The 1st ICBBs 2026

INTERNATIONAL CONFERENCE ON BIOTECHNOLOGY AND BIOMEDICAL SCIENCES

"Translational Advances in Stem Cell and Cancer Research: From Bench to Bedside"

1-2 August, 2026
08:00 GMT+7

GUMAYA TOWER HOTEL,
Semarang

PUBLICITY & PROCEEDING BOOK

Scopus Q3
Indonesian Journal of Biotechnology (IJBiotech)

Limited Quota **10**

Scopus Q4
International journal of Biomedicine (IJBM)

Limited Quota **10**

Sinta 1
Indonesian Journal of Cancer and Chemoprevention (IJCC)

Limited Quota **20**

Registration & Abstract Submission:

Deadline Abstract: 14 July 2026, Full Manuscript: 18 July 2026

Conference Registration Fee :

Participant	Non Presenter	Presenter
General Participants & Healthcare Practitioners	IDR 3,000,000	IDR 3,250,000
Undergraduate Students	IDR 1,000,000	IDR 1,250,000

Contents

SPEAKERS ABSTRACTS

1.1. ABSTRACT Prof. Dr. Akira Kurisaki

DIFFERENTIATION OF STOMACH TISSUE CELLS FROM STEM CELLS AND THEIR MECHANISMS

Akira Kurisaki

Laboratory of Stem Cell Technologies, Division of Biological Science, Graduate School of Science and Technology, Nara Institute of Science and Technology (NAIST), Nara, Japan

Abstract

The stomach is a unique organ that secrete various enzymes, gastric acid, and hormones. In the adult stomach tissues, defects in gastric tissue stem cell differentiation are associated with various gastric disorders, including atrophic gastritis, intestinal metaplasia, and gastric cancer. However, the mechanisms underlying the multilineage differentiation of gastric stem cells during healthy homeostasis remain poorly understood. Using a single-cell RNA sequencing method, we analyzed the gene expression dynamics of progenitor cell differentiation toward pit cell, neck cell, and parietal cell lineages in healthy adult mouse corpus tissues. Enrichment analysis of pseudotime-dependent genes and a gastric organoid assay revealed that EGFR-ERK signaling promotes pit cell differentiation, whereas NF-κB signaling maintains gastric progenitor cells in an undifferentiated state. In addition, pharmacological inhibition of EGFR in vivo resulted in fewer pit cells. Although activation of EGFR signaling in gastric progenitor cells has been suggested as one of the major inducers of gastric cancers, our findings unexpectedly identified that EGFR signaling exerts a differentiation-promoting function, not a mitogenic function, in normal gastric homeostasis.

1.2. ABSTRACK Prof. Dr. Rajesh Ramasamy

From Bench to Bedside: Harnessing MSC Immunomodulation in the Age of Precision Medicine

Rajesh Ramasamy

Stem cell & immunomodulation Research Group, Immunology Unit, Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia

rajesh@upm.edu.my

Mesenchymal stromal cells (MSCs) entered clinical evaluation based on the foundational hypothesis that they possess immunosuppressive properties across diverse environments. However, discrepancies in trial outcomes have prompted a reevaluation of this premise. Evidence indicates that MSC functions are conditional and largely influenced by the cytokine milieu at the site of action. The minimal profiling of MSCs defined by the International Society for Cellular Therapy (ISCT) (CD73, CD90, and CD105) identifies MSCs phenotypically, but does not predict their functional behaviour. In search of biomarkers of immunomodulation, vascular cell adhesion molecule-1 (VCAM-1/CD106) showed potential as an indicator of immunosuppressive potency. The mechanistic studies in murine and human models support an association, yet a clinical-grade human potency assay revealed that VCAM-1 expression did not correlate with T-cell suppression, unlike indoleamine 2,3-dioxygenase (IDO-1) and programmed death-ligand 1 (PD-L1). Moving from identity to activation, the roles of interferon-gamma and tumour necrosis factor-alpha are examined as licensing factors that modulate MSC functional programs. Once licensed, MSCs influence T-cell fate, including the regulation of exhaustion-associated checkpoints, with potential therapeutic benefits in autoimmune disorders but possible adverse effects within the tumour microenvironment. Clinically, these insights emphasise that potency assays should rely on immunologically validated markers rather than phenotypic convenience to ensure accurate assessment of MSC therapeutic potential.

1.3. ABSTRACT Dr. Shifu Chen

Presentation Title:

Precision Cancer Diagnosis and Monitoring with Liquid Biopsy and Artificial Intelligence

Abstract:

Dr. Chen will share his research experience in early diagnosis, precision treatment, and dynamic monitoring of tumors using technologies such as liquid biopsy and high-throughput sequencing.

Specifically, he will share some of his new research findings regarding diagnosing lung nodules with TCR-seq and AI, and cancer monitoring with MRD

1.4. ABSTRACT Faheem Ahmed Khan, B.Sc., M.S., Ph.D.

Title: Breaking the Barrier: Next-Generation Engineering of Adoptive T Cell Therapy for Solid Tumors

Abstract

Adoptive cell therapy (ACT), particularly chimeric antigen receptor (CAR) T cells, has revolutionized hematological cancer treatment, yet solid tumors present distinct clinical hurdles such as limited engraftment, off-tumor toxicity, and hostile tumor microenvironments (TME). This research highlights innovative engineering and combinatorial strategies to overcome these solid tumor barriers. To mitigate toxicity, a novel, chemically disruptible "STOP-CAR" was engineered using a human apolipoprotein E4 scaffold, enabling dynamic, reversible attenuation of CAR T cell activity *in vivo* via small molecule administration. To optimize *in vivo* fitness, expanding T cells with IL-7 and IL-15 preserves a robust central memory phenotype. Furthermore, fourth-generation (4G) CAR T cells co-expressing IL-15 exhibited superior persistence, reduced PD-1 expression, and favorable TME reprogramming. Addressing physical barriers, co-administering anti-VEGFA antibodies prevented target occlusion for VEGFR2-directed CAR T cells, effectively restoring their efficacy. Finally, rational combinatorial regimens like low-dose radiotherapy combined with cyclophosphamide and immune-modulating antibodies profoundly remodeled the TME, driving enhanced T cell infiltration. Collectively, these next-generation advancements offer a comprehensive framework to maximize the safety, fitness, and efficacy of ACT against solid tumors.

1.5. ABSTRACT Prof. Dr. dr. Amin Soebandrio, Ph. D., Sp.MK

Ethics in Regenerative Medicine
Amin Soebandrio
Committee for Stem Cell and Cell Development

Abstract.
Degenerative diseases encompass a range of conditions characterized by the progressive deterioration of cells, tissues, and organs. The goal of regenerative medicine is to replace or reboot tissues or organs damaged by disease, injury, age, or other factors, rather than treating symptoms with medication and procedures. Regenerative medicine could be delivered in the form of cell therapies, tissue-engineered products, gene therapies, or combination products. Four anchors of clinical ethics in this field are respect for persons, beneficence, justice, and integrity of science. Clinics in some countries sell unapproved stem cell interventions for chronic and terminal conditions. Marketing leans on the credibility of legitimate regenerative medicine and the desperation of patients without options. FDA and EMA have repeatedly warned of harms: infections, immunologic reactions, tumorigenesis, and worsened underlying disease. Under hype and hope, patients facing degenerative or terminal disease are uniquely vulnerable to exaggerated marketing claims. Potential problems with equity, access, and the cost frontier are that approved cell and gene therapies routinely exceed $1M per course; risk of a two-tier system (cutting-edge regenerative medicine for the well-insured, unproven clinics for everyone else); as well as LMIC access depends on technology transfer, regional manufacturing, and durable cold-chain capacity. What clinicians should carry forward is to track the guidance, stay clear of the lines, sharpen the consent, speak to the public, and defend the field (distinguish legitimate regenerative medicine from predatory clinics).

1.6. ABSTRACT Dr. dr. Eko Setiawan, Sp.B

"Bridging Bench to Bedside: Stem Cell Therapies for Advanced Wound Regeneration in Translational and Clinical Biomedical Research"

Eko Setiawan

Abstract:

Chronic wounds represent a significant global health burden, affecting millions of patients with diabetes, vascular insufficiency, and aging-related impairments, often leading to prolonged hospitalization, reduced quality of life, and increased healthcare costs. Traditional treatments frequently fail to achieve complete regeneration, resulting in fibrosis and scarring rather than functional tissue restoration. Stem cell-based approaches have emerged as a promising translational strategy to overcome these limitations by harnessing the regenerative, immunomodulatory, and paracrine capacities of various stem cell populations.

This presentation will explore the multifaceted roles of mesenchymal stem cells (MSCs) derived from bone marrow, adipose tissue, and other sources, alongside induced pluripotent stem cells (iPSCs) and embryonic stem cell derivatives, in wound healing. Key mechanisms include acceleration of re-epithelialization, promotion of angiogenesis via secretion of growth factors (e.g., VEGF, PDGF), modulation of inflammation through cytokine release, and enhancement of extracellular matrix remodeling. Preclinical evidence demonstrates significant improvements in wound closure rates, with MSC therapies reducing healing time by over 50% in diabetic models through restoration of disrupted signaling pathways such as Nrf2/Keap1.

Translational advancements, including exosome-based cell-free therapies, bioengineered scaffolds, and targeted delivery systems (e.g., hydrogels and microneedles), will be highlighted for their potential to improve cell survival, integration, and safety. Clinical studies have shown encouraging outcomes in chronic leg ulcers and diabetic foot wounds, with accelerated closure and minimal adverse effects, though challenges such as optimal dosing, long-term efficacy, immunogenicity, and regulatory hurdles remain.

Future perspectives will address personalized regenerative medicine, combination therapies with growth factors or gene editing, and ongoing trials aimed at achieving scarless healing. By integrating basic science insights with clinical applications, stem cell strategies hold transformative potential for revolutionizing wound management and advancing the field of regenerative biomedicine

1.7. ABSTRACT Wen Tai Chiu

YAP inactivation-mediated autophagy inhibition contributes to cisplatin resistance in ovarian cancer cells

Wen-Tai Chiu

Abstract

Background Cisplatin resistance remains a critical barrier in the treatment of high-grade serous ovarian cancer (HGSOC). Although HippoYAP signaling regulates cancer progression, its contribution to cisplatin resistance is still poorly understood. Here, we demonstrate that YAP is inactivated and sequestered in the cytoplasm of cisplatin-resistant ovarian cancer cells.

Results This cytosolic retention is mediated by Hippo kinases MST1/2 and LATS1/2, as well as ERK signaling, resulting in increased phosphorylation of YAP at its inhibitory site (Ser397) and reduced phosphorylation at its activating site (Tyr357). Restoration of YAP activity through genetic overexpression or pharmacological induction of nuclear YAP accumulation significantly reversed cisplatin resistance. Mechanistically, YAP inactivation impaired cisplatin-induced autophagy. Cisplatin robustly triggered autophagy in parental cells, as evidenced by LC3 puncta formation; however, this autophagic response was blunted in resistant cells. Overexpression of YAP further suppressed LC3 puncta formation and Beclin-1 expression, and increased p62 accumulation in cisplatin-resistant ovarian cancer cells. Autophagy inhibition using 3-methyladenine (3-MA) resensitized resistant cells to cisplatin.

Conclusion Collectively, these findings reveal that YAP inactivation contributes to cisplatin resistance by abrogating autophagy formation and identify YAP reactivation as a potential strategy to overcome chemoresistance in ovarian cancer.

1.8. ABSTRACT Dr. Shahid Ullah Khan PhD, Post doc

The beauty of Ru (II) Complexes: A Novel Antitumor Strategy in Triple Negative Breast Cancers

Presenter name: Shahid Ullah Khan PhD, Post doc

Type of presentation: Oral

Department of Biomedical Sciences, College of Medicine, Dubai Medical University (COM, DMU), Dubai 19099, United Arab Emirates

Email: shahid.zkd35@yahoo.com Tel: 00971558810175

Abstract

Introduction:

Cancer remains one of the most devastating diseases, contributing significantly to human mortality on a global scale. A critical factor in tumorigenesis and the development of drug resistance is the dysregulation of apoptosis. Ruthenium complexes are the leverage and emerged anticancer strategy to combat multiple forms of cancer cells.

Methods:

In this study, we synthesized 12 monofunctional ONS-donor salicylaldimine ligand-based Ru (II)(*p*-cymene) complexes (C1-C12). These complexes were characterized by ^{1}H NMR, ^{13}C NMR, UV and FT-IR spectroscopy and high-resolution electrospray mass spectrophotometric analysis. The structure of C7 was confirmed in solid state by single crystal X-ray analysis, that revealed the exact orientation of the ligand around Ru (II) center. These complexes were further investigated for their anticancer activity against MDA-MB-231, 4T1, U87MG and HeLa cancer cells. Using the 4T1 breast cancer orthotopic mouse model, we evaluated the efficacy of the most prominent complex (C8) in 4T1 breast cancer by bioluminescence metastatic windows, tumor weight and volume, hematoxylin and eosin (H&E) staining, immunohistochemistry (IHC) staining and hematological tests.

Results:

A dose-dependent manner reduction in cell viability and survival rates of cancer cells was observed following treatment with these complexes. We identified that C2, C8, and C11 exhibited the most potent anti-tumor effects among these tested complexes. The results from migration ability and live/dead imaging assays, as well as mitochondrial membrane potential (MMP) and clonogenic potential studies, revealed that these complexes demonstrated higher anti-tumor activities by enhancing caspase-3 and reducing Bcl-2 expression. Protein expression revealed apoptosis by up-regulating Caspase-3, cleaved caspase-3, TNF-α and down-regulating Bcl-2. Lasting survival and diminished tumor growth were observed in mice receiving the C8 treatment.

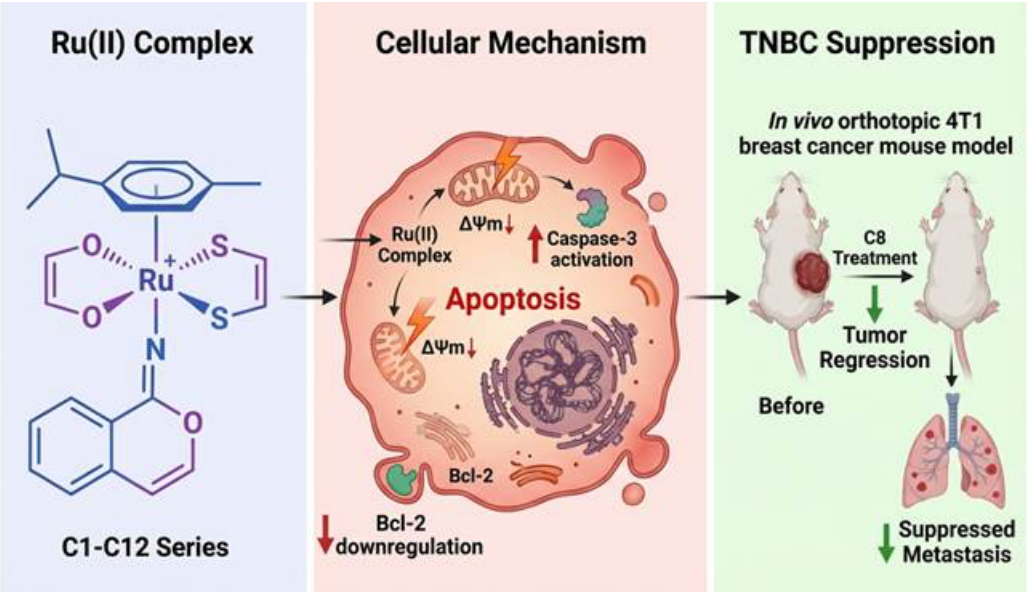
Conclusion:

These findings demonstrated the potential of those water-soluble monofunctional Ru (II) complexes for triple negative breast cancer treatment.

Keywords:

Breast cancer, 4T1 Orthotopic mouse model, Ruthenium arene complexes, Apoptosis central regulators

Graphical Abstract



Biography of Presenter:

Dr Shahid Ullah Khan is working as an Assistant Professor and Head of IRB, Department of Biomedical Sciences, College of Medicine, Dubai Medical University (COM, DMU), Dubai 19099, United Arab Emirates. He earned his Ph.D. degree in 'Genome Wide Association Studies and Post doc from HZAU, Wuhan, and SWU P. R. China in 2019, and 2025, respectively. He is recipient of several fellowships and awards such as: (i) World Top 0.5% and 2 % Scientists (ii) Young Scientist Award 2022, (iii) Asian Rank#01, Health and Biomedical Sciences (Biochemistry) Award , 2024, 2023, and 2022,(iii) World Scientists and University Ranking Award 2021 (iv) Agri Sciences China (Visiting Scientist-2020 at HZAU Wuhan, China, (v) Outstanding Research Awarded-2017 and 2019 ISO HZAU Wuhan China, (vi) OMG-2016 Award by HZAU Wuhan China, and (vii) Best Research Award-2022 by SCI-F (Biochemistry), around the globe. His current research activities are Genome Wide Association Studies, Nanotechnology and Natural Products etc. He has published over 150 research papers in peer reviewed international journals having 40 h-index and 804.6 IF. He has also contributed seven chapters in the book published by Springer Nature. He is editor and reviewers in various journals.

