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UNIVERSIDADE ESTADUAL PAULISTA ‘’JULIO DE MESQUITA FILHO’’
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Avaliação da expressão gênica de citocinas e fatores neurotróficos em células tronco mesenquimais caninas pré-condicionadas com extrato de canabis rico em canabidiol.

VINICIUS SKAU PERINO

Botucatu - SP
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VINICIUS SKAU PERINO

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LISTA DE SIGLAS E ABREVIATURAS

μM - Micro Molar

2-AcGs - 2-Acilgliceróis

2-AG - 2-Araquidonoilglicerol

2-AGE - éter 2-araquidonilglicerílico

AA - Ácido araquidônico

AEA - N-Araquidonoiletanolamina

Akt - quinase de proteína B

ANG-1 - Angiopoietina 1

AT- Tecido adiposo

AT-MSCs - Células tronco mesenquimais derivadas do tecido adiposo

AVC - acidente vascular cerebral

BDNF - Fator neurotrófico derivado do cérebro

BM-MSCs - células-tronco mesenquimais derivadas da medula óssea

cAMP - monofosfato de adenosina cíclico

Ca-NAT - N-aciltransferase dependente de cálcio

cAT-MSCs – Células Tronco Mesenquimais derivadas do tecido adiposo canino

CB1R - Receptor canabinóide tipo 1

CB2R - Receptor canabinóide tipo 2

CBD - Canabidiol

CBG - Canabigerol

CBGA - ácido canabigerólico

CBGV - cannabigerovarina

CCL2 - ligante de quimiocina 2

cDNA - DNA complementar

Células NK - Células exterminadoras naturais

CM - Grupo controle

COXs - Cicloxigenases

D1 - Grupo dose 1

D2 - Grupo dose 2

DAGL - Enzima diacilglicerol lipase

DAMPs - Padrões moleculares associados ao dano

DDIV - doença do disco intervertebral

DMEM F12 - Dulbecco's Modified Eagle Medium

DP - Polpa dentária

EA - Etanolamina

eCBs - Endocanabinóides

EMT - Transportador de membrana (genérico)

FAAH - Amida hidrolase de ácido graxo

FABPs - Proteínas de Ligação a Ácidos Graxos

GAPDH - Gliceraldeído-3- fosfato desidrogenase

GDNF - Fator neurotrófico derivado da linhagem das células da glia

GPCRs - Receptores acoplados a proteína G

HGF - Fator de crescimento de hepatócitos

hGMSCs - células-tronco mesenquimais da gengiva humana

HLA - moléculas de histocompatibilidade leucocitária

HLA-DR - Antígeno leucocitário humano-DR

HLA-G5 - antígeno Leucocitário Humano G5

IDO - Indoleamina-pirrol 2,3-dioxigenase

IL-10 - Interleucina 10

iNAT - N-Aciltransferase independente de cálcio

INF-γ - Interferon Gama

ISCT - International Society for Cellular Therapy

LIF - fator inibitório da leucemia

LPS - Lipopolissacarídeos

MAGL - Lipase Monoacilglicerol

MAPK - Proteino-quinases ativadas por mitógenos

MO - Medula óssea

MSCs - Células tronco mesenquimais

MTT - brometo de 3-[4,5-dimetil-tiazol-2-il] -2,5-difeniltetrazólio

MUO - meningoencefalomielite de origem desconhecida

NADA - N- N-araquidonoil dopamina

NAEs - N-Aciletanolaminas

NAPE - N-Acilfosfatidiletanolaminas

NAPE-PLD - N-Acilfosfatidiletanolamina fosfolipase D

NK – Células natural killer

nM - Nano Molar

NO - Óxido nítrico

NPCs - células progenitoras neurais

OAE - O-araquidonoil etanolamina

OCT-4 - Fator de transcrição de homeodomínio da família POU

PAMPs - Padrões moleculares associados a patógenos

PB - Sangue periférico

PCR - Reação em cadeia da polimerase

PDL-1 - ligantes de morte celular programada 1

PG - Prostaglandina

PGE2 - Prostaglandina E2

PI3K - fosfoinositídeo 3-quinase

PKA - proteína quinase A

PL - Placenta

PLC - Fosfolipase C

PPARs - Receptores ativados por proliferadores de peroxissoma

PRP - Plasma rico em plaquetas

PRRs - Receptores de reconhecimento de padrões

PtdCho - Fosfatidilcolina

PtdEt - Fosfatidiletanolamina

PTGES - Prostaglandina E sintaxe

PTGES 2 - Prostaglandina E sintaxe 2

PUFAs - Ácidos graxos poliinsaturados

qPCR - Reação em cadeia da polimerase em tempo real

RNA - Ácido Ribonucleico

RPS19 - proteína ribossomal S19

RPS5 - proteína ribossomal S5

SEC - Sistema Endocanabinóide

SF - Líquido sinovial

SFB - Soro fetal bovino

SNC - Sistema nervoso central

TGF - Fator de crescimento de fibroblasto

TGF-β1 - Fator de transformação do crescimento β1

Th17 - Células T auxiliares 17

THC - Δ9-tetrahidrocannabinol

THCV - tetra-hidrocanabivarina

TNF-α - Fator necrose tumoral alfa

TRPV1 - Receptores de potencial transitório do tipo vanilóide 1

TSG 6 - Proteína do gene 6 estimulada por TNF

UC - Cordão umbilical

VEGF - Fator de crescimento endotelial vascular

VGCC - canal de cálcio dependente de voltagem

SUMÁRIO

Perino, V. S. **Avaliação da expressão gênica de citocinas e fatores neurotróficos em células tronco mesenquimais caninas pré-condicionadas com extrato de canabis rico em canabidiol**. Botucatu, 2023. Dissertação (Mestrado) – Faculdade de Medicina Veterinária e Zootecnia, Campus de Botucatu, Universidade Estadual Paulista.

RESUMO

As células-tronco mesenquimais (MSCs) são caracterizadas como um tipo de célula-tronco multipotente conhecidas por possuir a capacidade de diferenciação em diversas linhagens celulares, modulação da secreção de moléculas bioativas (fatores neurotróficos, citocinas, entre outros), atua na reparação e regeneração tecidual, características que permitem sua aplicação em doenças degenerativas, imunomediadas e expressa seu enorme potencial dentro da medicina regenerativa. O uso terapêutico da canabis tem experimentado um crescimento significativo ao longo dos anos, em grande parte devido aos efeitos benéficos dos fitocanabinóides, como o canabidiol (CBD) e o Δ9-tetrahidrocannabinol (THC), dentre outros componentes da planta como os terpenos e flavonóides. Estudos têm demonstrado que o sistema endocanabinoide é responsável por funções biológicas cruciais, como neuroproteção, imunomodulação, modulação da dor e inflamação. O pré-condicionamento das células-tronco mesenquimais derivadas de tecido adiposo canino (cAT-MSCs) utilizando extrato de canabis rico em CBD é uma área emergente de pesquisa que explora os potenciais efeitos dos fitocanabinóides de aprimorar suas propriedades terapêuticas (imunomodulação/ efeitos anti-inflamatórios/ viabilidade e sobrevivência celular/ diferenciação e potencial Regenerativo). O CBD e o THC são os componentes mais estudados e desempenham um importante papel na proliferação, migração, diferenciação e modulação de citocinas e fatores neurotróficos das MSCs *in vitro*. O objetivo deste estudo *in vitro* foi avaliar a morfologia e viabilidade celular, assim como a expressão gênica de fatores neurotróficos (BDNF, GDNF e HGF) e citocinas (IL-10, IDO, TNF-α, INF-ɣ e PTGE2) após a estimulação das cAT-MSCs com extrato de canabis rico em CBD. Cinco amostras diferentes de cAT-MSCs, previamente isoladas, caracterizadas imunofenotipicamente (CD44+, CD90+, CD105+, CD34-, CD45-, MHC-II) e diferenciadas (osteogênica, adipogênica e condrogênica), foram pré-condicionadas com concentrações altas (2,25 μM) e baixas (225 nM) do extrato de cannabis rico em CBD por 24 horas. As cAT-MSCs estimuladas com baixa e alta concentração de CBD não apresentaram alterações na morfologia ou na atividade metabólica. O presente trabalho sugere que o perfil de expressão dos fatores neurotróficos (HGF e BDNF) das cAT-MSCs pode ser modulado pelos fitocanabinóides presentes no extrato de canabis rico em CBD, no entanto, o pré-condicionamento das cAT-MSCs com extrato de canabis rico em CBD é uma área de pesquisa relativamente nova, sendo necessário a realização de novos estudos para uma melhor análise do comportamento das cAT-MSCs frente a diferentes extratos, doses e tempo de estimulação *in vitro*.

Palavras-Chave: Fitocanabinóides; Sistema endocanabinóide; Imunomodulação; Priming; Célula Tronco Mesenquimal.

Perino, V. S. **Priming canine adipose-derived mesenchymal stem cells with CBD-rich cannabis extract modulates neurotrophic factors expression profile**. Botucatu, 2023. Dissertation (Master's) - Faculty of Veterinary Medicine and Animal Science, Botucatu Campus, São Paulo State University.

ABSTRACT

Mesenchymal stem cells (MSCs) are characterized as a type of multipotent stem cell known for their ability to differentiate into various cell lineages and modulate the secretion of bioactive molecules (neurotrophic factors, cytokines, among others). They also play a role in tissue repair and regeneration, making them applicable to degenerative and immune-mediated diseases, and showcasing their enormous potential in regenerative medicine. The therapeutic use of cannabis has experienced significant growth over the years, largely due to the beneficial effects of phytocannabinoids such as cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC), as well as other components of the plant like terpenes and flavonoids. Studies have demonstrated that the endocannabinoid system is responsible for crucial biological functions such as neuroprotection, immunomodulation, pain modulation, and inflammation. Preconditioning canine adipose tissue-derived mesenchymal stem cells (cAT-MSCs) using CBD-rich cannabis extract is an emerging area of research that explores the potential effects of phytocannabinoids in enhancing their therapeutic properties (immunomodulation, anti-inflammatory effects, viability and cell survival, differentiation, and regenerative potential). CBD and THC are the most studied components and play an important role in the proliferation, migration, differentiation, and modulation of cytokines and neurotrophic factors of MSCs in vitro. The objective of this in vitro study was to evaluate the cellular morphology and viability, as well as the gene expression of neurotrophic factors (BDNF, GDNF, and HGF) and cytokines (IL-10, IDO, TNF-α, INF-ɣ, and PTGE2) after stimulating cAT-MSCs with CBD-rich cannabis extract. Five different samples of cAT-MSCs, previously isolated, immunophenotypically characterized (CD44+, CD90+, CD105+, CD34-, CD45-, MHC-II), and differentiated (osteogenic, adipogenic, and chondrogenic), were preconditioned with high (2.25 μM) and low (225 nM) concentrations of CBD-rich cannabis extract for 24 hours. The cAT-MSCs stimulated with low and high concentrations of CBD showed no changes in morphology or metabolic activity. This study suggests that the expression profile of neurotrophic factors (HGF and BDNF) in cAT-MSCs can be modulated by the phytocannabinoids present in CBD-rich cannabis extract. However, preconditioning cAT-MSCs with CBD-rich cannabis extract is a relatively new area of research, and further studies are needed to better analyze the behavior of cAT-MSCs in response to different extracts, doses, and duration of in vitro stimulation.

Keywords: Phytocannabinoids; Endocannabinoid system; Immunomodulation; Priming; Mesenchymal Stem Cell.

5. BIBLIOGRAFIA

A. DOUGLAS KINGHORN et al. **Phytocannabinoids**. 1. ed. Cham: Springer International Publishing, 2017. v. 103

ABAME, M. A. et al. Chronic administration of synthetic cannabidiol induces antidepressant effects involving modulation of serotonin and noradrenaline levels in the hippocampus. **Neuroscience Letters**, v. 744, p. 135594, jan. 2021.

ABRAMS, D.; GUZMAN, M. Cannabis in cancer care. **Clinical Pharmacology & Therapeutics**, v. 97, n. 6, p. 575–586, jun. 2015.

ABUMAREE, M. H. et al. Human Placental Mesenchymal Stem Cells (pMSCs) Play a Role as Immune Suppressive Cells by Shifting Macrophage Differentiation from Inflammatory M1 to Anti-inflammatory M2 Macrophages. **Stem Cell Reviews and Reports**, v. 9, n. 5, p. 620–641, 28 out. 2013.

ADERMARK, L.; LOVINGER, D. M. Retrograde endocannabinoid signaling at striatal synapses requires a regulated postsynaptic release step. **Proceedings of the National Academy of Sciences**, v. 104, n. 51, p. 20564–20569, 18 dez. 2007.

AHANI-NAHAYATI, M. et al. Promoter Methylation Status of Survival-Related Genes in MOLT- 4 Cells Co-Cultured with Bone Marrow Mesenchymal Stem Cells under Hypoxic Conditions. **Cell journal**, v. 20, n. 2, p. 188–194, jul. 2018.

AHN, K.; MCKINNEY, M. K.; CRAVATT, B. F. Enzymatic Pathways That Regulate Endocannabinoid Signaling in the Nervous System. **Chemical Reviews**, v. 108, n. 5, p. 1687–1707, 1 maio 2008.

AHN, S. et al. A Cannabinoid Receptor Agonist N-Arachidonoyl Dopamine Inhibits Adipocyte Differentiation in Human Mesenchymal Stem Cells. **Biomolecules & Therapeutics**, v. 23, n. 3, p. 218–224, 31 maio 2015.

AIRAKSINEN, M. S.; SAARMA, M. The GDNF family: Signalling, biological functions and therapeutic value. **Nature Reviews Neuroscience**, v. 3, n. 5, p. 383–394, maio 2002.

ALDRICH, E. D. et al. Allogeneic Mesenchymal Stromal Cells for Cartilage Regeneration: A Review of in Vitro Evaluation, Clinical Experience, and Translational Opportunities. **Stem Cells Translational Medicine**, v. 10, n. 11, p. 1500–1515, 1 nov. 2021.

ALGER, B. E. Getting high on the endocannabinoid system. **Cerebrum : the Dana forum on brain science**, v. 2013, p. 14, nov. 2013.

ALIZADEH, E. et al. The effect of dimethyl sulfoxide on hepatic differentiation of mesenchymal stem cells. **Artificial Cells, Nanomedicine, and Biotechnology**, v. 44, n. 1, p. 157–164, 2 jan. 2016.

ALMEIDA, D. L.; DEVI, L. A. Diversity of molecular targets and signaling pathways for CBD. **Pharmacology Research & Perspectives**, v. 8, n. 6, 9 dez. 2020.

ALMOGI-HAZAN, O.; OR, R. Cannabis, the Endocannabinoid System and Immunity—the Journey from the Bedside to the Bench and Back. **International Journal of Molecular Sciences**, v. 21, n. 12, p. 4448, 23 jun. 2020.

ANAND, U. et al. Dose-Related Inhibition of Capsaicin Responses by Cannabinoids CBG, CBD, THC and their Combination in Cultured Sensory Neurons. **Journal of Pain Research**, v. Volume 14, p. 3603–3614, nov. 2021.

ANCANS, J. Cell therapy medicinal product regulatory framework in Europe and its application for MSC-based therapy development. **Frontiers in Immunology**, v. 3, 2012.

ANDIA, I.; MAFFULLI, N. Mesenchymal stromal cell products for intra-articular knee injections for conservative management of osteoarthritis. **Therapeutic Advances in Musculoskeletal Disease**, v. 13, p. 1759720X2199695, 18 jan. 2021.

ANDIA, I.; MARTIN, J. I.; MAFFULLI, N. Platelet-rich Plasma and Mesenchymal Stem Cells: Exciting, But … are we there Yet? **Sports Medicine and Arthroscopy Review**, v. 26, n. 2, p. 59–63, jun. 2018.

ANDRE, C. M.; HAUSMAN, J.-F.; GUERRIERO, G. Cannabis sativa: The Plant of the Thousand and One Molecules. **Frontiers in Plant Science**, v. 7, 4 fev. 2016.

ANKRUM, J. A.; ONG, J. F.; KARP, J. M. Mesenchymal stem cells: immune evasive, not immune privileged. **Nature Biotechnology**, v. 32, n. 3, p. 252–260, 23 mar. 2014.

ANSARI, S. et al. Human Periodontal Ligament- and Gingiva-derived Mesenchymal Stem Cells Promote Nerve Regeneration When Encapsulated in Alginate/Hyaluronic Acid 3D Scaffold. **Advanced Healthcare Materials**, v. 6, n. 24, p. 1700670, dez. 2017.

ANTONELLI, M. et al. New insights in hemp chemical composition: a comprehensive polar lipidome characterization by combining solid phase enrichment, high-resolution mass spectrometry, and cheminformatics. **Analytical and Bioanalytical Chemistry**, v. 412, n. 2, p. 413–423, 23 jan. 2020.

ARREAZA, G. et al. The cloned rat hydrolytic enzyme responsible for the breakdown of anandamide also catalyzes its formation via the condensation of arachidonic acid and ethanolamine. **Neuroscience Letters**, v. 234, n. 1, p. 59–62, set. 1997.

ASAKAWA, Y. et al. Isolation, Synthesis and Biological Activity of Grifolic Acid Derivatives from the Inedible Mushroom Albatrellus dispansus. **HETEROCYCLES**, v. 65, n. 10, p. 2431, 2005.

ASHTON, J.; GLASS, M. The Cannabinoid CB2 Receptor as a Target for Inflammation-Dependent Neurodegeneration. **Current Neuropharmacology**, v. 5, n. 2, p. 73–80, 1 jun. 2007.

AWAN, M. et al. Dimethyl sulfoxide: a central player since the dawn of cryobiology, is efficacy balanced by toxicity? **Regenerative Medicine**, v. 15, n. 3, p. 1463–1491, mar. 2020.

AZIZ, A. et al. Cannabinoids as Immune System Modulators: Cannabidiol Potential Therapeutic Approaches and Limitations. **Cannabis and Cannabinoid Research**, 22 nov. 2022.

BACALIA, K. M. A. et al. Cannabidiol Decreases Intestinal Inflammation in the Ovariectomized Murine Model of Postmenopause. **Biomedicines**, v. 11, n. 1, p. 74, 28 dez. 2022.

BALDARI, S. et al. Challenges and Strategies for Improving the Regenerative Effects of Mesenchymal Stromal Cell-Based Therapies. **International Journal of Molecular Sciences**, v. 18, n. 10, p. 2087, 2 out. 2017.

BARANOWSKA-KUCZKO, M. et al. Vasoprotective Endothelial Effects of Chronic Cannabidiol Treatment and Its Influence on the Endocannabinoid System in Rats with Primary and Secondary Hypertension. **Pharmaceuticals**, v. 14, n. 11, p. 1120, 31 out. 2021.

BARRACHINA, L. et al. Priming Equine Bone Marrow-Derived Mesenchymal Stem Cells with Proinflammatory Cytokines: Implications in Immunomodulation–Immunogenicity Balance, Cell Viability, and Differentiation Potential. **Stem Cells and Development**, v. 26, n. 1, p. 15–24, jan. 2017.

BARTOSH, T. J.; YLOSTALO, J. H. Efficacy of 3D Culture Priming is Maintained in Human Mesenchymal Stem Cells after Extensive Expansion of the Cells. **Cells**, v. 8, n. 9, p. 1031, 5 set. 2019.

BASWAN, S. M. et al. <p>Therapeutic Potential of Cannabidiol (CBD) for Skin Health and Disorders</p>. **Clinical, Cosmetic and Investigational Dermatology**, v. Volume 13, p. 927–942, dez. 2020.

BATTISTA, N. et al. The endocannabinoid system: an overview. **Frontiers in Behavioral Neuroscience**, v. 6, 2012.

BAUTISTA, J. L.; YU, S.; TIAN, L. Flavonoids in *Cannabis sativa* : Biosynthesis, Bioactivities, and Biotechnology. **ACS Omega**, v. 6, n. 8, p. 5119–5123, 2 mar. 2021.

BEHL, T. et al. Understanding the possible role of endocannabinoid system in obesity. **Prostaglandins & Other Lipid Mediators**, v. 152, p. 106520, fev. 2021.

BELLOCCHIO, L. et al. The Endocannabinoid System and Energy Metabolism. **Journal of Neuroendocrinology**, v. 20, n. 6, p. 850–857, jun. 2008.

BELTRAMO, M. et al. CB2 receptor-mediated antihyperalgesia: possible direct involvement of neural mechanisms. **European Journal of Neuroscience**, v. 23, n. 6, p. 1530–1538, mar. 2006.

