

BAB 5

KESIMPULAN DAN SARAN

5.1 Kesimpulan

1. Hidrogel liofilisat sekretom sel punca dari *cord-placental-junction* memberikan skor derajat keratinisasi yang lebih baik pada mencit model luka bakar derajat tiga dibandingkan dengan kelompok negatif dan kelompok standar pada hari ke-7 dan hari ke-14.
2. Hidrogel liofilisat sekretom sel punca dari *cord-placental-junction* memberikan skor perbaikan dermis pada mencit model luka bakar derajat tiga yang signifikan lebih baik dibandingkan dengan kelompok negatif dan kelompok standar hari ke-14 ($p=0,0015$; $p=0,0006$).

5.2 Saran

1. Melakukan studi lebih lanjut pada manusia untuk memastikan efektivitas dan keamanan penggunaan liofilisat sekretom MSC dalam terapi luka bakar.
2. Melakukan studi lebih lanjut mengenai optimasi formulasi hidrogel, terutama dalam hal pengaturan viskositas, stabilitas struktur, dan kompatibilitas dengan sekretom MSC, guna meningkatkan efektivitas dan aplikasi klinisnya.

DAFTAR PUSTAKA

- Alatyyat, S.M., Alasmari, H.M., Aleid, O.A., Abdel-maksoud, M.S., Elsherbiny, N., 2020. Umbilical cord stem cells: Background, processing and applications. *Tissue and Cell* **65**: 101351. <https://doi.org/10.1016/j.tice.2020.101351>
- Altunbek, M., Gezek, M., Gouveia, M.E.T., Camci-Unal, G., 2024. Development of a Sprayable Hydrogel-Based Wound Dressing: An In Vitro Model. *Gels* **10**, 176. <https://doi.org/10.3390/gels10030176>
- Alves, A., Miguel, S.P., Araujo, A.R.T.S., de Jesús Valle, M.J., Sánchez Navarro, A., Correia, I.J., Ribeiro, M.P., Coutinho, P., 2020. Xanthan Gum–Konjac Glucomannan Blend Hydrogel for Wound Healing. *Polymers* **12**: 99. <https://doi.org/10.3390/polym12010099>
- Ansari, P., Akther, S., Khan, J.T., Islam, S.S., Masud, Md.S.R., Rahman, A., Seidel, V., Abdel-Wahab, Y.H.A., 2022. Hyperglycaemia-Linked diabetic foot complications and their management using conventional and alternative therapies. *Applied Sciences* **12**: 11777. <https://doi.org/10.3390/app122211777>
- Arribas-López, E., Zand, N., Ojo, O., Snowden, M.J., Kochhar, T., 2021. The Effect of Amino Acids on Wound Healing: A Systematic Review and Meta-Analysis on Arginine and Glutamine. *Nutrients* **13**, 2498. <https://doi.org/10.3390/nu13082498>
- Arifka, M., Wilar, G., Elamin, K.M., Wathoni, N., 2022. Polymeric Hydrogels as Mesenchymal Stem Cell Secretome Delivery System in Biomedical Applications. *Polymers* **14**: 1218. <https://doi.org/10.3390/polym14061218>
- Arruda, I.F., Amendoeira, M.R.R., Bonifácio, T.F., Raso, C.N. da S., Elidio, H. da S.M., Coelho, J.W.R., da Silva, L.C.C.P., dos Santos, I.B., 2024. Humane Endpoints in Swiss Webster Mice Infected with *Toxoplasma gondii* RH Strain. *Animals* **14**: 1326. <https://doi.org/10.3390/ani14091326>
- auf dem Keller, U., Sabino, F., 2015. Matrix metalloproteinases in impaired wound healing. *Metalloproteinases In Medicine* **1**. <https://doi.org/10.2147/mnm.s68420>
- Baghaie, S., Khorasani, M.T., Zarrabi, A., Moshtaghian, J., 2017. Wound healing properties of PVA/starch/chitosan hydrogel membranes

