

REFERENCES

- Abdallah, H. Y., Ibrahim, M., El-Fadeal, N. M. A., Ali, D. A., Elsehrawy, G. G., Badr, R. E., & Hassoba, H. M. (2022). Pharmacogenomics of methotrexate pathway in rheumatoid arthritis patients: Approach toward personalized medicine. *Diagnostics*, **12**(7), 1–22.
- Achmad, A., Suryana, B. P. P., & Rahmayanti, T. Y. (2020). Efektifitas kepatuhan terapi metotreksat melalui *Disease Activity Score 28* (DAS28) pada pasien artritis rheumatoid. *Pharmaceutical Journal of Indonesia*, **5**(2):103-107.
- Aletaha, D., Neogi, T., Silman, A. J., Funovits, J., Felson, D. T., Bingham, C. O., Birnbaum, N. S., Burmester, G. R., Bykerk, V. P., Cohen, M. D., Combe, B., Costenbader, K. H., Dougados, M., Emery, P., Ferraccioli, G., Hazes, J. M. W., Hobbs, K., Huizinga, T. W. J., Kavanaugh, A., ... Hawker, G. (2010). 2010 rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis and Rheumatism*, **62**(9), 2569–2581.
- Alivernini, S., Firestein, G. S., & McInnes, I. B. (2022). The pathogenesis of rheumatoid arthritis. *Immunity*, **55**(12), 2255–2270.
- Al-Sofi, R. F., Bergmann, M. S., Nielsen, C. H., Andersen, V., Skov, L., & Loft, N. (2024). The association between genetics and response to treatment with biologics in patients with psoriasis, psoriatic arthritis, rheumatoid arthritis, and inflammatory bowel diseases: A systematic review and meta-analysis. *International Journal of Molecular Sciences*, **25**(11), 1–21.
- Auréal, M., Machuca-Gayet, I., & Coury, F. (2021). Rheumatoid arthritis in the view of osteoimmunology. *Biomolecules*, **11**(1), 48.
- Beltz, K., Tsang, D., Wang, J., Rose, S., Bao, Y., Wang, Y., Larkin, K., Rupp, S., Schrepfer, D., Datta, K., Gunderson, K., Sailor, C., Hansen, S., Dobosy, J., Lewis, L., Menezes, A., Walder, J., Behlke, M., & Chen, C. (2018). A high-performing and cost-effective SNP genotyping method using rhPCR and universal reporters. *Advances in Bioscience and Biotechnology*, **9**(9), 497–512.
- Black, R. J., Cross, M., Haile, L. M., Culbreth, G. T., Steinmetz, J. D., Hagins, H., Kopec, J. A., Brooks, P. M., Woolf, A. D., Ong, K. L., Kopansky-Giles, D. R., Dreinhoefer, K. E., Betteridge, N., Aali, A., Abbasifard, M., Abbasi-Kangevari, M., Abdurehman, A. M., Abedi, A., Abidi, H., ... March, L. M. (2023). Global, regional, and national burden of rheumatoid arthritis, 1990–2020, and projections to 2050: A systematic analysis of the Global Burden of Disease Study 2021. *The Lancet Rheumatology*, **5**(10), e594–e610.

- Boers, M. (2023). Viewpoint: Glucocorticoids in the treatment of rheumatoid arthritis: Points to (re)consider. *Rheumatology*, **62**(11), 3534–3537.
- Bustin, S. A., Benes, V., Nolan, T., & Pfaffl, M. W. (2005). Quantitative real-time RT-PCR: A perspective. *Journal of Molecular Endocrinology*, **34**(3), 597–601.
- Cen, H., Wen, Q. W., Zhang, H. Q., Yu, H., Zeng, Z., Jin, T., Wang, T. H., Qin, W., Huang, H., & Wu, X. D. (2022). Associations between genetic polymorphisms within transporter genes and clinical response to methotrexate in Chinese rheumatoid arthritis patients: A pilot study. *Pharmacogenomics and Personalized Medicine*, **15**, 327–339.
