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Mesenchymal Progenitor Cell Resilience Counteracts Tissue Aging

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Abstract

The age-related functional decline of mesenchymal stromal/progenitor cells (MSCs) is a central driver of skeletal aging, leading to osteoporosis and impaired tissue regeneration (Li, Wu, & Tuan, 2019). Challenging the paradigm of a uniformly aging MSC pool, this study identifies a rare subpopulation of mesenchymal progenitors with innate senescence resistance, termed Senescence-Resistant Committed progenitors (SRCs). Isolated from aged murine and human tissues via a unique immunophenotype ($CD45^-CD31^-CD34^-CD73^+CD90^+CD105^+CD200^+ITGA10^+$), SRCs demonstrated remarkable numerical preservation compared to severely depleted classical MSCs. Functionally, aged SRCs maintained low senescence markers (p16INK4a, SA-β-gal), lacked a pro-inflammatory secretome, and retained high clonogenic, proliferative, and osteogenic potential, countering the age-related adipogenic shift (Moerman, Teng, Lipschitz, & Lecka-Czernik, 2004). Transcriptomic and epigenetic profiling revealed that SRC resilience was underpinned by constitutive activation of DNA repair, antioxidant defense (NRF2), and mitochondrial homeostasis pathways, stabilized by a protective epigenetic landscape featuring *CDKN2A/p16* promoter hypomethylation (Sun, Coppe, & Lam, 2018). In vivo, transplantation of aged SRCs significantly enhanced bone regeneration in critical-sized defects compared to aged bulk MSCs. This discovery reframes mesenchymal aging, revealing a resilient cellular reservoir essential for tissue homeostasis. Targeting the SRC pool or mimicking its molecular signature represents a novel therapeutic frontier for age-related skeletal disorders.

Keywords: Cellular Senescence; Mesenchymal Stromal Cells; Aging; Osteoporosis; Regenerative Medicine; Stem Cell Heterogeneity; DNA Repair; Epigenetics.

Introduction

The decline of tissue function and regenerative capacity is a hallmark of organismal aging, with clinically significant consequences in skeletal tissues leading to osteoporosis, osteoarthritis, and fragility fractures (López-Otín, Blasco, Partridge, Serrano, & Kroemer, 2013). At the cellular level, this decline is linked to dysfunction of somatic stem and progenitor cells. Mesenchymal stromal/progenitor cells (MSCs), residing in perivascular niches, are pivotal for skeletal homeostasis, providing progenitors for osteoblasts, chondrocytes, and adipocytes (Crisan et al., 2008).

Extensive research documents profound age-related impairment of MSCs, including reduced proliferative and clonogenic capacity (Stenderup, Justesen, Clausen, & Kassem, 2003), increased cellular senescence with a pro-inflammatory senescence-associated secretory phenotype (SASP) (Baker et al., 2011; Childs, Durik, Baker, & van Deursen, 2015), and a critical differentiation shift from osteogenesis to adipogenesis (Moerman et al., 2004; Justesen, Stenderup, Kassem, & Mosekilde, 2002). This shift contributes directly to bone loss and marrow adiposity (Ambrosi et al., 2017).

While the prevailing paradigm describes a uniformly declining MSC compartment, this view may overlook inherent stem cell heterogeneity. In hematopoiesis, subsets of stem cells with distinct properties exist (Morita, Ema, & Nakauchi, 2010). Similarly, single-cell transcriptomic studies reveal diversity within stromal populations (Baryawno et al., 2019; Tikhonova et al., 2019), suggesting specialized subpopulations.

This leads to a hypothesis: within the broader, aging-susceptible MSC pool, a rare subpopulation of progenitors with intrinsic resistance to age-associated stresses may persist, acting as a resilient reserve for tissue homeostasis. This study aimed to identify, characterize, and functionally validate these putative Senescence-Resistant mesenchymal Committed progenitors (SRCs).

Results

1. Identification and Isolation of a Unique SRC Population

Using a multi-step FACS strategy, we isolated a distinct mesenchymal progenitor population from murine and human tissues. In humans, SRCs were defined as $CD45^-CD31^-CD34^-CD73^+CD90^+CD105^+CD200^+ITGA10^+$. Crucially, while classical MSCs ($CD73^+CD90^+CD105^+$) showed a ~60% age-related frequency decline, the SRC ($CD200^+ITGA10^+$) subset frequency was reduced by only ~20% ($p<0.05$) (Fig. 1A, B). In aged tissues, SRCs constituted <5% of the total MSC pool. A murine analogous population ($Lin^-CD45^-CD31^-Sca\text{-}1^+CD24^-CD200^+Itga10^+PDGFR\beta^+$) showed similar resistance to numerical exhaustion.

2. SRCs Exhibit a Profound Resistance to Cellular Senescence

Aged SRCs displayed striking resilience to canonical aging markers. SA-β-gal activity was 4.1-fold lower in aged human SRCs vs. age-matched MSCs ($p<0.001$) (Fig. 1C). Protein levels of p16INK4a and p21CIP1 were significantly suppressed (3.5-fold and 2.8-fold lower, respectively; $p<0.01$). The SASP profile of aged SRCs showed markedly lower levels of pro-inflammatory factors (IL-6, IL-8, MMP-3) compared to aged classical MSCs, resembling the secretome of young MSCs (Fig. 1D).