1.9. ABTRACT Rizal Azis, S.Si, M.Biotech., M.Sc., PhD

Xeno-free and chemically defined medium for expansion of UC-MSCs and differentiation of hiPSCs for disease modelling

Rizal Azis1,2, Nicholas R.F Hannan3

1Cellular and Regenerative Engineering (CARE) Lab, Biomedical Engineering, Faculty of Engineering, Universitas Indonesia, Depok, West Java, Indonesia

2Research Center for Biomedical Engineering, Faculty of Engineering, Universitas Indonesia, Depok, West Java, Indonesia

3Stem Cell Division, School of Medicine, Biodiscovery Institute, The University of Nottingham, University Park, Nottingham, United Kingdom

Abstract

Human induced pluripotent stem cells (hiPSCs) and umbilical cord-derived mesenchymal stromal cells (UC-MSCs) are important cell sources for regenerative medicine, disease modelling, and developmental biology studies. However, their broader application requires scalable and clinically compatible culture systems based on xeno-free and chemically defined conditions. In this study, we developed and optimized a xeno-free, chemically defined platform for both UC-MSC expansion and hiPSC differentiation. For UC-MSC culture, we established an in-house formulated medium that supported efficient cell expansion under xeno-free conditions. UC-MSCs cultured in this medium maintained their characteristic morphology and demonstrated population doubling time (PDT) and cumulative population doubling level (CPDL) values comparable to those obtained using commercially available xeno-free media, indicating that the formulated medium can serve as a cost-effective alternative for large-scale MSC expansion. To support advanced disease modelling applications, we further optimized a chemically defined, xeno-free differentiation protocol capable of generating multiple non-parenchymal cell types from a common hiPSC population. Following mesoderm induction, hiPSCs were directed into macrophages (MΦ), dendritic cells (DCs), fibroblasts (FBs), and vascular endothelial cells (VECs) through lineage-specific growth factor modulation. The differentiated cells were validated by mRNA sequencing and functional assays, including macrophage polarization, fibroblast activation, and endothelial tube formation. To demonstrate the utility of this platform, the generated non-parenchymal cells were combined with hiPSC-derived hepatocyte-like cells to produce multicellular tissue organoids. These organoids provide a more physiologically

relevant three-dimensional (3D) environment than conventional two-dimensional (2D) culture systems, enabling improved modelling of human tissue complexity and disease processes. In conclusion, we present an integrated xeno-free and chemically defined culture system that enables robust UC- MSC expansion and reproducible differentiation of hiPSCs into multiple functional cell types. This platform provides a scalable and clinically relevant approach for organoid generation, disease modelling, drug discovery, and regenerative medicine applications.

Keywords: human induced pluripotent stem cells (hiPSCs); Umbilical cord-derived mesenchymal stromal cells (UC-MSCs); Xeno-free medium; Chemically defined culture system; Disease modelling

ORAL PRESENTATION ABSTRACTS

2.1. . R. Vito Mahendra Ekasaputra

Mesenchymal Stem Cells (MSCs) Therapy on VEGF, CRP, TNF-α, Triglyceride, Pancreatic Beta Cells and Insulin Resistance in Obese Type 2 Diabetic Rat Model

Abstract

BACKGROUND: Obesity due to excess fat accumulation will cause chronic inflammation of

pancreatic cells and as the basis for insulin resistance (IR) and type 2 diabetes mellitus (T2DM).

Sleeve gastrectomy (SG) procedure increases insulin sensitivity which could reduce the chronic

inflammation that occurs in the body. Mesenchymal stem cells (MSCs) can also exhibit potential

immunomodulatory properties through their paracrine effects; however, the mechanism regarding

the combination of them could not be adequately explained. **AIM**: In this study, we explore the

potential of SG followed by injection of MSCs in type 2 diabetic rats with obesity in improving

IR. **MATERIALS AND METHODS**: This study used a pre and post-control group design with

24 rats divided into three groups: Control (C), SG, and SG + MSCs (SG+M). On day 10, the level

of VEGF, TNF-α, CRP, Triglyceride (TG), Pancreatic Beta Cells, and homeostasis model

assessment of IR (HOMA-IR) was evaluated using qRT-PCR, ELISA, and IHC. **RESULTS**: This

study showed a significant decrease of TNF-α (1.179 pg/mL), CRP(209 pg/mL), and TG levels

(82,83 ± 15,02pg/mL) in all treatment groups on day 10, in which SG + M group showed optimum

inhibition ($p < 0.05$). This result was in line with the optimum increase of VEGF (8,1500 ±

2,47397) and Pancreatic Beta Cell(10,1783±0,47) in SG + M group ($p < 0.05$). Moreover, our

study also revealed the optimum decrease of HOMA-IR in SG + M group on day (1049,8233 ±1,07303). **CONCLUSION**: A combination of SG and MSCs can optimally improve IR by inhibiting TNF-α, CRP, and TG level and upregulating VEGF and Pancreatic Beta Cells in an obese T2DM rat model.

KEYWORDS: *CRP, Insulin Resistance, MSCs, Pancreatic Beta Cells, TNF-α, Triglyceride,*

VEG

2.2. Yusrina Istanti

Original Research

Establishment and Validation of a Young Adult Rat Model of Caecal Slurry-Induced Sepsis for Investigating Early Intestinal Injury

Yusrina Istanti[1,2*]

[1]Student of Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University (UNISSULA), Semarang, 50112, Indonesia

[2] Pediatric Emergency and Intensive Care Division, Department of Anaesthesiology, Dr. Kariadi General Hospital, Semarang, 50244, Indonesia

Corresponding author: yit1st@gmail.com

Abstract. Background: Pediatric sepsis remains a leading cause of morbidity and mortality worldwide. Intestinal barrier dysfunction contributes to systemic inflammation and multiple organ dysfunction. Although the caecal slurry (CS) model is widely used, its relevance to early intestinal changes in pediatric sepsis remains unclear. **Objective:** To establish and validate an early CS-induced sepsis model and identify the optimal time point for evaluating intestinal injury and inflammatory responses**. Methods:** Young adult male Wistar rats were allocated to healthy control and caecal slurry groups evaluated at 9, 12, and 24 hours after induction. Chiu histopathological analysis included 8, 5, 10, and 14 animals in the healthy, 9-hour, 12-hour, and 24-hour groups, respectively, whereas NF-κB mRNA expression was assessed in three animals per group. Chiu scores were analysed using the Kruskal–Wallis test followed by Dunn's multiple-comparison test, while NF-κB expression was analysed using one-way ANOVA followed by Tukey's post hoc test. **Results**: CS induced early intestinal injury. Chiu scores were 0.00 ± 0.00, 2.40 ± 1.82, 2.20 ± 1.03, and 2.29 ± 1.38 in the healthy, 9-, 12-, and 24-hour groups, respectively (all post-CS groups vs. healthy, $p < 0.05$). NF-κB mRNA expression peaked at 9 hours (18.06 ± 10.02 vs. 2.16 ± 2.84 in healthy controls, $p < 0.05$) and declined at 12 hours (0.30 ± 0.28) and 24 hours (0.72 ± 0.46). **Conclusion**: The CS model reliably reproduced early sepsis-associated intestinal injury. The 9-hour post-CS time point was identified as the optimal window for investigating early sepsis-induced intestinal injury and may serve as a translational model for pediatric sepsis research.

Keywords: caecal slurry, pediatric sepsis, intestinal injury, NF-κB, animal model

2.3. Dian Rudy Yana

Efek Imunoregulasi Debiococo, Sinbiotik Kaya Vitamin D_2, terhadap IL-10 dan TGF-β pada Kolitis Eksperimental

Immunoregulatory Effects of Debiococo, a Vitamin D_2-Enriched Synbiotic, on IL-10 and TGF-β in Experimental Colitis

Dian Rudy Yana[1], Atina Hussaana[2]*, Siti Thomas Zulaikhah[3]

[1]Postgraduate Student of Biomedical Sciences, Faculty of Medicine, Universitas Islam Sultan Agung, Jl. Kaligawe KM 4, Semarang 50012, Indonesia
[2] Department of Pharmacology, Faculty of Medicine, Universitas Islam Sultan Agung, Jl. Kaligawe KM 4, Semarang 50012, Indonesia
[3] Department of Public Health, Faculty of Medicine, Universitas Islam Sultan Agung, Jl. Kaligawe KM 4, Semarang 50012, Indonesia

ABSTRAK

Latar Belakang: *Penelitian sebelumnya menunjukkan bahwa Debiococo, kombinasi serbuk jamur tiram teraktivasi UVB, probiotik, dan air kelapa muda, mampu mempertahankan integritas mukosa kolon serta meningkatkan kelangsungan hidup pada kolitis eksperimental.*
Tujuan: *Mengevaluasi pengaruh Debiococo terhadap kadar serum interleukin-10 (IL-10) dan transforming growth factor-beta (TGF-β) pada tikus kolitis yang diinduksi asam asetat.*
Metode: *Penelitian eksperimental dengan rancangan post-test only control group menggunakan 30 ekor tikus Wistar jantan yang dibagi menjadi lima kelompok: kontrol normal (G1), kontrol negatif (G2), kontrol positif sulfasalazin (G3), Debiococo dosis 1 (400 IU vitamin D_2 + 4 mL probiotik; G4), dan Debiococo dosis 2 (800 IU vitamin D_2 + 4 mL probiotik; G5). Kolitis diinduksi dengan pemberian intrarektal asam asetat 4%. Perlakuan diberikan selama 8 hari. Kadar IL-10 dan TGF-β serum diukur menggunakan metode ELISA.*
Hasil: *Kadar IL-10 tertinggi ditemukan pada kelompok kontrol negatif (120,64 ± 18,01 pg/mL) dan terendah pada kelompok Debiococo dosis 2 (86,00 ± 9,75 pg/mL). Kadar TGF-β tertinggi terdapat pada kelompok normal (285,82 ± 64,12 ng/L), sedangkan kelompok kontrol negatif mengalami penurunan menjadi (217,10 ± 41,00 ng/L). Pemberian Debiococo dosis 2 menunjukkan kadar TGF-β sebesar (223,53 ± 34,28 ng/L). Terdapat perbedaan bermakna antar kelompok untuk kedua parameter ($p < 0,05$).*

Kesimpulan: *Debiococo dosis 800 IU vitamin D_2 + 4 mL probiotik efektif menurunkan kadar IL-10 dan menunjukkan kecenderungan meningkatkan kadar TGF-β pada tikus kolitis terinduksi asam asetat.*

Kata kunci: *jamur tiram teraktivasi UVB; probiotik; IL-10; TGF-β; kolitis*

ABSTRACT

Background: Previous studies have shown that Debiococo, a formula of UVB-activated oyster mushroom powder, probiotics, and young coconut water, preserved colonic mucosal integrity and improved survival in experimental colitis.
Objectives: The aim was to assess Debiococo's impact on serum IL-10 and TGF-β levels in rats with acetic acid-induced colitis.
Methods: A post-test only control group design involved 30 male Wistar rats randomly divided into five groups (n=6 each): normal control (G1), negative control (G2), positive control treated with sulfasalazine (G3), Debiococo dose 1 (400 IU vitamin D_2 + 4 mL probiotic; G4), and Debiococo dose 2 (800 IU vitamin D_2 + 4 mL probiotic; G5). Colitis was induced by intrarectal administration of 4% acetic acid, and the treatments were administered for 8 days. Serum IL-10 and TGF-β levels were measured utilizing ELISA.
Results: The highest IL-10 level was observed in the negative control group (120.64 ± 18.01 pg/mL), while the lowest was found in the Debiococo dose 2 group (86.00 ± 9.75 pg/mL). The highest TGF-β level was observed in the normal control group (285.82 ± 64.12 ng/L), while the negative control group showed a lower level (217.10 ± 41.00 ng/L). Debiococo dose 2 showed a TGF-β level of 223.53 ± 34.28 ng/L. There were notable differences among the groups for both cytokines ($p < 0.05$).
Conclusions: Debiococo effectively lowered IL-10 levels and tended to elevate TGF-β levels in rats with acetic acid-induced colitis.

Keywords: UVB-activated oyster mushroom; Probiotic; IL-10; TGF-β; Colitis

*Correspondent:
Atina Hussaana
Department of Pharmacology, Faculty of Medicine, Universitas Islam Sultan Agung, Jl. Kaligawe KM 4, Semarang 50012, Indonesia
Email: atinahussaana@unissula.ac.id

2.4. Arif Zulkarnain

TISSUE ENGINEERING STRATEGIES FOR GROWTH PLATE INJURY REPAIR: A SYSTEMATIC REVIEW

Arif Zulkarnain[1], Dwikora Novembri Utomo[1,2], Lukas Widhiyanto[1,2]

[1]Doctoral Programme, Faculty of Medicine, Universitas Airlangga, Jawa Timur 60115, Surabaya, Indonesia

[2]Department of Orthopaedic and Traumatology, Faculty of Medicine,Universitas Airlangga, Dr. Soetomo General Academic Hospital, Jawa Timur 60115, Surabaya, Indonesia.

ABSTRACT

Background: Growth plate injuries can cause premature physeal closure, bone bridge formation, limb-length discrepancy, and angular deformity because of the limited regenerative capacity of physeal cartilage. Conventional surgical treatments are unable to restore native growth plate cartilage, leading to increasing interest in tissue engineering strategies for biological regeneration. This systematic review evaluated current tissue engineering approaches for growth plate injury repair and their regenerative outcomes.

Methods: A systematic search of PubMed/MEDLINE, Scopus, and ScienceDirect was performed for studies published between 2017 and 2026 following the PRISMA 2020 guidelines. Original studies investigating tissue engineering interventions for growth plate injury repair were included. Data on biomaterials, scaffolds, cell sources, regenerative strategies, and treatment outcomes were extracted and narratively synthesized because of methodological heterogeneity.

Results: Of 218 records identified, five preclinical studies met the inclusion criteria. Four studies used rabbit models and one used a rat model. Investigated strategies included extracellular matrix-derived scaffolds, three-dimensional (3D)-printed biomimetic scaffolds, stratified polycaprolactone scaffolds, GelMA-ACMMA composite hydrogels, and bone morphogenetic protein signaling modulation. Bone marrow-derived mesenchymal stem cells were the predominant cell source. Overall, tissue engineering strategies consistently reduced bone bridge formation, enhanced cartilage regeneration, improved histological organization, and promoted longitudinal bone growth. Biomimetic scaffold-based constructs combined with stem cells demonstrated the most favorable regenerative outcomes.

Conclusion: Current evidence suggests that tissue engineering is a promising approach for growth plate regeneration by integrating biomaterials, stem cells, and bioactive signaling. However, evidence remains limited to preclinical studies. Further standardized large-animal studies and clinical trials are required before these strategies can be translated into routine clinical practice.

Keywords : growth plate injury; physeal injury; tissue engineering; regenerative medicine; biomaterials; scaffold; mesenchymal stem cells; cartilage regeneration.

2.5. Nurul Hidayah

Original Research

Dendritic cell-Primed Cytotoxic T Lymphocytes Enhance Antitumor Activity Against HCT-116 Colorectal Cancer Cells Through Improved Cytotoxic Function

Nurul Hidayah[1*], Fauziah Novita Putri Rifai[2], Endah Agustina Lestari[3], Dian Respati Ayu[4], Nadya Audina Nurkhafiya Sadikin[5], Rita Agustina[6], Iffan Alif[1], Sugeng Ibrahim[7,8,9]

[1]Cancer Immunology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia
[2]Drug Discovery Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia
[3]Synthetic Biology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia
[4]Stem Cell Metabolites Laboratory, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[5]Cancer Biology Laboratory, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[6]Clinical Stem Cell and Cancer, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[7]Faculty of Medicine, Soegijapranata Catholic University, Semarang, Indonesia
[8]Faculty of Medicine, State Islamic University Walisongo, Semarang, Indonesia
[9]Stem Cell and Cancer Research (SCCR), Semarang, Indonesia

**Corresponding author: nurulhidayah@apu.ac.id*

Abstract. Background: Although colorectal cancer (CRC) is one of the most prevalent gastrointestinal malignancies, current therapeutic strategies provide limited clinical benefit. Adoptive cellular immunotherapy has emerged as a promising treatment modality for CRC. Dendritic cells (DCs), loaded with tumor lysate, efficiently prime tumor-specific cytotoxic T lymphocytes (CTLs) and have demonstrated favorable safety and therapeutic potential. Nevertheless, the antitumor efficacy of DC-primed CTLs remains limited, warranting further optimization to improve their cytotoxic activity. **Objective:** This study aims to analysed the antitumor activity of DC-Engineered CTLs against HCT-116 colorectal cancer cells. **Methods:** In the present study, $CD8^+$ T cells isolated from PBMCs of colorectal cancer were assigned to either a conventional CTL group or a DC-engineered CTL group. Conventional CTLs were activated using anti-CD3/CD28 beads and IL-2, whereas engineered CTLs underwent additional priming with mature dendritic cells (DC: T-cell ratio 1:10). After phenotypic characterization by flow cytometry, both CTL populations were directly co-cultured with HCT-116 cells at E:T ratios of 1:1, 5:1, and 10:1

for 24 h. HCT-116 cell viability and the secretion of perforin, granzyme B, IFN-γ, TNF-α, and IL-6 were subsequently evaluated. **Results:** DC-mediated priming significantly altered the T-cell phenotype, reduce the CD4:CD8 ratio compared with untreated controls ($p < 0.05$). In direct co-culture with HCT-116 for 24 h, engineered CTLs consistently exhibited greater cytotoxicity than conventional CTLs, reducing tumor cell viability to 63.6%, 58.1%, and 34.1% at effector-to-target (E:T) ratios of 1:1, 5:1, and 10:1, respectively, compared with 76.5%, 58.7%, and 47.6% in the conventional CTL group. This enhanced antitumor activity was accompanied by increased perforin secretion (120.3 vs. 109.1 pg/mL at E:T 10:1), while granzyme B levels remained comparable between groups. Engineered CTLs also maintained robust IFN-γ (2739 pg/mL) and TNF-α (424 pg/mL) production with minimal IL-6 secretion. **Conclusion:** Notably, DC-engineered CTLs exhibited enhanced antitumor activity compared with conventionally activated CTLs against HCT-116 colorectal cancer cells.

