References

Adams, G. D. J., Cook, I., & Ward, K. R. (2014). The Principles of Freeze-Drying. Methods in Molecular Biology, 121–143. DOI: 10.1007/978-1-4939-2193-5_4

Alonso, C., Martí, M., Barba, C., Carrer, V., Rubio, L., & Coderch, L. (2017). Skin permeation and antioxidant efficacy of topically applied resveratrol. *Archives of Dermatological Research, 309*(6), 423–431. DOI: 10.1007/s00403-017-1740-5

Ariyati, N., Kusworini, K., Nurdiana, N., & Wirohadidjojo, Y. W. (2019). Low degree hyaluronic acid crosslinking inducing the release of TGF-β1 in conditioned medium of wharton's jelly-derived stem cells. *Open Access Macedonian Journal of Medical Sciences, 7(*10), 1572.

Arsiccio, A., Giorsello, P., Marenco, L., & Pisano, R. (2019). Considerations on Protein Stability during Freezing and its Impact on the Freeze Drying Cycle: A Design Space Approach. *Journal of Pharmaceutical Sciences*. DOI: 10.1016/j.xphs.2019.10.022

Assegehegn, G., Brito-de la Fuente, E., Franco, J. M., & Gallegos, C. (2018). The Importance of Understanding the Freezing Step and its Impact on Freeze Drying Process Performance. *Journal of Pharmaceutical Sciences.* DOI: 10.1016/j.xphs.2018.11.039

Aubert, G., & Lansdorp, P. M. (2008). Telomeres and aging. *Physiological reviews, 88*(2), 557-579.

Bari, E., Perteghella, S., Di Silvestre, D., Sorlini, M., Catenacci, L., Sorrenti, 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(11), 190.

Bari, E., Ferrarotti, I., Torre, M. L., Corsico, A. G., & Perteghella, S. (2019). Mesenchymal stem/stromal cell secretome for lung regeneration: The long way through "pharmaceuticalization" for the best formulation. *Journal of Controlled Release*. DOI: 10.1016/j.jconrel.2019.07.022

Bakaltcheva, I., O'Sullivan, A. M., Hmel, P., & Ogbu, H. (2007). Freeze-dried whole plasma: Evaluating sucrose, trehalose, sorbitol, mannitol and glycine as stabilizers. Thrombosis Research, 120(1), 105–116. DOI: 10.1016/j.thromres.2006.07.005

Bhardwaj, G., & Webster, T. J. (2015). Increased NIH 3T3 fibroblast functions on cell culture dishes which mimic the nanometer fibers of natural tissues. *International Journal of Nanomedicine, 10*, 5293.

Boncler, M., Lukasiak, M., Dastych, J., Golanski, J., & Watala, C. (2019). Differentiated mitochondrial function in mouse 3T3 fibroblasts and human epithelial or endothelial cells in response to chemical exposure. *Basic & Clinical Pharmacology & Toxicology, 124*(2), 199-210.

Budgude, P., Kale, V., & Vaidya, A. (2020). Cryopreservation of mesenchymal stromal cell-derived extracellular vesicles using trehalose maintains their ability to expand hematopoietic stem cells in vitro. *Cryobiology*. DOI: 10.1016/j.cryobiol.2020.11.009

Bosutti, A., & Degens, H. (2015). The impact of resveratrol and hydrogen peroxide on muscle cell plasticity shows a dose-dependent interaction. *Scientific reports, 5*(1), 8093.

Chen, J., Liu, Y., Zhao, Z., & Qiu, J. (2021). Oxidative stress in the skin: Impact and related protection. International Journal of Cosmetic Science, 43(5), 495-509.

Chutipongtanate, S., Watcharatanyatip, K., Homvises, T., Jaturongkakul, K., & Thongboonkerd, V. (2012). Systematic comparisons of various spectrophotometric and colorimetric methods to measure concentrations of protein, peptide and amino acid: detectable limits, linear dynamic ranges, interferences, practicality and unit costs. *Talanta, 98*, 123-129.

