BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Li, Senlin	Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login) LISENLIN	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Shanxi Medical College, Taiyuan, PR China		1982	
Haerbin Medical University, Haerbin City, PR China	M. Med.	1985	Medicine
Peking Union Medical College, Peking, PR China		1989	Biochemistry and Molecular Biology
University of Geneva School of Medicine, Geneva, Switzerland	M.D.	1991	Medicine

A. Personal Statement

I will serve as mentor for Suzette Laing's F30 fellowship proposal. My background includes about 20 years of experience in basic and translational research relevant to human diseases. I was trained initially as MD and later in cell and molecular biology. I strongly believe that biomedical research should lead to defeating diseases and benefiting human health, and translational study is crucial in this process and endeavor. After several years' efforts, I have accumulated excellent knowledge on stem cell-based gene therapy for atherosclerosis and neurodegenerative diseases including specific training and expertise in most areas for this application. As PI, I laid the groundwork for the proposed research by developing super macrophage-specific promoters, using lentiviral vectors to transducer bone marrow stem cells, transplantation of these cells to reconstitute the hematopoietic system of the recipients, confirmation of transplantation efficiency, administration of high-fat diets to these animals, and conduction of the downstream work. As a result of my experience of over a decade as a principal investigator, I have been aware of the importance of having highly-qualified lab coworkers, frequent and efficient communication among project members, and constructing a realistic research/experimental plan and timeline. I have been mentoring/co-mentoring two graduate student conducting doctoral dissertation research (currently) and 14 post-doctoral fellows (4 currently). I also mentored 1 master student, 5 graduate research rotation students, as well as 5 summer high-school students. They included a good number of women and minority trainees. Among these trainees, some have become new faculty members (Drs. He, Imam, Li, Qiang).

B. Positions and Honors

Positions and Employment

1986-1989 Lecturer, Department of Child and Adolescent Health, Shanxi Medical College, Taiyuan, PR China
1989-1991 Investigator in Clinical Endocrinology, University of Geneva, Switzerland
1991-1992 Postdoctoral Fellow, Division of Clinical Biochemistry, University of Geneva, Switzerland
1992-1995 Postdoctoral Fellow, Fondation pour Recherches Medicales, University of Geneva, Switzerland
1995-1999 Senior Postdoctoral Fellow and Research Scientist, Department of Medicine, University of Texas Health Science Center, San Antonio, TX
2000-2006 Assistant Professor of Medicine & Barshop Center for Longevity and Aging Studies, UTHSCSA

2006-Present Associate Professor of Medicine, Pharmacology, and Barshop Center for Longevity and Aging Studies, UTHSCSA
2000-present Research Health Scientist (Health Science Specialist), South Texas Veterans Health Care System, Audie L. Murphy Division, San Antonio, TX

Professional Memberships

1998-present Member, American Association for the Advancement of Science
2004-present Member, American society of Gene therapy

Honors

1989-1991 World Health Organization Scholarship, University of Geneva, Switzerland
2002 Winner, Best Junior Faculty Poster, Department of Medicine 5th Annual Research Day, University of Texas Health Science Center, San Antonio, TX
2011 The first place winner for 2011 TINT (Technology Innovation in Novel Translation) Program

Patent

Li S, Clark RA. United States Patent No. 7,709,625 B2 issued May 4, 2010 entitled "Methods and compositions for bone marrow stem cell-derived macrophage delivery of genes for gene therapy" UTHSCSA/STTM Reference No.: 2004.006.HSCS

