



Jan 27, 2025

🌐 Unveiling Hub Genes and Biological Pathways: A Bioinformatics Analysis of Trauma-Induced Coagulopathy (TIC)

DOI

<https://dx.doi.org/10.17504/protocols.io.4r3l29bz4v1y/v1>

lin gang zhang¹, Bo Li¹, Jing Liu¹, Yanfeng Bian², Ying Zhou³, Ying Zhou¹

¹Yuncheng Central Hospital affiliated to Shanxi Medical University;

²Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital; ³Hebei province Xingtai Third People's Hospital



lin gang zhang

Yuncheng City Central Hospital

Create & collaborate more with a free account

Edit and publish protocols, collaborate in communities, share insights through comments, and track progress with run records.

Create free account

OPEN  ACCESS



DOI: <https://dx.doi.org/10.17504/protocols.io.4r3l29bz4v1y/v1>

Protocol Citation: lin gang zhang, Bo Li, Jing Liu, Yanfeng Bian, Ying Zhou, Ying Zhou 2025. Unveiling Hub Genes and Biological Pathways: A Bioinformatics Analysis of Trauma-Induced Coagulopathy (TIC). **protocols.io**

<https://dx.doi.org/10.17504/protocols.io.4r3l29bz4v1y/v1>

License: This is an open access protocol distributed under the terms of the **[Creative Commons Attribution License](#)**, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited

Protocol status: Working

We use this protocol and it's working

Created: January 25, 2025

Last Modified: January 27, 2025

Protocol Integer ID: 119067

Keywords: Biological Markers, Traumatic Coagulopathy, Bioinformatics, Differentially Expressed Genes, Pathway Analysis, Protein-Protein Interaction Network, Hub Genes, ROC Analysis., bioinformatics analysis of trauma, associated pathways in trauma, induced coagulopathy, bioinformatics analysis, pathway analysis, unveiling hub gene, using microarray dataset, hub gene, expressed gene, microarray datasets from the geo database, bioinformatics approach, associated pathway, novel biomarker, identification of key gene, protein interaction, biological pathway, key gene, trauma, protein, pathway

Funders Acknowledgements:

2023 Yuncheng City Basic Research Program (Free Exploration Category) Projects

Grant ID: YCKJ-2023052

Disclaimer

This protocol is under a Creative Commons license. Please credit the author(s) when using this protocol in your work.

Abstract

This protocol outlines a bioinformatics approach to identify hub genes and associated pathways in Trauma-Induced Coagulopathy (TIC) using microarray datasets from the GEO database. The methodology includes the identification of differentially expressed genes (DEGs), pathway analysis, and the construction of a Protein-Protein Interaction (PPI) network. The expected results include the identification of key genes and pathways associated with TIC, which could lead to novel biomarkers for its diagnosis and therapeutic targets.



Materials

Materials Required

Microarray Dataset:

Dataset Name: GSE223245

Source: Gene Expression Omnibus (GEO) Database

Description: This dataset includes gene expression data used for the identification of differentially expressed genes (DEGs) associated with trauma-induced coagulopathy (TIC).

Software and Tools:

R (v4.0 or higher): For statistical analysis and DEG identification.

Bioconductor packages: Used for data preprocessing and DEG analysis (e.g., limma, edgeR).

Cytoscape (v3.8.2 or higher): For constructing the Protein-Protein Interaction (PPI) network.

CytoHubba plugin: To identify hub genes in the PPI network.

MCODE plugin: For module detection in the PPI network.

CTD (Comparative Toxicogenomics Database): Used for further analysis of gene-disease associations.

Web Tools:

DAVID (Database for Annotation, Visualization, and Integrated Discovery): For GO and KEGG pathway enrichment analysis.

ROC Analysis Software:

R (v4.0 or higher): For conducting Receiver Operating Characteristic (ROC) curve analysis to evaluate the diagnostic potential of hub genes.

- 1 Data Acquisition
Objective: Obtain microarray datasets for analysis.
Action: Download the dataset GSE223245 from the Gene Expression Omnibus (GEO) database.
- 2 Identification of Differentially Expressed Genes (DEGs)
Objective: Identify the DEGs from the dataset.
Action: Process the dataset to extract upregulated and downregulated genes.
- 3 Functional Enrichment Analysis (GO and KEGG)
Objective: Perform gene functional enrichment analysis.
Action: Conduct Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses on the DEGs.
- 4 Construction of Gene-Concept Network
Objective: Establish a relationship between the genes and their functions.
Action: Construct a gene-concept network to visualize gene interactions and functions.
- 5 Construction of Protein-Protein Interaction (PPI) Network
Objective: Build a PPI network for further analysis.
Action: Use CytoHubba, MCODE, and CTD scores to identify hub genes linked to trauma-induced coagulopathy (TIC).
- 6 Identification of Hub Genes
Objective: Identify significant hub genes related to TIC.
Action: Analyze the PPI network to pinpoint crucial hub genes.
- 7 ROC Analysis of Hub Genes
Objective: Evaluate the diagnostic potential of the hub genes.
Action: Perform Receiver Operating Characteristic (ROC) analysis on the hub genes to assess their clinical relevance.

