

DAFTAR PUSTAKA

- Ackert-Bicknell, C.L., Anderson, L.C., Sheehan, S., Hill, W.G., Chang, B., Churchill, G.A., Chesler, E.J., Korstanje, R. and Peters, L.L., (2015). Aging research using mouse models. *Current protocols in mouse biology*, 5(2), pp.95-133.
- Ahsan, M., Sami, A., Haider, M. and Meeran, M., (2023). Central dogma of molecular biology: From dna to protein synthesis. *Journal of Physical, Biomedical and Biological Sciences*, 2023(1), pp.7-7.
- Aliyu, M., Zohora, F.T., Anka, A.U., Ali, K., Maleknia, S., Saffarioun, M. and Azizi, G., (2022). Interleukin-6 cytokine: An overview of the immune regulation, immune dysregulation, and therapeutic approach. *International immunopharmacology*, 111, p.109130.
- Azman, K.F. and Zakaria, R. (2019). ‘d-Galactose-induced accelerated aging model: an overview’, *Biogerontology*. Springer Netherlands, pp. 763–782. Available at: <https://doi.org/10.1007/s10522-019-09837-y>.
- Azman, K.F., Safdar, A. and Zakaria, R., (2021). D-galactose-induced liver aging model: Its underlying mechanisms and potential therapeutic interventions. *Experimental Gerontology*, 150, p.111372.
- Balasubramanian, P., Kiss, T., Gulej, R., Nyul Toth, A., Tarantini, S., Yabluchanskiy, A., Ungvari, Z. and Csiszar, A., (2024). Accelerated aging induced by an unhealthy high-fat diet: initial evidence for the role of Nrf2 deficiency and impaired stress resilience in cellular senescence. *Nutrients*, 16(7), p.952.
- Barber, R.D., Harmer, D.W., Coleman, R.A. and Clark, B.J., (2005). GAPDH as a housekeeping gene: analysis of GAPDH mRNA expression in a panel of 72 human tissues. *Physiological genomics*, 21(3), pp.389-395.
- Baidoo, N. and Sanger, G.J. (2024). ‘The human colon: Evidence for degenerative changes during aging and the physiological consequences’, *Neurogastroenterology and Motility* [Preprint]. John Wiley and Sons Inc. Available at: <https://doi.org/10.1111/nmo.14848>.

- Baixauli-Martín, J., Aliena-Valero, A., Castelló-Ruiz, M., Burguete, M.C., López-Morales, M.A., Muñoz-Espín, D., Torregrosa, G. and Salom, J.B., (2022). Brain cell senescence: a new therapeutic target for the acute treatment of ischemic stroke. *Journal of Neuropathology & Experimental Neurology*, 81(8), pp.614-620.
- Barbu, E., Popescu, M.R., Popescu, A.C. and Balanescu, S.M., (2022). Inflammation as a precursor of atherothrombosis, diabetes and early vascular aging. *International journal of molecular sciences*, 23(2), p.963.
- Bharucha, A. E., & Brookes, S. J. (2018). Neurophysiologic mechanisms of human large intestinal motility. *Physiology of the gastrointestinal tract*, 517-564.
- bin Imtiaz, M.K., Jaeger, B.N., Bottes, S., Machado, R.A., Vidmar, M., Moore, D.L. and Jessberger, S., (2021). Declining lamin B1 expression mediates age-dependent decreases of hippocampal stem cell activity. *Cell stem cell*, 28(5), pp.967-977.
- Bo-Htay, C., Palee, S., Apaijai, N., Chattipakorn, S.C. and Chattipakorn, N., (2018). Effects of d-galactose-induced ageing on the heart and its potential interventions. *Journal of Cellular and Molecular Medicine*, 22(3), pp.1392-1410.
- Bryda, E.C., (2013). The Mighty Mouse: the impact of rodents on advances in biomedical research. *Missouri medicine*, 110(3), p.207.
- Broad, J., Kung, V.W., Palmer, A., Elahi, S., Karami, A., Darreh-Shori, T., Ahmed, S., Thaha, M.A., Carroll, R., Chin-Aleong, J. and Martin, J.E., (2019). Changes in neuromuscular structure and functions of human colon during ageing are region-dependent. *Gut*, 68(7), pp.1210-1223.
- Buford, T. W. (2017). (Dis) Trust your gut: the gut microbiome in age-related inflammation, health, and disease. *Microbiome*, 5(1), 80.
- Buj, R., Leon, K.E., Anguelov, M.A. and Aird, K.M., (2021). Suppression of p16 alleviates the senescence-associated secretory phenotype. *Aging (Albany NY)*, 13(3), p.3290.

