BIOGRAPHICAL SKETCH

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NAME: Ling, Bruce Xuefeng

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

POSITION TITLE: Assistant Professor, Surgery

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 Date MM/YYYY	FIELD OF STUDY
Fudan University, Shanghai, China	B.S.	07/1990	Biochemistry
UCLA, LA, US	M.A.	01/1994	Molecular Biology
UCLA, LA, US	Ph.D.	01/1996	Biological Chemistry
Stanford University, Stanford, US	Postdoctoral Fellow	10/1998	Computer Science
Stanford University, Stanford, US	Postdoctoral Fellow	10/1998	Biomedicine
Leavey School of Business, Santa Clara University, US		03/2001	Business Administration

A. Personal Statement

With a diverse background in both academia and industry, I have built a multidisciplinary lab that is making significant translational advances in first-in-class disease diagnostics, population health analytics, and digital pathology.

As the PI for the Translational Medicine Program within Surgery, I have led multiple multi-omics biomarker discovery and AI-powered population health and digital pathology initiatives. These projects are part of a cutting-edge program that envisions a future with a wide range of diagnostic tools and AI solutions that will reshape clinical practice.

A significant focus of my career is the use of AI to decode real-world datasets of electronic health records, high-resolution LCMS-based liquid/tissue biopsy proteomics/metabolomics, and multiple modality medical imaging. For population health management, we use tens of millions of real-world state-wide EMRs to develop risk surveillance systems that forecast aspects like disease progression, resource utilization, and mortality across a diverse patient demographic with different social determinants. This can prompt timely clinical actions by simplifying intervention orders and crafting care strategies tailored to address modifiable patient risk components. For first-in-class molecular diagnostics, we have developed unique LCMS based multi-omic approaches that allow the simultaneous absolute quantification of thousands of metabolites and proteins in blood and Formalin-Fixed Paraffin-Embedded (FFPE) tissue pathological slides to predict clinical outcomes. Our collaborations with key opinion leaders in pregnancy disorder and pediatric diseases, such as Kawasaki disease, have been productive and have helped to fill critical unmet medical needs. For computer-aided pathology (CAP) and computer-aided medical imaging analytics (CAMIA), we have developed deep learning-based computational solutions to decode clinical outcome-correlating signals in pathological whole slide images and echocardiograms. Our multi-modality and multi-omics approaches shall synergize to promise the next generation of disease diagnostics and risk stratification solutions.

These translational innovations have formed the scientific foundations of several Silicon Valley start-ups in the realms of first-in-class diagnostics and population health management, namely HBI Solutions, Inc., Carmenta

Biosciences, Inc. (Stanford Spark Program's first exited enterprise), OncoOmicsDx, Inc., and mProbe, Inc. The core mission behind these bench-to-bed side endeavors is to craft next-generation diagnostic and predictive tools, aiming to elevate both preventive measures and treatments in upcoming years.

 Edwards LA, Feng F, Iqbal M, Fu Y, Sanyahumbi A, Hao S, McElhinney DB, Ling XB, Sable C, Luo J. Machine Learning for Pediatric Echocardiographic Mitral Regurgitation Detection. J Am Soc Echocardiogr. 2023;36(1):96-104 e4. Epub 20220930. doi: 10.1016/j.echo.2022.09.017. PubMed PMID: 36191670.
 Kuo HC, Hao S, Jin B, Chou CJ, Han Z, Chang LS, Huang YH, Hwa K, Whitin JC, Sylvester KG, Reddy CD, Chubb H, Ceresnak SR, Kanegaye JT, Tremoulet AH, Burns JC, McElhinney D, Cohen HJ, Ling XB. Single center blind testing of a US multi-center validated diagnostic algorithm for Kawasaki disease in Taiwan. Front Immunol. 2022;13:1031387. Epub 20221003. doi: 10.3389/fimmu.2022.1031387. PubMed PMID: 36263040; PMCID: PMC9575935.

