Journal of Muscle Biology. 2026;1(1):7–11.

Journal of Muscle Biology Editorial

The Wugeng China Initiative: A Muscle-centric Microcirculation Paradigm for Eliminating Lethal Stroke, Dementia, and Heart Attack – Operationalizing "Treating Pre-disease" Through the 4s Muscle Maintenance Model

Yue Zhang[1,2,3,#,*], Guisong Wang[4,#,*], Cibo Huang[5,6,7,#,*], Kamel Meguellati[8]

[1]Shenzhen Weilan Translational Institute of Biomicromolecules Research, Shenzhen, Guangdong, China

[2]Hezhou (the City of Longevity) Dongrong Yao Medicine Research Institute, Joint Institute of Shenzhen University and Hezhou Hospital for Traditional Chinese Medicine, Hezhou, Guangxi, China

[3]Integrated Chinese and Western Medicine Research Institute, TORAMI Avatar Longevity and Healthcare Hub, Zheng He Hospital, Changsha, Hunan, China

[4]Shanghai East Brain Research Institute, and Department of Neurosurgery, Renji Hospital, Shanghai Jiao Tong University, Shanghai, China College of Pharmacy, Jinan University, 855 Xingyu Avenue East, Guangzhou, 511436, China

[5]Shenzhen Hospital for Integrated Chinese and Western Medicine, Shenzhen, Guangdong, China

[6]Department of Rheumatology, Immunology and Gerontology, South-China Hospital of Shenzhen University, Shenzhen, Guangdong, China

[7]Department of Rheumatology and Immunology, National Center of Gerontology, Beijing Hospital, Beijing, China

[8]College of Pharmacy, Jinan University, 855 Xingyu Avenue East, Guangzhou, 511436, China

[#]Contributed equally

[*]Correspondence should be addressed to Yue Zhang, humanoids101@163.com; Cibo Huang, huangcibo1208@139.com; Guisong Wang, wangbo1718@126.com

Received date: February 21, 2026, **Accepted date:** March 03, 2026

Citation: Zhang Y, Wang G, Huang C, Meguellati K. The Wugeng China Initiative: A Muscle-Centric Microcirculation Paradigm for Eliminating Lethal Stroke, Dementia, and Heart Attack – Operationalizing "Treating Pre-disease" Through the 4s Muscle Maintenance Model. Journal of Muscle Biology. 2026;1(1):7–11.

Defining Wugeng China: The Disruptive Health Objective

"Wugeng" (无梗)—literally meaning "free of obstruction/infarction for stroke and dementia" represents a transformative national health goal for China: the annual elimination or near-zero incidence of lethal stroke, dementia, and heart attack through systematic preservation of the muscle-vascular-brain axis. These three conditions collectively account for over 70% of cardiovascular-cerebrovascular mortality in China [1].

The COVID-19 pandemic has amplified this urgency. SARS-CoV-2 infects host cells via ACE2 receptors abundantly expressed on vascular endothelium, causing direct endothelial injury and persistent dysfunction in long COVID affecting ~400 million globally [2–4]. The Wugeng China framework addresses this through an innovative 4S (Systemic, Standardized, Sustainable, Scalable) automobile maintenance model:

The 4s core principle

In the future, over 90% of people will be expected to achieve health through 4S, with less than 10% requiring medical intervention in China. People need annual maintenance when healthy, like automobile maintenance, one service cannot last years.

The Core Hypothesis: The Muscle-Vascular-Brain Axis

We propose that progressive microcirculatory endothelial dysfunction (MED) driven by sarcopenia (age-related muscle loss), myokine deficiency, and accelerated by COVID-19-induced ACE2 downregulation represents the universal pre-disease state underlying lethal stroke, dementia, and heart attack.

Skeletal muscle as the microcirculatory engine

Skeletal muscle comprises around 40% of body mass and houses the body's largest microvascular bed, functioning as a critical endocrine organ secreting 600+ myokines that regulate systemic vascular function [5,6]. Key myokines include:

Myokine	Function	Wugeng Relevance
Irisin (FNDC5)	Enhances endothelial function via AMPK-eNOS; crosses blood-brain barrier; promotes neurogenesis [7–9]	Prevents post-stroke cognitive dysfunction; improves cerebral microcirculation
IL-6	Induces VEGF, promotes angiogenesis, regulates inflammation [5,6,10]	Enhances muscle capillarization; supports cardiac and cerebral collateral circulation
FGF21	Protects against mitochondrial dysfunction, improves insulin sensitivity, acts as mitokine [11–13]	Metabolic protection, vascular anti-aging, stress adaptation
BDNF	Brain-derived neurotrophic factor; enhances synaptic plasticity, neurogenesis [9]	Cognitive protection, neurovascular coupling

