

葉麗 Li Ye



職稱/Position: 教授/Professor

課程主任/Program Director

學院/Faculty: 藥學院/School of Pharmacy

電郵/Email: lye@must.edu.mo

電話/Tel: (853) 8897-2831

辦公室/Office: E213c

地址/Address: 澳門氹仔偉龍馬路澳門科技大學/Macau University of Science and Technology, Avenida Wai Long, Taipa, Macau

教學科目: 免疫學與微生物學; 現代生物技術; 生物化學與分子生物學; 現代生物技術與新藥研究; 高等藥劑學

Teaching activity: Immunology and Microbiology; Modern Biotechnology; Biochemistry & Molecular Biology; Modern Biotechnology in Novel Drug Development; Advanced Pharmaceutics

研究方向: 單域抗體、抗體融合蛋白與重組細胞因子; 免疫檢查點抑制劑; 抗體-藥物偶聯物; 生物轉化與微生物發酵

Research interest: Single-domain antibody, Antibody fusion protein and recombinant cytokine; Immune checkpoint inhibitor; Antibody-drug conjugate; Biotransformation and Microbial Fermentation.

研究课题/Research project:

1. 澳門科學技術發展基金0019/2024/RIA1, 治療肺纖維化的吸入型盤狀蛋白結構域受體1(DDR1)單域抗體的研究與開發, 2024-10-30至2027-10-30, Mop212.5萬/Research and development of an inhalable Discoidin Domain Receptor 1 (DDR1) single-domain antibody for the treatment of pulmonary fibrosis. FDCT, No. 0019/2024/RIA1.

2. 澳門科學技術發展基金0148/2022/A3, 新型抗DDR1納米抗體-CD80融合蛋白通過重塑腫瘤微環境及雙重免疫檢查點阻斷治療胃癌的作用和成藥性研究, 2023-05-18至2026-05-18, MOP168萬/ The therapeutic effect of a novel anti-DDR1 nanobody-CD80 fusion protein on gastric cancer through remodeling tumor microenvironment and dual immune checkpoint blockade and its druggability. FDCT, No. 0148/2022/A3.
3. The cancer immunotherapeutical efficacy of immune checkpoint inhibitor SIRP α Fc fusion protein targeting tumor stroma collagen, Macau University of Science and Technology Faculty Research Grants (No. FRG-22-090-SP), 2022.10-2023.10
4. 廣東省教育廳科研平臺, 2023LSYS001, 介入醫學粵港澳高校聯合實驗室, 專案負責人 (澳門) / Guangdong-Hong Kong-Macao University Joint Laboratory of Interventional Medicine, Foundation of Guangdong Province (2023LSYS001).
5. 上海菌濟健康科技有限公司合作課題, 合成生物學在皮膚和消化道疾病中的應用開發 (2023.5-2026.5) / Application and Development of Synthetic Biology in Skin and Digestive Diseases.
6. 上海市科學技術委員會, 生物醫藥科技支撐專項, 20S11901600, 靶向PD-L1和Wnt信號治療腦膠質瘤的創新抗體-免疫啟動偶聯物研究與開發, 2020-10至2023-09/A novel Immune-stimulating Antibody Conjugates (ISAC) targeting PD-L1 and Wnt signaling for the treatment of glioma. Scientific and Innovative Action Plan of Shanghai, No. 20S11901600 (2020-2023).
7. 上海市科學技術委員會, 生物醫藥重點專案, 18431902800, 創新免疫檢查點抑制劑SIRP α -Fc融合蛋白的臨床前研究, 2018-04至2021-06/ Preclinical study of a novel immune checkpoint inhibitor SIRP α Fc fusion protein. Scientific and Innovative Action Plan of Shanghai, No. 18431902800 (2018-2021).
8. 國家自然科學基金面上專案, 81572979, 利用非天然氨基酸構建位點特異性IL2/sorafenib偶聯物及其抗腫瘤作用機制研究, 2016-01至2019-12/ Construction of site-specific IL-2/Sorafenib conjugates using unnatural amino acids and the antitumor activity and mechanism. National Natural Science Foundation of China, No. 81572979(2016-2019).

9. 上海高水準地方高校創新團隊“原創生物藥發現與轉化”(2021.10-2024.07)/Shanghai high-level local university innovation team “Cancer metastasis and original biologics”(2021-2024).

