OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

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| NAMELi, Lang | POSITION TITLEProfessor  |
| eRA COMMONS USER NAME (credential, e.g., agency login)LALI@IUPUI.EDU |
| 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 |
| Wuhan University of Technology | B.A. | 1992 | Mathematics |
| University of New Mexico | M.A. | 1996 | Statistics |
| University of Michigan | Ph.D. | 2001 | Biostatistics |
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1. **Personal Statement**

**Lang Li, PhD,** is aProfessor in the Department of Medical and Molecular Genetics. Dr. Li was trained as a biostatistician from the University of Michigan. His Ph.D. thesis is the statistical methodology development for pharmacokinetics and pharmacodynamics models. Since he joined Indiana University in 2001, his methodology research has spanned from statistics, pharmacokinetics, pharmacodynamics, and to pharmacogenomics. He has applied all these computational approaches to cancer research with particular focus on drug interaction and pharmcogenomics. His expertise is well demonstrated in his 140 publications. Administratively, Dr. Li serves as the Director of the Center for Computational Biology and Bioinformatics in the Indiana University School of Medicine. His center has 12 full time faculty members from various departments: including Biostatistics, Medical and Molecular Genetics, Molecular Biology and Biochemistry, Medicine, Radiology and Imaging Science. It is a truly multi-disciplinary research center. He will bring in the CCBB center resource and expertise into this spore grant proposal. Dr. Li has served as either the Biostatistics Core Director or the Bioinformatics Core Director in several NIH funded multi-institutional grants, including Breast Cancer Pharmacogenomics Consortium from NIGMS, Pediatric Pharmacology Program Project from NICHD, and Integrative Cancer Biology Program Project from NCI. Dr. Li also has an extensive track record in his own RO1s in drug interaction research from NIGMS, NIDDK and NLM. He has also had several collaborative publications in maternal therapeutics with the key investigators in this OPRC application, notably with Dr. Haas on the preliminary work in betamethasone pharmacogenetics. Therefore, Dr. Li’s expertise fits perfectly into this OPRC proposal. In the context of this U54 proposal, “PREGMED: The Indiana University Center for Pharmacogenetics and Therapeutics Research and Education in Maternal and Child Health”, Dr. Li will serve as a consulting statistician for the Bioinformatics and Modeling Core component. He will be responsible for the collaborative study design and analytical plans for both the clinical and basic/translational science research projects. He will also utilize his expertise in biostatistics education in the training component of the proposal.

1. **Positions and Honors**

**Positions and Employment**

1994–1995 Teaching Assistant, Department of Mathematics and Statistics, University of New Mexico

1996 Teaching Assistant, Department of Biostatistics, University of Michigan (September-December)

1999 Summer Intern, Clinical Pharmacology Department, AIZA Corporation, Clinical Pharmacology Department, Mountain View, CA

1997–2001 Research Assistant, Comprehensive Cancer Center, University of Michigan

2001 Assistant Professor of the Department of Medicine, Indiana University, Indianapolis, IN

2001 Adjunct Assistant Professor of the Department of Public Health, Indiana University, School of Medicine, Indianapolis, IN

2001 Adjunct Scientist of the Regenstrief Institute

2001 Adjunct Assistant Professor of the Clinical Pharmacology

2007-2010 Associate Professor of the Department of Medicine, Indiana University, Indianapolis, IN

2007 Director of Bioinformatics Core, School of Medicine, Indiana University, Indianapolis, IN.

2010 Associate Professor of the Department of Medical and Molecular Genetics, Biostatistics, Clinical Pharmacology, and BioHealth Informatics, Indiana University, Indianapolis, IN

2011 Associate Director of the Center for Computational Biology and Bioinformatics, Indiana University, IN

2011 Associate Director of the Indiana Institute of Personalized Medicine, Indiana University, IN

2013 Interim Director of Center for Computational Biology and Bioinformatics, Indiana University, IN

2014 Director of Center for Computational Biology and Bioinformatics, Indiana University, IN

2014 Professor of Medical and Molecular Genetics

**Other Experience and Professional Memberships**

1. Member, American Statistical Society
2. Member, International Biometrics Society

2002 Member, International Society of Computational Biology

1. Associate editor and editorial board, *Cancer Informatics*.

2010 Scientific Program Committee, American Society of Clinical Pharmacology

2013 Associate Editor, Pharmacometrics and System Pharmacology

2014 Strategic Planning Committee, American Society of Clinical Pharmacology

**Honors**

1997–1998 University of Michigan Fellowship (Cancer Center Trainee)