Sarcopenia-microcirculatory decline

Age-related muscle loss reduces microcirculatory reserve by:

- **Capillary rarefaction**: Reduced muscle VEGF/angiopoietin signaling decreases systemic microvascular density [14]
- **Myokine deficiency**: Loss of irisin, IL-6, and FGF21 impairs endothelial protection and angiogenesis [5,7,11]
- **Endothelial dysfunction**: Reduced IGF-1 signaling in aging muscle disrupts muscle-endothelial crosstalk, accelerating microvascular senescence [15]

Post-COVID amplification

SARS-CoV-2 infection accelerates attrition through ACE2 downregulation, reduced NO bioavailability, and persistent pro-thrombotic endothelial phenotype [2–4].

Dual-strategy approach

We further propose that "Activating Blood Circulation to Remove Stasis" (活血化瘀, Huó Xuè Huà Yū) package that we practice synergizes with muscle-targeted interventions by improving muscle perfusion, enhancing myokine delivery, and addressing hemorheological disturbances whenever necessary [16–18].

The Scientific Foundation: Microcirculatory Deterioration and Sarcopenia

The annual attrition law

Microcirculatory density declines ~1% annually after age 30, driven by sarcopenia-related myokine deficiency and capillary rarefaction [14,19]. Without annual 4S maintenance, this crosses the Wugeng Threshold (30% residual function), triggering stroke, dementia, or myocardial infarction [14,19].

Endothelial-to-mesenchymal transition (EndMT)

EndMT represents the fundamental mechanism wherein endothelial cells transform into mesenchymal cells [20]:

- **Stroke**: Cerebral microvascular EndMT reduces collateral circulation [20, 21].
- **Dementia**: Hippocampal microvascular EndMT causes chronic hypoperfusion; irisin deficiency impairs neurogenesis [22].
- **Heart attack**: Coronary microcirculatory EndMT precipitates plaque instability; FGF21 deficiency impairs cardiac protection [11,20].

Microcirculatory Environment Cleansing: Dual-Strategy Implementation

Defining microcirculatory environment cleansing (微血管环境清理)

Pathological Accumulation	Muscle-Centric Mechanism	TCM Syndrome
Capillary rarefaction	Reduced myokine (VEGF, angiopoietin) signaling	**Blood Stasis (瘀血)**
Myokine deficiency	Sarcopenia, physical inactivity	**Qi Stagnation (气滞)**
Microthrombosis	Post-COVID ACE2 downregulation, NETs formation [4]	**Blood Stasis (瘀血)**
Oxidative stress	Mitochondrial dysfunction, reduced FGF21 [11]	**Phlegm-Dampness (痰湿)**

Strategy A: Muscle-targeted MVAR (modern precision medicine)

Primary interventions

- **Myokine-enhancing exercise**: Resistance training to increase muscle capillarization by 20-40% and boost irisin/FGF21 secretion [5,7,11].

- **ACE2 pathway restoration**: Counter COVID-induced downregulation [2,3].
- **TGF-β modulation**: Suppress EndMT to preserve muscle-vascular coupling [20].
- **Glycocalyx regeneration**: Sulodexide for endothelial barrier repair [23].

Strategy B: TCM Huó Xuè Huà Yū (活血化瘀) package mechanisms

- **Huó Xuè (Activating Blood)**: Improves muscle capillary perfusion, enhancing myokine delivery to brain and heart [16–18].
- **Huà Yū (Resolving Stasis)**: Fibrinolytic activation, anti-thrombotic effects, addressing post-COVID microthrombosis [16–18].

Evidence base

- **Meta-analysis (Chen *et al.*, 2018)**: the RCTs (n>1,500) demonstrated Huoxue Huayu therapy reduced in-stent restenosis by 43% (RR=0.57) [16,17].
- **Systematic review (Gao *et al.*, 2025)**: the RCTs (n>3000) confirmed TCM formulas improved microcirculation (D-dimer, fibrinogen, endothelin) [18].
- **Xuefu Zhuyu Tang**: Improves hemorheology, enhances muscle pump efficiency [24–26].

