

DAFTAR PUSTAKA

- Aaron RK and Racine J. 2013. Pathogenesis and Epidemiology of Osteoarthritis. Rhode Island Medical Journal. 19-22
- Abbaszade I, Liu RQ, Yang F, Rosenfeld SA, Ross OH, Link JR et al. 1999. Cloning and characterization of ADAMTS11, an aggrecanase from the ADAMTS family. *J Biol Chem* 274:23443–23450
- Abraham S, Naveen AT, Kirtivasan V, Prasad GN, Karthik V, Rajesh V, Madhusankar N, Cherian KM. 2007. "Use of Bone Marrow derived Stem Cells in Patients with Cardiovascular Disorders". *Journal of Stem Cells and Regenerative Medicine.* 3(1): 28-29(2)
- Abraham AM, Goff I, Pearce MS, Francis RM and Birrell F. 2011. Reliability and validity of ultrasound imaging features of knee osteoarthritis in the community. *BMC Musculoskeletal Disorders* 12:70:1-8
- Abramson SB. 2008. Nitric oxide in inflammation and pain associated with osteoarthritis. *Arthritis Res Ther.* 10 Suppl 2:S2.
- Aggarwal S and Pittenger M F. 2005. Human mesenchymal stem cells modulate allogeneic immune cell responses. *Blood.* 105(4) : 1815-1822
- Allen RT, Robertson CM, Harwood FL, Sasho T, Williams SK, Pomerleau AC and Amiel D. 2004. Characterization of mature vs aged rabbit articular cartilage: analysis of cell density, apoptosis-related gene expression and mechanisms controlling chondrocyte apoptosis. *Ann Rheum Dis* 51:1219-1222. *OsteoArthritis and Cartilage* 12:917-923
- Almalki SG and Agrawal DK. 2016. Effects of matrix metalloproteinases on the fate of mesenchymal stem cells. *Stem Cell Research & Therapy.* 7:129
- Altman R, Asch E, Bloch D et al. 1986. Development of Criteria for the classification and Reporting of Osteoarthritis. *Arthritis and Rheumatism* 29(8):1039-1049
- Amin AR, Attur M, Abramson SB. 1999. Nitric oxide synthase and cyclooxygenases: distribution, regulation, and intervention in arthritis. *Curr Opin Rheumatol.* 11(3):202-9.
- Andia, I. and Maffulli, N. 2013. Platelet-rich plasma for managing pain and inflammation in osteoarthritis. *Nat. Rev. Rheumatol.* 141:1-10
- Andreas Ardhika Antoninus, Dwi Agustina, Laura Wijaya, Vincent Hariyanto, Yanti, Maurin Merlina, Benjamin Setiawan, Indra Bachtiar. 2012. Wharton's Jelly-Derived Mesenchymal Stem Cells: Isolation and Characterization. *CDK-196*, vol. 39 no. 8. 588-591

- Apte SS. 2004. A disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motifs: The ADAMTS family. *Cell Biol* 36:981–985.
- Aranapakam V, Grosu GT, Davis JM, Hu B, Ellingboe J, Baker JL, Skotnicki JS, Zask A, DiJoseph JF, Sung A, Sharr MA, Killar LM, Walter T, Jin G, Cowling R. 2003. Synthesis and Structure-Activity Relationship of α -Sulfonylhydroxamic Acids as Novel, Orally Active Matrix Metalloproteinase Inhibitors for the Treatment of Osteoarthritis. *J. Med. Chem.* 46:2361-2375.
- Assirelli E, Pulsatelli L, Dolzani P, Platano D, Olivotto E, Filardo G, Trisolino G, Facchini A, Borzi RM, Meliconi R. 2014. Human Osteoarthritic Cartilage Shows Reduced In Vivo Expression of IL-4, a Chondroprotective Cytokine that Differentially Modulates IL-1b-Stimulated Production of Chemokines and Matrix-Degrading Enzymes In Vitro. *Plos One*.9:1-13
- Ayala-Cuellar AP, Kang J-H, Jeung E-B and Cho K-C. 2017. Roles of Mesenchymal Stem Cells in Tissue Regeneration and Immunomodulation. *Biomol Ther*, 1-9
- Ayral X, Pickering EH, Woodworth TG, Mackillop N, Dougados M. 2001. Synovitis predicts the arthroscopic progression of medial tibiofemoral knee osteoarthritis. *Arthritis Rheum*. 44(Suppl. 9), 952
- Baksh D, Yao R, Tuan R. 2007. Comparison of proliferative and multilineage differentiation potential of human mesenchymal stem cells derived from umbilical cord and bone marrow. *Stem Cells*. 25(6):1384–92
- Batsali AK, Kastrinaki MC, Papadaki HA, Pontikoglou C. 2013. Mesenchymal Stem Cells Derived from Wharton's Jelly of the Umbilical Cord: Biological Properties and Emerging Clinical Applications. *Current Stem Cell Research and Therapy*. 8(2):144–155
- Bau B, Gebhard PM, Haag J, Knorr T, Bartnik E, Aigner T. 2002. Relative messenger RNA expression profiling of collagenases and aggrecanases in human articular chondrocytes in vivo and in vitro. *Arthritis Rheum* 46: 2648-57.
- Benito MJ, Veale DJ, Fitzgerald O, Van Den Berg WB, Bresnihan B. 2005. Synovial tissue inflammation in early and late osteoarthritis. *Ann Rheum Dis* 64: 1263-7.
- Blaney DEN, van der Kraan PM, van den Berg WB. 2007. TGF- β and osteoarthritis. *OsteoArthritis and Cartilage* 15, 597–604.
- Blom AB, Vanlent PLEM, Holthuysen et al. 2004. Synovial lining macrophages mediate osteophyte formation during experimental osteoarthritis. *Osteoarthritis and Cartilage* 12: 627-35.
- Blom AB, Lent PL, Libregts S et al. 2007. Crucial role of macrophages in matrix metalloproteinases-mediated cartilage destruction during experimental osteoarthritis. *Arthritis Rheum*. 56, 147–157

- Bodmer J-L, Schneider P, and Tschopp J. 2002. The molecular architecture of the TNF superfamily. *Trends in Biochemical Sciences.* 27(1):19–26
- Bondeson J, Wainwright SD, Lauder S, Amos N, Hughes CE. 2006. The role of synovial macrophages and macrophage-produced cytokines in driving aggrecanases, matrix metalloproteinases and other destructive and inflammatory responses in osteoarthritis. *Arthritis Res Ther.* 8: R187.
- Bondeson J, Lauder S, Wainwright S, et al. 2007. Adenoviral gene transfer of the endogenous inhibitor IkBa into human osteoarthritis synovial fibroblasts demonstrates that several matrix metalloproteinases and aggrecanases are nuclear factor- κ B-dependent. *J Rheumatol.* 34:523-33.
- Bongso A and Lee EH. 2005. Stem Cells: Their Definition, Classification and Sources. *Stem Cells: Exp Neurol.* 161: 67–84.
- Bongso A, Fong CY. 2013. The therapeutic potential, challenges and future clinical directions of stem cells from the Wharton's jelly of the human umbilical cord. *Stem Cell Rev.* 9(2):226–40.
- Bonnet CS, Walsh DA. 2005. Osteoarthritis, angiogenesis and inflammation. *Rheumatology (Oxford)* 44, 7–16
- Borderie D, Hilliquin P, Hernvann A, Lemarechal H, Menkes CJ, Ekindjian OG. 1999. Apoptosis induced by nitric oxide is associated with nuclear p53 protein expression in cultured osteoarthritic synoviocytes. *Osteoarthritis Cartilage.* 7(2):203-13.
- Bouffi C, Djouad F, Mathieu M, Noël D and Jorgensen C. 2009. Multipotent mesenchymal stromal cells and rheumatoid arthritis: risk or benefit?. *Rheumatology (Oxford)* 48:1185–1189
- Bou-Gharios G and de Crombrugghe B. Type I Collagen Structure, Synthesis, and Regulation : Principles of Bone Biology, 3rd edition. Academic Press. 2008. Inc. pp 285-318.
- Bourne RB, Chesworth BM, et al. 2010. Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? *Clin Orthop Relat.* 468:57–63.
- Braddock M and Quinn A. 2004. Targeting IL-1 in inflammatory disease: new opportunities for therapeutic intervention. *Nat Rev Drug Discov.* 3:330-339
- Brew K, Dinakarpandian D, Nagase H. 2000. Tissue inhibitors of metalloproteinases: evolution, structure and function. *Biochim Biophys Acta* 1477:267–283
- Burrage PS, Mix KS and Brinckerhoff CE. 2006. Matrix Metalloproteinases: Role In Arthritis. *Frontiers in Bioscience* 11, 529-543.

