

DAFTAR PUSTAKA

- Alexander, M., Hu, R., Runtsch, M.C., Kagele, D.A., Mosbrugger, T.L., Tolmachova, T., Seabra, M.C., Round, J.L., Ward, D.M., O'Connell, R.M., 2015. Exosome-delivered microRNAs modulate the inflammatory response to endotoxin. *Nat Commun* 6. <https://doi.org/10.1038/ncomms8321>
- BPOM, 2022. Peraturan Badan Pengawas Obat dan Makanan Nomor 10 Tahun 2022 tentang Pedoman Uji Toksisitas Praktikum Secara In Vivo.
- Brai, A., Poggialini, F., Vagaggini, C., Pasqualini, C., Simoni, S., Francardi, V., Dreassi, E., 2023. *Tenebrio molitor* as a Simple and Cheap Preclinical Pharmacokinetic and Toxicity Model. *Int J Mol Sci* 24. <https://doi.org/10.3390/ijms24032296>
- Burn, C.C., Peters, A., Day, M.J., Mason, G.J., n.d. Long-term effects of cage-cleaning frequency and bedding type on laboratory rat health, welfare, and handleability: a cross-laboratory study.
- Chen, J., Liu, S., Zou, J., Wang, Y., Ge, H., Hui, Y., Huang, S., Li, W., Na, W., Huang, X., Bai, L., Huang, Y., Qu, D., 2025. Comparison of efficacy of exosomes derived from human umbilical cord blood mesenchymal stem cells in treating mouse acute lung injury via different routes. *Front Pediatr* 13. <https://doi.org/10.3389/fped.2025.1560915>
- Choi, H., Kim, M.Y., Kim, D.H., Yun, H., Oh, B.K., Kim, S. Bin, Song, I.H., Park, H.S., Kim, S.E., Park, C., Choi, C., 2022. Quantitative Biodistribution and Pharmacokinetics Study of GMP-Grade Exosomes Labeled with⁸⁹Zr

Radioisotope in Mice and Rats. *Pharmaceutics* 14.

<https://doi.org/10.3390/pharmaceutics14061118>

Costa, E.L., Milhomem, A.C., De Moura Filho, R.M., Lino, R.S., 2016. Polymethyl methacrylate (Linnea Safe) causes local inflammatory response after intramuscular implant in BALB/c mice but it is not observed in distant organs. *J Bras Patol Med Lab* 52, 400–406. <https://doi.org/10.5935/1676-2444.20160058>

Dashnyam, K., Jin, G.Z., Kim, J.H., Perez, R., Jang, J.H., Kim, H.W., 2017. Promoting angiogenesis with mesoporous microcarriers through a synergistic action of delivered silicon ion and VEGF. *Biomaterials* 116, 145–157. <https://doi.org/10.1016/j.biomaterials.2016.11.053>

De Coppi, P., Grikscheit, T.C., 2021. Regeneration and tissue engineering: How pediatric surgeons contributed to building a new field to change the future of medicine. *Semin Pediatr Surg* 30. <https://doi.org/10.1016/j.sempedsurg.2021.151018>

Deguchi, K., Zambaiti, E., De Coppi, P., 2023. Regenerative medicine: current research and perspective in pediatric surgery. *Pediatr Surg Int*. <https://doi.org/10.1007/s00383-023-05438-6>

Ellistasari, E.Y., Kariosentono, H., Purwanto, B., Wasita, B., Riswiyant, R.C.A., Pamungkasari, E.P., Soetrisno, S., 2022. Exosomes Derived from Secretome Human Umbilical Vein Endothelial Cells (Exo-HUVEC) Ameliorate the Photo-Aging of Skin Fibroblast. *Clin Cosmet Investig Dermatol* 15, 1583–1591. <https://doi.org/10.2147/CCID.S371330>