C. Selected Peer-reviewed Publications

1. **Li S**, Vaugnat B, Gruaz NM, Eshkol A, Sizonenko PC, and Aubert ML. Binding kinetics of the long-acting gonadotropin-releasing hormone (GnRH) antagonist antide to rat pituitary GnRH receptors. *Endocrinology* 135:45-52, 1994.
2. **Li S**, Godson C, Roche E, Zhao SJ, Prentki M, and Schlegel W. Induction of *c-fos* in pituitary cells by thyrotrophin-releasing hormone and phorbol 12-myristate 13-acetate depends upon Ca^{2+} influx. *J Mol Endocrinol* 13:303-312, 1994.
3. **Li S**, Cougnon N, Bresson-Bepoldin L, Zhao SJ, and Schlegel W. *c-fos* mRNA and FOS protein expression are induced by Ca^{2+} influx in GH3B6 pituitary cells. *J Mol Endocrinol* 16:229-238, 1996.
4. **Li S**, Valente AJ, Zhao S-J, and Clark RA. PU.1 is essential for $p47^{phox}$ promoter activity in myeloid cells. *J Biol Chem* 272:17802-17809, 1997.
5. **Li S**, Schlegel W, Valente AJ, and Clark RA. Critical flanking sequences of PU.1 binding sites in myeloid-specific promoters. *J Biol Chem* 274:32453-32460, 1999.
6. Susini S, van Haasteren G, **Li S**, Prentki M, and Schlegel W. Essentiality of intron control in the induction of c-*fos* by glucose and glucoincretin peptides in INS-1 β-cells. *FASEB J* 14:128-136, 2000.
7. van Haasteren G, **Li S**, Ryser S, and Schlegel W. Essential contribution of intron sequences to Ca(2+)-dependent activation of c-fos transcription in pituitary cells. *Neuroendocrinology* 72:368-378, 2000.
8. Ryser S, Tortola S, van Haasteren G, Muda M, **Li S**, and Schlegel W. MAP kinase phosphatase-1 gene transcription in rat neuroendocrine cells is modulated by a calcium-sensitive block to elongation in the first exon. *J Biol Chem* 276:33319-33327, 2001.
9. **Li S**, Valente AJ, Wang L, Gamez MJ, and Clark RA. Transcriptional regulation of the $p67^{phox}$ gene: Role of AP-1 in concert with myeloid-specific transcription factors. *J Biol Chem* 276:39368-39378, 2001.
10. **Li S**, Valente AJ, and Clark RA. Multiple PU.1 binding is required for $p40^{phox}$ gene transcription in myeloid cells. *Blood* 99:4578-4587, 2002.
11. Clark RA, **Li S**, Pearson DW, Leidal KG, Clark JR, Denning GM, Reddick R, Krause K-H, and Valente AJ. Regulation of calreticulin expression during induction of differentiation in human myeloid cells: Evidence for remodeling of the endoplasmic reticulum. *J Biol Chem* 277:32369-32378, 2002.

12. Dong Z. Nishiyama J. Yi X. Venkatachalam MA. Denton M. Gu S. **Li S**. Qiang M. Gene promoter of apoptosis inhibitory protein IAP2: identification of enhancer elements and activation by severe hypoxia. *Biochem J* 364(Pt 2):413-21, 2002.

13. Zhao S, Venkatasubbarao K, **Li S**, Freeman JW. Requirement of a specific Sp1 site for HDAC-mediated repression of transforming growth factor bata type II receptor expression in human cancer cells. *Cancer Research* 63: 2624-2630, 2003.

14. He W, Qiang M, Ma W, Valente AJ, Quinones M, Wang W, Reddick, RL, Qifu X, Ahuja SS, Clark RA, Freeman GL, and **Li S**. Development of a synthetic promoter for macrophage gene therapy. *Human Gene Therapy* 11: 949-959, 2006.

15. Valente AJ, Zhou Q, Qiang M, Lu Z, He W, Ma W, Li G, Wang L, Banfi B, Krause K-H, Clark RA, and **Li S**. Regulation of NOX1 expression by GATA, HNF-1α and CDX transcription factors. *Free Radical Biology and Medicine* 44: 430-443, 2008.

16. Biju KC, Zhou Q, Li G, Imam SZ, Roberts RL, Morgan WW, Clark RA, and **Li S**. Macrophage-mediated GDNF delivery protects against dopaminergic neurodegeneration: A therapeutic strategy for Parkinson's disease. *Molecular Therapy* 18:1536-1544, 2010.

17. Imam SZ, Zhou Q, Yamamoto A, Valente AJ, Ali SF, Bains MC, Roberts JL, Kahle PJ, Clark RA, **Li S**. Novel Regulation of Parkin Function Through c-Abl-Mediated Tyrosine Phosphorylation: Implications for Parkinson's Disease. *Journal of Neuroscience* 31: 157–163, 2011.