Protocol references

1. Moore EE, Moore HB, Kornblith LZ, Neal MD, Hoffman M, Mutch NJ, et al. Trauma-induced coagulopathy. *Nat Rev Dis Primers*. 2021;7(1):30. Epub 2021/05/01. doi: 10.1038/s41572-021-00264-3. PubMed PMID: 33927200; PubMed Central PMCID: PMCPMC9107773.
2. Macfarlane RG, Biggs R. Fibrinolysis; its mechanism and significance. *Blood*. 1948;3(10):1167-87. Epub 1948/10/01. PubMed PMID: 18884682.
3. Vernon ST, Hansen T, Kott KA, Yang JY, O'Sullivan JF, Figtree GA. Utilizing state-of-the-art "omics" technology and bioinformatics to identify new biological mechanisms and biomarkers for coronary artery disease. *Microcirculation*. 2019;26(2):e12488. Epub 2018/06/30. doi: 10.1111/micc.12488. PubMed PMID: 29956866.
4. Liu K, Kang M, Li J, Qin W, Wang R. Prognostic value of the mRNA expression of members of the HSP90 family in non-small cell lung cancer. *Exp Ther Med*. 2019;17(4):2657-65. Epub 2019/04/02. doi: 10.3892/etm.2019.7228. PubMed PMID: 30930968; PubMed Central PMCID: PMCPMC6425268.
5. Barrett T, Wilhite SE, Ledoux P, Evangelista C, Kim IF, Tomashevsky M, et al. NCBI GEO: archive for functional genomics data sets--update. *Nucleic Acids Res*. 2013;41(Database issue): D991-5. Epub 2012/11/30. doi: 10.1093/nar/gks1193. PubMed PMID: 23193258; PubMed Central PMCID: PMCPMC3531084.
6. Gustavsson EK, Zhang D, Reynolds RH, Garcia-Ruiz S, Ryten M. ggtranscript: an R package for the visualization and interpretation of transcript isoforms using ggplot2. *Bioinformatics*. 2022;38(15):3844-6. Epub 2022/06/26. doi: 10.1093/bioinformatics/btac409. PubMed PMID: 35751589; PubMed Central PMCID: PMCPMC9344834.
7. Subramanian A, Tamayo P, Mootha VK, Mukherjee S, Ebert BL, Gillette MA, et al. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc Natl Acad Sci U S A*. 2005;102(43):15545-50. Epub 2005/10/04. doi: 10.1073/pnas.0506580102. PubMed PMID: 16199517; PubMed Central PMCID: PMCPMC1239896.
8. Yu G, Wang LG, Han Y, He QY. clusterProfiler: an R package for comparing biological themes among gene clusters. *Omics*. 2012;16(5):284-7. Epub 2012/03/30. doi: 10.1089/omi.2011.0118. PubMed PMID: 22455463; PubMed Central PMCID: PMCPMC3339379.
9. Li L, Lei Q, Zhang S, Kong L, Qin B. Screening and identification of key biomarkers in hepatocellular carcinoma: Evidence from bioinformatic analysis. *Oncol Rep*. 2017;38(5):2607-18. Epub 2017/09/14. doi: 10.3892/or.2017.5946. PubMed PMID: 28901457; PubMed Central PMCID: PMCPMC5780015.
10. Szklarczyk D, Gable AL, Nastou KC, Lyon D, Kirsch R, Pyysalo S, et al. The STRING database in 2021: customizable protein-protein networks, and functional characterization of user-uploaded gene/measurement sets. *Nucleic Acids Res*. 2021;49(D1): D605-d12. Epub 2020/11/26. doi: 10.1093/nar/gkaa1074. PubMed PMID: 33237311; PubMed Central PMCID: PMCPMC7779004.
11. Doncheva NT, Morris JH, Gorodkin J, Jensen LJ. Cytoscape StringApp: Network Analysis and Visualization of Proteomics Data. *J Proteome Res*. 2019;18(2):623-32. Epub 2018/11/20. doi: 10.1021/acs.jproteome.8b00702. PubMed PMID: 30450911; PubMed Central PMCID: PMCPMC6800166.
12. Tisherman SA, Schmicker RH, Brasel KJ, Bulger EM, Kerby JD, Minei JP, et al. Detailed description of all deaths in both the shock and traumatic brain injury hypertonic saline trials of the Resuscitation Outcomes Consortium. *Ann Surg*. 2015;261(3):586-90. Epub 2014/07/30. doi: 10.1097/sla.0000000000000837. PubMed PMID: 25072443; PubMed Central PMCID: PMCPMC4309746.

