

КОНФЛИКТ ИНТЕРЕСОВ

Автор заявляет об отсутствии конфликта интересов.

СПИСОК ЛИТЕРАТУРЫ

- Матвеева Д.К., Андреева Е.Р.* 2020. Регуляторная активность децеллюляризованного матрикса мультипотентных мезенхимных стромальных клеток. Цитология. Т. 62. № 10. С. 699. (*Matveeva D.K., Andreeva E.R.* 2020. Regulatory Activity of Decellularized Matrix of Multipotent Mesenchymal Stromal Cells. Tsitologia. V. 62. № 10. P. 699.)
<https://doi.org/10.31857/S004137712010003X>
- Нимирицкий П.П., Дусь Т.А., Григорьева О.А., Сагарадзе Г.Д., Ефименко А.Ю., Макаревич П.И.* 2016. Клеточные пласты из мезенхимных стромальных клеток жировой ткани человека и получение препаратов внеклеточного матрикса методом децеллюляризации. Технологии живых систем. Т. 13. № 6. С. 4. (*Nimiritskiy P.P., Dus' T.A., Grigor'eva O.A., Sagardzhe G.D., Efimenko A.Yu., Makarevich P.I.* 2016. Cell sheets from human adipose tissue mesenchymal stromal cells and derivation of decellularized native extracellular matrix components. Tekhnologii zhivyykh sistem = Technologies of living systems. V. 13. № 6. P. 4.)
- Ткачук В.А., Акопян Ж.А., Ефименко А.Ю., Григорьева О.А., Макаревич П.И., Нимирицкий П.П., Новоселецкая Е.С.* 2020. Пат. 2718907С1 Российская Федерация, МПК А61К35/28 С12Н5/775. Биоматериал на основе бесклеточного матрикса, производимого мезенхимными стромальными клетками человека, способ его получения и способ применения для стимуляции регенеративных процессов / заявитель и патентообладатель ФГБОУ ВО "Московский государственный университет имени М.В. Ломоносова" (МГУ). № 2018143484; заявл. 07.12.2018; опубл. 15.04.2020, Бюл. № 11. (*Tkachuk V.A., Akopyan Zh.A., Efimenko A.Yu., Grigoreva O.A., Makarevich P.I., Nimiritskiy P.P., Novoseletskaya E.S.* 2020. Invention 2718907C1 Russian Federation, Int. Cl. A61K35/28 C12N5/775. Biomaterial based on cell-free matrix produced by human mesenchymal stromal cells, method for preparing thereof and method of using thereof to stimulate regenerative processes. / proprietor FGBOU VO "Moskovskij gosudarstvennyj universitet imeni M.V. Lomonosova" (MGU) № 2018143484; date of filing 07.12.2018; date of publication 15.04.2020, Bull. № 11.)
- Aksel H., Sarkar D., Lin M.H., Buck A., Huang G.T.* 2022. Cell-derived Extracellular Matrix Proteins in Colloidal Microgel as a Self-Assembly Hydrogel for Regenerative Endodontics. J. Endod. V. 48. P. 527.
<https://doi.org/10.1016/j.joen.2022.01.011>
- Antich C., Jiménez G., de Vicente J., López-Ruiz E., Chocarro-Wrona C., Griñán-Lisón C., Carrillo E., Montañez E., Marchal J.A.* 2021. Development of a biomimetic hydrogel based on predifferentiated mesenchymal stem-cell-derived ECM for cartilage tissue engineering. Adv. Healthc. Mater. V. 10. P. e2001847.
<https://doi.org/10.1002/adhm.202001847>
- Assunção M., Dehghan-Baniani D., Yiu C.H.K., Später T., Beyer S., Blocki A.* 2020. Cell-derived extracellular matrix for tissue engineering and regenerative medicine. Front. Bioeng. Biotechnol. V. 8. P. 602009.