Keywords: Colorectal cancer, dendritic cells, cytotoxic T lymphocytes, adoptive cell therapy, immunotherapy.

2.6. Dendi Krisna Nugraha

Original Research

Evaluation of Proprietary Preservation Solutions for Short-Term Hypothermic Storage of Human Umbilical Cord-Derived Mesenchymal Stem Cells (UC-MSCs)

Risky Chandra Satria Irawan[1,2], Habibi[1], Dini Cahyani[1,3], Faheem Ahmed Khan[1], and Dendi Krisna Nugraha[1,2,*]

Affiliation(s)

[1] Stem Cell and Cancer Research (SCCR) Center, Semarang, Indonesia
[2]Deparment of Biomedical Sciences, Agung Putra University (APU), Semarang, Indonesia
[3]Department of Biotechnology, Agung Putra University (APU), Semarang, Indonesia

**Corresponding author: dendi@sccr.id*

Abstract. Efficient preservation of mesenchymal stem cells (MSCs) is essential for maintaining product quality during transportation and prior to clinical administration. This study evaluated two proprietary preservation solutions (Solution A and Solution B) for short-term hypothermic storage of human umbilical cord-derived MSCs using normal saline (NaCl) as a reference. Freshly harvested MSCs were suspended in each solution and stored at 4°C for up to 72 hours. Cell recovery, viability, morphology, attachment following re-culture, and expression of characteristic MSC surface markers were evaluated at predetermined time points. Both proprietary solutions effectively maintained MSC quality throughout storage. Cell recovery remained close to baseline for up to 72 hours, whereas recovery progressively declined in the NaCl group. Similarly, MSC viability remained high in both proprietary solutions during hypothermic storage. Microscopic examination showed that preserved MSCs retained their characteristic spindle-shaped morphology and adhesive properties after re-culture. Flow cytometric analysis further confirmed maintenance of the characteristic MSC immunophenotype, including high expression of CD73, CD90, CD105, and CD44 with minimal lineage marker expression, both immediately after storage and following re-culture. These findings demonstrate that Solution A and Solution B outperform normal saline in preserving the quality of human UC-MSCs during short-term hypothermic storage and support their potential application as preservation media for MSC transportation and other clinical workflows requiring temporary storage.

Keywords: mesenchymal stem cells, hypothermic storage, preservation solution, cell viability, cell therapy

2.7. Salindri Prawitasari

Original Research

Transcriptomic Profiling of Hypoxia-Preconditioned Mesenchymal Stem Cell Secretome (SH-MSC) Treatment Reveals Modulation of Hair Follicle-Associated Pathways in an Androgenetic Alopecia Mouse Model

Salindri Pawitasari[1,4*], Dini Cahyani[1,4], Naufal Sebastian Anggoro[2,4], Dendi Krisna Nugraha[2,4], Agung Putra[2,3,4], Faheem Ahmed Khan[4]

[1]Lecturer, Biotechnology Undergraduate Program, Agung Putra University, Semarang, Indonesia
[2]Lecturer, Biomedical Sciences Undergraduate Program, Agung Putra University, Semarang, Indonesia
[3]Lecturer, Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University (UNISSULA), Semarang, Indonesia
[4]Stem Cell and Cancer Research (SCCR), Semarang, Indonesia

**Corresponding author: salindriprawitasari@apu.ac.id*

Abstract. Androgenetic alopecia (AGA) is a common hair loss disorder affecting millions worldwide, with limited therapeutic options. SH-MSC has emerged as a promising regenerative therapy, yet its molecular mechanisms in AGA remain poorly understood. This study aimed to characterize the transcriptomic changes induced by SH-MSC treatment in an AGA mouse model using a comprehensive RNA-seq analysis pipeline. Four experimental groups were evaluated: healthy control (K1), NaCl negative control (K2), topical minoxidil positive control (K3), and SH-MSC injection treated group (K4). RNA sequencing was performed and analyzed using the TPM + edgeR (TMM) pipeline with a common BCV dispersion approach (BCV = 0.4) appropriate for unreplicated designs. Differential expression analysis, functional enrichment (GO, KEGG, Reactome), and targeted profiling of 60 hair follicle-associated genes were conducted. SH-MSC treatment induced 185 differentially expressed genes (FDR < 0.05) compared to NaCl control (79 upregulated, 106 downregulated), while minoxidil treatment yielded 141 DE genes. Notably, 228 genes differed between SH-MSC and minoxidil treatments, indicating distinct mechanisms of action. PCA revealed clear separation between treatment groups (PC1: 45.7%, PC2: 35.4% variance). Fifty hair

follicle marker genes were detected, including keratins (KRT5, KRT10, KRT14), androgen receptor (AR), 5α-reductase type 1 (SRD5A1), and WNT signaling components showing differential regulation. Functional enrichment implicated wound healing, hair cycle regulation, and androgen metabolism pathways. SH-MSC treatment induces distinct transcriptomic changes in AGA mouse models, modulating hair follicle-associated pathways through mechanisms partially overlapping but substantially different from minoxidil. These findings provide a molecular framework for understanding SH-MSC therapy in AGA and identify potential therapeutic targets.

Keywords: androgenetic alopecia, SH-MSC, RNA-seq, transcriptomics, hair follicle

2.8. Dian Respati Ayu

Original Research

Enhancement of Interleukin-10 Production via Co-Culture of PBMC with DSP30-Primed MSCs: A Preliminary Study for Clinical Application of Secretome

Dian Respati Ayu [1,*], Faheem Khan[2], Agung Putra[2], Jutadi[4], Rita Agustina[5], Dendi Krisna Nugraha[2], Dina Amalina[6], Risky Chandra Satria Irawan[3], and Fikriya Novita[3], Dini Cahyani[3]

Author Affiliations

[1]Department of Biomedical Science, Agung Putra University, Semarang, Indonesia.
[2]Stem Cell and Cancer Research Center (SCCR), Semarang, Indonesia
[3]Department of Biotechnology, Institut Karya Mulia Bangsa, Semarang, Indonesia
[4]Graduate Student of Biomedical Sciences, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.
[5]Department of Biomedical Science, Faculty of Medicine, UNISSULA, Semarang, Indonesia

**Corresponding author: Dianrespatiayu@apu.ac.id*

Abstract. : **Background:** Mesenchymal stem cell (MSC)-derived secretome is a promising cell-free therapeutic approach for regenerative medicine. This study investigated whether co-culture of peripheral blood mononuclear cells (PBMCs) with DSP30-primed MSCs could enhance the immunomodulatory profile of the resulting secretome, particularly interleukin-10 (IL-10) production. Methods: Human MSCs were primed with DSP30 and co-cultured with PBMCs at MSC:PBMC ratios of 1:3, 1:6, and 1:9. MSC identity was confirmed by flow cytometry. Conditioned media were analyzed for cytokines, growth factors, and total protein concentration using ELISA. Quality control assessments included endotoxin, mycoplasma, sterility, pH, and osmolality testing. The therapeutic potential of the secretome was evaluated in a degree IV burn wound model. **Results:** MSCs expressed CD90 (99.9%), CD105 (97.6%), and CD73 (100%). IL-10 production increased in a ratio-dependent manner, reaching 58 pg/mL in the 1:9 group. SDF-1 remained highly expressed across all groups, whereas HGF secretion was highest in the 1:3 group (5,759 pg/mL). VEGF and FGF-1 concentrations exceeded the assay detection limits. Total protein concentrations ranged from 4,992 to 5,288 µg/mL. Quality control testing demonstrated endotoxin levels below 1 EU/mL, negative mycoplasma results, and confirmed sterility. In vivo, secretome treatment accelerated wound closure and improved histological regeneration compared with untreated and silver sulfadiazine-

treated controls. **Conclusion:** PBMC co-culture enhances the immunomodulatory properties of DSP30-primed MSC secretome by increasing IL-10 production while preserving regenerative factor secretion. The resulting secretome demonstrated favorable quality attributes and promising wound-healing potential, supporting its further development as a cell-free regenerative therapy.

Keywords: Mesenchymal stem cells; Secretome; PBMC; Interleukin-10; Wound healing

2.9. Nadya Audina Nurkhafiya Sadikin

Original Research / Case Report / Review Article*
*(Please select and retain only the appropriate manuscript type for your submission)

Effects of Combined *Typhonium flagelliforme* and *Gynura procumbens* Extracts on the Growth of HCT116 Colorectal Cancer Cells In Vitro

Nadya Audina N.S[1*], Nurul Hidayah[2], M. Ariq Nazar[1], Psn Masruri Sulistiyanto[3] Ari, Dio Alif Utama[4]

[1]*Lecturer, Biomedical Science Undergraduate Program, Agung Putra University, Semarang, 50223, Indonesia*

[2]*Lecturer, Biotechnology Science Undergraduate Program, Agung Putra University, Semarang, 50223, Indonesia*

[3]*Research and Development, Stem Cell and Cancer Research (SCCR) Laboratory, Semarang, 50223, Indonesia*

[4]*Student of Biomedical Science Undergraduate Program, Agung Putra University, Semarang, 50223, Indonesia*

**Corresponding author: nadyaaudina@apu.ac.id*

Abstract. Colorectal cancer is one of the leading causes of cancer-related mortality worldwide, highlighting the need for alternative adjuvant therapies derived from natural products. This study aimed to investigate the cytotoxic activity of *Typhonium flagelliforme* (Keladi Tikus, KTE) and *Talinum paniculatum* (Umbi Dewa, UDE) extracts individually, and to evaluate their combined effects on colorectal cancer HCT116 cells. Cytotoxicity was assessed using the MTT assay across various concentrations of single and combined extracts. The IC_{50} values were calculated for each extract, and the interaction profile of the combination was analyzed using the Combination Index (CI). The results revealed that UDE exhibited stronger cytotoxicity (IC_{50} = 62.09 µg/mL; R^2 = 0.986) compared to KTE (IC_{50} = 73.47 µg/mL; R^2 = 0.83). The combination demonstrated diverse interactions: synergistic at low concentrations (KTE ¼ IC_{50} + UDE ¼ IC_{50}, CI = 0.48), additive at medium concentrations (½ IC_{50}), and antagonistic at higher concentrations (1 IC_{50}, CI = 1.87). These findings suggest that the combination of KTE and UDE is more effective at low to moderate doses, while high doses tend to reduce the therapeutic effect. Overall, this study indicates the potential of KTE and UDE combination as an adjuvant candidate for colorectal cancer therapy, although further molecular studies are required to elucidate the underlying mechanisms.

Keywords: Please provide 3–5 keywords that represent the main topics of the work. Keywords should be written in lowercase letters and separated by commas. Avoid using overly general terms or repeating words already included in the title whenever possible.

Example:

Keywords: *Typhonium flagelliforme, Talinum paniculatum*, Colorectal Cancer, Cytotoxicity, Combination Index.

2.10. Shelly Tjahyadewi

SECRETOME HYPOXIA MESENCHYMAL STEM CELL AS AN INNOVATIVE CELL-FREE THERAPY FOR CHRONIC RHINOSINUSITIS WITH NASAL POLYPS: A RAT MODEL STUDY

Shelly Tjahyadewi[1,2*]

Author Affiliations
1Faculty of Medicine, Universitas Islam Sultan Agung,Semarang Indonesia
2 Doctoral Study Program of Biomedicine Universitas Islam Sultan Agung,Semarang Indonesia

Corresponding Author Email Guidelines*
**Corresponding author:* shelly.tjayadewi@gmail.com

ABSTRACT

Introduction

Chronic rhinosinusitis with nasal polyps is a chronic inflammatory disease of the nasal and paranasal sinus mucosa lasting more than 12 weeks and characterized by nasal polyp formation. This disease is frequently dominated by type 2 inflammation involving IL-4, IL-5, IL-13, eosinophils, and IgE, leading to persistent mucosal inflammation, epithelial barrier dysfunction, and tissue remodeling. IL-5 plays an important role in eosinophil recruitment and activation, while reduced E-cadherin reflects impaired epithelial integrity. Increased TGF-β and periostin are associated with fibrosis, mucosal remodeling, and polyp persistence. Current treatment mainly relies on corticosteroids and biologic therapy. Corticosteroids can suppress inflammation and improve symptoms, but they may not fully prevent recurrence or restore structural mucosal damage. Biologic therapy offers a more targeted approach, but its use remains limited by high cost, patient selection requirements, and unequal access to healthcare services. These limitations highlight the need for a novel therapeutic approach that can suppress inflammation while promoting epithelial repair and reducing mucosal remodeling. Hypoxia-conditioned mesenchymal stem cell secretome has potential as a cell-free therapy because it contains paracrine factors and extracellular vesicles with immunomodulatory, regenerative, and anti-remodeling effects. This study evaluates the effect of hypoxia-conditioned mesenchymal stem cell secretome on IL-5, E-cadherin, TGF-β, periostin expression, and sinonasal histopathology in a rat model of chronic rhinosinusitis with nasal polyps.

Aim n scope :

This study aims to determine the effect of hypoxia-conditioned mesenchymal stem cell secretome on the improvement of chronic rhinosinusitis with nasal polyps in a rat model. The scope includes evaluation of IL-5, E-cadherin, TGF-β gene expression, periostin expression, and sinonasal histopathology compared with the control group.

Methods

This true experimental study used a post-test only control group design in Wistar rats with chronic rhinosinusitis with nasal polyps, divided into four groups: healthy control, disease control with NaCl, SH-MSC 75 µL, and SH-MSC 150 µL. The outcomes included IL-5, E-cadherin, and TGF-β gene expression, periostin expression, and sinonasal histopathology, assessed using RT-qPCR, immunohistochemistry, and hematoxylin-eosin staining

Keywords: chronic rhinosinusitis with nasal polyps; hypoxia-conditioned mesenchymal stem cell secretome; IL-5; E-cadherin; sinonasal tissue remodeling.

2.11. Rusyda Ayusti Anumillah

Review Article

Clinical Implication of Middle Cerebral Artery Anatomical Variations in Ischemic Stroke

Rusyda Ayusti Anumillah[1,*], Feda Anisah Makkiyah[2,3], Taufiq Fredrik Pasiak[2,4], Maria Selvester Thadeus[2], Sofia Wardhani[2], and Ratna Puspita[2]

[1]Anatomy Concentration, Master's Program in Biomedical Sciences, Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia
[2]Anatomy Division, Department of Biomedical Sciences, Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia
[3]Neurosurgery Division, Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia
[4]Neuroscience Division, Department of Biomedical Sciences, Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia

**Corresponding author: rusydaayusti@gmail.com*

Abstract. Background: The middle cerebral artery (MCA) is the most frequent site of large-vessel occlusion in ischemic stroke. Anatomical variations in branching and geometry significantly influence cerebral hemodynamics and vascular pathology. Objective: This systematic review evaluates MCA anatomical variants and their associations with stroke risk, infarct characteristics, endovascular treatment, detection and outcomes. Methods: Following PRISMA guidelines, 168 total records were identified from searches of PubMed, ScienceDirect, and Cochrane. Thirteen studies included and were evaluated for quality using the Newcastle-Ottawa Scale. Results: Common variations included bifurcation (48–69.9%), trifurcation (21–32%), and complex configurations (20%). Incomplete Circle of Willis and hypoplastic MCA segments were more prevalent in stroke populations (13.8–25%). High tortuosity and M1 arc length correlated with border-zone infarcts, while straight, thin segments were linked to large infarcts. Hemodynamic markers, such as low wall shear stress and high relative residence time are associated poorer functional outcome. Regarding endovascular treatment, the trifurcation pattern significantly reduced successful recanalization (57% vs. 91% for bifurcation) and increased procedural complications. Computed Tomography Angiography, Magnetic Resonance Angiography and High-Resolution Magnetic Resonance Vessel Wall Imaging (HRMR-VWI) used for analyses MCA morphology and plaque characteristics. Conclusion: MCA anatomical and hemodynamic variations including branching

patterns, vascular tortuosity, and vessel geometry influence stroke susceptibility, infarct distribution, thrombectomy success and outcome. Identifying these morphological markers via advanced imaging is essential for individualized therapeutic planning and improve clinical outcome.

