

## DAFTAR PUSTAKA

Abu-Raddad, L. J., Chemaitelly, H. and Bertollini, R. (2021). Severity of SARS-CoV-2 reinfections as compared with primary infections. *New England Journal of Medicine*, 385(26) ; 2487–2489. doi: 10.1056/nejmc2108120.

Ahmad, T., Chaudhuri, R., Joshi, M.C., Almatroudi, A., Rahmani, A.H., Ali, S.M. *et al.* (2020). COVID-19: the emerging immunopathological determinants for recovery or death. *Frontiers in Microbiology.*, 11: 588409. doi: 10.3389/fmicb.2020.588409.

Ahmed, F., Jo, D. H. and Lee, S. H. (2020). Can natural killer cells be a principal player in anti-SARS-CoV-2 immunity?. *Frontiers in Immunology.*, 11: 5886765 . doi: 10.3389/fimmu.2020.586765.

Al-Kuraishy, H. M. Al-Gareeb, A. I., Alkazmi, L., Habotta, O. A., Batiha, G. E. (2022). High-mobility group box 1 (HMGB1) in COVID-19 extrapolation of dangerous liaisons. *Inflammopharmacology*, 30: 811–820. doi: 10.1007/s10787-022-00988-y.

Alexandris, N., Lagoumintzis, G., Chasapis, C.T., Leonidas, D.D., Papadopoulos, G.E., Tzartos, S.J. *et al.* (2021). Nicotinic cholinergic system and COVID-19: In silico evaluation of nicotinic acetylcholine receptor agonists as potential therapeutic interventions. *Toxicology Reports.*, 8: 73–83. doi: 10.1016/j.toxrep.2020.12.013.

Allonso, D. Belgrano, F. S., Calzada, N., Guzmán, M. G., Vázquez, S., Mohana-Borges, R. (2012). Elevated serum levels of high mobility group box 1 (HMGB1) protein in dengue-infected patients are associated with disease symptoms and secondary infection. *Journal of Clinical Virology*, 55: 214–219. doi: 10.1016/j.jcv.2012.07.010.

Ambrożek-Latecka, M., Kozłowski, P., Hoser, G., Bandyszewska, M., Hanusek, K., Nowis, D. *et al.* (2024). SARS-CoV-2 and its ORF3a, E, and M viroporins activate inflammasome in human macrophages and induce of IL-1 $\alpha$  in pulmonary epithelial and endothelial cells. *Cell Death Discovery*, 10: 191. doi: 10.1038/s41420-024-01966-9.

Andersson, U. (2020). The cholinergic anti-inflammatory pathway alleviates acute lung injury. *Molecular Medicine*, 26: 64. doi: 10.1186/s10020-020-00184-0.

Andersson, U., Ottestad, W. and Tracey, K. J. (2020). Extracellular HMGB1: A therapeutic target in severe pulmonary inflammation including COVID-19?. *Molecular Medicine*, 26: 42. doi: 10.1186/s10020-020-00172-4.

Andersson, U., Yang, H. and Harris, H. (2018). High-mobility group box 1 protein (HMGB1) operates as an alarmin outside as well as inside cells. *Seminars in Immunology*, 38: 40–48. doi: 10.1016/j.smim.2018.02.011.

Andersson, U., Tracey, K. J. and Yang, H. (2021). Post-translational modification of HMGB1 disulfide bonds in stimulating and inhibiting inflammation. *Cells*, 10: 3323. doi: 10.3390/cells10123323.

Anggayasti, W. L., Mancera, R.L., Bottomley, S., Helmerhorst, E. (2017). The self-association of HMGB1 and its possible role in the binding to DNA and cell membrane receptors. *FEBS Letters*, 591: 282–294. doi: 10.1002/1873-3468.12545.

Angioni, R. Bonfanti, M., Caporale, N., Sánchez-Rodríguez, R., Munari, F., Savino, A., *et al.* (2023). RAGE engagement by SARS-CoV-2 enables monocyte infection and underlies COVID-19 severity. *Cell Reports Medicine*, 4: 101266. doi: 10.1016/j.xcrm.2023.101266.

Aucott, H., Sowinska, A., Harris, H.E., Lundback, P. (2018). Ligation of free HMGB1 to TLR2 in the absence of ligand is negatively regulated by the C-terminal tail domain. *Molecular Medicine*, 24: 19. doi: 10.1186/s10020-018-0021-x.

Bailly, C. and Vergoten, G. (2020). Glycyrrhizin: An alternative drug for the treatment of COVID-19 infection and the associated respiratory syndrome?. *Pharmacology and Therapeutics*, 214: 107618. doi: 10.1016/j.pharmthera.2020.107618.

Belgrano, F. S., De Abreu Da Silva, I.C., Bastos De Oliveira, F.M., Fantappiè, M.R., Mohana-Borges, R. (2013). Role of the acidic tail of high mobility group protein B1 (HMGB1) in protein stability and DNA bending. *PLoS ONE*, 8 (11): e79572. doi: 10.1371/journal.pone.0079572.

van den Berg, D. F. and te Velde, A. A. (2020). Severe COVID-19: NLRP3 inflammasome dysregulated. *Frontiers in Immunology*. 11: 1580. doi: 10.3389/fimmu.2020.01580.

Bertheloot, D. Naumovsk, A. L., Langhoff, P., Horvath, G. L., Jin, T., Xiao, T. S. *et al.* (2016). RAGE enhances TLR responses through binding and internalization of RNA. *J Immunol*, 197(10): 4118–4126. doi: 10.4049/jimmunol.1502169.

Bolay, H., Karadas, Ö., Oztürk, B., Sonkaya, R., Tasdelen, B., Bulut, T.D.S. *et al.* (2021). HMGB1, NLRP3, IL-6 and ACE2 levels are elevated in COVID-19 with headache: a window to the infection-related headache mechanism. *Journal of Headache and Pain*, 22: 94. doi: 10.1186/s10194-021-01306-7.

Bongoni, A. K., Klymiuk, N., Wolf, E., Ayares, D., Rieben, R., Cowan, P.J. (2016). Transgenic expression of human thrombomodulin inhibits HMGB1-induced

porcine aortic endothelial cell activation. *Transplantation*, 100(9): 1871–1879. doi: 10.1097/TP.0000000000001188.

Borges, R. C., Hohmann, M. S. and Borghi, S. M. (2020). Dendritic cells in COVID-19 immunopathogenesis: insights for a possible role in determining disease outcome. *International Reviews of Immunology*. doi: 10.1080/08830185.2020.1844195.

Boumaza, A., Gay, L., Mezouar, S., Bestion, E., Diallo, A.B., Michel, M., *et al.* (2021). Monocytes and macrophages, targets of severe acute respiratory syndrome coronavirus 2: the clue for coronavirus disease 2019 immunoparalysis. *The Journal of Infectious Diseases*, 224: 395–406. doi: 10.1093/infdis/jiab044.

Boutin, S., Hildebrand, D., Boulant, S., Kreuter, M., Rüter, J., Pallerla, S. R., *et al.* (2021). Host factors facilitating SARS-CoV-2 virus infection and replication in the lungs. *Cellular and Molecular Life Sciences*, 78: 5953–5976. doi: 10.1007/s00018-021-03889-5.

Browne, E., Kavanagh, S. and Devery, S. (2022). The Cytotoxicity of phorbol 12-myristate 13-acetate and lipopolysaccharide on THP-1 cells and an optimized differentiation protocol. *Medical Science Forum*, 11: 5. doi: 10.3390/bitap-12785.

Buehler, P. W., Humar, R. and Schaer, D. J. (2020). Haptoglobin therapeutics and compartmentalization of cell-free hemoglobin toxicity. *Trends in Molecular Medicine*, 26(7): 683–697. doi: 10.1016/j.molmed.2020.02.004.

Burhan, E., Susanto, A. D., Nasution, S. A., Eka, G., Pitoyo, C. W., Susilo, A., *dkk.* 2022. *Pedoman Tatalaksana COVID-19*. PDPI, PERKI, PAPDI, PERDATIN, IDAI.

Cahyani, I., Putro, E. W., Ridwanuloh, A. M., Wibowo, S., Hariyatun, Syahputra, G. *et al.* (2022). Genome profiling of SARS-CoV-2 in Indonesia, ASEAN and the neighbouring East Asian countries: features, challenges and achievements. *Viruses*, 14: 778. doi: 10.3390/v14040778.

Cavalli, G. and Dinarello, C. A. (2018). Anakinra therapy for non-cancer inflammatory diseases. *Frontiers in Pharmacology*, 9: 1157. doi: 10.3389/fphar.2018.01157.

Cazzato, G., Colagrande, A., Cimmino, A., Cicco, G., Scarcella, V.S., Tarantino, P. *et al.* (2021). HMGB1-TIM3-HO1: A new pathway of inflammation in skin of SARS-CoV-2 patients? a retrospective pilot study. *Biomolecules*, 11: 1219. doi: 10.3390/biom11081219.

