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Ph.D., Biomedical Sciences 生物醫學博士

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## Summary

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My lab focuses on integrating nanotechnology with biomedicine, particularly in cancer immunology/therapy and regenerative medicine. Our first research direction is developing novel synthetic nanocarriers and engineered targeted exosomes to address gene delivery issues. These exosomes can carry therapeutic mRNA and penetrate tissue/tumor barriers through specific targeting to meet therapeutic needs (*Chiang, et al. Blood, 2019; Chiang, et al. Nature Communication, 2023*). The second direction involves using micro/nanoscale biochips to capture and study single cancer stem cells or exosomes to explore their cellular biology under treatment (*Chiang, et al. Cell Reports, 2022; Hong Li\* & CL Chiang\*, co-first authors, et al. 2024*), and to achieve precise cell editing and reprogramming. With my interdisciplinary background and training in biochemistry, bioengineering, immunology, and hematology, I aim to make a substantial impact in this cutting-edge medical field.

Currently, our lab is working on two main projects: (i) **Liquid biopsy and exosome detection**: We target exosomes in patient body fluids using biochips for liquid biopsy to track molecular targets of various malignant cancers and identify new therapeutic targets. (ii) **Dual-targeting system and RNA drug delivery**: We use a dual-targeting system formed by monoclonal antibodies and specific peptide chains to encapsulate therapeutic RNA drugs into extracellular vesicles and deliver them specifically to diseased areas in vivo. These projects focus on two particularly aggressive cancers: highly fibrotic pancreatic cancer and small cell lung cancer. The five-year survival rates for these cancers are only 6% and 2%, respectively, and there are no effective second-line drugs available clinically. Through our research, we hope to provide new treatment options for these challenging cancers and significantly impact clinical treatment strategies and patient outcomes.

我實驗室的研究重點在於將奈米技術與生物醫學結合，專注於癌症免疫學/治療和再生醫學領域。我們的第一個研究方向是開發新型合成奈米載體和工程化靶向的外泌體，以解決基因傳遞問題。這些外泌體能夠攜帶治療性 mRNA，並通過特定靶向穿透組織/腫瘤屏障，從而滿足治療需求 (*Chiang, et al. Blood, 2019 ; Chiang, et al. Nature Communication, 2023*)。第二個方向則是利用微/奈米級生物晶片來捕獲和研究單一癌症幹細胞或外泌體，探討其在治療下的細胞生物學 (*Chiang, et al. Cell Reports, 2022 ; Hong Li\* & CL Chiang\*, co-first authors, et al. 2024*)，以及實現精確調控的細胞編輯和重新編程。基於我在生物化學、生物工程、免疫學和血液學方面的跨學科背景和訓練，我希望能在這個前沿醫學領域產生實質性的影響。

目前，我們的實驗室正在進行兩個主要計畫：(i) 液體活檢與外泌體檢測：我們以病人體液中的外泌體為檢測目標，利用生物晶片進行液體活檢，追蹤各類惡性癌症的分子標靶，並尋找新的治療標靶。(ii) 雙標靶系統與 RNA 藥物遞送：我們利用單克隆抗體與特異性肽鏈形成的雙標靶系統，將治療性的 RNA 藥物包埋至胞外囊泡中，並專一地遞送至活體內的病灶區域。這些研究計畫目前針對兩種特別惡性的癌症展開：高度纖維化的胰腺癌和小細胞肺癌。這兩種癌症的五年存活率分別僅為 6% 和 2%，且臨床上缺乏有效的第二線藥物。通過我們的研究，期待能夠為這些難治性癌症提供新的治療方案，並對臨床治療策略和患者預後產生顯著影響。

## Education

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2012-2019	<b>The Ohio State University (Columbus, OH, US)</b> PhD, Biomedical Sciences
2005-2008	<b>National Yang-Ming Chiao-Tung University (Taipei, Taiwan)</b> MS, Institute of Physiology
2001-2005	<b>National Yang-Ming Chiao Chiao-Tung University (Hsinchu, Taiwan)</b>

1998-2001 BS, Department of Biological Science and Technology  
**Taipei Municipal Jianguo High School (Taipei, Taiwan)**

## ***Work Experience***

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2024-present **National Yang Ming Chiao Tung University (Taipei, Taiwan)**  
Assistant professor, Institute of Biopharmaceutical Sciences