- Butov, A.A., Volkov, M.A., Anisimov, V.N., Sehl, M.E. and Yashin, A.I., (2002). A model of accelerated aging induced by 5-bromodeoxyuridine. *Biogerontology*, 3(3), pp.175-182.
- Cai, N., Wu, Y. and Huang, Y., (2022). Induction of accelerated aging in a mouse model. *Cells*, 11(9), p.1418.
- Camilleri, M., (2019). Leaky gut: mechanisms, measurement and clinical implications in humans. *Gut*, 68(8), pp.1516-1526.
- Capparelli, C., Chiavarina, B., Whitaker-Menezes, D., Pestell, T.G., Pestell, R.G., Hult, J., Andò, S., Howell, A., Martinez-Outschoorn, U.E., Sotgia, F. and Lisanti, M.P., (2012). CDK inhibitors (p16/p19/p21) induce senescence and autophagy in cancer-associated fibroblasts, “fueling” tumor growth via paracrine interactions, without an increase in neo-angiogenesis. *Cell cycle*, 11(19), pp.3599-3610.
- Chaffey, N., (2003). Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K. and Walter, P. Molecular biology of the cell. 4th edn.
- Chang, E. B., & Leung, P. S. (2014). Intestinal water and electrolyte transport. In *The Gastrointestinal System: Gastrointestinal, Nutritional and Hepatobiliary Physiology* (pp. 107-134). Dordrecht: Springer Netherlands.
- Chia, C.W., Egan, J.M. and Ferrucci, L., (2018). Age-related changes in glucose metabolism, hyperglycemia, and cardiovascular risk. *Circulation research*, 123(7), pp.886-904.
- Clay, D.E. and Fox, D.T., (2021). DNA damage responses during the cell cycle: insights from model organisms and beyond. *Genes*, 12(12), p.1882.
- Dalziel, J.E., Young, W., McKenzie, C.M., Haggarty, N.W. and Roy, N.C., (2017). Gastric emptying and gastrointestinal transit compared among native and hydrolyzed whey and casein milk proteins in an aged rat model. *Nutrients*, 9(12), p.1351.
- Dreesen, O., Chojnowski, A., Ong, P.F., Zhao, T.Y., Common, J.E., Lunny, D., Lane, E.B., Lee, S.J., Vardy, L.A., Stewart, C.L. and Colman, A., (2013). Lamin B1

- fluctuations have differential effects on cellular proliferation and senescence. *Journal of Cell Biology*, 200(5), pp.605-617.
- Drozdowski, L. and Thomson, A.B., (2006). Aging and the intestine. *World journal of gastroenterology: WJG*, 12(47), p.7578.
- Du, Z.H., Chen, J., Chen, Q.G., Zhou, L.Q., Bing, D., Liu, Y., Sun, Y.B., Li, P.J., Qi, F., Zhu, H.M. and Chu, H.Q., (2019). Expression patterns and implications of LaminB1 in Rat Cochleae. *Current Medical Science*, 39(2), pp.305-309.
- Eisenberg, E. and Levanon, E.Y., (2013). Human housekeeping genes, revisited. *TRENDS in Genetics*, 29(10), pp.569-574.
- El Oufir, L., Flourié, B., Bruley des Varannes, S., Barry, J.L., Cloarec, D., Bornet, F. and Galmiche, J.P., (1996). Relations between transit time, fermentation products, and hydrogen consuming flora in healthy humans. *Gut*, 38(6), pp.870-877.
- Engeland, K., (2022). Cell cycle regulation: p53-p21-RB signaling. *Cell Death & Differentiation*, 29(5), pp.946-960.
- Faget, D.V., Ren, Q. and Stewart, S.A., (2019). Unmasking senescence: context-dependent effects of SASP in cancer. *Nature Reviews Cancer*, 19(8), pp.439-453.
- Feng, X., Xing, J., Feng, G., Huang, D., Lu, X., Liu, S., Tan, W., Li, L. and Gu, Z., (2014). p16INK4A mediates age-related changes in mesenchymal stem cells derived from human dental pulp through the DNA damage and stress response. *Mechanisms of ageing and development*, 141, pp.46-55.
- Feringa, F.M., Raaijmakers, J.A., Hadders, M.A., Vaarting, C., Macurek, L., Heitink, L., Krenning, L. and Medema, R.H., (2018). Persistent repair intermediates induce senescence. *Nature communications*, 9(1), p.3923.
- Fernández, A., Quintana, E., Velasco, P., Moreno-Jimenez, B., de Andrés, B., Gaspar, M.L., Liste, I., Vilar, M., Mira, H. and Cano, E., (2021). Senescent accelerated prone 8 (SAMP8) mice as a model of age dependent neuroinflammation. *Journal of Neuroinflammation*, 18(1), p.75.

- Franceschi, C. and Campisi, J., (2014). Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, 69(Suppl_1), pp.S4-S9.
- Freund, A., Laberge, R.M., Demaria, M. and Campisi, J., (2012). Lamin B1 loss is a senescence-associated biomarker. *Molecular biology of the cell*, 23(11), pp.2066-2075.
- Forman, H.J., (2016). Redox signaling: An evolution from free radicals to aging. *Free Radical Biology and Medicine*, 97, pp.398-407.
- Furness, J.B., (2012). The enteric nervous system and neurogastroenterology. *Nature reviews Gastroenterology & hepatology*, 9(5), pp.286-294.
- Galluzzi, L., Yamazaki, T. and Kroemer, G., (2018). Linking cellular stress responses to systemic homeostasis. *Nature reviews Molecular cell biology*, 19(11), pp.731-745.
- García-Trejo, S.S., Gómez-Sierra, T., Eugenio-Pérez, D., Medina-Campos, O.N. and Pedraza-Chaverri, J., (2024). Protective effect of curcumin on D-galactose-induced senescence and oxidative stress in LLC-PK1 and HK-2 cells. *Antioxidants*, 13(4), p.415.
- Ghanbari, A., Danaie Fard, P., Azarmehr, N., Mahmoudi, R., Roozbehi, A., Zibara, K. and Hosseini, E., (2025). D-galactose induces senescence in adult mouse neural stem cells by imbalanced oxidant and antioxidant activity and differential expression of specific hub genes. *Molecular Neurobiology*, 62(4), pp.4250-4263.
- González-Gualda, E., Baker, A.G., Fruk, L. and Muñoz-Espín, D., (2021). A guide to assessing cellular senescence in vitro and in vivo. *The FEBS journal*, 288(1), pp.56-80.
- Gorgoulis, V., Adams, P.D., Alimonti, A., Bennett, D.C., Bischof, O., Bishop, C., Campisi, J., Collado, M., Evangelou, K., Ferbeyre, G. and Gil, J., (2019). Cellular senescence: defining a path forward. *Cell*, 179(4), pp.813-827.