Cortés-Ríos, J., Zárate, A. M., Figueroa, J. D., Medina, J., Fuentes-Lemus, E., Rodríguez-Fernández, M., ... & López-Alarcón, C. (2020). Protein quantification by bicinchoninic acid (BCA) assay follows complex kinetics and can be performed at short incubation times. *Analytical biochemistry, 608*, 113904.

Daneshmandi, L., Shah, S., Jafari, T., Bhattacharjee, M., Momah, D., Saveh-Shemshaki, N., … Laurencin, C. T. (2020). Emergence of the Stem Cell Secretome in Regenerative Engineering. *Trends in Biotechnology.* DOI: 10.1016/j.tibtech.2020.04.013

Damayanti, R. H., Rusdiana, T., & Wathoni, N. (2021). Mesenchymal stem cell secretome for dermatology application: a review. *Clinical, Cosmetic and Investigational Dermatology*, 14, 1401.

Davis, K. E., Joseph, S. J., & Janssen, P. H. (2005). Effects of growth medium, inoculum size, and incubation time on culturability and isolation of soil bacteria. *Applied and Environmental Microbiology*, 71(2), 826-834.

Doran, P. M. (2013). *Unit Operations*. Bioprocess Engineering Principles, 445–595. DOI: 10.1016/b978-0-12-220851-5.00011-3

Driscoll, J., Yan, I. K., & Patel, T. (2022). Development of a Lyophilized Off-the-Shelf Mesenchymal Stem Cell-Derived Acellular Therapeutic. Pharmaceutics, 14(4), 849.

Efimenko, A., Dzhoyashvili, N., Kalinina, N., Kochegura, T., Akchurin, R., Tkachuk, V., & Parfyonova, Y. (2014). Adipose-derived mesenchymal stromal cells from aged patients with coronary artery disease keep mesenchymal stromal cell properties but exhibit characteristics of aging and have impaired angiogenic potential. *Stem cells translational medicine, 3*(1), 32-41.

El Baradie, K. B. Y., Nouh, M., O'Brien III, F., Liu, Y., Fulzele, S., Eroglu, A., & Hamrick, M. W. (2020). Freeze-dried extracellular vesicles from adipose-derived stem cells prevent hypoxia-induced muscle cell injury. *Frontiers in Cell and Developmental Biology, 8*, 181.

Farage, M. A., Miller, K. W., Elsner, P., & Maibach, H. I. (2008). Intrinsic and extrinsic factors in skin ageing: a review. *International journal of cosmetic science, 30*(2), 87-95.

Fraile, M., Eiro, N., Costa, L. A., Martín, A., & Vizoso, F. J. (2022). Aging and Mesenchymal Stem Cells: Basic Concepts, Challenges and Strategies. Biology, 11(11), 1678.

González-Espinosa, D., Pérez-Romano, L., Guzmán-Soriano, B., Arias, E., Bongiovanni, C. M., & Gutierrez, A. A. (2007). Effects of pH-neutral, super-oxidised solution on human dermal fibroblasts in vitro. *International wound journal, 4*(3), 241-250.Goodman, S. R. (2007). Tools of the Cell Biologist. In *Medical Cell Biology*. essay, Elsevier Science.

Goodman, S. R. (2007). Tools of the Cell Biologist. In *Medical Cell Biology*. essay, Elsevier Science.

Hass, R., Kasper, C., Böhm, S., & Jacobs, R. (2011). Different populations and sources of human mesenchymal stem cells (MSC): A comparison of adult and neonatal tissue-derived MSC. *Cell*

Communication and Signaling, 9(1), 12. DOI: 10.1186/1478-811x-9-12

Hirsch, I., Prell, E., & Weiwad, M. (2014). Assessment of cell death studies by monitoring hydrogen peroxide in cell culture. *Analytical biochemistry, 456*, 22-24.