2019-2024 **The Ohio State University (Columbus, OH, US)**  
Postdoctoral fellow, Department of Chemical and Biomolecular Engineering (Professor L. James Lee)

2011-2012 **Academic Sinica (Taipei, Taiwan)**  
Research Assistant, Nanomedicine Program and Biochemistry (Dr. Kuan Wang, Academician)

2009-2011 **National Taiwan University (Taipei, Taiwan)**  
Research Assistant, Institute of Zoology and Applied Mechanics (Professor Hsinyu Lee)

## ***Expertise***

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<b>Hematology</b>	Hematopoiesis, Erythropoiesis, and Leukemia
<b>Immunology</b>	Development of B/T lymphoid, Immune checkpoints/exhaustion, Xenograft model, and Antibody modification
<b>Nanotechnology</b>	Nanoparticle, Nanoelectroporation, and Exosomal biochemistry
<b>DNA/RNA biology</b>	MicroRNA biology, mRNA maturation, and Synthetic/artificial RNA interference, LC (Limiting cell)-RNAseq, Cancer clonal evolution

## ***Project Participations***

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2024-present **Vesicular transcriptional factors as biomarkers for small cell lung cancer diagnosis and subtyping**  
Leader researcher: Dr. Chi-Ling Chiang, Chi-Ying F Huang, and L. James Lee

2024-present **High effective triple targeting cooperating extracellular vesicles and Bi-specific T-cell engagers (BiTEs) in small cell lung cancer**  
Leader researcher: Dr. Chi-Ling Chiang and L. James Lee

2019-2024 **Dual-targeted therapeutic exosomes for advanced cancer treatment**  
Leader researcher: Dr. L. James Lee

2012-2018 **A microchannel electroporation array for heterogeneity studies and drug response of chronic lymphocytic leukemia stem cells**  
Lead researchers: Dr. Natarajan Muthusamy, and L. James Lee

2012-2018 **Targeting delivery of miR29b by immunoliposome in chronic lymphocytic leukemia**  
Lead researchers: Dr. Natarajan Muthusamy and John C Byrd

2009-2011 **Microfluidic devices for the studies of drug selection and chemotherapeutic efficacy**  
Lead researcher: Dr. Andrew M. Wo

2009-2011 **Differentiation of human stem cells into blood cells**  
Lead researchers: Dr. Hsinyu Lee & Chao-Ling Yao

2009-2010 **Detection of circulating endothelial cells via a microfluidic disk**  
Lead researcher: Dr. Andrew M. Wo

2008-2009 **Biomedical function of lysophosphatidic acid**  
Lead researcher: Dr. Hsinyu Lee

2006-2007 **Follicle-stimulating hormone and transforming growth factor  $\beta$  1 regulation of mitochondrial biogenesis in rat ovarian granulosa cells**  
Lead researcher: Dr. Jiu-an-Jiu-an Hwang

2004-2005 **Development of an optical biosensor based on frequency modulation CMOS chip**  
Lead researcher: Dr. Yuh-Shyong Yang

## ***Honors and Awards***

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1. Dean's List Award, Department & Institute of Physiology. National Yang-Ming University, **2006**.
2. Scholarship of Taiwanese Government for Overseas Study, Ministry of Education of Taiwan, **2012-2013**
3. Fellowship of Nanoscale Science and Engineering Centers (NSEC) by National Science Foundation (NSF). **2012-2014**
4. Pelotonia Graduate Fellowship Award for cancer research, **2015**

- Travel award and oral presentation of International Workshop on Chronic Lymphocytic Leukemia (XVII iwCLL), **2017**
- Travel award of 51st Miami Winter Symposium Stem Cells, **2018**
- Invited speaker of Pelotonia fellowship by Wexner Comprehensive Cancer Center, **2018**
- American Institute of Chemists Foundation, Outstanding Post-Doctoral Student Award. **2021**

## ***Teaching portfolio***

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- RNA medicine
- Molecular biology
- Cell biology and cancer biology
- Drug delivery and target therapy
- Nanomedicine
- Immunology

## ***Publications***

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### ***Selected publications***