The Wugeng Muscle-Vascular Reserve Index (WMVRI)

So far, we formalize the 4S maintenance schedule through the AI-aided articulate Wugeng Muscle-Vascular Reserve Index (WMVRI):

WMVRI Score	Status	Primary Strategy	TCM Integration	Population Target
>0.7 (70%)	**Green**	Annual myokine-focused exercise	Wellness Qi regulation (optional)	Around 85% of population
0.3–0.7	**Yellow**	Resistance training + Huó Xuè Huà Yū	Primary therapy for muscle perfusion	12% at-risk population
<0.3 (30%)	**Red**	Emergency intervention + myokine replacement	Adjunctive TCM	3% require hospital care

Post-COVID adjustment

LC patients automatically classified as Yellow Status for 12 months.

4s station service integration

***4s station core services**:*

1. **Screening**: Annual DEXA muscle mass, serum irisin/FGF21, capillary imaging, sarcopenia index, post-COVID ACE2 autoantibodies.
2. **Muscle index**: Personalized exercise (irisin-boosting HIIT, resistance training for capillarization), myokine modulation.
3. **TCM evaluation**: Constitution identification; **Huó Xuè Huà Yū** package for Status muscle-perfusion optimization.
4. **Integrated monitoring**: tracking with muscle strength, gait speed, hemorheology.

Phase I: Green status maintenance (ages 20–30)

- **Muscle Target**: Maintain lean mass >90th percentile; serum irisin >15 ng/mL.
- **Exercise**: Combined aerobic + resistance to maximize myokine diversity [5,7].
- **Post-COVID**: 6-month enhanced monitoring.
- **TCM option**: Preventive Qi and Blood regulation.

Phase II: Yellow status restoration (ages 30–50, including all post-covid)

- **Muscle Target**: Reverse early sarcopenia; restore capillary density.
- **Exercise**: High-load resistance training (3×/week) to increase muscle capillarization by 25% [14].
- **TCM Primary**: **Huó Xuè Huà Yū therapy** (Xuefu Zhuyu Tang) for muscle microcirculation and myokine transport [16–18].

Phase III: Red status intervention (ages 50+, severe lc, advanced sarcopenia)

- **Interventions**: Myokine replacement (irisin analogs), intensive exercise rehabilitation.
- **TCM Adjunct**: Intensive muscle perfusion support, and beyond.

Implementation Through Muscle-Vascular Microphysiological Systems

The FDA Modernization Act 2.0 and NIH PAR-25-198 enable regulatory-qualified testing [27–29]. However, in near future, Wugeng Muscle-Vascular Digital Twins will need to integrate:

- **Muscle fiber-ECM-vascular units:** Patient-derived myocytes with endothelial co-culture to test myokine secretion.
- **Sarcopenia modeling**: Age-related muscle atrophy MPS to optimize MVAR protocols [30].
- **Post-COVID modeling**: ACE2-downregulated vasculature to test EER strategies [31].
- **TCM validation**: Huó Xuè Huà Yū compound testing for muscle perfusion enhancement.

Societal Implementation: Scaling the Muscle-Centric 4s Network

Infrastructure:

Towards 10 thousand nationwide Wugeng 4S Muscle Stations

Workforce:

- **Exercise myokine specialists**: Certified in irisin-boosting protocols, sarcopenia assessment, resistance training prescription.
- **Modern EER specialists**: Post-COVID cardiovascular rehabilitation, ACE2 pathway expertise.
- **TCM muscle practitioners**: Huó Xuè Huà Yū for muscle-perfusion optimization.

Computed economic model:

- **Green Status**: ¥500/year (muscle maintenance, exercise prescription).
- **Yellow Status (including all LC)**: ¥1,000/year (resistance training + Huó Xuè Huà Yū therapy + myokine monitoring).
- **Red Status**: Intensive intervention (vs. stroke/dementia/LC costs: ¥100,000–600,000).

Testable Predictions

1. **90/10 prediction**: Expect Annual 4S muscle maintenance achieves >90% Green/Yellow Status with <10% medical intervention in China.
2. **Sarcopenia reversal**: estimate that 12-week resistance training restores muscle capillarization and reduces arterial stiffness, preventing progression to Red Status [14].
3. **Myokine efficacy**: Theoretically Irisin-boosting exercise increases cerebral microcirculatory density by 15-20%, delaying dementia onset by 5-10 years [7,9]
4. **TCM-muscle synergy**: Yellow Status patients receiving resistance training + Huó Xuè Huà Yū show 30% faster WMVRI improvement than exercise alone (enhanced muscle perfusion → increased myokine delivery).