- with nano Zinc oxide as antibacterial wound dressing material. *Journal of Biomaterials Science, Polymer Edition* **28**: 2220–2241. <https://doi.org/10.1080/09205063.2017.1390383>
- Bahram, M., Mohseni, N., Moghtader, M., 2016. An Introduction to Hydrogels and Some Recent Applications, in: *Emerging Concepts in Analysis and Applications of Hydrogels*. InTech.
- Bari, E., Perteghella, S., Di Silvestre, D., Sorlini, M., Catenacci, L., Sorrenti, M., Marrubini, G., Rossi, R., Tripodo, G., Mauri, P., Marazzi, M., Torre, M.L., 2018. Pilot Production of Mesenchymal Stem/Stromal Freeze-Dried Secretome for Cell-Free Regenerative Nanomedicine: A Validated GMP-Compliant Process. *Cells* **7**: 190. <https://doi.org/10.3390/cells7110190>
- Bian, D., Wu, Y., Song, G., Azizi, R., Zamani, A., 2022. The application of mesenchymal stromal cells (MSCs) and their derivative exosome in skin wound healing: *a comprehensive review*. *Stem Cell Research & Therapy* **13**. <https://doi.org/10.1186/s13287-021-02697-9>
- Beeravolu, N., McKee, C., Alamri, A., Mikhael, S., Brown, C., Perez-Cruet, M., Chaudhry, G.R., 2017. Isolation and characterization of mesenchymal stromal cells from human umbilical cord and fetal placenta. *Journal of Visualized Experiments*. <https://doi.org/10.3791/55224>
- Bjelošević Žiberna, M., Planinšek, O., Ahlin Grabnar, P., 2023. Oral lyophilizates obtained using aggressive drying conditions: Effect of excipients. *Journal of Drug Delivery Science and Technology* **82**: 104379. <https://doi.org/10.1016/j.jddst.2023.104379>
- Bongso, A., Lee, E.H., 2005. *Stem Cells: From Bench to Bedside*. World Scientific.
- Bora, P., Majumdar, A.S., 2017. Adipose tissue-derived stromal vascular fraction in regenerative medicine: a brief review on biology and translation. *Stem Cell Research & Therapy* **8**. <https://doi.org/10.1186/s13287-017-0598-y>
- Bounds, E.J., Khan, M., Kok, S.J., 2023. *Electrical Burns*. StatPearls.
- Boxall, S.A., Jones, E., 2012. Markers for Characterization of Bone Marrow Multipotential Stromal Cells. *Stem Cells International*: 1–12. <https://doi.org/10.1155/2012/975871>

- Cañedo-Dorantes, L., Cañedo-Ayala, M., 2019. Skin Acute Wound Healing: A Comprehensive Review. *International Journal of Inflammation*: 1–15. <https://doi.org/10.1155/2019/3706315>
- Caplan, A.I., 2017. Mesenchymal Stem Cells: Time to Change the Name!. *Stem Cells Translational Medicine* **6**: 1445–1451. <https://doi.org/10.1002/sctm.17-0051>
- Chambers, I., Colby, D., Robertson, M., Nichols, J., Lee, S., Tweedie, S., Smith, A., 2003. Functional Expression Cloning of Nanog, a Pluripotency Sustaining Factor in Embryonic Stem Cells. *Cell* **113**: 643–655. [https://doi.org/10.1016/s0092-8674\(03\)00392-1](https://doi.org/10.1016/s0092-8674(03)00392-1)
- Chappell, J., Dalton, S., 2013. Roles for MYC in the Establishment and Maintenance of Pluripotency. *Cold Spring Harbor Perspectives in Medicine* **3**. <https://doi.org/10.1101/cshperspect.a014381>
- Chen, X., Oppenheim, J.J., Howard, O.M.Z., 2005. BALB/c mice have more CD4+CD25+ T regulatory cells and show greater susceptibility to suppression of their CD4+CD25– responder T cells than C57BL/6 mice. *Journal of Leukocyte Biology* **78**, 114–121. <https://doi.org/10.1189/jlb.0604341>
- Chen, J., Liu, Y., Zhang, J., Liang, H., Li, T., Yan, L., Zhou, L., Shan, L., Wang, H., 2022. External application of human umbilical cord-derived mesenchymal stem cells in hyaluronic acid gel repairs foot wound of type I and type II diabetic rats through paracrine action mode. Research Square Platform LLC
- Chia, R., Achilli, F., Festing, M.F.W., Fisher, E.M.C., 2005. The origins and uses of mouse outbred stocks. *Nature Genetics* **37**: 1181–1186. <https://doi.org/10.1038/ng1665>
- Chogan, F., Chen, Y., Wood, F., Jeschke, M.G., 2022. Skin Tissue Engineering Advances in Burns: A Brief Introduction to the Past, the Present, and the Future Potential. *Journal of Burn Care & Research* **44**: S1–S4. <https://doi.org/10.1093/jbcr/irac127>
- De Giacomo, A.F., Banffy, M.B., ElAttrache, N.S., 2019. Biologics in Orthopaedic Surgery, in: *Biologics in Orthopaedic Surgery. Elsevier*: 27–47.
- Dhaliwal, N.K., Abatti, L.E., Mitchell, J.A., 2019. KLF4 protein stability regulated by interaction with pluripotency transcription factors overrides transcriptional control. *Genes & Development* **33**: 1069–1082. <https://doi.org/10.1101/gad.324319.119>