- Grebenciucova, E. and VanHaerents, S., (2023). Interleukin 6: at the interface of human health and disease. *Frontiers in immunology*, 14, p.1255533.
- Han, H., Liu, Z., Yin, J., Gao, J., He, L., Wang, C., Hou, R., He, X., Wang, G., Li, T. and Yin, Y., (2021). D-galactose induces chronic oxidative stress and alters gut microbiota in weaned piglets. *Frontiers in physiology*, 12, p.634283.
- Hall, J.E. and Guyton, A.C., (2014). General principles of gastrointestinal function. *Guyton and Hal textbook of medical physiology*, 12th edn. Saunders Elsevier, 755.\
- Hasty, P., Campisi, J. and Sharp, Z.D., (2016). Do p53 stress responses impact organismal aging?. *Translational cancer research*, 5(6), p.685.
- Hernandez-Segura, A., de Jong, T.V., Melov, S., Guryev, V., Campisi, J. and Demaria, M., (2017). Unmasking transcriptional heterogeneity in senescent cells. *Current Biology*, 27(17), pp.2652-2660.
- Hinkal, G.W., Gatz, C.E., Parikh, N. and Donehower, L.A., (2009). Altered senescence, apoptosis, and DNA damage response in a mutant p53 model of accelerated aging. *Mechanisms of ageing and development*, 130(4), pp.262-271.
- Hor, Y.Y., Lew, L.C., Jaafar, M.H., Lau, A.S.Y., Ong, J.S., Kato, T., Nakanishi, Y., Azzam, G., Azlan, A., Ohno, H. and Liong, M.T., (2019). Lactobacillus sp. improved microbiota and metabolite profiles of aging rats. *Pharmacological Research*, 146, p.104312.
- Hosie, S., Abo-Shaban, T., Mou, K., Balasuriya, G.K., Mohsenipour, M., Alamoudi, M.U., Filippone, R.T., Belz, G.T., Franks, A.E., Bornstein, J.C. and Nurgali, K., (2024). Faster Gastrointestinal transit, reduced small intestinal smooth muscle tone and dysmotility in the Nlgn3R451C mouse model of autism. *International Journal of Molecular Sciences*, 25(2), p.832.
- Imerb, N., Thonusin, C., Pratchayasakul, W., Arunsak, B., Nawara, W., Ongnok, B., Aeimlapa, R., Charoenphandhu, N., Chattipakorn, N. and Chattipakorn, S.C.,

- (2022). D-galactose-induced aging aggravates obesity-induced bone dyshomeostasis. *Scientific reports*, 12(1), p.8580.
- Johmura, Y., Yamashita, E., Shimada, M., Nakanishi, K. and Nakanishi, M., (2016). Defective DNA repair increases susceptibility to senescence through extension of Chk1-mediated G2 checkpoint activation. *Scientific Reports*, 6(1), p.31194.
- Jung, W.K., Park, S.B., Kim, H.R., Ryu, H.Y., Kim, Y.H. and Kim, J., (2021). Advanced glycation end products increase salivary gland hypofunction in d-galactose-induced aging rats and its prevention by physical exercise. *Current Issues in Molecular Biology*, 43(3), pp.2059-2067.
- Kennedy, B.K., Berger, S.L., Brunet, A., Campisi, J., Cuervo, A.M., Epel, E.S., Franceschi, C., Lithgow, G.J., Morimoto, R.I., Pessin, J.E. and Rando, T.A., (2014). Geroscience: linking aging to chronic disease. *Cell*, 159(4), pp.709-713.
- Khan, H.A., Abdelhalim, M.A.K., Alhomida, A.S. and Al Ayed, M.S., (2013). Short Communication Transient increase in IL-1 β , IL-6 and TNF- α gene expression in rat liver exposed to gold nanoparticles. *Genetics and Molecular Research*, 12(4), pp.5851-5857.
- Kiela, P.R. and Ghishan, F.K., (2016). Physiology of intestinal absorption and secretion. *Best practice & research Clinical gastroenterology*, 30(2), pp.145-159.
- Kim, S., & Jazwinski, S. M. (2018). The gut microbiota and healthy aging: a mini-review. *Gerontology*, 64(6), 513-520.
- Kim, Y., (2023). The impact of altered lamin B1 levels on nuclear lamina structure and function in aging and human diseases. *Current Opinion in Cell Biology*, 85, p.102257.
- Kitazawa, K., Numa, K., Patel, S.K., King, C.D., Matsumoto, A., Sotozono, C., Desprez, P.Y., Schilling, B. and Campisi, J., (2023). Cellular senescence exacerbates features of aging in the eyes. *Aging biology*, 1(1), p.20230014.

