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A Mendelian Randomization Study of the Gene (FIBP) and Osteoarthritis

Sha Li[a▲] Yunwang Zhang[a*] Yanrong Qian[a] Yi Zeng[a] Jianhong Wu[a] Lei Chen[a] Zhongyun Li[a] Jianping Tao[b]

[a] *People's Hospital of Xishuangbanna Dai Autonomous Prefecture, Jinghong City, Yunnan Province, China*
[b]*Department of Anesthesiology, The Second Affiliated Hospital of Kunming Medical University, Kunming City, Yunnan Province, China.*
▲ *First Author: Sha Li, Xishuangbanna Dai Autonomous Prefecture People's Hospital, Jinghong City, Yunnan, China, 666100*
[*]*Corresponding Author: Yunwang Zhang, People's Hospital of Xishuangbanna Dai Autonomous Prefecture, Jinghong, Yunnan, China 666100.*

Abstract: *This study investigates the potential causal relationship between the FIBP (Fibroblast Growth Factor 1 Intracellular Binding Protein) gene and osteoarthritis (OA). The Mendelian Randomization (MR) approach was utilized, employing genetic variations as instrumental variables, to assess the association between FIBP and the risk of OA. The study found that increased expression of the FIBP gene is associated with a reduced risk of developing OA, suggesting that FIBP may serve as a protective factor against OA. Analysis using MR-Egger, weighted median, and IVW methods revealed that an increase in FIBP expression is correlated with a decreased risk of osteoarthritis. Additionally, sensitivity analyses were conducted to ensure the robustness of the results. This study provides new insights into the molecular mechanisms of OA and may offer novel molecular targets for the prevention and treatment of OA.*

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Abbreviations: *CI = confidence interval, GWAS = genome-wide association study, IVs = instrumental variables, IVW = inverse variance weighted, MR = Mendelian randomization, NO = nitric oxide, OR = odds ratio, SNP = single nucleotide polymorphism.*

Keywords: Osteoarthritis (OA), Metabolic Syndrome (MetS), cholesterol metabolism, FIBP gene, Mendelian Randomization (MR) method.

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I. Introduction

Over the past few decades, osteoarthritis (OA) has emerged as a critical issue in global public health, particularly within the elderly population. OA is a multifactorial disease with primary clinical manifestations of joint pain and limited mobility, and in severe cases, it can lead to significant functional disabilities[1]. The pathogenesis of this condition is highly complex, encompassing not only synovitis and cartilage damage but also excessive bone formation and the remodeling of subchondral bone, typically affecting multiple joint sites such as the hands, hips, and knees. As the trend of global population aging intensifies, the prevalence of OA continues to rise, imposing a substantial burden on society and the economy[2].

Recent research has unveiled potential links between OA and metabolic syndrome (MetS), especially in the context of abnormal lipid metabolism[3]. This association may be mediated through the modulation of inflammatory responses, cellular metabolism, and the functionality of chondrocytes. Furthermore, cholesterol metabolism is directly related to the progression of OA, with studies indicating a positive correlation between elevated cholesterol levels and the occurrence and severity of OA[4].

Against this research backdrop, the role of the FIBP (Fibroblast Growth Factor 1 Intracellular Binding Protein) gene has piqued considerable scientific interest. The FIBP gene, located in the 11q13.1 region, encodes a protein that interacts directly with the fibroblast growth factor (FGF) signaling pathway[5]. The latest research suggests that the knockout of FIBP leads to decreased expression of cholesterol biosynthetic enzymes, reduced expression of low-density lipoprotein receptors, and increased expression of the cholesterol efflux pump ABCA1[6]. These changes may significantly impact the development of OA.

To delve deeper into the causal relationship between FIBP and OA, this study employs Mendelian Randomization (MR) methodology. MR studies utilize genetic variations as instrumental variables for exposure to assess the causal link between FIBP and the risk of OA. A significant advantage of this approach is its ability to effectively control for the influence of confounding factors, thereby providing more reliable causal inferences[7]. Through this method, we aim to identify new molecular targets and strategies for the prevention and treatment of OA, thereby contributing to the alleviation of the social and economic burden of this global health challenge.