3. Huang Q, Hao S, You J, Yao X, Li Z, Schilling J, Thyparambil S, Liao WL, Zhou X, Mo L, Ladella S, Davies-Balch SR, Zhao H, Fan D, Whitin JC, Cohen HJ, McElhinney DB, Wong RJ, Shaw GM, Stevenson DK, Sylvester KG, <u>Ling XB</u>. Early-pregnancy prediction of risk for pre-eclampsia using maternal blood leptin/ceramide ratio: discovery and confirmation. BMJ Open. 2021;11(11):e050963. Epub 20211125. doi: 10.1136/bmjopen-2021-050963. PubMed PMID: 34824115; PMCID: PMC8627403.

4. <u>Ling XB</u>, Mellins ED, Sylvester KG, Cohen HJ. Urine peptidomics for clinical biomarker discovery. Adv Clin Chem. 2010;51:181-213. Epub 2010/09/23. doi: 10.1016/s0065-2423(10)51007-2. PubMed PMID: 20857622.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

Academic Appointments

Assistant Professor of Surgery, Stanford University
 Sr. Scientist, Translational Medicine Program, Dept. of Surgery, School of Medicine, Stanford
 University
 Sr. Scientist, Translational Medicine Program, Dept. of Pediatrics, School of Medicine, Stanford
 University

2006 Consultant, Biotechnology Core, Lucile Packard Children's Hospital, Stanford University

Industry Appointments

2010- Co-founder: HBI Solutions, Inc.; OncoOmicsDx CAP/CLIA Laboratory; Mprobe Inc.; Carmenta Biosciences, Inc.

- 2004-2005 Director, Research & Development Informatics, Amgen San Francisco.
- 2001-2004 Research Director, Tularik Inc.
- 2000-2001 Associate Director, R&D, DoubleTwist, Inc.
- 1999-2000 Genomic project lead, Pangea System, Inc.
- 1998-1999 Computation/Bioinformatics Scientist, Incyte Pharmaceuticals, Inc.

Other Experience and Professional Memberships Society Membership

Investigator, March of the Dimes Prematurity Research Center, Stanford University Professional member, American Heart Association

Service

2005- Member, Journal Editorial Board, Cancer Informatics
1997 Member, Medical Advisor Board, National Kidney Foundation of Northern California

Editorial Review

Ad hoc reviewer for: BMC medicine, PLOS ONE, PLOS Medicine, Molecular Cellular Proteomics, Bioinformatics, BMC bioinformatics, and EMBO medicine. JMIR mHealth and uHealth

<u>Honors</u>

- 2023 FDA contract award
- 2022 NIH STTR award
- 2022 NIH Technology Accelerator Challenge for Maternal Health
- 2021 NIH STTR award
- 2017 Stanford Spark Innovation Program Scholar

- 2014 American Heart Association Award
- 2014 Stanford Spark Innovation Program Scholar
- 2013 Stanford Cardiovascular Research Annual Retreat Clinical Research First Place Award
- 2013 Stanford Spark Innovation Program Scholar
- 2012 Stanford Spark Innovation Program Scholar
- 2011 Stanford Spark Innovation Program Scholar
- 1997Walter Berry Medical Research Award
- 1997National Kidney Foundation Research Award
- 1996Dean's Fellowship, Stanford University
- 1992 University Fellowship, UCLA, CA
- 1991University Fellowship, University of Iowa, IA
- 1990University Fellowship, Fudan University, China
- 1990Summa cum laude, Fudan University, China
- 1986 University Fellowship, Fudan University, China

C. Contribution to Science

 Epigenetics and histone code: As a Ph.D. student under Michael Grunstein in UCLA, I contributed to the understanding of the role of the histone H3/H4 N-termini and their post-translational modifications in gene regulation.

1. **Ling X**, Harkness TA, Schultz MC, Fisher-Adams G, Grunstein M. Yeast histone H3 and H4 amino termini are important for nucleosome assembly in vivo and in vitro: redundant and position-independent functions in assembly but not in gene regulation. Genes Dev. 1996;10(6):686-99. Epub 1996/03/15. doi: 10.1101/gad.10.6.686. PubMed PMID: 8598296.