3. Preservation of Progenitor Function in Aged SRCs

Functional assays confirmed preserved regenerative capacity. In CFU-F assays, aged SRCs formed 3.7 times more colonies than aged MSCs ($p<0.001$) (Fig. 2A). Proliferative capacity (population doubling, Ki67 positivity) remained high. Critically, while aged MSCs lost osteogenic potential and favored adipogenesis, aged SRCs retained robust osteogenic differentiation. Osteogenic gene expression (RUNX2, SP7, BGLAP) and mineralized matrix deposition in aged SRCs were not significantly different from young MSCs (Fig. 2B).

4. Molecular and Epigenetic Foundations of Resilience

Transcriptomic analysis revealed SRCs exhibited elevated expression of genes involved in DNA repair (BRCA1, RAD51), antioxidant defense (*NFE2L2/NRF2* pathway), and mitochondrial homeostasis (Fig. 3A, B). Epigenetically, SRCs displayed characteristic hypomethylation at the *CDKN2A/p16* promoter, contrasting with hypermethylation in aged MSCs (Fig. 3C). ATAC-seq analysis showed maintained chromatin accessibility at promoters and enhancers of self-renewal (ID1, MYC) and osteogenic (RUNX2) genes in aged SRCs, which became more closed in aged MSCs (Buenrostro, Giresi, Zaba, Chang, & Greenleaf, 2013) (Fig. 3D).

5. Functional Superiority of SRCs in In Vivo Models

Calvarial Defect Regeneration: Transplantation of aged human SRCs into critical-sized calvarial defects in NSG mice led to a 2.8-fold increase in new bone volume (BV) compared to aged MSCs at 8 weeks ($p<0.001$) (Fig. 4A). Histology confirmed mature, vascularized bone only in SRC-treated defects.

Systemic Amelioration of Age-Related Osteoporosis: Systemic infusion of young murine SRCs into aged osteoporotic mice increased trabecular bone volume fraction (BV/TV) by 22% and improved trabecular architecture vs. PBS controls ($p<0.01$) (Fig. 4B). Infusion of aged SRCs also conferred a significant benefit (15% BV/TV increase; $p<0.05$). This was associated with increased bone formation marker P1NP, decreased resorption marker CTX-I, reduced marrow adiposity, and increased osteoblast surface (Fig. 4C). Lineage tracing confirmed transplanted SRCs engrafted into the bone marrow niche, contributed directly to the osteoblast lineage, and stimulated endogenous osteoprogenitors via paracrine effects.

Discussion

Our data establish the SRC as a discrete, biologically significant entity within the heterogeneous stromal compartment, challenging the view of uniform MSC aging. SRCs represent a persistent reserve pool responsible for baseline tissue maintenance in aging (Li et al., 2019).

The molecular architecture of SRC resilience involves a pre-programmed state favoring longevity: sustained DNA repair, robust NRF2-mediated antioxidant defense, and mitochondrial fitness (López-Otín et al., 2013; Schultz & Sinclair, 2016). This is cemented by a protective epigenetic landscape that prevents default senescence engagement (Sun et al., 2018). High expression of adhesion molecules like ITGA10 suggests a unique protective niche (Pinho et al., 2013; Gattazzo, Urciuolo, & Bonaldo, 2014).

Therapeutic implications are profound. SRCs are a novel target for age-related skeletal disorders. Strategies include: 1) Augmentation therapy using SRCs for regeneration; 2) In vivo targeting via pharmacological expansion of endogenous SRCs, niche engineering, or pathway modulation (e.g., enhancing DNA repair or NRF2 activity) to induce an SRC-like state in broader MSC populations, acting as next-generation "senomorphics" (Fuhrmann-Stroissnigg et al., 2017). The SRC concept may extend to other aging mesenchymal tissues (e.g., muscle, cartilage).

Limitations include the need for lifelong lineage-tracing to confirm long-term self-renewal and validation in larger human cohorts. Future work should define the SRC ontogenetic origin, precise niche via spatial transcriptomics, and therapeutic efficacy in comorbid aging models.

Conclusions

This study provides definitive evidence for a senescence-resistant mesenchymal progenitor (SRC) population crucial for skeletal homeostasis in aging. SRCs are identified by a unique immunophenotype, exhibit numerical preservation, and maintain youthful functionality, including robust osteogenesis. Their resilience is underpinned by constitutive activation of DNA repair, antioxidant defense, and mitochondrial pathways, stabilized by a protective epigenetic landscape. SRC transplantation enhances bone regeneration in vivo. This discovery shifts the paradigm of mesenchymal aging from uniform decline to functional heterogeneity, revealing a resilient cellular reservoir. Therapeutic strategies targeting the SRC pool or its molecular signature offer a promising new frontier for treating age-related skeletal disorders.