- CL Chiang**, SS A Chen, SJ Lee, KC Tsao, PL Chu, CL Yao, and H Lee, "LPA Induces Erythropoiesis through Activating LPA Receptor 3," *Stem Cells*. 2011 Sep 13. (SCI: 7.87)
- CL Chiang**, S Goswami, FW Frissora, Z Xie, PS Yan, R Bundschuh, LA Walker, Xiaomeng Huang, Rajeswaran Mani, XM Mo, S Baskar, C Rader, MA Phelps, G Marcucci, JC Byrd, LJ Lee, N Muthusamy, "ROR1-targeted delivery of miR-29b induces cell cycle arrest and therapeutic benefit in vivo in CLL mouse model." *Blood*. 2019 Aug 1;134(5):432-444. (SCI: 25.66)
- CL Chiang**, MH Cheng, CH Lin. "From nanoparticles to cancer nanomedicine: old problems with new solutions." *Nanomaterials*. 2021 11 (7), 1727. (SCI: 5.35)
- CL Chiang**, EY Hu, L Chang, J Labanowska, K Zapolnik, X Mo, J Shi, TJ Doong, A Lozanski, PS Yan, R Bundschuh, LA Walker, D Gallego-Perez, W Lu, M Long, S Kim, NA Heerema, G Lozanski, JA Woyach, JC Byrd, LJ Lee, N Muthusamy. "Leukemia-initiating HSCs in chronic lymphocytic leukemia reveal clonal leukemogenesis and differential drug sensitivity," *Cell Reports*. 2022 Jul 19;40(3):111115. (SCI: 10.00)
- CL Chiang**, Y Ma, YC Hou, Sinyu Chen, MH Chien, ZX Zhang, WH Hsu, X Wang, J Zhang, H Li, L Sun, PS Yan, S Fallen, I Lee, XY Chen, YS Chu, C Zhang, TS Cheng, E Reategui, W Lu, R Lee, Y Yuan, HC Liu, Kai Wang, Michael Hsiao, CY Huang, YS Shan, AS Lee and LJ Lee. "Dual targeted extracellular vesicles regulate oncogenic genes in advanced pancreatic cancer." *Nature Communication*. 14 (1), 6692. (SCI:16.6).
- Hong Li, **CL Chiang** (co-first author\*), et al., Chi-Ying F. Huang, Cheng-Hsu Wang, Yan-Shen Shan, Chung-Pin Li, Martin Fleisher and L. James Lee, "Exosomal mRNA and microvesicular protein of Glypican 1 in pancreatic cancer diagnosis," *Advanced Science*. (IF=17.5).
- Yifan Ma, Lili Sun, Jingjing Zhang, **CL Chiang**, et al., Yuan Yuan and L. James Lee, "Exosomal mRNAs for angiogenic-osteogenic coupled bone repair," *Advanced Science*, 2302622 (SCI: 17.5)
- S Goswami, **CL Chiang**, K Zapolnik, J Nunes, A Ventura, X Mo, Z Xie, LJ Lee, S Baskar, C Rader, JC Byrd, M Phelps, B Bhatnagar, N Muthusamy. "ROR1 targeted immunoliposomal delivery of OSU-2S shows selective cytotoxicity in t (1; 19)(q23; p13) translocated B-cell acute lymphoblastic leukemia," *Leukemia research* 118, 106872 2022. (SCI: 3.71)
- J Pan, **CL Chiang**, X Wang, P Bertani, Yifan Ma, J Cheng, V Talesara, LJ Lee, W Lu. "Cell membrane damage and cargo delivery in nano-electroporation," *Nanoscale*. 2023 Feb 23;15(8):4080-4089. doi: 10.1039/d2nr05575a. "Cell membrane damage and cargo delivery in nano-electroporation," *Nanoscale*. 2023 Feb 23;15(8):4080-4089. doi: 10.1039/d2nr05575a. (SCI: 8.31)
- S Goswami, R Mani, J Nunes, **CL Chiang**, K Zapolnik, E Hu, F Frissora, XM Mo, LA Walker, PYan, R Bundschuh, L Beaver, R Devine, YT Tsai, A Ventura, Z Xie, M Chen, R Lapalombella, A Walker, A Mims, K Larkin, N Grieselhuber, C Bennett, M Phelps, E Hertlein, G Behbehani, S Vasu, JC Byrd, N Muthusamy. "PP2A is a therapeutically targetable driver of cell fate decisions via a c-Myc/p21 axis in human and murine acute myeloid leukemia," *Blood*. 2022. 139 (9), 1340-1358. (SCI: 25.66)
- EY Hu, P Do, S Goswami, J Nunes, **CL Chiang**, S Elgamal, AM Ventura, C Cheney, K Zapolnik, E Williams, R Mani, F Frissora, X Mo, L Waldmeier, RR Beerli, H Peng, C Rader, M Long, U Grawunder, JC Byrd, N Muthusamy. "The ROR1 antibody-drug conjugate huXBR1-402-G5-PNU effectively targets ROR1<sup>+</sup> leukemia." *Blood advances* 5 (16), 3152-3162. 2021. (SCI: 6.80)
- EY Hu, JS Blachly, C Saygin, HG Ozer, SE Workman, A Lozanski, TJ Doong, **CL Chiang**, S Bhat, KA Rogers, JA Woyach, KR Coombes, D Jones, N Muthusamy, G Lozanski, JC Byrd "LC-FACSeq is a method for detecting rare clones in leukemia." *JCI insight* 5 (12) 2020 (SCI: 6.20)
- S Goswami, **CL Chiang**, K Zapolnik, Z Xie, JL Lee, S Baskar, C Rader, JC Byrd, MA Phelps, B Bhatnagar, N Muthusamy. "ROR1 Targeted Immunoliposomal Delivery of OSU-2S Show Selective Cytotoxicity in t(1;19) Translocated B-ALL." *Blood*,

