Faculty Profile

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Indraneel Ghosh

Professor

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Honors

- Outstanding Faculty Award, Honors College, 2011
- Weed Endowed Chair, 2008
- NSF CAREER Award, 2006
- Research Innovation Award, 2002
- Leukemia Society Fellow, 1999

Education and Appointments

- Postdoctoral Fellow 1998-2001, Yale University, New Haven, Connecticut (Professor Andrew D. Hamilton & Professor Lynne Regan)
- Ph.D. 1992-1998, Purdue University, West Lafayette, Indiana (Professor Jean Chmielewski)
- B.S. 1988-1992, Hobart College, Geneva, New York

Research Interests

- Biochemistry
- Organic
- "Metabolism, Signaling, and Regulation"
- Bioanalytical
- Bioorganic
- Chemical Biology
- Materials and Polymer Chemistry
- Nucleic Acids and Genomes
- Protein and Membrane Biochemistry
- Structural Biology
- Synthesis/Synthetic Methods Development

Research Summary

Bioorganic Chemistry and Chemical Biology

Our group focuses upon:

A) Designing Inhibitors of Protein/Protein Interactions

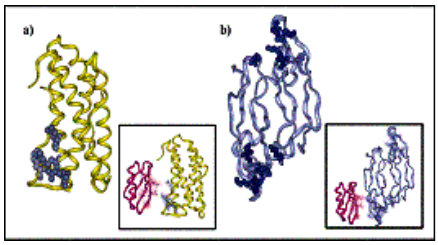
B) Constructing Macromolecules and Quantum Dots with Novel Functions

C) Designing Split-Protein Biosensors

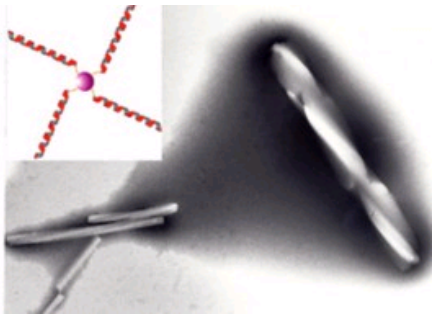
The broad objective of our research program in Bioorganic Chemistry and Chemical Biology is to construct protein therapeutics, protein mimetics, biomaterials, and biosensors. Our research at the University of Arizona is highly multidisciplinary and utilizes techniques in organic synthesis,

biochemistry, molecular biology, and a host of physical characterization methods. Our research motto is simple: *Unraveling mysteries and Enabling discoveries.*

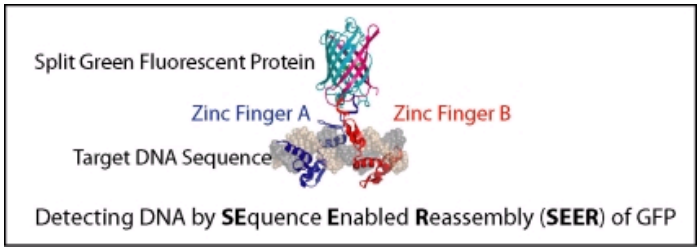
A) Targeted Therapeutics for Human Disease by Inhibition of Protein-Protein Interactions: We are developing novel therapeutics targeted towards protein-protein interactions utilizing evolved β-sheet scaffolds. We utilize a novel dual-surface selection phage-display methodology for identifying thermostable variants of small proteins that serve as rigid receptors for targeting a) gp120 (HIV AIDS); b) vascular endothelial growth factor (Cancer), c) thrombin (Heart Disease;) and d) beta-amyloid (Alzheimer's). Our receptors in principle can modulate and impair the *in vitro* and *in vivo* activities of the targeted proteins. Specific amino-acid residues selected from phage-display can be grafted upon small synthetic scaffolds.



B) Helical Supramolecules and Quantum Dots: We have recently constructed a new family of discrete supramolecules comprising designed peptides (coiled-coils) non-covalently assembled upon cognate peptides fused to a dendrimer core. These novel structures are being utilized for the multivalent display of proteins for protein inhibition and in the construction of novel biomaterials. We are also pursuing new approaches for labeling Quantum Dots with peptides to provide a means to image receptors on living cells.