- Goetz, R., Mohammadi, M., 2013. Exploring mechanisms of FGF signalling through the lens of structural biology. *Nat Rev Mol Cell Biol.* <https://doi.org/10.1038/nrm3528>
- Gu, Z., Yin, Z., Song, P., Wu, Y., He, Y., Zhu, M., Wu, Z., Zhao, S., Huang, H., Wang, H., Tong, C., Qi, Z., 2022. Safety and biodistribution of exosomes derived from human induced pluripotent stem cells. *Front Bioeng Biotechnol* 10. <https://doi.org/10.3389/fbioe.2022.949724>
- Ha, D.H., Kim, S.D., Lee, J., Kwon, H.H., Park, G.H., Yang, S.H., Jung, J.Y., Lee, J.H., Park, S.R., Youn, J., Lee, S.H., Kim, J.E., Lim, J., Lee, H.K., Cho, B.S., Yi, Y.W., 2020. Toxicological evaluation of exosomes derived from human adipose tissue-derived mesenchymal stem/stromal cells. *Regulatory Toxicology and Pharmacology* 115. <https://doi.org/10.1016/j.yrtph.2020.104686>
- Hajian, B., De Backer, J., Vos, W., Van Holsbeke, C., Ferreira, F., Quinn, D.A., Hufkens, A., Claes, R., de Backer, W., 2016. Pulmonary vascular effects of pulsed inhaled nitric oxide in COPD patients with pulmonary hypertension. *International Journal of COPD* 11, 1533–1541. <https://doi.org/10.2147/COPD.S106480>
- Harischandra, D.S., Ghaisas, S., Rokad, D., Kanthasamy, A.G., 2017. Exosomes in toxicology: Relevance to chemical exposure and pathogenesis of environmentally Linked Diseases. *Toxicological Sciences.* <https://doi.org/10.1093/toxsci/kfx074>

- Hassaan, N.A., Mansour, H.A., 2024. Exosomal therapy is a luxury area for regenerative medicine. *Tissue Cell*. <https://doi.org/10.1016/j.tice.2024.102570>
- He, S., Xia, T., Wang, H., Wei, L., Luo, X., Li, X., 2012. Multiple release of polyplexes of plasmids VEGF and bFGF from electrospun fibrous scaffolds towards regeneration of mature blood vessels. *Acta Biomater* 8, 2659–2669. <https://doi.org/10.1016/j.actbio.2012.03.044>
- Hou, Z., Qin, X., Hu, Y., Zhang, X., Li, G., Wu, J., Li, J., Sha, J., Chen, J., Xia, J., Wang, L., Gao, F., 2019. Longterm Exercise-Derived Exosomal miR-342-5p: A Novel Exerkine for Cardioprotection. *Circ Res* 124, 1386–1400. <https://doi.org/10.1161/CIRCRESAHA.118.314635>
- Jalabert, A., Vial, G., Guay, C., Wiklander, O.P.B., Nordin, J.Z., Aswad, H., Forterre, A., Meugnier, E., Pesenti, S., Regazzi, R., Danty-Berger, E., Ducreux, S., Vidal, H., El-Andaloussi, S., Rieusset, J., Rome, S., 2016. Exosome-like vesicles released from lipid-induced insulin-resistant muscles modulate gene expression and proliferation of beta recipient cells in mice. *Diabetologia* 59, 1049–1058. <https://doi.org/10.1007/s00125-016-3882-y>
- Jie, H.H., Lu, W.H., 2025. Exosome Secretion Regulation in Mice with Acute Lung Injury. *Journal of Inflammation Research* 18, 7151–7165. <https://doi.org/10.2147/JIR.S506693>
- Kamerkar, S., Lebleu, V.S., Sugimoto, H., Yang, S., Ruivo, C.F., Melo, S.A., Lee, J.J., Kalluri, R., 2017. Exosomes facilitate therapeutic targeting of oncogenic KRAS in pancreatic cancer. *Nature* 546, 498–503. <https://doi.org/10.1038/nature22341>

- Kandasamy, M., Anusuyadevi, M., Aigner, K.M., Unger, M.S., Kniewallner, K.M., Bessa de Sousa, D.M., Altendorfer, B., Mrowetz, H., Bogdahn, U., Aigner, L., 2020. TGF- β signaling: A therapeutic target to reinstate regenerative plasticity in vascular dementia? *Aging Dis.* <https://doi.org/10.14336/AD.2020.0222>
- Kang, M., Jordan, V., Blenkiron, C., Chamley, L.W., 2021. Biodistribution of extracellular vesicles following administration into animals: A systematic review. *J Extracell Vesicles.* <https://doi.org/10.1002/jev2.12085>
- Keshtkar, S., Azarpira, N., Ghahremani, M.H., 2018. Mesenchymal stem cell-derived extracellular vesicles: Novel frontiers in regenerative medicine. *Stem Cell Res Ther.* <https://doi.org/10.1186/s13287-018-0791-7>
- Kimiz-Gebologlu, I., Oncel, S.S., 2022. Exosomes: Large-scale production, isolation, drug loading efficiency, and biodistribution and uptake. *Journal of Controlled Release.* <https://doi.org/10.1016/j.jconrel.2022.05.027>
- Kocherova, I., Bryja, A., Mozdziak, P., Volponi, A.A., Dyszkiewicz-Konwińska, M., Piotrowska-Kempisty, H., Antosik, P., Bukowska, D., Bruska, M., Iżycki, D., Zabel, M., Nowicki, M., Kempisty, B., 2019. Human umbilical vein endothelial cells (HUVECs) co-culture with osteogenic cells: From molecular communication to engineering prevascularised bone grafts. *J Clin Med.* <https://doi.org/10.3390/jcm8101602>
- Laddha, A.P., Kulkarni, Y.A., 2019. VEGF and FGF-2: Promising targets for the treatment of respiratory disorders. *Respir Med.* <https://doi.org/10.1016/j.rmed.2019.08.003>