<https://doi.org/10.3389/fbioe.2020.602009>
- Carvalho M.S., Silva J.C., Udangawa R. N., Cabral J.M.S., Ferreira F.C., da Silva C.L., Linhardt R.J., Vashishth D.* 2019. Co-culture cell-derived extracellular matrix loaded electrospun microfibrous scaffolds for bone tissue engineering. Mater. Sci. Eng. C. Mater. Biol. Appl. V. 99. P. 479.
<https://doi.org/10.1016/j.msec.2019.01.127>
- Chan W.W., Yu F., Le Q.B., Chen S., Yee M., Choudhury D.* 2021. Towards Biomanufacturing of cell-derived matrices. Int. J. Mol. Sci. V. 22. P. 11929.
<https://doi.org/10.3390/ijms222111929>
- Chen Y., Zheng Y.L., Qiu D.B., Sun Y.P., Kuang S.J., Xu Y., He F., Gong Y.H., Zhang Z. G.* 2015. An extracellular matrix culture system for induced pluripotent stem cells derived from human dental pulp cells. Eur. Rev. Med. Pharmacol. Sci. V. 19. P. 4035.
- Chen Z., Wang L., Chen C., Sun J., Luo J., Cui W., Zhu C., Zhou X., Liu X., Yang H., Shi Q.* 2022. NSC-derived extracellular matrix-modified GelMA hydrogel fibrous scaffolds for spinal cord injury repair. NPG Asia Mater. V. 14. P. 20.
<https://doi.org/10.1038/s41427-022-00368-6>
- Cheng C.W., Solorio L.D., Alsberg E.* 2014. Decellularized tissue and cell-derived extracellular matrices as scaffolds for orthopaedic tissue engineering. Biotechnol. Adv. V. 32. P. 462.
<https://doi.org/10.1016/j.biotechadv.2013.12.012>
- Chiang C.-E., Fang Y.-Q., Ho C.-T., Assunção M., Lin S.-J., Wang Y.-C., Blocki A., Huang C.-C.* 2021. Bioactive Decellularized Extracellular Matrix Derived from 3D Stem Cell Spheroids under Macromolecular Crowding Serves as a Scaffold for Tissue Engineering. Adv. Healthcare Mater. V. 10. P. 2100024.
<https://doi.org/10.1002/adhm.202100024>
- Choi H.R., Cho K.A., Kang H.T., Lee J.B., Kaeberlein M., Suh Y., Chung I.K., Park S.C.* 2011. Restoration of senescent human diploid fibroblasts by modulation of the extracellular matrix. Aging Cell. V. 10. P. 148.
<https://doi.org/10.1111/j.1474-9726.2010.00654.x>
- Dikina A.D., Almeida H.V., Cao M., Kelly D.J., Alsberg E.* 2017. Scaffolds derived from ECM produced by chondrogenically induced human MSC condensates support human MSC chondrogenesis. ACS Biomater. Sci. Eng. V. 3. P. 1426.
<https://doi.org/10.1021/acsbiomaterials.6b00654>
- Du H.-C., Jiang L., Geng W.-X., Li J., Zhang R., Dang J.-G., Shu M.-G., Li L.-W.* 2017. Evaluation of xenogeneic extracellular matrix fabricated from CuCl₂-conditioned mesenchymal stem cell sheets as a bioactive wound dressing material. J. Biomater. Appl. V. 32(4). P. 472.
<https://doi.org/10.1177/0885328217731951>
- Gilkes D.M., Bajpai S., Chaturvedi P., Wirtz D., Semenza G.L.* 2013. Hypoxia-inducible factor 1 (HIF-1) promotes extracellular matrix remodeling under hypoxic conditions by inducing P4HA1, P4HA2, and PLOD2 expression in fibroblasts. J. Biol. Chem. V. 288. P. 10819.