2000 Student Awards (2001 ENAR Student Paper Competition)

2001 Excellent Paper Award (2001 ENAR Paper Competition)

2001 Excellent Paper Award (2001 JSM Paper Competition Biopharmaceutical Section)

2002 Travel Award (2002 ENAR Young Researcher Workshop)

**B. Selected peer-reviewed publications** (Publications selected from 140 peer-reviewed publications)

**Biostatistics Methodologies**

1. **Li L**, Huang J,Sun S, ShenJ, Unverzagt F, Gao S, Hendrie H, Hall K, and Hui S. Selecting Pre-Screening Items for EARLY INTERVENTION Trials of Dementia – A Case Study. Statistics in Medicine, 2004, 23, 271-283.
2. **Li L**, Desai M., Desta Z., and Flockhart D. QT analysis: a complex answer to a ‘simple’ problem. Statistics in Medicine, 2004, 23, 2625-2643.
3. **Li L**, Hui S, Desta Z, Todd S, Nguyen A and Flockhart D. Estimating a positive false discovery rate for variable selection in pharmacogenetic studies. Journal of Pharmaceutical Statistics, 2007, 17, 883-902.
4. Kim S. and **Li L**. A switching Markov chain Monte Carlo method for statistical identifiability of nonlinear pharmacokinetics models. Statistics in Sinica, 2012, 22, 1199-1215.

**Pharmacokinetics and Pharmacodynamics Modeling**

1. **Li L**, Brown M, Lee K. and Gupta S. Estimation and inference for a spline-enhanced nonlinear population pharmacokinetic model. Biometrics, 2002; 58, 601-611.
2. **Li L,** Lin X, Brown M, Gupta S. and Lee K. A population pharmacokinetic model with time-dependent covariates measured with errors. Biometrics, 2004, 60, 451-460.
3. Wang Z. Kim S., Quinney SK, Zhou J., and **Li L**., Non-compartment model/compartment model transformation. BMC System Biology, 2010, 4, 1:S8. PMC2880414

**Pregnancy Therapeutics and Modeling**

1. Quinney S.K., Mohammed A. N., Herbert M.F., Haas D.M., Clark S., Umans J.G., Caritis S.N., and **Li L**. A Semi-Mechanistic Metabolism Model of CYP3A Substrates in Pregnancy: Predicting Changes in Midazolam and Nifedipine Pharmacokinetic. Pharmacometrics and System Pharmacology 2012, 1, e2. PMC3603475
2. Haas DM, Dantzer J, Lehmann AS, Philips S, Skaar TC, McCormick CL, Hebbring SJ, Jung J, **Li L**. The impact of glucocorticoid polymorphisms on markers of neonatal respiratory disease after antenatal betamethasone administration. Am J Obstet Gynecol, 2013;208:215.e1-6.
3. Haas DM, Lehmann AS, Skaar T, Philips S, McCormick CL, Beagle K, Hebbring SJ, Dantzer J, **Li L**, Jung J. The impact of drug metabolizing enzyme polymorphisms on outcomes after antenatal corticosteroid use. Am J Obstet Gynecol, 2012;206:447.e17-24.

**Drug Interaction Prediction**

1. **Li L.,** Yu M., Chin R., Lucksiri A., Flockhart D., and Hall S. Drug-drug interaction prediction: A Bayesian meta-analysis approach. Statistics in Medicine, 2007, 26, 3700 - 3721.
2. Yu M., Kim S., Wang Z., Hall S, and **Li L**. Drug-drug interaction prediction: A Bayesian meta-analysis approach. Journal of Biopharmaceutical Statistics, 2008 18, 1063-1083.
3. Quinney S.K., Knopp S., Chang C., Hall S.D. and **Li L**. Integration of in vitro binding mechanism into the semi-physiologically based pharmacokinetic interaction model between ketoconazole and midazolam. 2013, Pharmacometrics and System Pharmacology, <http://www.nature.com/doifinder/10.1038/psp.2013.50>
4. Duke J., Han X., Wang Z., Overhage M., Subhadarshini A., Karnik SD, Rocha L.M., Li X., Strother M., Flockhart D., Quinney SK, and **Li L**. Literature based drug interaction discovery and its validation in the electronic medical record system. PLoS Computational Biology, 2012, 8(8):e1002614.

**Cancer Genomics and Epigenomics**

1. **Li L**., Cheng A. S. L., Jin V., Paik H. H., Fan M., Li X., Zhang W., Robarge J., Balch K., Davuluri R. V., Kim S., Huang T., Nephew K. A Mixture Model Based Discriminate Analysis for Identifying Ordered Transcription Factor Binding Site Pairs in Gene Promoters Directly Regulated by Estrogen Receptor-a. Bioinformatics, 2006, 22: 2210-2216.