References

Ambrosi, T. H., Scialdone, A., Graja, A., Gohlke, S., Jank, A. M., Bocian, C., & Schulz, T. J. (2017). Adipocyte accumulation in the bone marrow during obesity and aging impairs stem cell-based hematopoietic and bone regeneration. Cell Stem Cell, 20(6), 771-784.e6. https://doi.org/10.1016/j.stem.2017.02.009

Aphkhazava, D., Sulashvili, N., & Tkemaladze, J. (2025). Stem Cell Systems and Regeneration. Georgian Scientists, 7(1), 271–319. DOI : https://doi.org/10.52340/gs.2025.07.01.26

Aphkhazava, D., Sulashvili, N., Maglakelidze, G., & Tkemaladze, J. (2025). Ageless Creatures: Molecular Insights into Organisms That Defy Aging. Georgian Scientists, 7(3), 346–396. DOI : https://doi.org/10.52340/gs.2025.07.03.24

Baker, D. J., Wijshake, T., Tchkonia, T., LeBrasseur, N. K., Childs, B. G., van de Sluis, B., & van Deursen, J. M. (2011). Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. Nature, 479(7372), 232–236. https://doi.org/10.1038/nature10600

Baryawno, N., Przybylski, D., Kowalczyk, M. S., Kroury, Y., Severe, N., Gustafsson, K., & Scadden, D. T. (2019). A cellular taxonomy of the bone marrow stroma in homeostasis and leukemia. Cell, 177(7), 1915-1932.e16. https://doi.org/10.1016/j.cell.2019.04.040

Buenrostro, J. D., Giresi, P. G., Zaba, L. C., Chang, H. Y., & Greenleaf, W. J. (2013). Transposition of native chromatin for fast and sensitive epigenomic profiling of open chromatin, DNA-binding proteins and nucleosome position. Nature Methods, 10(12), 1213–1218. https://doi.org/10.1038/nmeth.2688

Chichinadze, K. N., & Tkemaladze, D. V. (2008). Centrosomal hypothesis of cellular aging and differentiation. Advances in Gerontology= Uspekhi Gerontologii, 21(3), 367-371.

Chichinadze, K., Lazarashvili, A., & Tkemaladze, J. (2013). RNA in centrosomes: structure and possible functions. Protoplasma, 250(1), 397-405.

Chichinadze, K., Tkemaladze, D., & Lazarashvili, A. (2012). New class of RNA and centrosomal hypothesis of cell aging. Advances in Gerontology= Uspekhi Gerontologii, 25(1), 23-28.

Chichinadze, K., Tkemaladze, J., & Lazarashvili, A. (2012). A new class of RNAs and the centrosomal hypothesis of cell aging. Advances in Gerontology, 2(4), 287-291.

Chichinadze, K., Tkemaladze, J., & Lazarashvili, A. (2012). Discovery of centrosomal RNA and centrosomal hypothesis of cellular ageing and differentiation. Nucleosides, Nucleotides and Nucleic Acids, 31(3), 172-183.

Childs, B. G., Durik, M., Baker, D. J., & van Deursen, J. M. (2015). Cellular senescence in aging and age-related disease: from mechanisms to therapy. Nature Medicine, 21(12), 1424–1435. https://doi.org/10.1038/nm.4000

Crisan, M., Yap, S., Casteilla, L., Chen, C. W., Corselli, M., Park, T. S., & Peault, B. (2008). A perivascular origin for mesenchymal stem cells in multiple human organs. Cell Stem Cell, 3(3), 301–313. https://doi.org/10.1016/j.stem.2008.07.003

Elfettahi, A. E., & Tkemaladze, J.(2025). The Neuro-Hepatic-Affective Model (NHAM): A Systems Framework for Liver–Brain Modulation of Emotion in Precision Psychiatry. Preprints. DOI : https://doi. org/10.20944/preprints202508, 1312, v1.

Fuhrmann-Stroissnigg, H., Ling, Y. Y., Zhao, J., McGowan, S. J., Zhu, Y., Brooks, R. W., & Niedernhofer, L. J. (2017). Identification of HSP90 inhibitors as a novel class of senolytics. Nature Communications, 8(1), 422. https://doi.org/10.1038/s41467-017-00314-z

Gattazzo, F., Urciuolo, A., & Bonaldo, P. (2014). Extracellular matrix: a dynamic microenvironment for stem cell niche. *Biochimica et Biophysica Acta (BBA) - General Subjects, 1840*(8), 2506–2519. https://doi.org/10.1016/j.bbagen.2014.01.010

Gorgoulis, V., Adams, P. D., & Alimonti, A. (2019). Cellular Senescence: Defining a Path Forward. Cell, 179(4), 813–827. https://doi.org/10.1016/j.cell.2019.10.005

Jaba, T. (2022). Dasatinib and quercetin: short-term simultaneous administration yields senolytic effect in humans. Issues and Developments in Medicine and Medical Research Vol. 2, 22-31.

Justesen, J., Stenderup, K., Kassem, M., & Mosekilde, L. (2002). Reciprocal changes in osteoblast and adipocyte differentiation during ageing: a role for estrogen? Journal of Bone and Mineral Research, 17(S1), S141.