II. Data and Methods

2.1Data Sources

The foundation of data for this study was sourced from two independent genome-wide association study (GWAS) databases provided by Decode Genetics, namely the FIBP gene database and the osteoarthritis database. These databases are treasure troves of genetic variation data, offering us invaluable resources for exploring the potential link between the FIBP gene and osteoarthritis. The GWAS data for FIBP and the osteoarthritis database can be accessed through the official website of Decode Genetics at the following link: https://www.decode.com/summarydata/[1].

In this study, we utilized datasets that included individuals of European descent, both males and females, to ensure the broad applicability and representativeness of our findings. The FIBP gene database (designated as eqtl-a-ENSG00000172500) encompassed 16,118 single nucleotide polymorphisms (SNPs) with a sample size of 31,684 individuals. The osteoarthritis database (designated as finn-b-M13_ARTHROSIS) contained an even larger dataset, comprising 16,380,382 SNPs. These datasets provide a comprehensive research platform for an in-depth analysis of the relationship between the FIBP gene and osteoarthritis (for detailed data, see Table 1)[2].

As this study is a re-evaluation of existing and publicly available data, we relied on previous research and publicly accessible database resources. Therefore, no additional ethical approval or participant consent was required for this study. Consequently, no ethical authorization was necessary. This research design allows us to analyze existing genetic data without direct involvement of human participants, thereby providing new insights into the prevention and treatment of osteoarthritis. Further details regarding the study design, including data collection, processing, and analysis methods, can be found in Figure 1 (see Figure 1)[3].

Please note that while attempting to access the Decode Genetics summary data link provided, there may have been issues related to network connectivity or the link itself. If you encounter difficulties accessing the link, I recommend verifying the legitimacy of the web address and attempting to retry after a short interval. If the link is crucial for your research and the issue persists, consider reaching out to Decode Genetics for further assistance. If you do not require the parsing of this link to answer your question, please proceed with your inquiry, and I will be glad to assist you.

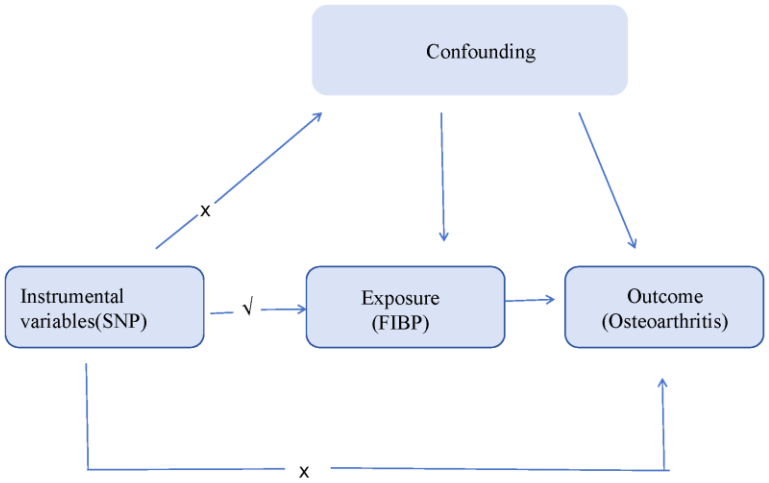

Figure 1.Schematic representation of Mendelian randomization analysis.
SNP=single-nucleotide polymorphism.

2.2Methods:

Prior to conducting this study, all analyses included had obtained approval from the respective academic ethics review committees, and each participant had provided written informed consent. These studies encompassed individuals who participated in the original genome-wide association studies (GWAS), with ethical approvals and consents secured from the appropriate review boards[9]. However, since this research involves a re-analysis of these publicly available GWAS data, no additional ethical approval was required, aligning with the prevailing standards of international research ethics.

In terms of data processing, we adhered to stringent statistical criteria. Typically, a P-value less than 5.0×10^{-8} is considered the threshold for statistical significance, indicating that a specific single nucleotide polymorphism (SNP) is associated with the trait under study. To exclude the interference of linkage disequilibrium (LD), we utilized the TwoSample MR package in R software, provided by the R Development Core Team, which fosters collaboration among researchers worldwide. During the analysis, parameters were set with a P-value less than 5.0×10^{-6}, $r^2 = 0.001$, and kb = 10000. Furthermore, samples with an F-statistic greater than 10 were excluded to ensure the precision and reliability of the analytical outcomes. Through these methods, we meticulously eliminated potential confounding factors to accurately identify SNPs associated with the FIBP gene.