- Kulaberoglu, Y., Hergovich, A. and Gundogdu R., (2016). The role of p53/p21/p16 in DNA damage signaling and DNA repair. In *Genome stability* (pp. 243-256). Academic Press.
- Kumar, M.V., Moore, R.L. and Scarpace, P.J., (1999). β 3-Adrenergic regulation of leptin, food intake, and adiposity is impaired with age. *Pflügers Archiv*, 438(5), pp.681-688.
- Lamech, L.T. and Haynes, C.M., (2015). The unpredictability of prolonged activation of stress response pathways. *The Journal of cell biology*, 209(6), p.781.
- Lee, S.J., Trostel, A., Le, P., Harinarayanan, R., FitzGerald, P.C. and Adhya, S., (2009). Cellular stress created by intermediary metabolite imbalances. *Proceedings of the National Academy of Sciences*, 106(46), pp.19515-19520.
- Lewis, S. J., & Heaton, K. W. (1997). Stool form scale as a useful guide to intestinal transit time. *Scandinavian journal of gastroenterology*, 32(9), 920-924.
- Li, J., Sun, Z., Cui, Y., Qin, L., Wu, F., Li, Y., Du, N. and Li, X., (2022). Knockdown of LMNB1 inhibits the proliferation of lung adenocarcinoma cells by inducing DNA damage and cell senescence. *Frontiers in oncology*, 12, p.913740.
- Li, N., He, Y., Wang, L., Mo, C., Zhang, J., Zhang, W., Li, J., Liao, Z., Tang, X. and Xiao, H., (2011). D-galactose induces necroptotic cell death in neuroblastoma cell lines. *Journal of cellular biochemistry*, 112(12), pp.3834-3844.
- Linton, P.J. and Thoman, M.L., (2014). Immunosenescence in monocytes, macrophages, and dendritic cells: lessons learned from the lung and heart. *Immunology letters*, 162(1), pp.290-297.
- Liu, J., (2017). Protective effects of Panax notoginseng saponins on testicular DNA damage in natural aging rats based on ATR/Chk1/P53 signal pathway. *Zhongcaoyao*, pp.935-940.
- López-Pingarrón, L., Almeida, H., Soria-Aznar, M., Reyes-Gonzales, M.C., Rodríguez-Moratinos, A.B., Muñoz-Hoyos, A. and García, J.J. (2023). Interstitial cells of Cajal and enteric nervous system in gastrointestinal and

- neurological pathology, relation to oxidative stress. *Current Issues in Molecular Biology*, 45(4), pp.3552-3572.
- Luo, Q.T., Ye, Y.C., Guo, W.M., Zhu, Q., Wang, S.S., Li, N., Wang, L., Cheng, C.S. and Fan, G., (2024). Senolytic treatment improve small intestine regeneration in aging. *Aging and Disease*, 15(4), p.1499.
- Lv, T., Wang, C., Zhou, J., Feng, X., Zhang, L. and Fan, Z., (2024). Mechanism and role of nuclear laminin B1 in cell senescence and malignant tumors. *Cell Death Discovery*, 10(1), p.269.
- Madsen, J.L. and Graff, J., (2004). Effects of ageing on gastrointestinal motor function. *Age and ageing*, 33(2), pp.154-159.
- Malvezzi, H., Dobo, C., Filippi, R.Z., Mendes do Nascimento, H., Palmieri da Silva e Sousa, L., Meola, J., Piccinato, C.A. and Podgaec, S., (2022). Altered p16Ink4a, IL-1 β , and Lamin b1 protein expression suggest cellular senescence in deep endometriotic lesions. *International Journal of Molecular Sciences*, 23(5), p.2476.
- Mari, A., Mahamid, M., Amara, H., Baker, F.A. and Yaccob, A., (2020). Chronic constipation in the elderly patient: updates in evaluation and management. *Korean journal of family medicine*, 41(3), p.139.
- Matt, S.M., Lawson, M.A. and Johnson, R.W., (2016). Aging and peripheral lipopolysaccharide can modulate epigenetic regulators and decrease IL-1 β promoter DNA methylation in microglia. *Neurobiology of aging*, 47, pp.1-9.
- Mawe, G.M., Sanders, K.M. and Camilleri, M. (2023). Overview of the enteric nervous system. In *Seminars in neurology* (Vol. 43, No. 04, pp. 495-505). Thieme Medical Publishers, Inc..
- McHugh, M.L. (2012) "Interrater reliability: the kappa statistic," *Biochemia Medica*, pp. 276–282. Available at: <https://doi.org/10.11613/BM.2012.031>.
- Meng, J., Liu, J., Chen, D., Kang, J., Huang, Y., Li, D., Duan, Y. and Wang, J., (2021). Integration of lncRNA and mRNA profiles to reveal the protective effects of Codonopsis pilosula extract on the gastrointestinal tract of mice subjected to

D-galactose-induced aging. *International Journal of Molecular Medicine*, 47(3), p.1.

Michaud, M., Balardy, L., Moulis, G., Gaudin, C., Peyrot, C., Vellas, B., Cesari, M. and Nourhashemi, F., (2013). Proinflammatory cytokines, aging, and age-related diseases. *Journal of the American Medical Directors Association*, 14(12), pp.877-882.

Mimura, S., Morishita, A., Kitaoka, A., Sasaki, K., Tai, H., Yano, R., Nakahara, M., Oura, K., Tadokoro, T., Fujita, K. and Tani, J., 2026. Constipation in Older Adults: Pathophysiology, Clinical Impact, and Management Strategies. *Geriatrics*, 11(2), p.47.