- Campbell J, Ciesielski CJ, Hunt AE et al. 2004. A novel mechanism for TNF- α regulation by p38 MAPK: involvement of NF- κ B with implications for therapy in rheumatoid arthritis. *Journal of Immunology.* 173(11):6928–6937.
- Caplan AI, Correa D. 2011. The MSC: an injury drugstore. *Cell Stem Cell.* 9(1):11–15.
- Carmona JU and Prades M. 2009. Pathophysiology of Osteoarthritis. Compendium Equine: Continuing Education for Veterinarians : 28-40
- Carrade Holt DD, Wood JA, Granick JL, Walker NJ, Clark KC, and Borjesson DL. 2014. Equine mesenchymal stem cells inhibit T cell proliferation through different mechanisms depending on tissue source. *Stem Cells Dev.* 23, 1258-1265.
- Catania JM, Chen G, Parrish AR. 2007. Role of matrix metalloproteinases in renal pathophysiologies. *Am J Physiol Renal Physiol* 292: F905–F911.
- Cerofolini L, Fields G B, Fragai M, Geraldes C F G C, Luchinat C, Parigi G et al. 2013. Examination of matrix metalloproteinase-1 (MMP-1) in solution: A preference for the pre-collagenolysis state. *J. Biol. Chem.* published online September 11, 2013
- Chai N-L, Zhang X-B, Chen S-W, Fan K-X, Linghu E-Q. 2016. Umbilical cord-derived mesenchymal stem cells alleviate liver fibrosis in rats. *World J Gastroenterol.* 22(26): 6036-6048.
- Chen M-S, Lin C-Y, Chiu Y-H, Chen C-P, Tsai P-J, and Wang H-S. 2018. IL-1 β -Induced Matrix Metalloprotease-1 Promotes Mesenchymal Stem Cell Migration via PAR1 and G-Protein-Coupled Signaling Pathway. *Stem Cells International.* Volume 2018, Article ID 3524759, 11 pages
- Choi H-S, Im S, Park J W, and Suh H J. 2016. Protective Effect of Deer Bone Oil on Cartilage Destruction in Rats with Monosodium Iodoacetate (MIA)-Induced Osteoarthritis. *Biol. Pharm. Bull.* 39(12), 2042–2051
- Chomarat P and Banchereau J. 1998. Interleukin-4 and interleukin-13: Their similarities and discrepancies. *Int. Rev. Immunol.* 17, 1–52
- Chowdhury T T, Bader D L, Lee D A. 2006. Anti-inflammatory effects of IL-4 and dynamic compression in IL-1 β stimulated chondrocytes. *Biochemical and Biophysical Research Communications* 339:241–247
- Chung JY, Song M, Ha CW, Kim JA, Lee CH, Park YB. 2014. Comparison of articular cartilage repair with different hydrogel-human umbilical cord blood-derived mesenchymal stem cell composites in a rat model. *Stem Cell Res Ther.* 5:39.
- Cillero-Pastor B, Martin M A, Arenas J, López-Armada M J, Blanco FJ. 2011. Effect of nitric oxide on mitochondrial activity of human synovial cells. *BMC Musculoskeletal Disorders* 12:42 .

- Cosenza S, Ruiz M, Toupet K, Jorgensen C & Noël D. 2017. Mesenchymal stem cells derived exosomes and microparticles protect cartilage and bone from degradation in osteoarthritis. *Scientific Reports* 7:16214: 1-12
- Curry TE and Osteen KG. 2003. The Matrix Metalloproteinase System: Changes, Regulation, and Impact throughout the Ovarian and Uterine Reproductive Cycle. *Endocrine Reviews* 24(4):428 – 465
- Curtis CL, Rees SG, Little CB, Flannery CR, Hughes CE, Wilson C, Dent CM, Otterness IG, Harwood JL, Caterson B. 2002. Pathologic indicators of degradation and inflammation in human osteoarthritic cartilage are abrogated by exposure to n-3 fatty acids. *Arthritis Rheum* 46:1544–1553
- Dahagin S, Bierma-Zeinstra SM, Ginai AZ, et al. 2005. Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability. *Ann Rheum Dis.* 64:682–687.
- Daheshia M and Yao J Q. 2008. The Interleukin 1 β Pathway in the Pathogenesis of Osteoarthritis. *J Rheumatol* 35:2306–12
- Dahlberg L, Billingham RC, Manner P, Nelson F, Webb G, Ionescu M, et al. 2000. Selective enhancement of collagenase-mediated cleavage of resident type II collagen in cultured osteoarthritic cartilage and arrest with a synthetic inhibitor that spares collagenase 1 (matrix metalloproteinase 1). *Arthritis Rheum* 43: 673–82
- De Coppi P, Bartsch G, Siddiqui MM, Xu T, Santos CC, Perin L, Mostoslavsky G, Serre AC, Snyder EY, Yoo JJ, Furth ME, Soker S, Atala A. 2007. Isolation of amniotic stem cell lines with potential for therapy. *Nature Biotechnology*. 25 (5): 100–106.
- Dedeepiya VD, Rao YY, Jayakrishnan GA, Parthiban JK, Baskar S, Manjunath SR, Senthilkumar R, Abraham SJ. 2012. Index of CD34+ Cells and Mononuclear Cells in the Bone Marrow of Spinal Cord Injury Patients of Different Age Groups: A Comparative Analysis. *Bone Marrow Res.* 2012: 787414.
- DeGroot J, Verzijl N, Marion J. G. Wenting-Van Wijk, Bank RA., Lafeber FP, Bijlsma WJ, and TeKoppele JM. 2001. Age-Related Decrease in Susceptibility of Human Articular Cartilage to Matrix Metalloproteinase-Mediated Degradation. *Arthritis Rheum.* 44(11): 2562–2571
- Del Carlo M, Jr., Loeser RF. 2002. Nitric oxide-mediated chondrocyte cell death requires the generation of additional reactive oxygen species. *Arthritis Rheum.* 46(2):394-403.
- Djouad F, Bouffi C, Ghannam S, et al. 2009. Mesenchymal stem cell: innovative therapeutic tools for rheumatic diseases. *Nat Rev Rheumatol.* 5:392–9.