Keywords: middle cerebral artery, anatomical variation, ischemic stroke

2.12. Minidian Fasitasari

Modulating TGF-β and TNF-α Levels with Gotu Kola Leaf Extract Cream on Acute Ultraviolet B Irradiated Skin Mice

Ririn Rahmayati[1], Atina Hussaana[2,3*], Minidian Fasitasari[2,4]

[1]Postgraduate of Biomedical Sciences, Faculty of Medicine, Universitas Islam Sultan Agung,Semarang, Indonesia

[2]Department of Biomedical Sciences, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

[3]Department of Pharmacology, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

[4]Department of Nutrition, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

*Corresponding author: atinahussaana@unissula.ac.id

Abstract

Acute UVB radiation causes epidermal damage and an inflammatory response by increasing ROS concentrations, leading to oxidative and DNA damage. Gotu kola (*Centella asiatica L.*) leaf extract contains triterpenoids and asiaticoside which have anti-inflammatory and antioxidant benefits. This study aims to determine the effect of Gotu kola leaf extract cream, hereafter referred toas GKC, on the expression of TGF-β and TNF-α when exposed to acute UVB. Experimental study with posttest only control group design was conducted on 24 Balb/c mice, divided into 4 groups. G1 was normal control group without UVB exposure. G2, G3 and G4, each exposed to UVB at a dose of 1 MED (*Minimum Erythema Dose*) or 360mJ/cm^2, for 5 days. G3 and G4 were given GKC 10% and 20%, respectively, for 5 days after each UVB exposure, while G2 received cream base. On the 6th day, mice were terminated, and the dorsal skin tissue samples were collected to analyze the expression of TGF-β and TNF- α via Immunohistochemistry staining. TGF-β expression in the treatment group decreased with increasing dose (G3=31.67±17.23, G4=15.83±11.14) compared to G2=68.33 ±22.28, and G1=2.50±4.18. Meanwhile, the expression of TNF- α also experienced a dose- dependent decrease (G3=38.33±13.29, G4=19.17±8.01) compared to the G2 =65, 00±12.25, and G1=10.00±6.32. There were significant decreases in TGF-β and TNF- α expression in GKC treatment groups ($p<0.05$). It can be concluded that topical administration of GKC can reduce the expression of TGF-β and TNF- α in the skin tissue of Balb/c mice exposed to acute UVB.

The novelty of this research lies in demonstrating the potential of GKC as a natural topical treatment to reduce inflammatory markers, specifically TGF-β and TNF- α in skin tissues exposed to UVB radiation. This study contributes to the development of alternative skincare therapies, potentially benefiting individuals seeking natural solutions for UV-induced skin inflammation and supporting advancements in dermatological science

Keywords: *Centella asiatica* L., Gotu kola, inflammation, photoprotection, sunburn, TGF-β, TNF- α, Ultraviolet-B

2.13. Sugeng Ibrahim

Case Report

Autologous Cytotoxic T Lymphocyte Therapy as an Adjuvant Immunotherapy in Epstein–Barr Virus-Positive Nasopharyngeal Carcinoma: a case report

Sugeng Ibrahim[1,2,3*], Agung Putra[1,4,5], Rita Agustina[6], Nurul Hidayah[7], Rakha Fahreza[8], Reynaldi Suryajaya[8], Dini Cahyani[9,] Yan Wisnu Pradjoko[10], Christina Hari Nawangsih[11], Dwi Antono[12]

[1]Stem Cell and Cancer Research (SCCR), Semarang, Indonesia
[2]Faculty of Medicine, Soegijapranata Catholic University, Semarang, Indonesia
[3]Faculty of Medicine, State Islamic University Walisongo, Semarang, Indonesia
[4]Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Indonesia
[5]Stem Cell Engineering, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[6]Clinical Stem Cell and Cancer, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[7]Cancer Immunology Laboratory, *Biotechnology, Agung Putra University,* Semarang, *Indonesia*
[8]Stem Cell Secretome Therapy, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[9]Immunology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia
[10]Department of Surgical Oncology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia.
[11]Department of Radiology Oncology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia.
[12]Department of Oncology, Kariadi Hospital, Semarang, Indonesia.

**Corresponding author: sugeng@unika.ac.id*

Abstract. Background: Nasopharyngeal carcinoma (NPC) is a highly invasive malignancy closely associated with Epstein–Barr virus (EBV) infection and is characterized by an immunosuppressive tumor microenvironment that contributes to disease progression and recurrence. Although radiotherapy remains the standard treatment for NPC, therapeutic options for patients with persistent or residual disease are limited. Adoptive cytotoxic T lymphocyte (CTL) therapy has emerged as a promising immunotherapeutic strategy to enhance tumor-specific immune responses.**Case Presentation:** A 54-year-old woman with EBV-positive NPC diagnosed in November 2023 presented with persistent cervical tumor involvement after surgical resection and

completion of 35x definitive radiotherapy. The patient subsequently received six cycles of autologous CTL therapy consisting of intravenous infusion of 10–20 × 10^6 viable cells per treatment, combined with bilateral peritumoral local injections. The patient was also encouraged to maintain a healthy lifestyle throughout the treatment period. **Results:** Serial clinical evaluations and photographic documentation demonstrated a clinically significant reduction in cervical tumor size after four CTL cycles, with further regression following completion of six treatment cycles. Follow-up PET-CT demonstrated no residual cervical mass or abnormal FDG uptake, indicating no imaging evidence of metabolically active disease. The treatment was well tolerated, and **n**o serious treatment-related adverse events were observed during the follow-up period. **Conclusion:** This case highlights the feasibility and favorable safety profile of autologous CTL therapy as an adjuvant immunotherapeutic approach for EBV-positive nasopharyngeal carcinoma following definitive radiotherapy.

Keywords: Nasopharyngeal carcinoma, Cytotoxic T lymphocyte therapy, Adoptive cell therapy, Epstein–Barr virus, Cancer immunotherapy, Case report

2.14. Soraya Rahmanisa

Original Research / ~~Case Report / Review Article~~*
*(Please select and retain only the appropriate manuscript type for your submission)

Osteogenic Differentiation of Human Mesenchymal Stem Cells on Substituted Chitosan Composite Scaffolds

(Use Times New Roman Font: 18 pt, Bold, Single spacing, Centered)

Soraya Rahmanisa[1,*] , Evi Kurniawaty[1], Rika Lisiswanti[2,] Syazili Mustofa[1], Risti Graharti [2], Indra Wibowo[3], Anggraini Barlian[3]

Author Affiliations

[1]Department of Biochemistry, Physiology, & Molecular Biology, Faculty of Medicine, Universitas Lampung, Bandar Lampung, Indonesia
[3]Department of Medical Education, Faculty of Medicine,Universitas Lampung, Bandar Lampung, Indonesia
3Department of Biology, School of Life Science, Institute of Technology Bandung, West Java, Indonesia

**Corresponding author: soraya.rahmanisa@fk.unila.ac.id*
If additional author email addresses are included, they may be listed on separate lines without an asterisk.

Abstract. Bone damage due to accidents or degenerative diseases such as osteoporosis has a high prevalence, and various methods have been developed to address this issue. Stem cell therapy can be used to enhance the regeneration of damaged or degenerative bone tissue. Stem cells can be engineered into bone cells so that they can be used as a cell-based therapy to replace damaged body tissue thru tissue engineering techniques. In tissue engineering techniques, there are three main factors: Cells; biofactors; and scaffold (the place where cells grow and differentiate).

Indonesia's biodiversity, especially in the sea, is highly potential in the development of tissue engineering techniques. One of the natural biodiversities from the sea is chitosan, which contains calcium carbonate, silica, and others that can serve as biomaterials for scaffolds as places for cells to grow and differentiate. The proposed research aims to test the biocompatibility of chitosan-based scaffolds derived from sea sponges of the Sangihe Islands in North Sulawesi, which can support the proliferation and differentiation of mesenchymal stem cells into bone cells. Various combinations of sponge biosilica and polycaprolactone (PCL) will be used to create the scaffold to support the growth and differentiation of mesenchymal stem cells into bone cells. Quantitative and qualitative analysis will be conducted, consisting of the creation of primary cell cultures derived from

human Wharton's jello stem cells, followed by the characterization of hWJ-MSC, isolation, and characterization testing of the scaffold. The mesenchymal stem cell grown optimal and differentiate into osteocyte at the end of 21 days of treatment.

Keywords: osteogenesis, bone, biomaterials, tissue engineering

2.15. Muhammad Rizki Yaznil

Immunological landscape and immunotherapy strategies in mucinous ovarian carcinoma: A scoping review

Muhammad Rizki Yaznil*[1,2], Muhammad Rusda[1,2], Deri Edianto[1,2], Adang Bachtiar[3,4], Agung Putra[5,6,7], Dodi Suardi[8], Henry Salim Siregar[2], Edy Ardiansyah[2]

Email: rizki.yaznil@usu.ac.id, m.rusda@usu.ac.id, deri.edianto@usu.ac.id, adang@ui.ac.id, profagung@sccr.id, rhidorhom@gmail.com, henrysalim@usu.ac.id, edy.ardiansyah@usu.ac.id

[1] Philosophy Doctor in Medicine Programme, Faculty of Medicine, Universitas Sumatera Utara, Medan 20155, Indonesia
[2] Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Sumatera Utara, Medan 20155, Indonesia
[3] Department of Health Administration and Policy, Faculty of Public Health, Universitas Indonesia, Depok 10430, Indonesia
[4] Health Institute of Medistra Lubuk Pakam, Lubuk Pakam 20514, Indonesia
[5] Stem Cell and Cancer Research (SCCR) Laboratory, Semarang 50223, Indonesia
[6] Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University (UNISSULA), Semarang 50112, Indonesia
[7] Biomedical Science Undergraduate Program, Agung Putra University (APU), Semarang 50223, Indonesia
[8] Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Padjadjaran, Bandung 40161, Indonesia

Author Contributions

Conceptualization: Y.M.R., R.M., E.D., B.A., P.A., S.D., S.H.S., A.E.; Data curation: Y.M.R., R.M., E.D., B.A., P.A., S.D., S.H.S., A.E.; Investigation: Y.M.R., R.M., E.D., B.A., P.A., S.D., S.H.S., A.E.; Methodology: Y.M.R., R.M., E.D., B.A., P.A., S.D.; Resources: Y.M.R., R.M., E.D., B.A.; Supervision: R.M., E.D., B.A., P.A., S.D., S.H.S., A.E.; Validation: Y.M.R., R.M., E.D., B.A., P.A., S.D., S.H.S., A.E.; Visualization: Y.M.R., S.D., E.D.; Writing - original draft: Y.M.R., R.M., E.D., B.A.,
S.D., S.H.S., A.E.; Writing - review & editing: Y.M.R., R.M., E.D., B.A., P.A., S.D., S.H.S., A.E.

Abstract

Mucinous ovarian carcinoma (MOC) is a rare epithelial ovarian cancer subtype characterized by frequent KRAS mutations, HER2 amplification in a subset of cases, mucin overexpression, platinum resistance, and limited evidence regarding its immunological profile and response to immunotherapy. This scoping review systematically mapped current evidence on MOC immunobiology and its implications for immunotherapy development. This scoping review followed an established scoping review methodology and reporting guideline. Literature searches of PubMed, Scopus, CENTRAL, Google Scholar, and ScienceDirect (February–March 2026) identified 3,272 records, of which 107 met the inclusion criteria. The MOC tumor microenvironment was consistently characterized by an immunosuppressive phenotype, including low tumor-infiltrating lymphocyte density (86% immune-depleted/cold tumors), lower PD-L1 expression than high-grade serous ovarian carcinoma, predominance of regulatory T cells and M2 tumor-associated macrophages, and frequent microsatellite-stable status. Mucins, particularly MUC5AC and MUC16/CA125, emerged as key immunosuppressive mediators and promising therapeutic targets. Direct immunotherapy evidence in MOC is extremely limited, encompassing only two studies that directly evaluated response in MOC. The MMR-deficient subset appears most suitable for immune checkpoint inhibitors, whereas MUC16-based CAR-T cells, mucin-targeted vaccines, and TA-MUC1 immunocytokines represent the most promising translational strategies. Further MOC-specific preclinical and clinical studies are urgently needed to advance effective immunotherapy.

Keywords: mucin; mucinous ovarian cancer; tumor microenvironment.

2.16. Chodidjah

PENGARUH PEMBERIAN GEL EKSTRAK MENGKUDU TERHADAP JUMLAH KADAR IL 6 , IL 10 dan DENSITAS KOLAGEN TIKUS JANTAN WISTAR YANG TERPAPAR SINAR UVB

*Chodidjah, **Titiek Sumarawati,*** Eni Widayati,

****Inez Aurelia Caesaria Amala dan **** Amalia Kamila Ullya
*Departemen Anatomi dan Program Doktor Ilmu Biomedis, Fakultas Kedokteran, Universitas Islam Sultan Agung, Semarang
**Departemen Kimia dan Program Doktor Ilmu Biomedis, Fakultas Kedokteran, Universitas Islam Sultan Agung, Semarang
*** Departemen Kimia, Fakultas Kedokteran, Universitas Islam Sultan Agung, Semarang
**** Mahasiswa Fakultas Kedokteran Universitas Islam Sultan Agung Semarang

ABSTRAK

Paparan radiasi sinar UVB dapat memicu inflamasi pada kulit dengan mengingkatkan ROS dan sitokin pro-inflamasi. IL6 serta degradasi kolagen. Mengku(*Morinda Citrifolia*) mengandung flavonoid memiliki efek antiinflamasi dapat membantu percepatan proses inflamasi ditandai dengan adanya produksi dari IL10. Penelitian ini bertujuan untuk mengetahui adakah efek pemberian topikal gel ekstrak mengkudu (*Morinda Citrifolia*) terhadap kadar IL6, IL-10 dan densitas koalgen pada kulit pasca paparan UVB

Penelitian eksperimental menggunakan desain *Post-test Only Control Group Design* pada 25 tikus jantan galur Wistar. Tikus dicukur pada punggung kemudian diinduksi sinar UVB pada dan dibagi menjadi lima kelompok: normal (G1), kontrol negatif (G2), kontrol positif retinoid (G3), perlakuan gel mengkudu 20% (G4) dan 30% (G5). Perlakuan diberikan selama tujuh hari, pengukuran kadar IL-6 dan IL10 metode ELISA serta densitas kolagen dengan pengecatan *Manson Trichrome*. Analisis statistik dengan *one-way* ANOVA serta *post hoc* LSD

Rerata kadar IL-6 pada kelompok normal 197,23 ± 1,80 ng/L, kelompok kontrol negatif 173,93 ± 1,21 ng/L, kelompok kontrol positif 157,02 ± 0,82 ng/L, kelompok perlakuan 20% 124,85 ± 0,52 ng/L, kelompok perlakuan 30% 109,55 ± 0,031 ng/L. Hasil pengujian *one-way* ANOVA menghasilkan nilai p=0,021 (p<0,05). Uji LSD menunjukkan perbedaan bermakna antara kelompok kontrol negatif dengan kelompok dosis 30 % sedangkan kelompok dosis 20 % dan kelompok retinoid tidak berbeda dengan kelompok kontrol negatif. Rerata kadar IL 10 dan Rerata densitas kolagen tidak menunjukkan

perbedaan bermakna.

Kesimpulan, terdapat pengaruh pemberian topikal gel buah mengkudu (*Morinda Citrifolia L.)* terhadap kadar IL-6, namun tidak berpengaruh terhadap kadar IL 10 densitas kolagen.

Kata Kunci: UVB, Mengkudu, IL-6, IL10, densitas kolagen, Inflamasi Kulit

The effect of Noni Extract gel administration on the level of IL6, IL10 and collagen density of male wistar rats exposed to UVB rays

*Chodidjah, **Titiek Sumarawati,*** Eni Widayati,
****Inez Aurelia Caesaria Amala dan **** Amalia Kamila Ullya

*Department of Anatomy and Doctoral Program in Biomedical Sciences, Faculty of Medicine, Sultan Agung Islamic University, Semarang
**Department of Chemistry and Doctoral Program in Biomedical Sciences, Faculty of Medicine, Sultan Agung Islamic University, Semarang
*** Department of Chemistry, Faculty of Medicine, Sultan Agung Islamic University, Semarang
****Students of the Faculty of Medicine, Sultan Agung Islamic University, Semarang

ABSTRACK

Ultraviolet B (UVB) radiation induces skin inflammation by increasing reactive oxygen species (ROS), stimulating pro-inflammatory cytokines such as interleukin-6 (IL-6), and promoting collagen degradation. *Morinda citrifolia* L. (noni) contains flavonoids with antioxidant and anti-inflammatory properties that may reduce UVB-induced skin damage. This study evaluated the effects of topical *Morinda citrifolia* fruit extract gel on IL-6 and IL-10 levels and collagen density following UVB exposure.

Methode :Twenty-five male Wistar rats were randomly assigned to five groups: normal control, UVB-exposed negative control, positive control treated with topical retinoid, 20% extract gel, and 30% extract gel (n = 5/group). Treatments were applied for seven days after UVB exposure. IL-6 and IL-10 levels were measured using enzyme-linked immunosorbent assay (ELISA), and collagen density was assessed by Masson's Trichrome staining. Data were analyzed using one-way ANOVA followed by the least significant difference (LSD) test.

Result IL-6 levels differed significantly among groups ($p = 0.021$), with the 30% *Morinda citrifolia* extract significantly reducing IL-6 compared with the negative control. In contrast, IL-10 levels and collagen density showed no significant differences. These findings suggest that topical *Morinda citrifolia* fruit extract gel, particularly at a 30% concentration, attenuates UVB-induced skin inflammation by reducing IL-6 expression but does not significantly affect IL-10 levels or collagen density.

Keywords: Ultraviolet B; *Morinda citrifolia*; IL-6; IL-10; collagen density; skin inflammation

2.17. Yudha Sudewo

Original Research

4-Vinylcyclohexene Diepoxide-Induced Diminished Ovarian Reserve in the Wistar Rat: A Dose-Comparative Endocrine, Cytological, and Folliculometric Characterization

Yudha Sudewo [1,2], Muhammad Fidel Ganis Siregar [1,2], Muhammad Rusda Harahap [1,2], Agung Putra [3,4], Budi Wiweko [5], Putri Chairani Eyanoer [2], Mohd. Rhiza Z. Tala [1,2], Indri Adriztina [2,] Nur Dina Amalina [3,6,7] , Fikriya Novita Sari [3,7]

[1] *Department of Obstetrics & Gynecology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*
[2] *Philosophy Doctor in Medicine Program, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*
[3] *Stem Cell and Cancer Research (SCCR) Indonesia, Semarang, Indonesia*
[4] *Biomedical Doctoral Program, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia*
[5] *Department of Obstetrics & Gynecology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia*
[6]*Pharmaceutical Sciences Study Program, Faculty of Medicine, Universitas Negeri Semarang, Semarang, Indonesia*
[7]*Biotechnology Undergraduate Program, Faculty of Health Sciences, Agung Putra University, Semarang, Indonesia*

*Corresponding author: yudha.sudewo@usu.ac.id

Abstract.