Conclusion

The Wugeng China initiative establishes skeletal muscle as the command center of microcirculatory health, expecting to integrate modern myokine science (irisin, FGF21, IL-6, resistance training) with TCM Huó Xuè Huà Yū (muscle perfusion optimization). By targeting sarcopenia reversal, myokine signaling restoration, and post-COVID endothelial repair, we may create a resilient dual-strategy framework.

The 4S model treats muscle as the "engine" requiring annual maintenance with 90% achieving health through muscle preservation, <10% requiring medical intervention in China. This muscle-centric approach honors both biomedical rigor and cultural medical heritage in the service of a singular goal: so far, what successfully hundreds of cases have been treated successfully is a promising signal towards a China free of lethal stroke, dementia, and heart attack.

References

1. Wang YJ, Li ZX, Gu HQ, Zhai Y, Zhou Q, Jiang Y, et al. China Stroke Statistics: an update on the 2019 report from the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, the Chinese Stroke Association, National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention and Institute for Global Neuroscience and Stroke Collaborations. Stroke Vasc Neurol. 2022 Oct;7(5):415–50.
2. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020 May 2;395(10234):1417–18.
3. Campagnole-Santos MJ, Peliky Fontes MA, Verano-Braga T, Haibara AS, Bader M, Santos RAS. ACE2/Angiotensin-(1-7)/Mas and the brain. Brain Res. 2025 Sep 15;1863:149739.
4. Stojanovic M, Djuric M, Nenadic I, Bojic S, Andrijevic A, Popovic A, et al. Vascular Complications of Long COVID-From Endothelial Dysfunction to Systemic Thrombosis: A Systematic Review. Int J Mol Sci. 2025 Dec 31;27(1):433.
5. Pedersen BK, Febbraio MA. Muscle as an endocrine organ:

focus on muscle-derived interleukin-6. Physiol Rev. 2008 Oct;88(4):1379–406.

6. Pedersen BK. Physical activity and muscle-brain crosstalk. Nat Rev Endocrinol. 2019 Jul;15(7):383–92.

7. Guo HH, Liang JJ, Pan RH, Zheng MF, Qiu YX, Jiang SS, et al. Irisin/FNDC5 Regulates Endothelial Function to Improve Post-Stroke-Induced Cognitive Dysfunction by Stimulating AMPK-eNOS Signaling. Brain Behav. 2025 Sep;15(9):e70767.

8. Ma C, Ding H, Deng Y, Liu H, Xiong X, Yang Y. Irisin: A New Code Uncover the Relationship of Skeletal Muscle and Cardiovascular Health During Exercise. Front Physiol. 2021 Feb 1;12:620608.

9. Wrann CD, White JP, Salogiannnis J, Laznik-Bogoslavski D, Wu J, Ma D, et al. Exercise induces hippocampal BDNF through a PGC-1α/FNDC5 pathway. Cell Metab. 2013 Nov 5;18(5):649–59.

10. Pedersen BK, Steensberg A, Fischer C, Keller C, Keller P, Plomgaard P, et al. The metabolic role of IL-6 produced during exercise: is IL-6 an exercise factor? Proc Nutr Soc. 2004 May;63(2):263–7.

11. Kim KH, Jeong YT, Oh H, Kim SH, Cho JM, Kim YN, et al. Autophagy deficiency leads to protection from obesity and insulin resistance by inducing Fgf21 as a mitokine. Nat Med. 2013 Jan;19(1):83–92.

12. Keipert S, Ost M, Johann K, Imber F, Jastroch M, van Schothorst EM, et al. Skeletal muscle mitochondrial uncoupling drives endocrine cross-talk through the induction of FGF21 as a myokine. Am J Physiol Endocrinol Metab. 2014 Mar 1;306(5):E469–82.

13. Kim KH, Kim SH, Min YK, Yang HM, Lee JB, Lee MS. Acute exercise induces FGF21 expression in mice and in healthy humans. PLoS One. 2013 May 7;8(5):e63517.

14. Prior SJ, Ryan AS, Blumenthal JB, Watson JM, Katzel LI, Goldberg AP. Sarcopenia Is Associated With Lower Skeletal Muscle Capillarization and Exercise Capacity in Older Adults. J Gerontol A Biol Sci Med Sci. 2016 Aug;71(8):1096–101.