- Du C, Jiang M, Wei X, Qin J, Xu H, Wang Y, Zhang Y, Zhou D, Xue H, Zheng S, and Zeng W. 2018. Transplantation of human matrix metalloproteinase-1 gene-modified bone marrow-derived mesenchymal stem cell attenuates CCL4-induced liver fibrosis in rats. *Int J Molecular Medicine*. 41: 3175-3184.
- Dubie T, Admassu B, Sisay T and Shiferaw H. 2014. Basic biology and therapeutic application of stem cells in various human and animal diseases. *J. Cell Biol. Genet.* 4(4):40-52
- Dunham J, Hoedt-Schmidt S, Kalbhen DA. 1993. Prolonged effect of iodoacetate on articular cartilage and its modification by an anti-rheumatic drug. *Int J Exp Pathol.* 74:283-9.
- Ea C-K, Deng L, Xia Z-P, Pineda G, and Chen ZJ. 2006. Activation of IKK by TNF α Requires Site-Specific Ubiquitination of RIP1 and Polyubiquitin Binding by NEMO. *Molecular Cell*.22(2):245–257.
- Elliott S, Hays E, Mayor M, Sporn M and Vincenti M. 2003. The triterpenoid CDDO inhibits expression of matrix metalloproteinase-1, matrix metalloproteinase-13 and Bcl-3 in primary human chondrocytes. *Arthritis Res Ther*, 5(5), R285-291
- Ellman MB, Yan D, Chen D and Im H-J. 2012. Biochemical Mediators Involved in Cartilage Degradation and the Induction of Pain in Osteoarthritis: Principles of Osteoarthritis- Its Definition, Character, Derivation and Modality-Related Recognition, Dr. Bruce M. Rothschild (Ed.), ISBN: 978-953-51-0063-8, InTech, Available from: <http://www.intechopen.com/books/principles-of-osteoarthritis-its-definition-character-derivation-and-modality-related-recognition/biochemical-mediators-involved-in-cartilage-degradation-and-the-induction-of-pain-in-osteoarthritis>
- Emadeddin M, Aghdami N, Taghiyar L, Fazeli R, Moghadasali R, Jahangir S, Farjad R, Baghaban E. 2012. Intra-articular injection of autologous mesenchymal stem cells in six patients with knee osteoarthritis. *Arch. Iran. Medicine*. 15: 422-428.
- Engel CK, Pirard B, Schimanski S, Kirsch R, Habermann J, Klingler O, Schlotte V, Weithmann KU, Wendt KU. 2005. Structural Basis for the Highly Selective Inhibition of MMP-13. *Chem.Biol.* 12:181-189.
- Fahmi H, Pelletier J.-P, Di Battista J. A, Cheung Ü H. S, Fernandes J. C and Martel-Pelletier J. 2002. Peroxisome proliferator-activated receptor gamma activators inhibit MMP-1 production in human synovial fibroblasts likely by reducing the binding of the activator protein 1. *J. OsteoArthritis Research Society Int.* 10 (2) : 100-108.
- Fan Z, Bau B, Yang H, Soeder S, Aigner T. 2005. Freshly isolated osteoarthritic chondrocytes are catabolically more active than normal chondrocytes, but less responsive to catabolic stimulation with interleukin-1 β . *Arthritis Rheum* 52:136-43.

- Farahat MN, Yanni G, Poston R, and Panayi GS. 1993. Cytokine expression in synovial membranes of patients with rheumatoid arthritis and osteoarthritis. *Annals of the Rheumatic Diseases* 52(12):870–875.
- Felson DT. 2006. Osteoarthritis of the Knee. *N Engl J Med.* 354(8): 841-848
- Fernandes JC, Martel-Pelletier J and Pelletier JP. 2002. The role of cytokines in osteoarthritis pathophysiology. *Biorheology* 39, 237-46.
- Fong CY, Richards M, Manasi N, Biswas A and Bongso A. 2007. Comparative growth behaviour and characterization of stem cells from human Wharton's jelly. *Reproductive biomedicine online* 15, 708-718
- Fong, CY, Chak L-L, Biswas A, Tan J-H, Gauthaman K, Chan W-K, Bongso A. 2011. Human Wharton's jelly stem cells have unique transcriptome profiles compared to human embryonic stem cells and other mesenchymal stem cells. *Stem cell reviews* 7, 1-16.
- Fosang AJ and Little CB. 2008. Drug insight: aggrecanases as therapeutic targets for osteoarthritis. *Nat Clin Pract Rheumatol.* 4:420–427.
- Freitag J, Bates D, Boyd R, Shah K, Barnard A, Huguenin L and Tenen A. 2016. Mesenchymal stem cell therapy in the treatment of osteoarthritis: reparative pathways, safety and efficacy—a review. *BMC Musculoskeletal Disorders.* 17:230:1-13
- Fuchs E and Segre J. 2000. Stem cells: a new lease on life. *Cell.* 100: 143–55.
- Gadani SP, Cronk JC, Norris GT, and Kipnis J. 2012. Interleukin-4: A Cytokine to Remember. *J Immunol.* 189(9): 4213–4219.
- Geha RS, Jabara HH, Brodeur SR. The regulation of immunoglobulin E class-switchrecombination. 2003. *Nat Rev Immunol.* 3:721–732.
- Gendron C, Kashiwagi M, Lim NH, Enghild JJ, Thøgersen IB, Hughes C, Caterson B, Nagase H. 2007. Proteolytic activities of human ADAMTS-5: Comparative studies with ADAMTS-4. *J Biol Chem* 282:18294–18306.
- Gieseke F, Böhringer J, Bussolari R, Dominici M, Handgretinger R, Müller I. 2010. Human multipotent mesenchymal stromal cells use galectin-1 to inhibit immune effector cells. *Blood* 116: 3770-3779
- Gimble JM, Katz AJ, Bunnell BA. 2007. Adipose-derived stem cells for regenerative medicine. *Circ Res.* 100 (9): 1249–60.
- Glennie, S., Soeiro, I., Dyson, P. J., Lam, E. W. and Dazzi, F. 2005. Bone marrow mesenchymal stem cells induce division arrest anergy of activated T cells. *Blood* 105, 2821-2827

- Glyn-Jones S, Palmer A J R, Agricola R, Price A J, Vincent T L, Weinans H, Carr A J. 2015. Osteoarthritis. *Lancet* 386: 376–87
- Goldring MB. 2000a. Osteoarthritis and cartilage: the role of cytokines. *Curr Rheumatol Rep* 2(6):459-65.
- Goldring MB. 2000b. The Role of the Chondrocyte in Osteoarthritis. *Arthritis Rheum.* 43(9):1916–1926
- Goldering MB and Goldering SR. 2007. Osteoarthritis. *Journal of Cellular Physiology Cell.* 626-634
- Goldring MB and Marcu KB. 2009. Cartilage homeostasis in health and rheumatic diseases. *Arthritis Res Ther.* 11:224
- Gomez DE, Alonso DF, Yoshiji H, Thorgeirsson UP. 1997. Tissue inhibitors of metalloproteinases: structure, regulation and biological functions. *Eur J Cell Biol* 74:111–122
- Gomis-Rüth FX. 2003. Structural aspects of the metzincin clan of metalloendopeptidases. *Mol Biotechnol.* 24:157–202
- Gordon S. Alternative activation of macrophages. 2003. *Nat Rev Immunol.* 3:23–35.
- Grell M, Douni E, Wajant H et al. 1995. The transmembrane form of tumor necrosis factor is the prime activating ligand of the 80 kDa tumor necrosis factor receptor. *Cell* 83(5):793–802.
- Guest D, Smith M, Allen W. 2010. Equine embryonic stem-like cells and mesenchymal stromal cells have different survival rates and migration patterns following their injection into damaged superficial digital flexor tendon. *Equine Vet. J.* 42: 636-642.
- Gulotta V, Kovacevic D, Packer D, Deng H, Rodeo S (2011). Bone marrow-derived mesenchymal stem cells transduced with scleraxis improve rotator cuff healing in a rat model. *Am. J. Sports Med.* 39: 1282-1289.
- Haas TL, Emmerich CH, Gerlach B et al. 2009. Recruitment of the linear ubiquitin chain assembly complex stabilizes the TNF-R1 signaling complex and is required for TNF-mediated gene induction. *Molecular Cell.* 36(5):831–844.
- Habib S and Ali A. 2011. Biochemistry of Nitric Oxide. *Ind J Clin Biochem* 26(1):3–17
- Han I, Yun M; Kim E-O, Kim B, Jung M-H, Kim S-H. 2014. Umbilical cord tissue-derived mesenchymal stem cells induce apoptosis in PC-3 prostate cancer cells through activation of JNK and downregulation of PI3K/AKT signaling. *Stem Cell Res Ther.* 5(54):1-9.

