## BIOGRAPHICAL SKETCH

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NAME: Ying Ge

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

POSITION TITLE: Professor

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 |
|---|---|---|---|
| Peking University, Beijing, P.R. China | BS | 1997 | Chemistry |
| Cornell University, Ithaca, NY | PhD | 2002 | Chemistry |

### A. Personal Statement

My career goal is to redefine molecular mechanisms in heart failure and cardiac regeneration through systems biology approaches and translate the bench discoveries to the clinic for precision medicine. My research is highly interdisciplinary that cuts across the traditional boundaries of chemistry, biology, and medicine. I received my Ph.D. from Cornell University under the joint supervision of Prof. Fred McLafferty, a pioneer in mass spectrometry, and Prof. Tadhg Begley, a well-known chemical biologist/enzymologist. Thus I have a strong background in chemical biology, analytical chemistry and extensive training/experience in mass spectrometry. After graduate school, I explored a career in pharmaceutical industry and had practical working experience in both drug discovery and development in pharmaceutical industry. Although I enjoyed my industrial experience, my ultimate interests were in academia for the freedom of pursuing independent research. In 2006, I joined UW-Madison to establish the Human Proteomics Program.

In 2012, I started my tenure track position in the Department of Cell and Regenerative Biology and Department of Chemistry at UW-Madison and have established a vibrant and externally funded research program in cardiac proteomics and systems biology. I have developed innovative technologies that can provide transformative insights into the understanding of cardiac disease and regeneration, to identify new molecular targets for diagnosis, and ultimately provide novel treatments for heart failure. I have published 136 papers including several in high impact journals. I have been awarded three NIH R01 grants and a high-end instrument grant. Moreover, I have been a regular reviewer for NIH, *ad hoc* reviewer for AHA, NSF and other domestic and international grant agencies.

I am very passionate about education and find genuine fulfillment in inspiring young scientists. My satisfaction comes when I see students develop critical thinking and problem-solving ability and thrive in their career development stages. In my lab, I aim to create a stimulating and nurturing research environment to train the young generation of scientists from diverse backgrounds. I have been mentoring students from chemistry, biology and medicine graduate programs. I have successfully mentored 10 post-doc associates, 7 PhD students, and 3 MD students (1 with honor thesis) as well as 25 undergraduate students at UW-Madison. I am currently mentoring 13 graduate students as well as 6 undergraduate students in my research group.

### B. Positions and Honors

**Positions and employment**

1998-2002 Research Assistant, Department of Chemistry, Cornell University
2002-2003 Research Scientist III, Department of Chemical Technologies, Wyeth Research
2003-2004 Senior Research Scientist I, Department of Chemical Technologies, Wyeth Research
2004-2006 Research Scientist, Group Leader, Department of Analytical Development, PPD, Inc.
2006-present Director of Mass Spectrometry, Human Proteomics Program, School of Medicine and Public

| | |
|---|---|
| | Health, University of Wisconsin-Madison |
| 2006-2012 | Assistant Scientist, Department of Physiology, School of Medicine and Public Health, University of Wisconsin-Madison |
| 2012-2015 | Assistant Professor, Department of Cell and Regenerative Biology, School of Medicine and Public Health, and Department of Chemistry, University of Wisconsin-Madison |
| 2015-2019 | Associate Professor, Department of Cell and Regenerative Biology, School of Medicine and Public Health, and Department of Chemistry, University of Wisconsin-Madison |
| 2019-present | Professor, Department of Cell and Regenerative Biology, School of Medicine and Public Health, and Department of Chemistry, University of Wisconsin-Madison |

**Selected Service, Other Experience and Professional Memberships**

| | |
|---|---|
| 2009 | Canada Foundation for Innovation Leaders Opportunity Fund Review Panel |
| 2010-2015 | *Ad hoc* reviewer for NIH Study Section (Myocardial Ischemia and Metabolism) |
| 2011 | NIH Special Emphasis Panel (Cardiovascular and Respiratory Sciences) |
| 2011 | National Science Foundation Major Research Instrumentation (MRI) Program |
| 2012 | *Ad hoc* reviewer Swiss Science Foundation |
| 2013-2015 | AHA Cardiac Biology Regulation –Bsci6 Review Panel |
| 2014 | *Ad hoc* reviewer for United Kingdom Medical Research Council |
| 2014 | *Ad hoc* reviewer for Austrian Science Fund |
| 2014 | NIH Program Project Review Panel |
| 2015 | NASA HERO Exercise and Cardiovascular Review Panel |
| 2015-present | Board of Directors for Top-down Proteomics Consortium |
| 2016-2018 | Board of Directors for American Society for Mass Spectrometry |
| 2016-2020 | Regular Member of NIH Study Section (Myocardial Ischemia and Metabolism) |
| 2021 | NIH Special Emphasis Panel(Cardiovascular and Respiratory Sciences) |