- Conti, V., Corbi, G., Costantino, M., De Bellis, E., Manzo, V., Sellitto, C., Stefanelli, B., Colucci, F., & Filippelli, A. (2020). Biomarkers to personalize the treatment of rheumatoid arthritis: Focus on autoantibodies and pharmacogenetics. *Biomolecules*, **10**(12), 1672.
- Cronstein, B. N., & Aune, T. M. (2020). Methotrexate and its mechanisms of action in inflammatory arthritis. *Nature Reviews Rheumatology*, **16**(3), 145–154.
- Delft, M. A. M. van, & Huizinga, T. W. J. (2020). An overview of autoantibodies in rheumatoid arthritis. *Journal of Autoimmunity*, **110**, 102392.
- DiPiro, J. T. (2023). *Pharmacotherapy: A pathophysiologic approach*. McGraw Hill.
- Dobosy, J. R., Rose, S. D., Beltz, K. R., Rupp, S. M., Powers, K. M., Behlke, M. A., & Walder, J. A. (2011). RNase H-dependent PCR (rhPCR): Improved specificity and single nucleotide polymorphism detection using blocked cleavable primers. *BMC Biotechnology*, **11**, 80.
- Eektimmerman, F., Swen, J. J., Madhar, M. B., Allaart, C. F., & Guchelaar, H. J. (2020). Predictive genetic biomarkers for the efficacy of methotrexate in rheumatoid arthritis: A systematic review. *The Pharmacogenomics Journal*, **20**(2), 159–168.
- Fraenkel, L., Bathon, J. M., England, B. R., St.Clair, E. W., Arayssi, T., Carandang, K., Deane, K. D., Genovese, M., Huston, K. K., Kerr, G., Kremer, J., Nakamura, M. C., Russell, L. A., Singh, J. A., Smith, B. J., Sparks, J. A., Venkatachalam, S., Weinblatt, M. E., Al-Gibbawi, M., ... Akl, E. A. (2021). 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Care and Research*, **73**(7), 924–939.
- GeneCards. (2025). *SLC19A1 gene: Solute carrier family 19 member 1*. GeneCards. Retrieved June 9, 2026, from <https://www.genecards.org/cgi-bin/carddisp.pl?gene=SLC19A1&keywords=SLC19A1>.
- Ghodke-Puranik, Y., Puranik, A. S., Shintre, P., Joshi, K., Patwardhan, B., Lamba, J. K., Niewold, T. B., & Chopra, A. (2015). Folate metabolic pathway

- single nucleotide polymorphisms: A predictive pharmacogenetic marker of methotrexate response in Indian (Asian) patients with rheumatoid arthritis. *Pharmacogenomics*, **16**(18), 2019–2034.
- Grabar, P. B., Leandro-García, L. J., Inglada-Pérez, L., Logar, D., Rodríguez-Antona, C., & Dolžan, V. (2012). Genetic variation in the *SLC19A1* gene and methotrexate toxicity in rheumatoid arthritis patients. *Pharmacogenomics*, **13**(14), 1583–1594.
- Green, M. R., & Sambrook, J. (2018). The basic polymerase chain reaction (PCR). *Cold Spring Harbor Protocols*, **2018**(5), pdb.prot095117.
- Hakamata, J., Kaneko, Y., Shimizu, M., Yamaoka, K., Maruyama, J., Takeuchi, T., Mochizuki, M., & Hashiguchi, M. (2018). Factors predicting the therapeutic response to methotrexate in Japanese patients with rheumatoid arthritis: A hospital-based cohort study. *Biological and Pharmaceutical Bulletin*, **41**(9), 1414–1422.
- Hidayat, R., Suryana, B. P. P., Wijaya, L. K., Ariane, A., Hellmi, R. Y., Adnan, E., & Sumariyono. (2021). *Diagnosis dan pengelolaan artritis reumatoid*. Perhimpunan Reumatologi Indonesia.