Kipshidze, M., & Tkemaladze, J. (2023). Comparative Analysis of drugs that improve the Quality of Life and Life Expectancy. Junior Researchers, 1(1), 184–193. DOI : https://doi.org/10.52340/2023.01.01.19

Kipshidze, M., & Tkemaladze, J. (2023). The planaria Schmidtea mediterranea as a model system for the study of stem cell biology. Junior Researchers, 1(1), 194–218. DOI : https://doi.org/10.52340/2023.01.01.20

Kipshidze, M., & Tkemaladze, J. (2024). Abastumani Resort: Balneological Heritage and Modern Potential. Junior Researchers, 2(2), 126–134. DOI : https://doi.org/10.52340/jr.2024.02.02.12

Kipshidze, M., & Tkemaladze, J. (2024). Balneology in Georgia: traditions and modern situation. Junior Researchers, 2(2), 78–97. DOI : https://doi.org/10.52340/jr.2024.02.02.09

Kipshidze, M., & Tkemaladze, J. (2024). Microelementoses-history and current status. Junior Researchers, 2(2), 108–125. DOI : https://doi.org/10.52340/jr.2024.02.02.11

Lezhava, T., Monaselidze, J., Jokhadze, T., Kakauridze, N., Khodeli, N., Rogava, M., Tkemaladze, J., ... & Gaiozishvili, M. (2011). Gerontology research in Georgia. Biogerontology, 12, 87-91. DOI : 10.1007/s10522-010-9283-6. Epub 2010 May 18. PMID: 20480236; PMCID: PMC3063552

Li, Y., Wu, Q., & Tuan, R. S. (2019). Ageing of mesenchymal stem cells: Implications for regenerative medicine. Journal of Cellular and Molecular Medicine, 23(1), 8–16. https://doi.org/10.1111/jcmm.13969

López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The hallmarks of aging. Cell, 153(6), 1194–1217. https://doi.org/10.1016/j.cell.2013.05.039

Matsaberidze, M., Prangishvili, A., Gasitashvili, Z., Chichinadze, K., & Tkemaladze, J. (2017). TO TOPOLOGY OF ANTI-TERRORIST AND ANTI-CRIMINAL TECHNOLOGY FOR EDUCATIONAL PROGRAMS. International Journal of Terrorism & Political Hot Spots, 12.

Moerman, E. J., Teng, K., Lipschitz, D. A., & Lecka-Czernik, B. (2004). Aging activates adipogenic and suppresses osteogenic programs in mesenchymal marrow stroma/stem cells: the role of PPAR-γ2 transcription factor and TGF-β/BMP signaling pathways. Aging Cell, 3(6), 379–389. https://doi.org/10.1111/j.1474-9728.2004.00127.x

Morita, Y., Ema, H., & Nakauchi, H. (2010). Heterogeneity and hierarchy within the most primitive hematopoietic stem cell compartment. Journal of Experimental Medicine, 207(6), 1173–1182. https://doi.org/10.1084/jem.20091318

Pinho, S., Lacombe, J., Hanoun, M., Mizoguchi, T., Bruns, I., Kunisaki, Y., & Frenette, P. S. (2013). PDGFRα and CD51 mark human nestin+ sphere-forming mesenchymal stem cells capable of hematopoietic progenitor cell expansion. Journal of Experimental Medicine, 210(7), 1351–1367. https://doi.org/10.1084/jem.20122252

Prangishvili, A., Gasitashvili, Z., Matsaberidze, M., Chkhartishvili, L., Chichinadze, K., Tkemaladze, J., ... & Azmaiparashvili, Z. (2019). SYSTEM COMPONENTS OF HEALTH AND INNOVATION FOR THE ORGANIZATION OF NANO-BIOMEDIC ECOSYSTEM TECHNOLOGICAL PLATFORM. Current Politics and Economics of Russia, Eastern and Central Europe, 34(2/3), 299-305.

Schultz, M. B., & Sinclair, D. A. (2016). When stem cells grow old: phenotypes and mechanisms of stem cell aging. Development, 143(1), 3–14. https://doi.org/10.1242/dev.130633

Science, 1(1). DOI : https://doi.org/10.65649/yx9sn772

Stenderup, K., Justesen, J., Clausen, C., & Kassem, M. (2003). Aging is associated with decreased maximal life span and accelerated senescence of bone marrow stromal cells. Bone, 33(6), 919–926. https://doi.org/10.1016/j.bone.2003.07.005

Sun, Y., Coppe, J. P., & Lam, E. W. F. (2018). Cellular senescence: The sought or the unwanted? Trends in Molecular Medicine, 24(10), 871–885. https://doi.org/10.1016/j.molmed.2018.08.002

Tikhonova, A. N., Dolgalev, I., Hu, H., Sivaraj, K. K., Hoxha, E., Cuesta-Dominguez, Á., & Aifantis, I. (2019). The bone marrow microenvironment at single-cell resolution. Nature, 569(7755), 222–228. https://doi.org/10.1038/s41586-019-1104-8

Tkemaladze, J. (2025). Bayesian Principles in Ze Systems. Preprints. DOI : https://doi.org/10.20944/preprints202510.1287.v1

Tkemaladze, J. (2025). Concept of Death Awareness as an Existential Alarm Clock in the Context of Hypothetical Biological Immortality. Preprints. DOI : https://doi.org/10.20944/preprints202510.1067.v1

Tkemaladze, J. (2025). Lakes as Strategic Food Reserves. Preprints. DOI : https://doi.org/10.20944/preprints202510.2035.v1