- Hsieh CS, Heimberger AB, Gold JS, O'Garra A, Murphy KM. Differential regulation of T helperphenotype development by interleukins 4 and 10 in an alpha beta T-cell-receptor transgenicsystem. 1992. Proc Natl Acad Sci U S A. 1992; 89:6065–6069.
- Hsieh FH, Lam BK, Penrose JF, Austen KF, Boyce JA. 2001. T helper cell type 2 cytokines coordinately regulate immunoglobulin E-dependent cysteinyl leukotriene production by human cord blood-derived mast cells: Profound induction of leukotriene C(4) synthase expression by interleukin 4. J. Exp. Med. 193, 123–133
- Ho IAW, Chan KYW, Ng W-H, Guo CM, Hui KM, Cheang P, Lam PYP. 2009. Matrix Metalloproteinase 1 Is Necessary for the Migration of Human Bone Marrow-Derived Mesenchymal Stem Cells Toward Human Glioma. Stem Cells. 27:1366–1375
- Horie M, Choi H, Lee R.H, Reger R.L, Ylostalo J, Muneta T, Sekiya I, Prockop D.J. 2012. Intra-articular injection of human mesenchymal stem cells (MSCs) promote rat meniscal regeneration by being activated to express Indian hedgehog that enhances expression of type II collagen. Osteoarthritis and Cartilage 20 : 1197-1207
- Houard, X., Goldring, M B., and Berenbaum, F., 2013, Homeostatic Mechanisms in Articular Cartilage and Role of Inflammation in Osteoarthritis, National Institute of Health Public Access, 15(11), 375, 1-19.
- Huang CY, Hung LF, Liang CC, Ho LJ. 2009. COX-2 and iNOS are critical in advanced glycation end product-activated chondrocytes in vitro. Eur J Clin Invest. 39(5):417-28.
- Hui W, Barksby HE, Young DA, Cawston TE, McKie N, Rowan AD. 2005. Oncostatin M in combination with tumour necrosis factor α induces a chondrocyte membrane associated aggrecanase that is distinct from ADAMTS aggrecanase-1 or -2. Ann Rheum Dis. 64(11):1624-32.
- Hu-Li J, Mizuguchi SEJ, Ohara J, Mosmann T, Paul WE. B cell stimulatory factor 1 (interleukin 4) is a potent costimulant for normal resting lymphocytes. 1987. J Exp Med. 159:7
- Idriss HT and Naismith JH. 2000. TNF alpha and the TNF receptor superfamily: structure-function relationship(s). Microscopy Research and Technique 50(3);184–195
- Inoue K, Masuko-Hongo K, Okamoto M, Nishioka K. 2005. Induction of vascular endothelial growth factor and matrix metalloproteinase-3 (stromelysin) by interleukin-1 in human articular chondrocytes and synoviocytes. Rheumatol Int 26:93-8.

Iyer S, Visse R, Nagase H, and Acharya KR. 2006. Crystal Structure of an Active Form of Human MMP-1. *J. Mol. Biol.* 362:78–88

Janusz M. J, Hookfin E. B, Heitmeyer S. A, Woessner J. F, Freemont A. J, Hoyland J. A, Brown K. K, Hsieh L. C, Almstead N. G, De B, Natchus M. G, Pikul S and Taiwo Y. O. 2001. Moderation of iodoacetate-induced experimental osteoarthritis in rats by matrix metalloproteinase inhibitors. *J. OsteoArthritis Research Society Int.* 9 (8): 751–760

Javanmard MZ, Asgari D, Karimipour M, Atabaki F, Farjah G, and Niakani A. 2015. Mesenchymal Stem Cells Inhibit Proteoglycan Degeneration in a Rat Model of Osteoarthritis. *Gene Cell Tissue.* 2(4):e31011: 1-5

Jiang Y, Jahagirdar BN, Reinhardt RL, Schwartz RE, Keene CD, Ortiz-Gonzalez XR, Reyes M, Lenvik T, Lund T, Blackstad M, Du J, Aldrich S, Lisberg A, Low WC, Largaespada DA, Verfaillie CM .2002. Pluripotency of mesenchymal stem cells derived from adult marrow. *Nature.* 418 (6893): 41–9

Jo CH, Lee YG, Shin WH, Kim H, Chai JW, Jeong EC, et al. 2014. Intra-articular injection of mesenchymal stem cells for the treatment of osteoarthritis of the knee: a proof-of concept clinical trial. *Stem Cells.* 32:1254–66.

Juni P, Reichenbach S, Dieppe P. 2006. Osteoarthritis: rational approach to treating the individual. *Best Pract Res Clin Rheumatol* 20:721-40.

Kalaszczynska I and Ferdyn K. 2015. Wharton's Jelly Derived Mesenchymal Stem Cells: Future of Regenerative Medicine? Recent Findings and Clinical Significance. *BioMed Research International*, Volume 2015, Article ID 430847, 11 pages

Kapoor M, Martel-Pelletier J, Lajeunesse D, Pelletier JP, Fahmi H. 2011. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. *Nat Rev Rheumatol.* 7(1):33-42.

Kashiwagi M, Enghild JJ, Gendron C, Hughes C, Caterson B, Itoh Y, Nagase H. 2004. Altered proteolytic activities of ADAMTS-4 expressed by C-terminal processing. *J Biol Chem* 279:10109–10119.

Kay A G, Long G, Tyler G, Stefan A, Broadfoot S J, Piccinini A M, Middleton J & Kehoe O. 2017. Mesenchymal Stem Cell-Conditioned Medium Reduces Disease Severity and Immune Responses in Inflammatory Arthritis. *Scientific Reports.* 7:18019

Kelly-Welch AE, Hanson EM, Boothby MR, Keegan AD. 2003. Interleukin-4 and interleukin-13 signaling connections maps. *Science* 300, 1527–1528

Kelly-Welch AE, Hanson EM, and Keegan AD. 2005. Interleukin-4 (IL-4) Pathway. *Sci. STKE* 2005. cm9.

- Kevorkian L, Young DA, Darrah C, et al. 2004. Expression profiling of metalloproteinases and their inhibitors in cartilage. *Arthritis Rheum.* 50:131–141.
- Kidd, B, 2012, Mechanisms of pain in osteoarthritis, Hiss Osteoarthritis Symposium, 8, 26-28
- Kim JS, Kroin JS, Buvanendran A, Li X, van Wijnen AJ, Tuman KJ, Im HJ. 2011. Characterization of a new animal model for evaluation and treatment of back pain due to lumbar facet joint osteoarthritis. *Arthritis Rheum.* 63:2966–73.
- Kim D-W, Staples M, Shinozuka K, Pantcheva P, Kang S-D and Borlongan CV. 2013. Wharton's Jelly-Derived Mesenchymal Stem Cells: Phenotypic Characterization and Optimizing Their Therapeutic Potential for Clinical Applications. *Int. J. Mol. Sci.* 14, 11692-11712.
- Kobayashi K, Imaizumi R, Sumichika H, Tanaka H, Goda M, Fukunari A, Komatsu H. 2003. Sodium iodoacetate-induced experimental osteoarthritis and associated pain model in rats. *J Vet Med Sci.* 65:1195–9
- Kobayashi M, Squires GR, Mousa A, et al. 2005. Role of interleukin-1 and tumor necrosis factor α in matrix degradation of human osteoarthritic cartilage. *Arthritis Rheum* 52:128-35.
- Koh YG, Choi Y-J. 2012. Infrapatellar fat pad-derived mesenchymal stem cell therapy for knee osteoarthritis. *The Knee* 19 : 902–907.
- Konttinen YT, Li T-F, Hukkanen M, Ma J, Xu J-W and Virtanen I. 2000. Fibroblast biology Signals targeting the synovial fibroblast in arthritis. *Arthritis Res* 2 :348–355
- Kuettner KE, Cole AA. 2005. Cartilage degeneration in different human joints. *Osteoarthritis Cartilage* 13(2):93-103.
- Kuroda Y, Kitada M, Wakao S, Nishikawa K, Tanimura Y, Makinoshima H, Goda M, Akashi H, Inutsuka A, Niwa A, Shigemoto T, Nabeshima Y, Nakahata T, Nabeshima Y, Fujiyoshi Y, Dezawa M. 2010. Unique multipotent cells in adult human mesenchymal cell populations. *Proc Natl Acad Sci U S A.* 107 (19): 8639–8643.
- Kuszczak, L., Trzeclak, T., Richter, M., Ratajczak, M C., 2015, Osteoarthritis and telomere shortening, *J Appl Genetics*, 56, 169-176
- Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. 2008. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part 2. *Arthritis Rheum* 58:26–35
- Lee A S, Ellman M B, Yan D, Kroin J S, Cole B J, van Wijnen A J, and Im H J. 2013. A current review of molecular mechanisms regarding osteoarthritis and pain, *Gene*, 527, 440-447