- Dodda, J.M., Deshmukh, K., Bezuidenhout, D., Yeh, Y.-C., 2023. Hydrogels: Definition, History, Classifications, Formation, Constitutive Characteristics, and Applications, in: *Multicomponent Hydrogels. The Royal Society of Chemistry*: 1–25.
- El Ayadi, A., Jay, J.W., Prasai, A., 2020. Current Approaches Targeting the Wound Healing Phases to Attenuate Fibrosis and Scarring. *International Journal of Molecular Sciences* **21**: 1105. <https://doi.org/10.3390/ijms21031105>
- Espinoza , J.A.G., Aguilar Aragon VB , Ortiz Villalobos EH, Manzano, R.A.G., Antonio, A.B., 2017. Burns: Definition, Classification, Pathophysiology and Initial Approach. *General Medicine: Open Access* 5. <https://doi.org/10.4172/2327-5146>
- Feng, R., Wen, J., 2015. Overview of the roles of Sox2 in stem cell and development. *Biological Chemistry* **396**: 883–891. <https://doi.org/10.1515/hsz-2014-0317>
- Fernández-Guarino, M., Hernández-Bule, M.L., Bacci, S., 2023. Cellular and Molecular Processes in Wound Healing. *Biomedicines* **11**: 2526. <https://doi.org/10.3390/biomedicines11092526>
- Gan, J., Dou, Y., Li, Y., Wang, Z., Wang, L., Liu, S., Li, Q., Yu, H., Liu, C., Han, C., Huang, Z., Zhang, J., Wang, C., Dong, L., 2018. Producing anti-inflammatory macrophages by nanoparticle-triggered clustering of mannose receptors. *Biomaterials* **178**: 95–108. <https://doi.org/10.1016/j.biomaterials.2018.06.015>
- Gargiulo, C., Pham, V.H., Thuy Hai, N., Nguyen, K.C.D., Phuc, P.V., Abe, K., Flores, V., Shiffman, M., 2015. Isolation and Characterization of Multipotent and Pluripotent Stem Cells from Human Peripheral Blood. *Stem Cell Discovery* **5**: 19–32. <https://doi.org/10.4236/scd.2015.53003>
- GBD. 2022. *Review for “The global burden of disease attributable to high fasting plasma glucose in 204 countries and territories, 1990-2019: An updated analysis for the Global Burden of Disease Study 2019”*.
- Goh, M., Du, M., Peng, W.R., Saw, P.E., Chen, Z., 2024. Advancing burn wound treatment: exploring hydrogel as a transdermal drug delivery system. *Drug Delivery* **31**. <https://doi.org/10.1080/10717544.2023.2300945>
- González-González, A., García-Sánchez, D., Dotta, M., Rodríguez-Rey, J.C., Pérez-Campo, F.M., 2020. Mesenchymal stem cells secretome: The

