OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Lu, Xinghua

eRA COMMONS USER NAME (credential, e.g., agency login): luxing

POSITION TITLE: Professor, Biomedical Informatics

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

| INSTITUTION AND LOCATION | DEGREE(if applicable) | Completion DateMM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Shandong Medical University | M.D. | 1984 | Medicine |
| Shandong Medical University | M.S. | 1988 | Cardiology |
| University of Connecticut Health Center | Ph.D. | 1998 | Pharmacology |
| University of Pittsburgh | Certificate | 2003 | Biomedical Informatics |

# A. Personal Statement

I have a long-standing interest and experience in studying cellular signaling systems throughout a decade of “wet-lab” research as a pharmacologist and two decades of “dry-lab” research as a computational biologist using machine learning and artificial intelligence approaches. I served as the Director of the Cancer Pathway Program in the Center of Causal Discovery, an NIH National Center of Excellence in Big Data to Knowledge (BD2K). For the last two decades, my research has concentrated on developing computational methods for studying cancer pathways and cancer pharmacogenomics, particularly using Bayesian causal network discovery and deep learning approaches for modeling signal transduction systems of cells. My computational methodology development works in the above fields have been published in *Science Signaling, Molecular Systems Biology, Cancer Research, PLoS Computational Biology,* and *Bioinformatics.* Our computational research also contributed to collaborative work on cancer signaling and immunology published in *Cancer Cell*, *Nature Communication*, *JCI,* etc.

My research in modeling cancer signaling systems lays a solid foundation for developing clinical decision support systems for precision oncology. We have developed a series of causal inference and deep learning models to infer the state of cellular signaling systems. We further use such information to build machine-learning (ML) models to predict whether cancer cells will respond to anticancer drugs. Our models perform well on large-scale drug screen data based on cell lines, patient-derived organoids, and patient-derived xenografts.

Most relevant to this project, we have developed an ML model called **col**on **ox**al**i**platin **s**ignature (COLOXIS) for predicting oxaliplatin benefits in colon cancers. The model performed well in a large cohort (N > 1,000) of colon cancer adjuvant patients from a real-world randomized clinical trial. This project aims to further refine and validate the model using a larger independent cohort combining patients from two large independent clinical trials. I will serve as the contact PI for this project, contributing to refining the COLOXIS model and evaluating the outcomes of validation experiments.

**Ongoing and recently completed projects that I would like to highlight include:**

**R01 LM012011 (**PI: Lu, X**)**  05/2020 – 04/2024

**Interpretable deep learning models for translational medicine**

This project aims to develop explainable AI models for discovering signaling pathways underlying physiological and pathological processes of cancer cells. The inferred pathway-activation information will be used to predict cancer cell responses to anti-cancer drugs in the precision oncology setting.

**1R01 CA254274-01A1 (**PI**:** Lu, B, Co-I: Lu, X**)** 06/16/2021 – 05/31/2026

**Study of the IL-33-driven immune cell organization underpinning responses to immune**

**checkpoint blockade cancer therapy**

Understanding the immune cellular organization driven by IL33 in the TME opens doors to the rationale design of novel combinational therapy to meet the pressing clinical need to improve responses to current cancer immunotherapy.

**R01 CA229431-01A1 (**PI: Wang, QM, Co-I: Lu, X**)** 07/02/2019 – 06/30/2024

**A novel mitotic regulatory axis in neuroendocrine prostate cancer**

Our study will define the role of PKD in mitotic regulation and contribute to the understanding of molecular mechanisms underlying TR-NEPC progression in late-stage mCRPC and uncover novel therapeutic strategies to treat this aggressive cancer.