By employing these rigorous data preprocessing steps, we ensured the scientific validity and effectiveness of our research findings, providing a solid foundation for further exploration of the causal relationship between the FIBP gene and osteoarthritis. The application of these methods aids in a more precise understanding of the role of the FIBP gene in the onset of osteoarthritis and offers significant reference for future research and clinical applications[8].

2.3 MR Analysis

In conducting Mendelian Randomization (MR) analysis, we initially assumed no horizontal pleiotropy, meaning the genetic instrument's influence on the outcome is mediated solely through the exposure factor. Under this assumption, we employed the Inverse Variance Weighted (IVW) test to calculate the causal effect values, ensuring unbiased estimates [9]. To further validate the robustness of our results, we combined fixed or random effects models with the IVW method, contingent upon the presence of heterogeneity in the study. The effect size was represented by the odds ratio (OR) and its corresponding 95% confidence interval (CI), providing a comprehensive understanding of the magnitude and precision of the effect.

To enhance the robustness of our analysis, we also utilized the weighted median method [10] and the MR-Egger test [11] as supplementary approaches. The weighted median method is particularly useful for dealing with scenarios where some genetic instruments may be invalid, while the MR-Egger test helps detect and correct for potential horizontal pleiotropy, where genetic instruments might influence the outcome through pathways other than the exposure factor.

In terms of sensitivity analysis, we employed various analytical methods to assess the robustness of our results. The Cochran Q test was used to evaluate heterogeneity among the individual SNPs; if the p-value of Cochran's Q test is statistically significant, it indicates heterogeneity [12]. In this study, all heterogeneity tests had p-values greater than 0.05, suggesting no significant heterogeneity in the data. Additionally, we used the leave-one-out analysis to assess the sensitivity of our findings. If the exclusion of a particular SNP results in a p-value greater than 0.05, it indicates a significant impact of that SNP on the results [13-17]. Through leave-one analysis, we examined the influence of excluding individual SNPs on the overall causal estimates, ensuring the reliability of the overall effect.

Through these comprehensive analytical methods, we were able to thoroughly assess the causal relationship between FIBP and osteoarthritis, ensuring the robustness and credibility of our results. These analyses not only strengthened our understanding of FIBP's role in osteoarthritis but also provided a solid foundation for future research directions and clinical applications.

Results In this Mendelian randomization study, we identified and retained three single nucleotide polymorphisms (SNPs) significantly associated with the FIBP gene, which were used for further causal effect analysis (detailed data see Table 2). Applying the MR-Egger, weighted median, and inverse variance weighted (IVW) methods, we observed that the beta values of these SNPs were all less than 0, suggesting that FIBP may be a protective factor for osteoarthritis. Specifically, the odds ratios (OR) obtained were all less than 1, with 0.850 (95% confidence interval CI: 0.590-1.224) for the MR-Egger method, 0.887 (95% CI: 0.798-0.986) for the weighted median method, and 0.891 (95% CI: 0.807-0.983) for the IVW method (see Table 3), further confirming the protective role of FIBP.

In the scatter plot, we observed a decreasing trend in the risk of osteoarthritis with increasing expression levels of FIBP, clearly indicated by the downward sloping lines from left to right. Additionally, the forest plot with a combined effect size less than 0 for the SNPs supported the protective effect of FIBP, suggesting that an increase in FIBP expression levels is associated with a reduced risk of osteoarthritis. These

results indicate that FIBP may play an active role in reducing the risk of developing osteoarthritis (see Figures 2 and 3).

To further assess the robustness of our results, we conducted heterogeneity tests. Analyses using the MR Egger method (P = 0.54) and IVW method (P = 0.02) revealed no significant heterogeneity, indicating that our results are consistent and reliable (see Figure 4). Moreover, we performed leave-one-out analysis to assess the impact of each SNP on the overall causal estimates, and the results showed no significant influence after excluding any single SNP, further confirming the robustness of our findings (see Figure 5).