CDC. (2024). The changing threat of COVID-19. *National Centre for Immunization and Respiratory Disease*. <https://www.cdc.gov/ncird/whats-new/changing-threat->

[covid-19.html. Diakses 21 November 2024.](#)

Cecchinato, V., D'Agostino, G., Raeli, L., Nerviani, A., Schiraldi, M., Danelon, G. *et al.* (2018). Redox-mediated mechanisms fuel monocyte responses to CXCL12/HMGB1 in active rheumatoid arthritis. *Frontiers in Immunology*, 9: 2118. doi: 10.3389/fimmu.2018.02118.

Cevik, M., Kuppalli, K., Kindrachuk, J, Peiris, M. (2020). Virology, transmission, and pathogenesis of SARS-CoV-2. *The BMJ*, 371: m3862. doi: 10.1136/bmj.m3862.

Chen, D., Bellussi, L. M., Cocca, S., Wang, J., Passali, G. C., Hao, X., *et al.* (2017). Glycyrrhetic acid suppressed HMGB1 release by up-regulation of SIRT6 in Nasal inflammation. *Journal of Biological Regulators and Homeostatic Agents*, 31(2): 269–277.

Chen, L. Long, X., Xu, Q., Tan, J., Wang, G., Cao, Y., *et al.* (2020a). Elevated serum levels of S100A8/A9 and HMGB1 at hospital admission are correlated with inferior clinical outcomes in COVID-19 patients. *Cellular and Molecular Immunology*, 17: 992–994. doi: 10.1038/s41423-020-0492-x.

Chen, R. Huang, Y., Quan, J., Liu, J., Wang, H., Billiar, T. R., *et al.* (2020b). HMGB1 as a potential biomarker and therapeutic target for severe. *Heliyon*, 6: e05672. doi: 10.1016/j.heliyon.2020.e05672.

Chitra, S., Nalini, G. and Lokeswari, T. (2014). Comparison of differentiation to macrophages in isolated monocytes from human peripheral blood and THP1 cells. *Sri Ramachandra Journal of Medicine*, 7(1).

Chrzanowski, J., Chrzanowska, A. and Graboń, W. (2021). Glycyrrhizin: An old weapon against a novel coronavirus. *Phytotherapy Research*, 35: 629–636. doi: 10.1002/ptr.6852.

Chu, X. H. Hu, H. Y., Godje, I. S. G., Zhu, L. J., Zhu, J. B., Feng, Y. L. (2023). Elevated HMGB1 and sRAGE levels in cerebrospinal fluid of aneurysmal subarachnoid hemorrhage patients. *Journal of Stroke and Cerebrovascular Diseases*, 32(5): 107061. doi: 10.1016/j.jstrokecerebrovasdis.2023.107061.

Cicco, S. Cicco, G., Racanelli, V., Vacca, A. (2020). Neutrophil extracellular traps (nets) and damage-associated molecular patterns (DAMPs): two potential targets for COVID-19 treatment. *Mediators of Inflammation*. doi:10.1155/2020/7527953.

Colavita, L., Ciprandi, G., Salpietro, A., Cuppari, C. (2020). HMGB1: A pleiotropic activity. *Pediatric Allergy and Immunology*, 31(S26): 63–65. doi: 10.1111/pai.13358.

Contoli, M., Papi, A., Tomassetti, L., Rizzo, P., Segal, F. V. D., Fortini, F., *et al.* (2021). Blood interferon- $\alpha$  levels and severity, outcomes, and inflammatory profiles in hospitalized COVID-19 patients. *Frontiers in Immunology*, 12: 648004. doi: 10.3389/fimmu.2021.648004.

Coutinho, L. L. C., Oliveira, C. N., Albuquerque, P. L.M.M., Mota, S. M.B., Meneses, G. C., Martins, A. M.C. *et al.* (2022). Elevated IL-18 predicts poor prognosis in critically ill COVID-19 patients at a Brazilian hospital in 2020-21. *Future Microbiology*, 17: 1287–1294. doi: 10.2217/fmb-2022-0057.

COVID-19 Treatment Guidelines Panel. (2024). Coronavirus Disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. <https://www.covid19treatmentguidelines.nih.gov/>. Diakses 1 Maret 2024.

Crayne, C. B. Albeituni, S., Nichols, K. E., and Cron, R. Q. (2019). The immunology of macrophage activation syndrome. *Frontiers in Immunology*, 10: 119. doi: 10.3389/fimmu.2019.00119.

Das, N. Dewan, V., Grace, P. M., Gunn, R. J., Tamura, R., Tzarum, N., *et al.* (2016). HMGB1 activates proinflammatory signaling via TLR5 leading to allodynia. *Cell Reports*, 17: 1128–1140. doi: 10.1016/j.celrep.2016.09.076.

Dash, S. P., Gupta, S. and Sarangi, P. P. (2024). Monocytes and macrophages: Origin, homing, differentiation, and functionality during inflammation. *Heliyon*, 10(8): e29686. doi: 10.1016/j.heliyon.2024.e29686

Deng, J., Ma, Y., Liu, Q., Du, M., Liu, M., Liu, J. (2023). Severity and outcomes of SAR-CoV-2 reinfection compared with primary infection: a systematic review and meta-analysis. *International Journal of Environmental Research and Public Health*, 20: 3335. doi: 10.3390/ijerph20043335

Diao, B. Wang, C., Tan, Y., Chen, X., Liu, Y., Ning, L., *et al.* (2020). Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). *Frontiers in Immunology*, 11: 827. doi: 10.3389/fimmu.2020.00827.

Du, A., Zheng, R., Disoma, C., Li, S., Chen, Z., Li, S., *et al.* (2021). Epigallocatechin-3-gallate, an active ingredient of traditional chinese medicines, inhibits the 3CLpro activity of SARS-CoV-2. *International Journal of Biological Macromolecule*, 176: 1–12. doi:10.1016/j.ijbiomac.2021.02.012.

Dubey, A., Lavanya, L., Sadananda, D., Gouthami, K., Elfansu, K., Singh, A *et al.* (2021). Inferences of carbon dioxide in present-day cell culture systems: an unacknowledged problem and perspectives. *Austin Therapeutics*, 6(1). doi: 10.26420/austintherapeutics.2021.1033.

Eiz-Vesper, B. and Schmetzer, H. M. (2020). Antigen-presenting cells: Potential of proven and new players in immune therapies. *Transfusion Medicine and Hemotherapy*, 47: 429–31. doi: 10.1159/000512729.

El-zayat, S. R., Sibaii, H. and Mannaa, F. A. (2019). Toll-like receptors activation, signaling, and targeting: an overview. *Bulletin of the National Research Centre*, 43: 187. <https://doi.org/10.1186/s42269-019-0227-2>.

El-Zayat, S. R., Sibaii, H. and Mannaa, F. A. (2019). Micronutrients and many important factors that affect the physiological functions of toll-like receptors. *Bulletin of the National Research Centre*, 43: 123. doi: 10.1186/s42269-019-0165z.

Fan, X. Song, J. W., Wang, S. Y., Cao, W. J., Wang, X. W., Zhou, M. J. *et al.* (2021). Changes of Damage Associated Molecular Patterns in COVID-19 Patients. *Infectious Diseases & Immunity*, 1(1): 20-27. doi:10.1097/01.ID9.0000733572.40970.6c.

Fantini, J. Di, C., Chahinian, H., and Yahi, N. (2020). Structural and molecular modeling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection. *International Journal of Antimicrobial Agents*, 55: 105960. doi:10.1016/j.ijantimicag.2020.105960.

Farooqui, A. Khan, F., Khan, I., Ansari, I. A. (2018). Glycyrrhizin induces reactive oxygen species-dependent apoptosis and cell cycle arrest at G0/G1 in HPV18+ human cervical cancer HeLa cell line. *Biomedicine and Pharmacotherapy*, 97: 752–764. doi: 10.1016/j.biopha.2017.10.147.

Farzi, R., Aghbash, P. S., Eslami, N., Azadi, A., Shamekh, A., *et al.* (2022). The role of antigen-presenting cells in the pathogenesis of COVID-19. *Pathology - Research and Practice*, 233: 153848. doi: 10.1016/j.prp.2022.153848.

Ferreira, A. C. Soares, V. C., de Azevedo-Quintanilha, I. G., Dias, S. da S. G., Fintelman-Rodrigues, N., Sacramento, C. Q., *et al.* (2021). SARS-CoV-2 engages inflammasome and pyroptosis in human primary monocytes. *Cell Death Discovery*, 7: 43. doi: 10.1038/s41420-021-00428-w.

Forrester, M. A., Wassall, H. J., Hall, L. S., Cao, H., Wilson, H. M., Barker, R. N. *et al.* (2018). Similarities and differences in surface receptor expression by THP-1 monocytes and differentiated macrophages polarized using seven different conditioning regimens. *Cellular Immunology*, 332: 58–76. doi: 10.1016/j.cellimm.2018.07.008.

Frediansyah, A., Nainu, F., Dhama, K., Mudatsir, Harapan, H. (2021). Remdesivir and its antiviral activity against COVID-19: A systematic review. *Clinical Epidemiology and Global Health*, 9 : 123–127. doi: 10.1016/j.cegh.2020.07.011.