C) Split-Protein Biosensors for Everything: Direct DNA Detection utilizing Sequence Enabled Reassembly (SEER): We have designed split protein systems that reassemble only in the presence of a specific DNA, modified DNA, or RNA sequence to allow for its direct detection. This approach utilizes rationally dissected proteins, such as the Green Fluorescent Protein (GFP), beta-Lactamase, and luciferase for construction of oligomerization-dependent protein reassembly systems and user defined nucleic acid targeting agents. This approach has potential for the direct detection of nucleic acid sequences implicated in human disease but more importantly has the for the design of new cancer therapeutics that respond to changes at the genetic level of an individual cell.



For reprints, please visit: http://www.chem.arizona.edu/ghosh/publications.html

Selected Publications

57. Jester, B.W.; Gaj, A.; Shomin, C.D.; Cox, K.J.; Ghosh, I."Testing the Promiscuity of Commercial Kinase Inhibitors against the AGC Kinase Group Using a Split-luciferase Screen" *J.*

Medicinal Chemistry , 2012, ASAP

56. Shekhawat, S.S.; Ghosh, I."Split-Protein Systems: Beyond Binary Protein-Protein Interactions" *Current Opinion in Chemical Biology* , 2011, 15,789-797

55. Shomin, C.D.; Resituto, E.; Cox, K.J.; Ghosh, I."Selection of cyclic-peptide inhibitors targeting Aurora kinase A: Problems and solutions." *Bioorg. Med. Chem.*, 2011,19,6743-6749

54. Badran, A.H.; Furman, J.L.; Ma, A.S.; Comi, T.J.; Porter, J.R.; Ghosh, I."Evaluating the Global CpG Methylation Status of Native DNA Utilizing a Bipartite Split-Luciferase Sensor" *Analytical Chem.*, 2011,83, 7151-7157

53. Shekhawat, S.S.; Campbell, S.T.; Ghosh, I. "A Comprehensive Panel of Turn-on Caspase Biosensors for Investigating Caspase Specificity and Caspase Activation Pathways" *ChemBioChem*, 2011,12,2353-2364

52. Furman, J.L.; Mok, P.W.; Badran, A.H.; Ghosh, I. "Turn-on DNA Damage Sensors for the Direct Detection of 8-Oxoguanine and Photoproducts in Native DNA" *J. Am. Chem. Soc.*, 2011,133, 12518-12527(Journal Cover)

51. Kox, K.J.; Shomin, C.D.; Ghosh, I."Tinkering outside the kinase ATP box: allosteric (type IV) and bivalent (type V) inhibitors of protein kinases" *Future Med. Chem.* , 2011, 3, 29-43

50. Furman, J.L.; Mok, P.W.;Shen,S.; Stains, C. I.; Ghosh, I. "A turn-on split-luciferase sensor for the direct detection of poly(ADP-ribose) as a marker for DNA repair and cell death" *Chem. Commun.*, 2011, 47, 397-399

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48. Jester, B.W.;Cox, K.J.;Gaj, A.; Shomin, C.D.; Porter, J.R.; Ghosh, I. "A Coiled Coil Enabled Split-Luciferase Three-Hybrid System: Applied Toward Profiling Inhibitors of Protein Kinases" *J. Am. Chem. Soc.*, 2010, 132, 11727-11735

47. Furman, J.L.;Badran A.H.;Oluyomi A.; Porter, J.R.; Stains, C.I.; Segal, D.J.; Ghosh, I. "A General Approach toward RNA-Templated Hierarchical Assembly of Split-Proteins" *J. Am. Chem. Soc.*, 2010, 132, 11692-11701

46. Stains, C.I.; Furman, J.L.; Porter, J.R.; Rajagopal, S.; Yuxing, L.; Wyatt, R.T.; Ghosh, I. "A General Approach for Receptor and Antibody-Targeted Detection of Native Proteins utilizing Split-Luciferase Reassembly" *ACS Chemical Biology*, 2010, 5, 943-952

45. Henchey, L.K.; Porter, J.R.; Ghosh, I.; Arora, P.S."High Specificity in Protein Recognition by Hydrogen Bond Surrogate alpha-Helices: Selective Inhibition of the p53/MDM2 Complex" *ChemBioChem*, 2010, 11,2104-2107