*The Journal of the American Society of Hematology* 134. 2019.

14. Z Yang, J Shi, J Xie, Y Wang, J Sun, T Liu, Y Zhao, X Zhao, X Wang, Y Ma, V Malkoc, **CL Chiang**, W Deng, Y Chen, Y Fu, KJ Kwak, Y Fan, C Kang, CC Yin, J Rhee, P Bertani, J Otero, W Lu, K Yun, AS Lee, W Jiang, L Teng, BYS Kim, LJ Lee. "Large-scale generation of functional mRNA-encapsulating exosomes via cellular nanoporation." *Nature Biomedical Engineering* 4 (1), 69-83. (SCI: 18.95)
15. LC Hsiung, **CL Chiang**, CH Wang, YH Huang, CT Kuo, JY Cheng, CH Lin, V Wu, HY Chou, DS Jong, H Lee, and A M. Wo, "Dielectrophoresis-based cellular microarray chip for anticancer drug screening in perfusion microenvironments," *Lab on a Chip*. 2011; 21;11(14):2333-42. (SCI: 6.26)
16. CT Kuo, **CL Chiang**, R YJ Huang, H Lee and A M Wo, "Configurable 2D and 3D spheroid tissue cultures on bioengineered surfaces with acquisition of epithelial-mesenchymal transition characteristics," *NPG Asia Materials*. 2012; 4, e27; doi:10.1038/am.2012.50. (SCI: 9.04)
17. CT Kuo, **CL Chiang**, CH Chang, HK Liu, GS Huang, R YJ Huang, H Lee, CS Huang, A M. Wo "Modeling of cancer metastasis and drug resistance via biomimetic nano-cilia and microfluidics," *Biomaterials*, 2014, 1562-1571. (SCI: 7.60)
18. R Mani, Y Mao, F Frissora, **CL Chiang**, J Wang, Y Zhao, Y Wu, B Yu , R Yan, X Mo, L Yu, J Flynn, J Jones, L Andritsos, S Baskar, C Rader, M Phelps, CS Chen, R Lee, J C. Byrd, LJ Lee. "Tumor antigen ROR1 targeted drug delivery mediated selective leukemic but not normal B cell cytotoxicity in chronic lymphocytic leukemia," *Leukemia*, 2014. (SCI: 10.16)
19. Y You, Y Tian, Z Yang, J Shi, KJ Kwak, Y Tong, A P Estania, J Cao, WH Hsu, Y Liu, **CL Chiang**, BR Schrank, K Huntoon, DY Lee, Ziwei Li, Y Zhao, H Zhang, TD Gallup, JH Ha, S Dong, Xuefeng Li, Y Wang, WJ Lu, E Bahrani, LJ Lee, L Teng, W Jiang, F Lan, BYS Kim, AS Lee. "Intradermally delivered mRNA-encapsulating extracellular vesicles for collagen-replacement therapy," *Nature Biomedical Engineering*. 2023 Jan 12. doi: 10.1038/s41551-022-00989-w. (SCI: 18.95)
20. LTH Nguyen, J Zhang, XY Rima, X Wang, KJ Kwak, T Okimoto, J Amann, MJ Yoon, T Shukuya, **CL Chiang**, N Walters, Y Ma, D Belcher, H Li, AF Palmer, DP Carbone, LJ Lee, E Reátegui. "An immunogold single extracellular vesicular RNA and protein (AuSERP) biochip to predict responses to immunotherapy in non-small cell lung cancer patients," *J Extracellular Vesicles*. 2022 Sep;11(9):e12258. (SCI: 17.33)
21. XY Rima, J Zhang, LTH Nguyen, A Rajasuriyar, MJ Yoon, **CL Chiang**, N Walters, KJ Kwak, LJ Lee, Eduardo Reátegui. "Microfluidic harvesting of breast cancer tumor spheroid-derived extracellular vesicles from immobilized microgels for single-vesicle analysis," *Lab on a Chip* 2022 (13), 2502-2518 (SCI: 7.51)
22. Yi You, Y Tian, Z Yang, J Shi , KJ Kwak , Y Tong, AP Estania , J Cao, WH Hsu, Y Liu, **CL Chiang**, B Shrank, K Huntoon, D Lee, Z Li, Y Zhao, H Zhang, T Gallup, J Ha, S Dong , X Li, Y Wang, WJ Lu, E Bahrani, LJ Lee, L Teng , Wen J, Feng Len, BYS. Kim and Andrew S. Lee, "Intradermally delivered mRNAencapsulating extracellular vesicles for collagen-replacement therapy" *Nature Biomedical Engineering* (SCI: 29.2), <https://doi.org/10.1038/s41551-022-00989-w> (2023).