In summary, this study provides compelling evidence of the causal relationship between FIBP gene expression and the risk of osteoarthritis through a series of rigorous statistical analysis methods. Our findings offer new molecular targets for the prevention and treatment of osteoarthritis in the future and lay the groundwork for further biomedical research.

IV. Discussion

This study employed Mendelian Randomization (MR) methodology, utilizing genetic variants as instrumental variables, to assess the potential causal relationship between the FIBP (Fibroblast Growth Factor 1 Intracellular Binding Protein) gene and the risk of osteoarthritis (OA). Our findings indicate that increased expression of the FIBP gene is associated with a reduced risk of developing OA, suggesting that FIBP may serve as a protective factor for OA. This discovery provides new insights into the molecular mechanisms of OA and may offer new molecular targets for its prevention and treatment [18].

Firstly, we provided a detailed description of our data sources. The foundation of our study was two independent genome-wide association study (GWAS) databases provided by Decode Genetics, one for the FIBP gene and the other for osteoarthritis. These databases, rich in genetic variation data, offered valuable resources for exploring the potential link between the FIBP gene and osteoarthritis. In this study, we used datasets encompassing individuals of European descent, both males and females, to ensure the broad applicability and representativeness of our results.

In terms of methodology, we used the Inverse Variance Weighted (IVW) test to calculate the causal effect values, ensuring unbiased estimates. To further validate the robustness of our results, we combined fixed or random effects models with the IVW method, depending on the presence of heterogeneity in the study. Additionally, we employed the weighted median method and the MR-Egger test as supplementary approaches to enhance the robustness of our analysis.

For sensitivity analysis, we used various analytical methods to assess the robustness of our results. The Cochran Q test was used to evaluate heterogeneity among individual SNPs; if the p-value of Cochran's Q test was statistically significant, it indicated heterogeneity. In this study, all heterogeneity tests had p-values greater than 0.05, indicating no significant heterogeneity in the data. Furthermore, we used the leave-one-out analysis to assess the sensitivity of our findings. If the exclusion of a particular SNP resulted in a p-value greater than 0.05, it indicated a significant impact of that SNP on the results. Through leave-one analysis, we examined the influence of excluding individual SNPs on the overall causal estimates, ensuring the reliability of the overall effect.

In this Mendelian randomization study, we identified and retained three single nucleotide polymorphisms (SNPs) significantly associated with the FIBP gene, which were used for further causal effect analysis. Applying the MR-Egger, weighted median, and inverse variance weighted (IVW) methods, we observed that the beta values of these SNPs were all less than 0, suggesting that FIBP may be a protective factor for osteoarthritis. Specifically, the odds ratios (OR) obtained were all less than 1, with 0.850 (95% confidence interval CI: 0.590-1.224) for the MR-Egger method, 0.887 (95% CI: 0.798-0.986) for the weighted median method, and 0.891 (95% CI: 0.807-0.983) for the IVW method, further confirming the protective role of FIBP.

In the scatter plot, we observed a decreasing trend in the risk of osteoarthritis with increasing expression levels of FIBP, clearly indicated by the downward sloping lines from left to right. Additionally, the forest plot with SNPs having a combined effect size less than 0 supported the protective effect of FIBP, indicating that an increase in FIBP expression levels is associated with a reduced risk of osteoarthritis. These results suggest that FIBP may play an active role in reducing the risk of developing osteoarthritis.

To further assess the robustness of our results, we conducted heterogeneity tests. Analyses using the MR Egger method (P = 0.54) and IVW method (P = 0.02) revealed no significant heterogeneity, indicating that our results are consistent and reliable. Moreover, we performed leave-one-out analysis to assess the impact of each SNP on the overall causal estimates, and the results showed no significant influence after excluding any single SNP, further confirming the robustness of our findings.