- Lejmi E, Perriraz N, Clément S, Morel P, Baertschiger R, Christofilopoulos P, et al. 2015. Inflammatory chemokines MIP-1 δ and MIP-3 α are involved in the migration of multipotent mesenchymal stromal cells induced by hepatoma cells. *Stem Cells Dev.* 2015;24:1223–35.
- Leonidou A, Lepetsos P, Mintzas M, Kenanidis E, Macheras G, Tzetis M, Potoupnis M & Tsiridis E. 2018. Inducible nitric oxide synthase as a target for osteoarthritis treatment. *Expert Opinion on Therapeutic Targets*: 1-20
- Li F, Xiong F, Zhang Y, Li Y, Zhao H, Cho SC et al. 2013. Therapeutic effects of human umbilical cord-derived mesenchymal stem cells against acute tubular necrosis quantified through measures of iNOS, BMP-7 and Bcl-2. *Open Journal of Regenerative Medicine* 2 (2): 31-38
- Lin T, Pajarin J, Nabeshima A, Lu L, Nathan K, Yao Z& Goodman S B. 2017. Establishment of NF- κ B sensing and interleukin-4 secreting mesenchymal stromal cells as an “on-demand” drug delivery system to modulate inflammation. *International Society for Cellular Therapy. Cytotherapy*. 19: 1025–1034
- Lotz M. 2001. Cytokines in cartilage injury and repair. *Clin Orthop*, S108-15.
- MacEwan DJ. 2002. TNF receptor subtype signalling: differences and cellular consequences. *Cellular Signalling*.14(6):477–492.
- Majore, I., Moretti, P., Stahl, F., Hass, R. & Kasper, C. 2011. Growth and differentiation properties of mesenchymal stromal cell populations derived from whole human umbilical cord. *Stem cell reviews* 7, 17-31, doi:10.1007/s1205-010-9165-y
- Malfait AM, Liu RQ, Ijiri K, Komiya S, Tortorella MD. 2002. Inhibition of ADAM-TS4 and ADAM-TS5 prevents aggrecan degradation in osteoarthritic cartilage. *J Biol Chem* 277:22201–8.
- Maneesh M, Jayalekshmi H, Suma T et all. 2005. Evidence for oxidative stress in osteoarthritis. *Indian journal of clinical biochemistry* 20 (1):129-130.
- Marcu KB, Otero M, Olivotto E, Borzi RM, and Goldring MB. 2010. NF- κ B signaling: multiple angles to target OA. *Current Drug Targets*. 11(5):599–613.
- Marini S, Fasciglione GF, Monteleone G, Maiotti M, Tarantino U, Coletta M. 2003. A correlation between knee cartilage degradation observed by arthroscopy and synovial proteinases activities. *Clinical Biochem*. 36 : 295–304
- Martel-Pelletier J. Pathophysiology of osteoarthritis. 2004. *Osteoarthritis Cartilage* 12(Suppl A):S31-S33.

- Martin MU and Wesche H. 2002. Summary and comparison of the signaling mechanisms of the Toll/interleukin-1 receptor family. *Biochimica et Biophysica Acta—Molecular Cell Research*, vol.1592(3):265–280.
- Massicotte F, Lajeunesse D, Benderdour M et al. 2002. Can altered production of interleukin-1 β , interleukin-6, transforming growth factor- α and prostaglandin E2 by isolated human subchondral osteoblasts identify two subgroups of osteoarthritic patients. *Osteoarthritis and Cartilage*. 10(6) 491–500
- Matsuzawa A, Tseng P-H, Vallabhapurapu S et al. 2008. Essential cytoplasmic translocation of a cytokine receptor-assembled signaling complex. *Science*.321(5889):663–668.
- McInnes IB, Leung BP, Field M, Wei XQ, Huang FP, Sturrock RD, Kinninmonth A, Weidner J, Mumford R, Liew FY. 1996. Production of nitric oxide in the synovial membrane of rheumatoid and osteoarthritis patients. *J Exp Med* 184:1519–24.
- Melchiorri C, Meliconi R, Frizziero L, Silvestri T, Pulsatelli L, Mazzetti I, et al. 1998. Enhanced and coordinated in vivo expression of inflammatory cytokines and nitric oxide synthase by chondrocytes from patients with osteoarthritis. *Arthritis Rheum.* 141(12):2165-74.
- Micheau O and Tschoopp J. 2003. Induction of TNF receptor I-mediated apoptosis via two sequential signaling complexes. *Cell* 114(2):181–190.
- Miljkovic Dj , Cvetkovic I, Stosic-Grujicic S and Trajkovic V. 2003. Mycophenolic acid inhibits activation of inducible nitric oxide synthase in rodent fibroblasts. *Clin Exp Immunol*.132:239 – 246
- Minshall C, Arkins S, Straza J, Conners J, Dantzer R, Freund GG, Kelley KW. IL-4 and insulin-likegrowth factor-I inhibit the decline in Bcl-2 and promote the survival of IL-3-deprived myeloidprogenitors. *J Immunol*. 1997; 159:1225–1232.
- Mitalipov S and Wolf D. 2009. Totipotency, pluripotency and nuclear reprogramming. *Adv. Biochem. Eng. Biotechnol.* Advances in Biochemical Engineering/Biotechnology. 114: 185–99.
- Mobasher A. 2013. The Future of Osteoarthritis Therapeutics: Targeted Pharmacological Therapy *Curr Rheumatol Rep*. 15:364.
- Moncada S and Higgs A. 1993. The L-arginine-nitric oxide pathway. *New England Journal of Medicine* 329:2002–2012.
- Murphy G and Nagase H. 2008. Reappraising metalloproteinases in rheumatoid arthritis and osteoarthritis: destruction or repair?. *Nat Clin Pract Rheumatol* 4:128–135.
- Murphy L, Schwartz TA, Helmick CG, et al. 2008. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis Rheum*. 59(9):1207–13.

- Nagase H, Woessner JF Jr. 1999. Matrix metalloproteinases. *J Biol Chem.* 274:21491–21494.
- Nagase H and Kashiwagi M. 2003. Aggrecanases and cartilage matrix degradation. *Arthritis Res Ther* 5:94–103.
- Nagase H, Visse R, Murphy G. 2006. Structure and function of matrix metalloproteinases and TIMPs. *Cardiovasc Res* 69: 562–573.
- Naito S, Shiomi T, Okada A, Kimura T, Chijiwa M, Fujita Y, Yatabe T, Komiya K, Enomoto H, Fujikawa K and Okada Y. 2007. Expression of ADAMTS4 (aggrecanase-1) in human osteoarthritic cartilage. *Pathology International.* 57: 703–711
- Nakagami H, Morishita R, et al. 2006. Adipose tissue-derived stromal cells as a novel option for regenerative cell therapy. *J Atheroscler Thromb.* 13(2):77.
- Narasipura SD, Wojciechowski JC, Charles N, Liesveld JL, King MR, 2008. P-Selectin coated microtube for enrichment of CD34+ hematopoietic stem and progenitor cells from human bone marrow. *Clin Chem.* 54 (1): 77–85.
- Nathan C and Xie Q. 1994. Regulation of biosynthesis of nitric oxide. *J Biol Chem.* 269:13725–8.
- Nelms K, Keegan AD, Zamorano J, Ryan JJ, Paul WE. 1999. The IL-4 receptor: Signaling mechanisms and biologic functions. *Annu. Rev. Immunol.* 17, 701–738 (1999)
- Nguyen J, Brunson D, Crespi CL, Penman BW, Wishnok JS, Tannenbaum SR. 1992. DNA damage and mutation in human cells exposed to nitric oxide. *Proc Natl Acad Sci USA.* 89: 3030–4
- Notoya K, Jovanovic DV, Reboul P, Martel-Pelletier J, Mineau F, Pelletier JP. 2000. The induction of cell death in human osteoarthritis chondrocytes by nitric oxide is related to the production of prostaglandin E2 via the induction of cyclooxygenase-2. *J Immunol.* 165(6):3402-10.
- Obermeyer T, Yonick D, Lauing K, Stock S, Nauer R, Strotman P, Shankar R, Gamelli R, Stover M, Callaci J (2012). Mesenchymal stem cells facilitate fracture repair in an alcohol-induced impaired healing model. *J. Orthop. Trauma.* 26: 712-718.
- Orita S, Ishikawa T, Miyagi M, Ochiai N, Inoue G, Eguchi Y, et al. 2011. Pain-related sensory innervation in monoiodoacetate-induced osteoarthritis in rat knees that gradually develops neuronal injury in addition to inflammatory pain. *BMC Musculoskelet Disord.* 12:134.

