2024.03

Tissue Engineering & Clinical Medicine Lab.

Principal Investigator:

Ming-Wei Lin, Ph.D.

Lab Introduction

1. Mitochondrial transplantation for therapeutic use: from cell to animal models
2. Regulation of mitochondrial metabolism, cancer stemness and tumor microenvironment by small natural compounds or extracellular vesicles
3. Degenerative diseases and treatment in experimental animal models

Contact Information:

TEL: +886-7-615-1100 ext. 5413

Email: ta990074@gmail.com; ed110876@edah.org.tw

Website : https://sites.google.com/view/eda-tissueclinical-lab/

Educations:

Ph.D. degree,

Institute of Basic Medical Sciences, National Cheng-Kung University Medical College, Tainan, Taiwan

Academic Experiences:

Duration	Department	Position
2021 to date	Dept. of Medical Research, E-Da Hospital/ E-Da Cancer Hospital, Kaohsiung, Taiwan	Associate Researcher
2020 to date	Dept. of of Nursing, I-Shou University College of Medicine, Kaohsiung, Taiwan	Assistant Professor
2018 ~2021	Dept. of Medical Research, E-Da Hospital, E-Da Cancer Hospital, Kaohsiung, Taiwan	Assistant Researcher
2016 ~2017	Center for Stem Cell Research, Kaohsiung Medical University, Kaohsiung, Taiwan	Assistant Research Fellow
2014~2016	Center for Stem Cell Research, Kaohsiung Medical University, Kaohsiung, Taiwan	Post-doctoral fellow
2012~2014	Chang Gung Memorial Hospital Gung Memorial Hospital, Kaohsiung, Taiwan	Post-doctoral fellow

2012	Department of Pharmacology, University of Minnesota, Minnesota, USA	Visiting Research Fellow
2010~2012	Graduate Institute of Clinical Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan	Post-doctoral fellow

Research Projects

Project titles	PI	Source	Duration
The application potential of mitochondrial therapy on wound healing and xenograft skin transplantation	MW Lin	MOST	2021/08~2024/07
The study of regulation of calcium signaling, mitochondrial metabolism and gastric cancer stemness by GRP78 inhibition by small natural compounds and clinical samples analysis	MW Lin	MOST	2017/11~2019/04
HDAC6 promotes gastric cancer cell stemness by upregulation of GRP78	MW Lin	I-Shou University	2023/5~2024/4
MEC-17 regulates gastric tumor microenvironment by promotion of acetylation modification-mediated GRP78 secretion	MW Lin	I-Shou University	2021/5~2022/4
Vascular protective effect of mitochondrial transplantation in a diabetic rat model of aortocaval fistula	MW Lin	EDa Hospital	2019/04~2020/03
Therapeutic potential and possible mechanism involved in peripheral nerve injury induced neuropathic pain treated by mitochondrial transplantation	MW Lin	NTU-EDa	2020/07~2021/06
Development of a new treatment paradigm for neuropathic pain by mitochondrial transplantation	MW Lin	NTU-EDa	2019/7~2020/6
Improvement of functional outcomes in rat with contusive spinal cord injury -implication of mitochondrial transplantation	MW Lin	NCKU-EDa	2018/01~2018/12
Improvement of functional outcomes in rat with contusive spinal cord injury by Cx43 inhibitors	MW Lin	NCKU-EDa	2019/01~2019/12
Regulation of circulating endothelial progenitor cell-derived extracellular vesicles (EPC-EV) in	MW Lin (as co-PI)	NSC	2023/08~2026/07

patients with pulmonary arterial hypertension and therapeutic potentials of EPC-EV in a rat model of pulmonary hypertension			
Taiwan-Singapore IP, Science and Technology Innovation Center	MW Lin (as co-PI)	MOST	2021/09-2024/08
The co-ordination of mitochondrial supply and demand between cancer cells and adjacent cells	MW Lin (as co-PI)	MOST	2020/8~2023/7
Mechanistic investigation of the differential effects of soluble and membrane-bound P-selectin in 2-hit hemorrhagic shock resuscitation models	MW Lin (as co-PI)	MOST	2018/08~2019/07
Application of NAD^+-dependent deacetylases, Sirtuin, for treatment of lung cancer	MW Lin (as co-PI)	MOST	2017/08~2018/07

