BIOGRAPHICAL SKETCH

NAME: **Jianjie Ma**

eRA COMMONS USER NAME: Jianjie_Ma

POSITION TITLE: William H Muller Endowed Professor, Director of Surgical Sciences

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Wuhan University (China)	B.S.	1983	Physics
Baylor College of Medicine	Ph.D.	1986-1989	Physiology & Biophysics
Rush University School of Medicine	Postdoctoral	1989-1991	Physiology & Biophysics

A. Personal Statement

My passion for research stems from the joy of working together with a team of complementary expertise, where a ripple of small ideas can mature into a deeper understanding of the human physiology. My current laboratory research focuses on diverse areas including regenerative medicine, aging biology, diabetes, Alzheimer's disease and cancer therapy.

I started my independent biomedical research career in 1991 as an Assistant Professor in Rush University School of Medicine. Subsequently, in 1992, I transitioned to Case Western Reserve University to establish my own laboratory. In 2001, Rutgers University – Robert Wood Johnson Medical School welcomed me as a University-named Professor, where I initiated the Graduate Program on Integrative Biology and Physiology. Later, I assumed the role of interim Chair of the Department of Physiology and Biophysics at Rutgers University. A decade later, our entire research group relocated to The Ohio State University, where I held the position of the Karl P. Klassen Chair of Thoracic Surgery and served as the Vice Chair of Research in the Department of Surgery. Since 2022, our research group has found a new home at the University of Virginia (UVA). Here, I am honored to serve as the William H Muller Professor of Thoracic Surgery and Director of the Division of Surgical Sciences within the Department of Surgery at UVA, facilitating collaboration with exceptional surgeons engaged in clinical and translational research.

Over the past 33 years of my academia research, I have mentored a diverse group of students and junior faculty members with various ethnic backgrounds. The guiding philosophy of our research has always emphasized the value of teamwork. Overseeing their growth and success is more valuable than mine. Many of my pre-doctoral, postdoctoral, and surgeon-scientist trainees have gone on to become leaders in academic, pharmaceutical industry, clinical care and research, and regulatory affairs at FDA or handling intellectual property.

As the Director of the Division of Surgical Sciences at UVA, my focus has been on creating a collaborative environment conducive to integrative team science. Our aim is to foster partnerships among surgeons, surgeon-scientists, and basic researchers to accelerate scientific discoveries. To achieve this, we have implemented a strategy of pairing every surgeon-scientist with one or more PhD researchers, promoting interdisciplinary collaboration across various fields.

In addition to strengthening collaborations within the Department of Surgery, I have established partnerships with clinical departments such as medicine, orthopedic surgery, plastic surgery, dermatology, and ophthalmology. Furthermore, we have fostered relationships with basic science departments including physiology and biophysics, biochemistry, pathology, microbiology, and biomedical engineering. By transcending departmental boundaries, we have extended our collaborations to different schools at UVA, including the School of Data Sciences and the School of Engineering, and School Arts and Science, facilitating cross-disciplinary research collaborations.

One of our notable achievements at UVA has been in the field of diabetes research. We have made

significant progress with the development of an "exercise pill" aimed at treating diabetes. This groundbreaking technology has garnered attention from both peers and the pharmaceutical industry, as evidenced by its recent feature in the Virginia Business Magazine: https://www.virginiabusiness.com/article/betting-on-biotech/.

