5.
BÖLÜM

Wharton Jölesi Mezenkimal Kök Hücre Eksozomlarının Klinik Hastalıklarda Kullanımı

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Eksozomlar endotelden, fibroblast ve kanser hücrelerine kadar bilinen tüm hücreler tarafından ekstraselüler ortama salınan, veziküler yapıda kesecikler-dir (1). Hücreler arası iletişim ve genetik materyal transferi gibi ana görevlerin yanında inflamasyon, anjiogenez ve immünolojik yanıtın düzenlenmesinde de rol almalarına rağmen, görevleri tam olarak aydınlatılmış değildir (2,3). Bu nanokeseciklerin içeriği köken aldığı hücre tipine göre değişmektedir. Kanser kök hücre kökenli eksozomlar bilhassa tümör oluşumu için mikroçevre düzenlemesi yaparken mezenkimal kök hücrelerden salgılanan eksozomların tedavi edici özellikleri baskındır. Son yıllarda özellikle kronik hastalıkların tedavisi başta olmak üzere pek çok hastalığın tedavisinde eksozom kullanımı denenmektedir. Mezenkimal kök hücre eksozomları ise bu tedaviler içinde en çok tercih edilen ajanlar olmuştur. Umbilikal kord wharton jölesi mezenkimal kök hücreleri (WJ-MKH) temini kolay, eldesi ağrısız, etik açıdan problem oluşturmayan aynı zamanda HLA matchde sıkıntı yaşanmayan hücrelerdir (4). WJ-MKH'den elde edilen eksozomlar da yine aynı avantajlara sahip tedavi edici kapasitesi yüksek olan biyoaktif ajanlardır.

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KAYNAKÇA

1. Théry C, Zitvogel L, Amigorena S. Exosomes: composition, biogenesis and function. Nat Rev Immunol 2002; 2:569-79.
2. Simons M, Raposo G. Exosomes-vesicular carriers for intercellular communication. Curr Opin Cell Biol 2009; 21:575-81.
3. Février B, Raposo G. Exosomes: endosomal-derived vesicles shipping extracellular messages. Curr Opin Cell Biol 2004; 16:415-21.
4. Ding D. C., Chang Y., Shyu W., Lin S., Human Umbilical Cord Mesenchymal Stem Cells: A New Era for Stem Cell Therapy 2015; Cell Transplantation 24: 339–347.
5. C. Olver and M. Vidal, "Proteomic analysis of secreted exosomes," Sub-Cellular Biochemistry, vol. 43, pp. 99–131, 2007.
6. S. Keller, M. P. Sanderson, A. Stoeck, and P. Altevogt, "Exosomes: from biogenesis and secretion to biological function," Immunology Letters, vol. 107, no. 2, pp. 102–108, 2006.
7. Sun L., Xu R., Sun X. Et al., Safety evaluation of exosomes derived from human umbilical cord mesenchymal stromal cell, Cytotherapy, 2016; 18: 413–422
8. Anderson JD, Johansson HJ, Graham CS, et al. Comprehensive proteomic analysis of mesenchymal stem cell exosomes reveals modulation of angiogenesis via nuclear factor-kappab signaling. Stem Cells. 2016; 34:601-613
9. Zhang B., Shen L., Shi H. et al., Exosomes from Human Umbilical Cord Mesenchymal Stem Cells: Identification, Purification, and Biological Characteristics, Vol 2016, Article ID 1929536, 11 pages Stem Cells International
10. Rohde E., Pachler K., Gimona M., Manufacturing and characterization of extracellular vesicles from umbilical cord–derived mesenchymal stromal cells for clinical testing, Cytotherapy, Vol 21, June 2019, Pages 581-592
11. Wang X-L., Zhao Y-Y., Sun L. et al., Exosomes derived from human umbilical cord mesenchymal stem cells improve myocardial repair via upregulation of Smad7, International Journal of Molecular Medicine, February 2018, Pages: 3063-3072
12. Zhao Y., Sun X., Cao W. et al., Exosomes Derived from Human Umbilical Cord Mesenchymal Stem Cells Relieve Acute Myocardial Ischemic Injury, Stem Cells International, 2015, Vol 2015, https://doi.org/10.1155/2015/761643
13. Arslan F., Lai R. C., Smeets M. B., et al., Mesenchymal stem cell-derived exosomes increase ATP levels, decrease oxidative stress and activate PI3K/Akt pathway to enhance myocardial viability and prevent adverse remodeling after myocardial ischemia/reperfusion injury, Stem Cell Research Vol 10, May 2013, Pages 301-312
14. Ma J., Zhao Y., Sun L. et al., Exosomes Derived from Akt-Modified Human Umbilical Cord Mesenchymal Stem Cells Improve Cardiac Regeneration and Promote Angiogenesis via Activating Platelet-Derived Growth Factor D, Tissue-Specific Progenitor and Stem Cells, September 2016, Vol 6, Pages 51-59
15. Northway W., Rosan C., Porter D. Y., Pulmonary Disease Following Respirator Therapy of Hyaline-Membrane Disease — Bronchopulmonary Dysplasia, The New England Journal of Medicine, Feb. 1967; 276:357-368
16. Willis G. R., Fernandez-Gonzalez A., Anastas J., et al., Mesenchymal Stromal Cell Exosomes Ameliorate Experimental Bronchopulmonary Dysplasia and Restore Lung Function through Macrophage Immunomodulation, American Journal of Respiratory and Critical Care Medicine, Jan 2018, Vol 197, Pages 104–116.