Publications:

Patent:

Method for treating Osteoarthritis (US 11590174 B2): ***Lin MW***, *Tsai HY, Jou IM, Wu CH*

Publications:

1. *Hung SY, Chen JL, Tu YK, Tsai HY, Lu PH, Jou IM, Mbuyisa L,* ***Lin MW****. Isoliquiritigenin inhibits apoptosis and ameliorates oxidative stress in rheumatoid arthritis chondrocytes through the Nrf2/HO-1-mediated pathway. Biomed Pharmacother. 2024;170:116006. (***corresponding author**)
2. *Kuo FC, Tsai HY, Cheng BL, Tsai KJ, Chen PC, Huang YB, Liu CJ, Wu DC, Wu MC, Huang B,* ***Lin MW****. Endothelial Mitochondria Transfer to Melanoma Induces M2-Type Macrophage Polarization and Promotes Tumor Growth by the Nrf2/HO-1-Mediated Pathway. Int J Mol Sci. 2024;25(3):1857. (***corresponding author**)
3. *Huang CC, Chiu HY, Lee PH, Fang SY,* ***Lin MW****, Chen HF, Lee JS*.* Mitochondrial transplantation attenuates traumatic neuropathic pain, neuroinflammation, and apoptosis in rats with nerve root ligation. Mol Pain. 2023;19:17448069231210423.
4. *Yang JL, Lin WL, Tai SB, Ciou YS, Chung CL, Chen JJ, Liu PF,* ***Lin MW****, Chen CL.* Suppression of TGFβ-Induced Interleukin-6 Secretion by Sinulariolide from Soft Corals through Attenuation of the p38-NF-kB Pathway in Carcinoma Cells. Int J Mol Sci. 2023;24(14):11656.
5. *Chen JL, Tai YS, Tsai HY, Hsieh CY, Chen CL, Liu CJ, Wu DC, Huang YB,* ***Lin MW*****.* Betulinic Acid Inhibits the Stemness of Gastric Cancer Cells by Regulating the GRP78-TGF-β1 Signaling Pathway and Macrophage Polarization. Molecules. 2023;28(4):1725. (***corresponding author**)
6. *Iha K, Sato A, Tsai HY, Sonoda H, Watabe S, Yoshimura T,* ***Lin MW****, Ito E*.* Gastric Cancer Cell-Derived Exosomal GRP78 Enhances Angiogenesis upon Stimulation of

Vascular Endothelial Cells. Curr Issues Mol Biol. 2022;44(12):6145-6157. (***corresponding author**)