2. Lenfant F, Mann RK, Thomsen B, Ling X, Grunstein M. All four core histone N-termini contain sequences required for the repression of basal transcription in yeast. EMBO J. 1996;15(15):3974-85. Epub 1996/08/01. PubMed PMID: 8670902; PMCID: PMC452117.

3. Thompson JS, Ling X, Grunstein M. Histone H3 amino terminus is required for telomeric and silent mating locus repression in yeast. Nature. 1994;369(6477):245-7. Epub 1994/05/19. doi: 10.1038/369245a0. PubMed PMID: 8183346.

 MOA of the immunosuppressive peptides: As a postdoctoral fellow with Alan Krensky in Stanford University, I contributed to the understanding of the mechanism of action of the potential immunosuppressive peptide drugs.

1. Jiang Y, Chen D, Lyu SC, **Ling X**, Krensky AM, Clayberger C. DQ 65-79, a peptide derived from HLA class II, induces I kappa B expression. J Immunol. 2002;168(7):3323-8. Epub 2002/03/22. doi: 10.4049/jimmunol.168.7.3323. PubMed PMID: 11907089.

2. **Ling X**, Tamaki T, Xiao Y, Kamangar S, Clayberger C, Lewis DB, Krensky AM. An immunosuppressive and anti-inflammatory HLA class I-derived peptide binds vascular cell adhesion molecule-1. Transplantation. 2000;70(4):662-7. Epub 2000/09/06. doi: 10.1097/00007890-200008270-00021. PubMed PMID: 10972226.

3. **Ling X**, Kamangar S, Boytim ML, Kelman Z, Huie P, Lyu SC, Sibley RK, Hurwitz J, Clayberger C, Krensky AM. Proliferating cell nuclear antigen as the cell cycle sensor for an HLA-derived peptide blocking T cell proliferation. J Immunol. 2000;164(12):6188-92. Epub 2000/06/08. doi: 10.4049/jimmunol.164.12.6188. PubMed PMID: 10843669.

3. <u>Decode the human genome</u>: After postdoctoral training in computer science and biomedicine at Stanford University, I began my career decoding the human genome draft during the goldrush for novel drug targets, such as unfound GPCRs and kinases. In 1999, my team at DoubleTwist delivered the *first* human genome database for commercial use. As the team leader, I also contributed to the science of human gene number estimation by comparing the HGP genome, Celera genome, and RefSeq database.

1. **Ling XB**. A machine to make a future - Biotech chronicles. J Clin Invest. 2005(115):2303-4.; PMCID: PMC1193899.

2. Li S, Cutler G, Liu JJ, Hoey T, Chen L, Schultz PG, Liao J, **Ling XB**. A comparative analysis of HGSC and Celera human genome assemblies and gene sets. Bioinformatics. 2003;19(13):1597-605. Epub 2003/09/12. doi: 10.1093/bioinformatics/btg219. PubMed PMID: 12967954.

3. Li S, Liao J, Cutler G, Hoey T, Hogenesch JB, Cooke MP, Schultz PG, **Ling XB**. Comparative analysis of human genome assemblies reveals genome-level differences. Genomics. 2002;80(2):138-9. Epub 2002/08/06. doi: 10.1006/geno.2002.6824. PubMed PMID: 12160725.

4. Pouliot Y, Gao J, Su QJ, Liu GG, **Ling XB**. DIAN: a novel algorithm for genome ontological classification. Genome research. 2001;11(10):1766-79. Epub 2001/10/10. doi: 10.1101/gr.183301. PubMed PMID: 11591654; PMCID: 311153.

4. <u>High throughput lead discovery powered by scientific computing</u>: The Human Genome Project revealed a vast number of new therapeutic targets. Modern high-throughput methodologies and screening robotics now generate unprecedented amounts of data for small molecule drug discovery. As research director under the biotech giant David Goeddel at Tularik Inc., I supervised the implementation of scientific computing and delivered the Tularik small molecule HTS Discovery Platform at scale. This significantly increased lead discovery throughput, resulting in high-quality drug candidates.