- cornerstone of cell-free regenerative medicine. *World Journal of Stem Cells* **12**: 1529–1552. <https://doi.org/10.4252/wjsc.v12.i12.1529>
- Greenhalgh, D.G., 2019. Management of Burns. *New England Journal of Medicine* **380**: 2349–2359. <https://doi.org/10.1056/nejmra1807442>
- Grubbs, H., Manna, B., 2023. *Wound Physiology*. StatPearls.
- Hirayama, D., Iida, T., Nakase, H., 2017. The Phagocytic Function of Macrophage-Enforcing Innate Immunity and Tissue Homeostasis. *International Journal of Molecular Sciences* **19**: 92. <https://doi.org/10.3390/ijms19010092>
- Hoang, D.M., Pham, P.T., Bach, T.Q., Ngo, A.T.L., Nguyen, Q.T., Phan, T.T.K., Nguyen, G.H., Le, P.T.T., Hoang, V.T., Forsyth, N.R., Heke, M., Nguyen, L.T., 2022. Stem cell-based therapy for human diseases. *Signal Transduction and Targeted Therapy* **7**. <https://doi.org/10.1038/s41392-022-01134-4>
- Hu, M.S., Borrelli, M.R., Lorenz, H.P., Longaker, M.T., Wan, D.C., 2018. Mesenchymal stromal cells and cutaneous wound healing: A comprehensive review of the background, role, and therapeutic potential. *Stem Cells International*: 1–13. <https://doi.org/10.1155/2018/6901983>
- IACUC. 2024. *Routes and Volumes of Administration in Mice*
- Jeschke, M.G., van Baar, M.E., Choudhry, M.A., Chung, K.K., Gibran, N.S., Logsetty, S., 2020. Burn injury. *Nature Reviews Disease Primers* **6**. <https://doi.org/10.1038/s41572-020-0145-5>
- Kawalec, A.M., 2020. Beverages and Burns in Children—The Challenge for Prevention. In: Safety Issues in Beverage Production. *Elsevier*: 485–514.
- Kemenkes. 2020. *Pedoman Nasional Pelayanan Kedokteran Tata Laksana Luka Bakar*.
- Kresnadi, A., Edward, M., Khang, G., Suroto, H., 2024. Characteristic Differences between Freeze-dried Tenogenic Secretomes and Freeze-dried Crude Secretomes of Mesenchymal Stem Cells under Hypoxic Conditions. *Biomolecular and Health Science Journal*. https://doi.org/10.4103/bhsj.bhsj_52_23

- Kucharzewski, M., Rojczyk, E., Wilemska-Kucharzewska, K., Wilk, R., Hudecki, J., Los, M.J., 2019. Novel trends in application of stem cells in skin wound healing. *European Journal of Pharmacology* **843**: 307–315. <https://doi.org/10.1016/j.ejphar.2018.12.012>
- Kuncorojakti, S., Pratama, A.Z.A., Antujala, C.A., Harijanto, C.T.B., Arsy, R.K., Kurniawan, P.A., Tjahjono, Y., Hendriati, L., Widodo, T., Aswin, A., Diyanoro, D., Wijaya, A.Y., Rodprasert, W., Susilowati, H., 2024. Acceleration of wound healing using adipose mesenchymal stem cell secretome hydrogel on partial-thickness cutaneous thermal burn wounds: An in vivo study in rats. *Veterinary World*: 1545–1554. <https://doi.org/10.14202/vetworld.2024.1545-1554>
- Kumar, R., E, K., Kumari, B., Kumar, A., Kumar, V., Janjua, D., Billah, A.M., 2022. Burn Injury Management, Pathophysiology and Its Future Prospectives. *Journal for Research in Applied Sciences and Biotechnology* **1**: 78–89. <https://doi.org/10.55544/jrasb.1.4.10>
- Li, M., Luan, F., Zhao, Y., Hao, H., Liu, J., Dong, L., Fu, X., Han, W., 2015. Mesenchymal stem cell-conditioned medium accelerates wound healing with fewer scars. *International Wound Journal* **14**: 64–73. <https://doi.org/10.1111/iwj.12551>
- Li, S., Yang, J., Sun, J., Chen, M., 2022. Adipose-Derived Mesenchymal Stem Cells Alleviate Hypertrophic Scar by Inhibiting Bioactivity and Inducing Apoptosis in Hypertrophic Scar Fibroblasts. *Cells* **11**, 4024. <https://doi.org/10.3390/cells11244024>
- Li, S.-N., Wu, J.-F., 2020. TGF- β /SMAD signaling regulation of mesenchymal stem cells in adipocyte commitment. *Stem Cell Research & Therapy* **11**. <https://doi.org/10.1186/s13287-020-1552-y>
- Li, Y., Deng, R., Chen, N., Pan, J., Pang, J., 2013. Review of Konjac Glucomannan: Isolation, Structure, Chain Conformation and Bioactivities. *Journal of Single Molecule Research* **1**: 7. <https://doi.org/10.12966/jsmr.07.03.2013>
- Lipsky, B.A., Senneville, É., Abbas, Z.G., Aragón-Sánchez, J., Diggle, M., Embil, J.M., Kono, S., Lavery, L.A., Malone, M., van Asten, S.A., Urbančič-Rovan, V., Peters, E.J.G., 2020. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). *Diabetes/Metabolism Research and Reviews* **36**. <https://doi.org/10.1002/dmrr.3280>