Fu, Y., Zhou, E., Wei, Z., Song, X., Liu, Z., Wang, T. *et al.* (2014). Glycyrrhizin inhibits lipopolysaccharide-induced inflammatory response by reducing TLR4 recruitment into lipid rafts in RAW264.7 cells. *Biochimica et Biophysica Acta - General Subjects*, 1840: 1755–1764. doi: 10.1016/j.bbagen.2014.01.024.

Gavriatopoulou, M., Korompoki, E., Fotiou, D., Ntanasis-Stathopoulos, I., Psaltopoulou, T., Kastritis, E. *et al.* (2020). Organ-specific manifestations of COVID-19 infection. *Clinical Experimental Medicine*, 20: 493–506. doi:10.1007/s10238-020-00648-x.

Greenhalgh, T., Sivan, M., Perlowski, A., Nikolich, J. (2024). Long COVID: a clinical update. *The Lancet*, 404(10453): 707–724. doi: 10.1016/S0140-6736(24)01136-X.

Grigorov, I., Pejić, S., Todorović, A., Drakulić, D., Veljković, F., Vukajlović, J.M., *et al.* (2023). Serum high-mobility group box 1 and heme oxygenase-1 as biomarkers in COVID-19 patients at hospital admission. *International Journal of Molecular Sciences*, 24: 13164. doi: 10.3390/ijms241713164.

Gomaa, A. A. and Abdel-Wadood, Y. A. (2021). The potential of glycyrrhizin and licorice extract in combating COVID-19 and associated conditions. *Phytomedicine Plus*, 1(3) : 100043. doi: 10.1016/j.phyplu.2021.100043.

Gong, W., Zheng, Y., Chao, F., Li, Y., Xu, Z., Huang, G., *et al.* (2010). The anti-inflammatory activity of HMGB1 A box is enhanced when fused with C-terminal acidic tail. *Journal of Biomedicine and Biotechnology*, 2010. doi: 10.1155/2010/915234.

Gowda, P., Patrick, S., Joshi, S. D., Kumawat, R. K., Sen, E. (2021). Glycyrrhizin prevents SARS-CoV-2 S1 and Orf3a induced high mobility group box 1 (HMGB1) release and inhibits viral replication. *Cytokine*, 142: 155496. doi: 10.1016/j.cyto.2021.155496.

Grégoire, M., Uhel, F., Lesouhaitier, M., Gacouin, A., Guirriec, M., Mourcin, F. *et al.* (2018). Impaired efferocytosis and neutrophil extracellular trap clearance by macrophages in ARDS. *European Respiratory Journal*, 52: 1702590. doi: 10.1183/13993003.02590-2017.

Gu, J. J., Chen, J. B., Zhang, J. H., Zhang, H., Wang, S. S. (2016). Recombinant human soluble thrombomodulin protects against brain injury in a CVST rat model, via downregulation of the HMGB1-RAGE axis. *Molecular Medicine Reports*, 14: 5217–5222. doi: 10.3892/mmr.2016.5891.

Guedes, A. R., Oliveira, M. S., Tavares, B. M., Luna-Muschi, A., Lazari, C. S., Montal, A. C. *et al.* (2023). Reinfection rate in a cohort of healthcare workers over

2 years of the COVID-19 pandemic. *Scientific Reports*, 13: 712. doi: 10.1038/s41598-022-25908-6.

Gu, X., Wang, S., Zhang, W., Li, C., Guo, L., Wang, Z. *et al.* (2023). Probing long COVID through a proteomic lens: a comprehensive two-year longitudinal cohort study of hospitalized survivors. *eBioMedicine*, 98: 104851. doi: 10.1016/j.ebiom.2023.104851.

Han, J. Sun, J., Zhang, G., and Chen, H. (2021). DCs-based therapies: Potential strategies in severe SARS-CoV-2 infection. *International Journal of Medical Sciences*, 18(2): 406–418. doi: 10.7150/ijms.47706.

Han, M. S., Byun, J. H., Cho, Y., Rim, J. H. (2021). RT-PCR for SARS-CoV-2: quantitative versus qualitative. *The Lancet Infectious Diseases*, 21: 165. doi: 10.1016/S1473-3099(20)30424-2.

Han, Y., Yuan, F., Deng, C., He, F., Zhang, Y., Shen, H., *et al.* (2019). Metformin decreases LPS-induced inflammatory response in rabbit annulus fibrosus stem/progenitor cells by blocking HMGB1 release. *Aging*, 11(22): 10252–10265. doi: 10.18632/aging.102453.

He, M. Bianchi, M. E., Coleman, T. R., Tracey, K. J., Al-Abed, Y. (2018). Exploring the biological functional mechanism of the HMGB1/TLR4/MD-2 complex by surface plasmon resonance. *Molecular Medicine*, 24: 21. doi: 10.1186/s10020-018-0023-8.

He, Q., You, H., Li, X., Liu, T., Wang, P., Wang, B. (2012). HMGB1 promotes the synthesis of pro-il-1 $\beta$  and pro-il-18 by activation of p38 MAPK and NF- $\kappa$ B through receptors for advanced glycation end-products in macrophages. *Asian Pacific Journal of Cancer Prevention*, 13: 1365–1370. doi:10.7314/APJCP.2012.13.4.1365.

Hedberg, P., Valik, J. K., Van Der Werff, S., Tanushi, H., Mendez, A. R., Granath, F., *et al.* (2022). Clinical phenotypes and outcomes of SARS-CoV-2, influenza, RSV and seven other respiratory viruses: A retrospective study using complete hospital data. *Thorax*, 77: 1–10. doi: 10.1136/thoraxjnl-2021-216949.

Hikmawati, I. and Setiyabudi, R. (2021). Epidemiology of COVID-19 in Indonesia: common source and propagated source as a cause for outbreaks. *Journal of Infection in Developing Countries*, 15(5) : 646–652. doi: 10.3855/JIDC.14240.

Horiuchi, T., Sakata, N., Narumi, Y., Kimura, T., Hayashi, T., Nagano, K., *et al.* (2017). Metformin directly binds the alarmin HMGB1 and inhibits its proinflammatory activity. *Journal of Biological Chemistry*, 292(20): 8436–8446. doi: 10.1074/jbc.M116.769380.

Hu, B., Guo, H., Zhou, P., and Shi, Z. L. (2021). Characteristics of SARS-CoV-2 and COVID-19. *Nature Reviews Microbiology*, 19(3): 141–154. doi: 10.1038/s41579-020-00459-7.

Ito, T., Thachil, J., Asakura, H., Levy, J. H., Iba, T. (2019). Thrombomodulin in disseminated intravascular coagulation and other critical conditions - A multifaceted anticoagulant protein with therapeutic potential. *Critical Care*, 23: 280. doi: 10.1186/s13054-019-2552-0.

Iwasaki, A. and Yang, Y. (2020). The potential danger of suboptimal antibody responses in COVID-19, *Nature Reviews Immunology*, 20(6): 339–341. doi: 10.1038/s41577-020-0321-6.

Jamilloux, Y., Henry, T., Belot, A., Viel, S., Fauter, M., El, T., Walzer, T., *et al.* (2020). Should we suppress or stimulate immune responses for COVID-19? Cytokine and anti-cytokine interventions. *Autoimmunity Reviews*, 19: 102567. doi:10.1016/j.autrev.2020.102567.

Jang, M. Park, Y. I., Cha, Y. E., Park, R., Namkoong, S., Lee, J. I., *et al.* (2020). Tea Polyphenols EGCG and theaflavin inhibit the activity of SARS-CoV-2 3CL-protease in vitro. *Evidence-based Complementary and Alternative Medicine*. doi: 10.1155/2020/5630838.

Jiang, C., Qu, X., Ke, H., Gong, W., Chen, R., Yang, W., *et al.* (2018). Association between the HMGB1/TLR4 signaling pathway and the clinicopathological features of ovarian cancer. *Molecular Medicine Reports*, 18(3): 3093–3098. doi: 10.3892/mmr.2018.9271.

Joffre, O. P., Segura, E., Savina, A., Amigorena, S.. (2012). Cross-presentation by dendritic cells. *Nature Reviews Immunology*, 12: 557–569. doi: 10.1038/nri3254.

Junqueira, D. R., Zorzela, L. M. and Perini, E. (2017). Unfractionated heparin versus low molecular weight heparins for avoiding heparin-induced thrombocytopenia in postoperative patients. *Cochrane Database of Systematic Reviews*, 4. doi: 10.1002/14651858.CD007557.pub3.

Kang, R. Chen, R., Zhang, Q., Hou, W., Wu, S., Cao, L. *et al.* (2014). HMGB1 in health and disease. *Molecular Aspects of Medicine*, 40: 1–116. doi: 10.1016/j.mam.2014.05.001.

Kaplanski, G. (2018). Interleukin-18: Biological properties and role in disease pathogenesis. *Immunological Reviews*, 281: 138–153. doi: 10.1111/imr.12616.

Kawase, A., Takashima, O., Tanaka, S., Shimada, H., Iwaki, M. (2022). Diclofenac-induced cytotoxicity in direct and indirect co-culture of Hepg2 cells with differentiated THP-1 Cells. *International Journal of Molecular Sciences*, 23:

8660. doi: 10.3390/ijms23158660.