<https://doi.org/10.1074/jbc.M112.442939>

- Grant R., Hay D., Callanan A.* 2018. From scaffold to structure: the synthetic production of cell derived extracellular matrix for liver tissue engineering. *Biomed. Phys. Eng. Express*. V. 4. P. 065015. <https://doi.org/10.1088/2057-1976/aacbe1>
- Gu Y., Zhu J., Xue C., Li Z., Ding F., Yang Y., Gu X.* 2014. Chitosan/silk fibroin-based, Schwann cell-derived extracellular matrix-modified scaffolds for bridging rat sciatic nerve gaps. *Biomaterials*. V. 35. P. 2253. <https://doi.org/10.1016/j.biomaterials.2013.11.087>
- Han S., Li Y.Y., Chan B.P.* 2016. Extracellular protease inhibition alters the phenotype of chondrogenically differentiating human mesenchymal stem cells (MSCs) in 3D collagen microspheres. *PLoS One*. V. 11. P. e0146928. <https://doi.org/10.1371/journal.pone.0146928>
- He S.K., Ning L.J., Yao X., Hu R.N., Cui J., Zhang Y., Ding W., Luo J.C., Qin T.W.* 2021. Hierarchically demineralized cortical bone combined with stem cell-derived extracellular matrix for regeneration of the tendon-bone interface. *Am. J. Sports Med.* V. 49. P. 1323. <https://doi.org/10.1177/0363546521994511>
- Hong Y., Koh I., Park K., Kim P.* 2017. On-Chip fabrication of a cell-derived extracellular matrix sheet. *ACS Biomater. Sci. Eng.* V. 3. P. 3546. <https://doi.org/10.1021/acsbomaterials.7b00613>
- Hoshiba T.* 2019. Decellularized extracellular matrix for cancer research. *Materials (Basel)*. V. 12. P. 1311. <https://doi.org/10.3390/ma12081311>
- Joergensen P., Rattan S.I.S.* 2014. Extracellular matrix modulates morphology, growth, oxidative stress response and functionality of human skin fibroblasts during aging in vitro. *J. Aging Sci.* V. 2. P. 122. <https://doi.org/10.4172/2329-8847.1000122>
- Junka R., Yu X.* 2020. Polymeric nanofibrous scaffolds laden with cell-derived extracellular matrix for bone regeneration. *Mater. Sci. Eng. C. Mater. Biol. Appl.* V. 113. P. 110981. <https://doi.org/10.1016/j.msec.2020.110981>
- Kim I.G., Hwang M.P., Park J.S., Kim S.H., Kim J.H., Kang H.J., Subbiah R., Ko U.H., Shin J.H., Kim C.H., Choi D., Park K.* 2019. Stretchable ECM patch enhances stem cell delivery for post-MI cardiovascular repair. *Adv. Healthc. Mater.* V. 8. P. e1900593. <https://doi.org/10.1002/adhm.201900593>
- Konofaos P., Szpalski C., Rogers G.F., Rae M.M., Bumgardner J., Warren S.M.* 2017. Biomaterials and their application in craniomaxillofacial surgery. *Comprehensive Biomat.* II. V. 7. P. 406. <https://doi.org/10.1016/B978-0-12-803581-8.10166-3>
- Kusuma G.D., Brennecke S.P., O'Connor A.J., Kalionis B., Heath D.E.* 2017. Decellularized extracellular matrices produced from immortal cell lines derived from different parts of the placenta support primary mesenchymal stem cell expansion. *PLoS One*. V. 12(2). P. e0171488. <https://doi.org/10.1371/journal.pone.0171488>
- Lai Y., Sun Y., Skinner C.M., Son E.L., Lu Z., Tuan R.S., Jilka R.L., Ling J., Chen X.D.* 2010. Reconstitution of marrow-derived extracellular matrix ex vivo: a robust culture system for expanding large-scale highly functional human mesenchymal stem cells. *Stem Cells Dev.* V. 19. P. 1095. <https://doi.org/10.1089/scd.2009.0217>