Minciullo, P.L., Catalano, A., Mandraffino, G., Casciaro, M., Crucitti, A., Maltese, G., Morabito, N., Lasco, A., Gangemi, S. and Basile, G., (2016). Inflammaging and anti-inflammaging: the role of cytokines in extreme longevity. *Archivum immunologiae et therapiae experimentalis*, 64(2), pp.111-126.

Mitchell, S.J., Scheibye-Knudsen, M., Longo, D.L. and de Cabo, R., 2015. Animal models of aging research: implications for human aging and age-related diseases. *Annu. Rev. Anim. Biosci.*, 3(1), pp.283-303.

Mosteiro, L., Pantoja, C., de Martino, A. and Serrano, M., (2018). Senescence promotes in vivo reprogramming through p16 INK 4a and IL-6. *Aging cell*, 17(2), p.e12711.

Murray-Nerger, L.A., Justice, J.L., Rekapalli, P., Hutton, J.E. and Cristea, I.M., (2021). Lamin B1 acetylation slows the G1 to S cell cycle transition through inhibition of DNA repair. *Nucleic acids research*, 49(4), pp.2044-2064.

Nakayasu, C., Kanemura, F., Hirano, Y., Shimizu, Y. and Tonosaki, K., (2000). Sensitivity of the olfactory sense declines with the aging in senescence-accelerated mouse (SAM-P1). *Physiology & behavior*, 70(1-2), pp.135-139.
Negussie, A. B., Dell, A. C., Davis, B. A., and Geibel, J. P. (2022). Colonic fluid and electrolyte transport 2022: an update. *Cells*, 11(10), 1712..

- Newman, A.B., Gottdiener, J.S., McBurnie, M.A., Hirsch, C.H., Kop, W.J., Tracy, R., Walston, J.D. and Fried, L.P., (2001). Associations of subclinical cardiovascular disease with frailty. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 56(3), pp.M158-M166.
- Nguyen, T.T., Dau, D.T., Nguyen, D.C., Nguyen, H.T., Ngo, P.T., Nguyen, T.Q., Han, B. and Hoang, B.X., (2017). Effects of Trang Phuc Linh plus-food supplement on irritable bowel syndrome induced by mustard oil. *Journal of medicinal food*, 20(4), pp.385-391.
- Nguyen, T. T., Baumann, P., Tüscher, O., Schick, S., and Endres, K. (2023). The aging enteric nervous system. *International journal of molecular sciences*, 24(11), 9471.
- O'Mahony, L., Holland, J., Jackson, J., Feighery, C., Hennessy, T.P.J. and Mealy, K., (1998). Quantitative intracellular cytokine measurement: age-related changes in proinflammatory cytokine production. *Clinical & Experimental Immunology*, 113(2), pp.213-219.
- O'Sullivan, E.A., Wallis, R., Mossa, F. and Bishop, C.L., (2024). The paradox of senescent-marker positive cancer cells: challenges and opportunities. *npj Aging*, 10(1), p.41.
- Oh, S. S. and Narver, H. L. (2024). Mouse and rat anesthesia and analgesia. *Current protocols*, 4(2), e995.
- Ock, S.A., Knott, J.G. and Choi, I., (2020). Involvement of CDKN1A (p21) in cellular senescence in response to heat and irradiation stress during preimplantation development. *Cell Stress and Chaperones*, 25(3), pp.503-508.
- Orjalo, A.V., Bhaumik, D., Gengler, B.K., Scott, G.K. and Campisi, J., (2009). Cell surface-bound IL-1 α is an upstream regulator of the senescence-associated IL-6/IL-8 cytokine network. *Proceedings of the National Academy of Sciences*, 106(40), pp.17031-17036.

- Ou, H.L. and Schumacher, B., (2018). DNA damage responses and p53 in the aging process. *Blood, The Journal of the American Society of Hematology*, 131(5), pp.488-495.
- Paletzki, R. F. and Gerfen, C. R. (2019). Basic neuroanatomical methods. *Current Protocols in Neuroscience*, 90(1), e84.
- Pan, H., Feng, W., Chen, M., Luan, H., Hu, Y., Zheng, X., Wang, S. and Mao, Y., (2021). Alginate oligosaccharide ameliorates D-Galactose-induced kidney aging in mice through activation of the Nrf2 signaling pathway. *BioMed research international*, 2021(1), p.6623328.
- Parameshwaran, K., Irwin, M.H., Steliou, K. and Pinkert, C.A., (2010). D-galactose effectiveness in modeling aging and therapeutic antioxidant treatment in mice. *Rejuvenation research*, 13(6), pp.729-735.
- Patejdl, R. (2024). Gastrointestinal motility function and dysfunction in the elderly patient: what are the effects of aging?. *Visceral Medicine*, 40(6), pp.324-329.
- Patel, B.A., Patel, N., Fidalgo, S., Wang, C., Ranson, R.N., Saffrey, M.J. and Yeoman, M.S., (2014). Impaired colonic motility and reduction in tachykinin signalling in the aged mouse. *Experimental gerontology*, 53, pp.24-30.
- Phillips, R.J., Pairitz, J.C. and Powley, T.L., (2007). Age-related neuronal loss in the submucosal plexus of the colon of Fischer 344 rats. *Neurobiology of aging*, 28(7), pp.1124-1137.
- Qian, Y. and Chen, X., (2012). Senescence regulation by the p53 protein family. *Cell senescence: methods and protocols*, pp.37-61.
- Rao, R., (2008). Oxidative stress-induced disruption of epithelial and endothelial tight junctions. *Frontiers in bioscience: a journal and virtual library*, 13, p.7210.
- Ren, J.L., Pan, J.S., Lu, Y.P., Sun, P. and Han, J., (2009). Inflammatory signaling and cellular senescence. *Cellular signalling*, 21(3), pp.378-383.
- Restuti, A.N.S., Yulianti, A. and Nuraini, N., (2018). Intervensi Bubuk Kakao Terhadap Perubahan Gula Darah Puasa Tikus Sprague Dawley Diabetes Melitus. *Dalam Jurnal Riset Kesehatan.[e-journal]*, 7(2), pp.57-60.