Kementrian Kesehatan RI (2024). Tidak benar pandemi COVID-19 disebut rekayasa.

<https://sehatnegeriku.kemkes.go.id/baca/umum/20241022/0946673/tidak-benar-pandemi-covid-19-disebut-rekayasa/>. Diakses 15 Oktober 2024

Kementerian Kesehatan RI (2020). Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MenKes/413/2020 Tentang Pedoman Pencegahan dan Pengendalian Coronavirus Disease 2019 (Covid-19). *MenKes/413/2020*, pp. 1–207. [https://infeksiemerging.kemkes.go.id/download/KMK\\_No.\\_HK.01.07-MENKES-413-2020\\_ttg\\_Pedoman\\_Pencegahan\\_dan\\_Pengendalian\\_COVID-19.pdf](https://infeksiemerging.kemkes.go.id/download/KMK_No._HK.01.07-MENKES-413-2020_ttg_Pedoman_Pencegahan_dan_Pengendalian_COVID-19.pdf). Diakses 10 Februari 2024.

Khoshkam, Z., Aftabi, Y., Stenvinkel, P., Lawrence, B. P., Rezaei, M. H., Ichihara, G., *et al.* (2021). Recovery scenario and immunity in COVID-19 disease: A new strategy to predict the potential of reinfection. *Journal of Advanced Research*, 31: 49–60. doi: 10.1016/j.jare.2020.12.013.

Kreitinger, J. M., Beamer, C. A., and Shepherd, D. M. (2016). Environmental Immunology: Lessons Learned from Exposure to a Select Panel of Immunotoxicants. *The Journal of Immunology*, 196: 3217–3225. doi: 10.4049/jimmunol.1502149.

Kreutmair, S., Unger, S., Núñez, N. G., Ingelfinger, F., Alberti, C., De Feo, D., *et al.* (2021). Distinct immunological signatures discriminate severe COVID-19 from non-SARS-CoV-2-driven critical pneumonia. *Immunity*, 54: 1578–1593. doi: 10.1016/j.immuni.2021.05.002.

Krysko, O., Kondakova, E., Vershinina, O., Galova, E., Blagonravova, A., Gorshkova, E., *et al.* (2021). Artificial intelligence predicts severity of COVID-19 based on correlation of exaggerated monocyte activation, excessive organ damage and hyperinflammatory syndrome: a prospective clinical study. *Frontiers in Immunology*, 12: 715072. doi: 10.3389/fimmu.2021.715072.

Kumar, P., Sobhanan, J., Takano, Y., and Biju, V. (2021). Molecular recognition in the infection, replication, and transmission of COVID-19-causing SARS-CoV-2: an emerging interface of infectious disease, biological chemistry, and nanoscience. *NPG Asia Materials*, 13: 14. doi: 10.1038/s41427-020-00275-8.

Kuzmich, N. N., Sivak, K. V., Chubarev, V. N., Porozov, Y. B., Savateeva-Lyubimova, T. N., Peri, F. (2017). TLR4 signaling pathway modulators as potential therapeutics in inflammation and sepsis. *Vaccines*, 5: 34. doi: 10.3390/vaccines5040034.

Kwak, M. S., Kim, H. S., Lkhamsuren, K., Kim, Y. H., Han, M. G., Shin, J. M., *et al.* (2019). Peroxiredoxin-mediated disulfide bond formation is required for nucleocytoplasmic translocation and secretion of HMGB1 in response to inflammatory stimuli. *Redox Biology*, 24: 101203. doi: 10.1016/j.redox.2019.101203.

Lagos, L. S., Luu, T. V., De Haan, B., Faas, M., De Vos, P. (2022). TLR2 and TLR4 activity in monocytes and macrophages after exposure to amoxicillin, ciprofloxacin, doxycycline and erythromycin. *Journal of Antimicrobial Chemotherapy*. 77: 2972–2983. doi: 10.1093/jac/dkac254.

Lakbar, I., Luque-Paz, D., Mege, J. L., Einav, S., Leone, M. (2020). COVID-19 gender susceptibility and outcomes: A systematic review. *PLoS ONE*, 15(11): e0241827. doi: 10.1371/journal.pone.0241827.

Lan, J., Luo, H., Wu, R., Wang, J., Zhou, B., Zhang, Y., *et al.* (2020). Internalization of HMGB1 (high mobility group box 1) promotes angiogenesis in endothelial cells. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 40: 2922–2940. doi: 10.1161/ATVBAHA.120.315151.

Land, W. G. (2020). Use of DAMPs and SAMPs as therapeutic targets or therapeutics: a note of caution. *Molecular Diagnosis and Therapy*, 24: 251–262. doi: 10.1007/s40291-020-00460-z.

Land, W. G. (2021). Role of DAMPs in respiratory virus-induced acute respiratory distress syndrome—with a preliminary reference to SARS-CoV-2 pneumonia. *Genes and Immunity*, 22(3): 141–160. doi: 10.1038/s41435-021-00140-w.

Lasky, J. A., Fuloria, J., Morrison, M. E., Lanier, R., Naderer, O., Brundage, T., *et al.* (2020). Design and rationale of a randomized, double-blind, placebo-controlled, phase 2/3 study evaluating dociparstat in acute lung injury associated with severe COVID-19. *Advances in Therapy*. doi: 10.1007/s12325-020-01539-z.

Latz, E. and Duewell, P. (2018). NLRP3 inflammasome activation in inflammaging. *Seminars in Immunology*, 40: 61–73. doi: 10.1016/j.smim.2018.09.001.

Leblanc, P. M., Doggett, T. A., Choi, J., Hancock, M. A., Durocher, Y., Frank, F., *et al.* (2014). An immunogenic peptide in the A-box of HMGB1 protein reverses apoptosis-induced tolerance through RAGE. *Journal of Biological Chemistry*, 289(11): 7777–7786. doi: 10.1074/jbc.M113.541474.

Lee, M. J. (2021). Quantifying SARS-CoV-2 viral load: current status and future prospects. *Expert Review of Molecular Diagnostics*, 21(10):1017–1023. doi: 10.1080/14737159.2021.1962709.

Lee, S. A., Kwak, M. S., Kim, S., Shin, J. S. (2014). The role of high mobility group box 1 in innate immunity. *Yonsei Medical Journal*, 55(5): 1165–1176. doi: 10.3349/ymj.2014.55.5.1165.

Lee, S. A., Lee, S. H., Kim, J. Y., Lee, W. S. (2019). Effects of glycyrrhizin on lipopolysaccharide-induced acute lung injury in a mouse model. *Journal of Thoracic Disease*, 11(4): 1287–1302. doi: 10.21037/jtd.2019.04.14.

Lega, S., Naviglio, S., Volpi, S., Tommasini, A. (2020). Recent insight into SARS-COV2 immunopathology and rationale for potential treatment and preventive strategies in COVID-19. *Vaccines*, 8: 224. doi: 10.3390/vaccines8020224.

Li, L., Ling, Y., Huang, M., Yin, T., Gou, S. M., Zhan, N. Y. *et al.* (2015). Heparin inhibits the inflammatory response induced by LPS and HMGB1 by blocking the binding of HMGB1 to the surface of macrophages. *Cytokine*, 72: 36–42. doi: 10.1016/j.cyto.2014.12.010.

Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., *et al.* (2020). Early transmission dynamics in Wuhan, China, of novel Coronavirus–infected pneumonia. *New England Journal of Medicine*, 382(13): 1199–1207. doi: 10.1056/nejmoa2001316.

Li, W., Ashok, M., Li, J., Yang, H., Sama, A. E., Wang, H. (2007). A major ingredient of green tea rescues mice from lethal sepsis partly by inhibiting HMGB1, *PLoS ONE*, 2(11): e1153. doi: 10.1371/journal.pone.0001153.

Li, Y., Wang, L., Zhang, B., Gao, F., Yang, C. M. (2019). Glycyrrhizin, an HMGB1 inhibitor, exhibits neuroprotective effects in rats after lithium-pilocarpine-induced status epilepticus. *Journal of Pharmacy and Pharmacology*, 71: 390–399. doi: 10.1111/jphp.13040.

Liang, S., Bao, C., Yang, Z., Liu, S., Sun, Y., Cao, W. *et al.* (2023). SARS-CoV-2 spike protein induces IL-18-mediated cardiopulmonary inflammation via reduced mitophagy. *Signal Transduction and Targeted Therapy*, 8: 108. doi: 10.1038/s41392-023-01368-w.

Liao, M., Liu, Y., Yuan, J., Wen, Y., Xu, G., Zhao, J., *et al.* (2020). Single-cell landscape of bronchoalveolar immune cells in patients with COVID-19. *Nature Medicine*, 26: 842–844. doi: 10.1038/s41591-020-0901-9.

Lim, T. K. (2016) *Glycyrrhiza glabra, Edible Medicinal and Non-Medicinal Plants*. Vol. 10. Springer Science+Business Media Dordrecht. doi: 10.1007/978-94-017-7276-1.