**C. Research Support**

# Ongoing Research Support

R01 DK102694 (Hennessy/Li) 07/01/14 – 06/30/18

NIH-NIDDK

Drug Interactions Involving Anti-diabetic Agents

This grant proposes both physiological based pharmacokinetics models and pharmaco-epidemiology studies to investigate the interactions between diabetic medications and their co-medications using claims data.

(Role: PI)

R01 GM10448301-A1 (Li) 08/01/14 – 06/30/18

NIH-NIGMS

A Translational Bioinformatics Approach in the Drug Interaction Research

In this grant proposal, drug interaction pairs will be mined from electronic medical record databases; and their interaction mechanisms will be investigated using cell based experiments. Our proposed bioinformatics drug interaction research represents an ideal model for the bi-directional translational research between basic science and clinical research. It will provide significant clinical and biological evidence for better drug interaction management in the patient health care system.

(Role: PI)

R01LM011945-01 (Li) 09/01/14 – 06/30/18

NIH-NLM

Evidence-based Drug-Interaction Discovery: In Vivo, In-Vitro and Clinical

In this project we propose to develop and use large-scale text-mining methods and tools to mine drug-interaction information from PubMed abstracts and from FDA drug labels. These tools will be designed to explicitly identify gaps across the three levels of DDI evidence, and to help close such gaps. While automated discovery of DDI mentions in text is an active research area, *no other text-based work is concerned with identifying explicit evidence for DDI, while separately taking into consideration the distinct types of interaction evidence.* As a follow-up step, we also propose to conduct selective molecular pharmacology experiments to close the identified knowledge-gaps at the *in vitro* evidence level.

(Role: PI)

P50 CA113001 (PI: Huang T.) 10/01/11-02/29/15

NCI

Interrogating Epigenetic Changes in Cancer Genomes

(Role: project PI for the epigenetics for the estrogen signaling pathway)

RR025761 (PI: Shekhar) 04/01/13 - 03/30/18

NIH-NCRR

Indiana Clinical and Translational Sciences Institute (CTSI)

To establish a new institute that facilitates clinical and translational biomedical research across the state

of Indiana. This is an institute established by the CTSA to Indiana and Purdue Universities.

(Role: co-I)

R01 HD062484 (PI: Renbarger) 01/01/11-12/31/15

NIH

Pharmacogenetic Determinants of Vincristine Toxicity and Response

To study Pharmacogenetic Determinants of Vincristine Toxicity and Response.

(Role: co-I)

U10 HD063094 (PI: Flockhart) 12/01/10-12/31/14

NIH

Indiana PREGMED

Grant is designed to use a novel approach to determine how pharmacokinetics of candidate selective

serotonin reuptake inhibitors changes during pregnancy and to determine whether these changes

affect SSRI efficacy.

(Role: co-I)

R01 GM088076 (PI: Skaar) 09/30/12-08/31/16

NIH

Regulation of drug metabolizing enzymes by miRNAs

The goal of this application is to investigate the regulation of the drug metabolizing enzymes by miRNAs.

(Role: co-I)

U54HD071598-01(PI: Renbarger) 09/26/11-06/30/16

NIH-NICHHD

Indiana University Center for Pediatric Pharmacology

(Role: co-I)

# Completed Research Project

RO1 GM74217 (PI: Li L) 04/01/05 – 03/31/11

Bayesian tools for physiologically-based pharmacokinetics models in drug-drug interaction research.

The aims are: (1) Bayesian PBPK models for published PK studies; (2) Probabilistic drug interaction prediction; and (3) Midazolam/ ketoconazole drug interaction model development.

(Role: PI)

RO1 GM078501-02 (PI: Desta Z.) 07/01/07 -- 06/30/11 CYP2B6 genetic variations and drug interactions

The goal of this grant is to determine the impact of CYP2B6genetic polymorphism on substrate drug metabolism and drug interactions

(Role: co-I).

UO1 GM61373 (PI: Flockhart A) 05/01/05 – 07/31/11

Consortium on Breast Cancer Pharmacogenetics (COBRA)

The goals of the project are (1) to determine the variability in the contributions of three genetically polymorphic enzymes (CYP2C9, CYP2D6 and CYP3A) to tamoxifen metabolism; (2) to test the hypothesis that CYP2D6, CYP3A or CYP2C9 genetics alter the pharmacokinetics of tamoxifen and its metabolites in a tamoxifen clinical trial; and (4) to test the hypothesis that genetics alter the toxicity of tamoxifen.

(Role: Bioinformatics and Biostatistics Core Director)

FDA 001756 (PI: Hall S.) 02/15/01 – 02/14/03

US DHHS

Effect of Echinacea on Cytochrome P450

The goals of this award are to conduct clinical pharmacology research that enhances the ability of the FDA to regulate drug use.

(Role: co-I)