Background: Diminished ovarian reserve (DOR) is a major cause of female subfertility, characterized by progressive follicular depletion. Human studies remain limited, necessitating reliable animal models. 4-Vinylcyclohexene diepoxide (VCD) selectively targets small follicles and mimics gradual ovarian decline, although variability in dosing and routes of administration has hindered standardization. **Objective:** This study aimed to define the endocrine, cytological, and histomorphometric alterations induced by VCD in Wistar rats, and to evaluate route- and dose-dependent effects to establish an optimized preclinical model of DOR. **Methods:** Female Wistar rats (~200 g) were assigned to five groups: control (NC), VCD 80 mg/kg/day intraperitoneal (T1), 160 mg/kg/day intraperitoneal (T2), 80 mg/kg/day subcutaneous (T3), and 160 mg/kg/day subcutaneous (T4). VCD was administered for 14 days, followed by a 40-day post-

exposure period. Body weight, serum FSH, estrous cyclicity, and ovarian histology were assessed. **Results:** Serum FSH levels increased in all treated groups, with a significant elevation in T4. The T2 group exhibited early mortality by day 8, indicating route-dependent toxicity at higher doses. No significant changes in body weight were observed. Histological analysis showed marked depletion of primordial and primary follicles, along with reductions in secondary and antral follicles, with the most pronounced effects in T4. Estrous cyclicity was disrupted, with prolonged diestrus and reduced proestrus and estrus phases. **Conclusion:** Subcutaneous administration of VCD at 160 mg/kg/day most effectively recapitulated key features of DOR, including elevated FSH, follicular depletion, and estrous cycle disruption, without affecting systemic body weight. This model provides a robust and reproducible platform for studying ovarian aging and evaluating therapeutic interventions to preserve ovarian reserve.

Keywords: diminished ovarian reserve, VCD, ovarian aging, follicular atresia, FSH, estrous cycle

2.18. Aliyah

Original Research

Effect of Lipid Diet Variations on Secondary Lamella Hyperplasia and Fusion in the Gills of Female Zebrafish (*Danio rerio*)

Aliyah[1], Dini Sri Damayanti[2,*] Noer Aini[3]

Author Affiliations

[1, 2, 3]*Department of Medical Education, Faculty of Medicine, Universitas Islam Malang, Malang, Indonesia*

**Corresponding author: dinisridamayanti@unisma.ac.id*

Abstract. Obesity is a global health problem with a continuously increasing prevalence. One of the main risk factors for obesity is a high-fat diet, which has been commonly used as an experimental model in metabolic research. Female zebrafish (*Danio rerio*) were selected as the animal model due to their similarity in lipid metabolism to mammals. The gills, as organs with thin and sensitive secondary lamellar structures, are potentially susceptible to histopathological changes resulting from metabolic stress induced by excessive fat intake. This study aimed to evaluate the effect of lipid diet variations on secondary lamella hyperplasia and fusion in the gills of female zebrafish over 28 days. This in vivo experimental study used a posttest-only control group design with 32 adult female zebrafish divided into four groups (n=8): standard pellet (P1), egg yolk+pellet (P2), *Artemia salina* (P3), and pure cholesterol 4%+pellet (P4). Histological sections of the gills were stained with Hematoxylin–Eosin and assessed for secondary lamella hyperplasia and fusion. Data were analyzed using the Kruskal–Wallis test. Secondary lamella hyperplasia and fusion were observed in all groups. Group P4 exhibited the highest hyperplasia percentage and differed significantly from P1 (95.30±1.09% vs 79.71±4.02%; $p<0.05$), but did not differ significantly from P2 or P3. No significant differences were found among groups in the secondary lamella fusion parameter. These findings suggest that dietary cholesterol has a greater impact on gill hyperplasia than other lipid sources. Female zebrafish may serve as an alternative model for evaluating high-fat diet-induced tissue alterations.

Keywords: zebrafish, high-fat diet, cholesterol, gill histopathology, hyperplasia.

2.19. Indra Adi Susianto

Case Report

Mesenchymal Stem Cell Secretome-Based Therapeutic Strategies for Ovarian Rejuvenation: A Focus on FSH and Estradiol Levels

Author:

Indra Adi Susianto[1,2,3], Ni Komang Yeni Dhanasari[1,4]Agung Putra[1,5,9], Syarief Thaufik Hidayat[6], Sugeng Ibrahim[1,7,9], Enzo MorenoAdisusianto[1,8], Dendi Krisna Nugraha[1,9], Nurul Hidayah[1,10]

1. Stem Cell and Cancer Research (SCCR) Laboratory, Semarang, Indonesia
2. Department of Reproductive Medicine, Soegijapranta Catholic University, Semarang, Indonesia
3. Department of Obstetrics & Gynecology, Anugerah Women & Children Hospital, Semarang, Indonesia
4. Department of Aesthetic Gynecology, Feminine Health & Intimate Care Center - Health360, Jakarta. Indonesia
5. Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Indonesia
6. Department of Obstetrics & Gynecology, Kariadi General Hospital, Semarang, Indonesia
7. Department of Molecular Biology, Soegijapranta Catholic University, Semarang, Indonesia.
8. Faculty of Medicine, Diponegoro University, Semarang, Indonesia
9. Department of Biomedical Sciences, Agung Putra University (APU), Semarang, Indonesia
10. Department of Biotechnology, Agung Putra University (APU), Semarang, Indonesia

Corresponding Author: *Indra Adi Susianto,*
Jl Kalisari Baru no 5, Semarang, Central Java, Indonesia,
indraadisusianto@unika.ac.id.
Scopus Author ID : 57946697800, Orcid Author ID : 0000-0002-5216-7131

Abstract

Background: Ovarian rejuvenation for Premature ovarian insufficiency (POI) offers a regenerative approach to restore ovarian function and microenvironment. MSC-derived secretome, rich in cytokines, growth factors, and vesicles, may promote follicle survival,

angiogenesis, tissue repair, and endocrine recovery. This study assesses MSC secretome therapy as an ovarian rejuvenation strategy for women with POI, focusing on changes in FSH and estradiol levels. **Methods**: A prospective observational study was conducted in 30 women with POI and infertility. Baseline demographic and reproductive characteristics were recorded. Serum FSH and estradiol levels were measured before treatment and at three months after intraovarian administration of the MSC secretome. Follicular development was assessed with transvaginal ultrasonography.**Results**: Participants had a mean age of 41.5 years and exhibited severely diminished ovarian reserve. Before treatment, mean serum FSH and estradiol levels were 36.17 mIU/mL and 15.17 pg/mL, respectively. Three months following MSC secretome therapy, mean FSH levels decreased markedly to 9.87 mIU/mL, while mean estradiol levels increased to 166.67 pg/mL. Ultrasonographic evaluation demonstrated improved follicular development, indicating enhanced ovarian responsiveness after treatment. **Conclusions:** MSC secretome therapy shows potential for ovarian rejuvenation, normalizing FSH, restoring estradiol, and improving follicular growth. It may recover ovarian endocrine function via regenerative and paracrine mechanisms, providing a cell-free strategy for POI-related fertility.

Keywords: premature ovarian insufficiency; ovarian rejuvenation; mesenchymal stem cell secretome; estradiol.

2.20. Nurina Tyagita

Chronic Stevia Administration Alters Metabolic and Renal Biomarkers in Healthy Sprague-Dawley Rats

KHANSA NABILA[1], ANINDYA LITUHAYU MAHESWARI[1], ANUGRAH AKBAR ROSYID P.[1], FINO FADILLA DAIMAR[1], MUHAMMAD FIKRI AKMAL[1], NORA ABILA DAVANZA[1], RAHMADINA PUTRI ANIZAR[1], AZIZAH HIKMA SAFITRI[2], NURINA TYAGITA*[2]

[1]Students of Faculty of Medicine, Universitas Islam Sultan Agung, Central Java, Indonesia

[2]Biochemistry Department, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Central Java, Indonesia

[*]Correspondence: Nurina Tyagita;

Address: Universitas Islam Sultan Agung, Semarang, Indonesia;

Email address: nurinatyagita@unissula.ac.id

ABSTRACT

Background: Stevia (*Stevia rebaudiana* Bertoni) is widely consumed as a natural non caloric sweetener. Although numerous studies have demonstrated its beneficial metabolic effects under pathological conditions, evidence regarding its long-term safety in healthy individuals remains limited. **Aim:** This study evaluated the effects of chronic stevia administration on metabolic profile, oxidative stress, inflammation, and renal function in healthy rats.

Methods: Twenty-four healthy male Wistar rats were randomly allocated into four groups: normal control, stevia at the acceptable daily intake/ADI (stevia1), stevia at twice the ADI/high dose (stevia2), and high fructose. Treatments were administered orally once daily for 28 days. Body weight, Lee index, systolic blood pressure, fasting and postprandial glucose, oral glucose tolerance, insulin homeostasis, oxidative biomarkers (MDA and SOD), inflammatory cytokines (TNF-α and IL-1), and renal function biomarkers (urea and creatinine) were evaluated.

Results: Stevia administered at the ADI produced minimal changes in glucose tolerance and systolic blood pressure. In contrast, chronic administration at high dose stevia was associated higher fasting and postprandial glucose concentrations, impaired oral glucose tolerance, higher HOMA-IR, lower HOMA-B, elevated MDA, reduced SOD activity, increased inflammatory cytokines, and higher serum urea and creatinine than the normal

control group. Nevertheless, these alterations remained less pronounced than those observed in the high fructose group.
Conclusion: Stevia administered at the recommended dose demonstrated a favorable safety profile in healthy rats. However, high dose stevia was associated with unfavorable metabolic, oxidative, inflammatory, and renal biomarker highlighting the importance of dose consideration during chronic stevia consumption.

Keywords: Stevia; healthy rats; metabolic

2.21. Mohamad Arif

Complete Diabetic Foot Ulcer Closure with Hypoxia-Preconditioned MSC Secretome Despite Treatment Refusal: A Case Report

Mohamad Arif [1]

1. Doctoral Program in Biomedical Science, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

Abstract

Diabetic foot ulcer remains one of the more feared chronic complications of diabetes mellitus, carrying a substantial risk of severe infection and amputation, particularly when standard management components such as sharp debridement and adequate glycemic control cannot be fully implemented. Secretome derived from mesenchymal stem cells (MSCs) subjected to hypoxic preconditioning is thought to carry greater therapeutic potential than secretome cultured under normoxic conditions, owing to an enhanced secretion of pro-angiogenic and anti-inflammatory mediators.

Case presentation. We report a 68-year-old man with a 7 x 6 x 2.5 cm ulcer over the right calcaneal region of roughly two months' duration, in the setting of previously undiagnosed type 2 diabetes mellitus (admission random glucose 310 mg/dL) and severe anemia (hemoglobin 6.5 g/dL). The patient declined insulin, blood transfusion, and wound debridement. As a clinical compromise, he was managed with co-amoxiclav, sitagliptin monotherapy, dietary counselling toward higher animal-protein intake, and adjunctive therapy with GMP-certified (CPOB) hypoxia-preconditioned UC-MSC secretome, given as a total of 12 ampoules (1.5 mL each) over four weeks through a combination of intramuscular injections into the vastus lateralis and gastrocnemius muscles together with perilesional injection. The wound showed progressive granulation at each visit and achieved complete closure by the eighth visit (end of week four), coinciding with improvement in random glucose (310 to 170 mg/dL) and hemoglobin (6.5 to 10.1 g/dL) without transfusion or insulin.

Conclusion. This case illustrates a possible clinical benefit of adjunctive hypoxia-preconditioned MSC secretome therapy in the healing of a refractory diabetic foot ulcer, although the concurrent improvement in glycemic and hematologic status limits any definitive causal claim regarding the secretome's contribution. Controlled studies with

larger cohorts are still needed to confirm its independent role in comparable clinical settings.

Keywords: *secretome, mesenchymal stem cells, hypoxia, chronic wound, diabetic foot ulcer*

2.22. Citra Primavita Mayangsari

Original Research

Immunomodulatory Effects of Mesenchymal Stem Cell Secretome on TNF-α and FoxP3 Expression in Busulfan-Induced Aplastic Anemia Mice

Citra Primavita Mayangsari[1,*], Harsono Salimo[2], Yulia Lanti Retno Dewi[2], Agung Putra[3,4,5], Betty Suryawati[2], Annang Giri Moelyo[6] , Nur Dina Amalina[3,5,7]

[1]Pediatrics Department, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang 50112, Indonesia
[2]Doctoral Program of Medical Science, Faculty of Medicine, Universitas Sebelas Maret, Surakarta 57126, Indonesia
[3]Stem Cell and Cancer Research (SCCR) Laboratory, Semarang 50112, Indonesia
[4]Department of Doctoral Biomedical Science, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang 50112, Indonesia
[5]Biotechnology Undergraduate Program, Agung Putra University, Semarang 50224, Indonesia
[6]Department of Child Health, Faculty of Medicine, Universitas Sebelas Maret/Dr.Moewardi Hospital, Surakarta 50112, Indonesia
[7]Pharmaceutical Sciences Study Program, Faculty of Medicine, Universitas Negeri Semarang, Semarang 50229, Indonesia

**Corresponding author: citraprimavita@gmail.com*

Abstract.
Aplastic anemia is a life-threatening bone marrow failure disorder characterized by pancytopenia, hypocellular marrow, and impaired hematopoiesis. Immune dysregulation is a central feature of its pathogenesis, involving excessive pro-inflammatory signaling and impaired regulatory T-cell function. Among the key mediators, TNF-α is a major cytokine associated with inflammatory suppression of hematopoiesis, whereas FoxP3 is an essential transcription factor involved in regulatory T-cell differentiation and immune tolerance. This study aimed to evaluate TNF-α and FoxP3 expression in a busulfan-induced aplastic anemia mouse model treated with hypoxic mesenchymal stem cell secretome (SH-MSCs). Thirty BALB/c mice were randomly assigned to five groups: healthy control, aplastic anemia control, aplastic anemia treated with standard medication, aplastic anemia treated with 200 µL SH-MSCs (325 µg protein/20 g body weight), and aplastic anemia treated with a combination of SH-MSCs and standard medication. Aplastic anemia was induced by intraperitoneal busulfan administration at 10 mg/kg body weight on days 1, 3, 8, 11, 15, 18, 21, and 23. The standard medication

consisted of methylprednisolone (1 mg/kg body weight, intraperitoneally) and cyclosporine (5 mg/kg body weight, orally), administered from day 24 to day 37. SH-MSCs were isolated from human umbilical cord tissue and cultured under hypoxic conditions (2% O_2) to obtain the secretome. TNF-α and FoxP3 gene expression were analyzed by quantitative real-time PCR on day 38. Busulfan-induced marrow injury was associated with increased TNF-α expression and decreased FoxP3 expression compared with the healthy group, indicating enhanced inflammation and impaired immune regulation. SH-MSCs in single- and combination therapy showed significantly reduced TNF-α expression and increased FoxP3 levels, especially in single therapy. These findings suggest that SH-MSC secretome, alone or in combination with standard therapy, may represent a promising strategy for immune modulation and marrow recovery in aplastic anemia.

Keywords: Anemia aplastic, inflammatory, T-regulator, immunotherapy, secretome MSCs

2.23. Luh Putu Widya Amritha Dewi

Cell-Free Regenerative Therapy Using Hypoxia UC-MSC Secretome Improves Functional Recovery in Subacute Ischemic Stroke: a case report

I Gusti Ngurah Putra Eka Santosa[1,2]*, Rindha Dwi Sihanto[1,3], Agung Putra[4,5,6], Rita Agustina[4,6], Sugeng Ibrahim[4,7,8], Nurul Hidayah[9,] Luh Putu Widya Amritha Dewi[10]

[1]Head of Stem Cell Services, Murni Teguh General Hospital Tuban, Bali, Indonesia
[2]Department of Biomedical Sciences, Faculty of Medicine, Mahasaraswati University Denpasar, Denpasar, Indonesia
[3]Lecturer, Medical Doctor Education Program, Mahasaraswati University Denpasar, Denpasar, Indonesia
[4]Stem Cell and Cancer Research (SCCR) Laboratory, Semarang, Indonesia
[5]Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University (UNISSULA), Semarang, Indonesia
[6]Biomedical Science Undergraduate Program, Agung Putra University, Semarang, Indonesia
[7]Faculty of Medicine, Universitas Islam Negeri Walisongo (UIN Walisongo), Semarang, Indonesia
[8]Faculty of Medicine, Soegijapranata Catholic University, Semarang, Indonesia
[9]Biotechnology Undergraduate Program, Agung Putra University, Semarang, Indonesia
[10]SAS Foundation

***Corresponding author** : ekasantosa@unmas.ac.id

ABSTRACT

Background: Ischemic stroke remains a leading cause of long-term disability, with limited therapeutic options to promote neuroregeneration in the subacute and chronic phases. Mesenchymal stem cell (MSC)-derived secretome has emerged as a promising cell-free therapy due to its paracrine effects, including modulation of inflammation, promotion of angiogenesis, and enhancement of neuroplasticity. **Case Presentation:** We report the case of a 65-year-old male with spastic paraparesis following ischemic stroke, presenting three months after onset with progressive bilateral lower limb weakness and loss of ambulatory function. Neurological examination revealed upper motor neuron signs with muscle strength graded 2/5 in both lower extremities. The patient had a history of uncontrolled hypertension and had shown limited improvement despite standard medical treatment and physiotherapy. **Intervention:** The patient received umbilical cord-derived MSC (UC-MSC) secretome therapy administered in four sessions over two weeks, in addition to standard pharmacological treatment (aspirin, candesartan, atorvastatin, and

citicoline) and intensive rehabilitation (3–5 sessions per week). **Outcome:** Following treatment, the patient demonstrated clinically meaningful improvement, including increased muscle strength and functional independence, with regained ability to ambulate. Laboratory findings remained stable, and no adverse events were observed during the treatment period. **Conclusion:** This case suggests that UC-MSC-derived secretome therapy may have potential as an adjunctive approach to enhance functional recovery in subacute to chronic ischemic stroke. Further studies with larger sample sizes and controlled designs are needed to confirm its efficacy and safety.
Keywords: Case report, Neuroregeneration, Ischemic stroke subacute, Stem cells, Secretome.