Liu, S., Yang, W., Li, Y., and Sun, C. (2023). Fetal bovine serum, an important factor affecting the reproducibility of cell experiments. *Scientific Reports*, 13: 1942.

doi: 10.1038/s41598-023-29060-7.

Liu, Q. Q., Cheng, A., Wang, Y., Li, H., Hu, L., Zhao, X., *et al.* (2020). Cytokines and their relationship with the severity and prognosis of coronavirus disease 2019 (COVID-19): A retrospective cohort study. *BMJ Open*, 10: e041471. doi: 10.1136/bmjopen-2020-041471.

Liu, T., Zhang, L., Joo, D., and Su, S. C. (2017). NF- $\kappa$ B signaling in inflammation. *Signal Transduction and Targeted Therapy*, 2: e17023. doi: 10.1038/sigtrans.2017.23.

Lotze, M. T. and Tracey, K. J. (2005). High-mobility group box 1 protein (HMGB1): Nuclear weapon in the immune arsenal. *Nature Reviews Immunology*, 5(4): 331–342. doi: 10.1038/nri1594.

Luan, Z., Hu, B., Wu, L., Jin, S., Ma, X., Zhang, J., *et al.* (2018). Unfractionated heparin alleviates human lung endothelial barrier dysfunction induced by high mobility group box 1 through regulation of p38-gsk3 $\beta$ -snail signaling pathway. *Cellular Physiology and Biochemistry*, 46: 1907–1918. doi: 10.1159/000489375.

Lundbäck, P., Stridh, P., Klevenvall, L., Jenkins, R. E., Fischer, M., Sundberg, E., *et al.* (2016). Characterization of the inflammatory properties of actively released hmgb1 in juvenile idiopathic arthritis. *Antioxidants and Redox Signaling*, 24(12): 605–619. doi: 10.1089/ars.2014.6039.

Mahboudi, H., Heidari, N. M., Rashidabadi, Z. I., Anbarestani, A. H., Karimi, S., Darestani, K. D. (2018). Prospect and competence of quantitative methods via real-time pcr in a comparative manner: an experimental review of current methods. *The Open Bioinformatics Journal*, 11: 1–11. doi: 10.2174/1875036201811010001.

Mandke, P. and Vasquez, K. M. (2019). Interactions of high mobility group box protein 1 (HMGB1) with nucleic acids: Implications in DNA repair and immune responses. *DNA Repair.*, 83: 102701. doi: 10.1016/j.dnarep.2019.102701.

Marongiu, L., Gornati, L., Artuso, I., Zanoni, I., and Granucci, F. (2019). Below the surface: The inner lives of TLR4 and TLR9. *Journal of Leukocyte Biology*, 106: 147–160. doi: 10.1002/JLB.3MIR1218-483RR.

Martinez, F. O., Combes, T. W., Orsenigo, F., and Gordon, S. (2020). Monocyte activation in systemic COVID-19 infection: Assay and rationale. *EBioMedicine*, 59: 102964. doi: 10.1016/j.ebiom.2020.102964.

Maugeri, N., De Lorenzo, R., Clementi, N., Diotti, R. A., Criscuolo, E., Godino, C., *et al.* (2021). Unconventional CD147-dependent platelet activation elicited by SARS-CoV-2 in COVID-19. *Journal of Thrombosis and Haemostasis*, 00: 1–15. doi: 10.1111/jth.15575.

Mazzoni, A., Salvati, L., Maggi, L., Capone, M., Vanni, A., Spinicci, M., *et al.* (2020). Impaired immune cell cytotoxicity in severe COVID-19 is IL-6 dependent. *Journal of Clinical Investigation*, 130(9): 4694–4703. doi: 10.1172/JCI138554.

Mdkhana, B., Sharif-Askari, N. S., Ramakrishnan, R. K., Goel, S., Hamid, Q., Halwani, R. (2021). Nucleic acid-sensing pathways during SARS-COV-2 infection: Expectations versus reality. *Journal of Inflammation Research*, 14: 199–216. doi: 10.2147/JIR.S277716.

Meng, X. Y., Li, B., Liu, S., Kang, H., Zhao, L., Zhou, R. (2016). EGCG in green tea induces aggregation of hmgb1 protein through large conformational changes with polarized charge redistribution. *Scientific Reports*, 6: 22128. doi: 10.1038/srep22128.

Merad, M. and Martin, J. C. (2020). Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. *Nature Reviews Immunology*, 20(6): 355–362. doi: 10.1038/s41577-020-0331-4.

Mizuno, T., Eguchi, Y., Tsujita, Y., Imashuku, Y., Tabata, T., Kitagawa, H. (2022) Mortality at 180 days is affected by serum haptoglobin levels in septic patients, *Acute Medicine & Surgery*, 9: e726. doi: 10.1002/ams2.726.

Moisy, D., Avilov, S.V., Jacob, Y., Laoide, B. M, Ge, X., Baudin, F. *et al.* (2012) HMGB1 Protein Binds to Influenza Virus Nucleoprotein and Promotes Viral Replication. *Journal of Virology*, 86(17): 9122–9133. doi: 10.1128/jvi.00789-12.

Morimoto, M., Nakano, T., Egashira, S., Irie, K., Matsuyama, K., Wada, M. *et al.* (2022). Haptoglobin regulates macrophage/ microglia-induced inflammation and prevents ischemic brain damage via binding to HMGB1. *Journal of the American Heart Association*, 11: e024424. doi: 10.1161/JAHA.121.024424.

Mu, S. W., Dang, Y., Wang, S. S., Gu, J. J. (2018). The role of high mobility group box 1 protein in acute cerebrovascular diseases (Review). *Biomedical Reports*, 9: 191–197. doi: 10.3892/br.2018.1127.

Mukaka, M. M. (2012). Statistics corner: A guide to appropriate use of correlation coefficient in medical research. *Malawi Medical Journal*, 24(3): 69–71.

Murgolo, N., Therien, A. G., Howell, B., Klein, D., Koeplinger, K., Lieberman, L. A., *et al.* (2021). SARS-CoV-2 tropism, entry, replication, and propagation: Considerations for drug discovery and development. *PLoS pathogens*, 17(2): e1009225. doi: 10.1371/journal.ppat.1009225.

Murray, R. Z. and Stow, J. L. (2014). Cytokine secretion in macrophages: SNAREs, Rabs, and membrane trafficking. *Frontiers in Immunology*, 5: 538. doi: 10.3389/fimmu.2014.00538.

Nanda, J. D., Jung, C. J., Satria, R. D., Jhan, M. K., Shen, T. J., Tseng, P. C. *et al.* (2021). Serum IL-18 is a potential biomarker for predicting severe dengue disease progression. *Journal of Immunology Research*, 2021. doi: 10.1155/2021/7652569.

Naqvi, A. A. T., Fatima, K., Mohammad, T., Fatima, U., Singh, I. K., Singh, A., *et al.* (2020). Insights into SARS-CoV-2 genome, structure, evolution, pathogenesis and therapies: Structural genomics approach. *BBA - Molecular Basis of Disease*, 1866: 165878. doi: 10.1016/j.bbadis.2020.165878

Okamoto, T. Tanigami, H., Suzuki, K., and Shimaoka, M. (2012). Thrombomodulin: A bifunctional modulator of inflammation and coagulation in sepsis, *Critical Care Research and Practice*. doi: 10.1155/2012/614545.

Okuma, Y., Liu, K., Wake, H., Liu, R., Nishimura, Y., Hui, Z. *et al.* (2014). Glycyrrhizin inhibits traumatic brain injury by reducing HMGB1-RAGE interaction. *Neuropharmacology*, 85: 18–26. doi: 10.1016/j.neuropharm.2014.05.007.

Olbei, M., Hautefort, I., Modos, D., Treveil, A., Poletti, M., Gul, L., *et al.* (2021). SARS-CoV-2 causes a different cytokine response compared to other cytokine storm-causing respiratory viruses in severely ill patients. *Frontiers in Immunology*, 12: 629193. doi: 10.3389/fimmu.2021.629193.

Oliveira, E. R. A., Póvoa, T. F., Nuovo, G. J., Allonso, D., Salomaõ, N. G., Basílio-De-Oliveira, C. *et al.* (2017). Dengue fatal cases present virus-specific HMGB1 response in peripheral organs *Scientific Reports*, 7: 16011. doi: 10.1038/s41598-017-16197-5.

Ong, S. P., Poh, C. M., Rénia, L., MacAry, P. A., and Ng, L. F.P. (2012). Dengue virus infection mediates HMGB1 release from monocytes involving PCAF acetylase complex and induces vascular leakage in endothelial cells. *PLoS ONE*, 7(7): e41932. doi: 10.1371/journal.pone.0041932

Özbay Kurt, F. G., Cicortas, B. A., Balzasch, B. M., De la Torre, C., Ast, V., Tavukcuoglu, E. *et al.* (2024). S100A9 and HMGB1 orchestrate MDSC-mediated immunosuppression in melanoma through TLR4 signaling. *Journal for ImmunoTherapy of Cancer*, 12: e009552. doi: 10.1136/jitc-2024-009552.