BENAVIDES, F. P. et al. Intrathecal Transplantation of Autologous and Allogeneic Bone Marrow-Derived Mesenchymal Stem Cells in Dogs. **Cell Transplantation**, v. 30, p. 096368972110344, 1 jan. 2021.

BERARDIS, S. et al. Use of mesenchymal stem cells to treat liver fibrosis: Current situation and future prospects. **World Journal of Gastroenterology**, v. 21, n. 3, p. 742, 2015.

BERCIK, P. et al. Chronic Gastrointestinal Inflammation Induces Anxiety-Like Behavior and Alters Central Nervous System Biochemistry in Mice. **Gastroenterology**, v. 139, n. 6, p. 2102- 2112.e1, dez. 2010.

BÉTOUS, R. et al. Human Adipose-Derived Stem Cells Expanded Under Ambient Oxygen Concentration Accumulate Oxidative DNA Lesions and Experience Procarcinogenic DNA Replication Stress. **Stem Cells Translational Medicine**, v. 6, n. 1, p. 68–76, 1 jan. 2017.

BEVAN, S.; QUALLO, T.; ANDERSSON, D. A. TRPV1. Em: [s.l: s.n.]. p. 207–245.

BIEBACK, K. et al. Human Alternatives to Fetal Bovine Serum for the Expansion of Mesenchymal Stromal Cells from Bone Marrow. **Stem Cells**, v. 27, n. 9, p. 2331–2341, 1 set. 2009.

BIELAWIEC, P. et al. Attenuation of Oxidative Stress and Inflammatory Response by Chronic Cannabidiol Administration Is Associated with Improved n-6/n-3 PUFA Ratio in the White and

Red Skeletal Muscle in a Rat Model of High-Fat Diet-Induced Obesity. **Nutrients**, v. 13, n. 5, p. 1603, 11 maio 2021.

BISOGNO, T. et al. Molecular targets for cannabidiol and its synthetic analogues: effect on vanilloid VR1 receptors and on the cellular uptake and enzymatic hydrolysis of anandamide. **British Journal of Pharmacology**, v. 134, n. 4, p. 845–852, out. 2001.

BISOGNO, T. et al. Cloning of the first sn1-DAG lipases points to the spatial and temporal regulation of endocannabinoid signaling in the brain. **Journal of Cell Biology**, v. 163, n. 3, p. 463–468, 10 nov. 2003.

BLANKMAN, J. L.; SIMON, G. M.; CRAVATT, B. F. A Comprehensive Profile of Brain Enzymes that Hydrolyze the Endocannabinoid 2-Arachidonoylglycerol. **Chemistry & Biology**, v. 14, n. 12, p. 1347–1356, dez. 2007.

BOGGS, D. L. et al. The dose-dependent psychomotor effects of intravenous delta-9-tetrahydrocannabinol (Δ^9 -THC) in humans. **Journal of Psychopharmacology**, v. 32, n. 12, p. 1308–1318, 26 dez. 2018.

BOIVIN, M. Cannabis Strains to Chemovars. Em: **Cannabinoids and Pain**. Cham: Springer International Publishing, 2021. p. 129–134.

BOLETI, A. P. DE A. et al. Biochemical aspects and therapeutic mechanisms of cannabidiol in epilepsy. **Neuroscience & Biobehavioral Reviews**, v. 132, p. 1214–1228, jan. 2022.

BONINI, S. A. et al. Cannabis sativa: A comprehensive ethnopharmacological review of a medicinal plant with a long history. **Journal of Ethnopharmacology**, v. 227, p. 300–315, dez. 2018.

BORNES, T. D.; ADESIDA, A. B.; JOMHA, N. M. Articular Cartilage Repair with Mesenchymal Stem Cells After Chondrogenic Priming: A Pilot Study. **Tissue Engineering Part A**, v. 24, n. 9–10, p. 761–774, maio 2018.

BOUGARNE, N. et al. Molecular Actions of PPARα in Lipid Metabolism and Inflammation. **Endocrine Reviews**, v. 39, n. 5, p. 760–802, 1 out. 2018.

BRADSHAW, H. B.; WALKER, J. M. The expanding field of cannabimimetic and related lipid mediators. **British Journal of Pharmacology**, v. 144, n. 4, p. 459–465, fev. 2005.

BRIDGEMAN, M. B.; ABAZIA, D. T. Medicinal Cannabis: History, Pharmacology, And Implications for the Acute Care Setting. **P & T : a peer-reviewed journal for formulary management**, v. 42, n. 3, p. 180–188, mar. 2017.

BRONDEEL, C. et al. Review: Mesenchymal Stem Cell Therapy in Canine Osteoarthritis Research: “Experientia Docet” (Experience Will Teach Us). **Frontiers in Veterinary Science**, v. 8, 19 maio 2021.

BURSTEIN, S. Cannabidiol (CBD) and its analogs: a review of their effects on inflammation. **Bioorganic & Medicinal Chemistry**, v. 23, n. 7, p. 1377–1385, abr. 2015.

BUTOWSKI, N. Novel and Prospective Molecular Targets for Therapy of Intracranial Gliomas. Em: [s.l: s.n.]. p. 66–78.

CADAS, H.; DI TOMASO, E.; PIOMELLI, D. Occurrence and Biosynthesis of Endogenous Cannabinoid Precursor, *N* -Arachidonoyl Phosphatidylethanolamine, in Rat Brain. **The Journal of Neuroscience**, v. 17, n. 4, p. 1226–1242, 15 fev. 1997.

CALPE-LÓPEZ, C.; GARCÍA-PARDO, M. P.; AGUILAR, M. A. Cannabidiol Treatment Might Promote Resilience to Cocaine and Methamphetamine Use Disorders: A Review of Possible Mechanisms. **Molecules**, v. 24, n. 14, p. 2583, 16 jul. 2019.

CAMPORA, L. et al. Cannabinoid receptor type 1 and 2 expression in the skin of healthy dogs and dogs with atopic dermatitis. **American Journal of Veterinary Research**, v. 73, n. 7, p. 988–995, jul. 2012.

CAO, W. et al. Mesenchymal stem cells and adaptive immune responses. **Immunology Letters**, v. 168, n. 2, p. 147–153, dez. 2015.

CAPLAN, A. I. Adult mesenchymal stem cells for tissue engineering versus regenerative medicine. **Journal of Cellular Physiology**, v. 213, n. 2, p. 341–347, nov. 2007.

CAPLAN, A. I. Mesenchymal Stem Cells: Time to Change the Name! **Stem Cells Translational Medicine**, v. 6, n. 6, p. 1445–1451, 1 jun. 2017.

CAPLAN, A. I.; DENNIS, J. E. Mesenchymal stem cells as trophic mediators. **Journal of Cellular Biochemistry**, v. 98, n. 5, p. 1076–1084, 1 ago. 2006.

CARNIEL, B. P.; DA ROCHA, N. S. Brain-derived neurotrophic factor (BDNF) and inflammatory markers: Perspectives for the management of depression. **Progress in Neuro-Psychopharmacology and Biological Psychiatry**, v. 108, p. 110151, jun. 2021.

CARRADE, D. D.; BORJESSON, D. L. Immunomodulation by mesenchymal stem cells in veterinary species. **Comparative medicine**, v. 63, n. 3, p. 207–17, jun. 2013.

CASEY, S.; VAUGHAN, C. Plant-Based Cannabinoids for the Treatment of Chronic Neuropathic Pain. **Medicines**, v. 5, n. 3, p. 67, 1 jul. 2018.

CASTONGUAY-PARADIS, S. et al. Dietary fatty acid intake and gut microbiota determine circulating endocannabinoidome signaling beyond the effect of body fat. **Scientific Reports**, v. 10, n. 1, p. 15975, 29 set. 2020.

CAVUOTO, P. et al. The expression of receptors for endocannabinoids in human and rodent skeletal muscle. **Biochemical and Biophysical Research Communications**, v. 364, n. 1, p. 105–110, dez. 2007.

CERRI, S. et al. Neuroprotective Potential of Adenosine A $_{2A}$ and Cannabinoid CB $_{1}$ Receptor Antagonists in an Animal Model of Parkinson Disease. **Journal of Neuropathology & Experimental Neurology**, v. 73, n. 5, p. 414–424, 1 maio 2014.

CERVENKA, I.; AGUDELO, L. Z.; RUAS, J. L. Kynurenines: Tryptophan’s metabolites in exercise, inflammation, and mental health. **Science**, v. 357, n. 6349, 28 jul. 2017.

CHANG, R. C. et al. Cannabidiol promotes adipogenesis of human and mouse mesenchymal stem cells via PPARγ by inducing lipogenesis but not lipolysis. **Biochemical Pharmacology**, v. 197, p. 114910, mar. 2022.

CHEN, L. et al. Correction: Conditioned Medium from Hypoxic Bone Marrow-Derived Mesenchymal Stem Cells Enhances Wound Healing in Mice. **PLOS ONE**, v. 10, n. 12, p. e0145565, 18 dez. 2015.

CHEN, X. et al. Structural determinants in the second intracellular loop of the human cannabinoid CB1 receptor mediate selective coupling to Gs and Gi. **British Journal of Pharmacology**, v. 161, n. 8, p. 1817–1834, dez. 2010.

CHENG, Z. et al. Targeted Migration of Mesenchymal Stem Cells Modified With CXCR4 Gene to Infarcted Myocardium Improves Cardiac Performance. **Molecular Therapy**, v. 16, n. 3, p. 571–579, mar. 2008.

CHEVALEYRE, V.; TAKAHASHI, K. A.; CASTILLO, P. E. ENDOCANNABINOID-MEDIATED SYNAPTIC PLASTICITY IN THE CNS. **Annual Review of Neuroscience**, v. 29, n. 1, p. 37–76, 21 jul. 2006.

CHICCA, A. et al. Uncovering the psychoactivity of a cannabinoid from liverworts associated with a legal high. **Science Advances**, v. 4, n. 10, 5 out. 2018.

CHILDS, E.; LUTZ, J. A.; DE WIT, H. Dose-related effects of delta-9-THC on emotional responses to acute psychosocial stress. **Drug and Alcohol Dependence**, v. 177, p. 136–144, ago. 2017.

CHINNADURAI, R. et al. IDO-Independent Suppression of T Cell Effector Function by IFN-γ–Licensed Human Mesenchymal Stromal Cells. **The Journal of Immunology**, v. 192, n. 4, p. 1491–1501, 15 fev. 2014.

CHIOCCHETTI, R. et al. Cellular Distribution of Canonical and Putative Cannabinoid Receptors in Canine Cervical Dorsal Root Ganglia. **Frontiers in Veterinary Science**, v. 6, 19 set. 2019.

CHIURCHIÙ, V.; LEUTI, A.; MACCARRONE, M. Bioactive Lipids and Chronic Inflammation: Managing the Fire Within. **Frontiers in Immunology**, v. 9, 29 jan. 2018.

CHON, S. Y.; HASSANAIN, H. H.; GUPTA, S. L. Cooperative Role of Interferon Regulatory Factor 1 and p91 (STAT1) Response Elements in Interferon-γ-inducible Expression of Human Indoleamine 2,3-Dioxygenase Gene. **Journal of Biological Chemistry**, v. 271, n. 29, p. 17247–17252, jul. 1996.

CITAL, S. et al. (EDS.). **Cannabis Therapy in Veterinary Medicine**. Cham: Springer International Publishing, 2021.

CITTI, C. et al. Pitfalls in the analysis of phytocannabinoids in cannabis inflorescence. **Analytical and Bioanalytical Chemistry**, v. 412, n. 17, p. 4009–4022, 14 jul. 2020.

COMPTON, A. C. et al. The immunomodulatory role of phytocannabinoids in an *in vitro* peri-implantitis model. **Journal of Dental Implant Research**, v. 41, n. 4, p. 102–112, 30 dez. 2022.

CONDIE, R. et al. Cannabinoid Inhibition of Adenylate Cyclase-mediated Signal Transduction and Interleukin 2 (IL-2) Expression in the Murine T-cell Line, EL4.IL-2. **Journal of Biological Chemistry**, v. 271, n. 22, p. 13175–13183, maio 1996.

CONTRERAS, R. A. et al. Mesenchymal Stem Cells Regulate the Innate and Adaptive Immune Responses Dampening Arthritis Progression. **Stem Cells International**, v. 2016, p. 1–10, 2016.

CORTRIGHT, D.; SZALLASI, A. TRP Channels and Pain. **Current Pharmaceutical Design**, v. 15, n. 15, p. 1736–1749, 1 maio 2009.

CRAVATT, B. F. et al. Molecular characterization of an enzyme that degrades neuromodulatory fatty-acid amides. **Nature**, v. 384, n. 6604, p. 83–87, nov. 1996.

CROCQ, M.-A. History of cannabis and the endocannabinoid system. **Dialogues in Clinical Neuroscience**, v. 22, n. 3, p. 223–228, 30 set. 2020.

CROFT, A. S. et al. The Application of Mesenchymal Stromal Cells and Their Homing Capabilities to Regenerate the Intervertebral Disc. **International Journal of Molecular Sciences**, v. 22, n. 7, p. 3519, 29 mar. 2021.

CUI, Y. et al. Functional collagen conduits combined with human mesenchymal stem cells promote regeneration after sciatic nerve transection in dogs. **Journal of Tissue Engineering and Regenerative Medicine**, v. 12, n. 5, p. 1285–1296, maio 2018.

DA SILVA MEIRELLES, L. et al. Mechanisms involved in the therapeutic properties of mesenchymal stem cells. **Cytokine & Growth Factor Reviews**, v. 20, n. 5–6, p. 419–427, out. 2009.

DAI, W.; GUPTA, S. L. Regulation of indoleamine 2,3-dioxygenase gene expression in human fibroblasts by interferon-gamma. Upstream control region discriminates between interferon-gamma and interferon-alpha. **Journal of Biological Chemistry**, v. 265, n. 32, p. 19871–19877, nov. 1990.

DALEY, G. Q. et al. Setting Global Standards for Stem Cell Research and Clinical Translation: The 2016 ISSCR Guidelines. **Stem Cell Reports**, v. 6, n. 6, p. 787–797, jun. 2016.

D'ANIELLO, E. et al. Identification and characterization of phytocannabinoids as novel dual PPARα/γ agonists by a computational and in vitro experimental approach. **Biochimica et Biophysica Acta (BBA) - General Subjects**, v. 1863, n. 3, p. 586–597, mar. 2019.

DAS, R. et al. The Role of Hypoxia in Bone Marrow–Derived Mesenchymal Stem Cells: Considerations for Regenerative Medicine Approaches. **Tissue Engineering Part B: Reviews**, v. 16, n. 2, p. 159–168, abr. 2010.

DAVIS, M. P. Cannabinoids in pain management: CB1, CB2 and non-classic receptor ligands. **Expert Opinion on Investigational Drugs**, v. 23, n. 8, p. 1123–1140, 16 ago. 2014.

DE WITTE, S. F. H. et al. Toward Development of iMesenchymal Stem Cells for Immunomodulatory Therapy. **Frontiers in Immunology**, v. 6, 6 jan. 2016.

DEANS, R. J.; MOSELEY, A. B. Mesenchymal stem cells. **Experimental Hematology**, v. 28, n. 8, p. 875–884, ago. 2000.

DEIANA, S. et al. Plasma and brain pharmacokinetic profile of cannabidiol (CBD), cannabidivarine (CBDV), Δ9-tetrahydrocannabivarin (THCV) and cannabigerol (CBG) in rats and mice following oral and intraperitoneal administration and CBD action on obsessive–compulsive behaviour. **Psychopharmacology**, v. 219, n. 3, p. 859–873, 28 fev. 2012.

DEUTSCH, D. G. et al. The Cellular Uptake of Anandamide Is Coupled to Its Breakdown by Fatty-acid Amide Hydrolase. **Journal of Biological Chemistry**, v. 276, n. 10, p. 6967–6973, mar. 2001.

DEUTSCH, D. G. A Personal Retrospective: Elevating Anandamide (AEA) by Targeting Fatty Acid Amide Hydrolase (FAAH) and the Fatty Acid Binding Proteins (FABPs). **Frontiers in Pharmacology**, v. 7, 13 out. 2016.

DEUTSCH, D. G.; CHIN, S. A. Enzymatic synthesis and degradation of anandamide, a cannabinoid receptor agonist. **Biochemical Pharmacology**, v. 46, n. 5, p. 791–796, set. 1993.

DEVANE, W. A. et al. Isolation and Structure of a Brain Constituent That Binds to the Cannabinoid Receptor. **Science**, v. 258, n. 5090, p. 1946–1949, 18 dez. 1992.

DEVANE, W. A.; AXELROD, J. Enzymatic synthesis of anandamide, an endogenous ligand for the cannabinoid receptor, by brain membranes. **Proceedings of the National Academy of Sciences**, v. 91, n. 14, p. 6698–6701, 5 jul. 1994.

DI MARZO, V. New approaches and challenges to targeting the endocannabinoid system. **Nature Reviews Drug Discovery**, v. 17, n. 9, p. 623–639, 17 set. 2018.

DI MARZO, V.; SILVESTRI, C. Lifestyle and Metabolic Syndrome: Contribution of the Endocannabinoidome. **Nutrients**, v. 11, n. 8, p. 1956, 20 ago. 2019.

DI TINCO, R. et al. Role of PD-L1 in licensing immunoregulatory function of dental pulp mesenchymal stem cells. **Stem Cell Research & Therapy**, v. 12, n. 1, p. 598, 4 dez. 2021.

DIMARINO, A. M.; CAPLAN, A. I.; BONFIELD, T. L. Mesenchymal Stem Cells in Tissue Repair. **Frontiers in Immunology**, v. 4, 2013.

DING, D.-C.; SHYU, W.-C.; LIN, S.-Z. Mesenchymal Stem Cells. **Cell Transplantation**, v. 20, n. 1, p. 5–14, 1 fev. 2011.

D'IPPOLITO, G. et al. Isolation and characterization of marrow-isolated adult multilineage inducible (MIAMI) cells. **Experimental Hematology**, v. 34, n. 11, p. 1608–1610, nov. 2006.

DJEUNGOUE-PETGA, M.-A.; HEBERT-CHATELAIN, E. Linking Mitochondria and Synaptic Transmission: The CB1 Receptor. **BioEssays**, v. 39, n. 12, p. 1700126, dez. 2017.

DOBACZEWSKI, M.; CHEN, W.; FRANGOGIANNIS, N. G. Transforming growth factor (TGF)-β signaling in cardiac remodeling. **Journal of Molecular and Cellular Cardiology**, v. 51, n. 4, p. 600–606, out. 2011.

DOMINICI, M. et al. Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. **Cytotherapy**, v. 8, n. 4, p. 315–317, 2006.

DUNN, C. M. et al. Interferon-Gamma Primed Human Clonal Mesenchymal Stromal Cell Sheets Exhibit Enhanced Immunosuppressive Function. **Cells**, v. 11, n. 23, p. 3738, 23 nov. 2022.

DURANTI, A. et al. The Endocannabinoid System as a Target for Neuroprotection/Neuroregeneration in Perinatal Hypoxic–Ischemic Brain Injury. **Biomedicines**, v. 11, n. 1, p. 28, 22 dez. 2022.

ECHEVERRY, C. et al. A Comparative In Vitro Study of the Neuroprotective Effect Induced by Cannabidiol, Cannabigerol, and Their Respective Acid Forms: Relevance of the 5-HT1A Receptors. **Neurotoxicity Research**, v. 39, n. 2, p. 335–348, 4 abr. 2021.

EGGENHOFER, E. et al. The Life and Fate of Mesenchymal Stem Cells. **Frontiers in Immunology**, v. 5, 19 maio 2014.

ELBATSH, M. M. et al. Anxiogenic-like effects of chronic cannabidiol administration in rats. **Psychopharmacology**, v. 221, n. 2, p. 239–247, 15 maio 2012.

ELMES, M. W. et al. Fatty Acid-binding Proteins (FABPs) Are Intracellular Carriers for Δ9-Tetrahydrocannabinol (THC) and Cannabidiol (CBD). **Journal of Biological Chemistry**, v. 290, n. 14, p. 8711–8721, abr. 2015.

ELSOHLY, M. A. et al. Phytochemistry of Cannabis sativa L. Em: [s.l: s.n.]. p. 1–36.

EPPS, D. E. et al. N-acylethanolamine accumulation in infarcted myocardium. **Biochemical and Biophysical Research Communications**, v. 90, n. 2, p. 628–633, set. 1979.

ESPAGNOLLE, N. et al. CD54-Mediated Interaction with Pro-inflammatory Macrophages Increases the Immunosuppressive Function of Human Mesenchymal Stromal Cells. **Stem Cell Reports**, v. 8, n. 4, p. 961–976, abr. 2017.

