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## Education

### Master of Public Health 2010-2011

Department of Public Health Sciences
University of Virginia（美国弗吉尼亚大学）, Charlottesville, VA, USA

Advisor: **Patrick Concannon, Ph.D.**

### Doctor of Philosophy 2003-2009

Department of Microbiology, Immunology, and Cancer Biology
University of Virginia（美国弗吉尼亚大学）, Charlottesville, VA, USA

Advisor: **Shu Man Fu, M.D., Ph.D.**

### Bachelor of Science 1999-2003

School of Life Sciences
Fudan University（复旦大学）, Shanghai, China

## Employment

### Principal Investigator

2022-present
International Center for Genetic Engineering and Biotechnology (ICGEB) China Regional Research Center
Taizhou, Jiangsu Province, China

### Research Assistant Scientist (research faculty member)

2019-2022
Department of Pathology, Immunology and Laboratory Medicine
University of Florida, Gainesville, FL, USA

### Postdoctoral Associate

(1) 2013-2019
Department of Pathology, Immunology and Laboratory Medicine

University of Florida, Gainesville, FL, USA
Advisor: **Patrick Concannon, Ph.D.**

(2) 2012-2013
Center for Public Health Genomics
University of Virginia, Charlottesville, VA, USA
Advisor: **Patrick Concannon, Ph.D.**

# Honors and Awards

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| 中国江苏省泰州市“凤城英才计划”113 生物医药专项高层次创新人才* [*This is a talent award from Taizhou city, Jiangsu Province, China.] | 2023 |
| JDRF (Juvenile Diabetes Research Foundation, USA) **Faculty** Transition Award* [*This is a grant awarded to new **faculty** members, not postdocs.] | 2019 |
| JDRF (Juvenile Diabetes Research Foundation, USA) Advanced Postdoctoral Fellowship Award | 2016 |
| ADA (American Diabetes Association, USA) Postdoctoral Fellowship Award | 2016 |
| The 2011 Pfizer Initiative in International Health— Center for Global Health Research in Infectious Disease Award University of Virginia, USA | 2011 |
| Shyr-Te Ju Research Award (University of Virginia, USA) | 2008 |
| 1st place at the 3rd National Young Investigators' Forum (Sponsored by National Kidney Foundation and Amgen, USA) | 2008 |
| 2nd place at the 3rd Mid-Atlantic Regional Young Investigators' Forum (Sponsored by National Kidney Foundation and Amgen, USA) | 2008 |

# Research Expertise and Accomplishments

## Expertise

My training and expertise spans genetics, immunology, and public health—with a focus on the pathogenesis of type 1 diabetes (T1D) and systemic lupus erythematosus (SLE), two common autoimmune diseases. As demonstrated by my publications, my research routinely uses multidisciplinary approaches across molecular and cell biology, genetics, immunology, proteomics, and bioinformatics.

## 1. Novel mechanisms of autoimmune disease

My studies on *UBASH3A*—a gene implicated in five different autoimmune diseases—have elucidated the mechanisms whereby *UBASH3A* and its genetic variants affect the risk for T1D and the function of human T cells, a crucial cell type that regulates immune response and

autoimmunity. My major findings are as follows:

- UBASH3A inhibits T-cell activation and function by dampening NF-κB signaling upon T-cell receptor (TCR) stimulation (Ge et al., 2017).
- UBASH3A regulates the synthesis and dynamics of TCR–CD3 complexes, thus suppressing the proximal TCR signaling pathway and T-cell activation (Ge et al., 2019).
- The minor alleles of rs80054410 and rs11203203 (two genetic variants in *UBASH3A*) increase risk for T1D by enhancing *UBASH3A* expression, resulting in decreased *IL2* expression in human primary T cells upon stimulation (Ge et al., 2017).
- The minor allele of rs1893592 (a genetic variant in *UBASH3A*) protects against T1D by altering the splicing and expression of *UBASH3A* in human T cells, leading to increased IL-2 production upon stimulation (Ge and Concannon, 2018).