- Lee, C., Kim, M.J., Kumar, A., Lee, H.W., Yang, Y., Kim, Y., 2025. Vascular endothelial growth factor signaling in health and disease: from molecular mechanisms to therapeutic perspectives. *Signal Transduct Target Ther.* <https://doi.org/10.1038/s41392-025-02249-0>
- Manca, S., Upadhyaya, B., Mutai, E., Desaulniers, A.T., Cederberg, R.A., White, B.R., Zempleni, J., 2018. Milk exosomes are bioavailable and distinct microRNA cargos have unique tissue distribution patterns. *Sci Rep* 8. <https://doi.org/10.1038/s41598-018-29780-1>
- Mao, A.S., Mooney, D.J., 2015. Regenerative medicine: Current therapies and future directions. *Proc Natl Acad Sci U S A* 112, 14452–14459. <https://doi.org/10.1073/pnas.1508520112>
- Medina-Leyte, D.J., Domínguez-Pérez, M., Mercado, I., Villarreal-Molina, M.T., Jacobo-Albavera, L., 2020. Use of human umbilical vein endothelial cells (HUVEC) as a model to study cardiovascular disease: A review. *Applied Sciences (Switzerland)* 10. <https://doi.org/10.3390/app10030938>
- Mohseni Meybodi, M.A., Nilforoushzadeh, M.A., KhandanDezfully, N., Mansouri, P., 2024. The safety and efficacy of adipose tissue-derived exosomes in treating mild to moderate plaque psoriasis: A clinical study. *Life Sci* 353. <https://doi.org/10.1016/j.lfs.2024.122915>
- Moreira, V.B., Mattaraira, V.G.M., Moura, A.S.A.M.T., 2015. Lifetime Reproductive Efficiency of BALBc Mouse Pairs after an Environmental Modification at 3 Mating Ages. *Journal of the American Association for Laboratory Animal Science* 54, 29–34.

- Ondondo, B., Brennan, C., Nicosia, A., Crome, S.J., Hanke, T., 2013. Absence of systemic toxicity changes following intramuscular administration of novel pSG2.HIVconsv DNA, ChAdV63.HIVconsv and MVA.HIVconsv vaccines to BALB/c mice. *Vaccine* 31, 5594–5601. <https://doi.org/10.1016/j.vaccine.2013.06.068>
- Passmore, M.R., Byrne, L., Obonyo, N.G., See Hoe, L.E., Boon, A.C., Diab, S.D., Dunster, K.R., Bisht, K., Tung, J.P., Fauzi, M.H., Narula, M., Pedersen, S.E., Esguerra-Lallen, A., Simonova, G., Sultana, A., Anstey, C.M., Shekar, K., Maitland, K., Suen, J.Y., Fraser, J.F., 2018. Inflammation and lung injury in an ovine model of fluid resuscitated endotoxemic shock. *Respir Res* 19, 231. <https://doi.org/10.1186/s12931-018-0935-4>
- Patel, S.A., Nilsson, M.B., Le, X., Cascone, T., Jain, R.K., Heymach, J. V., 2023. Molecular Mechanisms and Future Implications of VEGF/VEGFR in Cancer Therapy. *Clinical Cancer Research*. <https://doi.org/10.1158/1078-0432.CCR-22-1366>
- Qiu, P., Zhou, J., Zhang, J., Dong, Y., Liu, Y., 2021. Exosome: The Regulator of the Immune System in Sepsis. *Front Pharmacol*. <https://doi.org/10.3389/fphar.2021.671164>
- Rasouli, M., Alavi, M., D'Angelo, A., Sobhani, N., Roudi, R., Safari, F., 2024. Exploring the dichotomy of the mesenchymal stem cell secretome: Implications for tumor modulation via cell-signaling pathways. *Int Immunopharmacol*. <https://doi.org/10.1016/j.intimp.2024.113265>