2.24. Naufal Sebastian Anggoro

Original Research *

*(Please select and retain only the appropriate manuscript type for your submission)

A Transcriptomic Cancer Stem Cell Signature Derived from TCGA-COAD/READ Stratifies Prognosis and Is Independently Validated in an Asian Colorectal Cancer Cohort

Naufal Sebastian Anggoro[1], Achmad Dhani[2], Larasati Nikita Nareswari Kusnanto[2], Mohammad Ariq Nazar[1,*]

Author Affiliations

[1]*Department of Biomedical Engineering, Faculty of Health Science, Universitas Agung Putra, Semarang, Indonesia*

[2]*Stem Cell and Cancer Research Center (SCCR), Semarang, Indonesia*

Corresponding Author Email Guidelines

**Corresponding author: arqnazar@apu.ac.id*

Abstract.

Background: Cancer stem cell (CSC) markers in colorectal cancer (CRC) hold prognostic promise, but transcriptomic signatures integrating both CSC biology and genome-wide expression remain scarce and rarely validated in non-European populations. We aimed to construct a CSC-informed prognostic signature from The Cancer Genome Atlas (TCGA) CRC cohort and validate it in an independent Asian CRC cohort.

Methods: RNA-seq STAR-Counts and clinical data for 698 TCGA-COAD/READ samples were obtained via TCGAbiolinks. After quality control, 694 samples with 23,429 expressed genes entered differential expression analysis (DESeq2). A curated panel of 11 CRC CSC markers was intersected with co-expression modules from weighted gene correlation network analysis (WGCNA). CSC-associated genes were fed into LASSO-Cox regression (10-fold cross-validation) to derive a prognostic signature. The signature was independently validated in GSE107422 (N=110, Korean CRC) using logistic regression for recurrence prediction, with the closest available Southeast Asian CRC cohort (GSE220148, N=114, Thai CRC) serving as an expression reference.

Results: Among 11 CSC markers, LGR5 (log2FC=2.855, padj=1.67×10^{-40}), CD44 (log2FC=1.308, padj=2.74×10^{-52}), and ALDH1A1 (log2FC=−1.118, padj=1.28×10^{-6}) were significantly dysregulated in tumor versus normal. WGCNA (power=8) identified 3,941 CSC-associated genes, from which LASSO-Cox selected a 187-gene signature (lambda.min=0.0156). The signature stratified 609 TCGA patients into high- and low-risk

groups with highly significant survival separation (log-rank p≈0; adjusted HR=168.56, 95% CI: 23.24–1222.71, $p=3.95\times10^{-7}$; C-index=0.843). The proportional hazards assumption was satisfied (global p=0.41). In the independent Korean validation cohort, the signature significantly discriminated recurrence risk (OR=3.25, 95% CI: 1.40–7.54, p=0.006; AUC=0.640). Immune infiltration analysis revealed significant correlations between risk score and dendritic cells (ρ=0.144, $p=3.6\times10^{-4}$), NK cells (ρ=0.099, p=0.014), CD8 T cells (ρ=0.096, p=0.018), and inverse correlation with M2 macrophages (ρ=−0.103, p=0.011).

Conclusion: We present a novel 187-gene CSC-informed prognostic signature for CRC that demonstrates strong prognostic performance in TCGA and independent validation in an Asian cohort. The signature's association with multiple immune cell types suggests potential links between stemness and immune evasion. Further wet-lab validation and prospective studies in Indonesian and other Southeast Asian populations are warranted.

Keywords: colorectal cancer; cancer stem cells; prognostic signature; LASSO-Cox; WGCNA; Asian cohort validation; TCGA; immune infiltration

2.25. Friska Oktavrisa

Original Research

Effects of Mesenchymal Stem Cell Secretome on Epigenetic Regulation of SIRT1 and GLUT4 and Insulin Sensitivity in a Rat Model of Type 2 Diabetes

Friska Oktavrisa[1,2*]

[1]Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[2]Doctoral Program in Biomedical Sciences, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

**Corresponding author: foktavrisa@gmail.com*

Abstract. Type 2 diabetes mellitus (T2DM) is a major metabolic disorder characterized by insulin resistance and impaired glucose homeostasis, with epigenetic dysregulation contributing to altered expression of genes involved in insulin signaling. Sirtuin 1 (SIRT1) regulates cellular energy homeostasis and insulin signaling, whereas glucose transporter type 4 (GLUT4) mediates insulin-dependent glucose uptake in skeletal muscle and adipose tissue. Mesenchymal stem cell (MSC) secretome contains bioactive proteins, cytokines, growth factors, extracellular vesicles, and microRNAs that may modulate epigenetic pathways and restore metabolic gene expression. This study aims to determine the effect of MSC secretome on epigenetic regulation of SIRT1 and GLUT4 expression and insulin sensitivity in a T2DM model. A true experimental study with a post-test-only control group design will be conducted using male Wistar rats aged 8–12 weeks. T2DM will be induced by intraperitoneal nicotinamide followed by streptozotocin, and successful induction will be confirmed by fasting blood glucose above 200 mg/dL. Animals will be randomly allocated to control and MSC-secretome treatment groups. Epigenetic alterations related to SIRT1 and GLUT4 will be assessed, while gene expression will be quantified using reverse-transcription quantitative polymerase chain reaction. Fasting glucose and insulin levels will be measured, and insulin resistance will be estimated using the homeostatic model assessment for insulin resistance. MSC secretome is expected to enhance SIRT1 and GLUT4 expression, improve glucose utilization, and reduce insulin resistance. These findings may clarify its molecular mechanism and support its development as a cell-free regenerative strategy for T2DM.

Keywords: cell-free therapy, extracellular vesicles, glucose uptake, homeostatic model assessment, nicotinamide–streptozotocin model

2.26. Dirga Rachmad Aprianto

Original Research

Neuroprotective Potential of Secretome Hypoxia Mesenchymal Stem Cell in Acute Ischemic Stroke Rats

Dirga Rachmad Aprianto[1*], Agung Putra[1,2,3], Chodidjah[4], Titiek Sumarawati[1]

[1]Department of Doctoral Biomedical Science, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[2]Stem Cell and Cancer Research (SCCR) Laboratory, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[3]Department of Pathological Anatomy, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[4]Departement Anatomi, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

**Corresponding author: dirgarachmad@unissula.ac.id*

Background: Acute ischemic stroke induces neuroinflammation and apoptosis, contributing to brain injury. Hypoxia-conditioned mesenchymal stem cell secretome (SH-MSC) may exert anti-inflammatory and anti-apoptotic effects. **Objective:** To explore neurological, infarct, and molecular responses to SH-MSC in rats with acute ischemic stroke**. Methods:** This preliminary experimental study included healthy controls, untreated stroke rats, and SH-MSC-treated stroke rats. Stroke was induced by permanent ligation of the right common carotid artery. SH-MSC (300 µL) was administered intravenously 6 hours after induction. The modified Neurological Severity Score (mNSS) was assessed at 6 hours before treatment and at 24 and 72 hours. Brain infarction was qualitatively evaluated by TTC staining at 72 hours. IL-1β mRNA and caspase-3 protein expression were assessed by RT-qPCR and Western blot, respectively. **Results:** Median mNSS values in untreated stroke rats were 10 (7–10), 8.5 (8–10), and 9 (5–11) at 6, 24, and 72 hours, respectively. Corresponding values in SH-MSC-treated rats were 8 (6–11), 4.5 (3–6), and 3 (2–4), showing a greater descriptive decline over time. Representative TTC images suggested a smaller pale infarct area after treatment. Relative IL-1β expression was 2.60 ± 0.10 in untreated stroke rats and 1.29 ± 0.18 after SH-MSC treatment, versus 1.00 in healthy rats. Normalized caspase-3/β-actin expression was 0.92 ± 0.28 in untreated stroke rats, 0.33 ± 0.25 after SH-MSC treatment, and 0.47 ± 0.27 in

healthy rats**. Conclusion:** SH-MSC showed preliminary trends toward neurological recovery, a visually smaller infarct area, and lower IL-1β and normalized caspase-3 expression.

Keywords: acute ischemic stroke; caspase-3; IL-1β; mNSS; right common carotid artery ligation; SH-MSC.

POSTER PRESENTATION ABSTRACTS

3.1. Lusito

A Clinically Relevant Rat Model of Contrast-Induced Acute Kidney Injury Optimized for Preclinical Therapeutic Evaluation

Lusito
Department of Internal Medicine, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

Background
Contrast-induced acute kidney injury (CI-AKI) remains a major cause of hospital-acquired acute kidney injury. Existing rodent models vary in dehydration protocols and contrast media dosage, limiting reproducibility and preclinical applicability. This study aimed to identify an optimal protocol for establishing a clinically relevant rat model of CI-AKI using low-osmolar contrast medium.
Methods
A two-stage pilot study was conducted in male Sprague–Dawley rats. Pilot Study I validated a published protocol using iohexol (15 mL/kg) after either 6-hour or 72-hour dehydration. Renal injury was assessed by serial serum creatinine measurements and histopathology. Because functional AKI was not achieved, Pilot Study II increased the iohexol dose to 25 mL/kg while maintaining the same dehydration protocols.
Results
Iohexol at 15 mL/kg produced mild tubular injury but failed to induce functional AKI in either dehydration model. Increasing the iohexol dose to 25 mL/kg induced functional AKI only after 72-hour dehydration and was accompanied by severe tubular injury. In contrast, the 6-hour dehydration model remained insufficient to produce functional AKI.
Conclusions
Protocol optimization identified iohexol 25 mL/kg combined with 72-hour dehydration as the optimal protocol for reproducible CI-AKI induction. The optimized model demonstrated both structural kidney injury and functional renal impairment, providing a reliable platform for future preclinical evaluation of novel therapeutic interventions.
Keywords: contrast-induced acute kidney injury; iohexol; rat model; model optimization; preclinical study.

3.2. Yenny Purnama

Mesenchymal Stromal Cell Secretome as a Regulator of Immune Response and Its Potential as a Precision Immunomodulatory Therapy in Pediatric and Neonatal Sepsis: A Case Report

ABSTRACT

Background:

Pediatric and neonatal sepsis are critical conditions characterized by dysregulated host immune responses to infection, leading to systemic inflammation, multiple organ dysfunction, and increased mortality risk. Although antibiotics and supportive therapies remain the cornerstone of management, a proportion of patients continue to experience severe disease progression due to an imbalance between excessive pro-inflammatory activation and impaired resolution of inflammation. This highlights that sepsis pathogenesis is not solely determined by pathogen elimination but also by failure of host immune regulation.

Immunomodulatory-based therapeutic approaches have emerged as promising strategies to address the complexity of immune dysregulation in sepsis. Mesenchymal stromal cells (MSCs) have been extensively investigated as potential therapeutic agents due to their immunoregulatory properties mediated primarily through paracrine mechanisms. Current evidence indicates that the therapeutic effects of MSCs are largely attributed to their secretome, a complex collection of bioactive molecules including cytokines, growth factors, immunoregulatory proteins, lipids, and extracellular vesicles (EVs). MSC-derived secretome contributes to intercellular communication, inflammatory regulation, immune cell modulation, and tissue repair processes.

Case Report:

We report a case of severe pediatric/neonatal sepsis characterized by persistent inflammatory responses despite standard treatment with antibiotics and supportive therapy. The clinical course demonstrated features of immune dysregulation, including sustained inflammatory activation and increased risk of progressive organ dysfunction. This case highlights the potential role of MSC secretome-based approaches as a precision immunomodulatory strategy aimed at restoring immune homeostasis in severe sepsis.

MSC-derived secretome contains multiple bioactive components, particularly extracellular vesicles carrying microRNAs, regulatory proteins, and signaling molecules that may influence macrophage activation, dendritic cell function, T-cell responses, and inflammatory pathways. These mechanisms include suppression of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β), enhancement of anti-inflammatory mediators such as interleukin-10 (IL-10), and modulation of key inflammatory pathways including Toll-like receptor 4 (TLR4)/nuclear factor kappa B (NF-κB) signaling.

Discussion:

This case emphasizes the importance of shifting the therapeutic paradigm of sepsis from a pathogen-centered approach toward strategies aimed at restoring host immune homeostasis. MSC secretome represents a promising *cell-free therapy* platform because it preserves the biological activity of MSCs while potentially reducing the immunogenicity and safety concerns associated with direct cell transplantation. Furthermore, characterization of secretome components enables identification of specific bioactive molecules responsible for therapeutic effects, supporting the development of precision-based immunotherapy.

Recent experimental studies have demonstrated that MSC-derived extracellular vesicles can attenuate pathological inflammation, enhance immune regulation, reduce tissue injury, and improve outcomes in experimental models of sepsis. However, several challenges remain before clinical translation, including variability in MSC sources, heterogeneity of secretome composition, manufacturing standardization, product characterization, and the absence of validated biomarkers capable of predicting individual therapeutic responses.

Identification of a **secretome signature**, defined as a specific molecular profile associated with immunomodulatory potency, represents an important step toward developing personalized immunotherapy for pediatric and neonatal sepsis. This approach may enable patient-specific treatment strategies based on immune phenotype and biological characteristics.

Conclusion:

This case report highlights the potential role of MSC-derived secretome as a key regulator of immune responses and as a candidate precision immunomodulatory therapy for pediatric and neonatal sepsis. The secretome-based approach provides a novel therapeutic paradigm by targeting immune imbalance, inflammatory resolution, and tissue repair without relying on the administration of living cells. Further investigations are required to identify the specific secretome components associated with therapeutic efficacy and to establish personalized treatment strategies based on patient immune profiles.

Keywords:
Neonatal sepsis; pediatric sepsis; mesenchymal stromal cells; MSC secretome; extracellular vesicles; immunomodulation; precision therapy.

3.3. Reynaldi Suryajaya

Original Research

Synergistic Effects of Intradermal Hypoxia Mesenchymal Stem Cells-Derived Secretome and Topical Minoxidil on IGF-1 and MDA in Alopecia Rat Model
Short Title: *SH-MSCs and Topical Minoxidil in Alopecia Rat Model*

Reynaldi Suryajaya[1], Eko Setiawan[2], Hadi Sarosa[2], Agung Putra[3,4,8], Salindri Prawitasari[5]*, Nadya Audina Nurkhafiya Sadikin[6], Rakha Fahreza[1], Fikriya Novita Sari[7]

[1]*Stem Cell Secretome Therapy, Biomedical Sciences, Agung Putra University, Semarang, Indonesia*
[2]*Biomedical Science Master Program, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Indonesia*
[3]*Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Indonesia*
[4]*Stem Cell Engineering, Biomedical Sciences, Agung Putra University, Semarang, Indonesia*
[5]*Chemical and Nanobiotechnology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia*
[6]*Cancer Biology Laboratory, Biomedical Sciences, Agung Putra University, Semarang, Indonesia*
[7]*Immunology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia*
[8]*Stem Cell and Cancer Research (SCCR), Semarang, Indonesia*

**Corresponding author: salindriprawitasari@apu.ac.id*

Abstract. Background: Alopecia is characterized by excessive hair loss. Current standard therapies are ineffective and frequently cause side effects, thus requiring adjuvant therapies. Hypoxia mesenchymal stem cell-derived secretome (SH-MSCs) contains a broad range of paracrine factors, including cytokines, growth factors, and exosome-associated microRNAs (miRNAs), which reduce oxidative stress and enhance hair follicle regeneration. This study aimed to determine the synergistic effects of intradermal SH-MSCs and topical minoxidil on Insulin-like Growth Factor-1 (IGF-1) and Malondialdehyde (MDA) in alopecia rat model. **Methods:** This in vivo research used a randomized post-test only control group design with four groups: alopecia rat model receiving 0.9% NaCl, alopecia rat model receiving 5% topical minoxidil, alopecia rat

model receiving 100 µL SH-MSCs injection, and alopecia rat model receiving a combination of 100 µL SH-MSCs injection and 5% topical minoxidil. **Results:** IGF-1 and MDA levels in the rat skin were analyzed using the ELISA method. SH-MSCs administration in combination with 5% topical minoxidil significantly increased IGF-1 and decreased MDA levels in alopecia rat model. **Conclusions:** SH-MSCs improve alopecia condition by increasing IGF-1 and reducing MDA levels, indicating potential as an adjuvant therapy for alopecia.