**Selected Honors**

| | |
|---|---|
| 2007-2010 | American Heart Association Scientist Development Grant |
| 2011 | The Academy of Cardiovascular Research Excellence Young Investigator Award |
| 2014 | Shaw Scientist Finalist |
| 2016 | Georges Guiochon Faculty Fellowship |
| 2018 | H. I. Romnes Faculty Fellowship |
| 2019 | The Top 100 Analytical Scientist Power List (on a global scale) |
| 2020 | American Society for Mass Spectrometry Biemann Medal |
| 2020 | The Top 10 Analytical Scientist Power List (in North America) |

## C. Contribution to Science (from a total of 136 publications)

### 1. ***Technology Development for Top-Down Proteomics***

Proteomics is essential for deciphering how proteins interact as a system and for understanding the functions of cellular systems in human diseases. However, the unique characteristics of the human proteome, which include the large dynamic range of protein expression and the extreme complexity resulting from a plethora of post-translational modifications (PTMs) and sequence variations, make such analyses difficult. The emerging top-down mass spectrometry (MS)-based proteomics, which is based on analysis of intact proteins, is arguably the most powerful method to comprehensively characterize proteoforms that arise from genetic variations, alternative splicing, and PTMs. I have made significant advances in top-down MS for analysis of large intact proteins purified from complex biological samples including cell and tissue lysate as well as body fluids. We have shown that top-down MS has unique advantages for unraveling the molecular complexity, quantifying modified protein forms, deep sequencing of intact proteins, mapping modification sites with full sequence coverage, discovering unexpected modifications, identifying and quantifying positional isomers and determining the order of multiple modifications. Recently, we are employing a multi-pronged approach to address the challenges in top-down proteomics in a comprehensive manner by developing new MS-compatible surfactants for protein solubilization, novel materials and new strategies for multi-dimensional chromatography separation of proteins, novel nanomaterials for enrichment of low-abundance proteins. Additionally, we are developing a new comprehensive user-friendly software package for top-down proteomics.

a. Hwang, L.; Ayaz-Guner, S.; Cai, W.; Gregorich Z. R.; Jin, S.; **Ge, Y.*** Specific enrichment of phosphoproteins using functionalized multivalent nanoparticles, *J. Am. Chem. Soc*., **2015**, *137*, 2432-2435. PMCID: PMC4372338.
b. Cai, W.; Guner, H.; Gregorich, Z. R.; Chen, A. J.; Ayaz-Guner, S.; Peng, Y.; Valeja, S. G.; Liu, X.; **Ge, Y.*** MASH Suite Pro: A comprehensive software tool for top-down proteomics, *Mol. Cell Proteomics* **2016**, *15*, 703-714. PMCID: PMC4739683.
c. Brown, K. A.; Chen, B.; Guardado-Alvarez, T.; Lin, Z.; Hwang, L.; Ayaz-Guner, S.; Jin, S.; **Ge, Y.*** A cleavable surfactant for top-down proteomics. *Nature Methods* 2019, 16, 417-420. PMCID: PMC6532422.
d. Tiambeng T, Roberts DS, Brown KA, Zhu Y, Chen B, Wu Z, Mitchell SD, Guardado-Alvarez TM, Jin S, **Ge Y.*** Nanoproteomics enables proteoform-resolved analysis of low-abundance proteins in human serum. *Nature Commun.* **2020**, *11*, 3903. PMCID:PMC7411019