- Royo, F., Cossío, U., Ruiz De Angulo, A., Llop, J., Falcon-Perez, J.M., 2019. Modification of the glycosylation of extracellular vesicles alters their biodistribution in mice. *Nanoscale* 11, 1531–1537. <https://doi.org/10.1039/c8nr03900c>
- Shibuya, M., 2011. Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies. *Genes Cancer* 2, 1097–1105. <https://doi.org/10.1177/1947601911423031>
- Song, Y., Zhang, C., Zhang, J., Jiao, Z., Dong, N., Wang, G., Wang, Z., Wang, L., 2019. Localized injection of miRNA-21-enriched extracellular vesicles effectively restores cardiac function after myocardial infarction. *Theranostics* 9, 2346–2360. <https://doi.org/10.7150/thno.29945>
- Ståhl, A. lie, Johansson, K., Mossberg, M., Kahn, R., Karpman, D., 2019. Exosomes and microvesicles in normal physiology, pathophysiology, and renal diseases. *Pediatric Nephrology*. <https://doi.org/10.1007/s00467-017-3816-z>
- Stuelten, C.H., Zhang, Y.E., 2021. Transforming Growth Factor- β : An Agent of Change in the Tumor Microenvironment. *Front Cell Dev Biol*. <https://doi.org/10.3389/fcell.2021.764727>
- Türkeli, A., Yilmaz, Ö., Karaman, M., Kanik, E., Firinci, F., İnan, S., Yüksel, H., 2021. Anti-VEGF treatment suppresses remodeling factors and restores epithelial barrier function through the E-cadherin/ β -catenin signaling axis in experimental asthma models. *Exp Ther Med* 22. <https://doi.org/10.3892/etm.2021.10121>

- Tzavlaki, K., Moustakas, A., 2020. TGF- β signaling. *Biomolecules*.
<https://doi.org/10.3390/biom10030487>
- Wang, C., Bing, A., liu, H., Wang, X., Zhao, J., Lin, H., Jiao, H., 2022. High ambient humidity aggravates ammonia-induced respiratory mucosal inflammation by eliciting Th1/Th2 imbalance and NF- κ B pathway activation in laying hens. *Poult Sci* 101. <https://doi.org/10.1016/j.psj.2022.102028>
- Wei, L., Yan, W., Shah, W., Zhang, Z., Wang, M., Liu, B., Xue, Z., Cao, Y., Hou, X., Zhang, K., Yan, B., Wang, X., 2024. Advancements and challenges in stem cell transplantation for regenerative medicine. *Heliyon*.
<https://doi.org/10.1016/j.heliyon.2024.e35836>
- Xie, Y., Su, N., Yang, J., Tan, Q., Huang, S., Jin, M., Ni, Z., Zhang, B., Zhang, D., Luo, F., Chen, H., Sun, X., Feng, J.Q., Qi, H., Chen, L., 2020. FGF/FGFR signaling in health and disease. *Signal Transduct Target Ther*.
<https://doi.org/10.1038/s41392-020-00222-7>
- Xu, T., Huangfu, B., He, X., Huang, K., 2024. Exosomes as mediators of signal transmitters in biotoxins toxicity: a comprehensive review. *Cell Biol Toxicol*.
<https://doi.org/10.1007/s10565-024-09867-4>
- Yaghoubi, Y., Movassaghpour, A.A., Zamani, M., Talebi, M., Mehdizadeh, A., Yousefi, M., 2019. Human umbilical cord mesenchymal stem cells derived-exosomes in diseases treatment. *Life Sci*.
<https://doi.org/10.1016/j.lfs.2019.116733>

- Yi, Y.W., Lee, J.H., Kim, S.Y., Pack, C.G., Ha, D.H., Park, S.R., Youn, J., Cho, B.S., 2020. Advances in analysis of biodistribution of exosomes by molecular imaging. *Int J Mol Sci*. <https://doi.org/10.3390/ijms21020665>
- Yu, Y., Wang, Q., Wang, C., Shang, L., 2021. Living Materials for Regenerative Medicine. *Engineered Regeneration*. <https://doi.org/10.1016/j.engreg.2021.08.003>
- Zhang, C., Murphy, S. V., Atala, A., 2014. Regenerative medicine in urology. *Semin Pediatr Surg* 23, 106–111. <https://doi.org/10.1053/j.sempedsurg.2014.05.002>
- Zhang, Y., Xu, Y., Zhou, K., Kao, G., Xiao, J., 2021. MicroRNA-126 and VEGF enhance the function of endothelial progenitor cells in acute myocardial infarction. *Exp Ther Med* 23. <https://doi.org/10.3892/etm.2021.11065>
- Zhang, Yanlu, Zhang, Yi, Chopp, M., Zhang, Z.G., Mahmood, A., Xiong, Y., 2020. Mesenchymal Stem Cell–Derived Exosomes Improve Functional Recovery in Rats After Traumatic Brain Injury: A Dose-Response and Therapeutic Window Study. *Neurorehabil Neural Repair* 34, 616–626. <https://doi.org/10.1177/1545968320926164>