- Lee Y.J., Baek S.E., Lee S., Cho Y.W., Jeong Y.J., Kim K.J., Jun Y.J., Rhie J.W.* 2019. Wound-healing effect of adipose stem cell-derived extracellular matrix sheet on full-thickness skin defect rat model: histological and immunohistochemical study [published correction appears in *Int. Wound J.* 2019. V. 16. P. 873]. *Int. Wound J.* V. 16. P. 286. <https://doi.org/10.1111/iwj.13030>
- L'Heureux N., Dusserre N., Konig G., Victor B., Keire P., Wight T.N., Chronos N.A., Kyles A.E., Gregory C.R., Hoyt G., Robbins R.C., McAllister T.N.* 2006. Human tissue-engineered blood vessels for adult arterial revascularization. *Nat. Med.* V. 12. P. 361. <https://doi.org/10.1038/nm1364>
- Li M., Zhang A., Li J., Zhou J., Zheng Y., Zhang C., Xia D., Mao H., Zhao J.* 2020. Osteoblast/fibroblast coculture derived bioactive ECM with unique matrisome profile facilitates bone regeneration. *Bioact. Mater.* V. 5. P. 938. <https://doi.org/10.1016/j.bioactmat.2020.06.017>
- Lin H., Yang G., Tan J., Tuan R.S.* 2012. Influence of decellularized matrix derived from human mesenchymal stem cells on their proliferation, migration and multi-lineage differentiation potential. *Biomaterials*. V. 33. P. 4480. <https://doi.org/10.1016/j.biomaterials.2012.03.012>
- Malakpour-Permlid A., Buzzi I., Hegardt C., Johansson F., Oredsson S.* 2021. Identification of extracellular matrix proteins secreted by human dermal fibroblasts cultured in 3D electrospun scaffolds. *Sci. Rep.* V. 11. P. 6655. <https://doi.org/10.1038/s41598-021-85742-0>
- Marinkovic M., Sridharan R., Santarella F., Smith A., Garlick J.A., Kearney C.J.* 2021. Optimization of extracellular matrix production from human induced pluripotent stem cell-derived fibroblasts for scaffold fabrication for application in wound healing. *J. Biomed. Mater. Res. A*. V. 109. P. 1803. <https://doi.org/10.1002/jbm.a.37173>
- Massaro M.S., Pálek R., Rosendorf J., Červenková L., Liška V., Moulisová V.* 2021. Decellularized xenogeneic scaffolds in transplantation and tissue engineering: Immunogenicity versus positive cell stimulation. *Mater. Sci. Eng. C. Mater. Biol. Appl.* V. 127. P. 112203. <https://doi.org/10.1016/j.msec.2021.112203>
- Methe K.* 2020. Transplantation of normal and decellularized syngeneic, allogeneic and xenogeneic cardiac tissue in mice and non-human primates. Doctoral thesis. University of Gothenburg. Sahlgrenska Academy.
- Nellinger S., Mrcic I., Keller S., Heine S., Southan A., Bach M., Volz A.C., Chassé T., Kluger P.J.* 2022. Cell-derived and enzyme-based decellularized extracellular matrix exhibit compositional and structural differences that are relevant for its use as a biomaterial. *Biotechnol. Bioeng.* V. 119. P. 1142. <https://doi.org/10.1002/bit.28047>
- Novoseleitskaya E., Grigorieva O., Nimiritsky P., Basalova N., Er-emichev R., Milovskaya I., Kulebyakin K., Kulebyakina M., Rodionov S., Omelyanenko N., Efimenko A.* 2020. Mesenchymal stromal cell-produced components of extracellular

- matrix potentiate multipotent stem cell response to differentiation stimuli. *Front. Cell Dev. Biol.* V. 8. P. 555378. <https://doi.org/10.3389/fcell.2020.555378>
- Nyambat B., Manga Y.B., Chen C.H., Gankhuyag U., PratomWp A., Kumar Satapathy M., Chuang E.Y.* 2020. New insight into natural extracellular matrix: genipin cross-linked adipose-derived stem cell extracellular matrix gel for tissue engineering. *Int. J. Mol. Sci.* V. 21. P. 4864. <https://doi.org/10.3390/ijms21144864>