ESPOSITO, G. et al. Cannabidiol Reduces Aβ-Induced Neuroinflammation and Promotes Hippocampal Neurogenesis through PPARγ Involvement. **PLoS ONE**, v. 6, n. 12, p. e28668, 5 dez. 2011.

ESPOSITO, L. G. A. et al. Immune Responses Are Differentially Regulated by Root, Stem, Leaf, and Flower Extracts of Female and Male CBD Hemp (Cannabis sativa L.) Plants. **Immuno**, v. 1, n. 4, p. 369–379, 22 out. 2021.

FADDA, P. et al. Differential effects of THC- or CBD-rich cannabis extracts on working memory in rats. **Neuropharmacology**, v. 47, n. 8, p. 1170–1179, dez. 2004.

FAN, M. et al. Current Perspectives on Role of MSC in Renal Pathophysiology. **Frontiers in Physiology**, v. 9, 20 set. 2018.

FEGLEY, D. et al. Anandamide transport is independent of fatty-acid amide hydrolase activity and is blocked by the hydrolysis-resistant inhibitor AM1172. **Proceedings of the National Academy of Sciences**, v. 101, n. 23, p. 8756–8761, 8 jun. 2004.

FELLOUS, T. et al. Phytocannabinoids promote viability and functional adipogenesis of bone marrow-derived mesenchymal stem cells through different molecular targets. **Biochemical Pharmacology**, v. 175, p. 113859, maio 2020.

FIANI, B. et al. Current application of cannabidiol (CBD) in the management and treatment of neurological disorders. **Neurological Sciences**, v. 41, n. 11, p. 3085–3098, 16 nov. 2020.

FILIPIUC, L. E. et al. Major Phytocannabinoids and Their Related Compounds: Should We Only Search for Drugs That Act on Cannabinoid Receptors? **Pharmaceutics**, v. 13, n. 11, p. 1823, 1 nov. 2021.

FORRESTER, J. S.; MAKKAR, R. R.; MARBÁN, E. Long-Term Outcome of Stem Cell Therapy for Acute Myocardial Infarction. **Journal of the American College of Cardiology**, v. 53, n. 24, p. 2270–2272, jun. 2009.

FOWLER, C. J. Transport of endocannabinoids across the plasma membrane and within the cell. **FEBS Journal**, v. 280, n. 9, p. 1895–1904, maio 2013.

FRANCO, V.; PERUCCA, E. Pharmacological and Therapeutic Properties of Cannabidiol for Epilepsy. **Drugs**, v. 79, n. 13, p. 1435–1454, 1 set. 2019.

FRANÇOIS, M. et al. Human MSC Suppression Correlates With Cytokine Induction of Indoleamine 2,3-Dioxygenase and Bystander M2 Macrophage Differentiation. **Molecular Therapy**, v. 20, n. 1, p. 187–195, jan. 2012.

FREUNDT-REVILLA, J. et al. Spatial distribution of cannabinoid receptor type 1 (CB1) in normal canine central and peripheral nervous system. **PLOS ONE**, v. 12, n. 7, p. e0181064, 10 jul. 2017.

FU, Y. et al. Trophic Effects of Mesenchymal Stem Cells in Tissue Regeneration. **Tissue Engineering Part B: Reviews**, v. 23, n. 6, p. 515–528, dez. 2017.

GABRYŠOVÁ, L. et al. The Regulation of IL-10 Expression. Em: [s.l: s.n.]. p. 157–190.

GALIAZZO, G. et al. Localization of cannabinoid receptors CB1, CB2, GPR55, and PPARα in the canine gastrointestinal tract. **Histochemistry and Cell Biology**, v. 150, n. 2, p. 187–205, 7 ago. 2018.

GALIPEAU, J. et al. International Society for Cellular Therapy perspective on immune functional assays for mesenchymal stromal cells as potency release criterion for advanced phase clinical trials. **Cytotherapy**, v. 18, n. 2, p. 151–159, fev. 2016.

GALVE-ROPERH, I. et al. Mechanisms of Control of Neuron Survival by the Endocannabinoid System. **Current Pharmaceutical Design**, v. 14, n. 23, p. 2279–2288, 1 ago. 2008.

GAO, F. et al. Mesenchymal stem cells and immunomodulation: current status and future prospects. **Cell Death & Disease**, v. 7, n. 1, p. e2062–e2062, 21 jan. 2016.

GARCIA-ARENCIBIA, M.; GARCIA, C.; FERNANDEZ-RUIZ, J. Cannabinoids and Parkinsons Disease. **CNS & Neurological Disorders - Drug Targets**, v. 8, n. 6, p. 432–439, 1 dez. 2009.

GARCÍA-GUTIÉRREZ, M. S. et al. Cannabidiol: A Potential New Alternative for the Treatment of Anxiety, Depression, and Psychotic Disorders. **Biomolecules**, v. 10, n. 11, p. 1575, 19 nov. 2020.

GARG, P. et al. Prospective Review of Mesenchymal Stem Cells Differentiation into Osteoblasts. **Orthopaedic Surgery**, v. 9, n. 1, p. 13–19, fev. 2017.

GAUR, U.; AGGARWAL, B. B. Regulation of proliferation, survival and apoptosis by members of the TNF superfamily. **Biochemical Pharmacology**, v. 66, n. 8, p. 1403–1408, out. 2003.

GHORBEL, M. T. et al. Reconstruction of the pulmonary artery by a novel biodegradable conduit engineered with perinatal stem cell-derived vascular smooth muscle cells enables physiological vascular growth in a large animal model of congenital heart disease. **Biomaterials**, v. 217, p. 119284, out. 2019.

GIACOPPO, S. et al. Target regulation of PI3K/Akt/mTOR pathway by cannabidiol in treatment of experimental multiple sclerosis. **Fitoterapia**, v. 116, p. 77–84, jan. 2017.

GLASS, M.; NORTHUP, J. K. Agonist Selective Regulation of G Proteins by Cannabinoid CB $_1$ and CB $_2$ Receptors. **Molecular Pharmacology**, v. 56, n. 6, p. 1362–1369, 1 dez. 1999.

GONG, J.-P. et al. Cannabinoid CB2 receptors: Immunohistochemical localization in rat brain. **Brain Research**, v. 1071, n. 1, p. 10–23, fev. 2006.

GONZÁLEZ-FERNÁNDEZ, M. L. et al. Study on viability and chondrogenic differentiation of cryopreserved adipose tissue-derived mesenchymal stromal cells for future use in regenerative medicine. **Cryobiology**, v. 71, n. 2, p. 256–263, out. 2015.

GORE, A. V. et al. Mesenchymal stem cells increase T-regulatory cells and improve healing following trauma and hemorrhagic shock. **Journal of Trauma and Acute Care Surgery**, v. 79, n. 1, p. 48–52, jul. 2015.

GOULLÉ, J.-P.; SAUSSEREAU, E.; LACROIX, C. Pharmacocinétique du delta-9-tétrahydrocannabinol (THC). **Annales Pharmaceutiques Françaises**, v. 66, n. 4, p. 232–244, ago. 2008.

GRAU-VORSTER, M. et al. HLA-DR expression in clinical-grade bone marrow-derived multipotent mesenchymal stromal cells: a two-site study. **Stem Cell Research & Therapy**, v. 10, n. 1, p. 164, 13 dez. 2019.

GROUX, H. et al. Inhibitory and Stimulatory Effects of IL-10 on Human CD8+ T Cells. **The Journal of Immunology**, v. 160, n. 7, p. 3188–3193, 1 abr. 1998.

GU, Z. et al. Marijuana-Derived Cannabinoids Trigger a CB2/PI3K Axis of Suppression of the Innate Response to Oral Pathogens. **Frontiers in Immunology**, v. 10, 15 out. 2019.

GUERROUAHEN, B. S. et al. Enhancing Mesenchymal Stromal Cell Immunomodulation for Treating Conditions Influenced by the Immune System. **Stem Cells International**, v. 2019, p. 1–11, 5 ago. 2019.

GÜLCK, T.; MØLLER, B. L. Phytocannabinoids: Origins and Biosynthesis. **Trends in Plant Science**, v. 25, n. 10, p. 985–1004, out. 2020.

GUO, Y. et al. The therapeutic potential of mesenchymal stem cells for cardiovascular diseases. **Cell Death & Disease**, v. 11, n. 5, p. 349, 11 maio 2020.

GUO, Y. et al. Indoleamine 2,3-dioxygenase (Ido) inhibitors and their nanomedicines for cancer immunotherapy. **Biomaterials**, v. 276, p. 121018, set. 2021.

HACKE, A. C. M. et al. Probing the antioxidant activity of Δ^{9} -tetrahydrocannabinol and cannabidiol in *Cannabis sativa* extracts. **The Analyst**, v. 144, n. 16, p. 4952–4961, 2019.

HAJOS, N. et al. Endocannabinoid transport tightly controls 2-arachidonoyl glycerol actions in the hippocampus: effects of low temperature and the transport inhibitor AM404. **European Journal of Neuroscience**, v. 19, n. 11, p. 2991–2996, jun. 2004.

HAN, D. et al. Activation of cannabinoid receptor type II by AM1241 protects adipose-derived mesenchymal stem cells from oxidative damage and enhances their therapeutic efficacy in myocardial infarction mice *via* Stat3 activation. **Oncotarget**, v. 8, n. 39, p. 64853–64866, 12 set. 2017.

HAN, X. et al. Interleukin-17 enhances immunosuppression by mesenchymal stem cells. **Cell Death & Differentiation**, v. 21, n. 11, p. 1758–1768, 18 nov. 2014.

HANUŠ, L. O. et al. Phytocannabinoids: a unified critical inventory. **Natural Product Reports**, v. 33, n. 12, p. 1357–1392, 2016.

HÄRING, M. et al. Identification of the cannabinoid receptor type 1 in serotonergic cells of raphe nuclei in mice. **Neuroscience**, v. 146, n. 3, p. 1212–1219, maio 2007.

HARRELL, C. R.; DJONOV, V.; VOLAREVIC, V. The Cross-Talk between Mesenchymal Stem Cells and Immune Cells in Tissue Repair and Regeneration. **International Journal of Molecular Sciences**, v. 22, n. 5, p. 2472, 1 mar. 2021.

HASAN, A. et al. Mesenchymal Stem Cells in the Treatment of Traumatic Brain Injury. **Frontiers in Neurology**, v. 8, 20 fev. 2017.

HASSAN, S. et al. Cannabidiol enhances microglial phagocytosis via transient receptor potential (TRP) channel activation. **British Journal of Pharmacology**, v. 171, n. 9, p. 2426–2439, maio 2014.

HAZEKAMP, A.; FISCHEDICK, J. T. Cannabis - from cultivar to chemovar. **Drug Testing and Analysis**, v. 4, n. 7–8, p. 660–667, jul. 2012.

HELLMANN, J. et al. Atf3 negatively regulates Ptgs2/Cox2 expression during acute inflammation. **Prostaglandins & Other Lipid Mediators**, v. 116–117, p. 49–56, jan. 2015.

HELLWIG, V. et al. Activities of Prenylphenol Derivatives from Fruitbodies of Albatrellus spp. on the Human and Rat Vanilloid Receptor 1 (VR1) and Characterisation of the Novel Natural Product, Confluentin. **Archiv der Pharmazie**, v. 336, n. 2, p. 119–126, abr. 2003.

HEMATTI, P. Mesenchymal stromal cells and fibroblasts: a case of mistaken identity? **Cytotherapy**, v. 14, n. 5, p. 516–521, maio 2012.

HERKENHAM, M. et al. Cannabinoid receptor localization in brain. **Proceedings of the National Academy of Sciences**, v. 87, n. 5, p. 1932–1936, mar. 1990.

HERKENHAM, M. et al. Characterization and localization of cannabinoid receptors in rat brain: a quantitative in vitro autoradiographic study. **The Journal of Neuroscience**, v. 11, n. 2, p. 563–583, 1 fev. 1991.

HESAMI, M. et al. Current status and future prospects in cannabinoid production through in vitro culture and synthetic biology. **Biotechnology Advances**, v. 62, p. 108074, jan. 2023.

HILLARD, C. J. The Endocannabinoid Signaling System in the CNS. Em: [s.l: s.n.]. p. 1–47.

HILLARD, C. J. Circulating Endocannabinoids: From Whence Do They Come and Where are They Going? **Neuropsychopharmacology**, v. 43, n. 1, p. 155–172, 27 jan. 2018.

HILLIG, K. W. Genetic evidence for speciation in Cannabis (Cannabaceae). **Genetic Resources and Crop Evolution**, v. 52, n. 2, p. 161–180, mar. 2005.

HORWITZ, E. M. et al. Clarification of the nomenclature for MSC: The International Society for Cellular Therapy position statement. **Cytotherapy**, v. 7, n. 5, p. 393–395, 2005.

HOSOGANE, N. et al. Stromal derived factor-1 regulates bone morphogenetic protein 2-induced osteogenic differentiation of primary mesenchymal stem cells. **The International Journal of Biochemistry & Cell Biology**, v. 42, n. 7, p. 1132–1141, jul. 2010a.

HOSOGANE, N. et al. Stromal derived factor-1 regulates bone morphogenetic protein 2-induced osteogenic differentiation of primary mesenchymal stem cells. **The International Journal of Biochemistry & Cell Biology**, v. 42, n. 7, p. 1132–1141, jul. 2010b.

HOWLETT, A. C.; ABOOD, M. E. CB 1 and CB 2 Receptor Pharmacology. Em: [s.l: s.n.]. p. 169–206.

HUNG, K.-C. et al. Water-based polyurethane 3D printed scaffolds with controlled release function for customized cartilage tissue engineering. **Biomaterials**, v. 83, p. 156–168, mar. 2016.

HUSSAIN, T. et al. Demystifying the liverwort Radula marginata, a critical review on its taxonomy, genetics, cannabinoid phytochemistry and pharmacology. **Phytochemistry Reviews**, v. 18, n. 3, p. 953–965, 10 jun. 2019.

I. KHAN, M. et al. The Therapeutic Aspects of the Endocannabinoid System (ECS) for Cancer and their Development: From Nature to Laboratory. **Current Pharmaceutical Design**, v. 22, n. 12, p. 1756–1766, 29 mar. 2016.

IANNOTTI, F. A. et al. Nonpsychotropic Plant Cannabinoids, Cannabidivarin (CBDV) and Cannabidiol (CBD), Activate and Desensitize Transient Receptor Potential Vanilloid 1 (TRPV1) Channels in Vitro: Potential for the Treatment of Neuronal Hyperexcitability. **ACS Chemical Neuroscience**, v. 5, n. 11, p. 1131–1141, 19 nov. 2014.

IBSEN, M. S.; CONNOR, M.; GLASS, M. Cannabinoid CB $_1$ and CB $_2$ Receptor Signaling and Bias. **Cannabis and Cannabinoid Research**, v. 2, n. 1, p. 48–60, jan. 2017.

IDO, A. et al. Translational research on HGF: A phase I/II study of recombinant human HGF for the treatment of fulminant hepatic failure. **Hepatology Research**, v. 38, p. S88–S92, nov. 2008.

IGNATOWSKA-JANKOWSKA, B. M. et al. A Cannabinoid CB1 Receptor-Positive Allosteric Modulator Reduces Neuropathic Pain in the Mouse with No Psychoactive Effects. **Neuropsychopharmacology**, v. 40, n. 13, p. 2948–2959, 8 dez. 2015.

IP, W. K. E. et al. Anti-inflammatory effect of IL-10 mediated by metabolic reprogramming of macrophages. **Science**, v. 356, n. 6337, p. 513–519, 5 maio 2017.

IZADPANAH, R. et al. Characterization of Multipotent Mesenchymal Stem Cells from the Bone Marrow of Rhesus Macaques. **Stem Cells and Development**, v. 14, n. 4, p. 440–451, ago. 2005.

JENNY, M. et al. Δ9-Tetrahydrocannabinol and cannabidiol modulate mitogen-induced tryptophan degradation and neopterin formation in peripheral blood mononuclear cells in vitro. **Journal of Neuroimmunology**, v. 207, n. 1–2, p. 75–82, fev. 2009.

JIN, X.-H. et al. Discovery and Characterization of a Ca2+-independent Phosphatidylethanolamine N-Acyltransferase Generating the Anandamide Precursor and Its Congeners. **Journal of Biological Chemistry**, v. 282, n. 6, p. 3614–3623, fev. 2007.

JOCA, S. et al. Putative effects of cannabidiol in depression and synaptic plasticity. Em: **The Neuroscience of Depression**. [s.l.] Elsevier, 2021. p. 459–467.

JONES, F. K. et al. Syndecan-3 regulates MSC adhesion, ERK and AKT signalling in vitro and its deletion enhances MSC efficacy in a model of inflammatory arthritis in vivo. **Scientific Reports**, v. 10, n. 1, p. 20487, 24 nov. 2020.

JONES, N. A. et al. Cannabidiol exerts anti-convulsant effects in animal models of temporal lobe and partial seizures. **Seizure**, v. 21, n. 5, p. 344–352, jun. 2012.

JOSHI, N.; ONAIVI, E. S. Endocannabinoid System Components: Overview and Tissue Distribution. Em: [s.l: s.n.]. p. 1–12.

JULIEN, B. et al. Antifibrogenic role of the cannabinoid receptor CB2 in the liver. **Gastroenterology**, v. 128, n. 3, p. 742–755, mar. 2005.

KACZOCHA, M.; HAJ-DAHMANE, S. Mechanisms of endocannabinoid transport in the brain. **British Journal of Pharmacology**, v. 179, n. 17, p. 4300–4310, 27 set. 2022.

KADLE, R. L. et al. Microenvironmental cues enhance mesenchymal stem cell-mediated immunomodulation and regulatory T-cell expansion. **PLOS ONE**, v. 13, n. 3, p. e0193178, 7 mar. 2018.

KALVALA, A. K. et al. Cannabidiol-Loaded Extracellular Vesicles from Human Umbilical Cord Mesenchymal Stem Cells Alleviate Paclitaxel-Induced Peripheral Neuropathy. **Pharmaceutics**, v. 15, n. 2, p. 554, 7 fev. 2023.

KAMALI, A. et al. Cannabidiol-loaded microspheres incorporated into osteoconductive scaffold enhance mesenchymal stem cell recruitment and regeneration of critical-sized bone defects. **Materials Science and Engineering: C**, v. 101, p. 64–75, ago. 2019.

KANG, H. et al. The Therapeutic Effects of Human Mesenchymal Stem Cells Primed with Sphingosine-1 Phosphate on Pulmonary Artery Hypertension. **Stem Cells and Development**, v. 24, n. 14, p. 1658–1671, 15 jul. 2015.

KANG, M.; LEE, J.; PARK, S. Cannabidiol induces osteoblast differentiation via angiopoietin1 and p38 <scp>MAPK</scp>. **Environmental Toxicology**, v. 35, n. 12, p. 1318–1325, 13 dez. 2020.

KAY, A. G. et al. Therapeutic Effects of Hypoxic and Pro-Inflammatory Priming of Mesenchymal Stem Cell-Derived Extracellular Vesicles in Inflammatory Arthritis. **International Journal of Molecular Sciences**, v. 23, n. 1, p. 126, 23 dez. 2021.

KE, J. et al. Prostaglandin E2 (PGE2) promotes proliferation and invasion by enhancing SUMO-1 activity via EP4 receptor in endometrial cancer. **Tumor Biology**, v. 37, n. 9, p. 12203–12211, 26 set. 2016.

KELLY, D. J.; JACOBS, C. R. The role of mechanical signals in regulating chondrogenesis and osteogenesis of mesenchymal stem cells. **Birth Defects Research Part C: Embryo Today: Reviews**, v. 90, n. 1, p. 75–85, mar. 2010.

KHAN, I.; MAHFOOZ, S.; HATIBOGLU, M. A. Herbal Medicine for Glioblastoma: Current and Future Prospects. **Medicinal Chemistry**, v. 16, n. 8, p. 1022–1043, 23 nov. 2020.

KHAVANDI, M.; RAO, P. P. N.; BEAZELY, M. A. Differential Effects of Endocannabinoids on Amyloid-Beta Aggregation and Toxicity. **International Journal of Molecular Sciences**, v. 24, n. 2, p. 911, 4 jan. 2023.

KHOURY, M.; COHEN, I.; BAR-SELA, G. “The Two Sides of the Same Coin”—Medical Cannabis, Cannabinoids and Immunity: Pros and Cons Explained. **Pharmaceutics**, v. 14, n. 2, p. 389, 10 fev. 2022.

