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Therapeutic Potential of iPSC-Derived Extracellular Vesicles in Dermatology: Applications and Challenges

Mini Review

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Author Details

Hao Yun Chang

Department of Family Medicine, Renai Branch,Taiwan

*Corresponding author

Hao Yun Chang, Department of Family Medicine, Renai Branch, Taipei City Hospital, Taipei City, Taiwan

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Abstract

Extracellular vesicles (EVs), including exosomes, microvesicles, and apoptotic bodies, are critical players in cellular communication and have significant potential in dermatology. Induced pluripotent stem cell (iPSC)-derived EVs, particularly exosomes, offer a promising avenue for skin regeneration and treatment of dermatological conditions. iPSCs, with their ability to differentiate into any cell type, provide a scalable and personalized source of EVs. These iPSC-derived extracellular vesicles demonstrate superior anti-inflammatory and regenerative properties compared to those from other cell sources. They show potential in treating a range of skin issues, including chronic wounds, scars, inflammatory diseases, and cosmetic concerns. Despite their promise, challenges such as low production yield, stability, and delivery efficiency must be addressed to fully harness their therapeutic benefits. This review highlights the current applications, mechanisms, and future directions of iPSC-derived EVs in dermatology, emphasizing their transformative potential in skin health and disease management.

Introduction

Extracellular vesicles (EVs) are nano-sized vesicles secreted by cells that play a crucial role in intercellular communication by transporting proteins, nucleic acids, and lipids. EVs are classified into three subtypes: exosomes, microvesicles, and apoptotic bodies, with exosomes receiving the most attention due to their involvement in tissue repair and immune modulation[1,2]. Induced pluripotent stem cell (iPSC)-derived EVs, especially exosomes, are emerging as promising tools in dermatology for skin regeneration and therapeutic interventions. iPSCs, first discovered by Yamanaka, can be derived from somatic cells and have the ability to differentiate into any cell type, offering personalized and regenerative therapies for various skin conditions[3-6].

Subtypes of Extracellular Vesicles and Their Role in Skin Regeneration

The three subtypes of EVs differ in size, origin, and function[1,2]:

a. Exosomes (30-150nm) are formed within multivesicular bodies and released via fusion with the plasma membrane. They have gained recognition for transporting bioactive molecules that influence processes like immune modulation and tissue repair.

b. Microvesicles (100-1,000nm) bud from the plasma membrane and are involved in cell signaling and inflammation. However, their role in dermatology is less understood compared to exosomes.

c. Apoptotic bodies (1-5μm) form during programmed cell death and mainly contain cellular debris, playing a minimal role in therapeutic applications.

Exosomes derived from skin cells and stem cells have demonstrated the ability to promote tissue regeneration by transporting growth factors and cytokines that aid in wound healing, angiogenesis, and immune modulation. This makes exosomes valuable in treating conditions such as scars, wounds, and inflammatory skin diseases[4].

iPSC-Derived EVs in Skin Therapy

iPSC-derived EVs have unique advantages over EVs from other cell sources like mesenchymal stem cells (MSCs). iPSCs provide a scalable, renewable source of EVs with consistent production, while MSC-derived EVs face limitations such as donor variability and finite expansion potential[7]. iPSC-EVs possess anti-inflammatory and pro-regenerative properties, making them more effective in preclinical models of wound healing and inflammation resolution. They also reduce skin aging markers and promote collagen synthesis, demonstrating potential in anti-aging and cosmetic applications[8].

Applications of iPSC-EVs in Dermatology

iPSC-derived EVs have shown promise in several areas of dermatology[9,10]:

Wound Healing

iPSC-EVs enhance tissue repair by promoting collagen production, cell proliferation, and angiogenesis, particularly in chronic wounds like diabetic ulcers.

Scar Treatment

iPSC-EVs support tissue remodeling and reduce fibrosis in hypertrophic scars and keloids, influencing collagen synthesis and cell behavior.

Inflammatory Skin Diseases

In conditions such as psoriasis and eczema, iPSC-EVs modulate immune responses and reduce inflammation, aiding tissue repair and symptom relief.

Pigmentation Disorders

iPSC-EVs have potential in treating disorders like vitiligo by regulating melanocyte activity and normalizing pigment distribution.

Cosmetic Applications

iPSC-EVs improve skin texture and rejuvenation by increasing collagen and elastin production, reducing signs of aging such as wrinkles and fine lines.

Challenges in iPSC-EV Applications

Despite their potential, several challenges must be addressed to optimize the use of iPSC-derived EVs[11]:

Production Yield

Current methods for iPSC-EV production result in low yields, limiting scalability. Techniques to enhance exosome production, such as chemical treatments, require further refinement.

Stability and Storage

iPSC-EVs are prone to aggregation, which can reduce their efficacy. Freezing at -20°C to −80°C helps preserve their cargo, but improved storage methods are needed to ensure long-term stability.

Delivery Efficiency

Ensuring that iPSC-EVs are effectively delivered to target cells while maintaining their bioactive properties remains a challenge. Strategies to improve delivery efficiency, such as targeting specific tissues, are needed to enhance their therapeutic impact.

Conclusion

iPSC-derived extracellular vesicles (iPSC-EVs) represent a promising frontier in dermatological therapies, particularly for skin regeneration, wound healing, and cosmetic applications. Their ability to modulate immune responses, reduce inflammation, and promote tissue repair positions them as a powerful tool in treating skin conditions such as scars, chronic wounds, and inflammatory diseases. However, challenges such as optimizing production, improving storage stability, and enhancing delivery efficiency must be addressed to fully realize their clinical potential. Continued research and technological advancements will be essential in integrating iPSC-EVs into future dermatological treatments.

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