15. Gulej R, Csik B, Faakye J, Tarantini S, Shanmugarama S, Chandragiri SS, et al. Endothelial deficiency of insulin-like growth factor-1 receptor leads to blood-brain barrier disruption and accelerated endothelial senescence in mice, mimicking aspects of the brain aging phenotype. Microcirculation. 2024 Feb;31(2):e12840.

16. Chen R, Xiao Y, Chen M, He J, Huang M, Hong X, et al. A traditional Chinese medicine therapy for coronary heart disease after percutaneous coronary intervention: a meta-analysis of randomized, double-blind, placebo-controlled trials. Biosci Rep. 2018 Oct 17;38(5):BSR20180973.

17. Chen R, Xiao Y, Chen M, He J, Huang M, Hong X, et al. A traditional Chinese medicine therapy for coronary heart disease after percutaneous coronary intervention: a meta-analysis of randomized, double-blind, placebo-controlled trials. Biosci Rep. 2018 Oct 17;38(5):BSR20180973.

18. Gao J, Han C, Dai N, Wang W, Jin T, Du D, et al. Traditional Chinese medicine formulas alleviated acute pancreatitis via improvement of microcirculation: A systematic review and meta-analysis. Chin Herb Med. 2024 Dec 15;17(3):584–600.

19. Kasal DA, Sena V, Huguenin GVB, De Lorenzo A, Tibirica E. Microvascular endothelial dysfunction in vascular senescence and disease. Front Cardiovasc Med. 2025 Feb 18;12:1505516.

20. Xu Y, Kovacic JC. Endothelial to Mesenchymal Transition in Health and Disease. Annu Rev Physiol. 2023 Feb 10;85:245–67.

21. Jiang H, Zhou Y, Zhang W, Li H, Ma W, Ji X, et al. Molecular mechanisms of endothelial–mesenchymal transition and its pathophysiological feature in cerebrovascular disease. Cell & Bioscience. 2025 Apr 19;15(1):49.

22. Tarantini S, Tran CHT, Gordon GR, Ungvari Z, Csiszar A. Impaired neurovascular coupling in aging and Alzheimer's disease: Contribution of astrocyte dysfunction and endothelial impairment to cognitive decline. Exp Gerontol. 2017 Aug;94:52–8.

23. Inoda A, Suzuki K, Tomita H, Okada H. Glycocalyx shedding as a clinical biomarker in critical illness. Exp Mol Pathol. 2025 Dec;144:104997.

24. Yang T, Li X, Lu Z, Han X, Zhao M. Effectiveness and safety of Xuefu Zhuyu decoction for treating coronary heart disease angina: A systematic review and meta-analysis. Medicine (Baltimore). 2019 Mar;98(9):e14708.

25. Hou Y, Li X, Wang X, Dong T, Yang J. The effect of Huoxue Huayu decoction on restenosis after percutaneous coronary intervention in patients with coronary heart disease: A protocol for systematic review and meta-analysis. Medicine (Baltimore). 2022 Jan 28;101(4):e28677.

26. Wang D, Wang P, Zhang R, Xi X. Efficacy and safety of Xuefu Zhuyu decoction combined with Western medicine for angina pectoris in coronary heart disease: a protocol for systematic review and meta-analysis. Medicine. 2020 Dec 11;99(50):e23195.

27. Hesperos. Hesperos Demonstrates First Digital Twin of Human Disease Using Organ-on-a-Chip Platform. United States. Hesperos, Inc. 2025.

28. National Institutes of Health. Engineering Next-Generation Human Nervous System Microphysiological Systems (R01 Clinical Trials Not Allowed). Funding Opportunity Announcement PAR-25-198. November 6, 2024. Available at: https://grants.nih.gov/grants/guide/pa-files/PAR-25-198.html.

29. Zhang Y, Chen H, Huang C. Optimizing health-span: advances in stem cell medicine and longevity research. Med Rev (2021). 2023 Oct 10;3(4):351–5.

30. Abdelrahman Z, Wang X, Wang D, Zhang T, Zhang Y, Wang X, et al. Identification of novel pathways and immune profiles related to sarcopenia. Front Med (Lausanne). 2023 Apr 17;10:928285.

31. Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty. 2020 Apr 28;9(1):45.