KIGERL, K. A. et al. Identification of Two Distinct Macrophage Subsets with Divergent Effects Causing either Neurotoxicity or Regeneration in the Injured Mouse Spinal Cord. **The Journal of Neuroscience**, v. 29, n. 43, p. 13435–13444, 28 out. 2009.

KILARU, A.; CHAPMAN, K. D. The endocannabinoid system. **Essays in Biochemistry**, v. 64, n. 3, p. 485–499, 23 set. 2020.

KIM, D. S. et al. Enhanced Immunosuppressive Properties of Human Mesenchymal Stem Cells Primed by Interferon-γ. **EBioMedicine**, v. 28, p. 261–273, fev. 2018.

KIM, M. et al. Exosomes from IL-1β-Primed Mesenchymal Stem Cells Inhibited IL-1β- and TNF-α-Mediated Inflammatory Responses in Osteoarthritic SW982 Cells. **Tissue Engineering and Regenerative Medicine**, v. 18, n. 4, p. 525–536, 25 ago. 2021.

KIM, Y. et al. Transplantation of adipose derived mesenchymal stem cells for acute thoracolumbar disc disease with no deep pain perception in dogs. **Journal of Veterinary Science**, v. 17, n. 1, p. 123, 2016.

KIRILLY, E.; HUNYADY, L.; BAGDY, G. Opposing local effects of endocannabinoids on the activity of noradrenergic neurons and release of noradrenaline: relevance for their role in depression and in the actions of CB1 receptor antagonists. **Journal of Neural Transmission**, v. 120, n. 1, p. 177–186, 19 jan. 2013.

KLAHN, P. Cannabinoids-Promising Antimicrobial Drugs or Intoxicants with Benefits? **Antibiotics**, v. 9, n. 6, p. 297, 2 jun. 2020.

KLEIN, T. W. Cannabinoid-based drugs as anti-inflammatory therapeutics. **Nature Reviews Immunology**, v. 5, n. 5, p. 400–411, maio 2005.

KOENDERS, M. I.; VAN DEN BERG, W. B. Novel therapeutic targets in rheumatoid arthritis. **Trends in Pharmacological Sciences**, v. 36, n. 4, p. 189–195, abr. 2015.

KOGAN, N. M.; MECHOULAM, R. Cannabinoids in health and disease. **Dialogues in Clinical Neuroscience**, v. 9, n. 4, p. 413–430, 31 dez. 2007.

KONGKADEE, K. et al. Anti-inflammation and gingival wound healing activities of Cannabis sativa L. subsp. sativa (hemp) extract and cannabidiol: An in vitro study. **Archives of Oral Biology**, v. 140, p. 105464, ago. 2022.

KOPUSTINSKIENE, D. M. et al. Cannabis sativa L. Bioactive Compounds and Their Protective Role in Oxidative Stress and Inflammation. **Antioxidants**, v. 11, n. 4, p. 660, 29 mar. 2022.

KORAM, K. The Legalization of Cannabis and the Question of Reparations. **Journal of International Economic Law**, v. 25, n. 2, p. 294–311, 9 ago. 2022.

KÖSE, S. et al. Human bone marrow mesenchymal stem cells secrete endocannabinoids that stimulate in vitro hematopoietic stem cell migration effectively comparable to beta-adrenergic stimulation. **Experimental Hematology**, v. 57, p. 30- 41.e1, jan. 2018.

KOWALCZUK, A. et al. Cannabidiol (CBD) Protects Adipose-Derived Mesenchymal Stem Cells (ASCs) against Endoplasmic Reticulum Stress Development and Its Complications. **International Journal of Environmental Research and Public Health**, v. 19, n. 17, p. 10864, 31 ago. 2022.

KOWIAŃSKI, P. et al. BDNF: A Key Factor with Multipotent Impact on Brain Signaling and Synaptic Plasticity. **Cellular and Molecular Neurobiology**, v. 38, n. 3, p. 579–593, 16 abr. 2018.

KOZAK, K.; PRUSAKIEWICZ, J.; MARNETT, L. Oxidative Metabolism of Endocannabinoids by COX-2. **Current Pharmaceutical Design**, v. 10, n. 6, p. 659–667, 1 fev. 2004.

KOZAK, K. R. et al. 15-Lipoxygenase Metabolism of 2-Arachidonylglycerol. **Journal of Biological Chemistry**, v. 277, n. 26, p. 23278–23286, jun. 2002.

KOZELA, E. et al. Cannabinoids Δ9-Tetrahydrocannabinol and Cannabidiol Differentially Inhibit the Lipopolysaccharide-activated NF-κB and Interferon-β/STAT Proinflammatory Pathways in BV-2 Microglial Cells. **Journal of Biological Chemistry**, v. 285, n. 3, p. 1616–1626, jan. 2010.

KOZELA, E. et al. Cannabinoids Decrease the Th17 Inflammatory Autoimmune Phenotype. **Journal of Neuroimmune Pharmacology**, v. 8, n. 5, p. 1265–1276, 28 dez. 2013.

KRAWCZENKO, A. et al. Microvesicles from Human Immortalized Cell Lines of Endothelial Progenitor Cells and Mesenchymal Stem/Stromal Cells of Adipose Tissue Origin as Carriers of Bioactive Factors Facilitating Angiogenesis. **Stem Cells International**, v. 2020, p. 1–17, 15 jun. 2020.

KRUEGER, T. E. G. et al. Concise Review: Mesenchymal Stem Cell-Based Drug Delivery: The Good, the Bad, the Ugly, and the Promise. **Stem Cells Translational Medicine**, v. 7, n. 9, p. 651–663, 1 set. 2018.

KRUSZKA, K. K.; GROSS, R. W. The ATP- and CoA-independent synthesis of arachidonoylethanolamide. A novel mechanism underlying the synthesis of the endogenous ligand of the cannabinoid receptor. **Journal of Biological Chemistry**, v. 269, n. 20, p. 14345–14348, maio 1994.

KUDDUS, M.; GINAWI, I.; ALHAZIMI, A. Cannabis sativa: An ancient wild edible plant of India. **Emirates Journal of Food and Agriculture**, v. 25, n. 10, p. 736, 2013.

KUWAHARA, Y. et al. Extracellular Vesicles Derived From Canine Mesenchymal Stromal Cells in Serum Free Culture Medium Have Anti-inflammatory Effect on Microglial Cells. **Frontiers in Veterinary Science**, v. 8, 28 abr. 2021.

KWAN CHEUNG, K. A. et al. The Interplay between the Endocannabinoid System, Epilepsy and Cannabinoids. **International Journal of Molecular Sciences**, v. 20, n. 23, p. 6079, 2 dez. 2019.

LAHA, D. et al. The Role of Tumor Necrosis Factor in Manipulating the Immunological Response of Tumor Microenvironment. **Frontiers in Immunology**, v. 12, 27 abr. 2021.

LANKFORD, L. Early gestation chorionic villi-derived stromal cells for fetal tissue engineering. **World Journal of Stem Cells**, v. 7, n. 1, p. 195, 2015.

LARONI, A.; ROSBO, N. K. DE; UCCELLI, A. Mesenchymal stem cells for the treatment of neurological diseases: Immunoregulation beyond neuroprotection. **Immunology Letters**, v. 168, n. 2, p. 183–190, dez. 2015.

LE BLANC, K.; DAVIES, L. C. Mesenchymal stromal cells and the innate immune response. **Immunology Letters**, v. 168, n. 2, p. 140–146, dez. 2015.

LEE, H.-J.; JUNG, H.; KIM, D.-K. IDO and CD40 May Be Key Molecules for Immunomodulatory Capacity of the Primed Tonsil-Derived Mesenchymal Stem Cells. **International Journal of Molecular Sciences**, v. 22, n. 11, p. 5772, 28 maio 2021.

LEE, J.-H. et al. Effects of VEGF and FGF-2 on proliferation and differentiation of human periodontal ligament stem cells. **Cell and Tissue Research**, v. 348, n. 3, p. 475–484, 23 jun. 2012.

LEONG, N. L. et al. Tendon and Ligament Healing and Current Approaches to Tendon and Ligament Regeneration. **Journal of Orthopaedic Research**, v. 38, n. 1, p. 7–12, 30 jan. 2020.

LI, D. et al. Low levels of TGF-β1 enhance human umbilical cord-derived mesenchymal stem cell fibronectin production and extend survival time in a rat model of lipopolysaccharide-induced acute lung injury. **Molecular Medicine Reports**, v. 14, n. 2, p. 1681–1692, ago. 2016.

LI, D. et al. Analysis of Anti-Cancer and Anti-Inflammatory Properties of 25 High-THC Cannabis Extracts. **Molecules**, v. 27, n. 18, p. 6057, 16 set. 2022a.

LI, L. et al. Cannabidiol Promotes Osteogenic Differentiation of Bone Marrow Mesenchymal Stem Cells in the Inflammatory Microenvironment via the CB2-dependent p38 MAPK Signaling Pathway. **International Journal of Stem Cells**, v. 15, n. 4, p. 405–414, 30 nov. 2022b.

LI, W. et al. The role of TNF-α in the fate regulation and functional reprogramming of mesenchymal stem cells in an inflammatory microenvironment. **Frontiers in Immunology**, v. 14, 6 fev. 2023.

LIBRO, R. et al. Cannabidiol Modulates the Immunophenotype and Inhibits the Activation of the Inflammasome in Human Gingival Mesenchymal Stem Cells. **Frontiers in Physiology**, v. 7, 24 nov. 2016a.

LIBRO, R. et al. Cannabidiol Modulates the Expression of Alzheimer's Disease-Related Genes in Mesenchymal Stem Cells. **International Journal of Molecular Sciences**, v. 18, n. 1, p. 26, 23 dez. 2016b.

LIEN, C.-Y. et al. Restoration of Bone Mass and Strength in Glucocorticoid-Treated Mice by Systemic Transplantation of CXCR4 and Cbfa-1 Co-Expressing Mesenchymal Stem Cells. **Journal of Bone and Mineral Research**, v. 24, n. 5, p. 837–848, maio 2009.

LIM, J. et al. Valproic acid enforces the priming effect of sphingosine-1 phosphate on human mesenchymal stem cells. **International Journal of Molecular Medicine**, v. 40, n. 3, p. 739–747, set. 2017.

LIN, L. et al. Fatty acid amide hydrolase (FAAH) regulates hypercapnia/ischemia-induced increases in n-acylethanolamines in mouse brain. **Journal of Neurochemistry**, v. 142, n. 5, p. 662–671, set. 2017a.

LIN, L.-F. H. et al. GDNF: a Glial Cell Line-Derived Neurotrophic Factor for Midbrain Dopaminergic Neurons. **Science**, v. 260, n. 5111, p. 1130–1132, 21 maio 1993.

LIN, T. et al. Preconditioning of murine mesenchymal stem cells synergistically enhanced immunomodulation and osteogenesis. **Stem Cell Research & Therapy**, v. 8, n. 1, p. 277, 6 dez. 2017b.

LIPSKY, R. H.; MARINI, A. M. Brain-Derived Neurotrophic Factor in Neuronal Survival and Behavior-Related Plasticity. **Annals of the New York Academy of Sciences**, v. 1122, n. 1, p. 130–143, dez. 2007.

LIU, J. et al. A biosynthetic pathway for anandamide. **Proceedings of the National Academy of Sciences**, v. 103, n. 36, p. 13345–13350, 5 set. 2006.

LIU, J.; LIU, Q.; CHEN, X. The Immunomodulatory Effects of Mesenchymal Stem Cells on Regulatory B Cells. **Frontiers in Immunology**, v. 11, 14 ago. 2020.

LIU, W. et al. Exosome-shuttled miR-216a-5p from hypoxic preconditioned mesenchymal stem cells repair traumatic spinal cord injury by shifting microglial M1/M2 polarization. **Journal of Neuroinflammation**, v. 17, n. 1, p. 47, 4 dez. 2020.

LIVAK, K. J.; SCHMITTGEN, T. D. Analysis of Relative Gene Expression Data Using Real-Time Quantitative PCR and the $2^{-\Delta\Delta CT}$ Method. **Methods**, v. 25, n. 4, p. 402–408, dez. 2001.

LOMBARD, C.; NAGARKATTI, M.; NAGARKATTI, P. CB2 cannabinoid receptor agonist, JWH-015, triggers apoptosis in immune cells: Potential role for CB2-selective ligands as immunosuppressive agents. **Clinical Immunology**, v. 122, n. 3, p. 259–270, mar. 2007.

LOWE, H. et al. The Endocannabinoid System: A Potential Target for the Treatment of Various Diseases. **International Journal of Molecular Sciences**, v. 22, n. 17, p. 9472, 31 ago. 2021.

LU, H.-C.; MACKIE, K. Review of the Endocannabinoid System. **Biological Psychiatry: Cognitive Neuroscience and Neuroimaging**, v. 6, n. 6, p. 607–615, jun. 2021.

LUKOMSKA, B. et al. Challenges and Controversies in Human Mesenchymal Stem Cell Therapy. **Stem Cells International**, v. 2019, p. 1–10, 9 abr. 2019.

LUO, Y. et al. Co-culture with TM4 cells enhances the proliferation and migration of rat adipose-derived mesenchymal stem cells with high stemness. **Cytotechnology**, v. 70, n. 5, p. 1409–1422, 21 out. 2018.

LUTZ, B. On-demand activation of the endocannabinoid system in the control of neuronal excitability and epileptiform seizures. **Biochemical Pharmacology**, v. 68, n. 9, p. 1691–1698, nov. 2004.

LUZ-CRAWFORD, P. et al. Mesenchymal Stem Cell-Derived Interleukin 1 Receptor Antagonist Promotes Macrophage Polarization and Inhibits B Cell Differentiation. **Stem Cells**, v. 34, n. 2, p. 483–492, 1 fev. 2016.

MA, H. et al. A Network Pharmacology Approach to Identify Potential Molecular Targets for Cannabidiol's Anti-Inflammatory Activity. **Cannabis and Cannabinoid Research**, v. 6, n. 4, p. 288–299, 1 ago. 2021.

MACCARRONE, M. et al. The Endocannabinoid System and Its Relevance for Nutrition. **Annual Review of Nutrition**, v. 30, n. 1, p. 423–440, 1 jul. 2010.

MACCARRONE, M.; DAINESE, E.; ODDI, S. Intracellular trafficking of anandamide: new concepts for signaling. **Trends in Biochemical Sciences**, v. 35, n. 11, p. 601–608, nov. 2010.

MAEDA, A. Recruitment of Mesenchymal Stem Cells to Damaged Sites by Plant-Derived Components. **Frontiers in Cell and Developmental Biology**, v. 8, 9 jun. 2020.

MAGGINI, J. et al. Mouse Bone Marrow-Derived Mesenchymal Stromal Cells Turn Activated Macrophages into a Regulatory-Like Profile. **PLoS ONE**, v. 5, n. 2, p. e9252, 16 fev. 2010.

MÁNDI, Y.; VÉCSEI, L. The kynurenine system and immunoregulation. **Journal of Neural Transmission**, v. 119, n. 2, p. 197–209, 9 fev. 2012.

MANGAL, N. et al. Cannabinoids in the landscape of cancer. **Journal of Cancer Research and Clinical Oncology**, v. 147, n. 9, p. 2507–2534, 14 set. 2021.

MANGIERI, C. W. et al. Perioperative hepatocyte growth factor (HGF) infusions improve hepatic regeneration following portal branch ligation (PBL) in rodents. **Surgical Endoscopy**, v. 31, n. 7, p. 2789–2797, 17 jul. 2017.

MARKOV, A. et al. Mesenchymal stem/stromal cells as a valuable source for the treatment of immune-mediated disorders. **Stem Cell Research & Therapy**, v. 12, n. 1, p. 192, 18 mar. 2021.

MARTIN, I. et al. Challenges for mesenchymal stromal cell therapies. **Science Translational Medicine**, v. 11, n. 480, 20 fev. 2019.

MARTINELLO, T. et al. Canine adipose-derived-mesenchymal stem cells do not lose stem features after a long-term cryopreservation. **Research in Veterinary Science**, v. 91, n. 1, p. 18–24, ago. 2011.

MARX, C. et al. Acupoint Injection of Autologous Stromal Vascular Fraction and Allogeneic Adipose-Derived Stem Cells to Treat Hip Dysplasia in Dogs. **Stem Cells International**, v. 2014, p. 1–6, 2014.

MATHEW, S. A.; CHANDRAVANSHI, B.; BHONDE, R. Hypoxia primed placental mesenchymal stem cells for wound healing. **Life Sciences**, v. 182, p. 85–92, ago. 2017.

MATSUDA, L. A.; BONNER, T. I.; LOLAIT, S. J. Localization of cannabinoid receptor mRNA in rat brain. **The Journal of Comparative Neurology**, v. 327, n. 4, p. 535–550, 22 jan. 1993.

MAUMUS, M. et al. Utility of a Mouse Model of Osteoarthritis to Demonstrate Cartilage Protection by IFNγ-Primed Equine Mesenchymal Stem Cells. **Frontiers in Immunology**, v. 7, 27 set. 2016.

MAURYA, N.; VELMURUGAN, B. K. Therapeutic applications of cannabinoids. **Chemico-Biological Interactions**, v. 293, p. 77–88, set. 2018.

MCDONALD, J. et al. Effects of THC on Behavioral Measures of Impulsivity in Humans. **Neuropsychopharmacology**, v. 28, n. 7, p. 1356–1365, 3 jul. 2003.

MEAD, B. et al. TNFα-Mediated Priming of Mesenchymal Stem Cells Enhances Their Neuroprotective Effect on Retinal Ganglion Cells. **Investigative Opthalmology & Visual Science**, v. 61, n. 2, p. 6, 7 fev. 2020.

MECCARIELLO, R. Endocannabinoid System in Health and Disease: Current Situation and Future Perspectives. **International Journal of Molecular Sciences**, v. 21, n. 10, p. 3549, 18 maio 2020.

MECHOULAM, R. et al. Enantiomeric cannabinoids: stereospecificity of psychotropic activity. **Experientia**, v. 44, n. 9, p. 762–764, set. 1988.

MEERAN, M. F. et al. <scp>CB2</scp> receptor-selective agonists as candidates for targeting infection, inflammation, and immunity in <scp>SARS-CoV</scp> -2 infections. **Drug Development Research**, v. 82, n. 1, p. 7–11, 15 fev. 2021.

MEISEL, R. et al. Human but not murine multipotent mesenchymal stromal cells exhibit broad-spectrum antimicrobial effector function mediated by indoleamine 2,3-dioxygenase. **Leukemia**, v. 25, n. 4, p. 648–654, 18 abr. 2011.

MELAS, P. A. et al. Cannabidiol as a Potential Treatment for Anxiety and Mood Disorders: Molecular Targets and Epigenetic Insights from Preclinical Research. **International Journal of Molecular Sciences**, v. 22, n. 4, p. 1863, 13 fev. 2021.

MELLOR, A. L.; LEMOS, H.; HUANG, L. Indoleamine 2,3-Dioxygenase and Tolerance: Where Are We Now? **Frontiers in Immunology**, v. 8, 27 out. 2017.

MILLER, H. et al. Role of marijuana components on the regenerative ability of stem cells. **Cell Biochemistry and Function**, v. 39, n. 3, p. 432–441, 21 abr. 2021.

MOLDRICH, G.; WENGER, T. Localization of the CB1 cannabinoid receptor in the rat brain. An immunohistochemical study☆. **Peptides**, v. 21, n. 11, p. 1735–1742, nov. 2000.

MOORE, S. A. et al. Identification of a high-affinity binding site involved in the transport of endocannabinoids. **Proceedings of the National Academy of Sciences**, v. 102, n. 49, p. 17852–17857, 6 dez. 2005.

MORELLI, M. B. et al. The transient receptor potential vanilloid-2 cation channel impairs glioblastoma stem-like cell proliferation and promotes differentiation. **International Journal of Cancer**, v. 131, n. 7, p. E1067–E1077, 1 out. 2012.

MORELLI, M. B. et al. The effects of cannabidiol and its synergism with bortezomib in multiple myeloma cell lines. A role for transient receptor potential vanilloid type-2. **International Journal of Cancer**, v. 134, n. 11, p. 2534–2546, 1 jun. 2014.

MORENA, M. et al. Neurobiological Interactions Between Stress and the Endocannabinoid System. **Neuropsychopharmacology**, v. 41, n. 1, p. 80–102, 12 jan. 2016.

MORI, M. A. et al. Cannabidiol reduces neuroinflammation and promotes neuroplasticity and functional recovery after brain ischemia. **Progress in Neuro-Psychopharmacology and Biological Psychiatry**, v. 75, p. 94–105, abr. 2017.

