

Letter to Editor

## Exosome therapy in atopic dermatitis – A way to look forward

Nidhi Sharma<sup>1</sup>, Farhat Khan<sup>2</sup>, Priyadarshini Sahu<sup>3</sup>

<sup>1</sup>Department of Dermatology, Gurgaon, Skin Health Clinic, Gurgaon, Haryana, <sup>2</sup>Department of Dermatology, Topiwala National Medical College, Mumbai, Maharashtra, <sup>3</sup>Department of Dermatology, Dr Bansal Skin “n” Laser Center, Chandigarh, India.

Sir,

Exosomes contain lipids, nucleic acids, and proteins and are nanosized vesicles. It acts as a communicating channel between the cells and mediate membrane transport. Exosomes are released by almost every cell of the body and are released in different body fluids and in the cultured cells.<sup>[1]</sup> Because of this property, they are considered as bio-markers for the various treatments including aging and several chronic inflammatory diseases include atopic dermatitis (AD) and eczema. Herein, we discuss about the use of exosome therapy in AD.

Lipid bi-layered vesicles are called as extracellular vesicles which are released by almost every cell of the body in the extracellular space. It is divided into apoptotic bodies, that is, 500–2000 nm in diameter, microvesicles, that is, 200–1000 nm in diameter and exosomes, that is, 30–200 nm in diameter.<sup>[2]</sup> They are the nano-sized vesicles carrying the ability to travel in between different cells and deliver their contents, which constitutes lipids, proteins, and nucleic acids. Since they carry such unique property, exosomes were thought they can be used for various diseases as an intriguing cell-free therapy.

Multiple treatment options for AD were suggested but they are associated with various side effects. This limit us from using many topical and oral therapies for the longer time. Hence, there is an unavailing need to come up with some novel therapies which is effective and safe for AD. Therefore, the introduction of exosomes therapy in the AD can benefit the patients.

Initially, exosomes were considered as metabolic byproducts of cells and they help discarding off all the cellular waste from the body,<sup>[3]</sup> but now newer studies have tracked down that they serve as an essential mediators of intracellular communication by transferring genetic materials such as mRNA, microRNA, and DNA and proteins.<sup>[4]</sup> Recent study by Lai *et al.* gave the evidence that mesenchymal stem cells (MSCs)-derived exosomes (MSC-exosomes) molecules helps

in tissue regeneration and plays an important role in the various diseases.<sup>[5]</sup>

AD is an allergic response to various stimuli. Multiple studies were conducted that showed this allergic response can be subdue by MSCs derived from bone marrow or human umbilical cord blood by multiple targets modulation.<sup>[6]</sup> Nonetheless, there remedial effects were not satisfactory. It causes potential malignant effect, poor engraftment efficiency, non-specific differentiation, unwanted immune responses, and difficulty of quality control and short half-life before administration.<sup>[7]</sup> Exosomes carries a great property of not replicating. Therefore, when these molecules are used in cancer therapy, this potentially reduces the risk of tumor formation. Sterilizing the exosomes can easily be done by filtration. The shelf-life of exosomes is more lasting than cells themselves. As they are tiny molecules, they can penetrate the blood vessels with ease and circulate throughout the body and reaches sites of injury. In addition, even when the exosomes are repetitively administered in a long run, they have not bring forth any toxic effects.<sup>[8]</sup>

Cho *et al.*<sup>[9]</sup> found the therapeutic effect of exosomes in mouse model, obtained from human adipose tissue-derived mesenchymal stem cell-derived exosomes (ASC-exosomes) on AD. He found that there was significant decrease in the AD symptoms, marked reduction in the serum immunoglobulin E levels, significant reduction in eosinophils numbers although carrying no effect on other cells like neutrophils or white blood cells. It also reduced the infiltrated mast cells and reduced the up-regulated mRNA levels of interleukin (IL)-4, IL-31, IL-23, and tumor necrosis factor alpha in the skin lesion analyzed by the quantitative real-time polymerase chain reaction. Therefore, ASC-exosomes can be effectively used for defective epidermal barrier repair.

AD is primarily the dysfunction of the skin barrier and the immune response to the environment. Defective keratinocyte differentiation causes decreased levels of antimicrobial peptide, ceramide, and filaggrin. With the administration of

\*Corresponding author: Priyadarshini Sahu, Department of Dermatology, Dr Bansal Skin “n” Laser Center, Chandigarh, India. [supriyadarshini1986@gmail.com](mailto:supriyadarshini1986@gmail.com)

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the subcutaneous ASC-exosomes, studies showed that there was effective increase the production of very-long acyl chain ceramide by a *de novo* synthesis pathway along with the sphingoid bases including sphingosine and sphingosine-1-phosphate.<sup>[10]</sup>

In conclusion, we want to highlight the potential use of the exosomes therapy in skin conditions. Exosomes significantly cause downregulation of the inflammatory markers proofed by many studies conducted in the recent times. Altogether, studies that have been done on the use of exosomes therapy in various chronic inflammatory skin diseases are somewhat superficial, and further research is required to elucidate the roles of exosomes. To make a point that the use of exosomes therapy in humans are lagging behind and various studies and trials are required to find out its efficacy and safety. We are hoping that these tiny molecules will provide wonders in the coming times for the various treatments.

#### Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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#### Conflicts of interest

There are no conflicts of interest.

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