

Authors/Year of Publication	Level of Evidence (I-VI) *	Subject n=	Type of Study	Proposed Mechanism of Action	Outcome
Hu et al. ¹³ (2020)	N/A**	Mouse (n= 4)	Animal study	DP spheroid-exos promoted development of HFs via miR-218-5p-mediated β -catenin regulation (downregulated SFRP2, a WNT signaling inhibitor)	Promoted hair regeneration
Zhou et al. ¹⁴ (2018)	N/A**	Human ORSCs (n= N/A)	In-vitro study	DPC-exos upregulated β -catenin and Shh levels	Promoted hair follicle growth and development
		Mouse (n= 12)	Animal study		
Kwack et al. ⁴⁰ (2019)	N/A**	Human hair follicles (n= N/A)	In-vitro study	DPC-exos promoted hair growth and regeneration by regulating the activity of follicular dermal and epidermal cells	Promoted hair growth and regeneration, prevention of hair loss
		Mouse (n= N/A)	Animal study		

Yan et al. ⁴⁴ (2019)	N/A**	Cashmere goat HFSCs (n= N/A)	In-vitro study	Overexpression of miR-22-5p in DPC-exos inhibited HFSCs proliferation by targeting LEF1 gene	Regulated hair growth
Ogawa et al. ⁴⁵ (2021)	N/A**	Mouse (n= 18)	Animal study	Fistein-treated-HaCaT cell-derived exos promoted HFSCs activity via activating β -catenin	Promoted hair growth
Yang et al. ⁴⁶ (2019)	N/A**	Mouse (n= N/A)	Animal study	MSC-exos delivered through microneedle-based approach provided a sustained delivery of HFSCs activators, therefore enhancing the exosomes' effects in hair regeneration	Promoted hair regeneration and pigmentation
Huh and Kwon ⁴⁷ (2019)	N/A (abstract)	-	In-vitro study	MSC-exos stimulated proliferation of HFs, accelerated telogen-anagen progression, and protected HFs from ROS and androgen	Increased hair thickness and density
		Human (n= 20)	Pilot study		

*Per American Society of Plastic Surgeons Rating Levels of Evidence and Grading Recommendations: Evidence Rating Scale for Therapeutic Studies.⁵ **Animal/laboratory studies are considered not ratable in American Society of Plastic Surgeons Rating Levels of Evidence and Grading

Recommendations pyramid scheme.

Abbreviations: human keratinocyte (HaCaT), hair follicle stem cells (HFSCs), dermal papilla-derived exosomes (DPC-exos), dermal papilla spheroid-derived exosomes (DP spheroid-exos), mesenchymal stem cell-derived exosomes (MSC-exos), dermal papilla (DP), dermal papilla cells (DPCs), hair follicles (HFs), keratinocyte growth factor (KGF), hepatocyte growth factor (HGF), insulin-like growth factor 1 (IGF-1), secreted frizzled-related protein 2 (SFRP2), Wingless-related integration site (WNT), outer root sheath cells (ORSCs), lymphoid enhancer binding factor 1 (LEF1), reactive oxygen species (ROS), sonic hedgehog (Shh)

Table, Supplementary Digital Content 3. A table that summarizes the mechanism of exosomes in hair restoration.