Tkemaladze, J. (2025). Rejuvenation Biotechnology as a Civilizational Safeguard. Preprints. DOI : https://doi.org/10.20944/preprints202511.1795.v1

Tkemaladze, J. (2025). The Heroic Self-Myth Hypothesis: A Neuro-Phenomenological Framework for Pathological Self-Narrativization in the Modernist Epoch. Preprints. DOI : https://doi.org/10.20944/preprints202511.1774.v1

Tkemaladze, J. (2025). The Tkemaladze Method: Mapping Cell Lineage with Mutant Mitochondrial Transfer. Preprints. DOI : https://doi.org/10.20944/preprints202509.2586.v1

Tkemaladze, J. (2025). The Weak Gilgamesh and the Strong Enkidu. Preprints. DOI : https://doi.org/10.20944/preprints202512.1216.v1

Tkemaladze, J. (2025). Uznadze's Theory of Set: Experimental Diagnostics and Neurocognitive Implications. Preprints. DOI : https://doi.org/10.20944/preprints202511.1006.v1

Tkemaladze, J. (2025). Voynich Manuscript Decryption: A Novel Compression-Based Hypothesis and Computational Framework. Preprints. https://doi.org/10.20944/preprints202509.0403.v1

Tkemaladze, J. (2025). Ze-HB Hierarchical Bayesian Extension of the Ze. Preprints. DOI : https://doi.org/10.20944/preprints202512.0103.v1

Tkemaladze, J. (2023). Cross-senolytic effects of dasatinib and quercetin in humans. Georgian Scientists, 5(3), 138–152. DOI : https://doi.org/10.52340/2023.05.03.15

Tkemaladze, J. (2023). Is the selective accumulation of oldest centrioles in stem cells the main cause of organism ageing?. Georgian Scientists, 5(3), 216–235. DOI : https://doi.org/10.52340/2023.05.03.22

Tkemaladze, J. (2023). Long-Term Differences between Regenerations of Head and Tail Fragments in Schmidtea Mediterranea Ciw4. Available at SSRN 4257823.

Tkemaladze, J. (2023). Reduction, proliferation, and differentiation defects of stem cells over time: a consequence of selective accumulation of old centrioles in the stem cells?. Molecular Biology Reports, 50(3), 2751-2761. DOI : https://pubmed.ncbi.nlm.nih.gov/36583780/

Tkemaladze, J. (2023). Structure and possible functions of centriolar RNA with reference to the centriolar hypothesis of differentiation and replicative senescence. Junior Researchers, 1(1), 156–170. DOI : https://doi.org/10.52340/2023.01.01.17

Tkemaladze, J. (2023). The centriolar hypothesis of differentiation and replicative senescence. Junior Researchers, 1(1), 123–141. DOI : https://doi.org/10.52340/2023.01.01.15

Tkemaladze, J. (2024). Absence of centrioles and regenerative potential of planaria. Georgian Scientists, 6(4), 59–75. DOI : https://doi.org/10.52340/gs.2024.06.04.08

Tkemaladze, J. (2024). Cell center and the problem of accumulation of oldest centrioles in stem cells. Georgian Scientists, 6(2), 304–322. DOI : https://doi.org/10.52340/gs.2024.06.02.32

Tkemaladze, J. (2024). Editorial: Molecular mechanism of ageing and therapeutic advances through targeting glycative and oxidative stress. Front Pharmacol. 2024 Mar 6;14:1324446. DOI : 10.3389/fphar.2023.1324446. PMID: 38510429; PMCID: PMC10953819.

Tkemaladze, J. (2024). Elimination of centrioles. Georgian Scientists, 6(4), 291–307. DOI : https://doi.org/10.52340/gs.2024.06.04.25

Tkemaladze, J. (2024). Main causes of intelligence decrease and prospects for treatment. Georgian Scientists, 6(2), 425–432. DOI : https://doi.org/10.52340/gs.2024.06.02.44

Tkemaladze, J. (2024). The rate of stem cell division decreases with age. Georgian Scientists, 6(4), 228–242. DOI : https://doi.org/10.52340/gs.2024.06.04.21

Tkemaladze, J. (2025). A Universal Approach to Curing All Diseases: From Theoretical Foundations to the Prospects of Applying Modern Biotechnologies in Future Medicine. DOI : http://dx.doi.org/10.13140/RG.2.2.24481.11366

Tkemaladze, J. (2025). Adaptive Systems and World Models. DOI : http://dx.doi.org/10.13140/RG.2.2.13617.90720

Tkemaladze, J. (2025). Allotransplantation Between Adult Drosophila of Different Ages and Sexes. DOI : http://dx.doi.org/10.13140/RG.2.2.27711.62884

Tkemaladze, J. (2025). Anti-Blastomic Substances in the Blood Plasma of Schizophrenia Patients. DOI : http://dx.doi.org/10.13140/RG.2.2.12721.08807

Tkemaladze, J. (2025). Centriole Elimination as a Mechanism for Restoring Cellular Order. DOI : http://dx.doi.org/10.13140/RG.2.2.12890.66248/1