- Hillen, J., Geyer, C., Heitzmann, M., Beckmann, D., Krause, A., Winkler, I., Pavenstädt, H., Bremer, C., Pap, T., & Korb-Pap, A. (2017). Structural cartilage damage attracts circulating rheumatoid arthritis synovial fibroblasts into affected joints. *Arthritis Research and Therapy*, **19**(1), 1–11.
- Integrated DNA Technologies. (2023). *rhAmp SNP genotyping protocol* (Version 3).
- Jabbar, A., Zulfiqar, F., Mahnoor, M., Mushtaq, N., Zaman, M. H., Din, A. S. U., Khan, M. A., & Ahmad, H. I. (2021). Advances and perspectives in the application of CRISPR-Cas9 in livestock. *Molecular Biotechnology*, **63**(9), 757–767.
- James, H. M., Gillis, D., Hissaria, P., Lester, S., Somogyi, A. A., Cleland, L. G., & Proudman, S. M. (2008). Common polymorphisms in the folate pathway predict efficacy of combination regimens containing methotrexate and sulfasalazine in early rheumatoid arthritis. *Journal of Rheumatology*, **35**(4), 562–571.
- Jandu, J. S., & Goyal, A. (2020). *Rheumatoid arthritis*. StatPearls Publishing.
- Jenko, B., Tomšič, M., Jekić, B., Milić, V., Dolžan, V., & Praprotnik, S. (2018). Clinical pharmacogenetic models of treatment response to methotrexate monotherapy in Slovenian and Serbian rheumatoid arthritis patients: Differences in patient's management may preclude generalization of the models. *Frontiers in Pharmacology*, **9**, 20.

- Kolan, S. S., Li, G., Grimolizzi, F., Sexton, J., Goll, G., Kvien, T. K., Sundlisæter, N. P., Zucknick, M., Lillegraven, S., Haavardsholm, E. A., & Skålhegg, B. S. (2022). Identification of SNPs associated with methotrexate treatment outcomes in patients with early rheumatoid arthritis. *Frontiers in Pharmacology*, **13**, 1075603.
- Kuang, J., Yan, X., Genders, A. J., Granata, C., & Bishop, D. J. (2018). An overview of technical considerations when using quantitative real-time PCR analysis of gene expression in human exercise research. *PLOS ONE*, **13**(5), e0196438.
- Lee, P. Y., Costumbrado, J., Hsu, C.-Y., & Kim, Y. H. (2012). Agarose gel electrophoresis for the separation of DNA fragments. *Journal of Visualized Experiments*, **62**, 3923.
- Li, X., Hu, M., Li, W., Gu, L., Chen, M., Ding, H., Vanarsa, K., & Du, Y. (2016). The association between reduced folate carrier-1 gene 80G/A polymorphism and methotrexate efficacy or methotrexate-related toxicity in rheumatoid arthritis: A meta-analysis. *International Immunopharmacology*, **38**, 8–15.
- Lima, A., Bernardes, M., Azevedo, R., Monteiro, J., Sousa, H., Medeiros, R., & Seabra, V. (2014). *SLC19A1*, *SLC46A1*, and *SLCO1B1* polymorphisms as predictors of methotrexate-related toxicity in Portuguese rheumatoid arthritis patients. *Toxicological Sciences*, **142**(1), 196–209.
- Lima, A., Bernardes, M., Sousa, H., Azevedo, R., Costa, L., Ventura, F., Seabra, V., & Medeiros, R. (2014). *SLC19A1* 80G allele as a biomarker of methotrexate-related gastrointestinal toxicity in Portuguese rheumatoid arthritis patients. *Pharmacogenomics*, **15**(6), 807–820.