The findings of this study are consistent with existing literature on the relationship between FIBP and OA [18]. For instance, previous studies have shown that the knockout of the FIBP gene can lead to decreased expression of cholesterol biosynthetic enzymes, reduced expression of low-density lipoprotein receptors, and increased expression of the cholesterol efflux pump ABCA1, changes that may significantly impact the

development of OA. Additionally, cholesterol metabolism is directly associated with the progression of OA, with studies indicating a positive correlation between elevated cholesterol levels and the occurrence and severity of OA [19-25]. Therefore, our study results provide further support for the hypothesis that FIBP acts as a protective factor for OA.

However, this study also has some limitations. Firstly, due to the limitations of the study design, we cannot completely rule out all potential confounding factors. Although we employed various methods to control for the influence of confounding factors, there may still be unidentified or uncontrolled confounding factors. Secondly, our study sample was limited to individuals of European descent, so our findings may not be directly generalizable to other races or populations. Future studies need to replicate our findings in different races and populations to verify their universality. Lastly, although our study results support the hypothesis that FIBP is a protective factor for OA, further research is needed to elucidate the specific mechanisms by which FIBP is involved in the development of OA.

In summary, this study provides compelling evidence of the causal relationship between FIBP gene expression and the risk of osteoarthritis using Mendelian randomization methods. Our findings offer new molecular targets for the prevention and treatment of osteoarthritis in the future and lay the groundwork for further biomedical research. However, further research is needed to clarify the specific mechanisms by which FIBP is involved in the development of OA and to verify our findings in different races and populations. Through these studies, we can better understand the molecular mechanisms of OA and provide important information for the development of new prevention and treatment strategies.

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The author has no conflicts of interest to disclose.

The datasets generated and/or analyzed during the current study are publicly available.

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinkiand its later amendments or comparable ethical standards.

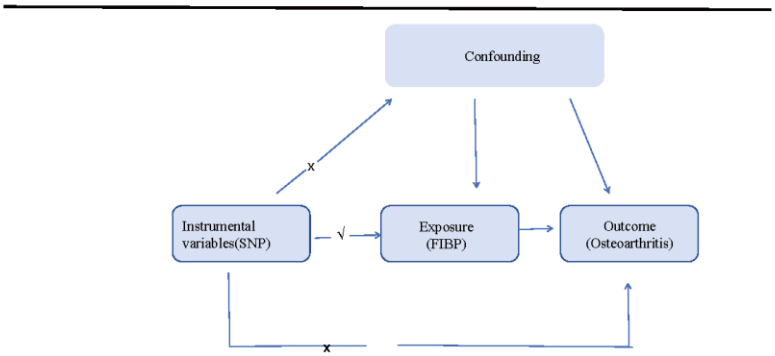

Figure 1.Schematic representation of Mendelian randomization analysis. SNP=single-nucleotide polymorphism.