Ling XB. High throughput screening informatics. Comb Chem High Throughput Screen.
 2008;11(3):249-57. Epub 2008/03/14. doi: 10.2174/138620708783877726. PubMed PMID: 18336217.
 Li WX, Li L, Eksterowicz J, Ling XB, Cardozo M. Significance analysis and multiple pharmacophore models for differentiating P-glycoprotein substrates. Journal of chemical information and modeling.
 2007;47(6):2429-38. Epub 2007/10/25. doi: 10.1021/ci700284p. PubMed PMID: 17956085.
 Pei L, Peng Y, Yang Y, Ling XB, Van Eyndhoven WG, Nguyen KC, Rubin M, Hoey T, Powers S, Li J. PRC17, a novel oncogene encoding a Rab GTPase-activating protein, is amplified in prostate cancer. Cancer Res. 2002;62(19):5420-4. Epub 2002/10/03. PubMed PMID: 12359748.

5. Peptidomics/Metabolomics/Proteomics: Collaborating with industrial giant Thermo Fisher, my Stanford laboratory focused on the development of unique LCMS based multi-omic approaches that allow the simultaneous absolute quantification of thousands of metabolites and proteins in blood and FFPE pathological slides to predict clinical outcomes. For FFPE pathological slides, our laser capture micro dissection (LCM) of tumor population in the FFPE specimens can retain the spatial and morphological context. In the field of precision oncology, our clinical analytic workflow, with laser capture micro dissection of the tumor cells in FFPE specimens and then quantitative LCMS/MS profiling, can precisely quantify therapeutic targets within the targeted tumor, and link the results to clinical outcomes to stratify the patients to achieve precision medicine. LCM can allow us to physically and precisely separate the cancer and cancer microenvironment for the cancer cellular drug target expression quantifications. My laboratory leverages high throughput biology data sets through analytics production to provide a more technically and bioinformatically tractable, physiologically relevant, chemically comprehensive, and cost effective assessment of multi-factorial non-communicable diseases. We have employed a comprehensive unbiased multi-omics' approach, integrating big datasets of genomics, metabolomics, and proteomics to define the multi-omics molecular "portrait" and relative health risk against the population baseline.

Thyparambil S, Liao W-L, An E, Tian Y, Heaton R, Sylvester KG, Ling XB. Expression of antibody-drug conjugates (ADC) biomarkers in colorectal cancer. Journal of Clinical Oncology. 2020;38(4_suppl):17-.
 Zheng L, Zhang Y, Hao S, Chen L, Sun Z, Yan C, Whitin JC, Jang T, Merchant M, McElhinney DB, Sylvester KG, Cohen HJ, Recht L, Yao X, Ling XB. A proteomic clock for malignant gliomas: The role of the environment in tumorigenesis at the presymptomatic stage. PLoS One. 2019;14(10):e0223558. Epub 2019/10/11. doi: 10.1371/journal.pone.0223558. PubMed PMID: 31600288; PMCID: PMC6786640.
 Tan Z, Liu R, Zheng L, Hao S, Fu C, Li Z, Deng X, Jang T, Merchant M, Whitin JC, Guo M, Cohen HJ, Recht L, Ling XB. Cerebrospinal fluid protein dynamic driver network: At the crossroads of brain tumorigenesis. Methods. 2015;83:36-43. Epub 2015/05/20. doi: 10.1016/j.ymeth.2015.05.004. PubMed PMID: 25982164.

4. **Ling XB**, Mellins ED, Sylvester KG, Cohen HJ. Urine peptidomics for clinical biomarker discovery. Adv Clin Chem. 2010;51:181-213. Epub 2010/09/23. doi: 10.1016/s0065-2423(10)51007-2. PubMed PMID: 20857622.

