stone M.J., Gupta S., Snyder, N., & Regan L. (2001) "Comparison of protein backbone entropy beta sheet stability: NMR-derived dynamics of protein G B1 Domain Mutants" **J. Am. Chem. Soc.** 123:185-6.

Bishop B., Koay D.C., Sartorelli A.C., Regan L. (2001) "Reengineering granulocyte colony-stimulating factor for enhanced stability" **J. Biol. Chem.** 276:33465-70.

Marino SF, **Shechner D.** & Regan L. (2001) "'Morphs' (MRFs): metal-reversible folding domains for differential IgG binding" **Chem. Biol.** 8:1221-9.

Ramirez-Alvarado M. & Regan L. (2002) "Does the location of a mutation determine the ability to form amyloid fibrils?" **J. Mol. Biol.** 323:17-22.

Ramirez-Alvarado M., Cocco M.J. & Regan L. (2003) "Mutations in the B1 domain of protein G that delay the onset of amyloid fibril formation in vitro" **Protein Sci.** 12:567-76.

Khurana R., Ionescu-Zanetti C., Pope M., Li J., Nielson L., Ramirez-Alvarado M., Regan L., Fink A.L. & Carter S.A. (2003) "A general model for amyloid fibril assembly based on morphological studies using atomic force microscopy" **Biophys J.** 85:1135-44.

Main E.R., Xiong Y., Cocco M.J., D'Andrea L. & Regan L. (2003) "Design of stable α -helical arrays from an idealized TPR motif" **Structure** 11:497-508.

D'Andrea L. & Regan L. (2003) "TPR proteins: the versatile helix" **Trends in Biol. Sci.** 28:655-62.

Magliery T.J. & Regan L. (2004) "A cell-based screen for function of the four-helix bundle protein Rop: a new tool for combinatorial experiments in biophysics" **Protein Eng. Des. Sel.** 17:77-83.

Magliery T.J. & Regan L. (2004) "Combinatorial approaches to protein stability and structure" **Eur. J. Biochem.** 271:1595-608.

Magliery T.J. & Regan L. (2004) "Library approaches to biophysical problems" **Eur. J. Biochem.** 271:1593-4.

Wilson C.G., Kajander T. & Regan L. (2004) "The crystal structure of Nlpl. A prokaryotic tetratricopeptide repeat protein with a globular fold" **FEBS J.** 272:166-79

Cortajarena A.L., Kajander T., Pan W., Cocco M. J. & Regan L. (2004) "Protein design to understand peptide ligand recognition by tetratricopeptide repeat proteins" **Protein Eng. Des. Sel.** 17:399-409.

Wilson C.G.M., Magliery, T.J. & Regan L. (2004) "Detecting protein-protein interactions with GFP-fragment reassembly" **Nature Methods** 1:255-262

Magliery T.J. & Regan L. (2004) "Beyond consensus: statistical free energies reveal hidden interactions in the design of a TPR motif" **J. Mol. Biol.** 343:731-45.

Magliery T.J., Wilson C.G.M., Pan W., Hamilton A. & Regan L. (2005) "Detecting protein-protein interactions with a GFP-fragment reassembly trap: scope and mechanism" **J. Am. Chem. Soc.** 127:146-151

Pozdnyakova I. & Regan L. (2005) "New insights into Fragile X syndrome. Relating genotype to phenotype at the molecular level" **FEBS J.** 272:872-8.

Main E.R., Stott K., Jackson S.E. & Regan L. (2005) "Local and Long-range Stability in Tandemly Arrayed Tetratricopeptide Repeats" **Proc. Natl. Acad. Sci. (USA)** in press.