Parrish, W., Rosas-Ballina, M., Gallowitsch-Puerta, M., Ochani, M., Ochani, K., Yang, L.H., *et al.* (2008). Modulation of TNF release by choline requires  $\alpha 7$  subunit nachr mediated signaling. *Molecular Medicine*, 14: 567–574. doi: 10.2119/2008-00079.Parrish.

Passos, F. R. S., Heimfarth, L., Monteiro, B. S., Correa, C. B., de Moura, T. R., Araújo, A. A. de S., *et al.* (2020). Oxidative stress and inflammatory markers in patients with COVID-19: Potential role of RAGE, HMGB1, GFAP and COX-2 in

disease severity. *International Immunopharmacology*, 104: 108502. doi : 10.1016/j.intimp.2021.108502.

Patel, M. C., Shirey, K. A., Boukhvalova, M. S., Vogel, S. N., Blanco, J. C.G. (2018). Serum high-mobility-group box 1 as a biomarker and a therapeutic target during respiratory virus infections. *mBio*, 9: e00246. doi: 10.1128/mBio.00246-18.

Pellerin, F. A., Caneparo, C., Pellerin, È., Chabaud, S., Pelletier, M., Bolduc, S. (2021). Heat-inactivation of fetal and newborn sera did not impair the expansion and scaffold engineering potentials of fibroblasts. *Bioengineering*, 8: 184. doi: 10.3390/bioengineering8110184.

Petrarca, L., Manganelli, V., Nenna, R., Frassanito, A., Ben David, S., Mancino, E., *et al.* (2022) HMGB1 in pediatric COVID-19 infection and MIS-C: a pilot study. *Front. Pediatr.* 10: 868269. doi: 10.3389/fped.2022.868269.

Pinto, S. M., Kim, H., Subbannayya, Y., Giambelluca, M. S., Bösl, K., Ryan, L. *et al.* (2021). Comparative proteomic analysis reveals varying impact on immune responses in phorbol 12-myristate-13-acetate-mediated THP-1 monocyte-to-macrophage differentiation. *Frontiers in Immunology*, 12: 679458. doi: 10.3389/fimmu.2021.679458.

Piroth, L., Cottenet, J., Mariet, A. S., Bonniaud, P., Blot, M., Tubert-Bitter, P., *et al.* (2021). Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study. *The Lancet Respiratory Medicine*, 9: 251–259. doi: 10.1016/S2213-2600(20)30527-0.

Polatoğlu, I., Oncu-Oner, T., Dalman, I., Ozdogan, S. (2023). COVID-19 in early 2023: Structure, replication mechanism, variants of SARS-CoV-2, diagnostic tests, and vaccine & drug development studies. *Medicine Communications*, 4(2): e228. doi: 10.1002/mco2.228.

Polticelli, F., Bocedi, A., Minervini, G., Ascenzi, P. (2008). Human haptoglobin structure and function - A molecular modeling study. *Federation of European Biochemical Societies Journal*, 275: 5648–5656. doi: 10.1111/j.1742-4658.2008.06690.x.

Public Health England (2020) *Understanding cycle threshold (Ct) in SARS-CoV-2 RT-PCR: A guide for health protection teams*. 1st edn, Public Health England. 1st edn. London, UK: PHE. <https://www.gov.uk/government/publications/cycle-threshold-ct-in-sars-cov-2-rt-pcr>.

Quan, C., Li, C., Ma, H., Li, Y. (2021). Immunopathogenesis of coronavirus-induced acute respiratory distress syndrome (ARDS): potential infection-associated

hemophagocytic lymphohistiocytosis. *Clinical Microbiology Reviews*, 34: e00074-20. doi: 10.1128/CMR.00074-20.0A.

Rabaan, A. A., Tirupathi, R., Sule, A. A., Aldali, J., Al Mutair, A., Alhumaid, S. *et al.* (2021). Viral dynamics and real-time RT-PCR Ct values correlation with disease severity in COVID-19. *Diagnostics*, 11: 1091. doi: 10.3390/diagnostics11061091.

Ramanathan, K., Antognini, D., Combes, A., Paden, M., Zakhary, B., Ogino, M. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet*, 395.

Rayavara, K., Kurosky, A., Stafford, S. J., Garg, N. J., Brasier, A. R., Garofalo, R. P., *et al.* (2018). Proinflammatory effects of respiratory syncytial virus-induced epithelial HMGB1 on human innate immune cell activation. *The Journal of Immunology*, 201: 2753–2766. doi: 10.4049/jimmunol.1800558.

Ren, W., Zhao, L., Sun, Y., Wang, X., Shi, X. (2023). HMGB1 and toll-like receptors: potential therapeutic targets in autoimmune diseases. *Molecular Medicine*, 29: 117. doi: 10.1186/s10020-023-00717-3.

Rena, G., Hardie, D. G. and Pearson, E. R. (2017). The mechanisms of action of metformin. *Diabetologia*, 60: 1577–1585. doi: 10.1007/s00125-017-4342-z.

Rheinheimer, J., de Souza, B. M., Cardoso, N. S., Bauer, A. C., Crispim, D. (2017). Current role of the NLRP3 inflammasome on obesity and insulin resistance: A systematic review. *Metabolism: Clinical and Experimental*, 74: 1–9. doi: 10.1016/j.metabol.2017.06.002.

Richard, S. A. (2021). Exploring the pivotal immunomodulatory and anti-inflammatory potentials of glycyrrhizic and glycyrrhetic acids. *Mediators of Inflammation*. doi: 10.1155/2021/6699560.

Rodrigues, T. S., de Sá, K. S.G., Ishimoto, A. Y., Becerra, A., Oliveira, S., Almeida, L. *et al.* (2020). Inflammasomes are activated in response to SARS-CoV-2 infection and are associated with COVID-19 severity in patients. *Journal of Experimental Medicine*, 218(3): e20201707. doi: 10.1084/JEM.20201707.

Roh, J. S. and Sohn, D. H. (2018). Damage-Associated Molecular Patterns in Inflammatory Diseases', *Immune Network*, 18(4): e27. doi: 10.4110/in.2018.18.e27.

Rubas, N. C., Peres, R., Kunihiro, B. P., Allan, N. P., Phankitnirundorn, K., Wells, R. K. *et al.* (2024). HMGB1 mediates microbiome-immune axis dysregulation underlying reduced neutralization capacity in obesity-related post-acute sequelae of SARS-CoV-2. *Scientific Reports*, 14: 355. doi: 10.1038/s41598-023-50027-1.

Sahanic, S., Hilbe, R., Dünser, C., Tymoszuk, P., Löffler-Ragg, J., Rieder, D. *et al.* (2023). SARS-CoV-2 activates the TLR4/MyD88 pathway in human macrophages: A possible correlation with strong pro-inflammatory responses in severe COVID-19. *Heliyon*, 9; e21893. doi: 10.1016/j.heliyon.2023.e21893.

Sanchez-Quintero, M. J., Torres, M. J., Blazquez, A. B., Gómez, E., Fernandez, T. D., Doña, I. *et al.* (2013). Synergistic effect between amoxicillin and tlr ligands on dendritic cells from amoxicillin-delayed allergic patients. *PLoS ONE*, 8(9): e74198. doi: 10.1371/journal.pone.0074198.

Satış, H., Özger, H. S., Yıldız, P. A., Hızıl, K., Gulbahar, Ö., Erbaş, G., *et al.* (2021). Prognostic value of interleukin-18 and its association with other inflammatory markers and disease severity in COVID-19. *Cytokine*, 137: 155302. doi: 10.1016/j.cyto.2020.155302.

Schuhenn, J., Meisterb, T. L., Todt, D., Bracht, T., Schork, K., Billaud, J. N., *et al.* (2022). Differential interferon- $\alpha$  subtype induced immune signatures are associated with suppression of SARS-CoV-2 infection. *Proceedings of the National Academy of Sciences of the United States of America*, 119(8): e2111600119. doi : 10.1073/pnas.2111600119.

Sellegounder, D., Zafari, P., Rajabinejad, M., Taghadosi, M., and Kapahi, P. (2021). Advanced glycation end products (AGEs) and its receptor, RAGE, modulate age-dependent COVID-19 morbidity and mortality. A review and hypothesis. *International Immunopharmacology*, 98: 107806. doi: 10.1016/j.intimp.2021.107806.

Shang, J., Wan, Y., Luo, C., Ye, G., Geng, Q., Auerbach, A., *et al.* (2020). Cell entry mechanisms of SARS-CoV-2. *Proceedings of the National Academy of Sciences of the United States of America*, 117(21): 11727-11734. doi: 10.1073/pnas.2003138117.

Shi, X., Yu, L., Zhang, Y., Liu, Z., Zhang, H., Zhang, Y., *et al.* (2020). Glycyrrhetic acid alleviates hepatic inflammation injury in viral hepatitis disease via a HMGB1-TLR4 signaling pathway. *International Immunopharmacology*, 84: 106578. doi: 10.1016/j.intimp.2020.106578.

Shirato, K. and Kizaki, T. (2021). SARS-CoV-2 spike protein S1 subunit induces pro-inflammatory responses via toll-like receptor 4 signaling in murine and human macrophages. *Heliyon*, 7: e06187. doi: 10.1016/j.heliyon.2021.e06187.