6. <u>Kawasaki disease diagnosis</u>: Kawasaki disease (KD) is an acute systemic vasculitis that currently ranks as the primary cause of acquired heart disease in childhood in both the United States and Japan. Early diagnosis of KD during the acute phase is crucial for timely administration of anti-inflammatory therapies, effectively reducing the risk of coronary artery aneurysms (CAA). To improve clinical outcomes and optimize resource utilization, my Stanford laboratory has utilized machine learning approaches on electronic health record (EHR) datasets. In 2013, we conducted a study applying statistical learning to

clinical and laboratory test patterns for acute KD diagnosis. Subsequently, in 2016, we enhanced and validated this improved diagnostic algorithm at a single site in the United States (US). Expanding further, we conducted validation12 at five pediatric hospitals across the US, including Boston Children's Hospital in Boston, Massachusetts; Children's Hospital Colorado in Aurora, Colorado; Children's Hospital of Orange County in Orange, California; Nationwide Children's Hospital in Columbus, Ohio; and Rady Children's Hospital in San Diego, California. Recently, we successfully validated this algorithm through a blinded study at a single center in Taiwan, Asia. My laboratory is currently developing qPCR and immune detection methods to objectively diagnose KD from confounding febrile illness.

1. Kuo HC, Hao S, Jin B, Chou CJ, Han Z, Chang LS, Huang YH, Hwa K, Whitin JC, Sylvester KG, Reddy CD, Chubb H, Ceresnak SR, Kanegaye JT, Tremoulet AH, Burns JC, McElhinney D, Cohen HJ, **Ling XB.** Single center blind testing of a US multi-center validated diagnostic algorithm for Kawasaki disease in Taiwan. Front Immunol. 2022;13:1031387. Epub 20221003. doi: 10.3389/fimmu.2022.1031387. PubMed PMID: 36263040; PMCID: PMC9575935.

2. Hao S, **Ling XB**, Kanegaye JT, Bainto E, Dominguez SR, Heizer H, Jone PN, Anderson MS, Jaggi P, Baker A, Son MB, Newburger JW, Ashouri N, McElhinney DB, Burns JC, Whitin JC, Cohen HJ, Tremoulet AH, Pediatric Emergency Medicine Kawasaki Disease Research G. Multicentre validation of a computerbased tool for differentiation of acute Kawasaki disease from clinically similar febrile illnesses. Arch Dis Child. 2020;105(8):772-7. Epub 2020/03/07. doi: 10.1136/archdischild-2019-317980. PubMed PMID: 32139365.

Hao S, Jin B, Tan Z, Li Z, Ji J, Hu G, Wang Y, Deng X, Kanegaye JT, Tremoulet AH, Burns JC, Cohen HJ, Ling XB, Pediatric Emergency Medicine Kawasaki Disease Research G. A Classification Tool for Differentiation of Kawasaki Disease from Other Febrile Illnesses. J Pediatr. 2016;176:114-20 e8. Epub 2016/06/28. doi: 10.1016/j.jpeds.2016.05.060. PubMed PMID: 27344221; PMCID: PMC5003696.
 Ling XB, Kanegaye JT, Ji J, Peng S, Sato Y, Tremoulet A, Burns JC, Cohen HJ. Point-of-care differentiation of Kawasaki disease from other febrile illnesses. J Pediatr. 2013;162(1):183-8 e3. Epub 2012/07/24. doi: 10.1016/j.jpeds.2012.06.012. PubMed PMID: 22819274; PMCID: PMC4186670.

7. <u>Necrotizing enterocolitis diagnosis and outcome prediction</u>: Necrotizing enterocolitis (NEC) is an inflammatory condition that predominantly affects the digestive system of newborns. Despite extensive research efforts spanning decades, NEC continues to be a prominent cause of illness and death among infants in neonatal intensive care units (NICUs). It has now become the most prevalent surgical emergency in newborns, surpassing all other gastrointestinal (GI) disorders that require surgical intervention in terms of the associated health issues and fatalities. Although we have yet to fully comprehend the precise mechanisms behind NEC, recent advancements in clinical knowledge suggest a shift in emphasis towards preventing the condition and identifying high-risk infants or those with progressive disease at an earlier stage. Through a collaborative effort with NEC specialist Karl Sylvester, our laboratory has employed advanced metabolomic and proteomic techniques to create cutting-edge personalized clinical tools for diagnosing and forecasting the clinical outcomes of NEC.

