

NAME Gabriela Chiosis		POSITION TITLE Frederick R. Adler Chair	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Bucharest, Romania	BS	1991	Chemistry
Twente University, Netherlands	Visiting res	1991-1993	Medical sensors
Columbia University, New York	MA	1993-1994	Chemistry
Columbia University, New York	PhD	1994-1998	Bioorganic chemistry
Memorial Sloan-Kettering Cancer Center, NY	postdoc	1998-2001	Tumor Cell Biology

A. Positions and Honors

Positions and Employment

1991-1993	Visiting Researcher, University of Twente – MESA Institute Enschede, The Netherlands
1993-1994	Teaching Assistant (Organic Chemistry), Columbia University, New York
1998-2001	Research Fellow, Cancer Research, Memorial Sloan-Kettering Cancer Center, New York
2001	Senior research scientist, Memorial Sloan-Kettering Cancer Center, NY
2001-	Assistant Laboratory Member and Assistant Attending, Department of Medicine, Memorial Hospital for Cancer & Allied Diseases, New York
2005-	Assistant Member and Laboratory Head, Program in Molecular Pharmacology and Chemistry, Sloan-Kettering Institute, New York
2005-	Assistant Professor, Program in Pharmacology, Weill Graduate School of Medical Sciences, Cornell University
2005-	Program faculty, Tri-Institutional Training Program in Chemical Biology, Sloan-Kettering Institute for Cancer Center, Cornell University and The Rockefeller University
2005-	Faculty, Cancer Biology, Gerstner Sloan-Kettering Graduate School
2006-	Frederick R. Adler Chair for Junior Faculty

Other Experience and Professional Memberships: **1997-** Member American Chemical Society **2000-** Member American Association for Advancement of Science **2000-** Member American Association for Cancer Research; **2002** Member NIH/NCI-Molecular target drug discovery for cancer committee; **2003-** Member Society of Biomolecular Screening; **2003** Member NIH/NCI-RAND committee; **2004-** Member New York Academy of Science; **2005** National Toxicology Program advisory committee member; **2005** Susan G. Komen breast cancer foundation reviewer, Treatment; **2006** Guest editor for Current Topics in Medicinal Chemistry on an issue focused on heat shock proteins as targets in medicinal chemistry and drug discovery; **2006** reviewer in the DOD Congressionally Directed Medical Research Program (CDMRP) Breast Cancer Research Program; **2006** Susan G. Komen breast cancer foundation reviewer, Treatment; **2007-2009** Member, American Chemical Society, medicinal chemistry long-range planning committee; **2007** reviewer in the DOD CDMRP Breast Cancer Research Program

Honors and awards **1990** Award of Excellence - University of Bucharest; **1991** European Community research grant recipient – development of medical sensors; **1998** Leukemia Research Foundation post-doctoral fellowship; **2000** Susan G. Komen post-doctoral fellowship; **2001** Highlighted in "This Week in Science", *Science*, 293, 2001. **2001** Featured in C&EN landmarks, December 10, 2001, Volume 79, Number 50 as one of the Top 10 accomplishments for 2001 in GENOMICS AND MEDICINE **2001** Cover of Chemistry & Biology, March 2001 (Cell press) for the design and discovery of novel Hsp90 inhibitors; **2001** Highlighted in The Journal of Medicinal Chemistry (vol. 45, page 1553, 2002); **2002** Experimental therapeutics award; **2003** AACR – Cancer Research and Prevention Career Development Award in Translational Lung Cancer Research, in Memory of Duffy Wall; **2003** Experimental therapeutics award; **2003** Cover of Chemistry&Biology July 2003; **2004** Cover of Journal of Biomolecular Screening August 2004; **2004** Highlighted in the August issue of Nature Reviews Drug Discovery for the novel purine(PU)-scaffold Hsp90 inhibitors; **2004** PU24FCI highlighted in the November issue of Nature Reviews Drug Discovery and Molecular Cell Biology; **2004** NIH Roadmap Initiative grant awarded for the development of HTS assays probing Hsp90 inhibition; **2004** Featured in NYSTAR Newsletter – New York state office of science, technology & academic research; **2004** Translational & Integrative Medicine Award for the Pre-Clinical Evaluation of Novel Synthetic Hsp90 Inhibitors in Breast Cancer; **2005** Susan G. Komen Breast Cancer Translational Research Award; **2006** CNF2024, first synthetic Hsp90 inhibitor based on the PU-Hsp90 inhibitor scaffold enters Phase I clinical trials in patients with advanced cancers; **2007** "Identification of Potent Water Soluble