- Orita S, Ishikawa T, Miyagi M, Ochiai N, Inoue G, Eguchi Y, et al. 2012. Percutaneously absorbed NSAIDs attenuate local production of proinflammatory cytokines and suppress the expression of c-Fos in the spinal cord of a rodent model of knee osteoarthritis. *J Orthop Sci.* 17:77-86.
- Palmer G, Guerne P-A, Mezin F et al. 2002. Production of interleukin-1 receptor antagonist by human articular chondrocytes," *Arthritis Research*, 4(3): 226–231.
- Pelletier JP, Jovanovic D, Fernandes JC, Manning P, Connor JR, Currie MG, et al. 1998. Reduced progression of experimental osteoarthritis *in vivo* by selective inhibition of inducible nitric oxide synthase. *Arthritis Rheum.* 41(7):1275-86.
- Pelletier JP, Martel-Pelletier J, Abramson SB. 2001. Osteoarthritis, an inflammatory disease : Potential Implication for the Selection of New Therapeutic Targets. *Arthritis Rheum* 44: 1237-47
- Pernis AB and Rothman PB 2002. JAK-STAT signaling in asthma. *J. Clin. Invest.* 109, 1279–1283
- Pessler F, Dai L, Diaz-Torne C et al. 2008. The synovitis of “non-inflammatory” orthopaedic arthropathies: a quantitative histological and immunohistochemical analysis. *Ann. Rheum. Dis.* 67, 1184–1187.
- Plumas, J., Chaperot, L, Richard, M. J., Molens, J. P., Bensa, J. C. and Favrot, M. C. 2005. Mesenchymal stem cells induce apoptosis of activated T cells. *Leukemia* 19, 1597-1604.
- Ponte AL , Marais E, Gallay N, Langonne A, Delorme B, Herault O, Charbord P, Domenech J. 2007. The In Vitro Migration Capacity of Human Bone Marrow Mesenchymal Stem Cells Comparison of Chemokine and Growth Factor Chemotactic Activities. *Stem Cells.* 25:1737–1745
- Poole A.R. 2000. Cartilage in health and disease. In: *Arthritis and Allied Conditions: A Textbook of rheumatology.* 14th Edition. Edited by Koopman, W.J., Williams & Wilkins, Baltimore.
- Porter S, Clark IM, Kevorkian L, Edwards DR. 2005. The ADAMTS metallo-proteinases. *Biochem J* 386:15–27.
- Pratta MA, Scherle PA, Yang G, Liu RQ, Newton RC. 2003. Induction of aggrecanase-1 (ADAM-TS4) by interleukin-1 occurs through activation of constitutively produced protein. *Arthritis Rheum* 48: 119-33
- Presle N, Cipolletta C, Jouzeau JY, Abid A, Netter P, Terlain B. 1999. Cartilage protection by nitric oxide synthase inhibitors after intraarticular injection of interleukin-1beta in rats. *Arthritis Rheum.* 42(10):2094-102.

- Racz GZ, Kadar K, Foldes A, Kallo K, Perczel-Kovach K, Keremi B, Nagy A, Varga G. 2014. Immunomodulatory and potential therapeutic role of mesenchymal stem cells in periodontitis. *J Physiol Pharmacol.* 65(3):327–339
- Rai MF and Sandell LJ. 2011. Inflammatory mediators: tracing links between obesity and osteoarthritis. *Crit Rev Eukaryot Gene Expr.* 21:131–142.
- Rai MF, Graeve T, Twardziok S, Schmidt MF. 2011. Evidence for regulated interleukin-4 expression in chondrocyte-scaffolds under in vitro inflammatory conditions. *PLoS One* 6:e25749.
- Raspollini MR, Castiglione F, Degl’Innocenti DR, Garbini F, Coccia ME, Taddei GL. 2005. Difference in expression of matrix metalloproteinase-2 and matrix metalloproteinase-9 in patients with persistent ovarian cysts. *Fertil. Steril.* 84: 1049–1052.
- Rehman J, Traktuev D, Li J, Merfeld-Clauss S, Temm-Grove C J., Bovenkerk J E, Pell C L, Johnstone B H, Considine RV, March K L. 2004. Secretion of Angiogenic and Antiapoptotic Factors by Human Adipose Stromal Cells. *Circulation.* 109:1292–1298.
- Ren G, Zhang L, Zhao X, Xu G, Zhang Y, Roberts A I, Zhao R C, and Shi Y. 2008. Mesenchymal Stem Cell-Mediated Immunosuppression Occurs via Concerted Action of Chemokines and Nitric Oxide. *Cell Stem Cell* 2, 141–150.
- Rhee, K. J., Lee, J. I. and Eom, Y. W. 2015. Mesenchymal Stem Cell-Mediated Effects of Tumor Support or Suppression. *Int. J. Mol. Sci.* 16, 30015–30033.
- Richardson DW and Dodge GR. 2000. Effects of interleukin-1beta and tumor necrosis factor-alpha on expression of matrix-related genes by cultured equine articular chondrocytes. *Am J Vet Res.* 61(6):624–30.
- Rodriguez M, Cabal-Hierro L, Carcedo MT et al. 2011. NF-kB signal triggering and termination by tumor necrosis factor receptor 2. *Journal of Biological Chemistry.* 286(26):22814–22824.
- Roman-Blas JA and Jimenez SA. 2006. NF-kB as a potential therapeutic target in osteoarthritis and rheumatoid arthritis. *Osteoarthritis and Cartilage,* 14(9):839–848
- Sato K, Ozaki K, Oh I, Meguro A, Hatanaka K, Nagai T, Muroi K and Ozawa K. 2007 Nitric oxide plays a critical role in suppression of T-cell proliferation by mesenchymal stem cells. *Blood* 109, 228–234

Saulnier N, Viguier E, Perrier-Groult E, Chenu C, Pillet E, Roger T, Maddens S, Boulocher C. 2015. Intra-articular administration of xenogeneic neonatal Mesenchymal Stromal Cells early after meniscal injury down-regulates metalloproteinase gene expression in synovium and prevents cartilage degradation in a rabbit model of osteoarthritis. *Osteoarthritis Cartilage*. 23:122-133.

Schöler HR. 2007. The Potential of Stem Cells: An Inventory. In Nikolaus Knoepffler; Dagmar Schipanski; Stefan Lorenz Sorgner. *Human biotechnology as Social Challenge*. Ashgate Publishing. p. 28.

Seder RA, Paul WE, Davis MM, Fazekas de St Groth B. The presence of interleukin 4 during invitro priming determines the lymphokine-producing potential of CD4+ T cells from T cell receptortransgenic mice. 1992. *The Journal of experimental medicine*. 176:1091–1098.