Izutsu, K. (2018). *Applications of Freezing and Freeze-Drying in Pharmaceutical Formulations. Survival Strategies in Extreme Cold and Desiccation, 371–383*. DOI: 10.1007/978-981-13-1244-1_20

Jain, N. K., & Roy, I. (2008). Effect of trehalose on protein structure. *Protein Science, NA–NA*. DOI: 10.1002/pro.3 https://sci-hub.se/10.1002/pro.3

Jassam, S. A. (2016). *Role of CD15 and CD15s in the Cellular Mechanisms of Cancer Cell Metastasis from Lung to the Brain* (Doctoral dissertation, University of Portsmouth).

Jeon, Y. K., Jang, Y. H., Yoo, D. R., Kim, S. N., Lee, S. K., & Nam, M. J. (2010). Mesenchymal stem cells' interaction with skin: Wound-healing effect on fibroblast cells and skin tissue. *Wound Repair and Regeneration, 18*(6), 655–661. DOI: 10.1111/j.1524-475x.2010.00636.x

Kaleci, B., & Koyutürk, M. (2020). Efficacy of resveratrol in the wound healing process by reducing oxidative stress and promoting fibroblast cell proliferation and migration. *Dermatologic Therapy*. DOI: 10.1111/dth.14357

Kamiloglu, S., Sari, G., Ozdal, T., & Capanoglu, E. (2020). Guidelines for cell viability assays. *Food Frontiers, 1*(3), 332-349.

Katerji, M., Filippova, M., & Duerksen-Hughes, P. (2019). Approaches and methods to measure oxidative stress in clinical samples: Research applications in the cancer field. *Oxidative medicine and cellular longevity.*

Kasper, J. C., & Friess, W. (2011). The freezing step in lyophilization: Physico-chemical fundamentals, freezing methods and consequences on process performance and quality attributes of biopharmaceuticals. *European Journal of Pharmaceutics and Biopharmaceutics, 78*(2), 248–263. DOI: 10.1016/j.ejpb.2011.03.010

Kisiel, M. A., & Klar, A. S. (2019). Isolation and Culture of Human Dermal Fibroblasts. *Methods in Molecular Biology, 71–78*. doi:10.1007/978-1-4939-9473-1_6

Koganti, V. R., Shalaev, E. Y., Berry, M. R., Osterberg, T., Youssef, M., Hiebert, D. N., ... & Zhang, L. (2011). Investigation of design space for freeze-drying: use of modeling for primary drying segment of a freeze-drying cycle. *Aaps Pharmscitech, 12*, *854-861*.

Kuete, V., Karaosmanoğlu, O., & Sivas, H. (2017). Anticancer Activities of African Medicinal Spices and Vegetables. *Medicinal Spices and Vegetables from Africa, 271–297*. DOI: 10.1016/b978-0-12-809286-6.00010-8

Lago, J. C., & Puzzi, M. B. (2019). The effect of aging in primary human dermal fibroblasts. *PLoS One, 14*(7), e0219165.

Lim, C. T., Lolli, F., Thomas, J. D., Kola, B., & Korbonits, M. (2012). Measurement of AMP-Activated Protein Kinase Activity and Expression in Response to Ghrelin. *Ghrelin, 271–287*. DOI: 10.1016/b978-0-12-381272-8.00017-9

Lobo, V., Patil, A., Phatak, A., & Chandra, N. (2010). Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacognosy reviews, 4*(8), 118.

López-García, J., Lehocký, M., Humpolíček, P., & Sáha, P. (2014). HaCaT keratinocytes response on antimicrobial atelocollagen substrates: extent of cytotoxicity, cell viability and proliferation. *Journal of functional biomaterials, 5*(2), 43-57.

Lü, J. M., Lin, P. H., Yao, Q., & Chen, C. (2010). Chemical and molecular mechanisms of antioxidants: experimental approaches and model systems. *Journal of cellular and molecular medicine, 14*(4), 840-860.