7. *Tsurusawa N, Iha K, Sato A, Tsai HY, Sonoda H, Watabe S, Yoshimura T, Wu DC,* ***Lin MW*****, Ito E*.* Ultrasensitive detection of GRP78 in exosomes and observation of migration and proliferation of cancer cells by application of GRP78-containing exosomes. Cancers. 2022; 14:3887. (***corresponding author**)
8. *Lee CH, Tsai HY, Chen CL, Chen JL, Lu CC, Fang YP, Wu DC, Huang YB,* ***Lin MW****. Isoliquiritigenin inhibits gastric cancer stemness, modulates tumor microenvironment, and suppresses tumor growth through glucose-regulated protein 78 downregulation. Biomedicines. 2022;10(6):1350. (***corresponding author**)
9. ***Lin MW****, Fang SY, Hsu JC, Huang CY, Lee PH, Huang CC, Chen HF, Lam CF, Lee JS*.* Mitochondrial transplantation attenuates neural damage and improves locomotor function after traumatic spinal cord injury in rats. Front Neurosci. 2022;16:800883. **(first author)**
10. *Tai YS, Ma YS, Chen CL, Tsai HY, Tsai CC, Wu MC, Chen CY,* ***Lin MW****. Resveratrol analog 4-bromo-resveratrol inhibits gastric cancer stemness through the SIRT3-c-Jun N-terminal kinase signaling pathway. Curr Issues Mol Biol. 2022;44, 63–72. (***corresponding author**)
11. *Iha K, Tsurusawa N, Tsai HY,* ***Lin MW****, Sonoda H, Watabe S, Yoshimura T, Ito E*.* Ultrasensitive ELISA detection of proteins in separated lumen and membrane fractions of cancer cell exosomes. Anal Biochem. 2022; 654:114831.
12. *Hsu CH, Roan JN, Fang SY, Chiu MH, Cheng TT, Huang CC,* ***Lin MW****, Lam CF*.* Transplantation of viable mitochondria improves right ventricular performance and pulmonary artery remodeling in rats with pulmonary arterial hypertension. J Thorac Cardiovasc Surg. 2022;163(5):e361-e373.
13. *Pang YL, Fang SY, Cheng TT, Huang CC,* ***Lin MW****, Lam CF, Chen KB.* Viable Allogeneic Mitochondria Transplantation Improves Gas Exchange and Alveolar-Capillary Permeability in Rats with Endotoxin-Induced Acute Lung Injuries. Int J Med Sci. 2022;19(6):1036-1046.
14. *Tsai KJ, Tsai HY, Tsai CC, Chen TY, Hsieh TH, Chen CL, Mbuyisa L, Huang YB,* ***Lin MW****. Luteolin inhibits breast cancer stemness and enhances chemosensitivity through the Nrf2-mediated pathway Molecules. 2021;26(21):6452. (***corresponding author**)
15. ***Lin MW****, *Chen CI, Cheng TT, Huang CC, Tsai JW, Feng GM, Hwang TZ, Lam. CF*.* Prolonged preoperative fasting induces postoperative insulin resistance by ER-stress mediated Glut4 down-regulation in skeletal muscles. Int J Med Sci. 2021;18(5):1189-1197. **(first /*corresponding author)**
16. *Fang SY, Chen JL, Chiu MH, Huang CC,* ***Lin MW****, Lam CF*.* Distinct phenotypic expressions of macrophages in neonatal lungs. Experimental and Therapeutic Medicine.

Exp Ther Med. 2021;21: 369.

17. *Huang CY, Yang JL, Chen JJ, Tai SB, Yeh YH, Liu PF,* ***Lin MW****, Chung CL, Chen CL*.* Fluoroquinolones suppress TGF-β and PMA-Induced MMP-9 production in cancer cells: implications in repurposing quinolone antibiotics for cancer treatment. Int J Mol Sci. 2021;22(21):11602.
18. *Fang SY, Roan JN, Lee JS, Chiu MH,* ***Lin MW****, Liu CC, Lam CF*.* Transplantation of viable mitochondria attenuates neurologic injury after spinal cord ischemia. J Thorac Cardiovasc Surg. 2021;161(5):e337-e347.
19. ***Lin MW****, Chen YH, Yang HB, Lin CC, Hung SY*.* Galantamine inhibits Aβ1-42-induced neurotoxicity by enhancing α7nAChR expression as a cargo carrier for LC3 binding and Aβ1-42 engulfment during autophagic degradation. Neurotherapeutics. 2020;17(2):676-689. **(first author)**
20. *Tsai CC, Chen TY, Tsai KJ,* ***Lin MW****, Hsu CY, Wu DC, Tsai EM, Hsieh TH*.* NF-κB/miR-18a-3p and miR-4286/BZRAP1 axis may mediate carcinogenesis in Helicobacter pylori-Associated gastric cancer. Biomed Pharmacother. 2020;132:110869.
21. *Hsu CH, Roan JN, Fang SY, Chiu MH, Cheng TT, Huang CC,* ***Lin MW****, Lam CF*.* Transplantation of viable mitochondria improves right ventricular performance and pulmonary artery remodeling in rats with pulmonary arterial hypertension. J Thorac Cardiovasc Surg. 2020:S0022-5223(20)32372-2.
22. ***Lin MW****, Lin CC, Chen YH, Yang HB, Hung SY*.* Celastrol inhibits dopaminergic neuronal death of Parkinson's disease through activating mitophagy. Antioxidants. 2019; 9(1), 37. **(first author)**
23. *Chiou HC,* ***Lin MW****, Hsiao PJ, Chen CL, Chiao S, Lin TY, Chen YC, Wu DC, Lin MH*.* Dulaglutide modulates the development of tissue-infiltrating Th1/Th17 cells and the pathogenicity of encephalitogenic Th1 cells in the central nervous system. Int J Mol Sci. 2019; 20(7): 1584. (SCI)
24. *Tai YS, Yang SC, Hsieh YC, Huang YB, Wu PC, Tsai MJ, Tsai YH,* ***Lin MW*.*** A novel model for studying voltage-gated ion channel gene expression during reversible ischemic stroke. Int J Med Sci. 2019; 16(1):60-67.（***corresponding author**）
25. *Wu PC, Hsu WL, Chen CL, Lam CF, Huang YB, Huang CC, Lin MH,* ***Lin MW****.* Morphine induces fibroblast activation through up-regulation of connexin 43 expression: implication of fibrosis in wound healing. Int J Med Sci. 2018;15(9):875-882.（***corresponding author**）
26. *Chen CL, Wu DC, Liu MY,* ***Lin MW****, Huang HT, Huang YB, Chen LC, Chen YY, Chen JJ, Yang PH, Kao YC, Chen PY.* Cholest-4-en-3-one attenuates TGF-β responsiveness by inducing TGF-β receptors degradation in Mv1Lu cells and colorectal adenocarcinoma cells. J Recept Signal Transduct Res. 2017 ;37(2):189-199.
27. ***Lin MW****, Huang YB, Chen CL, Wu PC, Chou CY, Wu PC, Hung SY.* A formulation study