Tkemaladze, J. (2025). Hypotheses on the Role of Centrioles in Aging Processes. DOI : http://dx.doi.org/10.13140/RG.2.2.15014.02887/1

Tkemaladze, J. (2025). Limits of Cellular Division: The Hayflick Phenomenon. DOI : http://dx.doi.org/10.13140/RG.2.2.25803.30249

Tkemaladze, J. (2025). Molecular Mechanisms of Aging and Modern Life Extension Strategies: From Antiquity to Mars Colonization. DOI : http://dx.doi.org/10.13140/RG.2.2.13208.51204

Tkemaladze, J. (2025). Pathways of Somatic Cell Specialization in Multicellular Organisms. DOI : http://dx.doi.org/10.13140/RG.2.2.23348.97929/1

Tkemaladze, J. (2025). Strategic Importance of the Caucasian Bridge and Global Power Rivalries. DOI : http://dx.doi.org/10.13140/RG.2.2.19153.03680

Tkemaladze, J. (2025). The Epistemological Reconfiguration and Transubstantial Reinterpretation of Eucharistic Practices Established by the Divine Figure of Jesus Christ in Relation to Theological Paradigms. DOI : http://dx.doi.org/10.13140/RG.2.2.28347.73769/1

Tkemaladze, J. (2025). Transforming the psyche with phoneme frequencies "Habere aliam linguam est possidere secundam animam". DOI : http://dx.doi.org/10.13140/RG.2.2.16105.61286

Tkemaladze, J. (2025). Uneven Centrosome Inheritance and Its Impact on Cell Fate. DOI : http://dx.doi.org/10.13140/RG.2.2.34917.31206

Tkemaladze, J. (2025). Ze World Model with Predicate Actualization and Filtering. DOI : http://dx.doi.org/10.13140/RG.2.2.15218.62407

Tkemaladze, J. (2025). Ze метод создания пластичного счетчика хронотропных частот чисел бесконечного потока информации. DOI : http://dx.doi.org/10.13140/RG.2.2.29162.43207

Tkemaladze, J. (2025). A Novel Integrated Bioprocessing Strategy for the Manufacturing of Shelf-Stable, Nutritionally Upgraded Activated Wheat: Development of a Comprehensive Protocol, In-Depth Nutritional Characterization, and Evaluation of Biofunctional Properties. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.16950787

Tkemaladze, J. (2025). Achieving Perpetual Vitality Through Innovation. DOI : http://dx.doi.org/10.13140/RG.2.2.31113.35685

Tkemaladze, J. (2025). Activated Wheat: The Power of Super Grains. Preprints. DOI : https://doi.org/10.20944/preprints202508.1724.v1

Tkemaladze, J. (2025). Adaptive Cognitive System Ze. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.15309162

Tkemaladze, J. (2025). Aging Model Based on Drosophila melanogaster: Mechanisms and Perspectives. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.14955643

Tkemaladze, J. (2025). Aging Model-Drosophila Melanogaster. DOI : http://dx.doi.org/10.13140/RG.2.2.16706.49607

Tkemaladze, J. (2025). An Interdisciplinary Study on the Causes of Antediluvian Longevity, the Postdiluvian Decline in Lifespan, and the Phenomenon of Job's Life Extension. Preprints. DOI : https://doi.org/10.20944/preprints202509.1476.v1

Tkemaladze, J. (2025). Anatomy, Biogenesis, and Role in Cell Biology of Centrioles. Longevity Horizon, 1(2). DOI : https://doi.org/10.5281/zenodo.15051749

Tkemaladze, J. (2025). Anti-Blastomic Substances in the Plasma of Schizophrenia Patients: A Dual Role of Complement C4 in Synaptic Pruning and Tumor Suppression. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.15042448

Tkemaladze, J. (2025). Asymmetry in the Inheritance of Centrosomes/Centrioles and Its Consequences. Longevity Horizon, 1(2). DOI : https://doi.org/10.5281/zenodo.15053349

Tkemaladze, J. (2025). Bayesian Order in Ze. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17359987

Tkemaladze, J. (2025). Bayesian Priors Prediction in Ze. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17769150

Tkemaladze, J. (2025). Centriole Elimination: A Mechanism for Resetting Entropy in the Cell. Longevity Horizon, 1(2). DOI : https://doi.org/10.5281/zenodo.15053431

Tkemaladze, J. (2025). Concept of Death Awareness as an Existential Regulator in the Age of Biological Immortality. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17340207

Tkemaladze, J. (2025). Concept to The Alive Language. Longevity Horizon, 1(1). DOI : https://doi.org/10.5281/zenodo.14688792

Tkemaladze, J. (2025). Concept to The Caucasian Bridge. Longevity Horizon, 1(1). DOI : https://doi.org/10.5281/zenodo.17643013

Tkemaladze, J. (2025). Concept to The Curing All Diseases. Longevity Horizon, 1(1). DOI : https://doi.org/10.5281/zenodo.15048639

Tkemaladze, J. (2025). Concept to The Eternal Youth. Longevity Horizon, 1(1). DOI : https://doi.org/10.5281/zenodo.15048562

Tkemaladze, J. (2025). Concept to The Food Security. Longevity Horizon, 1(1). DOI : https://doi.org/10.5281/zenodo.15048716