- Martí, M., Mulero, L., Pardo, C., Morera, C., Carrió, M., Laricchia-Robbio, L., Esteban, C.R., Belmonte, J.C.I., 2013. Characterization of pluripotent stem cells. *Nature Protocols* **8**: 223–253. <https://doi.org/10.1038/nprot.2012.154>
- Martin, K.E., Hunckler, M.D., Chee, E., Caplin, J.D., Barber, G.F., Kalelkar, P.P., Schneider, R.S., García, A.J., 2023. Hydrolytic hydrogels tune mesenchymal stem cell persistence and immunomodulation for enhanced diabetic cutaneous wound healing. *Biomaterials* **301**: 122256. <https://doi.org/10.1016/j.biomaterials.2023.122256>
- Masaki, S., Maeda, I., Kawamoto, T., 2022. Conservative Management of Full-thickness Burn Wounds Using Advanced Moist Dressings: A Case Report. *Wounds: a compendium of clinical research and practice* **34**: 42–46. <https://doi.org/10.25270/wnds/21030>
- Maskan Bermudez, N., Sa, B.C., Hargis, A., Yaghi, M., Mervis, J., 2024. Skin Grafting for Dermatologists: Past, Present, and Future. *Current Dermatology Reports* **13**: 47–54. <https://doi.org/10.1007/s13671-024-00427-x>
- McLaughlin, E.S., 2012. *Burns: Prevention, Causes and Treatment*.
- Mo, F., Zhang, M., Duan, X., Lin, C., Sun, D., You, T., 2022. Recent Advances in Nanozymes for Bacteria-Infected Wound Therapy. *International Journal of Nanomedicine* **17**, 5947–5990. <https://doi.org/10.2147/ijn.s382796>
- Muhammad, S.A., Abbas, A.Y., Saidu, Y., Fakurazi, S., Bilbis, L.S., 2020. Therapeutic efficacy of mesenchymal stromal cells and secretome in pulmonary arterial hypertension: A systematic review and meta-analysis. *Biochimie* **168**: 156–168. <https://doi.org/10.1016/j.biochi.2019.10.016>
- Nagamura-Inoue, T., 2014. Umbilical cord-derived mesenchymal stem cells: Their advantages and potential clinical utility. *World Journal of Stem Cells* **6**: 195. <https://doi.org/10.4252/wjsc.v6.i2.195>
- Nirenjen, S., Narayanan, J., Tamilanban, T., Subramaniam, V., Chitra, V., Fuloria, N.K., Wong, L.S., Ramachawolran, G., Sekar, M., Gupta, G., Fuloria, S., Chinni, S.V., Selvaraj, S., 2023. Exploring the contribution of pro-inflammatory cytokines to impaired wound healing in diabetes. *Frontiers in Immunology* **14**. <https://doi.org/10.3389/fimmu.2023.1216321>