13. Eastridge BJ, Mabry RL, Seguin P, Cantrell J, Tops T, Uribe P, et al. Death on the battlefield (2001-2011): implications for the future of combat casualty care. *J Trauma Acute Care Surg.* 2012;73(6 Suppl 5): S431-7. Epub 2012/12/05. doi: 10.1097/TA.0b013e3182755dcc. PubMed PMID: 23192066.
14. Fox EE, Holcomb JB, Wade CE, Bulger EM, Tilley BC. Earlier Endpoints are Required for Hemorrhagic Shock Trials Among Severely Injured Patients. *Shock.* 2017;47(5):567-73. Epub 2017/02/17. doi: 10.1097/shk.0000000000000788. PubMed PMID: 28207628; PubMed Central PMCID: PMC5392160.
15. Moore HB, Moore EE, Chapman MP, McVane K, Bryskiewicz G, Blechar R, et al. Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial. *Lancet.* 2018;392(10144):283-91. Epub 2018/07/24. doi: 10.1016/s0140-6736(18)31553-8. PubMed PMID: 30032977; PubMed Central PMCID: PMC6284829.
16. Sperry JL, Guyette FX, Brown JB, Yazer MH, Triulzi DJ, Early-Young BJ, et al. Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock. *N Engl J Med.* 2018;379(4):315-26. Epub 2018/07/26. doi: 10.1056/NEJMoa1802345. PubMed PMID: 30044935.
17. Kalkwarf KJ, Drake SA, Yang Y, Thetford C, Myers L, Brock M, et al. Bleeding to death in a big city: An analysis of all trauma deaths from hemorrhage in a metropolitan area during 1 year. *J Trauma Acute Care Surg.* 2020;89(4):716-22. Epub 2020/06/27. doi: 10.1097/ta.0000000000002833. PubMed PMID: 32590562.
18. Moore HB, Moore EE, Gonzalez E, Chapman MP, Chin TL, Silliman CC, et al. Hyperfibrinolysis, physiologic fibrinolysis, and fibrinolysis shutdown: the spectrum of postinjury fibrinolysis and relevance to antifibrinolytic therapy. *J Trauma Acute Care Surg.* 2014;77(6):811-7; discussion 7. Epub 2014/07/23. doi: 10.1097/ta.0000000000000341. PubMed PMID: 25051384; PubMed Central PMCID: PMC4370273.
19. Simmons JW, Powell MF. Acute traumatic coagulopathy: pathophysiology and resuscitation. *British Journal of Anaesthesia.* 2016; 117: iii31-iii43. doi: 10.1093/bja/aew328.
20. Brohi K, Gruen RL, Holcomb JB. Why are bleeding trauma patients still dying? *Intensive Care Med.* 2019;45(5):709-11. Epub 2019/02/12. doi: 10.1007/s00134-019-05560-x. PubMed PMID: 30741331.
21. Hoffman M, Pawlinski R. Hemostasis: old system, new players, new directions. *Thromb Res.* 2014;133 Suppl 1: S1-2. Epub 2014/04/25. doi: 10.1016/j.thromres.2014.03.001. PubMed PMID: 24759130.
22. Ivashkiv LB, Donlin LT. Regulation of type I interferon responses. *Nat Rev Immunol.* 2014;14(1):36-49. Epub 2013/12/24. doi: 10.1038/nri3581. PubMed PMID: 24362405; PubMed Central PMCID: PMC4084561.
23. Seo JY, Yaneva R, Cresswell P. Viperin: a multifunctional, interferon-inducible protein that regulates virus replication. *Cell Host Microbe.* 2011;10(6):534-9. Epub 2011/12/20. doi: 10.1016/j.chom.2011.11.004. PubMed PMID: 22177558; PubMed Central PMCID: PMC3246677.
24. Kurokawa C, Iankov ID, Galanis E. A key anti-viral protein, RSAD2/VIPERIN, restricts the release of measles virus from infected cells. *Virus Res.* 2019; 263:145-50. Epub 2019/01/27. doi: 10.1016/j.virusres.2019.01.014. PubMed PMID: 30684519; PubMed Central PMCID: PMC6615567.
25. Zhu H, Zheng J, Zhou Y, Wu T, Zhu T. Knockdown of RSAD2 attenuates B cell hyperactivity in patients with primary Sjögren's syndrome (pSS) via suppressing NF-kb signaling pathway. *Mol Cell Biochem.* 2021;476(5):2029-37. Epub 2021/01/30. doi: 10.1007/s11010-021-04070-z. PubMed PMID: 33512636.
26. Zhou X, Michal JJ, Zhang L, Ding B, Lunney JK, Liu B, et al. Interferon induced IFIT family genes in host antiviral defense. *Int J Biol Sci.* 2013;9(2):200-8. Epub 2013/03/06. doi: 10.7150/ijbs.5613. PubMed PMID: 23459883; PubMed Central PMCID: PMC3584916.
27. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet.* 2020;395(10229):1033-4. Epub 2020/03/21. doi: 10.1016/s0140-6736(20)30628-0. PubMed PMID: 32192578; PubMed Central PMCID: PMC7270045.