Another significant milestone in our team's research endeavors at UVA is the discovery and humanization of a novel monoclonal antibody against CitH3 (hCitH3-mAb), a critical component of NETosis-mediated immune regulation. This breakthrough has led to the establishment of HTIC, Inc., a UVA-spinoff biotechnology company dedicated to advancing hCitH3-mAb as a therapeutic for conditions such as diabetic foot ulcers and sepsis-induced multi-organ injuries.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2022-present	William H. Muller Endowed Professor of Thoracic Surgery Director, Division of Surgical Sciences Department of Surgery, University of Virginia (UVA)
2022-present	Executive Committee for the Department of Surgery at UVA
2022-present	Member of the Promotion& Tenure Committee for School of Medicine, UVA
2019-2022	Vice Chair of Research, Department of Surgery, The Ohio State University (OSU)
2019-2022	Executive Council Member, Department of Surgery, OSU
2012-2022	Professor and Karl P. Klassen Chair of Thoracic Surgery Director, Division of Surgical and Biomedical Sciences Investigator, Davis Heart and Lung Research Institute, OSU
2009-2012	Acting Chair, Department of Physiology and Biophysics, Rutgers University - Robert Wood Johnson Medical School (RWJMS)
2008-2012	Professor, Department of Medicine, RWJMS
2008-2012	Chief, Division of Developmental Medicine & Research, RWJMS
2002-2012	Founder and Director, Graduate Program in Physiology and Integrative Biology Joint Program between RWJMS and Rutgers University
2002-2012	Member, The Gerontological Institute of RWJMS
2001-2012	University-named Professor, RWJMS
2001-2012	Member, The Cancer Institute of New Jersey
1999-2000	Visiting Professor, Department of Pharmacology, University of Tokyo
1996-2001	Associate Professor with Tenure Department of Physiology and Biophysics, Case Western Reserve University (CWRU)
1992-1996	Assistant Professor, Department of Physiology and Biophysics, CWRU
1991-1992	Assistant Professor, Department of Physiology, Rush University School of Medicine

Scientific Appointments

2024	Expert Reviewer, European Science Foundation
2024	Founder, MGMedicine, Inc.
2023	Planning and Design of the Manning Institute of Biotechnology - Vivarium Focus Group Leader
2023	Planning of the Manning Institute of Biotechnology – Research Space Focus Group Leader
2023	Founder, HTIC, Inc.
2021	External Reviewer, Swiss National Science Foundation
2020	Ad hoc member, PBKD Study Section; NIH Review of K and F Applications
2019	Ad hoc member, SMEP Study Section; NINR Special Emphasis Panel
2019	NIH Director’s New Innovator Award (DP2), Editorial Panel
2019-present	Editorial Board Member, Molecular and Cellular Biochemistry
2018	ZRG MOSS C-02 Special Emphasis Panel Review
2017	NIH Director's New Innovator Award (DP2), Editorial Panel
2017	Vascular Surgery Division, Chair Search Committee
2016	Expert Panel Board Member of National Science Foundation of China (NSFC)
2010-2014	NIH Study Section, Chartered Member on SMEP
2010-2014	Guest Professor, School of Medicine, Nankai University
2009-2012	Internal Advisory Board Member for the Cancer Institute of New Jersey
2012-present	Editorial Board Member, Current Biology

2009	Member of the Global Musculoskeletal Experts Forum – Merck Co.
2008-present	Founder, TRIM-edicine, Inc.
2007-2010	Guest Professor, Institute of Molecular Medicine, Peking University
2006-2007	Special Emphasis Panel for NCCAM Program Project Review
2005-2007	Special Emphasis Panel for NIA Program Project Review
2004-2008	Guest Professor, College of Life Sciences, Wuhan University
2003-present	Member of the Teaching Staff for Bioscience2000
2002-2012	Founder and Director, Graduate Program in Physiology and Integrative Biology Joint Program between RWJMS and Rutgers University
2002-2008	Editorial Board Member, Journal of Biological Chemistry
2002-2008	Editorial Board Member, Cell Research
2002-2006	NIH Study Section, Chartered Member on NTRC
2001-2002	Special Emphasis Panel for NIDDK Program Project Review
1996-2001	Associate Professor with Tenure, Department of Physiology and Biophysics Case Western Reserve University (CWRU)
1992-1996	Assistant Professor, Department of Physiology and Biophysics, CWRU
1991-1992	Assistant Professor, Department of Physiology, Rush University School of Medicine

Honors

2024	Dean's Excellence of Research Award (senior faculty), School of Medicine, UVA
2024	Invitation to present to the UVA Health Board on translation medicine
2023	Highlight of our research in Virginia Business magnizine
2018	TEDx Talk – "Regenerative Medicine: Finding a Pixie Dust to Save Human Lives"
2018	Selected by the Board of Trustees of OSU – highlight on translational research
2017	WexMed<LIVE> - Discovery & Innovation in Medicine "Targeting Tissue Repair in Regenerative Medicine"
2016-present	Honorary Chief Scientist, Beijing ATAP Biopharma Biotechnology Company
2012	Excellence in Medical Research Award – UMDNJ Foundation
2009	Plenary Lecture - Annual Meeting of Associations of Chairs for Physiology
2007-2010	Outstanding Young Investigator Award from Chinese Natural Science Foundation
2001-2012	University-named Professor, University of Medicine and Dentistry of New Jersey
1999-2000	Research Fellow, Japan Society for the Promotion of Sciences
1994-1999	Established Investigator of American Heart Association
1990-1992	Muscular Dystrophy Association Research Fellow
1983	China-US Physics Examination Application Fellowship (Sponsored by Professor T.D. Lee)