MORRIS, G. et al. The endocannabinoidome in neuropsychiatry: Opportunities and potential risks. **Pharmacological Research**, v. 170, p. 105729, ago. 2021.

MOSHAVERINIA, A. et al. Bone Regeneration Potential of Stem Cells Derived from Periodontal Ligament or Gingival Tissue Sources Encapsulated in RGD-Modified Alginate Scaffold. **Tissue Engineering Part A**, p. 131106060201007, 6 nov. 2013.

MOSSER, D. M.; EDWARDS, J. P. Exploring the full spectrum of macrophage activation. **Nature Reviews Immunology**, v. 8, n. 12, p. 958–969, dez. 2008.

MUCCIOLI, G. G. Endocannabinoid biosynthesis and inactivation, from simple to complex. **Drug Discovery Today**, v. 15, n. 11–12, p. 474–483, jun. 2010.

MÜLLER-VAHL, K. R. et al. Cerebrospinal fluid endocannabinoid levels in Gilles de la Tourette syndrome. **Neuropsychopharmacology**, v. 45, n. 8, p. 1323–1329, 9 jul. 2020.

MURRAY, I. R. et al. Natural history of mesenchymal stem cells, from vessel walls to culture vessels. **Cellular and Molecular Life Sciences**, v. 71, n. 8, p. 1353–1374, 25 abr. 2014.

MUSHAHARY, D. et al. Isolation, cultivation, and characterization of human mesenchymal stem cells. **Cytometry Part A**, v. 93, n. 1, p. 19–31, jan. 2018.

MŰZES, G.; SIPOS, F. Mesenchymal Stem Cell-Derived Secretome: A Potential Therapeutic Option for Autoimmune and Immune-Mediated Inflammatory Diseases. **Cells**, v. 11, n. 15, p. 2300, 26 jul. 2022.

NABISSI, M. et al. Cannabidiol stimulates Aml-1a-dependent glial differentiation and inhibits glioma stem-like cells proliferation by inducing autophagy in a TRPV2-dependent manner. **International Journal of Cancer**, v. 137, n. 8, p. 1855–1869, 15 out. 2015.

NAIM-FEIL, E. et al. The Cannabis Plant as a Complex System: Interrelationships between Cannabinoid Compositions, Morphological, Physiological and Phenological Traits. **Plants**, v. 12, n. 3, p. 493, 21 jan. 2023.

NAJAR, M. et al. Immune-Related Antigens, Surface Molecules and Regulatory Factors in Human-Derived Mesenchymal Stromal Cells: The Expression and Impact of Inflammatory Priming. **Stem Cell Reviews and Reports**, v. 8, n. 4, p. 1188–1198, 15 dez. 2012.

NAJAR, M. et al. Mesenchymal stromal cells and immunomodulation: A gathering of regulatory immune cells. **Cytotherapy**, v. 18, n. 2, p. 160–171, fev. 2016.

NAJAR, M. et al. Insights into inflammatory priming of mesenchymal stromal cells: functional biological impacts. **Inflammation Research**, v. 67, n. 6, p. 467–477, 23 jun. 2018.

NAMDAR, D. et al. Terpenoids and Phytocannabinoids Co-Produced in Cannabis Sativa Strains Show Specific Interaction for Cell Cytotoxic Activity. **Molecules**, v. 24, n. 17, p. 3031, 21 ago. 2019.

NAVARRETE, F. et al. Endocannabinoid System Components as Potential Biomarkers in Psychiatry. **Frontiers in Psychiatry**, v. 11, 27 abr. 2020.

NICOLUSSI, S.; GERTSCH, J. Endocannabinoid Transport Revisited. Em: [s.l: s.n.]. p. 441–485.

NIE, Y. et al. Defective phenotype of mesenchymal stem cells in patients with systemic lupus erythematosus. **Lupus**, v. 19, n. 7, p. 850–859, 1 jun. 2010.

NIZZOLI, G. et al. IL-10 promotes homeostatic proliferation of human $CD8^+$ memory T cells and, when produced by $CD1c^+$ DCs, shapes naive $CD8^+$ T-cell priming. **European Journal of Immunology**, v. 46, n. 7, p. 1622–1632, jul. 2016.

NOMURA, D. K. et al. Endocannabinoid Hydrolysis Generates Brain Prostaglandins That Promote Neuroinflammation. **Science**, v. 334, n. 6057, p. 809–813, 11 nov. 2011.

NORONHA, N. DE C. et al. Priming approaches to improve the efficacy of mesenchymal stromal cell-based therapies. **Stem Cell Research & Therapy**, v. 10, n. 1, p. 131, 2 dez. 2019.

NOWAK-STĘPNIOWSKA, A. et al. Insight in Hypoxia-Mimetic Agents as Potential Tools for Mesenchymal Stem Cell Priming in Regenerative Medicine. **Stem Cells International**, v. 2022, p. 1–24, 26 mar. 2022.

NYILAS, R. et al. Enzymatic Machinery for Endocannabinoid Biosynthesis Associated with Calcium Stores in Glutamatergic Axon Terminals. **Journal of Neuroscience**, v. 28, n. 5, p. 1058–1063, 30 jan. 2008.

NYÍRI, G. et al. $GABA_B$ and CB_1 cannabinoid receptor expression identifies two types of septal cholinergic neurons. **European Journal of Neuroscience**, v. 21, n. 11, p. 3034–3042, jun. 2005.

ODDI, S. et al. Pitfalls and solutions in assaying anandamide transport in cells. **Journal of Lipid Research**, v. 51, n. 8, p. 2435–2444, ago. 2010.

ODDI, S.; SCIPIONI, L.; MACCARRONE, M. Endocannabinoid system and adult neurogenesis: a focused review. **Current Opinion in Pharmacology**, v. 50, p. 25–32, fev. 2020.

OKAMOTO, Y. et al. Molecular Characterization of a Phospholipase D Generating Anandamide and Its Congeners. **Journal of Biological Chemistry**, v. 279, n. 7, p. 5298–5305, fev. 2004.

OKAMOTO, Y.; TSUBOI, K.; UEDA, N. Chapter 1 Enzymatic Formation of Anandamide. Em: [s.l: s.n.]. p. 1–24.

OKINE, B. N.; GASPAR, J. C.; FINN, D. P. PPARs and pain. **British Journal of Pharmacology**, v. 176, n. 10, p. 1421–1442, maio 2019.

O'SULLIVAN, S. E. Cannabinoids go nuclear: evidence for activation of peroxisome proliferator-activated receptors. **British Journal of Pharmacology**, v. 152, n. 5, p. 576–582, nov. 2007.

PACHER, P.; BÁTKAI, S.; KUNOS, G. The Endocannabinoid System as an Emerging Target of Pharmacotherapy. **Pharmacological Reviews**, v. 58, n. 3, p. 389–462, set. 2006.

PACHER, P.; STEFFENS, S. The emerging role of the endocannabinoid system in cardiovascular disease. **Seminars in Immunopathology**, v. 31, n. 1, p. 63–77, 9 jun. 2009.

PACINI, S. Deterministic and stochastic approaches in the clinical application of mesenchymal stromal cells (MSCs). **Frontiers in Cell and Developmental Biology**, v. 2, 12 set. 2014.

PAGANO, C.; ROSSATO, M.; VETTOR, R. Endocannabinoids, Adipose Tissue and Lipid Metabolism. **Journal of Neuroendocrinology**, v. 20, n. s1, p. 124–129, maio 2008.

PAGANO, S. et al. Biological effects of Cannabidiol on normal human healthy cell populations: Systematic review of the literature. **Biomedicine & Pharmacotherapy**, v. 132, p. 110728, dez. 2020.

PAN, H. et al. Cannabidiol Attenuates Cisplatin-Induced Nephrotoxicity by Decreasing Oxidative/Nitrosative Stress, Inflammation, and Cell Death. **Journal of Pharmacology and Experimental Therapeutics**, v. 328, n. 3, p. 708–714, mar. 2009.

PARK, B.-W. et al. In vivo priming of human mesenchymal stem cells with hepatocyte growth factor–engineered mesenchymal stem cells promotes therapeutic potential for cardiac repair. **Science Advances**, v. 6, n. 13, 27 mar. 2020a.

PARK, H.-S. et al. Anti-microbial and anti-inflammatory effects of Cheonwangbosim-dan against *Helicobacter pylori*- induced gastritis. **Journal of Veterinary Science**, v. 21, 2020b.

PARK, S. E. et al. Exposure of Mesenchymal Stem Cells to an Alzheimer's Disease Environment Enhances Therapeutic Effects. **Stem Cells International**, v. 2021, p. 1–14, 16 mar. 2021.

PARK, Y.; WATKINS, B. A. Endocannabinoids and aging—Inflammation, neuroplasticity, mood and pain. Em: [s.l: s.n.]. p. 129–172.

PATEL, S. et al. The endocannabinoid system as a target for novel anxiolytic drugs. **Neuroscience & Biobehavioral Reviews**, v. 76, p. 56–66, maio 2017.

PEREZ, E. et al. In Vitro and Clinical Evaluation of Cannabigerol (CBG) Produced via Yeast Biosynthesis: A Cannabinoid with a Broad Range of Anti-Inflammatory and Skin Health-Boosting Properties. **Molecules**, v. 27, n. 2, p. 491, 13 jan. 2022.

PERTWEE, R. G. Cannabinoid receptors and pain. **Progress in Neurobiology**, v. 63, n. 5, p. 569–611, abr. 2001.

PERTWEE, R. G. et al. International Union of Basic and Clinical Pharmacology. LXXIX. Cannabinoid Receptors and Their Ligands: Beyond CB_1 and CB_2. **Pharmacological Reviews**, v. 62, n. 4, p. 588–631, 15 dez. 2010.

PETRESCU, N. B. et al. Cannabidiol and Vitamin D3 Impact on Osteogenic Differentiation of Human Dental Mesenchymal Stem Cells. **Medicina**, v. 56, n. 11, p. 607, 12 nov. 2020.

PETROCELLIS, L. DE; CASCIO, M. G.; MARZO, V. DI. The endocannabinoid system: a general view and latest additions. **British Journal of Pharmacology**, v. 141, n. 5, p. 765–774, mar. 2004.

PEYRAVIAN, N. et al. The Anti-Inflammatory Effects of Cannabidiol (CBD) on Acne. **Journal of Inflammation Research**, v. Volume 15, p. 2795–2801, maio 2022.

PIOMELLI, D. More surprises lying ahead. The endocannabinoids keep us guessing. **Neuropharmacology**, v. 76, p. 228–234, jan. 2014.

PISANTI, S.; BIFULCO, M. Medical *Cannabis* : A plurimillennial history of an evergreen. **Journal of Cellular Physiology**, v. 234, n. 6, p. 8342–8351, 11 jun. 2019.

PITTENGER, M. F. et al. Multilineage Potential of Adult Human Mesenchymal Stem Cells. **Science**, v. 284, n. 5411, p. 143–147, 2 abr. 1999.

POOMANI, M. S. et al. Mesenchymal Stem Cell (MSCs) Therapy for Ischemic Heart Disease: A Promising Frontier. **Global Heart**, v. 17, n. 1, 3 mar. 2022.

PORTER, A. C. et al. Characterization of a Novel Endocannabinoid, Virodhamine, with Antagonist Activity at the CB1 Receptor. **Journal of Pharmacology and Experimental Therapeutics**, v. 301, n. 3, p. 1020–1024, 1 jun. 2002.

POTSCHKA, H. et al. Cannabidiol in canine epilepsy. **The Veterinary Journal**, v. 290, p. 105913, dez. 2022.

PRASANNA, S. J. et al. Pro-Inflammatory Cytokines, IFNγ and TNFα, Influence Immune Properties of Human Bone Marrow and Wharton Jelly Mesenchymal Stem Cells Differentially. **PLoS ONE**, v. 5, n. 2, p. e9016, 2 fev. 2010.

PREMKUMAR, L.; SIKAND, P. TRPV1: A Target for Next Generation Analgesics. **Current Neuropharmacology**, v. 6, n. 2, p. 151–163, 1 jun. 2008.

PREMOLI, M. et al. Cannabidiol: Recent advances and new insights for neuropsychiatric disorders treatment. **Life Sciences**, v. 224, p. 120–127, maio 2019.

PROCACCIA, S. et al. Cannabis for Medical Use: Versatile Plant Rather Than a Single Drug. **Frontiers in Pharmacology**, v. 13, 25 abr. 2022.

PROCKOP, D. J.; YOUN OH, J. Mesenchymal Stem/Stromal Cells (MSCs): Role as Guardians of Inflammation. **Molecular Therapy**, v. 20, n. 1, p. 14–20, jan. 2012.

PRYCE, G.; BAKER, D. Control of Spasticity in a Multiple Sclerosis Model is mediated by CB_1, not CB_2, Cannabinoid Receptors. **British Journal of Pharmacology**, v. 150, n. 4, p. 519–525, fev. 2007.

QI, X. et al. Investigation of in vitro odonto/osteogenic capacity of cannabidiol on human dental pulp cell. **Journal of Dentistry**, v. 109, p. 103673, jun. 2021.

QIN, Y.; ZHANG, C. Endothelial progenitor cell-derived extracellular vesicle-meditated cell-to-cell communication regulates the proliferation and osteoblastic differentiation of bone mesenchymal stromal cells. **Molecular Medicine Reports**, v. 16, n. 5, p. 7018–7024, maio 2017.

QUAGHEBEUR, K. et al. Cannabiorci- and 8-chlorocannabiorcichromenic acid as fungal antagonists from Cylindrocarpon olidum. **Phytochemistry**, v. 37, n. 1, p. 159–161, jan. 1994.

RADMANESH, F. et al. The immunomodulatory effects of mesenchymal stromal cell-based therapy in human and animal models of systemic lupus erythematosus. **IUBMB Life**, v. 72, n. 11, p. 2366–2381, 2 nov. 2020.

RADWAN, M. M. et al. Cannabinoids, Phenolics, Terpenes and Alkaloids of Cannabis. **Molecules**, v. 26, n. 9, p. 2774, 8 maio 2021.

RAHMAN, I. A. S. et al. New players in the fatty acyl ethanolamide metabolism. **Pharmacological Research**, v. 86, p. 1–10, ago. 2014.

RAHN, E. J.; HOHMANN, A. G. Cannabinoids as pharmacotherapies for neuropathic pain: From the bench to the bedside. **Neurotherapeutics**, v. 6, n. 4, p. 713–737, out. 2009.

RAMAN, P. et al. 15-Deoxy-$\Delta^{12,14}$-prostaglandin J_2-Glycerol Ester, a Putative Metabolite of 2-Arachidonyl Glycerol, Activates Peroxisome Proliferator Activated Receptor γ. **Molecular Pharmacology**, v. 80, n. 1, p. 201–209, jul. 2011.

RAMER, R.; SCHWARZ, R.; HINZ, B. Modulation of the Endocannabinoid System as a Potential Anticancer Strategy. **Frontiers in Pharmacology**, v. 10, 9 maio 2019.

RAUSCH, S. M. et al. SNPs in PTGS2 and LTA predict pain and quality of life in long term lung cancer survivors. **Lung Cancer**, v. 77, n. 1, p. 217–223, jul. 2012.

RAVINET TRILLOU, C. et al. CB1 cannabinoid receptor knockout in mice leads to leanness, resistance to diet-induced obesity and enhanced leptin sensitivity. **International Journal of Obesity**, v. 28, n. 4, p. 640–648, 10 abr. 2004.

REDDY, D. S.; GOLUB, V. M. The Pharmacological Basis of Cannabis Therapy for Epilepsy. **Journal of Pharmacology and Experimental Therapeutics**, v. 357, n. 1, p. 45–55, 1 mar. 2016.

REDDY, P. V. et al. N-acylation of dog heart ethanolamine phospholipids by transacylase activity. **Biochimica et Biophysica Acta (BBA) - Lipids and Lipid Metabolism**, v. 750, n. 3, p. 472–480, mar. 1983.

REGMI, S. et al. Mesenchymal stromal cells for the treatment of Alzheimer's disease: Strategies and limitations. **Frontiers in Molecular Neuroscience**, v. 15, 6 out. 2022.

REINDERS, M. E. J. et al. Proinflammatory functions of vascular endothelial growth factor in alloimmunity. **Journal of Clinical Investigation**, v. 112, n. 11, p. 1655–1665, 1 dez. 2003.

REISENBERG, M. et al. The diacylglycerol lipases: structure, regulation and roles in and beyond endocannabinoid signalling. **Philosophical Transactions of the Royal Society B: Biological Sciences**, v. 367, n. 1607, p. 3264–3275, 5 dez. 2012.

REN, J. et al. Mesenchymal Stem Cells and their Exosomes: Promising Therapeutics for Chronic Pain. **Current Stem Cell Research & Therapy**, v. 14, n. 8, p. 644–653, 27 nov. 2019.

RENNICK, D. M.; FORT, M. M.; DAVIDSON, N. J. Studies with IL-10-/- mice: an overview. **Journal of Leukocyte Biology**, v. 61, n. 4, p. 389–396, 1 abr. 1997.

RIGGS, P. K. et al. A pilot study of the effects of cannabis on appetite hormones in HIV-infected adult men. **Brain Research**, v. 1431, p. 46–52, jan. 2012.

RINALDI, V. et al. Expression of cannabinoid receptors CB1 and CB2 in canine cutaneous mast cell tumours. **Research in Veterinary Science**, v. 152, p. 530–536, dez. 2022.

RIVERA, P. et al. Obesity-dependent cannabinoid modulation of proliferation in adult neurogenic regions. **European Journal of Neuroscience**, v. 33, n. 9, p. 1577–1586, maio 2011.

ROCKWELL, C. E.; KAMINSKI, N. E. A Cyclooxygenase Metabolite of Anandamide Causes Inhibition of Interleukin-2 Secretion in Murine Splenocytes. **Journal of Pharmacology and Experimental Therapeutics**, v. 311, n. 2, p. 683–690, nov. 2004.

RODRIGUES DA SILVA, N. et al. Cannabidiol attenuates behavioral changes in a rodent model of schizophrenia through 5-HT1A, but not CB1 and CB2 receptors. **Pharmacological Research**, v. 156, p. 104749, jun. 2020.

RODRÍGUEZ DE FONSECA, F. et al. THE ENDOCANNABINOID SYSTEM: PHYSIOLOGY AND PHARMACOLOGY. **Alcohol and Alcoholism**, v. 40, n. 1, p. 2–14, 1 jan. 2005.

RODRÍGUEZ MESA, X. M. et al. Therapeutic Prospects of Cannabinoids in the Immunomodulation of Prevalent Autoimmune Diseases. **Cannabis and Cannabinoid Research**, v. 6, n. 3, p. 196–210, 1 jun. 2021.

RODRÍGUEZ SÁNCHEZ, D. N. et al. Canine Adipose-Derived Mesenchymal Stromal Cells Enhance Neuroregeneration in a Rat Model of Sciatic Nerve Crush Injury. **Cell Transplantation**, v. 28, n. 1, p. 47–54, 28 jan. 2019.

ROSSI, F. et al. The Cannabinoid Receptor Type 2 as Mediator of Mesenchymal Stromal Cell Immunosuppressive Properties. **PLoS ONE**, v. 8, n. 11, p. e80022, 27 nov. 2013.

RUAN, X. et al. Exosomes from Suxiao Jiuxin pill-treated cardiac mesenchymal stem cells decrease H3K27 demethylase UTX expression in mouse cardiomyocytes in vitro. **Acta Pharmacologica Sinica**, v. 39, n. 4, p. 579–586, 15 abr. 2018.

RUBINO, T. et al. Cellular Mechanisms Underlying the Anxiolytic Effect of Low Doses of Peripheral Δ9-Tetrahydrocannabinol in Rats. **Neuropsychopharmacology**, v. 32, n. 9, p. 2036–2045, 7 set. 2007.

RUBINO, T. et al. CB1 receptor stimulation in specific brain areas differently modulate anxiety-related behaviour. **Neuropharmacology**, v. 54, n. 1, p. 151–160, jan. 2008.

RUHL, T. et al. The endocannabinoid receptors CB1 and CB2 affect the regenerative potential of adipose tissue MSCs. **Experimental Cell Research**, v. 389, n. 1, p. 111881, abr. 2020.

RUHL, T. et al. Genetic deletion of the cannabinoid receptors CB1 and CB2 enhances inflammation with diverging effects on skin wound healing in mice. **Life Sciences**, v. 285, p. 120018, nov. 2021.