Purine-Scaffold Inhibitors of the Heat Shock Protein 90", published in Journal of Medicinal Chemistry featured on the ACS Publications website as "Hot Paper" and "Number 1 most cited"; 2007 SynCure Cancer Foundation award' 2007 Manhasset Women's Coalition Against Breast Cancer award; 2007 Alzdiscovery award;

B. Selected peer-reviewed publications

1. VanVeggel FCJM, Chiosis G, Cameron RB, Reinhoudt DN. Preorganized Metallomacrocycles - Selective Receptor for Ammonia. *Supramolecular Chem.* **1994**; 3:177-183.
2. Kremer FJB, Chiosis G, Engbersen JFJ, Reinhoudt DN. Improved Guannidinium Ion-Selectivity by Novel Calix[4]arene and Calix[6]arene Receptor Molecules on CHEMFETs. *J. Chem. Soc. Perkin Trans2.* **1994**; 4: 677-681.
3. Vanaxelcastelli V, Cacciapaglia R, Chiosis G, VanVeggel FCJM, Mandolini L, Reinhoudt DN. The Uranyl Unit as Electrophilic Catalyst of Acyl Transfer Reactions. *Inorg. Chem. Acta* **1996**; 246:181-193.
4. Chiosis G. Study Into the Cyclization of an Epoxy-Alcohol to the Energetically Disfavored Product by Peptides from Non-biased Combinatorial Libraries. *Tetrahedron Lett.* **2000**; 41:801-806.
5. Zheng FF, Kuduk SD, Chiosis G, Munster PN, Sepp-Lorenzino L, Danishefsky SJ, Rosen N. Identification of a Geldanamycin Dimer That Induces the Selective Degradation of HER-family Tyrosine Kinases. *Cancer Res.* **2000**; 60:2090-2095.
6. Chiosis G, Rosen N, Sepp-Lorenzino L. LY294002-Geldanamycin Heterodimers as Selective Inhibitors of the PI3K and PI3K-related Family. *Bioorg. Med. Chem. Lett.* **2001**; 11: 909-915.
7. Chiosis G, Timaul MN, Lucas B, Munster PN, Zheng FF, Sepp-Lorenzino L, Rosen N. A Small Molecule Designed to Bind to the Adenine Nucleotide Pocket of Hsp90 Causes Her2 Degradation and the Growth Arrest and Differentiation of Breast Cancer Cells. *Chem. Biol.* **2001**; 8:289-299.
8. Chiosis G, Boneca IG. Selective Cleavage of D-Ala-D-Lac by Small Molecules: Re-Sensitizing Resistant Bacteria to Vancomycin. *Science* **2001**; 293: 1484-1487. **Must Read Faculty of 1000 Biology**
9. Lucas B, Rosen N, Chiosis G. Facile synthesis of 9-Alkyl-8-benzyl-9H-purin-6-ylamine Derivatives. *J. Comb. Chem.* **2001**; 3: 518-520.
10. Boneca IG, Chiosis G. A new strategy for fighting vancomycin resistant-enterococci. *APUA Newsletter* **2002**; 20: 1-3.
11. Chiosis G, Huezio H, Lucas B, Rosen N. Development of a Purine-based Novel Class of Hsp90 Binders That Inhibit the Proliferation of Cancer Cells and Induce the Degradation of Her2 Tyrosine Kinase. *Bioorg. Med. Chem.* **2002**; 10: 3555-3564.
12. Chiosis G, Rosen N, Lucas B. Development of novel hsp90 inhibitors as cancer therapeutics. *Am. Chem. Soc.* 224: 228-MEDI Part 2, **2002**.
13. Chiosis G, Huezio H, Rosen N, Mimnaugh E, Whitesell L, Neckers L. 17AAG - Low target binding affinity and potent whole cell potency: finding an explanation. *Eur. J. Cancer* **2002**; 38: 203B.
14. Gorre ME, Ellwood-Yen K, Chiosis G, Rosen N, Sawyers C. BCR-ABL point mutants isolated from patients with STI571-resistant chronic myeloid leukemia remain sensitive to inhibitors of the BCR-ABL chaperone heat shock protein 90. *Blood* **2002**; 100(8): 3041-3044.
15. Basso DB, Solit DB, Chiosis G, Giri B, Tschlis P, Rosen N. Akt forms an intracellular complex with hsp90 and Cdc37 and is destabilized by inhibitors of Hsp90 function. *J. Biol. Chem.* **2002**; 277(42): 39858-39866.
16. Chiosis G, Huezio H, Rosen N, Mimnaugh E, Whitesell L, Neckers L. 17AAG - Low target binding affinity and potent cell activity: Finding an explanation. *Molec. Cancer Ther.* **2003**; 2: 123-129.
17. Yamamoto K, Garbaccio RM, Stachel SJ, Solit DB, Chiosis G, Rosen N, Danishefsky SJ. Target Oriented Total Synthesis as a Resource in the Discovery of Potentially Valuable Agents in Oncology: Cyclopropanadicol. *Angew. Chemie* **2003**, 42: 1280-1284.
18. Boneca IG, Chiosis G. Vancomycin resistance: Occurrence, mechanism and therapeutic approaches. *Expert Opinion on Therapeutic Targets*, **2003**; 7(3), 311-328.
19. Chiosis G, Lucas B, Huezio H, Solit D, Basso A, Rosen N. Development of purine-scaffold small molecule inhibitors of Hsp90. *Curr. Cancer Drug Targets* **2003**, 3, 363-368.
20. Huezio H, Vilenchik M, Rosen N, Chiosis G. Microtiter cell-based assay for the detection of agents that alter cellular levels of Her2 and EGFR. *Chem Biol.* **2003**, 10(7), 629-634.
21. Llauger L, Felts S, Huezio H, Rosen N, Chiosis G. Synthesis of novel fluorescent probes for the molecular chaperone Hsp90. *Bioorg. Med. Chem. Lett.* **2003**, 13, 3975-3978.
22. He H, Llauger L, Rosen N, Chiosis G. General Method for the Synthesis of 8-Arylsulfanyl Adenine Derivatives, *J. Org. Chem.* **2004**, 69, 3230-3232.
23. Vilenchik M, Solit D, Basso M, Huezio H, Lucas B, Huazhong H, Rosen N, Spampinato C, Modrich P, Chiosis G. Targeting wide-range oncogenic transformation via PU24FCI, a specific inhibitor of tumor Hsp90. *Chem. Biol.* **2004**, 11, 787-797.
24. Kim J, Felts S, He H, Llauger L, Huezio H, Rosen N, Chiosis G. Development of a fluorescence polarization assay for the molecular chaperone Hsp90. *J. Biomolecular Screening* **2004**, 9(5):375-81.
25. Chiosis G, Vilenchik M, Kim J, Solit D. Hsp90 – the vulnerable chaperone. *Drug Discovery Today*, **2004**, 9(20):881-8.
26. Llauger L, He H, Chiosis G. Synthesis of 8-arylsulfoxyl/sulfonyl adenines. *Tet. Lett.* **2004**, 45, 9549-9552.