## 2. *The Role of Myofilament Modifications in Heart Failure*

A major biological research objective in my lab is to understand how myofilament modifications regulate cardiac contractility in health and disease using top-down proteomics in conjunction with *in vivo*, *ex vivo*, and *in vitro* functional measurements. Myofilament proteins of the sarcomeres not only play essential roles in cardiac contractility, but are also critical elements in signal reception and transduction during the onset and progression to heart failure (HF). I have made important contributions to myofilament proteomics and muscle biology. We have comprehensively characterized all types of detectable PTMs including phosphorylation, acetylation, proteolytic degradation, splicing isoforms and single amino acid polymorphisms of cardiac troponin (cTn)/tropomyosin (Tm), a key thin filament regulatory complex, purified directly from animal and human heart tissues. Furthermore, we have identified all the phosphorylation sites in a thick filament protein, cardiac myosin-binding protein C. More importantly, we have linked altered myofilament PTMs to contractile dysfunction in HF using both animal models and human clinical samples.

a. **Ge, Y.***; Rybakova, I.; Xu, Q.; Moss, R. L. Top-down high resolution mass spectrometry of cardiac myosin binding protein C revealed that truncation alters protein phosphorylation state, *Proc. Natl. Acad. Sci. U. S. A.* 200*9,106,* 12658-12663*.* PMCID: PMC2722289 *This article is a PNAS Direct Submission
b. Zhang, J.; Guy, J. M.; Norman, H. A.; Chen, Y.; Dong, X.; Wang, S.; Kohmoto, T.; Young, K. H.; Moss, R. L.; **Ge, Y.*** Top-Down quantitative proteomics identified phosphorylation of cardiac troponin I as a candidate biomarker for chronic heart failure, *J. Proteome Res.* 2011, 10,4054-4065*.* PMCID: PMC3170873
c. Peng, Y.; Gregorich Z. R.; Valeja, S. G.; Zhang, H.; Cai, W.; Chen, Y.; Guner, H.; Chen, A. J.; Schwahn, D. J.; Hacker, T. A.; Liu, X.; **Ge, Y.*** Top-down proteomics reveals concerted reductions in myofilament and Z-disc protein phosphorylation after acute myocardial infarction, *Mol. Cell. Proteomics* 2014, *13*, 2752-2764. PMCID: PMC4189000.
d. Tucholski, T.; Cai, W.; Gregorich, Z.; Bayne, E.; Mitchell, S.; de Lange, W.; McIlwain, S.; Wrobbel, M.; Karp, H.; Hite, Z.; Vikhorev, P. G., Marston, S. B.; Lal, S.; Li, A.; dos Remedios, C.; Kohmoto, T.; Hermsen, J.; Kamp, T.; Ralphe J. C.; Moss, R.L.; **Ge, Y.*** Distinct hypertrophic cardiomyopathy genotypes result in convergent sarcomeric proteoform profiles revealed by top-down proteomics, *Proc. Natl. Acad. Sci. U. S. A.* 2020, 117, 24691-24700. PMCID:PMC7547245 *This article is a PNAS Direct Submission.

## 3. *Stem Cell and Cardiac Regeneration*

A new direction in my research program is to investigate the molecular mechanism in cardiac regeneration via systems biology approaches. The stem cell treatments have beneficial functional improvement for post-MI left ventricular (LV) remodeling, however, the underlying mechanisms remain poorly defined. Thus, we are undertaking a systems biology approach to comprehensively delineate the molecular signaling pathways underlying cardiac regeneration in response to stem cell transplantation (in collaboration with Prof. Jianyi Zhang). Using a swine acute myocardial infarction model with tri-lineage cardiovascular cell transplantation, we provided the direct evidence that the functionally beneficial effects of cell therapy is accompanied by changes in the protein expression profiles of the myocardial cells in the recipient myocardium—leading to the induction of beneficial signaling pathways Recently, we demonstrated that the MI-induced changes in sarcomeric proteins phosphorylation were reversed by cell transplantation of human cardiac muscle patches derived from human induced-pluripotent stem cells in clinically relevant dimensions four weeks after MI injury. Moreover, we are harnessing the power of innovative top-down proteomics-based systems biology with patient specific hiPSC-derived cardiomyocytes (CMs) in engineered cardiac tissue to study hypertrophic cardiomyopathy (HCM) (in collaboration with Prof. Prof. Timothy Kamp and Carter Raphe).