## 2. Genetic architecture of autoimmune disease in humans

My findings on *UBASH3A*, *PTPN22*, and *IFIH1* have deepened our understanding of the genetic architecture of autoimmune disease in humans, as these genes are each implicated in multiple autoimmune diseases.

- I have shown that risk for T1D in humans is determined by the joint effect of several genetic variants in *UBASH3A*, not by their individual effects—thus revealing the importance of genetic interaction in T1D (Ge and Concannon, 2018).
- I have identified and characterized rare genetic variants in *PTPN22* and *IFIH1* that confer risk for T1D, demonstrating that rare variants, in addition to common variants, contribute to autoimmune disease in humans (Ge et al., 2016; Gorman et al., 2017).

## 3. Novel regulators of IL-2 production with therapeutic implications

IL-2 plays fundamental roles in the immune system. Moreover, IL-2 contributes to various human disorders and is dysregulated in several autoimmune diseases; hence, IL-2 is being developed in clinical trials as a new therapy. I have identified novel regulators of IL-2 production, and my findings can inform the design of future clinical trials targeting IL-2.

- I have revealed a previously unrecognized role of UBASH3A in IL-2 regulation: UBASH3A inhibits IL-2 production in stimulated human T cells by suppressing the proximal TCR and NF-κB signaling pathways (Ge and Concannon, 2018; Ge et al., 2017, 2019).
- I have shown that T1D-relevant variants in *UBASH3A* affect IL-2 production in human T cells (Ge et al., 2017; Ge and Concannon, 2018).

## 4. Molecular determinants of disease traits

Autoimmune diseases are heterogeneous in clinical manifestation and responsiveness to therapy; however, the causes of this heterogeneity are largely unknown. I have addressed this critical issue by identifying novel molecular determinants of clinical traits of autoimmune disease, thus paving the way for personalized prevention and treatment of the disease.

- I have uncovered previously unknown effects of *UBASH3A* and its genetic variants on IL-2 production, thus providing new mechanistic insights into how IL-2 levels are low in some patients with T1D or SLE (Ge et al., 2017; Ge and Concannon, 2018).
- My studies using a mouse model of SLE (i.e., NZM2328) have revealed that acute and chronic glomerulonephritis—two distinct clinical traits of SLE—are under separate genetic control (Ge et al., 2013).
- I have identified a 1.3-Mb region on chromosome 1 that confers susceptibility to chronic glomerulonephritis in NZM2328 mice (Ge et al., 2013).

### 5. Function of ubiquitination in human T cells

Ubiquitination (a post-translational modification) regulates various cellular processes (e.g., protein degradation, NF-κB signaling), thus playing important and diverse roles. However, the function of ubiquitination in human T cells has not been well defined. I have addressed this knowledge gap by showing that UBASH3A interacts with specific types of polyubiquitin chains, resulting in inhibition of NF-κB signaling and *IL2* expression in human T cells (Ge et al., 2017).

## Research Interests

- Elucidate the molecular networks underlying autoimmune response and specific clinical traits of autoimmune disease in humans for the development of personalized therapeutics
- Develop novel preventive and therapeutic strategies for autoimmune disease, such as new biomarkers, biologics, polygenic risk scores for autoimmunity, and diagnostic assays

## Publications

### Peer-reviewed publications

1. Zhao, Z., Qiao, H., **Ge, Y.**, Kannapel C.C., Sung, S.J., Gaskin, F., Tung, K.S.K. & Fu, S.M. (2021). Autoimmune experimental orchitis and chronic glomerulonephritis with end stage renal disease are controlled by Cgnz1 for susceptibility to end organ damage. ***Clinical Immunology***, 224, 108675. PMID: 33482358.

2. **Ge, Y.**, Paisie, T.K., Chen, S. & Concannon, P. (2019). UBASH3A regulates the synthesis and dynamics of T-cell receptor-CD3 complexes. ***Journal of Immunology***, 203(11), 2827-2836. PMCID: PMC6938261.