- Nguyen, T.T., Mobashery, S., Chang, M., 2023. Roles of Matrix Metalloproteinases in Cutaneous Wound Healing, in: Wound Healing - New Insights into Ancient Challenges. InTech
- Noor, A., Preuss, C.V., 2024. *Amphotericin B*. StatPearls.
- Noorbakhsh, S.I., Bonar, E.M., Polinski, R., Amin, M.S., 2021. Educational Case: Burn Injury—Pathophysiology, Classification, and Treatment. *Academic Pathology* **8**.
<https://doi.org/10.1177/23742895211057239>
- Novita, B.D., Wasiyastuti, W., Tjahjono, Y., Wijaya, H., Hadinugroho, W., Wijaya, S., Soegianto, L., Theodora, I., Widoretno, E.T.W., Samsudin, K., Julian, A., 2024. Glucomannan is a promising isoniazid's enhancer that inducing macrophage phagocytosis. *Journal of Advanced Pharmaceutical Technology & Research* **15**: 237–241. https://doi.org/10.4103/japtr.japtr_96_24
- Nugroho, R. A. (2018). *Mengenal Mencit Sebagai Hewan Laboratorium*. Mulawarman University Press.
- Phillipson, M., Kubes, P., 2019. The Healing Power of Neutrophils. *Trends in Immunology* **40**: 635–647.
<https://doi.org/10.1016/j.it.2019.05.001>
- Rogulska, O., Vackova, I., Prazak, S., Turnovcova, K., Kubinova, S., Bacakova, L., Jendelova, P., Petrenko, Y., 2024. Storage conditions affect the composition of the lyophilized secretome of multipotent mesenchymal stromal cells. *Scientific Reports* **14**.
<https://doi.org/10.1038/s41598-024-60787-z>
- Saladin, K., Mcfarland, R.K., Gan, C.A., Cushman, H.N., 2017. *Essentials of Anatomy and Physiology*. McGraw-Hill Education, New York.
- Schaefer, T.J., Szymanski, K.D., 2023. *Burn Evaluation and Management*. StatPearls.
- Schaefer, T.J., Tannan, S.C., 2023. *Thermal Burns*. StatPearls.
- Shareghi-oskoue, O., Aghebati-Maleki, L., Yousefi, M., 2021. Transplantation of human umbilical cord mesenchymal stem cells to treat premature ovarian failure. *Stem Cell Research & Therapy* **12**.
<https://doi.org/10.1186/s13287-021-02529-w>