學歷/Education

- 2010 復旦大學，博士學位/PhD, School of Pharmacy, Fudan University, Shanghai, China
- 2001 復旦大學，碩士學位/Master, School of Pharmacy, Fudan University, Shanghai, China
- 1992 上海醫科大學，學士學位/Bachelor, School of Pharmacy, Shanghai Medical University, Shanghai, China.

工作經驗/Work experience

- 2022- 澳門科技大學，教授/ Professor, Macau University of Science and Technology
- 2011-2022 復旦大學，副教授/Associate professor, Fudan University, Shanghai, China
- 1997-2011 復旦大學，講師/ Lecturer, Fudan University, Shanghai, China
- 1992-1997 上海醫科大學，助教/ Assistant, Shanghai Medical University, Shanghai, China

代表性文章/Publications

1. Huang X, Kuerban K, Fan J, Pan D, Chen H, Jiayang Liu, Wang S, Ju D, Zhu YZ, Liu J, Ye L*. IL-2-loaded liposomes modified with sorafenib derivative exert a synergistic anti-melanoma effect via improving tumor immune microenvironment and enhancing antiangiogenic activity. *Asian Journal Pharmaceutical Sciences*, 2024 (accepted). Reference: AJPS_101020
2. Pan D, Liu J, Huang X, Wang S, Kuerban K, Yan Y, Zhu YZ, **Ye L***. Challenges and New Directions in Therapeutic Cancer Vaccine Development. *Vaccines*. 2024; 12(12):1341. <https://doi.org/10.3390/vaccines12121341>
3. Liu J, Xu T, Pan D, Fan J, Fu Y, Huang X, Zhao W, Dong X, Zhang S, Kuerban K, Huang X, Wang S, Chen H, He Y, Zhu YZ, Wang C, **Ye L***. A collagen-binding SIRPαFc fusion protein for targeted cancer immunotherapy. *International Immunopharmacology*. 2023,124:110951.

4. Li J, Zhang Y, Ye F, Qian P, Qin Z, Li D, **Ye L***, Feng L*. DKK1 Promotes Epithelial–Mesenchymal Transition and Cisplatin Resistance in Gastric Cancer via Activation of the PI3K/AKT Pathway. *Cancers*. 2023, 15, 4756.
5. Liu J, Pan D, Huang X, Wang S, Chen H, Zhu YZ, **Ye L***. Targeting collagen in tumor extracellular matrix as a novel targeted strategy in cancer immunotherapy. *Frontiers in Oncology*. 2023, 13:1225483.
6. Cai M, Huang X, Huang X, Ju D, Zhu YZ, **Ye L***. Research progress of interleukin-15 in cancer immunotherapy. *Front. Pharmacol*. 2023, 14:1184703.
7. Wang S, Hu P, Fan J, Zou J, Hong W, Huang X, Pan D, Chen H, Zhu YZ, **Ye L***. CD80-Fc fusion protein as a potential cancer immunotherapy strategy. *Antibody Therapeutics*. 2024, 7(1): 28-36.
8. Wang S, Fu Y, Kuerban K, Liu J, Huang X, Pan D, Chen H, Zhu YZ, **Ye L***. Discoidin domain receptor 1 (DDR1) is a potential target correlated with tumor invasion and immune infiltration in gastric cancer. *Front. Immunol*. 2022; 13:933165.
9. Liu J, Meng Z, Xu T, Kuerban K, Wang S, Zhang X, Fan J, Ju D, Tian W, Huang X, Huang X, Pan D, Chen H, Zhao W and **Ye L***. A SIRPaFc Fusion Protein Conjugated with the Collagen-Binding Domain for Targeted Immunotherapy of Non-Small Cell Lung Cancer. *Front. Immunol*. 2022;13:845217.
10. 张慧, 陈华宁, 库德莱迪 •库尔班, 王松娜, 赵缜, **叶丽***. Wnt/ β -catenin信号通路与癌症发生发展. *中国生物工程杂志*. 2022;42:47-54.
11. Li J, Zhang H, Bei S, Zhang X, Li H, **Ye L***, Feng L* Disruption of Wnt/ β -catenin pathway elevates the sensitivity of gastric cancer cells to PD-1 antibody. *Curr Mol Pharmacol*. 2022, 15, 557-569.
12. Zhang H, Bi Y, Wei Y, Liu J, Kuerban K, **Ye L***. Blocking Wnt/ β -catenin Signal Amplifies Anti-PD-1 Therapeutic Efficacy by Inhibiting Tumor Growth, Migration, and Promoting Immune Infiltration in Glioblastomas. *Molecular cancer therapeutics*. 2021;20(7):1305-1315.
13. Kuerban K, Gao X, Zhang H, Liu J, Dong M, Wu L, Ye R, Feng M, **Ye L***. Doxorubicin-loaded bacterial outer-membrane vesicles exert enhanced anti-

tumor efficacy in non-small-cell lung cancer. *Acta Pharmaceutica Sinica B*. 2020;10(8): 1534-1548.