3. **Ge, Y.** & Concannon, P. (2018). Molecular-genetic characterization of common, noncoding *UBASH3A* variants associated with type 1 diabetes. ***European Journal of Human Genetics***, 26(7), 1060-1064. PMCID: PMC6018660.
[**Accompanying commentary**: Todd, J.A. (2018). Evidence that UBASH3 is a causal gene for type 1 diabetes. ***European Journal of Human Genetics***, 26(7), 925-927. PMCID: PMC6018710]

4. Gorman, J.A., Hundhausen, C., Errett, J.S., Stone, A.E., Allenspach, E.J., **Ge, Y.**, Arkatkar, T., Clough, C., Dai, X., Khim, S., Pestal, K., Liggitt, D., Cerosaletti, K., Stetson, D.B., James, R.G., Oukka, M., Concannon, P., Gale, M. Jr., Buckner, J.H. & Rawlings, D.J. (2017). The A946T variant of the RNA sensor IFIH1 mediates an interferon program that limits viral infection but increases the risk for autoimmunity. ***Nature Immunology***, 18(7), 744-752. PMCID: PMC5697900.

5. **Ge, Y.**, Paisie, T.K., Newman, J.R.B., McIntyre, L.M. & Concannon, P. (2017). UBASH3A mediates risk for type 1 diabetes through inhibition of T-cell receptor-induced NF-κB signaling. ***Diabetes***, 66(7), 2033-2043. PMCID: PMC5482087.
[**Accompanying commentary**: Todd, J.A. (2018). Evidence that UBASH3 is a causal gene for type 1 diabetes. ***European Journal of Human Genetics***, 26(7), 925-927. PMCID: PMC6018710]

6. Sung, S.J., **Ge, Y.**, Dai, C., Wang, H., Fu, S.M., Sharma, R., Hahn, Y.S., Yu, J., Le, T.H., Okusa, M.D., Bolton, W.K. & Lawler, J.R. (2017). Dependence of glomerulonephritis induction on novel

intraglomerular alternatively activated bone marrow–derived macrophages and Mac-1 and PD-L1 in lupus-prone NZM2328 mice. ***Journal of Immunology***, 198(7), 2589-2601. PMCID: PMC5360484.

7. **Ge, Y.**, Onengut-Gumuscu, S., Quinlan, A.R., Mackey, A.J., Wright, J.A., Buckner, J.H., Habib, T., Rich, S.S. & Concannon, P. (2016). Targeted deep sequencing in multiple-affected sibships of European ancestry identifies rare deleterious variants in *PTPN22* that confer risk for type 1 diabetes. ***Diabetes***, 65(3), 794-802. PMCID: PMC4764149.

8. **Ge, Y.**, Jiang, C., Sung, S.S., Bagavant, H., Dai, C., Wang, H., Kannapell, C.C., Cathro, H.P., Gaskin, F. & Fu, S.M. (2013). Cgnz1 allele confers kidney resistance to damage preventing progression of immune complex-mediated acute lupus glomerulonephritis. ***Journal of Experimental Medicine***, 210(11), 2387-2401. PMCID: PMC3804943.

9. Sim, D.L., Bagavant, H., Scindia, Y.M., **Ge, Y.**, Gaskin, F., Fu, S.M. & Deshmukh, U.S. (2009). Genetic complementation results in augmented autoantibody responses to lupus-associated antigens. ***Journal of Immunology***, 183(5), 3505-3511. PMCID: PMC2837801.

### Non-peer-reviewed publication

1. **Ge, Y**., Brown, M.G., Wang, H. & Fu, S.M. (2012). Genetic approach to study lupus glomerulonephritis. ***Methods in Molecular Biology***, 900, 271-290. PMCID: PMC3873643.

## Invited Oral Presentations

2021 Annual Academic Conference & 2022
Academic Forum of World-Class Universities
(Zhejiang University, China)
**Ge, Y.** Unexpected roles for UBASH3A in T-cell signaling and autoimmunity.

