**重庆市自然科学奖公示**

1. **项目名称**：非编码RNA调控的代谢重编程促肿瘤转移复发的新功能与分子机制

**二、提名单位：**重庆市渝中区人民政府

**三、提名等级：**重庆市自然科学奖 二等奖

**四、主要完成单位：**重庆医科大学

**五、主要完成人：**柳满然、杨丽萍、秦旖璐、刘水清、万雪颖

**六、项目简介：**

本项目针对肿瘤转移这一临床难题，围绕肿瘤转移过程的代谢变化、转移相关代谢重塑的分子调控，非编码RNA（ncRNA）对代谢重塑的影响，代谢产物活化的特异信号通路对癌细胞转移、肿瘤干细胞（CSC）特征与转移潜能影响，肿瘤微环境基质成纤维细胞（CAFs）与癌细胞互作，深入研究了ncRNA调控的肿瘤代谢变化及微环境对CSC干性维持、肿瘤转移复发的生理病理作用及内在分子机制。鉴定到一系列转移相关新型和标志性ncRNA、蛋白、代谢物，阐明了这些ncRNA的生物调控模式，深入研究并揭示ncRNA调控的代谢变化，尤其是脂代谢重塑是胃癌、乳腺癌等多种转移癌细胞的普遍病理特征。研究成果为阐述肿瘤转移复发，揭示肿瘤转移内在机制、寻找新靶向和治疗策略提供了重要依据。取得的重要成果归纳如下：

1. 发现并鉴定一系列特异表达或新型非编码RNA（ncRNAs）为肿瘤转移复发“新标志”；发现并证实一系列转移特异蛋白、代谢产物；鉴定并阐明低氧驱动的标志ncRNA在肿瘤转移复发中临床价值。

2. 揭示并阐明新型ncRNAs的调控作用方式。经体内外分子生物实验，证实转移相关ncRNA通过直接调控邻近基因表达，与RBP结合或3'-UTR结合调控靶基因mRNA稳定性，通过ceRNA竞争机制调控靶基因表达等方式在肿瘤转移中发挥作用。

3. 发现并阐明新型ncRNA介导代谢重塑调控CSC干性特征与肿瘤转移复发的新功能新机制。新发现低氧EMT化癌细胞、CSC的糖代谢变化及其调控机制；创新发现非经典mirtron类miRNA、新型lnRNA重塑肿瘤脂质代谢，引起活性代谢产物累积激活与转移、CSC相关的多种信号，维持CSC干性、肿瘤转移及化疗耐受。

4. 创新发现微环境CAF通过外泌体、特异细胞因子促肿瘤转移复发的新功能新机制。揭示CAF中自噬泡与多囊泡体偶联促外泌体释放，助力肿瘤转移的全新功能与分子机制。

这一系列创新成果，为揭示肿瘤转移复发及其密切相关的CSC特征提供了全新认知与观点；为转移性肿瘤分子诊断、临床治疗、开发新型靶向药物提供了靶标与重要理论基础。项目研究已发表高影响力的SCI论文近30篇，符合成果申报条件的SCI论文20篇（IF>5.0以上的17篇；其中12篇IF>8.0；7篇IF>10.0，最高IF23.168）。研究成果得到了国内外同行的高度认可，总引用次数达到1401次，他引总次数1337次。Cancer Discovery，Molecular Cancer，Advanced Science等一流专业期刊给予了高度评价。

