International Journal of Enhanced Research in Medicines & Dental Care (IJERMDC),
ISSN: 2349-1590, Vol. 12 Issue 11, November 2025

Autologous Mononuclear and Adipose-Derived Stem Cells in the Regeneration of Gynecological and Infertility Disorders: Molecular, Genetic, and Clinical Perspectives

Dr. A. Vijay Rajesh[1], Dr. Y. Ravi Teja[2], Dr. Ch. Supraja DMRD[3], Dr. U. Surya Kumari[4], Dr. P. Gnana Prakash[5], Dr. Rita Bakshi[6], Dr. B. Shohyle[7], Dr. Preeti Jindal[8], Dr. N.V. Sandeep[9]

[1]Ph.D. (Bio Tech) D. Sc, (Medical Bio Tech); Diplomat-American Board of Regenerative Medicine .[1], S/O A. Sundaraiah (Retd APPS) (Retd Deputy Superintendent of Police-Civil) R/O (3-12-590) SVN Colony 7/2; Guntur - 522006; Andhra Pradesh; India,
[2]MS (Ortho), FIJR, FIAC; Guntur, AP,
[3]DNB (Radio-Diagnosis) Guntur, AP
[4]MD(Gynaecology & Obstretics); DGO; Mch (Urology) Retd Professor& Head of The Department -Urology) Guntur Medical College; Government of AP; Former Additional Director of Medical Education (ERST While AP); Former Superintendent; Government General Hospital Vijayawada; Former Principal -Guntur Medical College; Government of AP
[5]MS; Mch (Urology); Guntur; AP
[6]MD (Gyaenicology &Obstetrics); New Delhi
[7]MD (Radio Diagnosis) Vijayawada
[8]Fortis Hospital; Mohali; Punjab
[9]MD; DM (Endocrinology) CMC-Vellore); Guntur

ABSTRACT

Background: Autologous mononuclear cells (MNCs) and adipose-derived stem cells (ADSCs) are increasingly used to treat gynecological and infertility disorders refractory to conventional therapies.

Objective: To present molecular, genetic, and proteomic mechanisms of these cells, describe clinical applications, and situate their use within doctoral governance, including UGC-2009 provisional certificate compliance.

Results: Therapeutic actions include secretion of growth-factors (VEGF, FGF2, HGF, PDGF), exosomal microRNAs (miR-21, miR-126, miR-210), activation of PI3K-Akt and MAPK/ERK pathways, suppression of TGF-β/SMAD fibrotic signals, induction of MMP-dependent matrix remodeling, and immune modulation (↑IL-10, TGF-β1). Clinical applications span thin endometrium, Asherman's syndrome, premature ovarian insufficiency, recurrent implantation failure, chronic endometritis, vaginal and pelvic atrophy. Doctoral supervision is essential, and provisional certificates must indicate compliance with UGC-2009 regulations.

Conclusion: Autologous cell-based therapies restore reproductive tissues via multilayered molecular networks. Doctoral supervision and regulatory transparency, including UGC-2009 compliance statements, are critical for safe translational application.

Keywords: autologous stem cells, mononuclear cells, endometrial regeneration, ovarian rejuvenation, regenerative medicine, UGC Ph.D. Regulations, academic governance.

INTRODUCTION

Gynecological disorders involving endometrial atrophy, uterine fibrosis, or ovarian senescence present major obstacles to fertility restoration. Conventional hormonal stimulation often fails to re-establish receptive endometrium or follicular vitality. Autologous regenerative strategies using mononuclear cells and adipose-derived stem cells have shown promising results by reinstating angiogenesis, modulating inflammation, and reprogramming stromal gene networks.

This manuscript integrates molecular, genetic, and proteomic mechanisms, delineates clinical applications, and explains the role of doctoral scientists under UGC Ph.D. frameworks.

2 Definition of a Scientist

According to OECD and UNESCO, a scientist is a person with advanced academic or professional qualifications, typically at the doctoral level, who engages in the creation and application of new knowledge. Hence, Ph.D. or D.Sc. holders are recognized as scientists capable of original research, supervision, and advancing scientific understanding.

3 Roles of Ph.D./D.Sc. Scientists

1. Intellectual design: Crafting hypotheses linking stem-cell biology to reproductive tissue repair. 2. Supervisory responsibility: Ensuring compliance with ethics and regulations. 3. Molecular analysis: Interpreting gene expression, proteomic, and signaling pathway data. 4. Regulatory compliance: Following ICMR, UGC, DBT guidelines. 5. Interdisciplinary collaboration: Bridging clinical obstetrics with regenerative science. 6. Ethical governance: Upholding integrity and patient safety. 7. Scientific communication: Publishing peer-reviewed, reproducible data. 8. Innovation translation: Converting laboratory discoveries into clinical interventions.