Luo, C., Liu, Z., Mi, S., & Li, L. (2020). Quantitative investigation on the effects of ice crystal size on freeze-drying: The primary drying step. *Drying Technology, 1–13*. DOI: 10.1080/07373937.2020.1806865

Makridakis, M., Roubelakis, M. G., & Vlahou, A. (2013). Stem cells: Insights into the secretome. *Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics, 1834(11), 2380–2384*. DOI: 10.1016/j.bbapap.2013.01.032

Mallick, K. K., & Winnett, J. (2014). 3D bioceramic foams for bone tissue engineering. *Bone Substitute*

Biomaterials, 118–141. DOI: 10.1533/9780857099037.2.118

Marino, L., Castaldi, M. A., Rosamilio, R., Ragni, E., Vitolo, R., Fulgione, C., ... & Selleri, C. (2019). Mesenchymal stem cells from the Wharton's jelly of the human umbilical cord: biological properties and therapeutic potential. *Int J stem cells, 12*(2), 218-226.

Mahaseth, T., & Kuzminov, A. (2017). Potentiation of hydrogen peroxide toxicity: From catalase inhibition to stable DNA-iron complexes. *Mutation Research/Reviews in Mutation Research, 773*, 274-281.

Meiliana, A., Dewi, N. M., & Wijaya, A. (2019). Mesenchymal stem cell secretome: Cell-free therapeutic strategy in regenerative medicine. *The Indonesian Biomedical Journal, 11*(2), 113-24.

Mirabdollahi, M., Haghjooyjavanmard, S., & Sadeghi-aliabadi, H. (2019). An anticancer effect of umbilical cord-derived mesenchymal stem cell secretome on the breast cancer cell line. *Cell and Tissue Banking.* DOI: 10.1007/s10561-019-09781-8

Mocchi, M., Grolli, S., Dotti, S., Di Silvestre, D., Villa, R., Berni, P., ... & Perteghella, S. (2021). Equine mesenchymal stem/stromal cells freeze-dried secretome (Lyosecretome) for the treatment of musculoskeletal diseases: production process validation and batch release test for clinical use. Pharmaceuticals, 14(6), 553.

Mocchi, M., Bari, E., Marrubini, G., Bonda, A. F., Perteghella, S., Tartara, F., … Segale, L. (2021). Freeze-Dried Mesenchymal Stem Cell-Secretome Pharmaceuticalization: Optimization of Formulation and Manufacturing Process Robustness. Pharmaceutics, 13(8), 1129. DOI: 10.3390/pharmaceutics13081129

Olson, B.J.S.C. 2016. Assays for determination of protein concentration. *Curr. Protoc. Pharmacol.* 73:A.3A.1-A.3A.32. DOI: 10.1002/cpph.3

Otieno, B. A., Krause, C. E., & Rusling, J. F. (2016). Bioconjugation of Antibodies and Enzyme Labels onto Magnetic Beads. *Rational Design of Enzyme-Nanomaterials, 135–150*. DOI: 10.1016/bs.mie.2015.10.005

Park, S. R., Kim, J. W., Jun, H. S., Roh, J. Y., Lee, H. Y., & Hong, I. S. (2018). Stem cell secretome and its effect on cellular mechanisms relevant to wound healing. *Molecular Therapy, 26*(2), 606-617.

Pinho, A. G., Cibrão, J. R., Silva, N. A., Monteiro, S., & Salgado, A. J. (2020). Cell secretome: Basic insights and therapeutic opportunities for CNS disorders. *Pharmaceuticals, 13*(2), 31.

Putri, W. E., Endaryaoihonto, A., Rantam, F. A., & Prakoeswa, C. R. S. (2019). Mesenchymal Stem Cells-Conditioned Medium (SECRETOME) in Skin Aging: A Systematic Review. *International Journal of Pharmaceutical Research*, 13(2), 613-635.

Rahimi, B., Panahi, M., Saraygord-Afshari, N., Taheri, N., Bilici, M., Jafari, D., & Alizadeh, E. (2021). *The secretome of mesenchymal stem cells and oxidative stress: challenges and opportunities in cell-free regenerative medicine*. Molecular Biology Reports. DOI: 10.1007/s11033-021-06360-7

Rahimi, A. M., Cai, M., & Hoyer-Fender, S. (2022). Heterogeneity of the NIH3T3 Fibroblast Cell Line. *Cells, 11*(17), 2677.