Shakibaei M, Schulze-Tanzil G, John T, and Mobasheri A. 2005. Curcumin protects human chondrocytes from IL-1 β -induced inhibition of collagen type II and β 1-integrin expression and activation of caspase-3: an immunomorphological study. *Annals of Anatomy*.187(5-6):487–497.

Shu C C, Ravi V, Zaki S, Smith S M, Schiavinato A, Smith M M, Little C B. 2016. The Effects Of Intra-Articular Injection Of Mesenchymal Stem Cells Versus Hyaluronan Hexadecylamide-Derivative on Post-Traumatic OA: The Relationship Between Synovial Inflammation, Structural Pathology and Pain Sensitisation. *Osteoarthritis and Cartilage* 24:S63-S534

Singh JA, Kundukulam J, et al. 2011. Early postoperative mortality following joint arthroplasty: a systematic review. *J Rheumatol*. 38:1507–13.

Singer, N. G. and Caplan, A. I. (2011) Mesenchymal stem cells: mechanisms of inflammation. *Annu. Rev. Pathol.* 6, 457-478.

Skalnikova H, Motlik J, Gadher SJ, Kovarova H. 2011. Mapping of the secretome of primary isolates of mammalian cells, stem cells and derived cell lines. *Proteomics*. 11:691–708

Sohn DH, Sokolove J, Sharpe O et al. 2012. Plasma proteins present in osteoarthritic synovial fluid can stimulate cytokine production via Toll-like receptor 4. *Arthritis Research and Therapy*.14(1):articleR7.

Somia H, Abd-Allah, Sally M. Shalaby, Heba F. Pasha, Amal S. El-Shal, and Amany M. Abou El-Saoud. 2012. Variation of Matrix Metalloproteinase 1 and 3 Haplotypes and Their Serum Levels in Patients with Rheumatoid Arthritis and Osteoarthritis. *Genetic Testing And Molecular Biomarkers*.16(1):15–20

Song R-H, Tortorella MD, Malfait A-M et al. 2007. Aggrecan degradation in human articular cartilage explants is mediated by both ADAMTS4 and ADAMTS5. *Arthritis Rheum* 56: 575-85

- SooHoo N, Lieberman J, et al. 2006. Factors predicting complication rates following total knee replacement. *J Bone Joint Surg Am.* 88(3):480–5.
- Stöve J, Huch K, Günther K-P, and Scharf HP. 2000. Interleukin-1 β induces different gene expression of stromelysin, aggrecan and tumor-necrosis-factor-stimulated gene 6 in human osteoarthritic chondrocytes in vitro. *Pathobiology.* 68(3):144–149.
- Stracke JO, Fosang AJ, Last K, Mercuri FA, Pendas AM, Llano E, et al. 2000. Matrix metalloproteinases 19 and 20 cleave aggrecan and cartilage oligomeric matrix protein (COMP). *FEBS Lett* 478: 52–6.
- Studer RK, Levicoff E, Georgescu H, Miller L, Jaffurs D, Evans CH. 2000. Nitric oxide inhibits chondrocyte response to IGF-I: inhibition of IGF-IRbeta tyrosine phosphorylation. *Am J Physiol Cell Physiol.* 279(4):C961–9.
- Subramaniyan R, Amalorpavanathan J, Shankar R, et al. September 2011. Application of autologous bone marrow mononuclear cells in six patients with advanced chronic critical limb ischemia as a result of diabetes: our experience. *Cyotherapy.* 13 (8): 993–9.
- Sze SK, de Kleijn DP, Lai RC, et al. 2007. Elucidating the secretion proteome of human embryonic stem cell-derived mesenchymal stem cells. *Mol Cell Proteomics* 6:1680–1689
- Takahashi K and Yamanaka S. 2006. Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors. *Cell* 126, 663–676.
- Tamura M, Kawabata A, Ohta N, Uppalapati L, Becker KG, Troyer D. 2011. Wharton's Jelly Stem Cells as Agents for Cancer Therapy. *The Open Tissue Engineering and Regenerative Medicine Journal.* 4:39–47.
- Tan RJ and Liu Y. 2012. Matrix metalloproteinases in kidney homeostasis and diseases. *Am J Physiol Renal Physiol* 302: F1351–F1361
- Tan C-Q, Gao X, Guo L, and Huang H. 2014. Exogenous IL-4-Expressing Bone Marrow Mesenchymal Stem Cells for the Treatment of Autoimmune Sensorineural Hearing Loss in a Guinea Pig Model. *BioMed Research Int.* 2014:2–10
- Tang BL. 2001. ADAMTS: a novel family of extracellular matrix proteases. *Int J Biochem Cell Biol.* 33:33–44.
- Tetlow LC, Adlam DJ, Woolley DE. 2001. Matrix metalloproteinase and proinflammatory cytokine production by chondrocytes of human osteoarthritic cartilage: associations with degenerative changes. *Arthritis Rheum* 44:585–94.

Terai S, Ishikawa T, Omori K, Aoyama K, Marumoto Y, Urata Y, Yokoyama Y, Uchida K, Yamasaki T, Fujii Y, Okita K, Sakaida I. 2006. Improved liver function in patients with liver cirrhosis after autologous bone marrow cell infusion therapy. *Stem Cells*. 24 (10): 2292–8.

Tortorella MD, Pratta M, Liu RQ, Abbaszade I, Ross H, Burn T, Arner EC. 2000. The thrombospondin motif of aggrecanase -1 (ADAMTS-4) is critical for aggrecan substrate recognition and cleavage. *J Biol Chem*. (in press)

Tortorella MD, Malfait AM, Deccico C, Arner E. 2001. The role of ADAM-TS4 (aggrecanase-1) and ADAM-TS5 (aggrecanase-2) in a model of cartilage degradation. *Osteoarthritis Cartilage* 9: 539-52.

Tortorella MD, Liu RQ, Burn T, et al. 2002. Characterization of human aggrecanase 2 (ADAM-TS5): substrate specificity studies and comparison with aggrecanase 1 (ADAM-TS4). *Matrix Biol*. 21:499–511.

Troyer, D. L. & Weiss, M. L. 2008. Wharton's jelly-derived cells are a primitive stromal cell population. *Stem Cells* 26, 591-599, doi:10.1634/stemcells.2007-0439

Uccelli A, Moretta L, Pistoia V. 2008. Mesenchymal stem cells in health and disease. *Nature* 8 : 726-736.

Uchida K, Ueno M, Naruse K, Urabe K, Onuma K, Sakai R, Itoman M, Takaso M. 2012. Bone marrow engrafted cells after mice umbilical cord blood transplantation differentiate into osteoblastic cells in response to fracture and placement of titanium screws. *Exp. Anim.* 61: 427-33

Ulloa-Montoya F, Verfaillie CM, Hu WS. 2005. Culture systems for pluripotent stem cells. *J Biosci Bioeng*. 100 (1): 12–27.

van Buul GM, Villafuertes E, Bos PK, Waarsing JH, Kops N, Narcisi R, et al. 2012. Mesenchymal stem cells secrete factors that inhibit inflammatory processes in short-term osteoarthritic synovium and cartilage explant culture. *Osteoarthritis Cartilage* 20:1186 –1196.

van Buul GM, Siebelt M, Leijs MJC, Bos PK, Waarsing JH, Kops N, et al. 2014. Mesenchymal Stem Cells Reduce Pain But Not Degenerative Changes in a Mono-Iodoacetate Rat Model of Osteoarthritis. *J Orthop Res* 32:1167–1174.

van der Kraan PM, Vitters EL, van Beuningen HM, van de Loo FA, van den Berg WB. 2000. Role of nitric oxide in the inhibition of BMP-2-mediated stimulation of proteoglycan synthesis in articular cartilage. *Osteoarthritis Cartilage*. 8(2):82-6.

Van Lent PLEM, Blom AB, Van Der Kraan P et al. 2004. Cricial role of synovial lining macrophages in the promotion of transforming growth factor beta-mediated osteophyte formation. *Arthritis Rheum* 50: 103-11.