of 5-aminolevulinic encapsulated in DPPC liposomes in melanoma treatment. Int J Med Sci. 2016;13(7):483-9. **(first author)**

28. *Wu CY, Hsu WL, Wang CH, Liang JL, Tsai MH, Yen CJ, Li HW, Chiu SJ, Chang CH, Huang YB,* ***Lin MW*,*** *Yoshioka T*.* A novel strategy for TNF-alpha production by 2-APB induced downregulated SOCE and upregulated HSP70 in O. tsutsugamushi-infected human macrophages. PLoS One. 2016;11(7):e0159299. （***corresponding author**）
29. *Tsai MJ*,* ***Lin MW**** *, Huang YB, Kuo YM, Tsai YH.* The Influence of Acute Hyperglycemia in an Animal Model of Lacunar Stroke That Is Induced by Artificial Particle Embolization. Int J Med Sci. 2016;13(5):347-56. **(*co-first author)**
30. *Chen CL, Chen CY, Chen YP, Huang YB,* ***Lin MW****, Wu DC, Huang HT, Liu MY, Chang HW, Kao YC, Yang PH.* Betulinic acid enhances TGF-β signaling by altering TGF-β receptors partitioning between lipid-raft/caveolae and non-caveolae membrane microdomains in mink lung epithelial cells. J Biomed Sci. 2016;23:30.
31. *Yang JC*,* ***Lin MW**** *, Rau CS*, Jeng SF, Lu TH, Wu YC, Chen YC, Tzeng SL, Wu CJ, Hsieh CH.* Altered exosomal protein expression in the serum of NF-κB knockout mice following skeletal muscle ischemia-reperfusion injury. J Biomed Sci. 2015:10;22:40. **(*co-first author)**
32. *Rau CS*,* ***Lin MW****, *Wu SC*, Wu YC, Lu TH, Tzeng SL, Chen YC, Wu CJ, Hsieh CH.* Regulatory and effector helper T-cell profile after nerve xenografting in the Toll-like receptor-deficient mice. Int J Med Sci. 2015;12:650-4. **(*co-first author)**
33. *Chen CL, Chen YP,* ***Lin MW****, Huang YB, Chang FR, Duh TH, Wu DC, Wu WC*. Euphol from *Euphorbia tirucalli* negatively modulates TGF-β responsiveness via TGF-β receptor segregation inside membrane rafts. PLoS One. 2015;10(10):e0140249.
34. *Hsu WL, Lu JH, Noda M, Wu CY, Liu JD, Sakakibara M, Tsai MH, Yu HS,* ***Lin MW****, Huang YB, Yan SJ, Yoshioka T.* Derinat protects skin against ultraviolet-B (UVB)-induced cellular damage. Molecules. 2015;20(11):20297-311.
35. *Huang YB,* ***Lin MW****, fLiu MY, Chen CL.* Composite of decellular adipose tissue with chitosan-based scaffold for tissue engineering with adipose-derived stem cells. J Biomater Tissue Eng. 2015:5:56-63.
36. *Wu CY*,* ***Lin MW**** *, Wu DC*, Huang YB, Huang HT, Chen CL.* The role of phosphoinositide-regulated actin reorganization in chemotaxis and cell migration. Br J Pharmacol. 2014;171:5541-54. **(*co-first author)**
37. *Huang YB*,* ***Lin MW**** *, Chao Y, Huang CT, Tsail YH, Wu PC.* Anti-oxidant activity and attenuation of bladder hyperactivity by the flavonoid compound kaempferol. Int J Urol. 2014: 21:94-8. **(*co-first author)**
38. *Yang JC, Wu SC, Rau CS, Lu TH, Wu YC, Chen YC,* ***Lin MW****, Tzeng SL, Wu CJ, Hsieh CH.* Inhibition of the phosphoinositide 3-kinase pathway decreases innate resistance to