14. Wang K, Kuerban K, Wan Q, Yu Z, **Ye L***, Chen Y*. Introduction of Mercaptoethyl at Sorafenib Pyridine-2-Amide Motif as a Potentially Effective Chain to Further get Sorafenib-PEG-DGL. *Molecules*. 2020;25: 573.
15. Dong M, Ye T, Bi Y, Wang Q, Kuerban K, Li J, Feng M, Wang K, Chen Y, **Ye L***. A novel hybrid of 3-benzyl coumarin seco-B-ring derivative and phenylsulfonylfuroxan induces apoptosis and autophagy in non-small-cell lung cancer. *Phytomedicine*. 2019;52: 79-88.
16. Ji Y, Wang Q, Zhao Q, Zhao S, Li L, Sun G, **Ye L***. Autophagy suppression enhances DNA damage and cell death upon treatment with PARP inhibitor Niraparib in laryngeal squamous cell carcinoma. *Applied Microbiol Biotechnol*. 2019;103:9557-9568.
17. Zhang X#, Wang Y#, Fan J, Chen W, Luan J, Mei X, Wang S, Li Y, **Ye L**, Li S, Tian W, Yin K*, Dianwen Ju*. Blocking CD47 efficiently potentiated therapeutic effects of anti-angiogenic therapy in non-small cell lung cancer. *J Immunother Cancer*. 2019;7:346.
18. Gu Z, Fu A, **Ye L**, Kuerban K, Wang Y, Cao Z. Ultra-Sensitive Chemiluminescence Biosensor for Nuclease and Bacteria Determination Based on Hemin-Encapsulated Mesoporous Silica Nanoparticle. *ACS Sensors* (2019), DOI:10.1021/acssensors.9b01303.
19. Qi F, Zhang C, Jiang S, Wang Q, Kuerban K, Luo M, Dong M, Zhou X, Wu L, Jiang B, **Ye L***. S-ethyl ethanethiosulfinate, a derivative of allicin, induces metacaspase-dependent apoptosis through ROS generation in *Penicillium chrysogenum*. *Biosci Rep*, 2019(39): BSR20190167.
20. Wang Y, Wang Q, Kuerban K, Dong M, Qi F, Li G, Ling J, Qiu W, Zhang W, **Ye L***. Colonic electrical stimulation promotes colonic motility through regeneration of myenteric plexus neurons in slow transit constipation beagles. *Biosci Rep*, 2019(39): BSR20182405.
21. Dong M, Meng Z, Kuerban K, Qi F, Liu J, Wei Y, Wang Q, Jiang S, Feng M, **Ye L***. Diosgenin promotes anti-tumor immunity and PD-1 antibody efficacy against melanoma by regulating intestinal microbiota. *Cell Death Dis*. 2018;9:1039.