17. Chaubey S., Thueson S., Ponnalagu D. et al., Early gestational mesenchymal stem cell secretome attenuates experimental bronchopulmonary dysplasia in part via exosome-associated factor TSG-6, Stem Cell Research & Therapy, June 2018, 9:173
18. Hao Y., Ran Y., Lu B. et al., Therapeutic Effects of Human Umbilical Cord–Derived Mesenchymal Stem Cells on Canine Radiation-Induced Lung Injury, International Journal of Radiation Oncology*Biology*Physics Vol 102, October 2018, Pages 407-416.
19. Xian P., Hei Y., Wang R. et al., Mesenchymal stem cell-derived exosomes as a nanotherapeutic agent for amelioration of inflammation-induced astrocyte alterations in mice, Theranostics, Aug 2019; 9(20): Pages 5956–5975
20. Chudickova M., Vackova I., Urdzikova L.M. et al., The Effect of Wharton Jelly-Derived Mesenchymal Stromal Cells and Their Conditioned Media in the Treatment of a Rat Spinal Cord Injury, Int. J. Mol. Sci. 2019, 20(18), 4516.
21. Joerger-Messerli M., Oppliger B., Spinelli M. et al., Extracellular Vesicles Derived from Wharton's Jelly Mesenchymal Stem Cells Prevent and Resolve Programmed Cell Death Mediated by Perinatal Hypoxia-Ischemia in Neuronal Cells, Cell Transplantation, March 2018, Vol. 27 Pages 168–180.
22. Ding M., Shen Y., Wang P. et al., Exosomes Isolated From Human Umbilical Cord Mesenchymal Stem Cells Alleviate Neuroinflammation and Reduce Amyloid-Beta Deposition by Modulating Microglial Activation in Alzheimer's Disease, Neurochemical Research, Sep 2018, Vol 43, Pages 2165–2177,
23. Joerger-Messerli M., Spinelli M., Oppliger B. et al., Neuro-protective and -regenerative effects of exosomes derived from Wharton's jelly mesenchymal stem cells, Jan 2017, Vol 216, Pages 236-237
24. Zhao G., Liu Z., Zuo K. et al., MSC-derived exosomes attenuate cell death through suppressing AIF nucleus translocation and enhance cutaneous wound healing, Stem Cell Research & Therapy, 2020, 11:174
25. Bakhtyar N., Jeschke M. G., Herer E. et al., Exosomes from acellular Wharton's jelly of the human umbilical cord promotes skin wound healing, Stem Cell Research & Therapy, July 2018, 9, Art. Number:193
26. Li X., Liu L., Yang J. et al., Exosome Derived From Human Umbilical Cord Mesenchymal Stem Cell Mediates MiR-181c Attenuating Burn-induced Excessive Inflammation, June 2016, Volume 8, Pages 72-82.
27. Liu J., Yan Z., Yang F. et al., Exosomes Derived from Human Umbilical Cord Mesenchymal Stem Cells Accelerate Cutaneous Wound Healing by Enhancing Angiogenesis through Delivering Angiopoietin-2, Stem Cell Reviews and Reports, 2020, https://doi.org/10.1007/s12015-020-09992-7
28. Zhou J., Tan X., Tan Y. et al., Mesenchymal Stem Cell Derived Exosomes in Cancer Progression, Metastasis and Drug Delivery, J Cancer. Aug 2018; 9, Pages 3129–3137
29. Ghorbani S., Maleki M., Inhibition of Cervical Cancer Cell Line Hela by Human Wharton's Jelly Stem Cells Through Induction of Apoptosis, Gene, Cell and Tissue: 2020, 7; e99206
30. Ding Y., Cao F., Sun H. et al., Exosomes derived from human umbilical cord mesenchymal stromal cells deliver exogenous miR-145-5p to inhibit pancreatic ductal adenocarcinoma progression, Cancer Letters Vol 442, February 2019, Pages 351-361