- Shi, G., Jin, Y., 2010. Role of Oct4 in maintaining and regaining stem cell pluripotency. *Stem Cell Research & Therapy* **1**. <https://doi.org/10.1186/scrt39>
- Shukla, S.K., Sharma, A.K., Gupta, V., Yashavarddhan, M.H., 2019. Pharmacological control of inflammation in wound healing. *Journal of Tissue Viability* **28**: 218–222. <https://doi.org/10.1016/j.jtv.2019.09.002>
- Siersbæk, M.S., Ditzel, N., Hejbøl, E.K., Præstholm, S.M., Markussen, L.K., Avolio, F., Li, L., Lehtonen, L., Hansen, A.K., Schrøder, H.D., Krych, L., Mandrup, S., Langhorn, L., Bollen, P., Grøntved, L., 2020. C57BL/6J substrain differences in response to high-fat diet intervention. *Scientific Reports* **10**. <https://doi.org/10.1038/s41598-020-70765-w>
- Soliman, H., Theret, M., Scott, W., Hill, L., Underhill, T.M., Hinz, B., Rossi, F.M.V., 2021. Multipotent stromal cells: One name, multiple identities. *Cell Stem Cell* **28**: 1690–1707. <https://doi.org/10.1016/j.stem.2021.09.001>
- Spronk, I., Edgar, D.W., van Baar, M.E., Wood, F.M., Van Loey, N.E.E., Middelkoop, E., Renneberg, B., Öster, C., Orwelius, L., Moi, A.L., Nieuwenhuis, M., van der Vlies, C.H., Polinder, S., Haagsma, J.A., 2020. Improved and standardized method for assessing years lived with disability after burns and its application to estimate the non-fatal burden of disease of burn injuries in Australia, New Zealand and the Netherlands. *BMC Public Health* **20**. <https://doi.org/10.1186/s12889-020-8233-8>
- Stipcevic, T., Piljac, A., Piljac, G., 2006. Enhanced healing of full-thickness burn wounds using di-rhamnolipid. *Burns* **32**: 24–34. <https://doi.org/10.1016/j.burns.2005.07.004>
- Stone II, R., Natesan, S., Kowalczewski, C.J., Mangum, L.H., Clay, N.E., Clohessy, R.M., Carlsson, A.H., Tassin, D.H., Chan, R.K., Rizzo, J.A., Christy, R.J., 2018. Advancements in Regenerative Strategies Through the Continuum of Burn Care. *Frontiers in Pharmacology* **9**. <https://doi.org/10.3389/fphar.2018.00672>
- Stylianou, N., Buchan, I., Dunn, K.W., 2015. A review of the international Burn Injury Database (iBID) for England and Wales: descriptive analysis of burn injuries 2003–2011. *BMJ Open* **5**: 6184. <https://doi.org/10.1136/bmjopen-2014-006184>

- Tan, S.T., Aisyah, P.B., Firmansyah, Y., Nathasia, N., Budi, E., Hendrawan, S., 2023. Effectiveness of secretome from human umbilical cord mesenchymal stem cells in gel (10% sm-hucmsc gel) for chronic wounds (diabetic and trophic ulcer) – phase 2 clinical trial. *Journal of Multidisciplinary Healthcare Volume 16*: 1763–1777. <https://doi.org/10.2147/jmdh.s408162>
- Tatullo, M., Gargiulo, I.C., Dipalma, G., Ballini, A., Inchingolo, A.M., Paduanelli, G., Nguyen, C. đấng K., Inchingolo, A.D., Makeeva, I., Scacco, S., Nuzzolese, M., De Vito, D., Inchingolo, F., 2020. Stem cells and regenerative medicine, in: Translational Systems Medicine and Oral Disease. *Elsevier*: 387–407.
- Togarrati, P., Dinglasan, N., Desai, S., Ryan, W., Muench, M., 2018. CD29 is highly expressed on epithelial, myoepithelial, and mesenchymal stromal cells of human salivary glands. *Oral Diseases 24*: 561–572. <https://doi.org/10.1111/odi.12812>
- Tortora, G.J., Derrickson, B., 2016. *Principles of Anatomy and Physiology*. Wiley.
- Oryan, A., Alemzadeh, E., Moshiri, A., 2017. Burn wound healing: present concepts, treatment strategies and future directions. *Journal of Wound Care 26*: 5–19. <https://doi.org/10.12968/jowc.2017.26.1.5>
- van de Vyver, M., Boodhoo, K., Frazier, T., Hamel, K., Kopcewicz, M., Levi, B., Maartens, M., Machcinska, S., Nunez, J., Pagani, C., Rogers, E., Walendzik, K., Wisniewska, J., Gawronska-Kozak, B., Gimble, J.M., 2021. Histology Scoring System for Murine Cutaneous Wounds. *Stem Cells and Development 30*: 1141–1152. <https://doi.org/10.1089/scd.2021.0124>
- VanHoy, T.B., Metheny, H., Patel, B.C., 2023. *Chemical Burns*. StatPearls.
- Vizoso, F., Eiro, N., Cid, S., Schneider, J., Perez-Fernandez, R., 2017. Mesenchymal Stem Cell Secretome: Toward Cell-Free Therapeutic Strategies in Regenerative Medicine. *International Journal of Molecular Sciences 18*: 1852. <https://doi.org/10.3390/ijms18091852>
- Wang, C., Dou, Z., Qin, F., Chen, H., Shen, Y., Zhang, G.-A., 2022. Epidemiology and risk prediction of patients with severe burns admitted to a burn intensive care unit in a burn center in beijing: A 5-year retrospective study. *Heliyon 8*: 12572. <https://doi.org/10.1016/j.heliyon.2022.e12572>