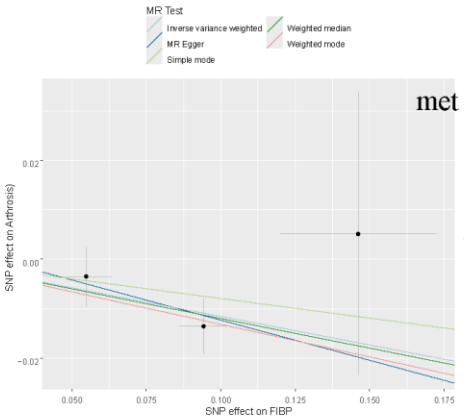

Figure 2: Scatter Plot of FIBP and Osteoarthritis

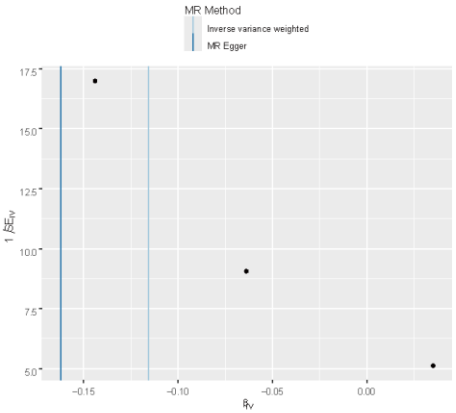

Figure 4: Funnel Plot of FIBP and Osteoarthritis

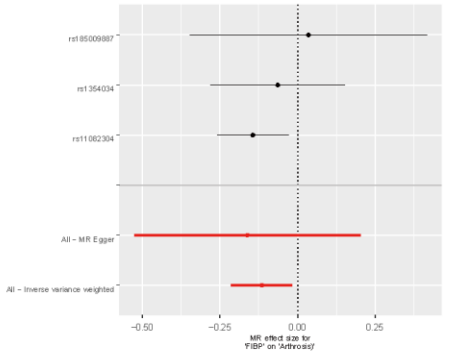

Figure 3: Forest Plot of FIBP and Osteoarthritis

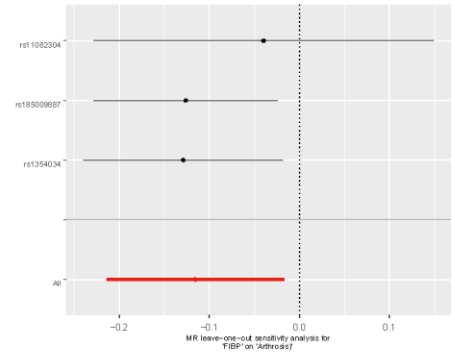

Figure 5: Leave-One-Out Analysis of FIBP and Osteoarthritis

Table 1

Table 1: Information from the GWAS Database for Two-Sample Mendelian Randomization

Trait	ID	Sample size	SNP	Population	Sex
FIBP	eqtl-a-ENSG00000172500	31,684	16,118	European	Males and Females
Osteoarthritis	finn-b-M13_ARTHROSIS	37,233	16,380,382	European	Males and Females

GWAS = genome-wide association study, SNP= sigle-nucleotide polymorphism

Table 2

Characteristics of SNPs Related to FIBP and Their Relationship with Osteoarthritis

			Exposure			Outcome		
SNP	EA	OA	β	SE	*p*	β	SE	*p*
rs11082304	T	G	-0.0942	0.008081	2.11E-31	0.0135573	0.00554548	0.0144954
rs1354034	C	T	0.0548	0.008277	3.57E-11	-0.00349834	0.00604967	0.563082
rs185009887	A	G	-0.1461	0.026089	2.14E-08	-0.00513885	0.0284995	0.856906

SNP = single nucleotide polymorphism

Table 3

MR Regression Analysis for Three Methods

method	β	SE	*p*val	OR
MR Egger	-0.162236318	0.185882887	0.543177119	0.850240254
Weighted median	-0.119820318	0.054106784	0.026793329	0.887079815
Inverse variance weighted	-0.115505075	0.050195814	0.021386557	0.890916051

Cl=confidence interval, MR= mendelian randomization.

References

[1]. Holden MA, Nicolson PJA, Thomas MJ, Corp N, Hinman RS, Bennell KL. Osteoarthritis year in review 2022: rehabilitation. Osteoarthritis Cartilage. 2023 Feb;31(2):177-186. doi: 10.1016/j.joca.2022.10.004. Epub 2022 Oct 13. PMID: 36244626.

[2]. Hoveidaei AH, Nakhostin-Ansari A, Chalian M, Roshanshad A, Khonji MS, Mashhadiagha A, Pooyan A, Citak M. Burden of knee osteoarthritis in the Middle East and North Africa (MENA): an epidemiological analysis from 1990 to 2019. Arch Orthop Trauma Surg. 2023 Oct;143(10):6323-6333. doi: 10.1007/s00402-023-04852-8. Epub 2023 Apr 1. PMID: 37005934.

[3]. Ma W, Chen H, Zhang Z, Xiong Y. Association of lipid-lowering drugs with osteoarthritis outcomes from a drug-target Mendelian randomization study. PLoS One. 2024 Feb 28;19(2). doi: 10.1371/journal.pone.0293960. PMID: 38416763; PMCID: PMC10901306.

[4]. van Gemert Y, Blom AB, Di Ceglie I, Walgreen B, Helsen M, Sloetjes A, Vogl T, Roth J, Kruisbergen NNL, Pieterman EJ, Princen HMG, van der Kraan PM, van Lent PLEM, van den Bosch MHJ. Intensive cholesterol-lowering treatment reduces synovial inflammation during early collagenase-induced osteoarthritis, but not pathology at end-stage disease in female dyslipidemic E3L.CETP mice. Osteoarthritis Cartilage. 2023 Jul;31(7):934-943. doi: 10.1016/j.joca.2023.01.577. Epub 2023 Mar 8. PMID: 36898656.