C. Contribution to Science

1. About 35 years ago, as I transitioned from Physics to Physiology, I was fortunate to be introduced to the wonders of calcium (Ca) signaling and excitation-contraction coupling. During this time, I contributed to the discovery of the ryanodine receptor as a functional Ca release channel. I received three years of training in Molecular Physiology and Biophysics at Baylor College of Medicine, earning my Ph.D. in 1989. In 2002, we identified store-operated Ca entry (SOCE) in skeletal muscle, challenging the prevailing belief that SOCE existed only in non-excitable cells. Our studies highlighted SOCE's critical role in muscle exercise, fatigue, and aging, inspiring further research into its molecular mechanisms in excitation-contraction coupling. In 2005, we identified Ca sparks in mammalian skeletal muscle as a stress-response signal for muscle function, opening new avenues for investigating the fundamental events of Ca signaling in physiology and disease. In 2006, we extended this work by linking Ca sparks to dysfunctional Ca signaling in muscle aging and dystrophy. Both discoveries received editorial highlights in peer-reviewed journals, further underscoring their significance in the field

a. **Ma, J.**, Fill, M., Knudson, C.M., Campbell, K.P. and Coronado, R. (1988) Ryanodine receptor of skeletal muscle is a gap junction-type channel. *Science* **242:** 99-102. PMID: 2459777.
b. Pan Z, Yang D, Nagaraj RY, Nosek TA, Nishi M, Takeshima H, Cheng H, **Ma J.** (2002) Dysfunction of store operated calcium channel in muscle cells lacking mg29. *Nat Cell Biol.* **4:** 379-83. PMID: 11988740.
c. Wang X., Weisleder N., Collet C., Zhou J., Chu Y., Brotto M., Hirata Y., Zhao X., Pan Z., Cheng H., **Ma J.** (2005) Uncontrolled calcium sparks act as a dystrophic signal for mammalian skeletal muscle. *Nat Cell Biol.* **7:** 525-530. PMID: 15834406.
d. Weisleder N., Brotto M., Komazaki, S., Pan, Z., Nosek, T., Parness, J., Takeshima H, and **Ma J.** (2006) Muscle aging is associated with compromised Ca spark signaling and segregated intracellular Ca

release. *J. Cell Biol.* **174***:* 639-645*.* PMCID: PMC2064307.

2. Extending our work with Ca signaling, I initiated a research project with dissecting the functional crosstalk between endoplasmic reticulum Ca release and mitochondria signaling in controlling programmed cell death. We were the first group to show that synergistic movement of Ca and Bax contribute to mitochondria-dependent apoptosis. Along this research line, my graduate student identified an amphipathic tail anchoring peptide (ATAP) as a potent inducer of mitochondria permeability transition that triggers apoptotic cell death in a Bcl2- and Bax-independent manner. We conducted proof-of-concept studies targeting ATAP for the treatment of aggressive tumors using a xenograft model. Our findings suggest that packaging ATAP with nanoparticles could provide an effective therapeutic strategy for cancers that evade apoptotic regulation. Based on these discoveries, we have established a partnership with a pharmaceutical company to advance ATAP toward human clinical trials