Ramachandran, N., & Hiles, M. (2013). *Cytocompatibility testing of cell delivery devices may be crucial for cell therapies. Cytotherapy, 15(4), S50*. DOI: 10.1016/j.jcyt.2013.01.195

Rinnerthaler, M., Bischof, J., Streubel, M. K., Trost, A., & Richter, K. (2015). Oxidative stress in aging human skin. *Biomolecules, 5*(2), 545-589.

Romanov, Y. A., Volgina, N. E., Dugina, T. N., Kabaeva, N. V., & Sukhikh, G. T. (2019). Effect of Storage Conditions on the Integrity of Human Umbilical Cord Mesenchymal Stromal Cell-Derived Microvesicles. *Bulletin of Experimental Biology and Medicine*. DOI: 10.1007/s10517-019-04476-2

Sandonà, M., Di Pietro, L., Esposito, F., Ventura, A., Silini, A. R., Parolini, O., & Saccone, V. (2021). Mesenchymal stromal cells and their secretome: new therapeutic perspectives for skeletal muscle regeneration. Frontiers in Bioengineering and Biotechnology, 9, 652970.

Sagaradze, G., Grigorieva, O., Nimiritsky, P., Basalova, N., Kalinina, N., Akopyan, Z., & Efimenko, A. (2019). Conditioned medium from human mesenchymal stromal cells: towards the clinical translation. *International journal of molecular sciences, 20*(7), 1656.

Schultz, G. S., Chin, G. A., Moldawer, L., & Diegelmann, R. F. (2011). Principles of wound healing. *Mechanisms of vascular disease: a reference book for vascular specialists*, 423.

Severo, M. G., Zeferino, A. S., & Soccol, C. R. (2017). Development of a Rabies Vaccine in Cell Culture for Veterinary Use in the Lyophilized Form. *Current Developments in Biotechnology and Bioengineering, 523–560*. DOI: 10.1016/b978-0-444-63660-7.00021-8

Shabbir, A., Cox, A., Rodriguez-Menocal, L., Salgado, M., & Badiavas, E. V. (2015). Mesenchymal Stem Cell Exosomes Induce Proliferation and Migration of Normal and Chronic Wound Fibroblasts, and Enhance Angiogenesis In Vitro. *Stem Cells and Development, 24*(14), 1635–1647. DOI: 10.1089/scd.2014.0316

Sharifi-Rad, M., Anil Kumar, N. V., Zucca, P., Varoni, E. M., Dini, L., Panzarini, E., ... & Sharifi-Rad, J. (2020). Lifestyle, oxidative stress, and antioxidants: back and forth in the pathophysiology of chronic diseases. *Frontiers in physiology, 11*, 694.

Sheu, M. T., Jhan, H. J., Hsieh, C. M., Wang, C. J., & Ho, H. O. (2015). Efficacy of antioxidants as a complementary and alternative medicine (CAM) in combination with the chemotherapeutic agent doxorubicin. *Integrative Cancer Therapies, 14*(2), 184-195.

Shin, S., Lee, J., Kwon, Y., Park, K. S., Jeong, J. H., Choi, S. J., ... & Lee, C. (2021). Comparative proteomic analysis of the mesenchymal stem cells secretome from adipose, bone marrow, placenta and wharton's jelly. *International Journal of Molecular Sciences, 22*(2), 845.

Soydas, T., Yaprak Sarac, E., Cinar, S., Dogan, S., Solakoglu, S., Tuncdemir, M., & Kanigur Sultuybek, G. (2018). The protective effects of metformin in an in vitro model of aging 3T3 fibroblast under the high glucose conditions. *Journal of Physiology and Biochemistry, 74(*2), 273–281. DOI: 10.1007/s13105-018-0613-5

Stepanchenko, N. S., Novikova, G. V., & Moshkov, I. E. (2011). Protein quantification. *Russian Journal of Plant Physiology, 58(4), 737–742.* DOI: 10.1134/s1021443711040182

Tan, K. X., Chang, T., & Lin, X. (2022). Secretomes as an emerging class of bioactive ingredients for enhanced cosmeceutical applications. *Experimental Dermatology*, 31(5), 674-688.