Sinha, P., Matthay, M. A. and Calfee, C. S. (2020). Is a “cytokine Storm” relevant to COVID-19? *JAMA Internal Medicine*, 180(9): 1152–1154. doi: 10.1001/jamainternmed.2020.3313.

Sitapara, R. A., Gauthier, A. G., Valdés-Ferrer, S. I., Lin, M., Patel, V., Wang, M., *et al.* (2020). The  $\alpha 7$  nicotinic acetylcholine receptor agonist, GTS-21, attenuates hyperoxia-induced acute inflammatory lung injury by alleviating the accumulation of HMGB1 in the airways and the circulation. *Molecular Medicine*, 26: 63. doi: 10.1186/s10020-020-00177-z.

Sivakorn, C., Dechsanga, J., Jamjumrus, L., Boonnak, K., Schultz, M. J., Dorndorp, A. M., *et al.* (2021). High mobility group box 1 and interleukin 6 at intensive care unit admission as biomarkers in critically ill COVID-19 patients. *The American Journal of Tropical Medicine and Hygiene*, 0(0): 1–8. doi: 10.4269/ajtmh.21-0165.

Song, X., Hu, W., Yu, H., Zhao, L., Zhao, Y., Zhao, X., *et al.* (2020). Little to no expression of angiotensin-converting enzyme-2 on most human peripheral blood immune cells but highly expressed on tissue macrophages. *Cytometry*, 1–10. doi: 10.1002/cyto.a.24285.

Stevens, N. E., Chapman, M. J., Fraser, C. K., Kuchel, T. R., Hayball, J. D., Diener, K. R. (2017). Therapeutic targeting of HMGB1 during experimental sepsis modulates the inflammatory cytokine profile to one associated with improved clinical outcomes. *Scientific Reports*, 7: 5850. doi: 10.1038/s41598-017-06205-z.

Street, M. E. (2020). HMGB1: A possible crucial therapeutic target for COVID-19?. *Hormone Research in Paediatrics*, 93: 73–75. doi: 10.1159/000508291.

Sutiningsih, D., Rahatina, V. E. F., Prabowo, Y., Haryanto, A., Wibowo, M. A. (2020). Epidemiologic and clinical characteristics of patients with COVID-19 in Central Java, Indonesia. *E3S Web of Conferences*, 202: 12014. doi: 10.1051/e3sconf/202020212014.

Taha, S. I., Shata, A. K., Baioumy, S. A., Fouad, S. H., Anis, S. G., Mossad, I. M. *et al.* (2021). Toll-like receptor 4 polymorphisms (896A/G and 1196C/T) as an indicator of COVID-19 severity in a convenience sample of Egyptian patients. *Journal of Inflammation Research*, 14: 6293–6303. doi: 10.2147/JIR.S343246.

Tang, D., Comish, P. and Kang, R. (2020). The hallmarks of COVID-19 disease. *PLoS Pathogens*, 16(5) : 1–24. doi: 10.1371/journal.ppat.1008536.

Tang, D. Kang, R., Coyne, C. B., Zeh, H. J., Lotze, M. T (2012). PAMPs and DAMPs: signal 0s that spur autophagy and immunity. *Immunological Review*, 249: 158–175. doi: 10.1111/j.1600-065X.2012.01146.x.

Tang, N., Kido, T., Shi, J., McCafferty, E., Ford, J. M., Dal Bon, K. *et al.* (2024). Blood markers show neural consequences of long COVID-19. *Cells*, 13: 478. doi: 10.3390/cells13060478.

Tang, Y., Zhao, X., Antoine, D., Xiao, X., Wang, H., Andersson, U., *et al.* (2016). Regulation of posttranslational modifications of HMGB1 during immune responses. *Antioxidants and Redox Signaling*, 24(12): 620–634. doi: 10.1089/ars.2015.6409.

Tang, Y., Liu, J., Zhang, D., Xu, Z., Ji, J., Wen, C. (2020). Cytokine storm in COVID-19: the current evidence and treatment strategies. *Frontiers in Immunology*, 11: 1708. doi: 10.3389/fimmu.2020.01708.

Tatematsu, M., Funami, K., Seya, T., Matsumoto, M. (2018). Extracellular RNA sensing by pattern recognition receptors. *Journal of Innate Immunity*, 10: 398–406. doi: 10.1159/000494034.

Tedesco, S., De Majo, F., Kim, J., Trenti, A., Trevisi, L., Fadini, G. P. *et al.* (2018). Convenience versus biological significance: Are PMA-differentiated THP-1 cells a reliable substitute for blood-derived macrophages when studying in vitro polarization?. *Frontiers in Pharmacology*, 9(71). doi: 10.3389/fphar.2018.00071.

Tejaro, J. R. (2016). Type I interferons in viral control and immune regulation. *Current Opinion in Virology*, 16 : 31–40. doi: 10.1016/j.coviro.2016.01.001.

Tjan, L. H., Furukawa, K., Nagano, T., Kiri, T., Nishimura, M., Arie, J., *et al.* (2021). Early differences in cytokine production by severity of Coronavirus Disease 2019. *The Journal of infectious diseases*, 223: 1145–1149. doi: 10.1093/infdis/jiab005.

Torres-Ruiz, J., Absalón-Aguilar, A., Nuñez-Aguirre, M., Pérez-Fragoso, A., Carrillo-Vázquez, D. A., Maravillas-Montero, J. L., R. *et al.* (2021). Neutrophil extracellular traps contribute to COVID-19 hyperinflammation and humoral autoimmunity. *Cells*, 10: 2545. doi: 10.3390/cells10102545.

Trifonova, I., Ngoc, K., Nikolova, M., Emilova, R., Todorova, Y., Gladnishka, T. *et al.* (2023). Patterns of cytokine and chemokine expression in peripheral blood of patients with COVID-19 associated with disease severity. *International Journal of Immunopathology and Pharmacology*, 37: 1–12. doi: 10.1177/03946320231163681.

Trypsteen, W., Van Cleemput, J., van Snippenberg, W., Gerlo, S., Vandekerckhove, L. (2020). On the whereabouts of SARS-CoV-2 in the human body: A systematic review. *PLoS Pathogens*, 16(10) : e1009037. doi: 10.1371/journal.ppat.1009037.

Tsujita, R., Tsubota, M., Hayashi, Y., Saeki, H., Sekiguchi, F., Kawabata, A. (2018). Role of thrombin in soluble thrombomodulin-induced suppression of peripheral HMGB1-mediated allodynia in mice. *Journal of Neuroimmune Pharmacology*, 13: 179–188. doi: 10.1007/s11481-017-9773-2.

Ubanako, P., Xelwa, N. and Ntwasa, M. (2019). LPS induces inflammatory chemokines via TLR-4 signalling and enhances the Warburg effect in THP-1 cells. *PLoS ONE*, 14(9): e0222614. doi: 10.1371/journal.pone.0222614.

Vabret, N., Britton, G. J., Gruber, C., Hegde, S., Kim, J., Kuksin, M., *et al.* (2020). Immunology of COVID-19: current state of the science. *Immunity*, 52: 910–941. doi: 10.1016/j.immuni.2020.05.002.

van de Sand, L., Bormann, M., Alt, M., Schipper, L., Heilingloh, C. S., Steinmann, E., *et al.* (2021). Glycyrrhizin effectively inhibits sars-cov-2 replication by inhibiting the viral main protease. *Viruses*, 13: 609. doi: 10.3390/v13040609.

Vanpatten, S. and Al-Abed, Y. (2018). High mobility group box-1 (HMGB1): current wisdom and advancement as a potential drug target. *Journal of Medicinal Chemistry*, 61: 5093–5107. doi: 10.1021/acs.jmedchem.7b01136.

Velazquez-Salinas, L., Verdugo-Rodriguez, A., Rodriguez, L. L., Borca, M. V. (2019). The role of interleukin 6 during viral infections. *Frontiers in Microbiology*, 10: 1057. doi: 10.3389/fmicb.2019.01057.

Volchuk, A., Ye, A., Chi, L., Steinberg, B. E., Goldenberg, N. M. (2020). Indirect regulation of HMGB1 release by gasdermin D. *Nature Communications*, 11: 4561. doi: 10.1038/s41467-020-18443-3.

Wang, C., Xie, J., Zhao, L., Fei, X., Zhang, H., Tan, Y., Nie, X., *et al.* (2020). Alveolar macrophage dysfunction and cytokine storm in the pathogenesis of two severe COVID-19 patients. *EBioMedicine*, 57: 102833. doi: 10.1016/j.ebiom.2020.102833.

Wang, H., Liao, H., Ochani, M., Justiniani, M., Lin, X., Yang, L., *et al.* (2004). Cholinergic agonists inhibit HMGB1 release and improve survival in experimental sepsis. *Nature Medicine*, 10(11) : 1216–1221. doi: 10.1038/nm1124.

Wang, J. Li, R., Peng, Z., Hu, B., Rao, X., Li, J. (2020). HMGB1 participates in LPS-induced acute lung injury by activating the AIM2 inflammasome in macrophages and inducing polarization of M1 macrophages via TLR2, TLR4, and RAGE/NF- $\kappa$ B signaling pathways. *International Journal of Molecular Medicine*, 45: 61–80. doi: 10.3892/ijmm.2019.4402.