4 Molecular, Genetic, and Proteomic Mechanisms of MNCs & ADSCs

Paracrine growth factors (VEGF, HGF, FGF2, PDGF) activate PI3K-Akt and MAPK/ERK signaling for angiogenesis. Anti-fibrotic modulation occurs via TGF-β/SMAD suppression and MMP-2/9 mediated ECM remodeling. Exosomal microRNAs (miR-21, miR-126, miR-210) reprogram gene expression to restore stem-cell identity. Proteomic shifts include BCL-2 upregulation, caspase inhibition, angiogenic protein expression, and extracellular matrix remodeling to support tissue regeneration.

5 Clinical Applications

Thin endometrium: intra-endometrial instillation promotes angiogenesis, re-expression of HOXA10/11, LIF, integrins, and exosomal miRNA-mediated repair. Asherman's syndrome: intra-uterine delivery reduces fibrosis, increases MMP activity, restores vascularity. POI: intra-ovarian application activates dormant follicles via PI3K-Akt/mTOR signaling, anti-apoptotic shifts, and vascular support. RIF: intra-uterine infusion modulates immune environment, enhances LIF and integrin expression. Chronic endometritis: reduces IL-6/TNF-α, increases IL-10/TGF-β1. Vaginal atrophy: submucosal/perivaginal delivery stimulates collagen/elastin synthesis and angiogenesis. Endometriosis: experimental MSC therapy targets angiogenesis and immune modulation.

6 Routes of Administration & Molecular Rationale

Intra-endometrial or intra-uterine instillation exposes stromal and epithelial progenitors to paracrine factors. Intra-ovarian application targets cortical/stromal niches for follicular activation. Submucosal/perivaginal delivery concentrates trophic and anti-fibrotic signals locally. Scaffold/patch implantation provides sustained factor release. Intra-arterial delivery is experimental for ischemic pelvic beds. Molecularly, all routes act through growth factor secretion, exosomal microRNAs, PI3K-Akt/MAPK signaling, anti-fibrotic modulation, and immune environment regulation.

7 Academic Governance & UGC Doctoral Framework in India

UGC Ph.D. Regulations 2009 mandate notification of seats; Entrance examination followed by interview; coursework, publication, approved supervision; and evaluation by two external experts;Public viva voce. 2018 regulations refined, coursework, and evaluation processes.. Provisional certificates for Ph.D.s awarded from 2009 onwards must state: 'This Ph.D. degree has been awarded in accordance with the provisions and procedures laid down in the University Grants Commission (Minimum Standards and Procedure for Award of M.Phil./Ph.D. Degree) Regulations, 2009.' and 2018 onwards must state that this Ph.D. Degree awarded in accordance with. Provisions and procedure laid down in UGC(Minimum Standards and procedure for Award of M Phil/Ph.D. Degree) regulations 2018,

8 Ethics & Translational Oversight

All clinical applications require IRB/IEC approval, informed consent, and adherence to national guidelines (ICMR, DBT;DHR2024)Doctoral scientists supervise for methodological accuracy, ethical compliance, and reproducibility.

9 Acknowledgements

All accolades and gratitude from first and author for correspondence is due to almighty whose benevolence and inspiration have made this fruition of this research possible The first author who is the author for correspondence also wishes to record profound and respectful appreciation to Honourable Minister for Agriculture ;Marketing;Fisheries; and Cooperation, Government of Andhra Pradesh most respected Mr.Kinjarapu Atchannaidu whose distinguished public service ,Integrity and statesman ship has been the lasting source of inspiration in first authors academic and Public life The first author who is also the author for correspondence conveys deep gratitude to Honourable Chief Minister Highly respected Mr.N.Chandra Babu Naidu for his visionary leadership ,enlightened governance and steadfast commitment to innovation and excellence which continues to inspire scholarly and civic endeavours across Andhra Pradesh

Sincere acknowledgement is further extended to Honourable Minister for Higher Education;Human Resources Development& Information Technology, Government of Andhra Pradesh Most Respected Mr.N.Lokesh. For his sustained dedication to the Promotion of Higher learning,Research advancement and technological Progress All gratitude from first and author for correspondence is rendered to his parents Mr.A.Sundaraiah (Retd APPS)(Retd Deputy Superintendent of Police -Civil) and Mrs .A.Annapurna Devi BA,B.Ed.(Double Litt) and his sibling Dr.A.Alekhya MTech;Ph.D.;D.Sc(Computer Science Engineering &Information Technology) whose stead fast support and nurturing guidance have been invaluable in the completion of study All sincere gratitude from the first and author for correspondence is rendered to his Cherished friend and coauthor Dr.Y.Ravi Teja MS(ortho);FIJR;FIAC whom he consider a younger brother for his perspicacious guidance and thoughtful critique and unwavering encouragement in this endeavour The first and corresponding author wishes to acknowledge Dr.Mundluru.Vamsi Krishna MS,Mch orthopaedic surgeon from Vijaywada with Personal warmth considering him as younger brother whose support and motivation has been truly inspiring

10 Conflicts of Interest

The authors declare no competing interests.