**七、代表性论文专著目录：**

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| **序号** | **论文（专著）****名称/刊名****/作者** | **年卷页码****（xx年xx卷****xx页）** | **发表时间（年月日）** | **通讯作者（含共同）** | **第一作者（含共同）** | **国内作者** | **他引总次数** | **检索数据库** | **论文署名单位是否包含国外单位** |
| **1** | Mirtronic miR-4646-5p promotes gastric cancer metastasis by regulating ABHD16A and metabolite lysophosphatidylserines. /Cell Death & Differentiation. / Liping Yang, Yixuan Hou, Yan-e Du, Qiao Li, Fanlin Zhou, Yu Li, Huan Zeng, Ting Jin, Xueying Wan, Shengdong Guan, Rui Wang, Manran Liu. | 2021; 14(1):178. | 22021. Sep 3. | Manran Liu (柳满然) | Liping Yang (杨丽萍) | Liping Yang, Yixuan Hou, Yan-e Du, Qiao Li, Fanlin Zhou, Yu Li, Huan Zeng, Ting Jin, Xueying Wan, Shengdong Guan, Rui Wang, Manran Liu. | **20** | **Web of Science核心合集** | **否** |
| **2** | A novel lncRNA ROPM-mediated lipid metabolism governs breast cancer stem cell properties. /Journal of Hematology & Oncology. /Shuiqing Liu, Yan Sun, Yixuan Hou, Liping Yang, Xueying Wan, Yilu Qin, Yongcan Liu, Rui Wang, Pengpeng Zhu, Yong Teng, Manran Liu. | 2021; 14(1):178. | 2021,Oct 29. | Manran Liu (柳满然) | Shuiqing Liu (刘水清) | Shuiqing Liu, Yan Sun, Yixuan Hou, Liping Yang, Xueying Wan, Yilu Qin, Yongcan Liu, Rui Wang, Pengpeng Zhu, Manran Liu. | **102** | **Web of Science核心合集** | **是** |
| **3** | A Novel Long Non-Coding RNA lnc030 Maintains Breast Cancer Stem Cell Stemness by Stabilizing SQLE mRNA and Increasing Cholesterol Synthesis. /Advanced Science. / Yilu Qin, Yixuan Hou, Shuiqing Liu, Pengpeng Zhu, Xueying Wan, Maojia Zhao, Meixi Peng, Huan Zeng, Qiao Li, Ting Jin, Xiaojiang Cui, Manran Liu.  | 2021; 8(2): 2002232. | 2021, Jan. | Manran Liu (柳满然) | Yilu Qin (秦旖璐) | Yilu Qin, Yixuan Hou, Shuiqing Liu, Pengpeng Zhu, Xueying Wan, Maojia Zhao, Meixi Peng, Huan Zeng, Qiao Li, Ting Jin, Manran Liu.  | **68** | **Web of Science核心合集** | **是** |
| **4** | Hypoxia-stimulated ATM activation regulates autophagy-associated exosome release from cancer-associated fibroblasts to promote cancer cell invasion. / Journal of Extracellular Vesicles. /Lei Xi#, Meixi Peng#, Shuiqing Liu#, Yongcan Liu#, Xueying Wan#, Yixuan Hou, Yilu Qin, Liping Yang, Shanchun Chen, Huan Zeng, Yong Teng, Xiaojiang Cui, Manran Liu\*. | 2021; 10(11): e12146. | 2021, Sep 20. | Manran Liu (柳满然) | Lei Xi (席磊), Meixi Peng (彭美茜), Shuiqing Liu (刘水清), Yongcan Liu (刘永灿), Xueying Wan (万雪颖).  | Lei Xi#, Meixi Peng#, Shuiqing Liu#, Yongcan Liu#, Xueying Wan#, Yixuan Hou, Yilu Qin, Liping Yang, Shanchun Chen, Huan Zeng, Manran Liu. | **73** | **Web of Science核心合集** | **是** |
| **5** | FOSL2 promotes VEGF-independent angiogenesis by transcriptionnally activating Wnt5a in breast cancer-associated fibroblasts. / Theranostics. / Xueying Wan#, Shengdong Guan#, Yixuan Hou, Yilu Qin, Huan Zeng, Liping Yang, Yina Qiao, Shuiqing Liu, Qiao Li, Ting Jin, Yuxiang Qiu, Manran Liu.  | 2021; 11(10):4975-4991. | 2021, Mar 5. | Manran Liu (柳满然) |  Xueying Wan (万雪颖), Shengdong Guan（官胜东）. | Xueying Wan#, Shengdong Guan#, Yixuan Hou, Yilu Qin, Huan Zeng, Liping Yang, Yina Qiao, Shuiqing Liu, Qiao Li, Ting Jin, Yuxiang Qiu, Manran Liu. | **78** | **Web of Science核心合集** | **否** |
| **合 计** | **341** |  |  |