**Relevant publications:**

1. Ding, MQ., Chen, L., Cooper, GF., Young, JD., and **Lu, X**. (2017) Precision oncology beyond targeted therapy: Combining omics data with machine learning matches the majority of cancer cells to effective therapeutics. ***Molecular Cancer Research*** 16(2):269-278
2. Cai C, Cooper GF, Lu KN, Ma X, Xu S, Zhao Z, Chen X, Xue Y, Lee AV, Clark N, Chen V, Lu S, Chen L, Yu L, Hochheiser HS, Jiang X, Wang QJ, **Lu X**. (2019) Systematic discovery of the functional impact of somatic genome alterations in individual tumors through tumor-specific causal inference. ***PLoS Computational Biology*.** 2019 Jul; 15(7): e1007088. (doi: [10.1371/journal.pcbi.1007088](https://dx.doi.org/10.1371/journal.pcbi.1007088)). PMID:31276486; PMCID: PMC6650088
3. Tao, Y., Ren, S., Ding, MQ., Schwartz, R., and **Lu, X**. (2020) Predicting drug sensitivity of cancer cell lines via collaborative filtering with contextual attention. Proceedings of Machine Learning Research 1–A7, 2020
4. Ren, S., Tao, Y., Yu, K., Xue, Y., Schwartz, R., Lu, X. (2021) *De novo* prediction of cell-drug sensitivities using deep learning-based graph regularized matrix factorization. ***Pacific Symposium on Biocomputing 2022***.

**B. Positions and Honors**

2019 - President and Chief Scientist, DeepRx Inc.

2021 – 2022 Visiting professor (sabbatical, 11/21 – 03/22), Shezhen Bay Laboratory (SZBL), Shenzhen, Guangdong, China

2016 - Professor, Biomedical Informatics, Department of Biomedical Informatics, the University of Pittsburgh.

2010- 2016 Associate Professor, Biomedical Informatics, Department of Biomedical Informatics, University of Pittsburgh

2009-2010 Associate Professor, Bioinformatics, Dept Biochemistry and Molecular Biology, Medical University of South Carolina

2008-2010 Co-Directors, DOE GAANN training grant and NIGMS T32 training grant

2008-2010 Associate Professor, Bioinformatics, Dept Biostatistics, Bioinformatics and Epidemiology, Medical University of South Carolina

2007-2010 Director, Bioinformatics Division, Dept of Biostatistics, Bioinformatics and Epidemiology, Medical University of South Carolina

2006-2010 Director, NLM training program “Training of Toolmakers for Bio-Medical Informatics”, Dept of Biostatistics, Bioinformatics and Epidemiology, Medical University of South Carolina

2003-2008 Assistant Professor, Dept of Biostatistics, Bioinformatics and Epidemiology, Medical Univ. of South Carolina

2001-2003 National Library of Medicine training fellow, Center for Biomedical Informatics, University of Pittsburgh

1998-2001 Research Associate, Dept. of Pharmacology, University of Pittsburgh

1991-1993 Attending cardiologist, Dept of Emerg. Med., Shandong Provincial Hospital, Jinan, China

1988-1991 Chief Resident, Dept. of Emergency Medicine, Shandong Provincial Hospital, Jinan, China

1984-1985 Residency, Internal Medicine, Shengli Central Hospital, Dongying, China

# Honors and Awards

# 1997 SmithKline Beecham Award for outstanding graduate student research at New England Pharmacologists’ Meeting. Boston, MA

# 1998 Fogarty Postdoctoral Fellowship Award, National Institutes of Health

# 2001-2003 National Library of Medicine Training Fellowship award

# 2003 Lister Hill National Center for Biomedical Communication Summer Research Participation Program Fellowship

# 2004 International Society for Computation Biology travel award for PSB 2004

# 2005 The Third International Charleston Ceramide Conference travel award

# 2009 Outstanding Paper Award, AMIA Summit on Translational Bioinformatics, San Francisco, CA

2012 The 2nd place award in the Sage Bionetwork Breast Cancer Prognosis Challenge.

2019 Tied 1st Place award in the Partner Biobank Disease Challenge

# Professional Services

# 2007-2016 Ad hoc member, multiple NLM Special Panel Study Section, BDMA,

# 2007-2014 Program Committee service: IEEE 7th International Symposium on Bioinformatics & Bioengineering (BIBE 2007); (BMEI 2008); ICMS(2011); AMIA (2011); WABI (2012); ICBC (2012); (ACBIT’2013); BioVis (2014), APBC 2016.