27. Llauger L, He H, Kim J, Aguirre J, Rosen N, Peters U, Davies P, Chiosis G. 8-Arylsulfanyl and 8-Arylsulfoxyl Adenine Derivatives as Inhibitors of the Heat Shock Protein 90. *J. Med. Chem.* **2005**, 48, 2892-2905.
28. Chiosis G, Brodsky J. The journey of small molecule microarrays: From proteins to mammalian cells - are we there yet? *Trends Biotech.* **2005**, (6):271-4.
29. Chiosis G., Rodina A, Moulick K. Emerging Hsp90 inhibitors: from discovery to clinic. *Current medicinal chemistry-Anti-cancer agents.* **2006**, 6, 1-8.
30. He H, Zatorska D, Kim J, Aguirre J, Llauger L, She Y, Wu N, Immormino RM, Gewirth DT, Chiosis G. Identification of Potent Water-Soluble Purine-Scaffold Inhibitors of the Heat Shock Protein 90. *J. Med. Chem.* **2006**, 49(1):381-90.
31. Chiosis G. Targeting chaperones in transformed systems – a focus on Hsp90 and cancer. *Expert Opinion on Therapeutic Targets.* **2006**, 10(1):37-50.
32. De Martino G, Edler MC, La Regina G, Coluccia A, Barbera MC, Barrow D, Nicholson RI, Chiosis G, Brancale A, Hamel E, Artico M, Silvestri R. New Arylthioindoles: Potent Inhibitors of Tubulin Polymerization. 2. Structure-Activity Relationships and Molecular Modeling Studies. *J Med Chem.* **2006**, 49(3):947-954.
33. Chiosis G, Aguirre J, Nicchitta CV. Synthesis of Hsp90 dimerization modulators. *Bioorg. Med. Chem. Lett.* **2006**, 16:3529–3532.
34. Chu F, Maynard JC, Chiosis G, Nicchitta CV, Burlingame AL. Identification of novel quaternary domain interactions in the Hsp90 chaperone, GRP94. *Protein Science* **2006**, (6):1260-9.
35. Chiosis G. Molecular chaperones as targets in medicinal chemistry and drug discovery. *Curr. Top. Med. Chem.* **2006**, 6(11):1161.
36. Chiosis G. Discovery and Development of Purine-Scaffold Hsp90 Inhibitors. *Curr. Top. Med. Chem.* **2006**, 6(11):1183-1191.
37. Brodsky JF, Chiosis G. Hsp70 Molecular Chaperones: Emerging Roles in Human Disease and Identification of Small Molecule Modulators. *Curr. Top. Med. Chem.* **2006**, 6(11):1215-1225.
38. Chiosis G, Caldas Lopes E, Solit D. Hsp90 inhibitors – a chronicle from geldanamycin to today's agents. *Current Opinion in Investigational Drugs* **2006** (6):534-41.
39. Chiosis G, Neckers L. Tumor Selectivity of Hsp90 Inhibitors – The Explanation Remains Elusive. *ACS Chemical Biology* **2006**, (1):279-284.
40. Moulick K, Clement CC, Aguirre J, Kim J, Kang Y, Felts S, Chiosis G. Synthesis of a red-shifted fluorescence polarization probe for Hsp90. *Bioorg. Med. Chem. Lett.* **2006**, (16):4515–4518.
41. Immormino RM, Kang Y, Chiosis G, Gewirth DT. Structural and Quantum Chemical Studies of 8-aryl-sulfanyl adenine class Hsp90 inhibitors. *J Med Chem.* **2006** 49(16):4953-4960.
42. Chiosis G, Tao H. Purine-scaffold Hsp90 inhibitors. *iDrugs* **2006** 9(11):778-82.
43. Smith-Jones P, Kozirowski J, Usher C, Zatorska D, Chiosis G, Larson S. Radioiodinated heat shock protein 90 binding purine ligands. *J. Nucl. Med.* **2006**, 47; S1-91P.
44. Hieronymus H, Lamb J, Ross KN, Peng XP, Clement C, Rodina A, Nieto M, Du J, Stegmaier K, Raj SM, Maloney KN, Clardy J, Hahn WC, Chiosis G, Golub TR. Gene expression signature-based chemical genomic prediction identifies a novel class of HSP90 pathway modulators. *Cancer Cell* **2006** 10(4):321-30.
45. Luo W, Dou F, Rodina A, Chip S, Kim J, Zhao Q, Moulick K, Aguirre J, Wu N, Greengard P, Chiosis G. Roles of heat shock protein 90 in maintaining and facilitating the neurodegenerative phenotype in tauopathies. *Proc Natl Acad Sci U S A* **2007** (104), 9511-9516.
46. Du Y, Moulick K, Rodina A, Aguirre J, Felts S, Dingleline R, Fu H, Chiosis G. High-throughput screening fluorescence polarization assay for tumor-specific Hsp90. Accepted *J. Biomolecular Screening* **2007**
47. Rodina A, Vilenchik M, Moulick K, Aguirre J, Kim J, Chiang A, Litz J, Clement CC, She Y, Wu N, Felts S, Wipf P, Massague J, Jiang X, Brodsky LJ, Krystal GW, Chiosis G. Selective compounds define Hsp90 as a major inhibitor of apoptosis in small cell lung cancer. *Nat Chem Biol* **2007** Aug;3(8):498-507. **Recommended Faculty of 1000 Biology**
48. Didelot C, Brunet M, Joly A-L, De Thonel A, Chiosis G, Garrido C. Anti-Cancer Therapeutic Approaches Based on Intracellular and Extracellular Heat Shock Proteins. *Curr. Med. Chem.* 14, **2007**.
49. Chiosis G, Solit D. Development and applications of Hsp90 inhibitors. *Drug Discovery Today.* **2007**