- Roager, H.M., Hansen, L., Bahl, M.I., Frandsen, H.L., Carvalho, V., Gøbel, R.J., Dalgaard, M.D., Plichta, D.R., Sparholt, M.H., Vestergaard, H. and Hansen, T., (2016). Colonic transit time is related to bacterial metabolism and mucosal turnover in the gut. *Nature microbiology*, 1(9), p.16093.
- Robert, G. and Wagner, J.R., (2020). ROS-induced DNA damage as an underlying cause of aging. *Advances in Geriatric Medicine and Research*, 4(3).
- Roberts, S.B., Fuss, P., Heyman, M.B., Dallal, G.E. and Young, V.R., (1996). Effects of age on energy expenditure and substrate oxidation during experimental underfeeding in healthy men. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 51(2), pp.B158-B166.
- Romaniello, D., Gelfo, V., Pagano, F., Sgarzi, M., Morselli, A., Girone, C., Filippini, D.M., D'Uva, G. and Lauriola, M., 2023. IL-1 and senescence: Friends and foe of EGFR neutralization and immunotherapy. *Frontiers in Cell and Developmental Biology*, 10, p.1083743.
- Rubio, C., Lizárraga, E., Álvarez-Cilleros, D., Pérez-Pardo, P., Sanmartín-Salinas, P., Toledo-Lobo, M.V., Alvarez, C., Escrivá, F., Fernández-Lobato, M., Guijarro, L.G. and Valverde, A.M., (2021). Aging in male wistar rats associates with changes in intestinal microbiota, gut structure, and cholecystokinin-mediated gut–brain axis function. *The Journals of Gerontology: Series A*, 76(11), pp.1915-1921.
- Ruprecht, N.A., Singhal, S., Schaefer, K., Panda, O., Sens, D. and Singhal, S.K. (2024). A review: multi-omics approach to studying the association between ionizing radiation effects on biological aging. *Biology*, 13(2), p.98.
- Rutkute, K., Karakashian, A.A., Giltaiy, N.V., Dobierzewska, A. and Nikolova-Karakashian, M.N., (2007). Aging in rat causes hepatic hyperresponsiveness to interleukin-1 β which is mediated by neutral sphingomyelinase-2. *Hepatology*, 46(4), pp.1166-1176.
- Saad, R. J., Rao, S. S., Koch, K. L., Kuo, B., Parkman, H. P., McCallum, R. W., ... & Chey, W. D. (2010). Do stool form and frequency correlate with whole-gut

and colonic transit? Results from a multicenter study in constipated individuals and healthy controls. *Official journal of the American College of Gastroenterology* | *ACG*, 105(2), 403-411.

Sadigh-Eteghad, S., Majdi, A., McCann, S.K., Mahmoudi, J., Vafaei, M.S. and Macleod, M.R., (2017). D-galactose-induced brain ageing model: A systematic review and meta-analysis on cognitive outcomes and oxidative stress indices. *PloS one*, 12(8), p.e0184122.

Saffrey, M.J., (2013). Aging of the mammalian gastrointestinal tract: a complex organ system. *Age*, 36(3), pp.1019-1032.

Safwan-Zaiter, H., Wagner, N. and Wagner, K.D. (2022). P16INK4A—More than a senescence marker. *Life*, 12(9), p.1332.

Sanders, R., Mason, D.J., Foy, C.A. and Huggett, J.F., (2013). Evaluation of digital PCR for absolute RNA quantification. *PloS one*, 8(9), p.e75296.

Sanders, K.M., Ward, S.M. and Koh, S.D., 2014. Interstitial cells: regulators of smooth muscle function. *Physiological reviews*.

Sasaki, M., Kajiya, H., Ozeki, S., Okabe, K. and Ikebe, T., (2014). Reactive oxygen species promotes cellular senescence in normal human epidermal keratinocytes through epigenetic regulation of p16INK4a. *Biochemical and Biophysical Research Communications*, 452(3), pp.622-628.

Scarpace, P.J., Matheny, M., Moore, R.L. and Tümer, N., (2000). Impaired leptin responsiveness in aged rats. *Diabetes*, 49(3), pp.431-435.

Seiberling, K.A. and Conley, D.B., (2004). Aging and olfactory and taste function. *Otolaryngologic Clinics of North America*, 37(6), pp.1209-1228.

Shen, C.Y., Lu, C.H., Wu, C.H., Li, K.J., Kuo, Y.M., Hsieh, S.C. and Yu, C.L., (2020). The development of maillard reaction, and advanced glycation end product (AGE)-receptor for AGE (RAGE) signaling inhibitors as novel therapeutic strategies for patients with AGE-related diseases. *Molecules*, 25(23), p.5591.