# 2008-2010 Member, NLM Study Section, Biomedical Library and Informatics Research Committee (BLIRC), CSR/NIH

# 2008 - 2012 Associate Editor, *BMC Research Notes*

2018 - 2021 Exec Associate Editor, *The International Journal of Biological Sciences*

# 2019 - Editorial Board, *DNA Repair*

2020 - Regular member (2020 – 2024) of the CSR Study Section: Biomedical Informatics, Library and Data Sciences (BILDS)

2022 - Editorial Board, *Gene and Diseases*

# C. Contribution to Science

**C.1. Pharmacogenomics and translational medicine.** I have a long-standing interest in studying cellular signaling and using such information for translational research and application. We develop computational methods for predicting cancer cell responses to current anticancer drugs. Recently, we designed *deep learning* models to infer the state of cellular signaling systems and use the derived information to predict cancer cell drug responses. We are working on translating these models to real clinical settings to improve patient care.

1. Ding, MQ., Chen, L., Cooper, GF., Young, JD., and **Lu, X**. (2017) Precision oncology beyond targeted therapy: Combining omics data with machine learning matches the majority of cancer cells to effective therapeutics. ***Molecular Cancer Research*** 16(2):269-278
2. Tao, Y., Cai, C., Cohen, W., and **Lu, X** (2020) From genome to phenome: Predicting multiple cancer phenotypes based on somatic genomic alterations via the genomic impact transformer. Proceedings of ***Pacific Symposium on Biocomputing.***
3. Tao, Y., Ren, S., Ding, MQ., Schwartz, R., and **Lu, X**. (2020) Predicting drug sensitivity of cancer cell lines via collaborative filtering with contextual attention. Proceedings of Machine Learning Research 1–A7, 2020
4. Ren, S., Tao, Y., Yu, K., Xue, Y., Schwartz, R., Lu, X. (2021) *De novo* prediction of cell-drug sensitivities using deep learning-based graph regularized matrix factorization. ***Pacific Symposium on Biocomputing 2022***.

**C.2. Computational cancer biology.** My research has been concentrating on developing computational biology methodologies to study cancer signaling and disease mechanisms. We have designed gene-expression-module-based models for predicting breast cancer patient survival (the DREAM 7 Challenge), and our team won the 2nd best performance. Our algorithms for predicting signaling networks have won first place in the SBV IMPROVER Trans-species Network Inference Challenge.

1. Huang, T., Alvarez, AA, Pangeni, RP., Horbinski, C., Lu, S., Kim, SK., James, CD., Raizer, J., Kessler, J., Brenann, CW., Sulman, EP., Finocchiaro, G., Tan, M., Nishikawa, R., **Lu, X**., Nakano, I., Hu1, B., and Cheng, SY.. (2016) A Regulatory circuit of miR-125b/miR-20b and Wnt signaling controls GBM phenotypes through FZD6-mediated pathways. ***Nature Communication.* 7**:12885
2. Cai C, Cooper GF, Lu KN, Ma X, Xu S, Zhao Z, Chen X, Xue Y, Lee AV, Clark N, Chen V, Lu S, Chen L, Yu L, Hochheiser HS, Jiang X, Wang QJ, **Lu X**. (2019) Systematic discovery of the functional Impact of somatic genome alterations in individual tumors through tumor-specific causal inference. ***PLoS Computational Biology*.** 2019 Jul; 15(7): e1007088. (doi: [10.1371/journal.pcbi.1007088](https://dx.doi.org/10.1371/journal.pcbi.1007088)). PMID:31276486; PMCID: PMC6650088
3. Huang, T, Kim, CK., Alvarez, AA., Pangeni, RP., Shi, T, Sastry, N., Lu, S., Horbinski, C., Kessler, J., Nishikawa, R., Nakano, I., **Lu, X**, James, CD., Ying, XM., Hu, B., and Cheng, SY. (2017) MST4 phosphorylation of ATG4B regulates autophagic activity, tumorigenicity and radioresistance in cancer. ***Cancer Cell*** 32:840-855
4. Liu, Z, Cai, C., Ma, X., Liu, J, Chen, L., Lui, VWY. Cooper, GF., and **Lu, X** (2022) A novel Bayesian framework infers driver activation states and reveals pathway-oriented molecular subtypes in head and neck cancer. ***Cancers (Basel)***, 14(19):4825PMCID: [PMC9563147](http://www.ncbi.nlm.nih.gov/pmc/articles/pmc9563147/)

**C.3. Cancer immunology.** My group has developed a unique approach to studying cancer immune evasion mechanisms by combining single-cell transcriptome and individualized causal Bayesian networks. We hypothesize that cell-cell communications within an individual tumor define the immune environment of a tumor. We have developed a causal framework to infer the states of cells within a tumor and further infer how cells communicate with each other using causal Bayesian network algorithms.