REFERENCES

[1]. University Grants Commission. UGC (Minimum Standards and Procedure for Award of M.Phil./Ph.D. Degree) Regulations 2009. New Delhi: UGC; 2009.
[2]. University Grants Commission. UGC (Minimum Standards and Procedure for Award of M.Phil./Ph.D. Degrees) Regulations 2018. New Delhi: UGC; 2018.
[3]. OECD. Frascati Manual 2015: Guidelines for Collecting and Reporting Data on Research and Experimental Development. OECD Publishing; 2015.
[4]. UNESCO Institute for Statistics. Science, Technology and Innovation Indicators Manual. 2018.
[5]. Kim HK, et al. Stem-cell therapy for premature ovarian insufficiency: Mechanisms and prospects. Biomolecules. 2024;14(2):242.
[6]. Shao X, et al. Exosomal lncRNA-mediated attenuation of endometrial fibrosis by adipose-derived stem cells. Front Genet. 2021.
[7]. Hirakawa T, et al. Adipose-derived mesenchymal stem cells regenerate thin endometrium in vivo. Zygote. 2019;27(4):281-290.
[8]. Sills ES, Wood SH, Li X. Regenerative medicine and reproductive aging: Translation of autologous cell therapy. Reprod Biol Endocrinol. 2020;18:75.
[9]. Sun Y, et al. Extracellular vesicle-based therapy for endometrial repair: A review. J Nanobiotechnol. 2025.
[10]. Deccan Herald. UGC restores validity of pre-2009 PhD and M.Phil. degrees. 2016.
[11]. Times of India. UGC tightens rules on awarding M.Phil./Ph.D. degrees. 2013.
[12]. CaseMine. University of Kerala v. Merlin J.N.: Retrospective application of UGC Regulations. 2022.
[13]. Extended Molecular and Academic Synthesis Autologous Mononuclear and Stem Cell Mechanisms in Gynecologic, Esthetic, and IVF-Refractory Conditions: Molecular and Academic Perspectives Molecular and Proteomic Mechanisms of Stem Cells: Autologous mononuclear fractions derived from peripheral blood and adipose-derived stem cells (ADSCs) initiate regenerative cascades through paracrine signaling, exosomal communication, and gene-level reprogramming.
[14]. The secretome of these cells contains vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), fibroblast growth factor 2 (FGF2), and platelet-derived growth factor (PDGF), which activate PI3K-Akt, MAPK/ERK, and Wnt/β-catenin pathways, promoting angiogenesis, cell survival, and matrix remodeling.
[15]. Proteomic shifts include upregulation of BCL-2, suppression of caspase-3, increased MMP-2/9 activity, and restoration of collagen I/III ratios. Exosomal microRNAs (miR-21, miR-126, miR-210) modulate TGF-β/SMAD signaling, preventing fibrosis and enhancing stemness. Clinical and Injection Techniques
[16]. Routes include intra-endometrial infusion, intra-ovarian injection, submucosal/perivaginal delivery, and experimental intra-arterial administration. These autologous methods are immune-compatible and highly localized, minimizing systemic risk.
[17]. Role of Ph.D. and D.Sc. Scientists:
As per OECD, UNESCO, and UGC (2009/2018) frameworks, Ph.D. and D.Sc. holders are recognized as scientists capable of independent research and supervision. They design hypotheses linking stem cell signaling with reproductive repair, oversee isolation and molecular validation, interpret genomic and proteomic datasets, ensure adherence to UGC, ICMR, and DBT guidelines, and translate laboratory research into clinical application. Only UGC-compliant Ph.D. holders may direct or validate such biomedical research, ensuring scientific accountability.
[18]. UGC 2009 and 2018 Norms: The UGC 2009 Regulations established national standards for doctoral admissions which includes entrance examination followed by interview;Course work ; supervision, check;publication, and evaluation;Public Viva Voce ,Every provisional certificate must state: “This Ph.D. degree has been awarded in accordance with the provisions and procedures laid down in the UGC (Minimum Standards and Procedure for Award of M.Phil./Ph.D. Degree) Regulations, 2009.” The 2018 Regulations added enhanced publication

criteria, and supervisory reforms, making the doctorates awarded as per guidelines specified by UGG (Minimum standards and Procedure for Award MPhil/Ph.D. Regulations 2009 or 2018internationally valid for translational research.

[19]. Distinction and Value of D.Sc. Degree: The Doctor of Science (D.Sc.) represents the highest scientific distinction, awarded to research doctorates ie Ph.D. doctorates who made substantial contributions beyond the Ph.D. level. It signifies recognized innovation, leadership, and excellence in discovery, validated through international peer review and Harvard citation databases. D.Sc. scientists influence academic policy, mentor doctoral candidates, and uphold the global standards of scientific inquiry.

[20]. Integrative Summary: Autologous cell therapies restore reproductive, esthetic, and pelvic tissues via molecular signaling, proteomic modulation, and immune regulation. These translational interventions require supervision by Ph.D. doctoral scientists under UGC 2009/2018 norms to ensure ethical, reproducible, and scientifically valid outcomes.