Wang, S. and Zhang, Y. (2020). HMGB1 in inflammation and cancer. *Journal of Hematology and Oncology*, 13(1): 13–16. doi: 10.1186/s13045-020-00950-x.

Wang, Y., Tian, H., Zhang, L., Zhang, M., Guo, D., Wu, W., *et al.* (2020). Reduction of secondary transmission of SARS-CoV-2 in households by face mask

use, disinfection and social distancing: a cohort study in Beijing, China. *BMJ Global Health*, 5: e002794. doi: 10.1136/bmjgh-2020-002794.

Wei, J., Alfajaro, M. M., DeWeirdt, P. C., Hanna, R. E., Lu-Culligan, W. J., Cai, W. L. *et al.* (2021). Genome-wide CRISPR screens reveal host factors critical for SARS-CoV-2 infection. *Cell*, 184: 76-91. doi: 10.1016/j.cell.2020.10.028.

Weiskirchen, S., Schröder, S. K., Buhl, E. M., Weiskirchen, R. (2023). A beginner's guide to cell culture: practical advice for preventing needless problems. *Cells*, 12: 682. doi: 10.3390/cells12050682.

WHO (2020a). Listings of WHO's response to COVID-19. *World Health Organization*. <https://www.who.int/news/item/29-06-2020-covidtimeline>. Diakses 12 Maret 2021.

WHO (2020b). Naming the coronavirus disease (COVID-19) and the virus that causes it, *World Health Organization*. [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-\(covid-2019\)-and-the-virus-that-causes-it](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it). Diakses 12 Maret 2021.

WHO (2024). COVID-19 Dashboard, *World Health Organization*, <https://data.who.int/dashboards/covid19/>. Diakses 5 November 2024.

Wilk, A. J., Rustagi, A., Zhao, N. Q., Roque, J., Martínez-Colón, G. J., McKechnie, J. L., *et al.* (2020). A single-cell atlas of the peripheral immune response in patients with severe COVID-19. *Nature Medicine*, 26: 1070–1076. doi: 10.1038/s41591-020-0944-y.

Willis, W. L., Wang, L., Wada, T. T., Gardner, M., Abdouni, O., Hampton, J., Valiente, G. *et al.* (2018). The proinflammatory protein HMGB1 is a substrate of transglutaminase-2 and forms high-molecular-weight complexes with autoantigens. *Journal of Biological Chemistry*, 293(22): 8394–8409. doi: 10.1074/jbc.RA117.001078.

Wilopo, S. A. (2021). *Sampling dan Estimasi Besar Sampel. Aplikasi di Bidang Kedokteran dan Kesehatan Masyarakat*. Pusat Kesehatan Reproduksi, Fakultas Kedokteran, Kesehatan Masyarakat dan Keperawatan UGM, Ed. 1., pp. 67-69. Yogyakarta.

Wu, A. H., He, L., Long, W., Zhou, Q., Zhu, S., Wang, P., *et al.* (2015). Novel mechanisms of herbal therapies for inhibiting HMGB1 secretion or action. *Evidence-based Complementary and Alternative Medicine*. doi: 10.1155/2015/456305.

Wu, X., Cakmak, S., Wortmann, M., Hakimi, M., Zhang, J., Böckler, D., *et al.* (2016). Sex-and disease-specific inflammasome signatures in circulating blood leukocytes of patients with abdominal aortic aneurysm. *Molecular Medicine*, 22(7): 508–518. doi: 10.2119/molmed.2016.00035.

Xu, J., Jiang, Y., Wang, J., Shi, X., Liu, Q., Liu, Z., *et al.* (2014). Macrophage endocytosis of high-mobility group box 1 triggers pyroptosis. *Cell Death and Differentiation*, 21: 1229–1239. doi: 10.1038/cdd.2014.40.

Yanai, H., Ban, T., Wang, Z., Choi, M. K., Kawamura, T., Negishi, H., *et al.* (2009). HMGB proteins function as universal sentinels for nucleic-acid-mediated innate immune responses. *Nature*, 462(7269): 99–103. doi: 10.1038/nature08512.

Yang, H., Wang, H., Levine, Y. A., Gunasekaran, M. K., Wang, Y., Addorisio, M., *et al.* (2018). Identification of CD163 as an antiinflammatory receptor for HMGB1-haptoglobin complexes. *JCI insight*, 1 (7): e85375. doi: 10.1172/jci.insight.126617.

Yang, H., Liu, H., Zeng, Q., Imperato, G. H., Addorisio, M. E., Li, J., *et al.* (2019). Inhibition of HMGB1/RAGE-mediated endocytosis by HMGB1 antagonist box A, anti-HMGB1 antibodies, and cholinergic agonists suppresses inflammation. *Molecular Medicine*, 25: 1–13. doi: 10.1186/s10020-019-0081-6.

Yang, Z., Li, L., Chen, L., Yuan, W., Dong, L., Zhang, Y., *et al.* (2014). PARP-1 mediates LPS-induced HMGB1 release by macrophages through regulation of HMGB1 acetylation. *The Journal of Immunology*, 193: 6114–6123. doi: 10.4049/jimmunol.1400359.

Yao, H., Zhao, A., Han, Q., Wu, L., Yao, D., Wang, L. (2013). Correlation between serum high-mobility group box - 1 levels and high-sensitivity C-reactive protein and troponin I in patients with coronary artery disease. *Experimental dan Therapeutic Medicine*, 6: 121–124. doi: 10.3892/etm.2013.1095.

Yasuda, K., Nakanishi, K. and Tsutsui, H. (2019). Interleukin-18 in health and disease, *International Journal of Molecular Sciences*, 20: 649. doi: 10.3390/ijms20030649.

Yilla, M., Harcourt, B. H., Hickman, C. J., McGrew, M., Tamin, A., Goldsmith, C. S., *et al.* (2005). SARS-coronavirus replication in human peripheral monocytes/macrophages. *Virus Research*, 107: 93–101. doi: 10.1016/j.virusres.2004.09.004.

Yoshihiro, S., Sakuraya, M., Hayakawa, M., Ono, K., Hirata, A., Takaba, A., *et al.* (2019). Recombinant human-soluble thrombomodulin contributes to reduced mortality in sepsis patients with severe respiratory failure: a retrospective observational study using a multicenter dataset. *Shock*, 51(2): 174–179. doi: 10.1097/SHK.0000000000001148.

Yuan, J. S., Reed, A., Chen, F., Stewart, C. N. (2006). Statistical analysis of real-time PCR data. *BMC Bioinformatics*, 7: 85. doi: 10.1186/1471-2105-7-85.

Yuan, S., Liu, Z., Xu, Z., Liu, J., Zhang, J. (2020). High mobility group box 1 (HMGB1): A pivotal regulator of hematopoietic malignancies. *Journal of Hematology and Oncology*, 13: 1–19. doi: 10.1186/s13045-020-00920-3.

Yuan, Z., Shao, Z., Ma, L., Guo, R. (2023). Clinical Severity of SARS-CoV-2 Variants during COVID-19 Vaccination: A Systematic Review and Meta-Analysis. *Viruses*, 15: 1994. doi: 10.3390/v15101994.

Zakharova, E., Grandhi, J., Wewers, M. D., Gavrilin, M. A. (2010). Mycoplasma suppression of THP-1 cell TLR responses is corrected with antibiotics. *PLoS ONE*, 5(3); e9900. doi: 10.1371/journal.pone.0009900.

Zhao, F., Fang, Y., Deng, S., Li, X., Zhou, Y., Gong, Y., *et al.* (2017). Glycyrrhizin protects rats from sepsis by blocking HMGB1 signaling. *BioMed Research International*. doi: 10.1155/2017/9719647.

Zheng, D., Liwinski, T. and Elinav, E. (2020). Inflammasome activation and regulation: toward a better understanding of complex mechanisms. *Cell Discovery*, 6: 36. doi: 10.1038/s41421-020-0167-x.

Zheng, W., Huang, X., Lai, Y., Liu, X., Jiang, Y., Zhan, S., *et al.* (2021). Glycyrrhizic Acid for COVID-19: Findings of Targeting Pivotal Inflammatory Pathways Triggered by SARS-CoV-2. *Frontiers in Pharmacology*, 12: 631206. doi: 10.3389/fphar.2021.631206.

Zhong, H., Li, X., Zhou, S., Jiang, P., Liu, X., Ouyang, M. *et al.* (2020). Interplay between RAGE and TLR4 Regulates HMGB1-Induced Inflammation by Promoting Cell Surface Expression of RAGE and TLR4. *The Journal of Immunology*, 205(3): 767–775. doi: 10.4049/jimmunol.1900860.

Zhou, R., To, K. K. W., Wong, Y. C., Liu, L., Zhou, B., Li, X., *et al.* (2020). Acute SARS-CoV-2 Infection Impairs Dendritic Cell and T Cell Responses. *Immunity*, 53: 864-877.e5. doi: 10.1016/j.immuni.2020.07.026.