a. Ye, L.; Chang, Y. H.; Xiong Q.; Zhang P.; Somasundaram, P.; Lepley M.; Swingen C.; Su, L.; Wendel, J. S.; Guo, J.; Jang, A.; Rosenbush, D.; Zhang, L.; Greder, L.; Dutton, J. R.; Zhang, J.; Kamp, T. J.; Kaufman, D.S.; **Ge, Y.;** Zhang, J. Cardiac repair in a porcine model of acute myocardial infarction with human induced pluripotent stem cell-derived cardiovascular cells, *Cell Stem Cell* 2014, *15*, 750-761. PMCID: PMC4275050

b. Chang, Y.; Ye, L.; Cai, W.; Lee, Y-K.; Guner, H.; Lee, Y-S.; Kamp, T. J.; Zhang, J.; **Ge, Y.*** Quantitative proteomics reveals differential regulation of protein expression in recipient myocardium after trilineage cardiovascular cell transplantation, *Proteomics*, 2015, *15*, 2560-2567. PMCID: PMC4690722

c. Gao, L.; Gregorich, Z. R.; Zhu, W.; Mattapally, S.; Lou, X.; Borovjagin, A. V.; Walcott, G. P.; Pollard, A. E.; Fast, V. G.; **Ge, Y.;** Zhang, J. Large cardiac-muscle patches engineered from human induced-pluripotent stem-cell–derived cardiac cells improve recovery from myocardial infarction in swine. *Circulation,* 2018, 137, 1712-1730. PMCID:PMC5903991

d. Cai, W.; Zhang, J.; de Lange, W. J.; Gregorich, Z. R.; Karp, H.; Farrell, E. T.; Lin, Z.; Mitchell, S. D.; Tucholski, T.; McIlwain, S.; Ralphe, C. J.; Kamp, T. J.; **Ge, Y.*** Unbiased proteomics method to assess the maturation of human pluripotent stem cell-derived cardiomyocytes, *Circ. Res.* 2019*, 125,* 936-953. PMC-in process.

**For a more complete list of published work visit MyBibliography**
https://www.ncbi.nlm.nih.gov/sites/myncbi/ying.ge.1/bibliography/41605245/public/?sort=date&direction=descending

## D. Research Support

**Ongoing**

"Top-Down Proteomics of Myofilaments in Heart Failure"
Principal Investigator: **Ge** Agency: NIH/NHLBI
Type: R01 Period: 8/5/2011 – 11/30/2021
Goals: To develop top-down mass spectrometry-based proteomics technologies for analysis of key myofilament regulatory proteins and to understand the disease mechanism in left ventricular hypertrophy and failure using a pressure overload animal model and hypertrophic cardiomyopathy.
*Impact/Priority Score: 18, Percentile: 8.0 (reviewed by CCHF study section)*
*Renewal: Impact/Priority Score: 21, Percentile: 3.0 (reviewed by CCHF study section)*

"Enabling Top-down Proteomics through Material Chemistry and Nanotechnology"
Principal Investigator: **Ge and Jin (MPI)** Agency: NIH/NIGMS
Type: R01 Period: 9/22/2015 - 6/30/2024
Goals: To develop novel approaches enabled by nanotechnology and materials chemistry to address the challenges in top-down MS-based proteomics.
*Impact/Priority Score: 20, Percentile: 2.0 (reviewed by ISD study section)*
*Renewal Impact/Priority Score: 20, Percentile: 2.0 (reviewed by EBIT study section)*

"MASH Explorer, a Comprehensive Software Environment of Top-Down Proteomics"
Principal Investigator: **Ge** Agency: NIH/NIGMS
Type: R01 Period: 6/01/2018 - 3/31/2022
Goals: To develop MASH Explorer, a comprehensive, user-friendly, and universal software environment for top-down proteomics, to process data from various vendor formats and incorporate multiple algorithms for deconvolution and database search with user-friendly graphical interfaces
*Impact/Priority Score: 18, Percentile: 2.0 (reviewed by EBIT study section)*

"A Multi-Omics Approach to Discover Metabolic Critical Quality Attributes for Cardiomyocyte Biomanufacturing"
Principal Investigator: **Palecek** (**Ge, Co-investigator)** Agency: NIH/NHLBI
Type: R01 Period: 7/1/2019 – 6/30/2024
Goals: This study aims to provide fundamental new insights into metabolic transitions during iPSC-CM differentiation and maturation, will identify novel multivariate metabolic CQAs that will facilitate efforts to mature iPSC-CMs, and generate tools to enable assessment of iPSC-CM differentiation and maturation during biomanufacturing.