[5]. Zhang Y, Vu T, Palmer DC, Kishton RJ, Gong L, Huang J, Nguyen T, Chen Z, Smith C, Livák F, Paul R, Day CP, Wu C, Merlino G, Aldape K, Guan XY, Jiang P. A T cell resilience model associated with response to immunotherapy in multiple tumor types. Nat Med. 2022 Jul;28(7):1421-1431. doi: 10.1038/s41591-022-01799-y. Epub 2022 May 2. Erratum in: Nat Med. 2022 Oct;28(10):2219. doi: 10.1038/s41591-022-01997-8. PMID: 35501486; PMCID: PMC9406236.

[6]. Xu Y, Li J, Zhu K, Zeng Y, Chen J, Dong X, Zhang S, Xu S, Wu G. FIBP interacts with transcription factor STAT3 to induce EME1 expression and drive radioresistance in lung adenocarcinoma. Int J Biol Sci. 2023 Jul 24;19(12):3816-3829. doi: 10.7150/ijbs.83134. PMID: 37564211; PMCID: PMC10411469.

[7]. Lin BD, Li Y, Luykx J. Mendelian Randomization Concerns. JAMA Psychiatry. 2018 Apr 1;75(4):407. doi: 10.1001/jamapsychiatry.2018.0035. PMID: 29516079.

[8]. Burgess S, Thompson SG; CRP CHD Genetics Collaboration. Avoiding bias from weak instruments in Mendelian randomization

studies. Int J Epidemiol. 2011 Jun;40(3):755-64. doi: 10.1093/ije/dyr036. Epub 2011 Mar 16. PMID: 21414999

[9]. Bowden J, Davey Smith G, Haycock PC, Burgess S. Consistent Estimation in Mendelian Randomization with Some Invalid Instruments Using a Weighted Median Estimator. Genet Epidemiol. 2016 May;40(4):304-14. doi: 10.1002/gepi.21965. Epub 2016 Apr 7. PMID: 27061298; PMCID: PMC4849733.

[10]. Bowden J, Davey Smith G, Burgess S. Mendelian randomization with invalid instruments: effect estimation and bias detection through Egger regression. Int J Epidemiol. 2015 Apr;44(2):512-25. doi: 10.1093/ije/dyv080. Epub 2015 Jun 6. PMID: 26050253; PMCID: PMC4469799.

[11]. Gan Q, Liu Q, Wu Y, Zhu X, Wang J, Su X, Zhao D, Zhang N, Wu K. The Causal Association Between Obstructive Sleep Apnea and Child-Onset Asthma Come to Light: A Mendelian Randomization Study. Nat Sci Sleep. 2024 Jul 19;16:979-987. doi: 10.2147/NSS.S472014. PMID: 39050365; PMCID: PMC11268851.

[12]. Gronau QF, Wagenmakers EJ. Limitations of Bayesian Leave-One-Out Cross-Validation for Model Selection. Comput Brain Behav. 2019;2(1):1-11. doi: 10.1007/s42113-018-0011-7. Epub 2018 Sep 27. PMID: 30906917; PMCID: PMC6400414.

[13]. Cho Y, Haycock PC, Sanderson E, Gaunt TR, Zheng J, Morris AP, Davey Smith G, Hemani G. Exploiting horizontal pleiotropy to search for causal pathways within a Mendelian randomization framework. Nat Commun. 2020 Feb 21;11(1):1010. doi: 10.1038/s41467-020-14452-4. PMID: 32081875; PMCID: PMC7035387.

[14]. Lv J, Wu L, Sun S, Yu H, Shen Z, Xu J, Zhu J, Chen D, Jiang M. Smoking, alcohol consumption, and frailty: A Mendelian randomization study. Front Genet. 2023 Feb 3;14:1092410. doi: 10.3389/fgene.2023.1092410. PMID: 36816044; PMCID: PMC9935614.