lipopolysaccharide toxicity in TLR4 deficient mice. J Biomed Sci. 2014;21:20.

39. *Rau CS, Yang CS, Wu SC, Chen YC, Lu TH,* ***Lin MW,*** *Wu YC, Tzeng SL, Wu CJ, Hsieh CH.* Profiling circulating microRNA expression in a mouse model of nerve allotransplantation. J Biomed Sci. 2013;20:64.
40. ***Lin MW,*** *Lin AS, Wu DC, Wang SW, Chang FR, Wu YC, Huang YB.* Euphol from Euphorbia tirucalli selectively inhibits human gastric cancer cell growth through the induction of ERK1/2-mediated apoptosis. Food Chem Toxicol. 2012:50:4333–39. **(first author)**
41. *Hsu WL, Chiu YC,* ***Lin MW****, Chen CH, Lu JH, Yu HS, Yoshioka T.* Differential effects of arsenic on calcium signaling in primary keratinocytes and malignant (HSC-1) cells. Cell Calcium. 2012;52:161-9.
42. ***Lin MW****, Wang YJ, Liu SI, Lin AA, Lo YC, Wu SN.* Characterization of aconitine-induced block of delayed rectifier K^+ current in differentiated NG108-15 neuronal cells. Neuropharmacology. 2008;54:912-23. **(first author)**
43. *Wu SN,* ***Lin MW****, Wang YJ.* Stimulatory actions of di-8-butyl-amino-naphthyl-ethylene-pyridinium-propyl-sulfonate (di-8-ANEPPS), voltage-sensitive dye, on the BK_{Ca} channel in pituitary tumor (GH3) cells. Pflugers Arch. 2008;455:687-99.
44. *Wang YJ,* ***Lin MW****, Lin AA, Wu SN.* Riluzole-induced block of voltage-gated Na^+ current and activation of BK_{Ca} channels in cultured differentiated human skeletal muscle cells. Life Sci. 2008;82:11-20.
45. *Wang YJ,* ***Lin MW****, Lin AA, Peng H, Wu SN.* Evidence for state-dependent block of DPI 201-106, a synthetic inhibitor of Na^+ channel inactivation, on delayed-rectifier K^+ current in pituitary tumor (GH_3) cells. J Physiol Pharmacol. 2008;59:409-23.
46. *Huang CW, Huang CC,* ***Lin MW****, Tsai JJ, Wu SN.* The synergistic inhibitory actions of oxcarbazepine on voltage-gated sodium and potassium currents in differentiated NG108-15 neuronal cells and model neurons. Int J Neuropsychopharmacol. 2008;11:597-610.
47. *Wang YJ, Chen BS,* ***Lin MW****, Lin AA, Peng H, Sung RJ, Wu SN.* Time-dependent block of ultrarapid-delayed rectifier K^+ currents by aconitine, a potent cardiotoxin, in heart-derived H9c2 myoblasts and in neonatal rat ventricular myocytes. Toxicol Sci. 2008;106(2):454-63.
48. *Wu SN, Chen BS,* ***Lin MW****, Liu YC.* Contribution of slowly inactivating potassium current to delayed firing of action potentials in NG108-15 neuronal cells: experimental and theoretical studies. J Theor Biol. 2008;252:711-21.
49. *Wu SN, Pung H, Chen BS, Wang YJ, Wu PY,* ***Lin MW.*** Potent activation of