1. Chen, X., and Chen, L., et al (2022) An instance-specific causal framework for learning intercellular communication networks that define microenvironments of individual tumors. Under revision at the ***PLoS Computation Biology*** (preprint **doi:** https://doi.org/10.1101/2021.11.11.467838)
2. Kurten, C., Vujanovic, L., et al (2021) Investigating immune and non-immune cell interactions in head and neck tumors by single-cell RNA sequencing. ***Nature Communication*** 12:7338, PMCID: [PMC8683505](http://www.ncbi.nlm.nih.gov/pmc/articles/pmc8683505/)
3. Chen A, Jiang Y, Li Z, Wu L, Santiago U, Zou H, Cai C, Sharma V, Guan Y, McCarl LH, Ma J, Wu YL, Michel J, Shi Y, Konnikova L, Amankulor NM, Zinn PO, Kohanbash G, Sameer A, Lu S, **Lu X,** Sun D, Gittes GK, Wang Q, Xiao X, Yimlamai D, Pollack IF. Camacho CJ, Hu, B. (2021) Chitinase-3-like-1 protein complexes modulate macrophage-mediated immune suppression in glioblastoma. ***The Journal of Clinical Investigation***. 6;147552, PMCID: [PMC8363281](http://www.ncbi.nlm.nih.gov/pmc/articles/pmc8363281/)
4. Song, X, Zhou, Z, Li, H, Xue, Y, **Lu, X**, Bahar I, Kepp, O, Hung, M-C, Kroemer, G, and Wan, Y. (2020) Pharmacological suppression of B7-H4 glycosylation restores antitumor immunity in immune-cold breast cancers. ***Cancer Discovery*** (doi: 10.1158/2159-8290.CD-20-0402) PMCID: [PMC7710601](http://www.ncbi.nlm.nih.gov/pmc/articles/pmc7710601/)

# C.4. Statistical text mining of biomedical literature and automatic annotations. I have made significant contributions to text mining in the bioinformatics domain. Our 2006 paper [1] is one of the first papers introducing PTMs to the bioinformatics field, which motivated many follow-up studies of other groups, reflected by over 40 citations. Our efforts in modeling the semantic topics associated with genes/proteins further enabled us to assess if the functions of a set of genes are coherently related (functional coherence), automatic textual evidence identification and automatic function annotation of proteins, with numerous publications in Genome Biology, Bioinformatics and BMC Bioinformatics.

1. Zheng, B., McLean, D.C., and **Lu, X**. (2006) Identifying biological concepts from a protein-related corpus with a probabilistic topic model. (doi:10.1186/1471-2105-7-58). ***BMC Bioinformatics*** 7:58. PMID:16466569. PMCID:PMC1420333.
2. Zheng, B. and **Lu, X.** (2007) Novel metrics for evaluating the functional coherence of protein groups via protein-semantic-network. ***Genome Biology***, 8:R153 [PMCID:PMC2323239](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2323239/)
3. Chen, V., **Paisley, J**., and **Lu, X** (2017) Revealing common disease mechanisms shared by tumors of different tissues of origin through semantic representation of genomic alterations and topic modeling. ***BMC Genomics*** 18 (Suppl 2):105 (**Using nested hierarchical Dirichlet process, NHDP model)**
4. Jin, Q., Dhingra, B., Cohen, W., and Lu, X. (2018) AttentionMeSH: Simple, Effective and Interpretable Automatic MeSH Indexer. ***Proc of Empirical Methods in NLP.*** Brussel, Belgium.

A partial list of my publications is available at PubMed: <https://www.ncbi.nlm.nih.gov/myncbi/xinghua.lu.1/bibliography/public/>