RUHL, T.; KIM, B.-S.; BEIER, J. P. Cannabidiol restores differentiation capacity of LPS exposed adipose tissue mesenchymal stromal cells. **Experimental Cell Research**, v. 370, n. 2, p. 653–662, set. 2018.

RURALI, E. et al. New Strategies to Enhance Myocardial Regeneration: Expectations and Challenges from Preclinical Evidence. **Current Stem Cell Research & Therapy**, v. 15, n. 8, p. 696–710, 10 nov. 2020.

RUSSO, E. B. et al. Agonistic Properties of Cannabidiol at 5-HT1a Receptors. **Neurochemical Research**, v. 30, n. 8, p. 1037–1043, ago. 2005.

RYAN, D. et al. Cannabidiol Targets Mitochondria to Regulate Intracellular Ca $^{2+}$ Levels. **The Journal of Neuroscience**, v. 29, n. 7, p. 2053–2063, 18 fev. 2009.

RYSKAMP, D. et al. TRPV1 and Endocannabinoids: Emerging Molecular Signals that Modulate Mammalian Vision. **Cells**, v. 3, n. 3, p. 914–938, 12 set. 2014.

SAATCIOGLU, E. et al. Design and fabrication of electrospun polycaprolactone/chitosan scaffolds for ligament regeneration. **European Polymer Journal**, v. 148, p. 110357, abr. 2021.

SADATPOOR, S. OMID et al. Manipulated Mesenchymal Stem Cells Applications in Neurodegenerative Diseases. **International Journal of Stem Cells**, v. 13, n. 1, p. 24–45, 30 mar. 2020.

SÁNCHEZ, G. B.; AMORIM, R. M. **TRANSPLANTE DE CÉLULAS-TRONCO MESENQUIMAIS ALOGÊNICAS EM CÃES COM MENINGOENCEFALOMIELITE DE ORIGEM DESCONHECIDA**. Clínica veterinária—Botucatu: Universidade Estadual Paulista (Unesp), 5 fev. 2021.

SANTONI, G. et al. Transient Receptor Potential Cation Channels in Cancer Therapy. **Medical Sciences**, v. 7, n. 12, p. 108, 30 nov. 2019.

SASAKI, A. et al. Mesenchymal stem cells for cartilage regeneration in dogs. **World Journal of Stem Cells**, v. 11, n. 5, p. 254–269, 26 maio 2019.

SCHEPER, V. et al. BDNF-overexpressing human mesenchymal stem cells mediate increased neuronal protection *in vitro*. **Journal of Neuroscience Research**, v. 97, n. 11, p. 1414–1429, 30 nov. 2019.

SCHMID, H. H. O.; SCHMID, P. C.; NATARAJAN, V. N-Acylated glycerophospholipids and their derivatives. **Progress in Lipid Research**, v. 29, n. 1, p. 1–43, jan. 1990.

SCHMUHL, E. et al. Increase of mesenchymal stem cell migration by cannabidiol via activation of p42/44 MAPK. **Biochemical Pharmacology**, v. 87, n. 3, p. 489–501, fev. 2014.

SCHOUTEN, M.; DALLE, S.; KOPPO, K. Molecular Mechanisms Through Which Cannabidiol May Affect Skeletal Muscle Metabolism, Inflammation, Tissue Regeneration, and Anabolism: A Narrative Review. **Cannabis and Cannabinoid Research**, v. 7, n. 6, p. 745–757, 1 dez. 2022.

SELTZER, E. S. et al. Cannabidiol (CBD) as a Promising Anti-Cancer Drug. **Cancers**, v. 12, n. 11, p. 3203, 30 out. 2020.

SHAH, K.; ZHAO, A. G.; SUMER, H. New Approaches to Treat Osteoarthritis with Mesenchymal Stem Cells. **Stem Cells International**, v. 2018, p. 1–9, 16 set. 2018.

SHAHBAZI, F. et al. Cannabinoids and Cannabinoid Receptors: The Story so Far. **iScience**, v. 23, n. 7, p. 101301, jul. 2020.

SHAMMAA, R. et al. Mesenchymal Stem Cells Beyond Regenerative Medicine. **Frontiers in Cell and Developmental Biology**, v. 8, 18 fev. 2020.

SHARPE, L. et al. Cannabis, a cause for anxiety? A critical appraisal of the anxiogenic and anxiolytic properties. **Journal of Translational Medicine**, v. 18, n. 1, p. 374, 2 dez. 2020.

SHARUN, K. et al. Clinical evaluation following the percutaneous transplantation of allogenic bone marrow-derived mesenchymal stem cells (aBM-MSC) in dogs affected by vertebral compression fracture. **Veterinary and Animal Science**, v. 10, p. 100152, dez. 2020.

SHBIRO, L. et al. Effects of cannabidiol in males and females in two different rat models of depression. **Physiology & Behavior**, v. 201, p. 59–63, mar. 2019.

SHI, J. et al. Demineralized Bone Matrix Scaffolds Modified by CBD-SDF-1α Promote Bone Regeneration via Recruiting Endogenous Stem Cells. **ACS Applied Materials & Interfaces**, v. 8, n. 41, p. 27511–27522, 19 out. 2016.

SHI, Y. et al. Immunoregulatory mechanisms of mesenchymal stem and stromal cells in inflammatory diseases. **Nature Reviews Nephrology**, v. 14, n. 8, p. 493–507, 12 ago. 2018.

SHOWALTER, M. R. et al. Primed mesenchymal stem cells package exosomes with metabolites associated with immunomodulation. **Biochemical and Biophysical Research Communications**, v. 512, n. 4, p. 729–735, maio 2019.

SIMMONS, D. L.; BOTTING, R. M.; HLA, T. Cyclooxygenase Isozymes: The Biology of Prostaglandin Synthesis and Inhibition. **Pharmacological Reviews**, v. 56, n. 3, p. 387–437, set. 2004.

SINGER, N. G.; CAPLAN, A. I. Mesenchymal Stem Cells: Mechanisms of Inflammation. **Annual Review of Pathology: Mechanisms of Disease**, v. 6, n. 1, p. 457–478, 28 fev. 2011.

SIPP, D.; ROBEY, P. G.; TURNER, L. Clear up this stem-cell mess. **Nature**, v. 561, n. 7724, p. 455–457, 26 set. 2018.

SKELLEY, J. W. et al. Use of cannabidiol in anxiety and anxiety-related disorders. **Journal of the American Pharmacists Association**, v. 60, n. 1, p. 253–261, jan. 2020.

SOLIMAN, N. et al. Systematic review and meta-analysis of cannabinoids, cannabis-based medicines, and endocannabinoid system modulators tested for antinociceptive effects in animal models of injury-related or pathological persistent pain. **Pain**, v. 162, p. 26–26, 15 mar. 2020.

SONG, H. et al. l-Kynurenine-induced apoptosis in human NK cells is mediated by reactive oxygen species. **International Immunopharmacology**, v. 11, n. 8, p. 932–938, ago. 2011.

SOUNDARA RAJAN, T. et al. Cannabidiol Activates Neuronal Precursor Genes in Human Gingival Mesenchymal Stromal Cells. **Journal of Cellular Biochemistry**, v. 118, n. 6, p. 1531–1546, 29 jun. 2017.

SOUSA, B. R. et al. Human adult stem cells from diverse origins: An overview from multiparametric immunophenotyping to clinical applications. **Cytometry Part A**, v. 85, n. 1, p. 43–77, jan. 2014.

SPINELLA, G. et al. Overview of the Current Literature on the Most Common Neurological Diseases in Dogs with a Particular Focus on Rehabilitation. **Veterinary Sciences**, v. 9, n. 8, p. 429, 13 ago. 2022.

STEFKOV, G. et al. Analytical Techniques for Phytocannabinoid Profiling of Cannabis and Cannabis-Based Products—A Comprehensive Review. **Molecules**, v. 27, n. 3, p. 975, 1 fev. 2022.

STELLA, N. Endocannabinoid signaling in microglial cells. **Neuropharmacology**, v. 56, p. 244–253, jan. 2009.

STOTT, C. G. et al. The Proposed Multimodal Mechanism of Action of Cannabidiol (CBD) in Epilepsy: Modulation of Intracellular Calcium and Adenosine-mediated Signalling. **Epilepsy & Behavior**, v. 101, p. 106734, dez. 2019.

STRAUS, D. S.; GLASS, C. K. Anti-inflammatory actions of PPAR ligands: new insights on cellular and molecular mechanisms. **Trends in Immunology**, v. 28, n. 12, p. 551–558, dez. 2007.

SU, P. et al. Mesenchymal Stem Cell Migration during Bone Formation and Bone Diseases Therapy. **International Journal of Molecular Sciences**, v. 19, n. 8, p. 2343, 9 ago. 2018.

SUGIURA, T.; WAKU, K. 2-Arachidonoylglycerol and the cannabinoid receptors. **Chemistry and Physics of Lipids**, v. 108, n. 1–2, p. 89–106, nov. 2000.

SUN, Y.; DOLMETSCH, R. E. Investigating the Therapeutic Mechanism of Cannabidiol in a Human Induced Pluripotent Stem Cell (iPSC)-Based Model of Dravet Syndrome. **Cold Spring Harbor Symposia on Quantitative Biology**, v. 83, p. 185–191, 2018.

SUN, Y.-X. et al. Activation of Cannabinoid Receptor 2 Enhances Osteogenic Differentiation of Bone Marrow Derived Mesenchymal Stem Cells. **BioMed Research International**, v. 2015, p. 1–8, 2015.

SUNDA, F.; AROWOLO, A. A molecular basis for the anti-inflammatory and anti-fibrosis properties of cannabidiol. **The FASEB Journal**, v. 34, n. 11, p. 14083–14092, 3 nov. 2020.

TAKEDA, K. et al. Activation of p70S6 Kinase-1 in Mesenchymal Stem Cells Is Essential to Lung Tissue Repair. **Stem Cells Translational Medicine**, v. 7, n. 7, p. 551–558, 1 jul. 2018.

TANAKA, M. et al. Anti-Inflammatory Effects by Pharmacological Inhibition or Knockdown of Fatty Acid Amide Hydrolase in BV2 Microglial Cells. **Cells**, v. 8, n. 5, p. 491, 22 maio 2019.

TAVAKOLI, S. et al. Mesenchymal stromal cells; a new horizon in regenerative medicine. **Journal of Cellular Physiology**, v. 235, n. 12, p. 9185–9210, 26 dez. 2020.

TEJEDA-MARTÍNEZ, A. R. et al. Chronic Inhibition of FAAH Reduces Depressive-Like Behavior and Improves Dentate Gyrus Proliferation after Chronic Unpredictable Stress Exposure. **Behavioural Neurology**, v. 2021, p. 1–14, 24 mar. 2021.

TELI, P.; KALE, V.; VAIDYA, A. Extracellular vesicles isolated from mesenchymal stromal cells primed with neurotrophic factors and signaling modifiers as potential therapeutics for neurodegenerative diseases. **Current Research in Translational Medicine**, v. 69, n. 2, p. 103286, maio 2021.

THEEUWES, W. F. et al. The role of inflammation in mesenchymal stromal cell therapy in osteoarthritis, perspectives for post-traumatic osteoarthritis: a review. **Rheumatology**, v. 60, n. 3, p. 1042–1053, 2 mar. 2021.

TI, D. et al. LPS-preconditioned mesenchymal stromal cells modify macrophage polarization for resolution of chronic inflammation via exosome-shuttled let-7b. **Journal of Translational Medicine**, v. 13, n. 1, p. 308, 19 dez. 2015.

TRIVEDI, P.; HEMATTI, P. Derivation and immunological characterization of mesenchymal stromal cells from human embryonic stem cells. **Experimental Hematology**, v. 36, n. 3, p. 350–359, mar. 2008.

TU, Z. et al. Mesenchymal Stem Cells Inhibit Complement Activation by Secreting Factor H. **Stem Cells and Development**, v. 19, n. 11, p. 1803–1809, nov. 2010.

TURCOTTE, C. et al. The CB2 receptor and its role as a regulator of inflammation. **Cellular and Molecular Life Sciences**, v. 73, n. 23, p. 4449–4470, 11 dez. 2016.

TURNER, S. E. et al. Molecular Pharmacology of Phytocannabinoids. Em: [s.l: s.n.]. p. 61–101.

UCHIGASHIMA, M. et al. Subcellular Arrangement of Molecules for 2-Arachidonoyl-Glycerol-Mediated Retrograde Signaling and Its Physiological Contribution to Synaptic Modulation in the Striatum. **Journal of Neuroscience**, v. 27, n. 14, p. 3663–3676, 4 abr. 2007.

UEDA, N. et al. Biosynthesis and degradation of the endocannabinoid 2-arachidonoylglycerol. **BioFactors**, v. 37, n. 1, p. 1–7, jan. 2011.

ULLAH, M.; LIU, D. D.; THAKOR, A. S. Mesenchymal Stromal Cell Homing: Mechanisms and Strategies for Improvement. **iScience**, v. 15, p. 421–438, maio 2019.

VALERI, A.; MAZZON, E. Cannabinoids and Neurogenesis: The Promised Solution for Neurodegeneration? **Molecules**, v. 26, n. 20, p. 6313, 19 out. 2021.

VAN BAKEL, H. et al. The draft genome and transcriptome of Cannabis sativa. **Genome Biology**, v. 12, n. 10, p. R102, 2011.

VAN DER STELT, M.; DI MARZO, V. Endovanilloids. Putative endogenous ligands of transient receptor potential vanilloid 1 channels. **European Journal of Biochemistry**, v. 271, n. 10, p. 1827–1834, maio 2004.

VATER, C.; KASTEN, P.; STIEHLER, M. Culture media for the differentiation of mesenchymal stromal cells. **Acta Biomaterialia**, v. 7, n. 2, p. 463–477, fev. 2011.

VIADER, A. et al. A chemical proteomic atlas of brain serine hydrolases identifies cell type-specific pathways regulating neuroinflammation. **eLife**, v. 5, 18 jan. 2016.

VIDAL, R. et al. New Strategies in the Development of Antidepressants: Towards the Modulation of Neuroplasticity Pathways. **Current Pharmaceutical Design**, v. 17, n. 5, p. 521–533, 1 fev. 2011.

VIEIRA, N. M. et al. Isolation, Characterization, and Differentiation Potential of Canine Adipose-Derived Stem Cells. **Cell Transplantation**, v. 19, n. 3, p. 279–289, 1 mar. 2010.

VISWANATHAN, S. et al. Mesenchymal stem versus stromal cells: International Society for Cell & Gene Therapy (ISCT®) Mesenchymal Stromal Cell committee position statement on nomenclature. **Cytotherapy**, v. 21, n. 10, p. 1019–1024, out. 2019.

VOGA, M.; KOVAČ, V.; MAJDIC, G. Comparison of Canine and Feline Adipose-Derived Mesenchymal Stem Cells/Medicinal Signaling Cells With Regard to Cell Surface Marker Expression, Viability, Proliferation, and Differentiation Potential. **Frontiers in Veterinary Science**, v. 7, 13 jan. 2021.

WAGNER, W.; HO, A. D. Mesenchymal Stem Cell Preparations—Comparing Apples and Oranges. **Stem Cell Reviews**, v. 3, n. 4, p. 239–248, 18 dez. 2007.

WALKER, F. C.; SRIDHAR, P. R.; BALDRIDGE, M. T. Differential roles of interferons in innate responses to mucosal viral infections. **Trends in Immunology**, v. 42, n. 11, p. 1009–1023, nov. 2021.

WALTER, C. et al. Brain Mapping-Based Model of Δ9-Tetrahydrocannabinol Effects on Connectivity in the Pain Matrix. **Neuropsychopharmacology**, v. 41, n. 6, p. 1659–1669, 30 maio 2016.

WANG, B. et al. New AKT-dependent mechanisms of anti-COVID-19 action of high-CBD Cannabis sativa extracts. **Cell Death Discovery**, v. 8, n. 1, p. 110, 11 mar. 2022.

WANG, H. et al. Mesenchymal stem cells microvesicles stabilize endothelial barrier function partly mediated by hepatocyte growth factor (HGF). **Stem Cell Research & Therapy**, v. 8, n. 1, p. 211, 29 dez. 2017.

WANG, M.; YUAN, Q.; XIE, L. Mesenchymal Stem Cell-Based Immunomodulation: Properties and Clinical Application. **Stem Cells International**, v. 2018, p. 1–12, 14 jun. 2018.

WATT, G.; KARL, T. In vivo Evidence for Therapeutic Properties of Cannabidiol (CBD) for Alzheimer's Disease. **Frontiers in Pharmacology**, v. 8, 3 fev. 2017.

WEISS, L. et al. Cannabidiol lowers incidence of diabetes in non-obese diabetic mice. **Autoimmunity**, v. 39, n. 2, p. 143–151, 7 jan. 2006.

WELLNER, N. et al. N-acylation of phosphatidylethanolamine and its biological functions in mammals. **Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids**, v. 1831, n. 3, p. 652–662, mar. 2013.

WHELAN, D. S.; CAPLICE, N. M.; CLOVER, A. J. P. Mesenchymal stromal cell derived CCL2 is required for accelerated wound healing. **Scientific Reports**, v. 10, n. 1, p. 2642, 14 fev. 2020.

WIELAND, H. A. et al. Osteoarthritis — an untreatable disease? **Nature Reviews Drug Discovery**, v. 4, n. 4, p. 331–344, abr. 2005.

WILSON, A. J. et al. Characterisation of mesenchymal stromal cells in clinical trial reports: analysis of published descriptors. **Stem Cell Research & Therapy**, v. 12, n. 1, p. 360, 22 dez. 2021.

WILSON-POE, A. R. et al. Effects of inflammatory pain on CB1 receptor in the midbrain periaqueductal gray. **PAIN Reports**, v. 6, n. 1, p. e897, jan. 2021.

WINTER, J. TRPV1 distribution and regulation. Em: **Turning up the Heat on Pain: TRPV1 Receptors in Pain and Inflammation**. Basel: Birkhäuser Basel, 2005. p. 39–51.

WOODHAMS, S. G. et al. The Role of the Endocannabinoid System in Pain. Em: [s.l: s.n.]. p. 119–143.

WU, J. et al. Studies of involvement of G-protein coupled receptor-3 in cannabidiol effects on inflammatory responses of mouse primary astrocytes and microglia. **PLOS ONE**, v. 16, n. 5, p. e0251677, 13 maio 2021.

XIE, J. et al. Up-regulation of immunomodulatory effects of mouse bone-marrow derived mesenchymal stem cells by tetrahydrocannabinol pre-treatment involving cannabinoid receptor CB2. **Oncotarget**, v. 7, n. 6, p. 6436–6447, 9 fev. 2016.

XU, C. et al. Cross-Talking Between PPAR and WNT Signaling and its Regulation in Mesenchymal Stem Cell Differentiation. **Current Stem Cell Research & Therapy**, v. 11, n. 3, p. 247–254, 3 mar. 2016.

YAGI, H. et al. Mesenchymal Stem Cells: Mechanisms of Immunomodulation and Homing. **Cell Transplantation**, v. 19, n. 6–7, p. 667–679, 1 jun. 2010.

YANG, Y. et al. New chromane and chromene meroterpenoids from flowers of Rhododendron rubiginosum Franch. var. rubiginosum. **Fitoterapia**, v. 127, p. 396–401, jun. 2018.

YATES, M. L.; BARKER, E. L. Chapter 2 Organized Trafficking of Anandamide and Related Lipids. Em: [s.l: s.n.]. p. 25–53.

YEN, B. L. et al. Brief Report—Human Embryonic Stem Cell-Derived Mesenchymal Progenitors Possess Strong Immunosuppressive Effects Toward Natural Killer Cells as Well as T Lymphocytes. **Stem Cells**, v. 27, n. 2, p. 451–456, 1 fev. 2009.

YOSHIDA, T. Localization of Diacylglycerol Lipase- around Postsynaptic Spine Suggests Close Proximity between Production Site of an Endocannabinoid, 2-Arachidonoyl-glycerol, and Presynaptic Cannabinoid CB1 Receptor. **Journal of Neuroscience**, v. 26, n. 18, p. 4740–4751, 3 maio 2006.

YU, B.; ZHANG, X.; LI, X. Exosomes Derived from Mesenchymal Stem Cells. **International Journal of Molecular Sciences**, v. 15, n. 3, p. 4142–4157, 7 mar. 2014.

YU, C. H. J.; RUPASINGHE, H. P. V. Cannabidiol-based natural health products for companion animals: Recent advances in the management of anxiety, pain, and inflammation. **Research in Veterinary Science**, v. 140, p. 38–46, nov. 2021.