- van Meegeren ME, Roosendaal G, Jansen NW, et al. 2012. IL-4 alone and in combination with IL-10 protects against blood-induced cartilage damage. *Osteoarthr Cartil* 20:764–72.
- Varfolomeev E, Goncharov T, Fedorova AV et al. 2008. c-IAP1 and c-IAP2 are critical mediators of tumor necrosis factor α (TNF α)-induced NF- κ B activation. *Journal of Biological Chemistry*. 283(36): 24295–24299.
- Venkatesan AM, Davis JM, Grosu GT, Baker J, Zask A, Levin JI, Ellingboe J, Skotnicki JS, DiJoseph JF, Sung A, Jin G, Xu W, McCarthy DJ, Barone DJ. 2004. Synthesis and Structure-Activity Relationships of 4-alkynyoxy Phenyl Sulfanyl, Sulfinyl, and Sulfonyl Alkyl Hydroxamates as Tumor Necrosis Factor- α Converting Enzyme and Matrix Metalloproteinase Inhibitors. *Med. Chem.* 47, 6255-6269.
- Venugopal, P., Balasubramanian, S., Majumdar, A. S. & Ta, M. 2011. Isolation, characterization, and gene expression analysis of Wharton's jelly-derived mesenchymal stem cells under xeno-free culture conditions. *Stem Cells and Cloning-Advances and Applications* 4, 39-50
- Verma P and Dalal K. 2011. ADAMTS-4 and ADAMTS-5: Key Enzymes in Osteoarthritis. *Journal of Cellular Biochemistry* 112:3507–3514
- Voronkina I V, Smagina L V, Krylova T A, Musorina A S, and Poljanskaya G G. 2017. Analysis of Matrix Metalloproteinase Activity during Differentiation of Mesenchymal Stem Cells Isolated from Different Tissues of One Donor. *Cell and Tissue Biology*. 11(2): 95–103
- Vuolteenaho K, Moilanen T, Hamalainen M, Moilanen E. 2002. Effects of TNF α -antagonists on nitric oxide production in human cartilage. *Osteoarthritis Cartilage*. 10(4):327-32.
- Vuolteenaho K, Moilanen T, Knowles RG, Moilanen E. 2007. The role of nitric oxide in osteoarthritis. *Scand J Rheumatol*. 36(4):247-58.
- Vuolteenaho K, Koskinen A, Kukkonen M, Nieminen R, Paivarinta U, Moilanen T, et al. 2009. Leptin enhances synthesis of proinflammatory mediators in human osteoarthritic cartilage-mediator role of NO in leptin-induced PGE2, IL-6, and IL-8 production. *Mediators Inflamm*. 345838
- Wang W., Shen J., Jin H., Im H J., Sandy J., and Chen D., 2011, Recent progress in understanding molecular mechanisms of cartilage degeneration during osteoarthritis, National Institute of Health Public Access, 1240, 61-69
- Wang M, Yuan Q, and Xie L. 2018. Mesenchymal Stem Cell-Based Immunomodulation: Properties and Clinical Application. *Stem Cells International*. Vol. 2018, Article ID 3057624, 12 pages.

- Webb GR, Westacott CI, and Elson CJ. 1998. Osteoarthritic synovial fluid and synovium supernatants up-regulate tumor necrosis factor receptors on human articular chondrocytes. *Osteoarthritis and Cartilage* 6(3):167–176.
- Weinberg JB, Fermor B, Guilak F. 2007. Nitric oxide synthase and cyclooxygenase interactions in cartilage and meniscus: relationships to joint physiology, arthritis, and tissue repair. *Subcell Biochem*. 42:31-62.
- Westacott CI, Barakat AF, Wood L et al. 2000. Tumor necrosis factor alpha can contribute to focal loss of cartilage in osteoarthritis. *Osteoarthritis and Cartilage*.8(3):213–221.
- Widowati W, Afifah E, Mozef Tj, Sandra F, Rizal R, Amalia A, Arinta Y, Bachtiar I, Murti H. Effects of insulin-like growth factor-induced Wharton jelly mesenchymal stem cells toward chondrogenesis in an osteoarthritis model. 2018. *Iran J Basic Med Sci* 21:745-752.
- Wojdasiewicz P, Poniatowski ŁA, Szukiewicz D. 2014. The role of inflammatory and anti-inflammatory cytokines in the pathogenesis of osteoarthritis. *Mediat Inflamm*. 2014:561459.
- Wylde V, Hewlett S, et al. 2011. Persistent pain after joint replacement: prevalence, sensory qualities, and postoperative determinants. *Pain*. 152:566–72.
- Xu C, Ren G, Cao G, Chen Q, Shou P, Zheng C, Du L, Han X, Jiang M, Yang Q, Lin L, Wang G, Yu P, Zhang X, Cao W, Brewer G, Wang Y and Shi Y. 2013. MiR-155 Regulates Immune Modulatory Properties of Mesenchymal Stem Cells by Targeting TAK1-binding Protein 2. *J. Biol. Chem.* published online February 28, 2013
- Xu Y, Luo H, Chen F, Shi Y, Sun M. 2018. Human umbilical cord mesenchymal stem cells polarize RAW264.7 macrophages to an anti-inflammatory subpopulation. *Int J Clin Exp Pathol* 11(3):1446-1452
- Yamanishi Y, Boyle D, Clark M, Maki RA, Tortorella MD, Arner EC, et al. 2002. Expression and regulation of aggrecanase in arthritis: the role of TGF- β . *J Immunol* 168:1405–12.
- Yamin GE, Trisnawati L, Yusnayanti WN. 1999. Pedoman Praktek laboratorium yang benar. Jakarta: Departemen Kesehatan RI.
- Yan Z, Xiong J, Zhao C, Qin C, He. 2015. Decreasing cartilage damage in a rat model of osteoarthritis by intra-articular injection of deoxycholic acid. *Int J Clin Exp Med* 2015;8(6):9038-9045
- Yan M, Liu X, Dang O, Huang H, Yang F, and Li Y. 2017. Intra-Articular Injection of Human Synovial Membrane-Derived Mesenchymal Stem Cells in Murine Collagen-Induced Arthritis Assessment of Immunomodulatory Capacity In Vivo. *Stem Cells International*. Volume 2017, Article ID 9198328, 12 pages

Yorimitsu M, Nishida K, Shimizu A et.al., 2008. Intra-articular injection of interleukin-4 decreases nitric oxide production by chondrocytes and ameliorates subsequent destruction of cartilage in instability-induced osteoarthritis in rat knee joints. *Osteoarthritis Research Society Int.* 16(7):764-771.

Yun S, Ku S-K and Kwon Y-S. 2016. Adipose-derived mesenchymal stem cells and platelet-rich plasma synergistically ameliorate the surgical-induced osteoarthritis in Beagle dogs. *Journal of Orthopaedic Surgery and Research.* 11(9):1-12

Zamora R, Vodovotz Y, and Billiar TR. 2000. Inducible Nitric Oxide Synthase and Inflammatory Diseases. *Molecular Medicine* 6(5): 347–373

Zamorano J, Rivas MD, Pérez-G M. 2003. Interleukin-4: A multifunctional cytokine. *Immunologia.* 22(2):215-224

Zhang Y and Jordan JM. 2010. Epidemiology of osteoarthritis. *Clin Geriatr Med* 26:355-69.

Zhao S, Zhao Y, Guo J, Fei C, Zheng Q, Li X & Chang C. 2016. Downregulation of MMP1 in MDS-derived mesenchymal stromal cells reduces the capacity to restrict MDS cell proliferation. *Scientific Reports.* 7:43849

Zhou Z, Connell MC, and MacEwan DJ. 2007. TNFR1-induced NF- κ B, but not ERK, p38MAPK or JNK activation, mediates TNF-induced ICAM-1 and VCAM-1 expression on endothelial cells. *Cellular Signalling.* 19(6):1238–1248.