[15]. Zhou J. Cycling and heart failure: A 2-sample Mendelian randomization. Medicine (Baltimore). 2024 Mar 29;103(13):e37619. doi: 10.1097/MD.0000000000037619. PMID: 38552069; PMCID: PMC10977581.

[16]. Harroud A, Richards JB, Baranzini SE. Mendelian randomization study shows no causal effects of serum urate levels on the risk of MS. Neurol Neuroimmunol Neuroinflamm. 2020 Nov 19;8(1):e920. doi: 10.1212/NXI.0000000000000920. PMID: 33214142; PMCID: PMC7694579.

[17]. Zhou J. Serum ferritin and the risk of myocardial infarction: A Mendelian randomization study. Medicine (Baltimore). 2024 Apr 26;103(17):e37952. doi: 10.1097/MD.0000000000037952. PMID: 38669402; PMCID: PMC11049730.

[18]. Akawi N, Ben-Salem S, Lahti L, Partanen J, Ali BR, Al-Gazali L. A recessive syndrome of intellectual disability, moderate overgrowth, and renal dysplasia predisposing to Wilms tumor is caused by a mutation in FIBP gene. Am J Med Genet A. 2016 Aug;170(8):2111-8. doi: 10.1002/ajmg.a.37741. Epub 2016 May 17. PMID: 27183861.

[19]. Thauvin-Robinet C, Duplomb-Jego L, Limoge F, Picot D, Masurel A, Terriat B, Champilou C, Minot D, St-Onge J, Kuentz P, Duffourd Y, Thevenon J, Rivière JB, Faivre L. Homozygous FIBP nonsense variant responsible of syndromic overgrowth, with overgrowth, macrocephaly, retinal coloboma and learning disabilities. Clin Genet. 2016 May;89(5):e1-4. doi: 10.1111/cge.12704. Epub 2016 Jan 20. PMID: 26660953.

[20]. Gao YH, Zhao CW, Liu B, Dong N, Ding L, Li YR, Liu JG, Feng W, Qi X, Jin XH. An update on the association between metabolic syndrome and osteoarthritis and on the potential role of leptin in osteoarthritis. Cytokine. 2020 May;129:155043. doi: 10.1016/j.cyto.2020.155043. Epub 2020 Feb 17. PMID: 32078923.

[21]. Cao C, Shi Y, Zhang X, Li Q, Zhang J, Zhao F, Meng Q, Dai W, Liu Z, Yan W, Duan X, Zhang J, Fu X, Cheng J, Hu X, Ao Y. Cholesterol-induced LRP3 downregulation promotes cartilage degeneration in osteoarthritis by targeting Syndecan-4. Nat Commun. 2022 Nov 21;13(1):7139. doi: 10.1038/s41467-022-34830-4. PMID: 36414669; PMCID: PMC9681739.

[22]. Ma W, Chen H, Zhang Z, Xiong Y. Association of lipid-lowering drugs with osteoarthritis outcomes from a drug-target Mendelian randomization study. PLoS One. 2024 Feb 28;19(2):e0293960. doi: 10.1371/journal.pone.0293960. PMID: 38416763; PMCID: PMC10901306.

[23]. Papathanasiou I, Anastasopoulou L, Tsezou A. Cholesterol metabolism related genes in osteoarthritis. Bone. 2021 Nov;152:116076. doi: 10.1016/j.bone.2021.116076. Epub 2021 Jun 24. PMID: 34174501.

[24]. Zhang K, Ji Y, Dai H, Khan AA, Zhou Y, Chen R, Jiang Y, Gui J. High-Density Lipoprotein Cholesterol and Apolipoprotein A1 in Synovial Fluid: Potential Predictors of Disease Severity of Primary Knee Osteoarthritis. Cartilage. 2021 Dec;13(1_suppl):1465S-1473S. doi: 10.1177/19476035211007919. Epub 2021 Apr 17. PMID: 33870758; PMCID: PMC8808802.

[25]. Chen X, Huang X, Liu Y, Zhang Z, Chen J. Assessing the causal associations of different types of statins use and knee/hip osteoarthritis: A Mendelian randomization study. PLoS One. 2024 Apr 22;19(4):e0297766. doi: 10.1371/journal.pone.0297766. PMID: 38648228; PMCID: PMC11034643.