22. Wang Q, Guo Y, Jiang S, Dong M, Kuerban K, Li J, Feng M, Chen Y, **Ye L***. A hybrid of coumarin and phenylsulfonylfuroxan induces caspase-dependent apoptosis and cytoprotective autophagy in lung adenocarcinoma cells. *Phytomedicine*. 2018;39:160-167.
23. Song G, Yang D, Wang Y, Chris de Graaf, Zhou Q, Jiang S, Liu K, Cai X, Dai A, Lin G, Liu D, Wu F, Wu Y, Zhao S, **Ye L**, Han GW, Lau J, Wu B, Hanson MA, Liu Z, Wang M & Stevens RC. Human GLP-1 receptor transmembrane domain structure in complex with allosteric modulators. *Nature*. 2017;546: 312-315. doi:10.1038/nature22378.
24. Song P, Wang Z, Zhang X, Fan J, Li Y, Chen Q, Wang S, Liu P, Luan J, **Ye L***, Ju D*. The role of autophagy in asparaginase-induced immune suppression of macrophages. *Cell Death & Dis*. 2017;8: e2721.
25. Jiang S, Wang Q, Feng M, Li J, Guan Z, An D, Dong M, Peng Y, Kuerban K, **Ye L***. C2-ceramide enhances sorafenib-induced apoptosis via Caspase-dependent and PI3K/AKT/mTOR signaling pathways in HCC cells. *Appl. Microbiol Biotechnol*. 2017;101:1535-1546.
26. Hu X, Shi S, Wang H, Yu X, Wang Q, Jang S, Ju D, **Ye L***, Feng M*. Blocking autophagy improves the anti-tumor activity of afatinib in lung adenocarcinoma with activating EGFR mutations in vitro and in vivo. *Sci Rep*. 2017;7:4559.
27. Chen Q#, **Ye L#**, Fan J, Zhang X, Song P, Wang Z, Wang S, Li Y, Luan J, Wang Y, Chen W, Zai W, Yang P, Cao Z, Ju D. Autophagy suppression potentiates the anti-glioblastoma effect of asparaginase in vitro and in vivo. *Oncotarget*. 2017;8(53):91052-91066.
28. Li J, Wang W, Han L, Feng M, Lu H, Yang L, Hu X, Shi S, Jiang S, Wang Q, **Ye L***. Human apolipoprotein A-I exerts a prophylactic effect on high fat diet-induced atherosclerosis in a rabbit model via inflammation inhibition. *Acta Biochimica et Biophysica Sinica*. 2017, 49(2), 149-158.
29. Jiang S, Fan J, Wang Q, Ju D, Feng M, Li J, Guan Z, An D, Wang X, **Ye L***. Diosgenin induces ROS-dependent autophagy and cytotoxicity via mTOR signaling pathway in chronic myeloid leukemia cells. *Phytomedicine*. 2016, 23:

243-252.

30. **Ye L**, Fan J, Shi X, Tao Q, Ye D, Xian Z, Zeng X, Li Y, Feng M, Ju D. Tumor necrosis therapy antibody interleukin-2 fusion protein elicits prolonged and targeted antitumor effects in vivo. *Appl. Microbiol Biotechnol.* 2014, 98: 4053-4061.
31. Song P#, **Ye L#**, Fan J, Li Y, Zeng X, Wang Z, Wang S, Zhang G, Ping Yang, Cao Z, Ju D. Asparaginase induced apoptosis and cytoprotective autophagy in chronic myeloid leukemia cells. *Oncotarget.* 2015, 6(6): 3861-3873.
32. Feng M, Liao Z, Han L, Li J, **Ye L***. Enhancement of microbial hydroxylation of 13-ethylgon-4-ene-3,17-dione by *Metarhizium anisopliae* using nanoliposome technique. *J. Ind. Microbiol. Biotechnol.* 2014, 41(4): 619-627.
33. **Ye L#**, Zhang C#, Li J, Shi X, Feng M. Effects of external calcium on the biotransformation of ginsenoside Rb1 to ginsenoside Rd by *Paecilomyces bainier* 229-7. *World J. Microbiol. Biotechnol.* 2012, 28(3): 857-863.
34. **Ye L**, Liu X, Zhou W, Feng M, Shi X, Li J, Chen D, Zhou P. Microbial transformation of astragalosides to astragaloside IV by *Absidia corymbifera* AS2, *Process Biochem*, 2011, 46 (9) : 1724-1730.
35. **Ye L**, Zhou C, Zhou W, Zhou P, Chen D, Liu X, Shi X, Feng M. Biotransformation of ginsenoside Rb1 to ginsenoside Rd by highly substrate-tolerant *Paecilomyces bainier* 229-7, *Bioresour. Technol.*, 2010, 101 (20) : 7872-787.

授權專利/Licensed Patents

1. The application of *Metarhizium anisopliae* mutant in steroid hydroxylation. ZL 2011 1 0199550.7.
2. Microbial transformation of astragalosides to astragaloside IV by *Absidia corymbifera* AS2. ZL 2010 1 0615265.4
3. Biotransformation of ginsenoside Rb1 to ginsenoside Rd. ZL 2011 1 0207782.2
4. Optimization methods for biotransformation of desogestrel using nano-liposome technique. ZL 2013 1 048 4977.0

教材/Textbook

《生物技術藥物學》（2024，科學出版社，副主編）

《生物技術製藥》（2016和2021版，中國醫藥科技出版社，編委）

《生物製藥工藝學》（2016和2022版，人民衛生出版社，編委）
Associate Editor in Pharmacology of Anti-Cancer Drugs (specialty section of
Frontiers in Pharmacology and Frontiers in Oncology)