Shimi, T., Butin-Israeli, V., Adam, S.A., Hamanaka, R.B., Goldman, A.E., Lucas, C.A., Shumaker, D.K., Kosak, S.T., Chandel, N.S. and Goldman, R.D.,

- (2011). The role of nuclear lamin B1 in cell proliferation and senescence. *Genes & development*, 25(24), pp.2579-2593.
- Sholikhah, T.A., Dian, E.S., Yustina, A.A.S. and Susilowati, R., (2024). Prevention of colon enlargement by TNF- α antagonist in a streptozotocin-induced diabetic rat model. *Histol. Histopathol*, 39, pp.1443-1455.
- Shtutman, M., Chang, B.D., Schools, G.P. and Broude, E.V., (2016). Cellular model of p21-induced senescence. In *Oncogene-Induced Senescence: Methods and Protocols* (pp. 31-39). New York, NY: Springer New York.
- Singh, A.S. and Masuku, M.B., (2014). Sampling techniques & determination of sample size in applied statistics research: An overview. *International Journal of economics, commerce and management*, 2(11), pp.1-22.
- Singh, K., Khairnar, S.I., Sanghavi, A., Yadav, T.T., Gupta, N., Arora, J. and Katcher, H.L., (2024). E5 treatment showing improved health-span and lifespan in old Sprague Dawley rats. *Aging Cell*, 23(12), p.e14335.
- Sipos, F., Leiszter, K. and Tulassay, Z., (2011). Effect of ageing on colonic mucosal regeneration. *World Journal of Gastroenterology: WJG*, 17(25), p.2981.
- Smits, G.J. and Lefebvre, R.A., (1996). Influence of aging on gastric emptying of liquids, small intestine transit, and fecal output in rats. *Experimental Gerontology*, 31(5), pp.589-596.
- Soultanova, A., Mikulski, Z., Pfeil, U., Grau, V. and Kummer, W., (2016). Calcitonin peptide family members are differentially regulated by LPS and inhibit functions of rat alveolar NR8383 macrophages. *PLoS One*, 11(10), p.e0163483.
- Spehlmann, M.E., Manthey, C.F., Dann, S.M., Hanson, E., Sandhu, S.S., Liu, L.Y., Abdelmalak, F.K., Diamanti, M.A., Retzlaff, K., Scheller, J. and Rose-John, S., (2013). Trp53 deficiency protects against acute intestinal inflammation. *The Journal of Immunology*, 191(2), pp.837-847.

- Spencer, N.J. and Hu, H., (2020). Enteric nervous system: sensory transduction, neural circuits and gastrointestinal motility. *Nature reviews Gastroenterology & hepatology*, 17(6), pp.338-351.
- Sudakov, S.K., Alekseeva, E.V., Nazarova, G.A. and Bashkatova, V.G., (2021). Age-related individual behavioural characteristics of adult wistar rats. *Animals*, 11(8), p.2282.
- Suenaga, K., Takasawa, H., Watanabe, T., Wako, Y., Suzuki, T., Hamada, S. and Furihata, C., (2013). Differential gene expression profiling between genotoxic and non-genotoxic hepatocarcinogens in young rat liver determined by quantitative real-time PCR and principal component analysis. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 751(1), pp.73-83.
- Suzuki, T., Higgins, P.J. and Crawford, D.R., (2000). Control selection for RNA quantitation. *Biotechniques*, 29(2), pp.332-337.
- Takasugi, M., Yoshida, Y., Hara, E. and Ohtani, N., (2023). The role of cellular senescence and SASP in tumour microenvironment. *The FEBS journal*, 290(5), pp.1348-1361.
- Tan, C.L. and Anderson, E., (2020). The new central dogma of molecular biology. *Resonance*, 14(3), pp.1-32.
- Thevaranjan, N., Puchta, A., Schulz, C., Naidoo, A., Szamosi, J. C., Verschoor, C. P., ... & Bowdish, D. M. (2017). Age-associated microbial dysbiosis promotes intestinal permeability, systemic inflammation, and macrophage dysfunction. *Cell host & microbe*, 21(4), 455-466.
- Thiagarajah, J.R., Donowitz, M. and Verkman, A.S., 2015. Secretory diarrhoea: mechanisms and emerging therapies. *Nature reviews Gastroenterology & hepatology*, 12(8), pp.446-457.
- Tomobe, K. and Nomura, Y., (2009). Neurochemistry, neuropathology, and heredity in SAMP8: a mouse model of senescence. *Neurochemical research*, 34(4), pp.660-669.

- Tran, L. and Greenwood-Van Meerveld, B., (2014). In a non-human primate model, aging disrupts the neural control of intestinal smooth muscle contractility in a region-specific manner. *Neurogastroenterology & Motility*, 26(3), pp.410-418.
- Tylutka, A., Walas, Ł. and Zembron-Lacny, A., 2024. Level of IL-6, TNF, and IL-1 β and age-related diseases: a systematic review and meta-analysis. *Frontiers in immunology*, 15, p.1330386.
- Van Avondt, K., Strecker, J.K., Tulotta, C., Minnerup, J., Schulz, C. and Soehnlein, O., (2023). Neutrophils in aging and aging-related pathologies. *Immunological Reviews*, 314(1), pp.357-375.
- Vancamelbeke, M. and Vermeire, S., (2017). The intestinal barrier: a fundamental role in health and disease. *Expert review of gastroenterology & hepatology*, 11(9), pp.821-834.
- Vdoviaková, K., Petrovová, E., Maloveská, M., Krešáková, L., Teleky, J., Elias, M. Z. J., & Petrášová, D. (2016). Surgical anatomy of the gastrointestinal tract and its vasculature in the laboratory rat. *Gastroenterology research and practice*, 2016(1), 2632368.
- Vellers, H.L., Kleeberger, S.R. and Lightfoot, J.T., (2018). Inter-individual variation in adaptations to endurance and resistance exercise training: genetic approaches towards understanding a complex phenotype. *Mammalian Genome*, 29(1), pp.48-62.
- Vogel, C. and Marcotte, E.M., (2012). Insights into the regulation of protein abundance from proteomic and transcriptomic analyses. *Nature reviews genetics*, 13(4), pp.227-232.
- Vogelstein, B., Sur, S. and Prives, C., (2010). p53: the most frequently altered gene in human cancers. *Nature Education*, 3(9), p.6.
- von Muhlinen, N., Horikawa, I., Alam, F., Isogaya, K., Lissa, D., Vojtesek, B., Lane, D.P. and Harris, C.C., (2018). p53 isoforms regulate premature aging in human cells. *Oncogene*, 37(18), pp.2379-2393.