1. Sinclair TJ, Ye C, Chen Y, Zhang D, Li T, **Ling XB**, Cohen HJ, Shaw GM, Stevenson DK, Chace D, Clark RH, Sylvester KG. Progressive Metabolic Dysfunction and Nutritional Variability Precedes Necrotizing Enterocolitis. Nutrients. 2020;12(5). Epub 2020/05/06. doi: 10.3390/nu12051275. PubMed PMID: 32365850; PMCID: PMC7281969.

 Sylvester KG, Ling XB, Liu GY, Kastenberg ZJ, Ji J, Hu Z, Wu S, Peng S, Abdullah F, Brandt ML, Ehrenkranz RA, Harris MC, Lee TC, Simpson BJ, Bowers C, Moss RL. Urine protein biomarkers for the diagnosis and prognosis of necrotizing enterocolitis in infants. J Pediatr. 2014;164(3):607-12 e1-7. Epub 2014/01/18. doi: 10.1016/j.jpeds.2013.10.091. PubMed PMID: 24433829; PMCID: PMC4161235.
 Sylvester KG, Ling XB, Liu GY, Kastenberg ZJ, Ji J, Hu Z, Peng S, Lau K, Abdullah F, Brandt ML, Ehrenkranz RA, Harris MC, Lee TC, Simpson J, Bowers C, Moss RL. A novel urine peptide biomarkerbased algorithm for the prognosis of necrotising enterocolitis in human infants. Gut. 2014;63(8):1284-92. Epub 2013/09/21. doi: 10.1136/gutjnl-2013-305130. PubMed PMID: 24048736; PMCID: PMC4161026.
 Ji J, Ling XB, Zhao Y, Hu Z, Zheng X, Xu Z, Wen Q, Kastenberg ZJ, Li P, Abdullah F, Brandt ML, Ehrenkranz RA, Harris MC, Lee TC, Simpson BJ, Bowers C, Moss RL, Sylvester KG. A data-driven algorithm integrating clinical and laboratory features for the diagnosis and prognosis of necrotizing enterocolitis. PLoS One. 2014;9(2):e89860. Epub 2014/03/04. doi: 10.1371/journal.pone.0089860. PubMed PMID: 24587080; PMCID: PMC3938509. 8. <u>Transdisciplinary efforts for Pregnancy disorder prediction:</u> As a principal investigator at the March of the Dime Prematurity Center, I worked with center director David Stevenson to apply our blood/urine metabolomics and proteomics approaches to pregnancy disorders such as preeclampsia (PE) and preterm birth (PTB), where early diagnosis is essential for a good clinical outcome. We identified urine/blood metabolite markers that change over time during gestation, suggesting that a "metabolic clock" characterizes normal pregnancy and could be used as a reference to identify changes associated with PE or PTB. We discovered multiple blood or urine metabolite/protein panels with the potential to be FDA-approved molecular diagnostics for pregnancy-related issues.

1. Zhang Y, Sylvester KG, Jin B, Wong RJ, Schilling J, Chou CJ, Han Z, Luo RY, Tian L, Ladella S, Mo L, Maric I, Blumenfeld YJ, Darmstadt GL, Shaw GM, Stevenson DK, Whitin JC, Cohen HJ, McElhinney DB, Ling XB. Development of a Urine Metabolomics Biomarker-Based Prediction Model for Preeclampsia during Early Pregnancy. Metabolites. 2023;13(6). Epub 20230531. doi: 10.3390/metabo13060715. PubMed PMID: 37367874; PMCID: PMC10301596.

2. Sylvester KG, Hao S, You J, Zheng L, Tian L, Yao X, Mo L, Ladella S, Wong RJ, Shaw GM, Stevenson DK, Cohen HJ, Whitin JC, McElhinney DB, **Ling XB**. Maternal metabolic profiling to assess fetal gestational age and predict preterm delivery: a two-centre retrospective cohort study in the US. BMJ Open. 2020;10(12):e040647. Epub 2020/12/04. doi: 10.1136/bmjopen-2020-040647. PubMed PMID: 33268420; PMCID: PMC7713207.