44. Yu, Y.; Blair, S.; Gillespie, D.; Jensen, R.; Myszka, D.; Badran, A.H.; Ghosh, I.; Chagovetz, A. "Direct DNA Methylation Profiling Using Methyl Binding Domain Proteins" *Analytical Chemistry*, 2010, 82, 5012-5019

43. Meyer, S.C.; Ghosh, I. "Phage Display Technology in Biosensor Development" In *Recognition Receptors in Biosensors; Zourob, M., Ed. Springer: New York*; 2010, 723-751

42. Porter J.R.; Lockwood S.H.; Segal. D.J.; Ghosh, I."Seeing Genetic and Epigenetic Information without DNA Denaturation Using Sequence Enabled Reassembly (SEER)" *Engineered Zinc Finger Proteins: Protocols and Methods: Methods in Molecular Biology 649* Springer: New York; 2010, 649, 365-382

41. Shekhawat, S.S.; Porter, J.R.; Sriprasad, A.; Ghosh, I."An Autoinhibited Coiled-Coil Design Strategy for Split-Protein Protease Sensors" *J. Am. Chem. Soc.*, 2009, 131, 5284-5290

40. Furman, J.L.;Badran, A.H.; Shen, S.; Stains, C.I.;Hannallah, J.; Segal D.J.; Ghosh, I. "Systematic Evaluation of Split-fluorescent Proteins for the Direct Detection of Native and Methylated DNA" *Bioorg. Med. Chem. Lett.*, 2009, 19, 3748-51 *(special issue for Carlos F. Barbas III/featured Report in Faculty of 1000)*

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38. Deng, Z.; Lie, L.F.; Shen, S.; Ghosh, I.; Mansuripur, M; Muscat, A. J. "Water-Based Route to Ligand-Selective Synthesis of ZnSe and Cd-Doped ZnSe Quantum Dots with Tunable Ultraviolet A to Blue Photoluminescence" *Langmuir* 2009, 9, 434-442

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36. Ghosh, I. Creative Chemical Sensor Systems *J. Am. Chem. Soc.(Book Review)* 2008, 130,

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35. Ghosh, I. Quantum Dots: Applications in Biology *ChemBioChem, (Book Review)* 2008, 9, 157-158

34. Meyer, S.C.; Shomin, C.D.; Gaj, T.; Ghosh, I. "Tethering Small Molecules to a Phage Display Library: Discovery of a Selective Bivalent Inhibitor of Protein Kinase A" *J. Am. Chem. Soc.* 2007, 129, 13812-13813 (Featured Report in *ACS Chem. Biol., Mol. BioSys., and Faculty of 1000)*

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28. Zhou, M.; Nakatani, E.; Gronenberg, L.S.; Tokimoto, T.; Wirth, M.J.; Hruby, V.J.; Roberts, A.; Lynch, R.M.; Ghosh, I. "Peptide-Labeled Quantum Dots for Imaging GPCRs in Whole Cells and as Single Molecules" *Bioconjugate Chem.,* 2007, 18 (2), 323 -332

27. Zhou, M.; Ghosh, I. "Quantum Dots and Peptides: A Bright Future Together" *Biopolymers,* 2007, 88, 325-339

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21. Meyer, S.C.; Gaj, T.; Ghosh, I. "Highly Selective Cyclic Peptide Ligands for NeutrAvidin and Avidin Identified by Phage Display"*Chem. Biol. & Drug Des.* 2006, 68, 3-10 *(Journal Cover)*

20. Ooi, A.T.; Stains, C.I.; Ghosh, I. Segal, D.J. "SEquence-Enabled Reassembly of beta-Lactamase (SEER-LAC): A Sensitive Method for the Detection of Double-Stranded DNA"*Biochemistry* 2006, 46, 3620-3625

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13. Zhou, M; Ghosh, I. "Helical supramolecules and fibers utilizing leucine-zipper displaying dendrimers" *J. Am. Chem. Soc.*, 2004, 126, 734-735 *Research Highlighted in Chem. & Eng. News*, 2004, 82, 41

For publications prior to 2004 please see Vitae

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