Tanaka, M., Misawa, E., Yamauchi, K., Abe, F., & Ishizaki, C. (2015). Effects of plant sterols derived from Aloe vera gel on human dermal fibroblasts in vitro and on skin condition in Japanese women. *Clinical, cosmetic and investigational dermatology, 8*, 95.

Tchessalov, S., Shalaev, E., Bhatnagar, B., Nail, S., Alexeenko, A., Jameel, F., ... & Bhatt, S. (2022). Best Practices and Guidelines (2022) for Scale-Up and Tech Transfer in Freeze-Drying Based on Case Studies. Part 1: Challenges during Scale Up and Transfer. *AAPS PharmSciTech, 24*(1), 11.

Thakral, S., Sonje, J., Munjal, B., & Suryanarayanan, R. (2021). Stabilizers and their interaction with formulation components in frozen and freeze-dried protein formulations. *Advanced Drug Delivery Reviews, 173*, 1-19.

Walter, M. N., Wright, K. T., Fuller, H. R., MacNeil, S., & Johnson, W. E. B. (2010). Mesenchymal stem cell-conditioned medium accelerates skin wound healing: an in vitro study of fibroblast and keratinocyte scratch assays. *Experimental cell research*, 316(7), 1271-1281.

Wang, W. (2000). Lyophilization and development of solid protein pharmaceuticals. *International journal of pharmaceutics, 203*(1-2), 1-60.

Wang, T., Jian, Z., Baskys, A., Yang, J., Li, J., Guo, H., … Long, Q. (2020). MSC-derived exosomes protect against oxidative stress-induced skin injury via adaptive regulation of the NRF2 defense system. *Biomaterials, 120264*. DOI: 10.1016/j.biomaterials.2020.120264

Wang, Y., Nguyen, D. T., Yang, G., Anesi, J., Kelly, J., Chai, Z., ... & Golledge, J. (2021). A Modified MTS Proliferation Assay for Suspended Cells to Avoid the Interference by Hydralazine and β-Mercaptoethanol. *ASSAY and Drug Development Technologies, 19*(3), 184-190.

Wang, G.-Q., Pu, J., Yu, X.-Q., Xia, Y.-J., & Ai, L.-Z. (2020). Influence of freezing temperature before freeze-drying on the viability of various Lactobacillus plantarum strains. *Journal of Dairy Science*. DOI: 10.3168/jds.2019-17685

Xiao, X., Chen, H., Paerhati, P., Zhou, M., Yang, Z., Bai, S., & Yuan, Y. (2020). Establishment and Application of Engineered NIH 3T3 Cell Line with Stable Human RAGE Expression.

Pharmaceutical Fronts, 2(01), e23-e27.

Yu, L. X., Amidon, G., Khan, M. A., Hoag, S. W., Polli, J., Raju, G. K., & Woodcock, J. (2014). Understanding pharmaceutical quality by design. *The AAPS journal, 16*, 771-783.

Zhang, Y., Liu, S., Guo, W., Wang, M., Hao, C., Gao, S., … Guo, Q. (2018). Human umbilical cord Wharton's jelly mesenchymal stem cells combined with an acellular cartilage extracellular matrix scaffold improve cartilage repair compared with microfracture in a caprine model. *Osteoarthritis and Cartilage, 26*(7), 954–965. DOI: v10.1016/j.joca.2018.01.019

Zhang, L. X., Li, C. X., Kakar, M. U., Khan, M. S., Wu, P. F., Amir, R. M., ... & Li, J. H. (2021). Resveratrol (RV): A pharmacological review and call for further research. *Biomedicine & pharmacotherapy, 143*, 112164.

Zhang, X., Liu, X., Wan, F., You, W., Tan, X., Sheng, Q., ... & Zhao, H. (2022). Protective effect of resveratrol against hydrogen peroxide-induced oxidative stress in bovine skeletal muscle cells. *Meat Science, 185*, 108724.