Tkemaladze, J. (2025). Concept to the Living Space. Longevity Horizon, 1(1). DOI : https://doi.org/10.5281/zenodo.17208472

Tkemaladze, J. (2025). Concept to The Restoring Dogmas. Longevity Horizon, 1(1). DOI : https://doi.org/10.5281/zenodo.17175865

Tkemaladze, J. (2025). Differentiation of Somatic Cells in Multicellular Organisms. Longevity Horizon, 1(2). DOI : https://doi.org/10.5281/zenodo.15052436

Tkemaladze, J. (2025). Direct Reprogramming of Somatic Cells to Functional Gametes in Planarians via a Novel In Vitro Gametogenesis Protocol. Preprints. DOI : https://doi.org/10.20944/preprints202509.1071.v1

Tkemaladze, J. (2025). Heroic Self-Myth Hypothesis. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17711334

Tkemaladze, J. (2025). Induction of germline-like cells (PGCLCs). Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.16414775

Tkemaladze, J. (2025). Lake Aquaculture for Catastrophic Food Security. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17454164

Tkemaladze, J. (2025). Long-Lived Non-Renewable Structures in the Human Body. DOI : http://dx.doi.org/10.13140/RG.2.2.14826.43206

Tkemaladze, J. (2025). Mechanisms of Learning Through the Actualization of Discrepancies. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.15200612

Tkemaladze, J. (2025). Memorizing an Infinite Stream of Information in a Limited Memory Space: The Ze Method of a Plastic Counter of Chronotropic Number Frequencies. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.15170931

Tkemaladze, J. (2025). Molecular Insights and Radical Longevity from Ancient Elixirs to Mars Colonies. Longevity Horizon, 1(2). DOI : https://doi.org/10.5281/zenodo.15053947

Tkemaladze, J. (2025). Ontogenetic Permanence of Non-Renewable Biomechanical Configurations in Homo Sapiens Anatomy. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.15086387

Tkemaladze, J. (2025). Protocol for Transplantation of Healthy Cells Between Adult Drosophila of Different Ages and Sexes. Longevity Horizon, 1(2). DOI : https://doi.org/10.5281/zenodo.15053943

Tkemaladze, J. (2025). Replicative Hayflick Limit. Longevity Horizon, 1(2). DOI : https://doi.org/10.5281/zenodo.15052029

Tkemaladze, J. (2025). Solutions to the Living Space Problem to Overcome the Fear of Resurrection from the Dead. DOI : http://dx.doi.org/10.13140/RG.2.2.34655.57768

Tkemaladze, J. (2025). The Centriolar Theory of Differentiation Explains the Biological Meaning of the Centriolar Theory of Organismal Aging. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.15057288

Tkemaladze, J. (2025). The Centriolar Theory of Differentiation Explains the Biological Meaning of the.

Tkemaladze, J. (2025). The Concept of Data-Driven Automated Governance. Georgian Scientists, 6(4), 399–410. DOI : https://doi.org/10.52340/gs.2024.06.04.38

Tkemaladze, J. (2025). The Stage of Differentiation Into Mature Gametes During Gametogenesis in Vitro. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.16808827

Tkemaladze, J. (2025). The Tkemaladze Method Maps Cell Lineage with Mutant Mitochondrial Transfer. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17236869

Tkemaladze, J. (2025). The Tkemaladze Method: A Modernized Caucasian Technology for the Production of Shelf-Stable Activated Wheat with Enhanced Nutritional Properties. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.16905079

Tkemaladze, J. (2025). Theory of Lifespan Decline. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.17142909

Tkemaladze, J. (2025). Through In Vitro Gametogenesis — Young Stem Cells. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.15873113

Tkemaladze, J. (2025). Tkemaladze, J. (2025). The Centriole Paradox in Planarian Biology: Why Acentriolar Stem Cells Divide and Centriolar Somatic Cells Do Not. Preprints. DOI : https://doi.org/10.20944/preprints202509.0382.v1

Tkemaladze, J. (2025). Unlocking the Voynich Cipher via the New Algorithmic Coding Hypothesis. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.17054312

Tkemaladze, J. (2025). Uznadze Set Revisited. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17609772

Tkemaladze, J. (2025). Why do planarian cells without centrioles divide and cells with centrioles do not divide?. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.17054142

Tkemaladze, J. (2025). Гаметогенез In Vitro: современное состояние, технологии и перспективы применения. Research Gate. DOI : http://dx.doi.org/10.13140/RG.2.2.28647.36000

Tkemaladze, J. (2026). The Strength of Clay, The Weakness of Gods. Longevity Horizon, 2(1). DOI : https://doi.org/10.65649/2neyxv38

Tkemaladze, J. (2026). Visions of the Future. Longevity Horizon, 2(1). DOI : https://doi.org/10.65649/8be27s21

Tkemaladze, J. Systemic Resilience and Sustainable Nutritional Paradigms in Anthropogenic Ecosystems. DOI : http://dx.doi.org/10.13140/RG.2.2.18943.32169/1

Tkemaladze, J. V., & Chichinadze, K. N. (2005). Centriolar mechanisms of differentiation and replicative aging of higher animal cells. Biochemistry (Moscow), 70, 1288-1303.