 Wen Q, Liu LY, Yang T, Alev C, Wu S, Stevenson DK, Sheng G, Butte AJ, Ling XB. Peptidomic Identification of Serum Peptides Diagnosing Preeclampsia. PLoS One. 2013;8(6):e65571. Epub 2013/07/11. doi: 10.1371/journal.pone.0065571. PubMed PMID: 23840341; PMCID: PMC3686758.
 Liu LY, Yang T, Ji J, Wen Q, Morgan AA, Jin B, Chen G, Lyell DJ, Stevenson DK, Ling XB, Butte AJ. Integrating multiple 'omics' analyses identifies serological protein biomarkers for preeclampsia. BMC Med. 2013;11:236. Epub 2013/11/08. doi: 10.1186/1741-7015-11-236. PubMed PMID: 24195779; PMCID: PMC4226208.

9. Population health management: We need definitive diagnosis/prognosis risk stratification to better monitor disease progression and improve outcomes and cost-effectiveness. My lab's population risk analytics approach integrates structured and unstructured clinical data to risk-stratify the population for preventive or targeted care. Data-driven healthcare uses big data from treating millions of patients to provide the best and most personalized care. Big data-based business intelligence/artificial intelligence (BI/AI) in healthcare is improving practice quality and outcomes, and reducing practice-induced adverse events. For the past ten years, my laboratory has collaborated with multiple state health information exchange organizations to implement our vision of innovating healthcare management through disruptive big data-based solutions.

1. Zheng L, Wang O, Hao S, Ye C, Liu M, Xia M, Sabo AN, Markovic L, Stearns F, Kanov L, Sylvester KG, Widen E, McElhinney DB, Zhang W, Liao J, **Ling XB**. Development of an early-warning system for high-risk patients for suicide attempt using deep learning and electronic health records. Transl Psychiatry. 2020;10(1):72. Epub 2020/02/23. doi: 10.1038/s41398-020-0684-2. PubMed PMID: 32080165; PMCID: PMC7033212.

2. Wang Y, Luo J, Hao S, Xu H, Shin AY, Jin B, Liu R, Deng X, Wang L, Zheng L, Zhao Y, Zhu C, Hu Z, Fu C, Hao Y, Zhao Y, Jiang Y, Dai D, Culver DS, Alfreds ST, Todd R, Stearns F, Sylvester KG, Widen E, **Ling XB**. NLP based congestive heart failure case finding: A prospective analysis on statewide electronic medical records. Int J Med Inform. 2015;84(12):1039-47. Epub 2015/08/10. doi:

10.1016/j.ijmedinf.2015.06.007. PubMed PMID: 26254876.

3. Hu Z, Hao S, Jin B, Shin AY, Zhu C, Huang M, Wang Y, Zheng L, Dai D, Culver DS, Alfreds ST, Rogow T, Stearns F, Sylvester KG, Widen E, **Ling X**. Online Prediction of Health Care Utilization in the Next Six Months Based on Electronic Health Record Information: A Cohort and Validation Study. J Med Internet Res. 2015;17(9):e219. doi: 10.2196/jmir.4976. PubMed PMID: 26395541.

4. Hao S, Wang Y, Jin B, Shin AY, Zhu C, Huang M, Zheng L, Luo J, Hu Z, Fu C, Dai D, Wang Y, Culver DS, Alfreds ST, Rogow T, Stearns F, Sylvester KG, Widen E, **Ling XB**. Development, Validation and Deployment of a Real Time 30 Day Hospital Readmission Risk Assessment Tool in the Maine Healthcare Information Exchange. PLoS One. 2015;10(10):e0140271. Epub 2015/10/09. doi: 10.1371/journal.pone.0140271. PubMed PMID: 26448562; PMCID: PMC4598005.