18. Li G, Biju KC, Xu X, Zhou Q, Chen C, Valente AJ, He W, Reddick RL, Freeman GL, Ahuja SS, Clark RA and **Li S**. Macrophage LXRα gene therapy ameliorates atherosclerosis as well as hypertriglyceridemia in LDLR-/- mice. *Gene Therapy* 18: 835–841, 2011.

19. Levin MC, Lidberg U, Jirholt P, Adiels M, Wramstedt A, Gustafsson K, Greaves DR, **Li S,** Fazio S, Linton MF, Olofsson SO, Boren J, and Gjertsson I. Evaluation of macrophage-specific promoters using lentiviral delivery in mice, Gene Ther. doi:10.1038/gt.2011.195, 2011

D. Research Support

Ongoing Research Support

VA Merit Review Li (PI) 12/31/2011 – 12/31/2015
VA/BLR&D
Macrophage-mediated gene delivery of neurotrophic factors for Parkinson's disease
Using a chronic MPTP/probenecid mouse model and tetracycline-regulated GDNF-expressing lentivectors, we are investigating the efficacy of hematopoietic stem cell-based macrophage-mediated GDNF gene therapy to ameliorate the pathologic changes and neurological defects of PD. GDNF expression and secretion are switched on at different stages of degeneration of the nigrostriatal dopaminergic system. Moreover, the long-term safety issues are also addressed in the animals.

VA Merit Review Li (PI) 01/01/2009 – 12/31/2012
VA/BLR&D
Macrophage-mediated Gene Therapy of Atherosclerosis
The major goals of this proposal are to develop novel therapy for atherosclerosis by knocking down detrimental gene (such as PPAR delta) expression in macrophages using our macrophage-specific promoters combined with lentiviral transduction and hematopoietic stem cell transplantation.

2RO1DE015857-05A1 Sherry Abboud Werner (PI) 07/01/2008 – 06/30/2013
NIH
CSF-1 in Dental Biology
This proposal is to study the hypotheses: 1) cell-specific cis-acting elements in the -774 bp CSF-1 promoter direct gene expression inameloblast lineage cells during tooth development, 2) CSF-1 isoforms differentially regulate enamelmatrix and root formation and result in distinct phenotypes, and 3) lentiviral-mediated gene

deliveryof sCSF-1 to ameloblasts will rescue enamel/root defects in *op/opS* mice. CSF-1 is the growth factor for cells of the monocyte-macrophage lineage.
Role: Co-Investigator

AHAF Biju Chandu (PI) 07/2011 - 06/2013
iPS-derived microglia-based gene therapy for Alzheimer's
Postdoctoral Fellowship
Role: Mentor

IIMS/CTSA Li (PI) 06/2011 - 05/2012
Pilot Project
Preclinical study of a neuroprotective therapy for Parkinson's disease in nonhuman primate

Completed Research Support

R01 NS 046004-06 Li (PI) 07/15/2004-06/30/10
NIH/NINDS
Macrophage Gene Therapy of Neurodegenerative Diseases
The goal of this project is to develop gene therapy strategies for neurodegenerative diseases using *ex vivo* transduction of hematopoietic stem cells with lentiviral vectors expressing therapeutic genes driven by highly active macrophage-selective synthetic promoters.

VA Merit Review Li (PI) 10/01/2004 – 09/30/2007
VA/BLR&D
Macrophage-mediated Gene Therapy of Atherosclerosis
This proposal is to develop novel therapy for atherosclerosis by enhancing beneficial gene (LXRAα) expression in macrophages using our macrophage-specific promoters combined with lentiviral transduction and hematopoietic stem cell transplantation.

Scientist Development Grant Li (PI) 01/01/2001 – 12/31/2003
American Heart Association - 0030048N
Title: The Role of Calreticulin in Cardiac Development and Pathophysiology
This study investigates the function of calreticulin during cardiac development and in adult heart using transgenic and targeted gene knockout mice.