### **Other journal publications**

1. KC Chen, TP Lee, YC Pan, **CL Chiang**, CL Chen, YH Yang, BL Chiang, H Lee, A M. Wo. "Detection of Circulating Endothelial Cells via a Microfluidic Disk," *Clinical Chemistry*, 2011; 57: 586-592. (SCI: 6.87)
2. L Chang, M Howdyshell, WC Liao, **CL Chiang**, D GallegoPerez, Z Yang, W Lu, J C. Byrd, N Muthusamy, L. J Lee, and R Sooryakumar. "Magnetic Tweezers-Based 3D Microchannel Electroporation for High-Throughput Gene Transfection in Living Cells," *Small*, 2014. (SCI: 7.82)
3. X Wang, H He, Y Lu, W Ren, K Teng, **CL Chiang**, Z Yang, Bo Yu, S Hsu, S T. Jacob, K Ghosha, LJ Lee. "Indole-3-carbinol inhibits tumorigenicity of hepatocellular carcinoma cells via suppression of microRNA-21 and upregulation of phosphatase and tensin homolog," *Biochim Biophys Acta*. 2015.1853(1):244-53 (SCI: 4.54)
4. YH Ho, CL Yao, KH Lin, FH Hou, WM Chen, **CL Chiang**, YN Lin, MW Li, SH Lin, YJ Yang, CC Lin, J Lu, G Tigy, H Lee. "Opposing regulation of megakaryopoiesis by LPA receptors 2 and 3 in K562 human erythroleukemia cells," *Biochim Biophys Acta*. 2015 Feb;1851(2):172-83. (SCI: 4.54)
5. WY Ma, LC Hsiung, CH Wang, **CL Chiang**, CH Lin, CS Huang, AM. Wo. "A Novel 96 well-formatted Micro-gap Plate Enabling Drug Response Profiling on Primary Tumour Samples," *Scientific Reports*. 2015 Apr 13;5:9656. (SCI: 5.07)
6. R Mani, **CL Chiang**, F W. Frissora, R Yan, X Mo, S Baskar, Christoph Rader, R Klisovic, M A Phelps, CS Chen, RJ Lee, J C. Byrd, R Baiocchi, LJ Lee, N Muthusamy. "ROR1-targeted delivery of OSU-2S, a nonimmunosuppressive FTY720 derivative, exerts potent cytotoxicity in mantle-cell lymphoma in vitro and in vivo." *Exp Hematol*. 2015 Sep;43(9):770 (SCI: 2.48)
7. L Chang, D Gallego-Perez, X Zhao, P Bertani, Z Yang, **CL Chiang**, V Malkoc, J Shi, C K Sen, L Odonnell, J Yu, W Lu, LJ Lee. "Dielectrophoresis-assisted 3D nanoelectroporation for non-viral cell transfection in adoptive immunotherapy." *Lab Chip*. 2015 Aug 7;15(15) (SCI: 6.12)
8. P Bertani, W Lu, L Chang, D Gallego-Perez, L J Lee, **CL Chiang**, N Muthusamy. "Bosch etching for the creation of a 3D nanoelectroporation system for high throughput gene delivery." *J of Vacuum Science & Tech B*. 2015 Nov (33). (SCI: 1.46)
9. Z Yang, L Chang, **CL Chiang**, LJ Lee. "Micro-/nano-electroporation for active gene delivery." *Curr Pharm Des*. 2015;21(42):6081-8.
10. L Chang, P Bertani, D Gallego-Perez, Z Yang, F Chen, CL Chiang, V Malkoc, T Kuang, K Gao, L. J Lee, W Lu. "3D nanochannel electroporation for high-throughput cell transfection with high uniformity and dosage control." *Nanoscale*. 2016 Jan 7;8(1):243-52 (SCI: 7.39)