YU, S. et al. Fatty Acid-binding Protein 5 (FABP5) Regulates Cognitive Function Both by Decreasing Anandamide Levels and by Activating the Nuclear Receptor Peroxisome Proliferator-activated Receptor β/δ (PPARβ/δ) in the Brain. **Journal of Biological Chemistry**, v. 289, n. 18, p. 12748–12758, maio 2014.

YUAN, M. et al. Δ9-Tetrahydrocannabinol regulates Th1/Th2 cytokine balance in activated human T cells. **Journal of Neuroimmunology**, v. 133, n. 1–2, p. 124–131, dez. 2002.

YUN, C.; LEE, S. Potential and Therapeutic Efficacy of Cell-based Therapy Using Mesenchymal Stem Cells for Acute/chronic Kidney Disease. **International Journal of Molecular Sciences**, v. 20, n. 7, p. 1619, 1 abr. 2019.

ZEIRA, O. et al. Adult autologous mesenchymal stem cells for the treatment of suspected non-infectious inflammatory diseases of the canine central nervous system: safety, feasibility and preliminary clinical findings. **Journal of Neuroinflammation**, v. 12, n. 1, p. 181, 29 dez. 2015.

ZHAN, X.-S. et al. A Comparative Study of Biological Characteristics and Transcriptome Profiles of Mesenchymal Stem Cells from Different Canine Tissues. **International Journal of Molecular Sciences**, v. 20, n. 6, p. 1485, 25 mar. 2019.

ZHANG, R.; ZHENG, F. PPAR-γ and aging: one link through klotho? **Kidney International**, v. 74, n. 6, p. 702–704, set. 2008.

ZHANG, X. et al. RETRACTED ARTICLE: Overexpressing p130/E2F4 in mesenchymal stem cells facilitates the repair of injured alveolar epithelial cells in LPS-induced ARDS mice. **Stem Cell Research & Therapy**, v. 10, n. 1, p. 74, 6 dez. 2019.

ZHANG, Y. et al. An RNA-Sequencing Transcriptome and Splicing Database of Glia, Neurons, and Vascular Cells of the Cerebral Cortex. **Journal of Neuroscience**, v. 34, n. 36, p. 11929–11947, 3 set. 2014.

ZHOU, H. et al. MSC based gene delivery methods and strategies improve the therapeutic efficacy of neurological diseases. **Bioactive Materials**, v. 23, p. 409–437, maio 2023.

ZHOU, X.; HE, X.; REN, Y. Function of microglia and macrophages in secondary damage after spinal cord injury. **Neural Regeneration Research**, v. 9, n. 20, p. 1787, 2014.

ZOGOPOULOS, P. et al. The role of endocannabinoids in pain modulation. **Fundamental & Clinical Pharmacology**, v. 27, n. 1, p. 64–80, fev. 2013.

ZOU, C. et al. Identification of a Ferroptosis-Related Prognostic Gene PTGS2 Based on Risk Modeling and Immune Microenvironment of Early-Stage Cervical Cancer. **Journal of Oncology**, v. 2022, p. 1–32, 8 abr. 2022.

ZOU, S.; KUMAR, U. Cannabinoid Receptors and the Endocannabinoid System: Signaling and Function in the Central Nervous System. **International Journal of Molecular Sciences**, v. 19, n. 3, p. 833, 13 mar. 2018.

ZUARDI, A. W. History of cannabis as a medicine: a review. **Revista Brasileira de Psiquiatria**, v. 28, n. 2, p. 153–157, jun. 2006.

Conclusão

A conclusão deste estudo é que o pré-condicionamento das cAT-MSCs com o extrato de cannabis rico em CBD foi capaz de aumentar a expressão gênica de HGF e diminuir a expressão gênica de BDNF, especialmente na dose mais alta, embora não tenha sido capaz de influenciar a expressão gênica de GDNF, IDO, IL-10, TNF-α, INF-γ e PTGES2.

Considerações finais

A utilização da canabis no pré-condicionamento das MSCs no campo da medicina veterinária é uma área de pesquisa relativamente nova, e seus potenciais benefícios e riscos ainda não são totalmente compreendidos, sendo necessário estudos adicionais para avaliar os efeitos *in vitro* a partir de diferentes abordagens de pré-condicionamento, viabilidade das MSCs pré-condicionadas em relação a criopreservação, modificações epigenéticas geradas por diferentes abordagens de pré-condicionamento, eficácia para diferentes aplicações clínicas, as melhores fontes de isolamento e o uso de diferentes doses. No geral, a expressão de receptores canabinoides nas MSCs sugere que o SEC pode ter um papel importante na regulação do seu comportamento e função, e que o pré-condicionamento utilizando canabinoides como CBD podem ter potenciais aplicações terapêuticas no campo da medicina regenerativa.

Bibliografia

1. Cital S, Kramer K, Hughston L, et al., (eds). Cannabis Therapy in Veterinary Medicine. Springer International Publishing: Cham; 2021.; doi: 10.1007/978-3-030-68317-7.

2. Klahn P. Cannabinoids-Promising Antimicrobial Drugs or Intoxicants with Benefits? Antibiotics 2020;9(6):297; doi: 10.3390/antibiotics9060297.

3. Hesami M, Pepe M, Baiton A, et al. Current status and future prospects in cannabinoid production through in vitro culture and synthetic biology. Biotechnol Adv 2023;62:108074; doi: 10.1016/j.biotechadv.2022.108074.

4. Woodhams SG, Sagar DR, Burston JJ, et al. The Role of the Endocannabinoid System in Pain. 2015; pp. 119–143; doi: 10.1007/978-3-662-46450-2_7.

5. Duranti A, Beldarrain G, Álvarez A, et al. The Endocannabinoid System as a Target for Neuroprotection/Neuroregeneration in Perinatal Hypoxic–Ischemic Brain Injury. Biomedicines 2022;11(1):28; doi: 10.3390/biomedicines11010028.

6. Valeri A, Mazzon E. Cannabinoids and Neurogenesis: The Promised Solution for Neurodegeneration? Molecules 2021;26(20):6313; doi: 10.3390/molecules26206313.

7. D'Aniello E, Fellous T, Iannotti FA, et al. Identification and characterization of phytocannabinoids as novel dual PPARα/γ agonists by a computational and in vitro experimental approach. Biochimica et Biophysica Acta (BBA) - General Subjects 2019;1863(3):586–597; doi: 10.1016/j.bbagen.2019.01.002.

8. Compton AC, Abhyankar V, Stein S, et al. The immunomodulatory role of phytocannabinoids in an *in vitro* peri-implantitis model. Journal of Dental Implant Research 2022;41(4):102–112; doi: 10.54527/jdir.2022.41.4.102.

9. Jones NA, Glyn SE, Akiyama S, et al. Cannabidiol exerts anti-convulsant effects in animal models of temporal lobe and partial seizures. Seizure 2012;21(5):344–352; doi: 10.1016/j.seizure.2012.03.001.

10. Kilaru A, Chapman KD. The endocannabinoid system. Essays Biochem 2020;64(3):485–499; doi: 10.1042/EBC20190086.

11. Soliman N, Haroutounian S, Hohmann AG, et al. Systematic review and meta-analysis of cannabinoids, cannabis-based medicines, and endocannabinoid system modulators tested for antinociceptive effects in animal models of injury-related or pathological persistent pain. Pain 2020;162:26–26; doi: 10.1097/j.pain.0000000000002269.

12. Casey S, Vaughan C. Plant-Based Cannabinoids for the Treatment of Chronic Neuropathic Pain. Medicines 2018;5(3):67; doi: 10.3390/medicines5030067.

13. García-Gutiérrez MS, Navarrete F, Gasparyan A, et al. Cannabidiol: A Potential New Alternative for the Treatment of Anxiety, Depression, and Psychotic Disorders. Biomolecules 2020;10(11):1575; doi: 10.3390/biom10111575.

14. Melas PA, Scherma M, Fratta W, et al. Cannabidiol as a Potential Treatment for Anxiety and Mood Disorders: Molecular Targets and Epigenetic Insights from Preclinical Research. Int J Mol Sci 2021;22(4):1863; doi: 10.3390/ijms22041863.

15. Potschka H, Bhatti SFM, Tipold A, et al. Cannabidiol in canine epilepsy. The Veterinary Journal 2022;290:105913; doi: 10.1016/j.tvjl.2022.105913.

16. Klein TW. Cannabinoid-based drugs as anti-inflammatory therapeutics. Nat Rev Immunol 2005;5(5):400–411; doi: 10.1038/nri1602.

17. Yu CHJ, Rupasinghe HPV. Cannabidiol-based natural health products for companion animals: Recent advances in the management of anxiety, pain, and inflammation. Res Vet Sci 2021;140:38–46; doi: 10.1016/j.rvsc.2021.08.001.

18. Baranowska-Kuczko M, Kozłowska H, Kloza M, et al. Vasoprotective Endothelial Effects of Chronic Cannabidiol Treatment and Its Influence on the Endocannabinoid System in Rats with Primary and Secondary Hypertension. Pharmaceuticals 2021;14(11):1120; doi: 10.3390/ph14111120.

19. Caplan AI, Dennis JE. Mesenchymal stem cells as trophic mediators. J Cell Biochem 2006;98(5):1076–1084; doi: 10.1002/jcb.20886.

20. Shi Y, Wang Y, Li Q, et al. Immunoregulatory mechanisms of mesenchymal stem and stromal cells in inflammatory diseases. Nat Rev Nephrol 2018;14(8):493–507; doi: 10.1038/s41581-018-0023-5.

21. Shammaa R, El-Kadiry AE-H, Abusarah J, et al. Mesenchymal Stem Cells Beyond Regenerative Medicine. Front Cell Dev Biol 2020;8; doi: 10.3389/fcell.2020.00072.

22. Voga M, Kovač V, Majdic G. Comparison of Canine and Feline Adipose-Derived Mesenchymal Stem Cells/Medicinal Signaling Cells With Regard to Cell Surface Marker Expression, Viability, Proliferation, and Differentiation Potential. Front Vet Sci 2021;7; doi: 10.3389/fvets.2020.610240.

23. Radmanesh F, Mahmoudi M, Yazdanpanah E, et al. The immunomodulatory effects of mesenchymal stromal cell-based therapy in human and animal models of systemic lupus erythematosus. IUBMB Life 2020;72(11):2366–2381; doi: 10.1002/iub.2387.

24. Wang M, Yuan Q, Xie L. Mesenchymal Stem Cell-Based Immunomodulation: Properties and Clinical Application. Stem Cells Int 2018;2018:1–12; doi: 10.1155/2018/3057624.

25. Qin Y, Zhang C. Endothelial progenitor cell-derived extracellular vesicle-meditated cell-to-cell communication regulates the proliferation and osteoblastic differentiation of bone mesenchymal stromal cells. Mol Med Rep 2017;16(5):7018–7024; doi: 10.3892/mmr.2017.7403.

26. Harrell CR, Djonov V, Volarevic V. The Cross-Talk between Mesenchymal Stem Cells and Immune Cells in Tissue Repair and Regeneration. Int J Mol Sci 2021;22(5):2472; doi: 10.3390/ijms22052472.

27. Park B-W, Jung S-H, Das S, et al. In vivo priming of human mesenchymal stem cells with hepatocyte growth factor–engineered mesenchymal stem cells promotes therapeutic potential for cardiac repair. Sci Adv 2020;6(13); doi: 10.1126/sciadv.aay6994.

28. Barrachina L, Remacha AR, Romero A, et al. Priming Equine Bone Marrow-Derived Mesenchymal Stem Cells with Proinflammatory Cytokines: Implications in Immunomodulation–Immunogenicity Balance, Cell Viability, and Differentiation Potential. Stem Cells Dev 2017;26(1):15–24; doi: 10.1089/scd.2016.0209.

29. Kowalczuk A, Marycz K, Kornicka-Garbowska K, et al. Cannabidiol (CBD) Protects Adipose-Derived Mesenchymal Stem Cells (ASCs) against Endoplasmic Reticulum Stress Development and Its Complications. Int J Environ Res Public Health 2022;19(17):10864; doi: 10.3390/ijerph191710864.

30. Mathew SA, Chandravanshi B, Bhonde R. Hypoxia primed placental mesenchymal stem cells for wound healing. Life Sci 2017;182:85–92; doi: 10.1016/j.lfs.2017.06.016.

31. Bartosh TJ, Ylostalo JH. Efficacy of 3D Culture Priming is Maintained in Human Mesenchymal Stem Cells after Extensive Expansion of the Cells. Cells 2019;8(9):1031; doi: 10.3390/cells8091031.

32. Libro R, Diomede F, Scionti D, et al. Cannabidiol Modulates the Expression of Alzheimer's Disease-Related Genes in Mesenchymal Stem Cells. Int J Mol Sci 2016;18(1):26; doi: 10.3390/ijms18010026.

33. Petrescu NB, Jurj A, Sorițău O, et al. Cannabidiol and Vitamin D3 Impact on Osteogenic Differentiation of Human Dental Mesenchymal Stem Cells. Medicina (B Aires) 2020;56(11):607; doi: 10.3390/medicina56110607.

34. Chang RC, Thangavelu CS, Joloya EM, et al. Cannabidiol promotes adipogenesis of human and mouse mesenchymal stem cells via PPARγ by inducing lipogenesis but not lipolysis. Biochem Pharmacol 2022;197:114910; doi: 10.1016/j.bcp.2022.114910.

35. Fellous T, De Maio F, Kalkan H, et al. Phytocannabinoids promote viability and functional adipogenesis of bone marrow-derived mesenchymal stem cells through different molecular targets. Biochem Pharmacol 2020;175:113859; doi: 10.1016/j.bcp.2020.113859.

36. Miller H, De Leo N, Badach J, et al. Role of marijuana components on the regenerative ability of stem cells. Cell Biochem Funct 2021;39(3):432–441; doi: 10.1002/cbf.3609.

37. Kamali A, Oryan A, Hosseini S, et al. Cannabidiol-loaded microspheres incorporated into osteoconductive scaffold enhance mesenchymal stem cell recruitment and regeneration of critical-sized bone defects. Materials Science and Engineering: C 2019;101:64–75; doi: 10.1016/j.msec.2019.03.070.

38. Maeda A. Recruitment of Mesenchymal Stem Cells to Damaged Sites by Plant-Derived Components. Front Cell Dev Biol 2020;8; doi: 10.3389/fcell.2020.00437.

39. Nie Y, Lau C, Lie A, et al. Defective phenotype of mesenchymal stem cells in patients with systemic lupus erythematosus. Lupus 2010;19(7):850–859; doi: 10.1177/0961203309361482.

40. Lukomska B, Stanaszek L, Zuba-Surma E, et al. Challenges and Controversies in Human Mesenchymal Stem Cell Therapy. Stem Cells Int 2019;2019:1–10; doi: 10.1155/2019/9628536.

41. Hosogane N, Huang Z, Rawlins BA, et al. Stromal derived factor-1 regulates bone morphogenetic protein 2-induced osteogenic differentiation of primary mesenchymal stem cells. Int J Biochem Cell Biol 2010;42(7):1132–1141; doi: 10.1016/j.biocel.2010.03.020.

42. Martin I, Galipeau J, Kessler C, et al. Challenges for mesenchymal stromal cell therapies. Sci Transl Med 2019;11(480); doi: 10.1126/scitranslmed.aat2189.

43. Bieback K, Hecker A, Kocaömer A, et al. Human Alternatives to Fetal Bovine Serum for the Expansion of Mesenchymal Stromal Cells from Bone Marrow. Stem Cells 2009;27(9):2331–2341; doi: 10.1002/stem.139.

44. Pacini S. Deterministic and stochastic approaches in the clinical application of mesenchymal stromal cells (MSCs). Front Cell Dev Biol 2014;2; doi: 10.3389/fcell.2014.00050.

45. Krueger TEG, Thorek DLJ, Denmeade SR, et al. Concise Review: Mesenchymal Stem Cell-Based Drug Delivery: The Good, the Bad, the Ugly, and the Promise. Stem Cells Transl Med 2018;7(9):651–663; doi: 10.1002/sctm.18-0024.

46. Meisel R, Brockers S, Heseler K, et al. Human but not murine multipotent mesenchymal stromal cells exhibit broad-spectrum antimicrobial effector function mediated by indoleamine 2,3-dioxygenase. Leukemia 2011;25(4):648–654; doi: 10.1038/leu.2010.310.

47. Sousa BR, Parreira RC, Fonseca EA, et al. Human adult stem cells from diverse origins: An overview from multiparametric immunophenotyping to clinical applications. Cytometry Part A 2014;85(1):43–77; doi: 10.1002/cyto.a.22402.

48. Wagner W, Ho AD. Mesenchymal Stem Cell Preparations—Comparing Apples and Oranges. Stem Cell Rev 2007;3(4):239–248; doi: 10.1007/s12015-007-9001-1.

49. D'Ippolito G, Howard GA, Roos BA, et al. Isolation and characterization of marrow-isolated adult multilineage inducible (MIAMI) cells. Exp Hematol 2006;34(11):1608–1610; doi: 10.1016/j.exphem.2006.07.016.

50. Awan M, Buriak I, Fleck R, et al. Dimethyl sulfoxide: a central player since the dawn of cryobiology, is efficacy balanced by toxicity? Regenerative Med 2020;15(3):1463–1491; doi: 10.2217/rme-2019-0145.

51. Alizadeh E, Zarghami N, Eslaminejad MB, et al. The effect of dimethyl sulfoxide on hepatic differentiation of mesenchymal stem cells. Artif Cells Nanomed Biotechnol 2016;44(1):157–164; doi: 10.3109/21691401.2014.928778.

52. González-Fernández ML, Pérez-Castrillo S, Ordás-Fernández P, et al. Study on viability and chondrogenic differentiation of cryopreserved adipose tissue-derived mesenchymal stromal cells for future use in regenerative medicine. Cryobiology 2015;71(2):256–263; doi: 10.1016/j.cryobiol.2015.07.007.

53. Hematti P. Mesenchymal stromal cells and fibroblasts: a case of mistaken identity? Cytotherapy 2012;14(5):516–521; doi: 10.3109/14653249.2012.677822.

54. Martinello T, Bronzini I, Maccatrozzo L, et al. Canine adipose-derived-mesenchymal stem cells do not lose stem features after a long-term cryopreservation. Res Vet Sci 2011;91(1):18–24; doi: 10.1016/j.rvsc.2010.07.024.

55. Schmuhl E, Ramer R, Salamon A, et al. Increase of mesenchymal stem cell migration by cannabidiol via activation of p42/44 MAPK. Biochem Pharmacol 2014;87(3):489–501; doi: 10.1016/j.bcp.2013.11.016.

56. Ahn S, Yi S, Seo WJ, et al. A Cannabinoid Receptor Agonist N-Arachidonoyl Dopamine Inhibits Adipocyte Differentiation in Human Mesenchymal Stem Cells. Biomol Ther (Seoul) 2015;23(3):218–224; doi: 10.4062/biomolther.2014.137.

57. Kogan NM, Mechoulam R. Cannabinoids in health and disease. Dialogues Clin Neurosci 2007;9(4):413–430; doi: 10.31887/DCNS.2007.9.4/nkogan.

58. Ren J, Liu N, Sun N, et al. Mesenchymal Stem Cells and their Exosomes: Promising Therapeutics for Chronic Pain. Curr Stem Cell Res Ther 2019;14(8):644–653; doi: 10.2174/1574888X14666190912162504.

59. Li L, Feng J, Sun L, et al. Cannabidiol Promotes Osteogenic Differentiation of Bone Marrow Mesenchymal Stem Cells in the Inflammatory Microenvironment via the CB2-dependent p38 MAPK Signaling Pathway. Int J Stem Cells 2022;15(4):405–414; doi: 10.15283/ijsc21152.

60. Ruhl T, Kim B-S, Beier JP. Cannabidiol restores differentiation capacity of LPS exposed adipose tissue mesenchymal stromal cells. Exp Cell Res 2018;370(2):653–662; doi: 10.1016/j.yexcr.2018.07.030.

61. Rossi F, Bernardo ME, Bellini G, et al. The Cannabinoid Receptor Type 2 as Mediator of Mesenchymal Stromal Cell Immunosuppressive Properties. PLoS One 2013;8(11):e80022; doi: 10.1371/journal.pone.0080022.

62. Vidal R, Pilar-Cuellar F, dos Anjos S, et al. New Strategies in the Development of Antidepressants: Towards the Modulation of Neuroplasticity Pathways. Curr Pharm Des 2011;17(5):521–533; doi: 10.2174/138161211795164086.