- Ozguldez H.O., Cha J., Hong Y., Koh I., Kim P.* 2018. Nanoengineered, cell-derived extracellular matrix influences ECM-related gene expression of mesenchymal stem cells. *Biomater. Res.* V. 22. P. 32. <https://doi.org/10.1186/s40824-018-0141-y>
- Parmaksiz M., Dogan A., Odabas S., Elçin A.E., Elçin Y.M.* 2016. Clinical applications of decellularized extracellular matrices for tissue engineering and regenerative medicine. *Biomed. Mater.* V. 11. P. 022003. <https://doi.org/10.1088/1748-6041/11/2/022003>
- Ragelle H., Naba A., Larson B.L., Zhou F., Prijic M., Whittaker C.A., Del Rosario A., Langer R., Hynes R.O., Anderson D.G.* 2017. Comprehensive proteomic characterization of stem cell-derived extracellular matrices. *Biomaterials.* V. 128. P. 147. <https://doi.org/10.1016/j.biomaterials.2017.03.008>
- Raghunathan V.K.* 2018. Cell-derived matrices as a model to study ocular hypertension. In: *Glaucoma Research and Clinical Advances: 2018 to 2020*. Amsterdam: Kugler Publications. P. 69.
- Rao Pattabhi S., Martinez J.S., Keller T.C.* 3rd. 2014. Decellularized ECM effects on human mesenchymal stem cell stemness and differentiation. *Differentiation.* V. 88. P. 131. <https://doi.org/10.1016/j.diff.2014.12.005>
- Rubi-Sans G., Castaño O., Cano I., Mateos-Timoneda M.A., Perez-Amodio S., Engel E.* 2020. Engineering cell-derived matrices: from 3D models to advanced personalized therapies. *Adv. Funct. Mater.* V. 30. P. 2000496. <https://doi.org/10.1002/adfm.202000496>
- Rubi-Sans G., Nyga A., Rebollo E., Pérez-Amodio S., Otero J., Navajas D., Mateos-Timoneda M.A., Engel E.* 2021. Development of cell-derived matrices for three-dimensional in vitro cancer cell Models. *ACS Appl. Mater. Interfaces.* V. 13. P. 44108. <https://doi.org/10.1021/acsami.1c13630>
- Ruff S.M., Keller S., Wieland D.E., Wittmann V., Tovar G.E.M., Bach M., Kluge P.J.* 2017. clickECM: Development of a cell-derived extracellular matrix with azide functionalities. *Acta Biomater.* V. 52. P. 159. <https://doi.org/10.1016/j.actbio.2016.12.022>
- Schmuck E., Raval A.* 2016. Cardiac fibroblast-derived extracellular matrix and injectable formulations thereof for treatment of ischemic disease or injury. *Int. Publ. Number* WO2016197038A1
- Shamis Y., Hewitt K.J., Bear S.E., Alt-Holland A., Qari H., Margvelashvili M., Knight E.B., Smith A., Garlick J.A.* 2012. iP-SC-derived fibroblasts demonstrate augmented production and assembly of extracellular matrix proteins. *In vitro Cell Dev. Biol. Anim.* V. 48. P. 112. <https://doi.org/10.1007/s11626-011-9478-4>
- Sicari B.M., Rubin J.P., Dearth C.L., Wolf M.T., Ambrosio F., Boninger M., Turner N.J., Weber D.J., Simpson T.W., Wyse A., Brown E.H.P., Dziki J.L., Fisher L.E., Brown S., Badylak S.F.* 2014. An acellular biologic scaffold promotes skeletal muscle formation in mice and humans with volumetric muscle loss. *Sci. Transl. Med.* V. 6. P. 234ra58. <https://doi.org/10.1126/scitranslmed.3008085>
- Sonbol H.S.* 2018. Extracellular matrix remodeling in human disease. *J. Microsc. Ultrastruct.* V. 6. P. 123. https://doi.org/10.4103/JMAU.JMAU_4_18