a. Pan, Z., Bhat, M.B., Nieminen, A.L., and **Ma, J**. (2001) Synergistic movements of Ca and Bax in cells undergoing apoptosis. *J. Biol. Chem.* **276:** 32257-32263. PMID: 11413128.
b. Ko, J., Choi, K., Pan, Z., Lin, P., Weisleder, N., Kim, C.W., **Ma, J.** (2007) Tail-anchoring domain of Bfl-1 targets mitochondria and induces apoptosis by its amphipathic property. *J. Cell Sci.* 120: 2912-23.
c. De G, Ko JK, Tan T, Zhu H, Li H, **Ma J** (2014). Amphipathic tail-anchoring peptide is a promising therapeutic agent for prostate cancer treatment. *Oncotarget*. 5: 7734-47. PMCID: PMC4202157.
d. Li H, Lin PH, Gupta P, Li X, Zhao SL, Zhou X, Li Z, Wei S, Xu L, Han R, Lu J, Tan T, Yang DH, Chen ZS, Pawlik TM, Merritt RE, **Ma J.** (2021) MG53 suppresses tumor progression and stress granule formation by modulating G3BP2 activity in non-small cell lung cancer. *Mol Cancer*. 20(1):118. PMID: 34521423

3. For over thirty years, Dr. Takeshima and I have collaborated to develop a unique immuno-proteomic approach that has enabled the identification of novel genes involved in muscle and cardiovascular biology. Our work demonstrated that MG29, a muscle-specific synaptophysin family protein, regulates transverse-tubule biogenesis and intracellular calcium signaling in skeletal muscle. We also identified junctophilin (JP) as a critical linker that facilitates functional coupling between the transverse-tubule and SR membranes, essential for excitation-contraction coupling. Mutations in JP have been linked to impaired calcium signaling in human diseases. Additionally, we cloned and characterized TRIC, a trimeric intracellular cation channel, as a putative counter-ion channel that regulates calcium release from the endoplasmic/sarcoplasmic reticulum. In recognition of Dr. Takeshima's contributions, we are organizing an international symposium at UVA on March 22, 2025, titled *"Advancing Innovations in Translational Research into Human Applications*".

a. Weisleder N, Takeshima H, **Ma J** (2008). Immuno-proteomic approach to excitation--contraction coupling in skeletal and cardiac muscle: molecular insights revealed by the mitsugumins. *Cell Calcium.* 43: 1-8. PMCID: PMC3059838.
b. Yazawa M, Ferrante C, Feng J, Mio K, Ogura T, Zhang M, Lin PH, Pan Z, Komazaki S, Kato K, Nishi M, Zhao X, Weisleder N, Sato C, **Ma J**, Takeshima H (2007).TRIC channels are essential for Ca handling in intracellular stores. *Nature* 448: 78-82. PMID: 17611541.
c. Zhou X, Lin P, Yamazaki D, Park KH, Komazaki S, Chen SR, Takeshima H, **Ma J** (2014). Trimeric intracellular cation channels and sarcoplasmic/endoplasmic reticulum calcium homeostasis. *Circ Res.* 114: 706-16. PMCID: PMC3955254.
d. Chen K, Xu Z, Liu Y, Wang Z, Li Y, Xu X, Chen C, Xia T, Liao Q, Yao Y, Zeng C, He D, Yang Y, Tan T, Yi J, Zhou J, Zhu H, **Ma J***, Zeng C* (2017) (* - co-corresponding author) Irisin protects mitochondria function during pulmonary ischemia/reperfusion injury. *Sci Transl Med*. 29;9(418). PMCID: PMC5969805.

4. A major finding of our research was made in 2008, when we discovered MG53 as a key member of the cell membrane repair machinery. We solved the mechanism that underlies MG53's role in nucleating the assembly of the cell membrane repair machinery (**a**). My students have identified several interacting partners for MG53 that contribute to the tissue injury-repair and regeneration process in physiology and disease, and in modulation of stem cell regeneration associated with chronic tissue injuries (**b**). Facing the controversy brought out by a research group that proposes MG53 as a causative factor for diabetes, we and our co-workers have spent a series of efforts to show that "MG53 does not manifest the development of diabetes in db/db mice" (**c**). More recently, our team study has uncovered a new function for MG53 – as a novel mediator of anti-inflammation (**d**).

a. Cai C, Masumiya H, Weisleder N, Matsuda N, Nishi M, Hwang M, Ko JK, Lin P, Thornton A, Zhao X, Pan Z, Komazaki S, Brotto M, Takeshima H, **Ma J** (2009). MG53 nucleates assembly of cell membrane repair machinery. *Nat Cell Biol.* 11: 56-64. PMCID: PMC2990407.
   See commentary by P. McNeil. Membrane repair redux: redox of MG53. *Nat Cell Biol.* 11, 7 - 9 (2009)
b. Bian Z, Wang Q, Zhou X, Tan T, Park KH, Kramer HF, McDougal A, Laping NJ, Kumar S, Adesanya TMA, Sermersheim M, Yi F, Wang X, Wu J, Gumpper K, Jiang Q, He D, Lin PH, Li H, Guan F, Zhou J,