Keywords: *Alopecia; SH-MSCs; minoxidil; IGF-1, MDA*

3.4. Rita Agustina

Original Research

Hypoxia Mesenchymal Stem Cells-Derived Secretome Cream Modulates p50 and p65 Gene Expression in Atopic Dermatitis-Like Rat Model
Short Title: ***SH-MSCs Cream Modulates p50 and p65 in Atopic Dermatitis Rat***

Rita Agustina[1*], Agung Putra[2,3,9], Prasetyowati Subchan[4], Salindri Prawitasari[5], Iffan Alif[6], Risky Chandra Satria Irawan[7], Dian Respati Ayu[8]

[1]Clinical Stem Cell and Cancer, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[2]Biomedical Sciences Doctoral Program, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Indonesia
[3]Stem Cell Engineering, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[4]Biomedical Science Master Program, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Indonesia
[5]Chemical and Nanobiotechnology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia
[6]Cancer Immunology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia
[7]Stem Cell Biology Laboratory, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[8]Stem Cell Metabolites Laboratory, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[9]Stem Cell and Cancer Research (SCCR), Semarang, Indonesia

*Corresponding author: ritaagustina@apu.ac.id

ABSTRACT

Background: Atopic dermatitis is a chronic skin disease closely associated with a dysregulation of Th2 cell responses, resulting in an exaggerated inflammatory response, characterized by activation of the NF-κB transcription factor. Current therapies provide only temporary relief and may cause adverse effects. Therefore, safer and more effective treatments are needed, with hypoxia mesenchymal stem cells-derived secretome (SH-MSCs) representing a promising therapeutic approach. This study aimed to determine

the effect of SH-MSCs cream on p50 and p65 gene expression modulation in atopic dermatitis-like rat model.**Methods:** An in vivo post-test-only controlled study was conducted using 28 male Wistar rats randomly assigned to four groups (n = 6/group): healthy control, AD-like + base cream, AD-like + SH-MSC cream (100 µL/kg body weight), and AD-like + SH-MSC cream (200 µL/kg body weight). After 7 days of treatment, p50 and p65 gene expression was quantified by qRT-PCR. **Results:** SH-MSCs cream significantly downregulated both p50 and p65 expression compared with the base cream-treated AD-like group, with the 200 µL/kg body weight dose showing the greatest effect ($p < 0.05$). **Conclusions:** Topical SH-MSCs cream significantly downregulating p50 and p65 gene expression in an atopic dermatitis-like rat model, indicating its ability to modulate NF-κB-mediated inflammatory responses.

Keywords: *Hypoxia MSCs, SH-MSCs cream, atopic dermatitis, p50, p65*

3.5. Dita Eka Sartika Putri Dewi

Combination of Secretome Therapy and Erbium Laser for Enhancing Wound Healing: A Case Report

dr. Dita Eka Sartika Putri Dewi, MHKes, M.Kes, MM

Background

Wound healing following incision and drainage of an abscess is a complex biological process involving the sequential phases of hemostasis, inflammation, proliferation, and tissue remodeling. This process may be impaired by conditions such as diabetes mellitus, advanced age, infection, and vascular disorders, thereby increasing the risk of chronic wounds and scar formation. Secretome, a collection of bioactive factors secreted primarily by mesenchymal stem/stromal cells (MSCs), contains cytokines, growth factors, chemokines, proteins, lipids, and extracellular vesicles that promote angiogenesis, fibroblast proliferation, collagen synthesis, and tissue regeneration. This case report aims to evaluate the role of secretome therapy combined with erbium laser treatment in enhancing wound healing following post-incision and drainage of an abscess.

Objective

To describe the clinical outcomes of combination therapy using secretome and erbium laser in accelerating wound healing in a patient with a post-incision and drainage abscess wound.

Case Presentation

A 38-year-old woman with a delayed-healing post-drainage abscess wound that failed to demonstrate satisfactory improvement following conventional treatment received adjuvant therapy consisting of topical secretome combined with erbium laser treatment. Clinical evaluations were performed periodically by assessing wound size, granulation tissue formation, epithelialization, wound exudate, signs of inflammation, pain intensity, and serial photographic documentation throughout the observation period.

Results

Following combination therapy, progressive clinical improvement was observed, including a reduction in wound size, enhanced formation of healthy granulation tissue,

decreased local inflammation and wound exudate, accelerated epithelialization, and no significant adverse events during the observation period. The clinical response suggests that secretome may accelerate wound healing by modulating the wound microenvironment, while erbium laser treatment promotes tissue regeneration and remodeling without inducing additional scar formation.

Conclusion

The combination of secretome therapy and erbium laser treatment demonstrates promising potential as an adjuvant regenerative approach for enhancing wound healing through anti-inflammatory, pro-angiogenic, and tissue regenerative mechanisms. Although this case report provides encouraging clinical evidence, larger controlled clinical trials are required to confirm the efficacy, safety, optimal dosage, treatment frequency, and standardized production protocols of secretome before this therapeutic approach can be recommended for routine clinical practice.
Keywords: secretome, erbium laser, wound healing, regenerative therapy, mesenchymal stem cells, cell-free therapy.

3.6. Titik Kusumawinakhyu

The Therapeutic Potentials and Molecular Mechanisms of Curcumin and Secretome in Psoriasis: A Systematic Literature Review

Titik Kusumawinakhyu

Doctoral Programme Faculty of Medicine Universitas Islam Sultan Agung

Corresponding author: titikkusumawinakhyu@gmail.com

Abstract

Background: Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by hyperproliferation of keratinocytes and infiltration of inflammatory cells. Traditional systemic therapies often come with significant side effects, prompting the exploration of natural compounds and novel regenerative therapies. Curcumin, a polyphenol derived from *Curcuma longa*, and secretome (stem cell-conditioned medium) have emerged as promising therapeutic agents due to their potent anti-inflammatory, antioxidant, and immunomodulatory properties.

Objective: This systematic literature review aims to evaluate and synthesize current scientific evidence regarding the effects and underlying mechanisms of curcumin and secretome in the treatment and management of psoriasis.

Methods: A systematic search was conducted across major electronic databases, including PubMed, Scopus, ScienceDirect, and Google Scholar, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Studies published up to 2024-2026 investigating the in vitro, in vivo, or clinical therapeutic effects of curcumin and/or secretome on psoriasis were included. Data extraction focused on study designs, intervention types, molecular pathways, and clinical outcomes.

Results: The synthesized data revealed that both curcumin and secretome significantly alleviate psoriasis-like skin lesions. Curcumin exerts its anti-psoriatic effects primarily by downregulating the IL-23/IL-17 axis, inhibiting NF-κB activation, and reducing the expression of pro-inflammatory cytokines (TNF-α, IL-6). On the other hand, secretome—particularly from mesenchymal stem cells (MSCs)—exhibits profound immunomodulatory effects by promoting regulatory T cell (Treg) differentiation, suppressing dendritic cell activation, and facilitating tissue repair through paracrine factors. Interestingly, emerging evidence suggests that combining or formulation-targeting these two agents may offer a synergistic effect, enhancing bioavailability and therapeutic efficacy.

Conclusion: Both curcumin and secretome demonstrate substantial therapeutic potential against psoriasis by targeting multiple inflammatory pathways and restoring immune homeostasis. While curcumin offers a strong plant-based anti-inflammatory

approach, secretome provides advanced regenerative immunomodulation. Further robust clinical trials are warranted to establish standardized dosages, delivery methods, and long-term safety profiles for these therapies in psoriatic patients.

Keywords: Curcumin, Secretome, Psoriasis, Inflammation, Systematic Literature Review

3.7. Dimas Febriarto

Original Research / Case Report / Review Article*
*(Please select and retain only the appropriate manuscript type for your submission)

Mesenchymal Stem Cell-Based Interventions for Bone Fracture Healing in Humans and Animals: A Systematic Review and Meta-Analysis

Dimas Febriarto[1,*]

Author Affiliations

[1] Department of Orthopedic, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

**Corresponding author: drdimasf14@unissula.ac.id*

Abstract

Aim: To evaluate the efficacy and safety of mesenchymal stem cell (MSC) therapy for bone fracture healing in humans and animals, compared with standard treatment, and to identify knowledge gaps for future research. **Methods:** Systematic review and meta-analysis of studies (2015-2025) identified through MEDLINE, PubMed, Scopus, and Cochrane Library. We included randomized and non-randomized trials in humans and animal models (rats, mice, rabbits, primates) using MSC injections or implants (bone marrow, adipose, or umbilical cord sources) versus standard therapy. Data were extracted independently by two reviewers and analyzed using RevMan Web; risk of bias was assessed with Cochrane RoB-2. **Results:** Twenty-two studies were included. Meta-analysis showed no significant benefit at 3 months (OR 0.56; 95% CI 0.24-1.30; p=0.18). MSC therapy significantly improved healing rates at 6 months (OR 3.33; 95% CI 1.76-6.29; p=0.0002), 9 months (OR 2.21; 95% CI 1.03-4.74; p=0.04), and 12 months (OR 2.91; 95% CI 1.76-4.81; p<0.0001), with a positive trend beyond 12 months (OR 4.81; 95% CI 0.86-26.86; p=0.07). Bone marrow-derived MSCs exhibited the strongest effect. Adverse events were mild and occurred in <5% of cases; no safety concerns were identified**. Conclusion:** MSC therapy significantly accelerates fracture union from 6 months onward with an excellent safety profile. Benefits are not evident at 3 months, and long-term data remain limited.

Keywords: Mesenchymal stem cells,Bone fracture,Fracture healing,Non-union,Meta-analysis

3.8. Rivaldo Heru Setiawan

Cactaceae-Derived Bioactives in Cancer Therapy: A Systematic Review of Preclinical Mechanisms Targeting Apoptosis and Redox Signaling

Gabriela Valencia Putri Husodho[1], Anatalya Diah Ayu Kumalasari[1], Rivaldo Heru Setiawan[1], Hamdi Ramadhan Daulay[1], Desy Armalina[2], Indah Saraswati[3]

[1]Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia

[2]Department of Anatomy and Histology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia

[3]Department of Biochemistry and Clinical Biology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia

Abstract

Background:

Cancer continues to be a predominant cause of global morbidity and mortality, with conventional therapies frequently constrained by systemic toxicity, limited selectivity, and the development of drug resistance. These limitations have heightened interest in plant-derived bioactive compounds as alternative or complementary anticancer strategies. Members of the Cactaceae family, including Opuntia, Cereus, and related genera, are abundant in bioactive compounds such as flavonoids, betalains, and phenolic acids. Emerging preclinical evidence indicates that these compounds exert anticancer effects by modulating oxidative stress, inducing apoptosis, and regulating redox-sensitive signaling pathways. However, current evidence is fragmented across heterogeneous experimental models, and a comprehensive mechanistic synthesis remains absent..

Methods:

A comprehensive literature search was executed across the PubMed, ScienceDirect, EBSCO, and ProQuest databases, focusing on studies published within the past decade. The studies deemed eligible comprised both in vitro and in vivo investigations that assessed the anticancer properties of extracts or isolated compounds derived from the Cactaceae family. The selection of studies was independently conducted by multiple reviewers in accordance with predefined inclusion criteria. The methodological quality of the studies was evaluated using the SciRAP tool. A semi-quantitative vote-counting method was employed for outcomes related to apoptosis, while other findings were synthesized narratively, with particular attention to mechanistic pathways.

Results:
Seven studies satisfied the inclusion criteria, encompassing a range of cancer types, including cervical, breast, hepatic, colorectal, and hematological malignancies. All included studies (7/7; 100%, 95% CI: 59–100%; p = 0.0156) exhibited a pro-apoptotic effect of Cactaceae-derived interventions compared to controls. Mechanistically, these effects were linked to the upregulation of tumor suppressor pathways, notably p53, increased intracellular oxidative stress leading to mitochondrial dysfunction, and activation of caspase-dependent apoptosis. Furthermore, selective cytotoxicity toward cancer cells with minimal impact on normal cells was consistently observed. The dual role of antioxidant and pro-oxidant activity appears to be central to the redox modulation induced by these bioactive compounds.

Conclusion:
Cactaceae-derived compounds consistently demonstrate pro-apoptotic and redox-modulating effects in preclinical cancer models, indicating their potential as candidates for anticancer drug development. However, the current body of evidence is constrained by small sample sizes, methodological heterogeneity, and a lack of translational validation. Future research should prioritize standardized experimental designs, dose-response characterization, and integration with clinically relevant models to facilitate the transition toward therapeutic applications.

Keywords

Cactaceae; Apoptosis; Redox Signaling; Phytochemicals; Cancer Therapy; Preclinical Studies

3.9. 3.9 Dini Cahyani

Original Research

Short-Term Storage Stability of Human Umbilical Cord-Derived Human Mesenchymal Stem Cells (hUC-MSCs): A Multi-Timepoint Analysis

Dini Cahyani[1], Fikriya Novita Sari[1*], Dian Respati Ayu[2], Risky Chandra Satria Irawan[3], Agung Putra[4,6], Rita Agustina[5,6], Nur Dina Amalina[6]

[1]Immunology Laboratory, Biotechnology, Agung Putra University, Semarang, Indonesia
[2]Stem Cell Metabolites Laboratory, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[3]Stem Cell Biology, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[4]Stem Cell Engineering, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[5]Clinical Stem Cell and Cancer, Biomedical Sciences, Agung Putra University, Semarang, Indonesia
[6]Stem Cell and Cancer Research (SCCR), Semarang, Indonesia

**Corresponding author: fikriyanovitasari@apu.ac.id*

Abstract. Background: Human Umbilical Cord Mesenchymal Stem Cells (hUC-MSCs) are widely used in regenerative medicine, where maintaining cell quality during short-term storage is critical to ensure stability for safety, therapeutic efficacy, and regulatory compliance. **Objective:** This study aims to evaluate the effect of storage duration on MSC characteristics at several time-points, including viability assays, macroscopic observation, contamination assays, and immunophenotyping by flow cytometry. **Methods:** hUC-MSC products were prepared under standardized conditions. Final product was filled into sterile syringes containing 1–2 × 10^5 cells suspended in 6 mL of 0.9% NaCl solution and stored at controlled cold temperature (2–8°C). Assessments were conducted at 0, 12, 24, 48, and 72 hours post-storage. At each time-point, analyses were performed in duplicate. **Results:** This research showed that macroscopic observation does not reveal any color or particle formation changes. MSC viability remains relatively stable, above (90%) from 0-48 hours, and decreases at 72 hours. All replicates remained free of contamination with negative mycoplasma and endotoxin test results and confirmed sterility. The MSC immunophenotype profile shows surface marker percentages for positive markers at 0–48 hours (≥95%), while at 72 hours there is a decrease (≤95%), and negative markers remain (≤2%) from 0 to 72 hours. **Conclusion:** In conclusion, hUC-MSCs demonstrate optimal stability within 0–48 hours of cold storage (2–8°C), maintaining high viability and preserved cell quality. Viability is still within acceptable bounds even if there is a noticeable time-dependent reduction at 72 hours. These findings indicate a clearly

defined storage window, with <48 hours as the optimal condition, but until 72 hours still considered suitable for use.

Keywords: human-umbilical cord mesenchymal stem cell, immunophenotype, viability, storage-stability.

3.10. Ivo Devi Kristyani

EFFECTS OF DOXORUBICIN AND CYTOTOXIC T LYMPHOCYTES ON APOPTOSIS ACTIVATION IN MDA-MB-231 BREAST CANCER CELLS: AN IN VITRO STUDY

Ivo Devi Kristyani[1,2*]

[1]Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia

[2]Doctoral Study Program of Biomedical Sciences, Universitas Islam Sultan Agung, Semarang, Indonesia

*Corresponding author: [insert email address]

ABSTRACT

Introduction: Triple-negative breast cancer is an aggressive subtype with limited targeted treatment options and frequent resistance to apoptosis. Doxorubicin induces DNA damage and mitochondrial apoptosis, but its efficacy may be reduced by antiapoptotic mechanisms. Cytotoxic T lymphocytes (CTLs) eliminate tumor cells through perforin–granzyme release, Fas–Fas ligand interaction, and secretion of tumor necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ). Combining doxorubicin with CTLs may enhance tumor-cell susceptibility to immune-mediated killing, reduce B-cell lymphoma 2 (BCL-2) expression, and increase cleaved caspase-3 activation.

Aim and Scope: This study aims to determine the effects of doxorubicin, CTLs, and their combination on apoptosis activation and immune-inflammatory responses in MDA-MB-231 breast cancer cells. The evaluated outcomes are TNF-α and IFN-γ levels, BCL-2 expression, and cleaved caspase-3 expression.

Methods: This in vitro true experimental study uses a post-test-only control group design. MDA-MB-231 cells are divided into four groups: vehicle control, doxorubicin, CTL, and combined doxorubicin–CTL. Cells in the doxorubicin and combination groups are exposed to 250 nM doxorubicin for 48 hours. The CTL and combination groups are subsequently cocultured with activated human CD8+ CTLs for six hours at a predetermined effector-to-target ratio. TNF-α and IFN-γ concentrations are measured using enzyme-linked immunosorbent assays. BCL-2 and cleaved caspase-3 expression are assessed using Western blotting and quantified by densitometric analysis. Enhanced apoptosis is indicated by decreased BCL-2 expression and increased cleaved caspase-3 expression. This approach simultaneously characterizes immune effector activity, antiapoptotic regulation, and execution-phase apoptosis, providing mechanistic evidence for combining chemotherapy with cell-based immunotherapy against aggressive breast cancer in vitro models.