- Wang, Y., Beekman, J., Hew, J., Jackson, S., Issler-Fisher, A.C., Parungao, R., Lajevardi, S.S., Li, Z., Maitz, P.K.M., 2018. Burn injury: Challenges and advances in burn wound healing, infection, pain and scarring. *Advanced Drug Delivery Reviews* **123**: 3–17. <https://doi.org/10.1016/j.addr.2017.09.018>
- Warby, R., Maani, C.V., 2023. *Burn Classification*. StatPearls.
- Waters, M., Tadi, P., 2023. *Streptomycin*. StatPearls.
- Watt, S.M., Gullo, F., van der Garde, M., Markeson, D., Camicia, R., Khoo, C.P., Zwaginga, J.J., 2013. The angiogenic properties of mesenchymal stem/stromal cells and their therapeutic potential. *British Medical Bulletin* **108**: 25–53. <https://doi.org/10.1093/bmb/ldt031>
- World Health Organization: WHO, 2023. *Burns*. World Health Organization: WHO.
- Wu, S., Sun, S., Fu, W., Yang, Z., Yao, H., Zhang, Z., 2024. The Role and Prospects of Mesenchymal Stem Cells in Skin Repair and Regeneration. *Biomedicines* **12**: 743. <https://doi.org/10.3390/biomedicines12040743>
- Wu, Y., Su, M., Zhang, S., Xiao, L., Xiao, Y., Zhang, M., Bei, Y., Li, Meiyun, Zhang, F., Yuan, Q., Wu, S., Liu, J., Li, H., Yuan, X., Li, Meng, Li, Y., Gao, J., 2023. A mesenchymal stem cell-derived nanovesicle-biopotentiated bovine serum albumin-bridged gelatin hydrogel for enhanced diabetic wound therapy. *Materials & Design* **230**: 111960. <https://doi.org/10.1016/j.matdes.2023.111960>
- Yakupu, A., Zhang, J., Dong, W., Song, F., Dong, J., Lu, S., 2022. The epidemiological characteristic and trends of burns globally. *BMC Public Health* **22**. <https://doi.org/10.1186/s12889-022-13887-2>
- Yip, D.W., Gerriets, V., 2024. *Penicillin*. StatPearls.
- Zakrzewski, W., Dobrzyński, M., Szymonowicz, M., Rybak, Z., 2019. Stem cells: past, present, and future. *Stem Cell Research & Therapy* **10**. <https://doi.org/10.1186/s13287-019-1165-5>
- Zarei, F., Soleimaninejad, M., 2018. Role of growth factors and biomaterials in wound healing. *Artificial Cells, Nanomedicine, and Biotechnology* **46**: 906–911. <https://doi.org/10.1080/21691401.2018.1439836>

- Zhang, W., Ling, Y., Sun, Y., Xiao, F., Wang, L., 2023. Extracellular Vesicles Derived from Mesenchymal Stem Cells Promote Wound Healing and Skin Regeneration by Modulating Multiple Cellular Changes: A Brief Review. *Genes* **14**, 1516.
- Zhou, L., Hao, Q., Sugita, S., Naito, Y., He, H., Yeh, C., Lee, J.-W., 2021. Role of CD44 in increasing the potency of mesenchymal stem cell extracellular vesicles by hyaluronic acid in severe pneumonia. *Stem Cell Research & Therapy* **12**. <https://doi.org/10.1186/s13287-021-02329-2>
- Żwiercło, W., Piorun, K., Skórka-Majewicz, M., Maruszewska, A., Antoniewski, J., Gutowska, I., 2023. Burns: Classification, Pathophysiology, and Treatment: A Review. *International Journal of Molecular Sciences* **24**: 3749. <https://doi.org/10.3390/ijms24043749>