77th Scientific Sessions of the American Diabetes Association 2017
(in San Diego, USA)
**Ge, Y.**, Paisie, T.K. and Concannon, P. UBASH3A mediates risk for type 1 diabetes through inhibition of T-cell receptor-induced NF-κB signaling.

76th Scientific Sessions of the American Diabetes Association 2016
(in New Orleans, USA)
**Ge, Y.**, Onengut-Gumuscu, S., Quinlan, A.R., Mackey, A.J., Rich, S.S. and Concannon, P. Deep sequencing in multiple-affected sibships identifies rare variants contributing to risk of type 1 diabetes.

73rd Annual Scientific Meeting of the American College of Rheumatology 2009
(in Philadelphia, USA)
**Ge, Y.**, Jiang, C., Gaskin, F., Sung, S.S., Bagavant, H. and Fu, S.M. Pathogenesis of proliferative lupus nephritis: different genetic control for acute and chronic glomerulonephritis and new insights into the mechanism of immune complex mediated nephritis.

The Specialized Center of Research on Systemic Lupus Erythematosus Third Symposium (at the University of Virginia, USA) 2009
**Ge, Y.**, Jiang, C., Gaskin, F., Sung, S.S., Bagavant, H. and Fu, S.M. Identification of Cgnz1 genes which confer susceptibility to lupus nephritis in NZM2328 mice.

72nd Annual Scientific Meeting of the American College of Rheumatology (in San Francisco, USA) 2008
**Ge, Y.**, Jiang, C., Morris, A.M., Gaskin, F., Sung, S.S., Bagavant, H. and Fu, S.M. Acute glomerulonephritis without progression to chronic glomerulonephritis, renal failure and early mortality in female mice of congenic strain NZM2328.Lc1R27.

95th Annual Meeting of the American Association of Immunologists (in San Diego, USA) 2008
**Ge, Y.**, Jiang, C., Morris, A.M., Gaskin, F., Sung, S.S. and Fu, S.M. Characterization of a NZM2328 derived recombinant congenic strain which has an 8Mb C57L/J fragment on distal chromosome 1.

## Selected Poster Presentations

ASCB|EMBO Meeting (in San Diego, USA) 2018
**Ge, Y.**, Paisie, T.K., Chen, S. and Concannon, P. UBASH3A regulates the synthesis and dynamics of T-cell receptor-CD3 complexes.

70th Annual Scientific Meeting of the American College of Rheumatology (in Washington DC, USA) 2007
**Ge, Y.**, Jiang, C., Morris, A.M., Gaskin, F., Brown, M.G. and Fu, S.M. Linkage analysis of a (NZM2328 X Balb/cJ) F1 X NZM2328 backcross cohort to identify novel lupus-associated genetic loci in NZM2328 mice.

## Experience in Teaching and Global Health

- At ICGEB China Regional Research Center, I mentored two undergraduate students on their thesis work.
- At the University of Florida in the USA, I mentored three rotation students enrolled in the PhD program of the University of Florida Genetics Institute (UFGI). I also supervised a junior technician, who subsequently obtained a master's degree from UFGI.
- For my MPH summer project funded by the **2011 Pfizer Initiative in International Health**, I developed a diagnostic assay for tuberculosis at Kilimanjaro Clinical Research Institute (KCRI) in **Tanzania**, and I taught the local lab technicians how to perform this assay. I also lectured graduate students and researchers at KCRI on experimental techniques.
- At the University of Virginia in the USA, I taught and supervised two junior lab technicians, who subsequently enrolled in a Doctor of Veterinary Medicine program and a master's degree program.

## Service

Ad hoc reviewer: 2018-present

*Diabetes*, *Diabetes Care*, *Genes & Immunity*, and *The Journal of Immunology*

Panelist: 2020
JDRF (Juvenile Diabetes Research Foundation, USA) career development session for postdocs