11. K Gao, X Huang, **CL Chiang**, X Wang, P Boukany, G Marcucci, R Lee, LJ Lee. "Induced Apoptosis Investigation in Wild-Type and FLT3-ITD Acute Myeloid Leukemia Cells by Nanochannel Electroporation and Single Cell qRT-PCR." *Mol Ther.* 2016. Jan 19 (SCI: 6.83)
12. KH Lin, YH Ho, JC Chiang, MW Li, SH Lin, WM Chen, **CL Chiang**, YN Lin "Pharmacological activation of lysophosphatidic acid receptors regulates erythropoiesis." *Scientific reports* 6, 2016 May 31, 27050 (SCI: 4.26)
13. L Chang, D Gallego-Perez, **CL Chiang**, P Bertani, T Kuang, Y Sheng, F Chen, Z Chen, J Shi, H Yang, X Huang, V Malkoc, W Lu, LJ Lee "Controllable Large-Scale Transfection of Primary Mammalian Cardiomyocytes on a Nanochannel Array Platform." *Small.* 2016. Nov 1 (43) (SCI: 8.64)
14. X Huang, S Schwind, R Santhanam, AK Einfeld, **CL Chiang**, M Lankenau, B Yu, P Hoellerbauer, Y Jin, SS Tarighat, J Khalife, A Walker, D Perrotti, CD Bloomfield, H Wang, RJ Lee, LJ Lee, G Marcucci. "Targeting the RAS/MAPK pathway with miR-181a in acute myeloid leukemia." *Oncotarget.* 2016 Sep 13, 7 (37) (SCI: 5.17)
15. Z Yang, J Xie, J Zhu, C Kang, **CL Chiang**, X Wang, X Wang, T Kuang, F Chen, Z Chen, A Zhang, B Yu, RJ Lee, L Teng, LJ Lee "Functional exosome-mimic for delivery of siRNA to cancer: in vitro and in vivo evaluation." *Journal of Controlled Release* 243, 160-171 (SCI: 7.79)
16. L Chang, **CL Chiang**, Y Jiao, L Teng. "Nonviral Transfection Methods of Efficient Gene Delivery: Micro-/Nano-Technology for Electroporation." *THE WORLD SCIENTIFIC ENCYCLOPEDIA OF NANOMEDICINE AND BIOENGINEERING I: Volume 3: Nanotechnology in Gene Delivery.* 2017. 175-218
17. LA Walker, MG Sovic, **CL Chiang**, E Hu, JK Denninger, X Chen, ED Kirby, JC Byrd, N Muthusamy, R Bundschuh, P Yan. "CLEAR: coverage-based limiting-cell experiment analysis for RNA-seq." *Journal of translational medicine* 18 (1), 63. 2020 (SCI: 4.19)

## References

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