Kohr MJ, Zeng C, Zhu H, **Ma J.** Sustained elevation of mg53 in the bloodstream increases tissue regenerative capacity without compromising metabolic function. *Nat Commun.* 2019; 10: 4659.

c. Wang, Q, Bian,Z, Jiang,Q, Wang,X, Zhou,X, Park, KH, Hsueh, W, Whitson, BA, Haggard, E, Li, H, Chen, K, Cai, C, Tan, T, Zhu, H and **Ma, J** (2020). MG53 does not manifest the development of diabetes in db/db mice. *Diabetes* 69:1052-1064. doi: 10.2337/db19-0807. PMCID: PMC7171965.

d. Sermersheim, M, Kenney, AD, Lin, PH, McMichael, TM, Cai, C, Gumpper, K, Adesanya, TA, Li, H, Zhou, X, Park, KH, Yount, JS and **Ma, J.** (2020). MG53 suppresses interferon-β and inflammation via regulation of ryanodine receptor-mediated intracellular calcium signaling. *Nat Commun* 2020; 11: 3624.

5. The ultimate goal of our research is to translate the basic findings into clinical applications to treat human disease. Through partnership with pharmaceutical industries and collaboration with clinician scientist, we have begun to develop the proof-of-concept studies testing the recombinant human MG53 (rhMG53) protein for treatment of muscle injury (**a**), myocardial infarction and heart failure (**b**), drug toxicity and liver protection (**c**), corneal protection (**d**). We have now established the protocol for production and quality control of rhMG53 and the safety profile of rhMG53 in small and large animal species.

a. Weisleder N, Takizawa N, Lin P, Wang X, Cao C, Zhang Y, Tan T, Ferrante C, Zhu H, Chen PJ, Yan R, Sterling M, Zhao X, Hwang M, Takeshima M, Cai C, Cheng H, Takeshima H, Xiao RP, **Ma J** (2012). Recombinant MG53 protein modulates therapeutic cell membrane repair in treatment of muscular dystrophy. *Sci Transl Med.* 4: 139ra85. PMCID: PMC3777623 (cover page).

b. Wang, X., Li, X., Ong, H., Tan, T., Park, K.H., Bian, Z., Zou, X., Haggard, E., Janssen, P.M., Merritt, R.E., Pawlik, T.M., Whitson, B.A., Mokadam, N.A., Cao, L., Zhu, H., Cai, C*., **Ma, J***. (2021) MG53 suppresses NF-κB activation to mitigate age-related heart failure. *JCI Insight*. 6(17):148375. DOI: 10.1172/jci.insight.148375.

c. Han Y, Black S, Gong Z, Chen Z, Ko JK, Zhou Z, Xia T, Fang D, Yang D, Gu D, Zhang Z, Ren H, Duan X, Reader BF, Chen P, Li Y, Kim JL, Li Z, Xu X, Guo L, Zhou X, Haggard E, Zhu H, Tan T, Chen K, **Ma J***, Zeng C*. (2022) Membrane-delimited signaling and cytosolic action of MG53 preserve hepatocyte integrity during drug-induced liver injury. *J Hepatol*. 76(3):558-567. doi: 10.1016/j.jhep.2021.10.017.

d. Chandler HL, Tan T, Yang C, Gemensky-Metzler AJ, Wehrman RF, Jiang Q, Peterson CMW, Geng B, Zhou X, Wang Q, Kaili D, Adesanya TMA, Yi F, Zhu H, **Ma J.** (2019) MG53 Promotes Corneal Wound Healing and Mitigates Fibrotic Remodeling in Rodents. *Commun Biol*.;2:71. doi: 10.1038/s42003-019-0316-7. eCollection 2019. PMCID: PMC6382791.

For complete list of publication, please see:
https://pubmed.ncbi.nlm.nih.gov/?term=jianjie+ma&sort=date