- Wagner, K.D. and Wagner, N., (2022). The senescence markers p16INK4A, p14ARF/p19ARF, and p21 in organ development and homeostasis. *Cells*, 11(12), p.1966.
- Waldherr, A. and Fogtman, A., (2025). Radiation symptoms resemble laminopathies and the physical underlying cause may sit at the lamin A C-terminus. *Molecular Medicine*, 31(1), p.69.
- Wang, B., Han, J., Elisseeff, J.H. and Demaria, M., (2024). The senescence-associated secretory phenotype and its physiological and pathological implications. *Nature Reviews Molecular Cell Biology*, 25(12), pp.958-978.
- Wang, Y., Ren, K., Tan, J. and Mao, Y., (2023). Alginate oligosaccharide alleviates aging-related intestinal mucosal barrier dysfunction by blocking FGF1-mediated TLR4/NF- κ B p65 pathway. *Phytomedicine*, 116, p.154806.
- Wang, Y., Goh, L. L., & Chin, K.-Y. (2026). D-galactose-induced osteoporosis in rodents—Model development, skeletal characteristics, and optimal dosing regimens: A scoping review. *Biomolecules and Biomedicine*. <https://doi.org/10.17305/bb.2026.13914>.
- Wiemer, M. and Osiewacz, H.D. (2014). Effect of paraquat-induced oxidative stress on gene expression and aging of the filamentous ascomycete *Podospora anserina*. *Microbial Cell*, 1(7), p.225.
- Wilson, M.M. and Morley, J., (2003). Impaired cognitive function and mental performance in mild dehydration. *European journal of clinical nutrition*, 57(2), pp.S24-S29.
- Wiskur, B. and Greenwood-Van Meerveld, B., (2010). The aging colon: the role of enteric neurodegeneration in constipation. *Current gastroenterology reports*, 12(6), pp.507-512.
- Xie, D., Jiang, L., Lin, Y. and Liu, Z., (2020). Antioxidant activity of selenium-enriched *Chrysomya megacephala* (Fabricius) larvae powder and its impact on intestinal microflora in D-galactose induced aging mice. *BMC complementary medicine and therapies*, 20(1), p.264.

- Xu, J., Chen, Y., Liu, S. and Hou, X., (2013). Electroacupuncture regulates apoptosis/proliferation of intramuscular interstitial cells of cajal and restores colonic motility in diabetic constipation rats. *Evidence-Based Complementary and Alternative Medicine*, 2013(1), p.584179.
- Yosef, R., Pilpel, N., Papismadov, N., Gal, H., Ovadya, Y., Vadai, E., Miller, S., Porat, Z., Ben-Dor, S. and Krizhanovsky, V., (2017). p21 maintains senescent cell viability under persistent DNA damage response by restraining JNK and caspase signaling. *The EMBO journal*, 36(15), pp.2280-2295.
- Zeng, X.L., Yang, X.N. and Liu, X.J., (2022). Resveratrol attenuates cigarette smoke extract induced cellular senescence in human airway epithelial cells by regulating the miR-34a/SIRT1/NF- κ B pathway. *Medicine*, 101(46), p.e31944.
- Zhao, J., Tian, F., Zhao, N., Zhai, Q., Zhang, H. and Chen, W., (2017). Effects of probiotics on d-galactose-induced oxidative stress in plasma: A meta-analysis of animal models. *Journal of Functional Foods*, 39, pp.44-49.
- Zhang, P., Wu, P., Li, C., Deng, R. and Chen, X.D., (2025). Modeling age-related gastrointestinal changes in food digestion: Progress and challenges in transitioning from in vivo studies to physiologically relevant in vitro systems. *Current Opinion in Food Science*, p.101357.
- Zhang, X. X., He, S. H., Liang, X., Li, W., Li, T. F., & Li, D. F. (2021). Aging, cell senescence, the pathogenesis and targeted therapies of osteoarthritis. *Frontiers in Pharmacology*, 12, 728100.
- Zheng, Y., Chen, X., Ding, C., Liu, X., Chi, L. and Zhang, S., (2024). Absciscic acid ameliorates d-galactose-induced aging in mice by modulating AMPK-SIRT1-p53 pathway and intestinal flora. *Heliyon*, 10(6).
- Zhu, J., Mu, X., Zeng, J., Xu, C., Liu, J., Zhang, M., Li, C., Chen, J., Li, T. and Wang, Y., (2014). Ginsenoside Rg1 prevents cognitive impairment and hippocampus senescence in a rat model of D-galactose-induced aging. *PloS one*, 9(6), p.e101291.

