

叶丽 Li Ye



职称/Position: 教授/Professor

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教学科目: 免疫学与微生物学; 现代生物技术; 生物化学与分子生物学; 现代生物技术与新药研究; 高等药剂学

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

研究方向: 单域抗体、抗体融合蛋白与重组细胞因子; 免疫检查点抑制剂; 抗体-药物偶联物; 生物转化与微生物发酵

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. 澳门科学技术发展基金0148/2022/A3, 新型抗DDR1纳米抗体-CD80融合蛋白通过重塑肿瘤微环境及双重免疫检查点阻断治疗胃癌的作用和成药性研究, 2023-05-18至2026-05-18, MOP168万/ 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.
2. 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

3. 广东省教育厅科研平台, 2023LSYS001, 介入医学粤港澳高校联合实验室, 项目负责人 (澳门) / Guangdong-Hong Kong-Macao University Joint Laboratory of Interventional Medicine, Foundation of Guangdong Province (2023LSYS001).
4. 上海菌济健康科技有限公司合作课题, 合成生物学在皮肤和消化道疾病中的应用开发 (2023.5-2026.5) / Application and Development of Synthetic Biology in Skin and Digestive Diseases.
5. 上海市科学技术委员会, 生物医药科技支撑专项, 20S11901600, 靶向PD-L1和Wnt信号治疗脑胶质瘤的创新抗体-免疫启动偶联物研究与开发, 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).
6. 上海市科学技术委员会, 生物医药重点项目, 18431902800, 创新免疫检查点抑制剂SIRP α -Fc融合蛋白的临床前研究, 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).
7. 国家自然科学基金面上项目, 81572979, 利用非天然氨基酸构建位点特异性IL2/sorafenib偶联物及其抗肿瘤作用机制研究, 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).
8. 上海高水平地方高校创新团队“原创生物药发现与转化”(2021.10-2024.07) /Shanghai high-level local university innovation team “Cancer metastasis and original biologics”(2021-2024).

学历/Education

2010 复旦大学, 博士学位/PhD, School of Pharmacy, Fudan University, Shanghai, China

2001 复旦大学，硕士学位 /Master, School of Pharmacy, Fudan University, Shanghai, China

1992 上海医科大学，学士学位/Bachelor, School of Pharmacy, Shanghai Medical University, Shanghai, China.

工作经验/Work experience

2022- 澳门科技大学，教授/ Professor, Macau University of Science and Technology

2011-2022 复旦大学，副教授/Associate professor, Fudan University, Shanghai, China

1997-2011 复旦大学，讲师/ Lecturer, Fudan University, Shanghai, China

1992-1997 上海医科大学，助教/ Assistant, Shanghai Medical University, Shanghai, China

代表性文章/Publications

1. 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.
2. 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.
3. 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.
4. 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.
5. 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.
6. 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.

7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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.
13. 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.
14. 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.
15. 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.

16. 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.
17. 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.
18. 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.
19. 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.
20. 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.
21. 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.
22. 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.
23. 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.

24. 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.
25. 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.
26. 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.
27. 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.
28. **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.
29. 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.
30. 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.
31. **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.

32. **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.
33. **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.

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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

《生物技术药物学》（2023，科学出版社，副主编）
《生物技术制药》（2016和2021版，中国医药科技出版社，编委）
《生物制药工艺学》（2016和2022版，人民卫生出版社，编委）

Associate Editor in Pharmacology of Anti-Cancer Drugs (specialty section of
Frontiers in Pharmacology and Frontiers in Oncology)