large-conductance Ca^{2+}-activated K^+ channels by diphenylurea NS1643 in pituitary tumor (GH_3) cells. Mol Pharmacol. 2008;74:1696-704.

50. *Lam CF, Chang PJ, Huang YS, Sung YH, Huang CC,* ***Lin MW****, Liu YC, Tsai YC.* Prolonged use of high-dose morphine impairs angiogenesis and mobilization of endothelial progenitor cells in mice. Anesth Analg. 2008;107:686-92.
51. *Lam CF, Liu YC, Hsu JK, Yeh PA, Su TY, Huang CC,* ***Lin MW****, Wu PC, Chang PJ, Tsai YC.* Autologous transplantation of endothelial progenitor cells attenuates acute lung injury in rabbits. Anesthesiology. 2008;108:392-401.
52. *Wang YJ,* ***Lin MW****, Wu SN, Sung RJ.* The activation by estrogen receptor agonists of the BK_{Ca}-channel in human cardiac fibroblasts. Biochem Pharmacol. 2007;73:1347-57.
53. *Wu SN, Wang YJ,* ***Lin MW****.* Potent stimulation of large-conductance Ca^{2+}-activated K^+ channels by rottlerin, an inhibitor of protein kinase C-delta, in pituitary tumor (GH_3) cells and in cortical neuronal (HCN-1A) cells. J Cell Physiol. 2007;210:655-66.
54. ***Lin MW****, Wu AZ, Ting WH, Li CL, Cheng KS, Wu SN.* Changes in membrane cholesterol of pituitary tumor (GH_3) cells regulate the activity of large-conductance Ca^{2+}-activated K^+ channels. Chin J Physiol. 2006;49:1-13. **(first author)**
55. *Wu SN, Wu AZ,* ***Lin MW****.* Pharmacological roles of the large-conductance calcium-activated potassium channel. Curr Top Med Chem. 2006;6(10):1025-30.
56. *Wang YJ, Sung RJ,* ***Lin MW****, Wu SN.* Contribution of BK_{Ca}-channel activity in human cardiac fibroblasts to electrical coupling of cardiomyocytes-fibroblasts. J Membr Biol. 2006;213:175-85.
57. *Chen LW,* ***Lin MW****, Hsu CM.* Different pathways leading to activation of extracellular signal-regulated kinase and p38 MAP kinase by formyl-methionyl-leucyl-phenylalanine or platelet activating factor in human neutrophils. J Biomed Sci. 2005;12:311-9.
58. ***Lin MW****, Yang SR, Huang MH, Wu SN.* Stimulatory actions of caffeic acid phenethyl ester, a known inhibitor of NF-κB activation, on Ca^{2+}-activated K^+ current in pituitary GH_3 cells. J Biol Chem. 2004;279:26885-92. **(first author)**
59. *Wu CM,* ***Lin MW****, Cheng JT, Wang YM, Huang YW, Sun WZ, Lin CR.* Regulated, electroporation-mediated delivery of pro-opiomelanocortin gene suppresses chronic constriction injury-induced neuropathic pain in rats. Gene Ther. 2004;11:933-40.
60. *Lan CY, Tan PH, Cheng JT, Lu HF,* ***Lin MW****, Hsiao PN, Lin CR.* Immunoneutralization of c-Fos using intrathecal antibody electroporation attenuates chronic constrictive injury-induced hyperalgesia and regulates preprodynorphin expression in rats.

Anesthesiology. 2003;99:938-46.

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