

## Matrix Metalloproteinases as Therapeutic Targets of Cancer and Cardiovascular Diseases

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### Research/Technology Overview:

(Start typing here, or paste appropriate portion of abstract.) A research/technology overview and advantages over current state-of-the-art and ongoing national research programs.

Matrix metalloproteinases (MMPs, matrixins) are a family of zinc-endopeptidases that are believed to participate in angiogenesis, embryonic development, morphogenesis, reproduction, tissue resorption and remodeling, arthritis, and tumor growth, progression, invasion, and metastasis through breakdown of the extracellular matrix (ECM), cell surface proteins, and processing growth factors, cytokines, and chemokines. At least twenty three human MMPs have been reported and more MMPs have been reported in vertebrates. Many MMPs such as membrane type 1 matrix metalloproteinase (MT1-MMP) are reported to play multiple functions in ECM remodeling, development, growth, morphogenesis and disease conditions. Selectively inhibit certain MMP enzymes, specifically those modulating certain diseases, physiological conditions and disease conditions are highly desirable.

Novel substituted heterocyclic mercaptosulfide compounds, precursors, and derivatives are developed and tested to be potent and relatively selective inhibitors of matrix metalloproteinases (MMPs), e.g. membrane type 1 MMP,

gelatinase B, gelatinase A, collagenases, matrilysins, metalloelastase, and stromelysin-1. These compounds contain new zinc-binding functional groups and groups probing deep versus shallow enzyme active site S1' pockets, respectively. They are relatively stable in buffers, cell culture media, and serum, and more water-soluble.

**Target Industry Overview:**

(Start typing here, or paste portion of abstract.) A target industry overview and the potential commercial impact of the research that has been augmented by the convergence of at least two of Information Technology, Biotechnology and Nanotechnology.

Pharmaceutical and Biotechnology Industries.

**Commercial Applications:**

(Start typing here, or paste appropriate portion of abstract.) A clear link of commercial significant application(s) in innovative new technologies or products that might result from the research.

These inhibitors will be used for the control of physiological and pathological processes in which metalloproteases play roles, e.g. the prevention and treatments of cancer invasion, angiogenesis, and metastasis; stroke and cardiovascular diseases; arthritic diseases; periodontal disease; multiple sclerosis; inflammation; pain; corneal ulceration; bacterial meningitis; diabetic complications; wound healing; kidney diseases; neurodegenerative diseases; AIDS; organ transplantation; the control of fertility and reproductive capabilities; blister formation; allergy; bone remodeling; osteoporosis; asthma; anti-aging; anti-bacterial activities; industrial manufacturing of extracellular matrix/collagen products, cosmetics, and beauty products. These inhibitors can be used for human beings, animals, and other organisms.

**Stage of Technology Development and Commercialization:**

(Start typing here, or paste appropriate portion of abstract.) The stage of technology development and commercialization activities.

A provisional patent application was filed by the four co-inventors: Drs. Martin A. Schwartz, Yonghao Jin, Douglas R. Hurst, and Qing-Xiang Sang in year 2003 and the full patent application will be filed in year 2004.

## Qing-Xiang (Amy) SANG, Ph.D., Associate Professor of Chemistry, Biochemistry, and Biomedical Sciences

### Institution and Contact Information

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Institute of Molecular Biophysics, Florida State University

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### Education

B.S. in Biology, Hunan Normal University, P.R.C. 1984.

Ph.D. in Cell Biology and Anatomy, Georgetown University Medical School,  
Washington D.C., 1990. (Mentors, Drs. Steve W. Byers and Martin Dym).  
Dissertation title: Testicular metalloproteinases; regulation by hormones and  
Sertoli-peritubular cell interactions *in vitro*.

### Professional Experience

Graduate Research and Teaching Assistant in Cell Biology and Tumor Biology,  
Department of Biology, Xiamen University, PRC, 1984-86.

Research Assistant in Cell Biology and Reproductive Biology, Georgetown  
University Medical School, 1986-89.

Teaching Assistant, Georgetown University Medical School, taught class M91  
Gross Anatomy, 1987.

Postdoctoral Research Associate in Enzymology, Protein Chemistry, and  
Metallobiochemistry, Department of Chemistry and Institute of Molecular  
Biophysics, The Florida State University, January 1990-April 1992. Mentor,  
Professor Harold E. van Wart.

N.I.H. Postdoctoral Fellow in Enzymology, Protein Chemistry, Metallobiochemistry, and Molecular Biology, Department of Chemistry and Institute of Molecular Biophysics, The Florida State University, May 1992-September 1993. Sponsor, Dr. Harold E. van Wart.

Assistant Scholar/Scientist (Research Assistant Professor), Biochemistry Division, Department of Chemistry and Institute of Molecular Biophysics, The Florida State University. September 1993-August 1997.

Assistant Professor (tenure-track), Biochemistry Division, Department of Chemistry and Biochemistry and Institute of Molecular Biophysics. College of Arts and Sciences. The Florida State University. August 1997- August 2003.

Courtesy Assistant Professor, Department of Biomedical Sciences, College of Medicine. Florida State University. January 2002-August 2003.

Associate Professor (tenured), Department of Chemistry and Biochemistry and Institute of Molecular Biophysics, Florida State University and Courtesy Associate Professor, Department of Biomedical Sciences, College of Medicine. August 2003-present

## Professional Awards and Honors

### HONORS AND AWARDS

Georgetown University Medical School Competitive Graduate Fellowship, 1986-1989.

Student Travel Award, American Society for Cell Biology, 1989.

Individual National Research Service Award from Public Health Service, National Institutes of Health Individual Postdoctoral Fellowship (F32, NIH, NIGMS 14336), May 1992-September 1993.

Henry F. Abel Research Award, American Cancer Society, the Florida Division, 1994-1995.

Elsa U. Pardee Foundation Award, 1995.

The RGK Foundation Award, 1994-1995.

The Gustavus and Louise Pfeiffer Foundation Award, 1996.

Robert J. Boucek, M.D. Research Award, to the highest merit rated researcher for the American Heart Association, Florida Affiliate, 1996-1997.

Elsa U. Pardee Foundation Award, 1997.

The Gustavus and Louise Pfeiffer Foundation Award, 1997.

First-Year Assistant Professor Award, Florida State University, Council on Research and Creativity (CRC). 1997-1998.

FIRST Award (R29). National Cancer Institute, National Institutes of Health. 1998-2003.

Travel Award from NATO Advanced Study Institute for attending a Conference on Vascular Endothelium: Mechanisms of Cell Signaling, Crete, Greece. June 20-29, 1998.

The Gustavus and Louise Pfeiffer Foundation Award, 1999.

Elsa U. Pardee Foundation Award, 2000.

Pilot Award, American Cancer Society, Florida Division, 2001-2002.

Florida State University Program Enhancement Grant Award, 2001-2003.

U.S. Army Prostate Cancer Research Program New Investigator Award, Department of Defense, 2002-2005.

Developing Scholar Award, Florida State University, 2003-2004.

## PROFESSIONAL MEMBERSHIPS

Associate Member, American Society for Cell Biology, 1988-1992.

Member, American Society for Cell Biology, 1992-1997.

Associate Member, Sigma Xi, the Scientific Research Society, 1989-1991.

Member, Sigma Xi, the Scientific Research Society, 1991-1992.

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Member of American Association for the Advancement of Science, 1995-2002

Member of American Society for Biochemistry and Molecular Biology, 1998-

Member of American Association for Cancer Research, 2001-

Member of the International Proteolysis Society, 2001-