Patents

1. Chiosis G, Rosen N. Small Molecule Compositions for Binding to HSP90. MSKCC. WO0236075, May 10, 2002; US2004180814, May 27, 2004.
2. Chiosis G, Boneca IG, Still WC. Method for Re-Sensitizing Vancomycin Resistant Bacteria Using Agents Which Selectively Cleave a Cell Wall Depsipeptide. Columbia U-Rockefeller U. US2004180814, September 19, 2004.
3. Chiosis G, Rosen N, Huezo H. Assays for Detection of Bioactive Compounds that Interact with Heat Shock Protein 90. Memorial Sloan-Kettering Cancer Center, WO2005012482, February 10, 2005; US2007178537, August 2, 2007.
4. Chiosis G, He H, Llauger L, Kim J, Smith-Jones P, Larson S. Small-molecule HSP90 inhibitors. MSKCC. WO2006084030, August 10, 2006.
5. Chiosis G, Gold B. Stimulation of neurite outgrowth by small molecules. UOHS and MSKCC. WO2006130469 December 12, 2007.

Principal Investigator/Program Director (Last, First, Middle):

CHIOSIS, GABRIELA

6. Chiosis G, Dou F, Luo W, Greengard P. Treatment of neurodegenerative diseases through inhibition of HSP90. MSKCC and Rockefeller U, Provisional Application No.: 60/806,427, 2006.