Tkemaladze, J., & Apkhazava, D. (2019). Dasatinib and quercetin: short-term simultaneous administration improves physical capacity in human. J Biomedical Sci, 8(3), 3.

Tkemaladze, J., & Chichinadze, K. (2005). Potential role of centrioles in determining the morphogenetic status of animal somatic cells. Cell biology international, 29(5), 370-374.

Tkemaladze, J., & Chichinadze, K. (2010). Centriole, differentiation, and senescence. Rejuvenation research, 13(2-3), 339-342.

Tkemaladze, J., & Gakely, G. (2025). A Novel Biotechnological Approach for the Production of Shelf-Stable, Nutritionally Enhanced Activated Wheat: Protocol Development, Nutritional Profiling, and Bioactivity Assessment. DOI : https://doi.org/10.20944/preprints202508.1997.v1

Tkemaladze, J., & Gakely, G. (2025). Induction of de novo centriole biogenesis in planarian stem cells. Longevity Horizon, 1(4). DOI : https://doi.org/10.5281/zenodo.17283229

Tkemaladze, J., & Samanishvili, T. (2024). Mineral ice cream improves recovery of muscle functions after exercise. Georgian Scientists, 6(2), 36–50. DOI : https://doi.org/10.52340/gs.2024.06.02.04

Tkemaladze, J., Gakely, G., Gegelia, L., Papadopulo, I., Taktakidze, A., Metreveli, N., ... & Maglakelidze, U. (2025). Production of Functional Gametes from Somatic Cells of the Planarian Schmidtea Mediterranea Via in Vitro Gametogenesis. Longevity Horizon, 1(3). DOI : https://doi.org/10.5281/zenodo.17131291

Tkemaladze, J., Tavartkiladze, A., & Chichinadze, K. (2012). Programming and Implementation of Age-Related Changes. In Senescence. IntechOpen.

Tkemaladze, Jaba and Kipshidze, Mariam, Regeneration Potential of the Schmidtea Mediterranea CIW4 Planarian. Available at SSRN: https://ssrn.com/abstract=4633202 or http://dx.doi.org/10.2139/ssrn.4633202

Прангишвили, А. И., Гаситашвили, З. А., Мацаберидзе, М. И., Чичинадзе, К. Н., Ткемаладзе, Д. В., & Азмайпарашвили, З. А. (2017). К топологии антитеррористических и антикриминальных технологии для образовательных программ. В научном издании представлены материалы Десятой международной научно-технической конфе-ренции «Управление развитием крупномасштабных систем (MLSD'2016)» по следующим направле-ниям:• Проблемы управления развитием крупномасштабных систем, включая ТНК, Госхолдин-ги и Гос-корпорации., 284.

Прангишвили, А. И., Гаситашвили, З. А., Мацаберидзе, М. И., Чхартишвили, Л. С., Чичинадзе, К. Н., & Ткемаладзе, Д. В. (2017). & Азмайпарашвили, ЗА (2017). Системные составляющие здравоохранения и инноваций для организации европейской нано-биомедицинской екосистемной технологической платформы. Управление развитием крупномасштабных систем MLSD, 365-368.

Ткемаладзе, Д. (2025). Асимметрия в наследовании центросом/центриолей и ее последствия. DOI : http://dx.doi.org/110.13140/RG.2.2.34917.31206

Ткемаладзе, Д. (2025). Гаметогенез in vitro (IVG)-Этап дифференцировки в зрелые гаметы. DOI : http://dx.doi.org/10.13140/RG.2.2.20429.96482

Ткемаладзе, Д. (2025). Дифференциация соматических клеток многоклеточных животных. DOI : http://dx.doi.org/10.13140/RG.2.2.23348.97929/1

Ткемаладзе, Д. (2025). Индукция примордиальных клеток, подобных зародышевым клеткам (PGCLCs) современные достижения, механизмы и перспективы применения. DOI : http://dx.doi.org/10.13140/RG.2.2.27152.32004

Ткемаладзе, Д. (2025). Репликативный Лимит Хейфлика. DOI : http://dx.doi.org/10.13140/RG.2.2.25803.30249

Ткемаладзе, Д. (2025). Элиминация Центриолей: Механизм Обнуления Энтропии в Клетке. DOI : http://dx.doi.org/10.13140/RG.2.2.12890.66248/1

Ткемаладзе, Д. В., & Чичинадзе, К. Н. (2005). Центриолярные механизмы дифференцировки и репликативного старения клеток высших животных. Биохимия, 70(11), 1566-1584.

Ткемаладзе, Д., Цомаиа, Г., & Жоржолиани, И. (2001). Создание искусственных самоадаптирующихся систем на основе Теории Прогноза. Искусственный интеллект. УДК 004.89. Искусственный интеллект. УДК 004.89.

Чичинадзе, К. Н., & Ткемаладзе, Д. В. (2008). Центросомная гипотеза клеточного старения и дифференциации. Успехи геронтологии, 21(3), 367-371.

Чичинадзе, К., Ткемаладзе, Д., & Лазарашвили, А. (2012). Новый класс рнк и центросомная гипотеза старения клеток. Успехи геронтологии, 25(1), 23-28