28. Ahmad F, Kannan M, Ansari AW. Role of SARS-CoV-2 -induced cytokines and growth factors in coagulopathy and thromboembolism. *Cytokine Growth Factor Rev.* 2022; 63:58-68. Epub 2021/11/10. doi: 10.1016/j.cytogfr.2021.10.007. PubMed PMID: 34750061; PubMed Central PMCID: PMC8541834.
29. Imaizumi T, Hashimoto S, Sato R, Umetsu H, Aizawa T, Watanabe S, et al. IFIT Proteins Are Involved in CXCL10 Expression in Human Glomerular Endothelial Cells Treated with a Toll-Like Receptor 3 Agonist. *Kidney Blood Press Res.* 2021;46(1):74-83. Epub 2020/12/17. doi: 10.1159/000511915. PubMed PMID: 33326977.
30. Leisching G, Wiid I, Baker B. OAS1, 2, and 3: Significance During Active Tuberculosis? *J Infect Dis.* 2018;217(10):1517-21. Epub 2018/02/17. doi: 10.1093/infdis/jiy084. PubMed PMID: 29452387.
31. Fagone P, Nunnari G, Lazzara F, Longo A, Cambria D, Distefano G, et al. Induction of OAS gene family in HIV monocyte infected patients with high and low viral load. *Antiviral Res.* 2016; 131:66-73. Epub 2016/04/25. doi: 10.1016/j.antiviral.2016.04.009. PubMed PMID: 27107898.
32. McDowell IC, Modak TH, Lane CE, Gomez-Chiarri M. Multi-species protein similarity clustering reveals novel expanded immune gene families in the eastern oyster *Crassostrea virginica*. *Fish Shellfish Immunol.* 2016; 53:13-23. Epub 2016/04/02. doi: 10.1016/j.fsi.2016.03.157. PubMed PMID: 27033806.
33. Miyashita M, Oshiumi H, Matsumoto M, Seya T. DDX60, a DEXD/H box helicase, is a novel antiviral factor promoting RIG-I-like receptor-mediated signaling. *Mol Cell Biol.* 2011;31(18):3802-19. Epub 2011/07/28. doi: 10.1128/mcb.01368-10. PubMed PMID: 21791617; PubMed Central PMCID: PMC3165724.
34. Onomoto K, Jogi M, Yoo JS, Narita R, Morimoto S, Takemura A, et al. Critical role of an antiviral stress granule containing RIG-I and PKR in viral detection and innate immunity. *PLoS One.* 2012;7(8):e43031. Epub 2012/08/23. doi: 10.1371/journal.pone.0043031. PubMed PMID: 22912779; PubMed Central PMCID: PMC3418241 study was partly funded by Nippon Boehringer Ingelheim. There are no patents, products in development or marketed products to declare. This does not alter the authors' adherence to all the PLoS ONE policies on sharing data and materials, as detailed online in the guide for authors.
35. Mathieu NA, Paparisto E, Barr SD, Spratt DE. HERC5 and the ISGylation Pathway: Critical Modulators of the Antiviral Immune Response. *Viruses.* 2021;13(6). Epub 2021/07/03. doi: 10.3390/v13061102. PubMed PMID: 34207696; PubMed Central PMCID: PMC8228270.
36. Paparisto E, Woods MW, Coleman MD, Moghadasi SA, Kochar DS, Tom SK, et al. Evolution-Guided Structural and Functional Analyses of the HERC Family Reveal an Ancient Marine Origin and Determinants of Antiviral Activity. *J Virol.* 2018;92(13). Epub 2018/04/20. doi: 10.1128/jvi.00528-18. PubMed PMID: 29669830; PubMed Central PMCID: PMC6002735.
37. Woods MW, Tong JG, Tom SK, Szabo PA, Cavanagh PC, Dikeakos JD, et al. Interferon-induced HERC5 is evolving under positive selection and inhibits HIV-1 particle production by a novel mechanism targeting Rev/RRE-dependent RNA nuclear export. *Retrovirology.* 2014; 11:27. Epub 2014/04/04. doi: 10.1186/1742-4690-11-27. PubMed PMID: 24693865; PubMed Central PMCID: PMC4021598.