"KCNJ2 Mutation-Induced Arrhythmia Mechanisms in CPVT Phenotypes"
Principal Investigator: **Eckhardt** (**Ge, Co-investigator)** Agency: NIH/NHLBI
Type: R01 Period: 8/1/2018 – 7/31/2022

Goals: to determine the biophysical properties, $Ca^{2+}$ sensitivity, phosphorylation state and arrhythmia mechanism of KCNJ2 (ion channel Kir2.1) mutations associated with a catecholaminergic polymorphic ventricular tachycardia or an Adersen-Tawil syndrome phenotype and compare that to a heart failure model.

"Signaling Pathways in Skin Patterning and Polarity"
Principal Investigator: **Chang** (**Ge, Co-investigator)** Agency: NIH/NIGMS
Type: R01 Period: 4/1/2019 – 6/30/2024
Goals: to reveal fundamental insights into the mechanisms of the mammalian planar cell polarity (PCP) pathway and improve our understanding of the pathogenesis of PCP-related diseases.

"Epithelial Innate Signaling in Airway Inflammation and Remodeling"
Principal Investigator: **Garofalo** (**Ge, Co-investigator)** Agency: NIH/NIAID
Type: P01 Period: 9/1/2018 – 8/31/2023
Goals: To test the hypothesis that NFkB/RelA-activated BRD4 HAT- chromatin remodeling complex (CRC) links RSV infection with the remodeling program.

**"**Role of RIP3-laden Extracellular Vesicles in Thrombosis and Aortic Aneurysm"
Principal Investigator: **Liu** (**Ge, Co-investigator)** Agency: NIH/NHLBI
Type: R01 Period: 07/01/20-06/30/25
Goals: This project aims to Investigate the molecular mechanisms that govern how RIP3 is sorted into extracellular vesicles (EVs) and how RIP3 stimulates coagulation during aneurysm development. We will test the hypothesis that EVs convey signals from stressed smooth muscle cells and thereby promote thrombosis during the development of aortic aneurysm.

"Post-transcriptional Regulation of RNA binding Proteins in Heart Failure"
Principal Investigator: **Guo** (**Ge, Co-investigator)** Agency: NIH/NHLBI
Type: R01 Period: 8/15/20-07/31/24
Goals: This project aims to determine the functional roles of RBM20 phosphorylation and genetic mutations on phosphorylation sites in the pathogenesis of heart failure as well as the molecular/cellular mechanisms of RBM20 mediated posttranscriptional regulation of heart failure through cofactors and RBM20 isoforms.

**Completed**

"Comprehensive Analysis of Antibody Drug-Conjugate Variants"
Principal Investigator: **Ge** Agency: Abbvie, Inc.
Type: Research collaboration Period: 09/07/17-09/06/20
Goals**:** To develop novel liquid chromatography mass spectrometry methods for in-depth analytical characterization and understanding of the origin and control of antibody drug-conjugate variants.

"Deciphering Myofilament Modifications in Ischemic Cardiomyopathy"
Principal Investigator: **Ge** Agency: NIH/NHLBI
Type: R01 Period: 3/1/2013 - 2/28/2018 (NCE)
Goals: To understand the molecular mechanism in ischemic cardiomyopathy and identify novel targets for diagnosis and treatment of ischemic heart diseases through identification of ischemia-induced myofilament protein modifications.
*Impact/Priority Score: 17, Percentile: 6.0 (reviewed by MIM study section)*

"Ultra High-Resolution Mass Spectrometer for Biomedical Research"
Principal Investigator: **Ge** Agency: NIH/Office of the Director
Type: High-end instrument grant Period: 3/1/2015-2/29/2016
Goals: To obtain an ultrahigh-resolution Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer to support 21 NIH-funded research projects at the University of Wisconsin (UW)-Madison.

"Bioenergetics in Hypertrophied and Remodeled Left Ventricle"
Principal Investigator: Zhang (**Ge**, **Co-investigator**) Agency: NIH/NHLBI
Type: R01 Period: 8/10/2012-8/31/2016
Goals: To determine the energetics in hypertrophied and remodeled left ventricle towards a better understanding of the underlying mechanism in heart failure.