Keywords: triple-negative breast cancer; MDA-MB-231; doxorubicin; cytotoxic T lymphocytes; apoptosis

3.11. Shelly Tjahyadewi

Original Research / Case Report / Review Article*
*(Please select and retain only the appropriate manuscript type for your submission)

THE EFFECT OF GARLIC SKIN EXTRACT (*Allium sativum Linn)* ON THE NUMBER OF NITRIC OXIDE,TNF ALPHA AND NEUTROPHILS IN ACUTE BACTERIAL SINUSITIS
(Experimental Study of Male White Rats *Rattus Novergicus Sprague Dawley* Strain induced by *Staphylococcus aureus*)

Shelly Tjahyadewi[1,2*] Andina Putri Aulia[1] Renny Swasti Wijayanti[1]

Author Affiliations
1Faculty of Medicine, Universitas Islam Sultan Agung,Semarang Indonesia
2 Doctoral Study Program of Biomedicine Universitas Islam Sultan Agung,Semarang Indonesia

Corresponding Author Email Guidelines*
**Corresponding author:* shelly.tjayadewi@gmail.com*
If additional author email addresses are included, they may be listed on separate lines without an asterisk.

Abstract.

Background: acute bacterial sinusitis an inflammatory process and can cause an increase in the number of leukocytes and the number of neutrophils. the content of flavonoids in garlic skin can inhibit the inflammatory process through the process of inhibiting the accumulation of leukocytes and neutrophils in the inflamed area. **objective:** this study was conducted to determine the effect of garlic peel extract (allium sativum linn) on number of nitric oxid,TNF alpha and neutrophils levels in acute bacterial rhinosinusitis so that can be used as adjuvant therapy in suppressing the inflammatory process in acute bacterial rhinosinusitis. **Methods:** This study is an experimental study with post-test only control group design. There were 28 male Sprague Dawley rats divided into 4 groups, including the control group, the group of bacterial acute sinusitis rats without treatment, the group of bacterial acute sinusitis rats treated with amoxicillin and prednisolone antibiotics, and a group of bacterial acute sinusitis rats treated with amoxicillin antibiotics and garlic peel extractResults: Based on the results of the One Way Anova test, the p value < 0.001 showed that there were at least two groups that had a significant difference, namely the effect of giving garlic peel extract (Allium sativum linn) on the number of Nitric Oxide, TNF-alpha, and neutrophil levels. The results of the LSD Post Hoc Test showed a significant difference between group K against P1, P2 and P3, group P1 against P2 and P3. And there was no significant difference between the P2 and P3 groups ($p < 0.05$). **Conclusion :** The administration of garlic skin extract (Allium sativum Linn) affected the

levels of NO, TNF-alpha, and neutrophil in rats with acute bacterial sinusitis induced by Staphylococcus aureus.

Keywords: *Keywords: sinusitis; Garlic ; Anti-inflammatory; Nitric Oxide; Neutrophils; TNF-alpha.*

3.12. Agus Widiyatmoko

Nanoparticle Encapsulation of Umbilical Cord-Derived Mesenchymal Stem Cell Secretome: A Structured Review of an Emerging Cell-Free Therapeutic Delivery Strategy

Widiyatmoko A[1], Putra A[2], Sumarawati T[2], Munir D[3]

[1] Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta (FKIK UMY), Yogyakarta, Indonesia
[2] Faculty of Medicine, Sultan Agung Islamic University (FK UNISSULA), Semarang, Indonesia
[3] Faculty of Medicine, Universitas Prima Indonesia (FK UNPRIMA), Medan, Indonesia

Corresponding author: Widiyatmoko A **Email:** aguswidi@umy.ac.id

Background: Umbilical cord-derived mesenchymal stem cell (UC-MSC) secretome comprises soluble cytokines, chemokines, growth factors, extracellular matrix-related proteins, lipid mediators, nucleic acids, and extracellular vesicles that collectively mediate immunomodulatory, anti-inflammatory, anti-apoptotic, angiogenic, and tissue-regenerative effects [1,2]. However, the therapeutic translation of unencapsulated secretome is restricted by enzymatic degradation, physicochemical instability, rapid systemic clearance, nonspecific tissue distribution, and the need for repeated administration [2,3].
Objective: This review evaluates the scientific rationale, formulation approaches, therapeutic potential, limitations, and translational requirements of nanoparticle-based encapsulation of UC-MSC secretome.
Novelty: Unlike previous reviews that predominantly discuss MSC secretome, isolated extracellular vesicles, or hydrogel-based delivery separately, this review integrates evidence concerning the encapsulation of the whole UC-MSC secretome within nanosized lipid and polymeric carriers. It also distinguishes direct evidence for whole-secretome encapsulation from indirect evidence derived from conditioned-medium, extracellular-vesicle, and biomaterial-delivery studies.
Materials and Methods: A structured narrative search of peer-reviewed literature indexed in Scite was conducted using combinations of the terms “UC-MSC,” “umbilical cord mesenchymal stem cell,” “secretome,” “conditioned medium,” “extracellular vesicle,” “nanoparticle,” “lipid nanoparticle,” “liposome,” “PLGA,” “chitosan,” “alginate,” and “controlled release.” Original experimental studies and relevant reviews published from 2015 to July 2026 were considered. Evidence was synthesized according to secretome composition, carrier materials, physicochemical characterization, release behavior, preservation of biological activity, preclinical efficacy, and translational limitations. Publications with retraction notices were excluded.
Results: UC-MSC secretome contains heterogeneous but therapeutically relevant

interleukins and paracrine mediators, although its composition varies according to donor characteristics, culture conditions, oxygen tension, passage number, conditioning protocols, and processing methods [1,10]. Delivery-system studies indicate that polymeric and lipid-based carriers can protect biologically active cargo, increase local retention, and enable sustained or controlled release [2,3]. Conditioned medium has been successfully incorporated into chitosan-based nanoparticles, demonstrating the technical feasibility of producing particles with measurable size, morphology, and surface charge [4]. In UC-MSC-specific studies, a chitosan-collagen thermosensitive hydrogel carrying UC-MSC-conditioned medium accelerated wound closure and improved tissue regeneration in experimental burn injury [5]. Similarly, composite biomaterials delivering UC-MSC-derived exosomes improved wound-repair responses [6]. UC-MSC extracellular vesicles have also functioned as natural nanocarriers capable of transferring regulatory microRNAs and other biologically active molecules to injured renal tubular cells [7]. Preliminary veterinary evidence further suggests that chitosan-based nanoparticle systems may enhance the neuroprotective activity of umbilical cord MSC-conditioned medium [8]. Nevertheless, direct comparative studies evaluating whole human UC-MSC secretome encapsulated in lipid nanoparticles, liposomes, PLGA, or chitosan-alginate nanoparticles remain scarce.

Discussion: The available evidence supports nanoparticle encapsulation as a plausible strategy to overcome the short biological half-life and uncontrolled biodistribution of UC-MSC secretome. Lipid nanoparticles and liposomes may be particularly suitable for combined hydrophilic, lipid, protein, and nucleic-acid cargo, whereas PLGA offers tunable biodegradation and sustained release. Chitosan- and alginate-based nanoparticles provide biocompatibility, ionic cross-linking, and potential mucoadhesive or local-retention properties. However, encapsulation may selectively retain or exclude secretome components, alter protein conformation, damage extracellular vesicles, or modify biological potency. Translation therefore requires simultaneous characterization of particle size, polydispersity index, zeta potential, morphology, encapsulation efficiency, loading capacity, release kinetics, sterility, endotoxin levels, storage stability, biodistribution, toxicity, and post-encapsulation biological activity [2–4,9,10].

Conclusion: Nanoparticle encapsulation of UC-MSC secretome represents a promising platform for developing stable, targeted, and controlled cell-free regenerative therapies. Current evidence demonstrates formulation feasibility and improved biological retention or efficacy in several preclinical delivery models, but direct evidence for whole human UC-MSC secretome encapsulation remains limited. Standardized secretome manufacturing, mechanism-based carrier selection, validated potency assays, pharmacokinetic studies, long-term safety assessment, and well-designed disease-specific preclinical and clinical trials are required before routine clinical translation.

Acknowledgement: The authors gratefully acknowledge academic support from the Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta; the Faculty of Medicine, Sultan Agung Islamic University; and the Faculty of Medicine, Universitas Prima Indonesia.

Keywords: UC-MSC secretome; nanoparticle encapsulation; conditioned medium; lipid nanoparticle; chitosan; controlled release; cell-free therapy; regenerative medicine

3.13. Santi Cintya Dewi

Black Rice Extract Attenuates UVB-Induced Hyperpigmentation by Inhibiting IL-1b and MITF Gene Expression

Santi Chintya Dewi[1*], Titiek Sumarawati[2], Prasetyowati Subchan[2], Setyo Trisnadi[2], Joko Wahyu Wibowo[2], Chodijah Chodijah[2], Agung Putra[2,3,4], Nur Dina Amalina[4,5]

[1]Postgraduate Student, Faculty of Medicine, Sultan Agung Islamic University (UNISSULA), Semarang, Indonesia
[2]Department of Postgraduate Biomedical Science, Medical Faculty, Sultan Agung Islamic University (UNISSULA), Semarang, Indonesia,
[3]Department of Pathology, Medical Faculty, Sultan Agung Islamic University (UNISSULA), Semarang, Indonesia
[4]Stem Cell and Cancer Research Indonesia, Semarang, Indonesia
[5]Pharmaceutical Sciences Department, Faculty of Medicine, Universitas Negeri Semarang, Semarang, Indonesia
*Corresponding author email: Professmail16@gmail.com
Phone number: +62 877 8551 8212

Abstract

This study investigated the effects of black rice extract on ultraviolet-B (UVB)-induced hyperpigmentation in C57BL/6J mice, with a focus on the expression of the interleukin-1β (IL-1β) and melanocyte-inducing transcription factor (MITF) genes. Black rice extract was obtained via ethanol maceration, yielding 8.70% and exhibiting high flavonoid content (90.30±4.02mg/100g) and potent antioxidant activity (IC_{50} = 67.98±8.16 ppm). UVB irradiation (390 mJ/cm2) induced visible skin darkening in mice after 14 days. Gene expression analysis using qRT-PCR revealed that black rice extract cream (BREC) at concentrations of 7.5% and 15% significantly reduced IL-1β expression compared to the negative control group ($p < 0.05$). BREC also decreased MITF expression, with the 15% concentration showing the lowest levels (0.93±0.18) compared to the negative control (2.09±1.30). Statistical analysis revealed significant differences in IL-1β and MITF expression among treatment groups ($p < 0.05$). These findings suggest that black rice extract effectively mitigates UVB-induced hyperpigmentation by modulating the expression of IL-1β and MITF genes in a dose-dependent manner.

Keywords: Black rice extract, interleukin-1 beta, melanocyte-inducing transcription factor, ultraviolet-B.

3.14. Hanifah

Synergistic Effect of Curcumin and Adoptive Cytotoxic T Lymphocytes in Inducing Cervical Cancer Cell Death via Multitarget Modulation of p53, Cleaved Caspase-3, PD-L1, TGF-β, Perforin/Granzyme B, and IFN-γ

AUTHORS:

[dr. Hanifah, SpOG]1*, [Promoter Prof. Dr. dr. H. Agung Putra, M.Si.Med]1, [Co-Promoter Prof. Dr. Dra. Atina H,M.Si.Apt]1,[Co-Promoter Dr. dr. Chodidjah, M.Kes]2.

AFFILIATION:

1Doctoral Program in Biomedical Science, Faculty of Medicine, Universitas Islam Sultan Agung (UNISSULA), Semarang, Central Java, Indonesia

*Corresponding Author Email: [drhanifah9@gmail.com]

ABSTRACT

Background: Cervical cancer driven by high-risk Human Papillomavirus (HPV) persistently evades host immune surveillance through tumor-suppressor degradation (p53) and over-expression of immunosuppressive and imun checkpoints (PD-L1 and TGF-β). Although Adoptive Cytotoxic T Lymphocyte (CTL) therapy offers targeted tumor-lytic capabilities, its clinical efficacy is frequently hindered by T-cell exhaustion within the tumor microenvironment. Phytochemical chemosensitization using curcumin presents a promising strategy to reverse immune evasion and sensitize tumor cells to CTL-mediated lysis.

Objective: To evaluate the synergistic antitumor efficacy of combined curcumin and adoptive CTL therapy against human cervical cancer cell lines (HeLa and SiHa) and to elucidate the underlying molecular mechanisms through the integrative modulation of apoptotic, immunosuppressive, and lytic biomarkers (p53, Cleaved Caspase-3, PD-L1, TGF-β, Perforin, Granzyme B, and IFN-γ).

Translational Significance & Benefits: This research provides a first-in-class molecular framework demonstrating how phytochemical chemosensitization coordinately reverses tumor immune evasion while restoring CTL-driven apoptosis. Clinically, priming solid cervical tumors with curcumin before adoptive cell transfer offers a novel strategy to prevent T-cell burnout, lower required cell doses, and minimize treatment-related toxicities, serving as a solid pre-clinical foundation for affordable adjuvant phyto-immunotherapy.

Hypothesis: We hypothesized that pre-treatment with curcumin acts as an immunomodulatory sensitizer that downregulates PD-L1 and TGF-β, thereby restoring CTL lytic machinery (Perforin, Granzyme B, and IFN-γ) and synergistically (CI<1.0) accelerating p53/Caspase-3-dependent apoptosis in cervical cancer cells (HeLa/SiHa) compared to either monotherapy.

Methods: An in vitro true experimental design was conducted using independent biological triplicates (n=3). Cervical cancer cells (HeLa/SiHa) were pre-treated with curcumin (IC 50 dose determined by CCK-8 assay) for 24 hours prior to co-culturing with human CD8+ CTLs (isolated via MACS) at an Effector:Target (E:T) ratio of 5:1. Cell viability and apoptosis rates were quantified using Annexin V-FITC/PI flow cytometry. Surface PD-L1, intracellular p53, and Cleaved Caspase-3 were measured by flow cytometry and Western Blotting. Soluble TGF-β, Perforin, Granzyme B, and IFN-γ levels in culture supernatants were measured using Sandwich ELISA. Pharmacological synergy was evaluated using Chou-Talalay's Combination Index (CI) algorithm via CompuSyn software.

Results: Combinatorial treatment demonstrated strong synergistic cytotoxicity (CI=0.42), yielding significantly higher total apoptosis (78.4%) than curcumin (32.1%) or CTL (41.2%) monotherapies ($p<0.001$). Curcumin pre-treatment markedly downregulated surface PD-L1 and soluble TGF-β ($p<0.01$). Reversing this immunosuppressive barrier restored CTL effector function, causing a significant surge in Perforin, Granzyme B, and IFN-γ release ($p<0.001$). Consequently, boosted CTL lytic activity synchronized with HPV-E6 suppression, reactivating p53 and accelerating Cleaved Caspase-3 execution ($p<0.001$).

Conclusion: Curcumin acts as a potent immunomodulatory sensitizer that reverses the immunosuppressive microenvironment of cervical cancer cells, thereby synergistically boosting the lytic capacity of adoptive CTLs. Dual targeting of intrinsic apoptotic pathways (p53/Caspase-3) and immune checkpoint blockade (PD-L1/TGF-β) provides a compelling translational rationale for novel phyto-immunotherapeutic combination regimens in advanced cervical cancer.

Keywords: Curcumin; Adoptive CTL Therapy; Cervical Cancer; Apoptosis; Immune Checkpoint; Synergy Index.

3.15. Churriyyatul Anam

Abstract

Background: Ischemic stroke is one of the leading causes of mortality and long-term disability worldwide. Cerebral ischemia triggers oxidative stress, inflammation, blood-brain barrier disruption, neuronal apoptosis, and infarct expansion. Previous experimental studies demonstrated that glutathione supplementation significantly reduced matrix metalloproteinase-9 (MMP-9) levels and infarct area in Wistar rat models of ischemic stroke. In another study, hypoxia-conditioned mesenchymal stem cell (MSC) secretome increased vascular endothelial growth factor (VEGF) expression, reduced glial fibrillary acidic protein (GFAP) expression, and significantly decreased cerebral infarct area.

Objective: To summarize previous experimental evidence and propose the scientific rationale for combining MSC-derived secretome and glutathione as a multi-target neuroprotective strategy for ischemic stroke.

Methods: This poster reviews findings from two previous experimental animal studies evaluating glutathione supplementation and hypoxia-conditioned MSC secretome therapy in rodent models of ischemic stroke. The biological mechanisms of both therapies were integrated to identify their potential complementary neuroprotective effects.

Results: Previous studies demonstrated that glutathione reduced oxidative stress, suppressed MMP-9 activity, and significantly decreased infarct area compared with the control group. Hypoxia-conditioned MSC secretome promoted neuroprotection by increasing VEGF expression, reducing GFAP expression, and decreasing cerebral infarction. These findings indicate that both therapies target different but complementary molecular pathways involved in ischemic brain injury.

Conclusion: Based on the available evidence, the combination of MSC-derived secretome and glutathione represents a promising multi-target therapeutic strategy for ischemic stroke by simultaneously modulating oxidative stress, inflammation, angiogenesis, and neuronal survival. Further experimental studies are required to verify the efficacy, safety, and potential synergistic effects of this combination before clinical application.

Keywords: Ischemic stroke; mesenchymal stem cell secretome; glutathione; neuroprotection; infarct area; MMP-9; VEGF; GFAP.