- Tang C., Jin C., Li X., Li J., Du X., Yan C., Lu S., Wei B., Xu Y., Wang L.* 2019. Evaluation of an autologous bone mesenchymal stem cell-derived extracellular matrix scaffold in a rabbit and minipig model of cartilage repair. *Med. Sci. Monit.* V. 25. P. 7342. <https://doi.org/10.12659/MSM.916481>
- Theocharis A.D., Manou D., Karamanos N.K.* 2019. The extracellular matrix as a multitasking player in disease. *FEBS J.* V. 286. P. 2830. <https://doi.org/10.1111/febs.14818>
- Thompson R.E., Pardieck J., Smith L., Kenny P., Crawford L., Shoichet M., Sakiyama-Elbert S.* 2018. Effect of hyaluronic acid hydrogels containing astrocyte-derived extracellular matrix and/or V2a interneurons on histologic outcomes following spinal cord injury. *Biomaterials.* V. 162. P. 208. <https://doi.org/10.1016/j.biomaterials.2018.02.013>
- Vuoristo S., Toivonen S., Weltner J., Mikkola M., Ustinov J., Trokovic R., Palgi J., Lund R., Tuuri T., Otonkoski T.* 2013. A novel feeder-free culture system for human pluripotent stem cell culture and induced pluripotent stem cell derivation. *PLoS One.* V. 8. P. e76205. <https://doi.org/10.1371/journal.pone.0076205>
- Weber B., Dijkman P.E., Scherman J., Sanders B., Emmert M.Y., Grünfelder J., Verbeek R., Bracher M., Black M., Franz T., Kortsmi J., Modregger P., Peter S., Stamparoni M., Robert J. et al.* 2013. Off-the-shelf human decellularized tissue-engineered heart valves in a non-human primate model. *Biomaterials.* V. 34. P. 7269. <https://doi.org/10.1016/j.biomaterials.2013.04.059>
- Xiong G.F., Xu R.* 2016. Function of cancer cell-derived extracellular matrix in tumor progression. *J. Cancer Metastasis Treat.* V. 2. P. 357. <https://doi.org/10.20517/2394-4722.2016.08>
- Yu X., He Y., Chen Z., Qian Y., Wang J., Ji Z., Tan X., Li L., Lin M.* 2019. Autologous decellularized extracellular matrix protects against H₂O₂-induced senescence and aging in adipose-derived stem cells and stimulates proliferation *in vitro*. *Biosci. Rep.* V. 39. P. BSR20182137. <https://doi.org/10.1042/BSR20182137>
- Zhang X., Liu Y., Clark K.L., Padgett A.M., Alexander P.G., Dai J., Zhu W., Lin H.* 2020. Mesenchymal stem cell-derived extracellular matrix (mECM): a bioactive and versatile scaffold for musculoskeletal tissue engineering. *Biomed. Mater.* V. 16. P. 012002. <https://doi.org/10.1088/1748-605X/abb6b3>
- Zhu W., Cao L., Song C., Pang X., Jiang H., Guo C.* 2021. Cell-derived decellularized extracellular matrix scaffolds for articular cartilage repair. *Int. J. Artif. Organs.* V. 44. P. 269. <https://doi.org/10.1177/0391398820953866>

The Potential of Decellularized Cell-Derived Matrices for Biomedical Applications

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Decellularized extracellular matrices show a great promise as materials for tissue engineering and regenerative medicine. Recently, there has been an increasing interest in the use of cell-derived extracellular matrices (CD-ECMs). The present mini-review focuses on advantages and disadvantages of the CD-ECMs, describes the variety of approaches to modify the CD-ECMs and discusses the CD-ECMs application fields. In particular, CD-ECMs were shown to serve as cell culture substrate, as base for biocompatible scaffold production, as drug for cell-free therapy and as component of disease models.

Keywords: decellularized matrix, cell-free matrix, cell-free therapy, tissue engineering, regenerative medicine