- Lucena-Aguilar, G., Sánchez-López, A. M., Barberán-Aceituno, C., Carrillo-Ávila, J. A., López-Guerrero, J. A., & Aguilar-Quesada, R. (2016). DNA source selection for downstream applications based on DNA quality indicators analysis. *Biopreservation and Biobanking*, **14**(4), 264–270.
- Lwanga, S. K., & Lemeshow, S. (1991). *Sample size determination in health studies: A practical manual*. World Health Organization.
- Maksimovic, V., Pavlovic-Popovic, Z., Vukmirovic, S., Cvejic, J., Mooranian, A., Al-Salami, H., Mikov, M., & Golocorbin-Kon, S. (2020). Molecular mechanism of action and pharmacokinetic properties of methotrexate. *Molecular Biology Reports*, **47**(6), 4699–4708.
- Malinowski, D., Piotrowska, K., Drożdżik, M., & Pawlik, A. (2024). Solute carrier transporters in synovial membrane and Hoffa's pad of patients with rheumatoid arthritis. *Archivum Immunologiae et Therapiae Experimentalis*, **72**, 14.

- Masoumi, M., Solaymani, M., Abbasifard, M., Houshmandfar, S., Iravani, P., Saeedi-Boroujeni, A., & Karami, J. (2025). The genetic puzzle of rheumatoid arthritis: Causes, progression, and treatment. *Biochemistry and Biophysics Reports*, **43**, 102148.
- Miller, F. W. (2023). The increasing prevalence of autoimmunity and autoimmune diseases: An urgent call to action for improved understanding, diagnosis, treatment, and prevention. *Current Opinion in Immunology*, **80**, 102266.
- National Center for Biotechnology Information. (2025). *SLC19A1 solute carrier family 19 member 1 [Homo sapiens (human)]*. National Library of Medicine. Retrieved June 9, 2025, from <https://www.ncbi.nlm.nih.gov/gene/?term=SLC19A1>
- Nomair, A. M., Abdelati, A., Dwedar, F. I., Elnemr, R., Kamel, Y. N., & Nomeir, H. M. (2024). The impact of folate pathway variants on the outcome of methotrexate therapy in rheumatoid arthritis patients. *Clinical Rheumatology*, **43**(3), 971–983.
- Onda, K., Honma, T., & Masuyama, K. (2023). Methotrexate-related adverse events and impact of concomitant treatment with folic acid and tumor necrosis factor-alpha inhibitors: An assessment using the FDA adverse event reporting system. *Frontiers in Pharmacology*, **14**, 1030832.
- Owen, S. A., Hider, S. L., Martin, P., Bruce, I. N., Barton, A., & Thomson, W. (2013). Genetic polymorphisms in key methotrexate pathway genes are associated with response to treatment in rheumatoid arthritis patients. *The Pharmacogenomics Journal*, **13**(3), 227–234.
- Padyukov, L. (2022). Genetics of rheumatoid arthritis. *Seminars in Immunopathology*, **44**(1), 47–62.
- Palmowski, A., Nielsen, S. M., Boyadzhieva, Z., Schneider, A., Pankow, A., Hartman, L., Silva, J. A. P. D., Kirwan, J., Wassenberg, S., Dejaco, C., Christensen, R., Boers, M., & Buttgerit, F. (2023). Safety and efficacy associated with long-term low-dose glucocorticoids in rheumatoid arthritis: A systematic review and meta-analysis. *Rheumatology*, **62**(8), 2652–2660.
- Paramaiswari, A., Kertia, N., Achadiono, D., Sinarta, A., & Nugroho, D. (2025). Predictors of persistent high disease activity after methotrexate treatment in rheumatoid arthritis patients. *Universa Medicina*, **44**(2), 141–151.
- PharmGKB. (2025). *Methotrexate pathway*. PharmGKB. Retrieved March 9, 2025, from <https://www.pharmgkb.org/pathway/PA165334955>.
- PubChem. (2025). *Methotrexate*. National Library of Medicine. Retrieved March 9, 2025, from <https://pubchem.ncbi.nlm>.