63. Park Y, Watkins BA. Endocannabinoids and Aging—Inflammation, Neuroplasticity, Mood and Pain. 2021; pp. 129–172; doi: 10.1016/bs.vh.2020.12.007.

64. Oddi S, Scipioni L, Maccarrone M. Endocannabinoid system and adult neurogenesis: a focused review. Curr Opin Pharmacol 2020;50:25–32; doi: 10.1016/j.coph.2019.11.002.

65. Galve-Roperh I, Aguado T, Palazuelos J, et al. Mechanisms of Control of Neuron Survival by the Endocannabinoid System. Curr Pharm Des 2008;14(23):2279–2288; doi: 10.2174/138161208785740117.

66. Bisogno T, Hanuš L, De Petrocellis L, et al. Molecular targets for cannabidiol and its synthetic analogues: effect on vanilloid VR1 receptors and on the cellular uptake and enzymatic hydrolysis of anandamide. Br J Pharmacol 2001;134(4):845–852; doi: 10.1038/sj.bjp.0704327.

67. Rodrigues da Silva N, Gomes FV, Sonego AB, et al. Cannabidiol attenuates behavioral changes in a rodent model of schizophrenia through 5-HT1A, but not CB1 and CB2 receptors. Pharmacol Res 2020;156:104749; doi: 10.1016/j.phrs.2020.104749.

68. Elmes MW, Kaczocha M, Berger WT, et al. Fatty Acid-binding Proteins (FABPs) Are Intracellular Carriers for Δ9-Tetrahydrocannabinol (THC) and Cannabidiol (CBD). Journal of Biological Chemistry 2015;290(14):8711–8721; doi: 10.1074/jbc.M114.618447.

69. ElBatsh MM, Assareh N, Marsden CA, et al. Anxiogenic-like effects of chronic cannabidiol administration in rats. Psychopharmacology (Berl) 2012;221(2):239–247; doi: 10.1007/s00213-011-2566-z.

70. Carniel BP, da Rocha NS. Brain-derived neurotrophic factor (BDNF) and inflammatory markers: Perspectives for the management of depression. Prog Neuropsychopharmacol Biol Psychiatry 2021;108:110151; doi: 10.1016/j.pnpbp.2020.110151.

71. Bercik P, Verdu EF, Foster JA, et al. Chronic Gastrointestinal Inflammation Induces Anxiety-Like Behavior and Alters Central Nervous System Biochemistry in Mice. Gastroenterology 2010;139(6):2102-2112.e1; doi: 10.1053/j.gastro.2010.06.063.

72. Giacoppo S, Pollastro F, Grassi G, et al. Target regulation of PI3K/Akt/mTOR pathway by cannabidiol in treatment of experimental multiple sclerosis. Fitoterapia 2017;116:77–84; doi: 10.1016/j.fitote.2016.11.010.

73. Mori MA, Meyer E, Soares LM, et al. Cannabidiol reduces neuroinflammation and promotes neuroplasticity and functional recovery after brain ischemia. Prog Neuropsychopharmacol Biol Psychiatry 2017;75:94–105; doi: 10.1016/j.pnpbp.2016.11.005.

74. Lin L-FH, Doherty DH, Lile JD, et al. GDNF: a Glial Cell Line-Derived Neurotrophic Factor for Midbrain Dopaminergic Neurons. Science (1979) 1993;260(5111):1130–1132; doi: 10.1126/science.8493557.

75. Airaksinen MS, Saarma M. The GDNF family: Signalling, biological functions and therapeutic value. Nat Rev Neurosci 2002;3(5):383–394; doi: 10.1038/nrn812.

76. Anand U, Oldfield C, Pacchetti B, et al. Dose-Related Inhibition of Capsaicin Responses by Cannabinoids CBG, CBD, THC and their Combination in Cultured Sensory Neurons. J Pain Res 2021;Volume 14:3603–3614; doi: 10.2147/JPR.S336773.

77. Stott CG, Nichol K, Jones NA, et al. The Proposed Multimodal Mechanism of Action of Cannabidiol (CBD) in Epilepsy: Modulation of Intracellular Calcium and Adenosine-mediated Signalling. Epilepsy & Behavior 2019;101:106734; doi: 10.1016/j.yebeh.2019.08.009.

78. Wang H, Zheng R, Chen Q, et al. Mesenchymal stem cells microvesicles stabilize endothelial barrier function partly mediated by hepatocyte growth factor (HGF). Stem Cell Res Ther 2017;8(1):211; doi: 10.1186/s13287-017-0662-7.

79. Rurali E, Vinci MC, Bassetti B, et al. New Strategies to Enhance Myocardial Regeneration: Expectations and Challenges from Preclinical Evidence. Curr Stem Cell Res Ther 2020;15(8):696–710; doi: 10.2174/1574888X15666200225124451.

80. Han D, Li X, Fan W-S, et al. Activation of cannabinoid receptor type II by AM1241 protects adipose-derived mesenchymal stem cells from oxidative damage and enhances their therapeutic efficacy in myocardial infarction mice *via* Stat3 activation. Oncotarget 2017;8(39):64853–64866; doi: 10.18632/oncotarget.17614.

81. Kozela E, Pietr M, Juknat A, et al. Cannabinoids Δ9-Tetrahydrocannabinol and Cannabidiol Differentially Inhibit the Lipopolysaccharide-activated NF-κB and Interferon-β/STAT Proinflammatory Pathways in BV-2 Microglial Cells. Journal of Biological Chemistry 2010;285(3):1616–1626; doi: 10.1074/jbc.M109.069294.

82. Baswan SM, Klosner AE, Glynn K, et al. <p>Therapeutic Potential of Cannabidiol (CBD) for Skin Health and Disorders</p>. Clin Cosmet Investig Dermatol 2020;Volume 13:927–942; doi: 10.2147/CCID.S286411.

83. Kongkadee K, Wisuitiprot W, Ingkaninan K, et al. Anti-inflammation and gingival wound healing activities of Cannabis sativa L. subsp. sativa (hemp) extract and cannabidiol: An in vitro study. Arch Oral Biol 2022;140:105464; doi: 10.1016/j.archoralbio.2022.105464.

84. Rivera P, Romero-Zerbo Y, Pavón FJ, et al. Obesity-dependent cannabinoid modulation of proliferation in adult neurogenic regions. European Journal of Neuroscience 2011;33(9):1577–1586; doi: 10.1111/j.1460-9568.2011.07650.x.

85. Tejeda-Martínez AR, Viveros-Paredes JM, Hidalgo-Franco G V., et al. Chronic Inhibition of FAAH Reduces Depressive-Like Behavior and Improves Dentate Gyrus Proliferation after Chronic Unpredictable Stress Exposure. Behavioural Neurology 2021;2021:1–14; doi: 10.1155/2021/6651492.

86. Kang M, Lee J, Park S. Cannabidiol induces osteoblast differentiation via angiopoietin1 and p38 <scp>MAPK</scp>. Environ Toxicol 2020;35(12):1318–1325; doi: 10.1002/tox.22996.

87. Qi X, Liu C, Li G, et al. Investigation of in vitro odonto/osteogenic capacity of cannabidiol on human dental pulp cell. J Dent 2021;109:103673; doi: 10.1016/j.jdent.2021.103673.

88. Bielawiec P, Harasim-Symbor E, Sztolsztener K, et al. Attenuation of Oxidative Stress and Inflammatory Response by Chronic Cannabidiol Administration Is Associated with Improved n-6/n-3 PUFA Ratio in the White and Red Skeletal Muscle in a Rat Model of High-Fat Diet-Induced Obesity. Nutrients 2021;13(5):1603; doi: 10.3390/nu13051603.

89. Hassan S, Eldeeb K, Millns PJ, et al. Cannabidiol enhances microglial phagocytosis via transient receptor potential (TRP) channel activation. Br J Pharmacol 2014;171(9):2426–2439; doi: 10.1111/bph.12615.

90. Shi J, Sun J, Zhang W, et al. Demineralized Bone Matrix Scaffolds Modified by CBD-SDF-1α Promote Bone Regeneration via Recruiting Endogenous Stem Cells. ACS Appl Mater Interfaces 2016;8(41):27511–27522; doi: 10.1021/acsami.6b08685.

91. Schouten M, Dalle S, Koppo K. Molecular Mechanisms Through Which Cannabidiol May Affect Skeletal Muscle Metabolism, Inflammation, Tissue Regeneration, and Anabolism: A Narrative Review. Cannabis Cannabinoid Res 2022;7(6):745–757; doi: 10.1089/can.2022.0220.

92. Sun Y, Dolmetsch RE. Investigating the Therapeutic Mechanism of Cannabidiol in a Human Induced Pluripotent Stem Cell (iPSC)-Based Model of Dravet Syndrome. Cold Spring Harb Symp Quant Biol 2018;83:185–191; doi: 10.1101/sqb.2018.83.038174.

93. Pan H, Mukhopadhyay P, Rajesh M, et al. Cannabidiol Attenuates Cisplatin-Induced Nephrotoxicity by Decreasing Oxidative/Nitrosative Stress, Inflammation, and Cell Death. Journal of Pharmacology and Experimental Therapeutics 2009;328(3):708–714; doi: 10.1124/jpet.108.147181.

94. Wu J, Chen N, Liu Y, et al. Studies of involvement of G-protein coupled receptor-3 in cannabidiol effects on inflammatory responses of mouse primary astrocytes and microglia. PLoS One 2021;16(5):e0251677; doi: 10.1371/journal.pone.0251677.

95. Seltzer ES, Watters AK, MacKenzie D, et al. Cannabidiol (CBD) as a Promising Anti-Cancer Drug. Cancers (Basel) 2020;12(11):3203; doi: 10.3390/cancers12113203.

96. Nabissi M, Morelli MB, Amantini C, et al. Cannabidiol stimulates Aml-1a-dependent glial differentiation and inhibits glioma stem-like cells proliferation by inducing autophagy in a TRPV2-dependent manner. Int J Cancer 2015;137(8):1855–1869; doi: 10.1002/ijc.29573.

97. Santoni G, Maggi F, Morelli MB, et al. Transient Receptor Potential Cation Channels in Cancer Therapy. Medical Sciences 2019;7(12):108; doi: 10.3390/medsci7120108.

98. Morelli MB, Nabissi M, Amantini C, et al. The transient receptor potential vanilloid-2 cation channel impairs glioblastoma stem-like cell proliferation and promotes differentiation. Int J Cancer 2012;131(7):E1067–E1077; doi: 10.1002/ijc.27588.

99. Morelli MB, Offidani M, Alesiani F, et al. The effects of cannabidiol and its synergism with bortezomib in multiple myeloma cell lines. A role for transient receptor potential vanilloid type-2. Int J Cancer 2014;134(11):2534–2546; doi: 10.1002/ijc.28591.

100. Butowski N. Novel and Prospective Molecular Targets for Therapy of Intracranial Gliomas. 2018; pp. 66–78; doi: 10.1159/000469681.

101. Khan I, Mahfooz S, Hatiboglu MA. Herbal Medicine for Glioblastoma: Current and Future Prospects. Med Chem (Los Angeles) 2020;16(8):1022–1043; doi: 10.2174/1573406416666200130100833.

102. Berardis S, Dwisthi Sattwika P, Najimi M, et al. Use of mesenchymal stem cells to treat liver fibrosis: Current situation and future prospects. World J Gastroenterol 2015;21(3):742; doi: 10.3748/wjg.v21.i3.742.

103. Mangieri CW, McCartt JC, Strode MA, et al. Perioperative hepatocyte growth factor (HGF) infusions improve hepatic regeneration following portal branch ligation (PBL) in rodents. Surg Endosc 2017;31(7):2789–2797; doi: 10.1007/s00464-016-5288-9.

104. Ido A, Moriuchi A, Marusawa H, et al. Translational research on HGF: A phase I/II study of recombinant human HGF for the treatment of fulminant hepatic failure. Hepatology Research 2008;38:S88–S92; doi: 10.1111/j.1872-034X.2008.00432.x.

105. Julien B, Grenard P, Teixeira-Clerc F, et al. Antifibrogenic role of the cannabinoid receptor CB2 in the liver. Gastroenterology 2005;128(3):742–755; doi: 10.1053/j.gastro.2004.12.050.

106. Aziz A, Nguyen LC, Oumeslakht L, et al. Cannabinoids as Immune System Modulators: Cannabidiol Potential Therapeutic Approaches and Limitations. Cannabis Cannabinoid Res 2022; doi: 10.1089/can.2022.0133.

107. Jenny M, Santer E, Pirich E, et al. Δ9-Tetrahydrocannabinol and cannabidiol modulate mitogen-induced tryptophan degradation and neopterin formation in peripheral blood mononuclear cells in vitro. J Neuroimmunol 2009;207(1–2):75–82; doi: 10.1016/j.jneuroim.2008.12.004.

108. Pagano S, Coniglio M, Valenti C, et al. Biological effects of Cannabidiol on normal human healthy cell populations: Systematic review of the literature. Biomedicine & Pharmacotherapy 2020;132:110728; doi: 10.1016/j.biopha.2020.110728.

109. Guo Y, Liu Y, Wu W, et al. Indoleamine 2,3-dioxygenase (Ido) inhibitors and their nanomedicines for cancer immunotherapy. Biomaterials 2021;276:121018; doi: 10.1016/j.biomaterials.2021.121018.

110. Kadle RL, Abdou SA, Villarreal-Ponce AP, et al. Microenvironmental cues enhance mesenchymal stem cell-mediated immunomodulation and regulatory T-cell expansion. PLoS One 2018;13(3):e0193178; doi: 10.1371/journal.pone.0193178.

111. Lee H-J, Jung H, Kim D-K. IDO and CD40 May Be Key Molecules for Immunomodulatory Capacity of the Primed Tonsil-Derived Mesenchymal Stem Cells. Int J Mol Sci 2021;22(11):5772; doi: 10.3390/ijms22115772.

112. Mellor AL, Lemos H, Huang L. Indoleamine 2,3-Dioxygenase and Tolerance: Where Are We Now? Front Immunol 2017;8; doi: 10.3389/fimmu.2017.01360.

113. Singer NG, Caplan AI. Mesenchymal Stem Cells: Mechanisms of Inflammation. Annual Review of Pathology: Mechanisms of Disease 2011;6(1):457–478; doi: 10.1146/annurev-pathol-011110-130230.

114. Gu Z, Singh S, Niyogi RG, et al. Marijuana-Derived Cannabinoids Trigger a CB2/PI3K Axis of Suppression of the Innate Response to Oral Pathogens. Front Immunol 2019;10; doi: 10.3389/fimmu.2019.02288.

115. Kozela E, Juknat A, Kaushansky N, et al. Cannabinoids Decrease the Th17 Inflammatory Autoimmune Phenotype. Journal of Neuroimmune Pharmacology 2013;8(5):1265–1276; doi: 10.1007/s11481-013-9493-1.

116. Weiss L, Zeira M, Reich S, et al. Cannabidiol lowers incidence of diabetes in non-obese diabetic mice. Autoimmunity 2006;39(2):143–151; doi: 10.1080/08916930500356674.

117. Rennick DM, Fort MM, Davidson NJ. Studies with IL-10-/- mice: an overview. J Leukoc Biol 1997;61(4):389–396; doi: 10.1002/jlb.61.4.389.

118. Gabryšová L, Howes A, Saraiva M, et al. The Regulation of IL-10 Expression. 2014; pp. 157–190; doi: 10.1007/978-3-662-43492-5_8.

119. Groux H, Bigler M, de Vries JE, et al. Inhibitory and Stimulatory Effects of IL-10 on Human CD8+ T Cells. The Journal of Immunology 1998;160(7):3188–3193; doi: 10.4049/jimmunol.160.7.3188.

120. Nizzoli G, Larghi P, Paroni M, et al. IL-10 promotes homeostatic proliferation of human CD8 + memory T cells and, when produced by CD1c + DCs, shapes naive CD8 + T-cell priming. Eur J Immunol 2016;46(7):1622–1632; doi: 10.1002/eji.201546136.

121. Ip WKE, Hoshi N, Shouval DS, et al. Anti-inflammatory effect of IL-10 mediated by metabolic reprogramming of macrophages. Science (1979) 2017;356(6337):513–519; doi: 10.1126/science.aal3535.

122. Li W, Liu Q, Shi J, et al. The role of TNF-α in the fate regulation and functional reprogramming of mesenchymal stem cells in an inflammatory microenvironment. Front Immunol 2023;14; doi: 10.3389/fimmu.2023.1074863.

123. Gaur U, Aggarwal BB. Regulation of proliferation, survival and apoptosis by members of the TNF superfamily. Biochem Pharmacol 2003;66(8):1403–1408; doi: 10.1016/S0006-2952(03)00490-8.

124. Laha D, Grant R, Mishra P, et al. The Role of Tumor Necrosis Factor in Manipulating the Immunological Response of Tumor Microenvironment. Front Immunol 2021;12; doi: 10.3389/fimmu.2021.656908.

125. Walker FC, Sridhar PR, Baldridge MT. Differential roles of interferons in innate responses to mucosal viral infections. Trends Immunol 2021;42(11):1009–1023; doi: 10.1016/j.it.2021.09.003.

126. Rodríguez Mesa XM, Moreno Vergara AF, Contreras Bolaños LA, et al. Therapeutic Prospects of Cannabinoids in the Immunomodulation of Prevalent Autoimmune Diseases. Cannabis Cannabinoid Res 2021;6(3):196–210; doi: 10.1089/can.2020.0183.

127. Peyravian N, Deo S, Daunert S, et al. The Anti-Inflammatory Effects of Cannabidiol (CBD) on Acne. J Inflamm Res 2022;Volume 15:2795–2801; doi: 10.2147/JIR.S355489.

128. Abame MA, He Y, Wu S, et al. Chronic administration of synthetic cannabidiol induces antidepressant effects involving modulation of serotonin and noradrenaline levels in the hippocampus. Neurosci Lett 2021;744:135594; doi: 10.1016/j.neulet.2020.135594.

129. Ma H, Xu F, Liu C, et al. A Network Pharmacology Approach to Identify Potential Molecular Targets for Cannabidiol's Anti-Inflammatory Activity. Cannabis Cannabinoid Res 2021;6(4):288–299; doi: 10.1089/can.2020.0025.

130. Zou C, Xu F, Shen J, et al. Identification of a Ferroptosis-Related Prognostic Gene PTGS2 Based on Risk Modeling and Immune Microenvironment of Early-Stage Cervical Cancer. J Oncol 2022;2022:1–32; doi: 10.1155/2022/3997562.

131. Rausch SM, Gonzalez BD, Clark MM, et al. SNPs in PTGS2 and LTA predict pain and quality of life in long term lung cancer survivors. Lung Cancer 2012;77(1):217–223; doi: 10.1016/j.lungcan.2012.02.017.

132. Ke J, Yang Y, Che Q, et al. Prostaglandin E2 (PGE2) promotes proliferation and invasion by enhancing SUMO-1 activity via EP4 receptor in endometrial cancer. Tumor Biology 2016;37(9):12203–12211; doi: 10.1007/s13277-016-5087-x.

133. Bacalia KMA, Tveter KM, Palmer H, et al. Cannabidiol Decreases Intestinal Inflammation in the Ovariectomized Murine Model of Postmenopause. Biomedicines 2022;11(1):74; doi: 10.3390/biomedicines11010074.

134. Hellmann J, Tang Y, Zhang MJ, et al. Atf3 negatively regulates Ptgs2/Cox2 expression during acute inflammation. Prostaglandins Other Lipid Mediat 2015;116–117:49–56; doi: 10.1016/j.prostaglandins.2015.01.001.

135. Tanaka M, Yagyu K, Sackett S, et al. Anti-Inflammatory Effects by Pharmacological Inhibition or Knockdown of Fatty Acid Amide Hydrolase in BV2 Microglial Cells. Cells 2019;8(5):491; doi: 10.3390/cells8050491.

136. Park H-S, Jeong H-Y, Kim Y-S, et al. Anti-microbial and anti-inflammatory effects of Cheonwangbosim-dan against *Helicobacter pylori*- induced gastritis. J Vet Sci 2020;21; doi: 10.4142/jvs.2020.21.e39.

137. Esposito LGA, Overbaugh E, Xiong J, et al. Immune Responses Are Differentially Regulated by Root, Stem, Leaf, and Flower Extracts of Female and Male CBD Hemp (Cannabis sativa L.) Plants. Immuno 2021;1(4):369–379; doi: 10.3390/immuno1040025.

138. Wang B, Li D, Fiselier A, et al. New AKT-dependent mechanisms of anti-COVID-19 action of high-CBD Cannabis sativa extracts. Cell Death Discov 2022;8(1):110; doi: 10.1038/s41420-022-00876-y.