Ming-Chih Lai (賴銘志), Ph. D.

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Research Interests

1. RNA Metabolism (Transcription, Pre-mRNA Splicing, mRNA Export & Translation)
2. Cancer Research (Human Colorectal Cancer)
3. Molecular Virology (HIV, EBV, HPV)
4. Innate immunity

Education

Ph.D. (2008) Institute of Life Sciences, National Defense Medical College
M.S. (1994) Institute of Biomedical Science, National Tsing Hua University
B.S. (1992) Department of Food Science, National Chung Hsing University

Professional Experience

Assistant Professor (2014-present)	Department of Biomedical Sciences, Chang Gung University
Assistant Researcher (2010-2014)	Department of Physiology, National Cheng Kung University
Postdoctoral Fellow (2008-2010)	Institute of Biomedical Sciences, Academia Sinica
Research Assistant (1997-2008)	Institute of Biomedical Sciences, Academia Sinica
Research Assistant (1996-1997)	Department of Medical Research and Education, Taipei Veterans General Hospital

Honors

2008 Excellent Poster Award, The 16th Symposium on Recent Advances in Cellular and Molecular Biology
2006 Excellent Thesis Award & The President Award, The 1st TienTe Lee Medical Technology Award

2001 Second-class Research Award, National Science Council

2000 Second-class Research Award, National Science Council

Publications

1. **M. -C. Lai***, C. -M. Chang and H. S. Sun*. Hypoxia induces autophagy through translational up-regulation of lysosomal proteins in human colon cancer cells. ***PLOS ONE*** (2016) 11(4): e0153627
2. **M. -C. Lai***, H. S. Sun, S. -W. Wang and W. -Y. Tarn*. DDX3 functions in antiviral innate immunity through translational control of PACT. ***FEBS J.*** (2016) 283(1): 88-101
3. T. -M. Chen, Y. -H. Shih, J. T. -C. Tseng, **M. -C. Lai**, C. -H. Wu, Y. -H. Li, S. -J. Tsai and H. S. Sun. Overexpression of FGF9 in colon cancer cells is mediated by hypoxia-induced translational activation. ***Nucleic Acids Res.*** (2014) 42: 2932-2944
4. **M. -C. Lai**, S. -W. Wang, L. Cheng, W. -Y. Tarn, S. -J. Tsai and H. S. Sun. Human DDX3 interacts with the HIV-1 Tat protein to facilitate viral mRNA translation. ***PLOS ONE*** (2013) 8(7): e68665
5. W. -Y. Tarn and **M. -C. Lai***. Translational control of cyclins. ***Cell Div.*** (2011) 6(1):5
6. **M. -C. Lai**, W. -C. Chang, S. -Y. Shieh and W. -Y. Tarn. DDX3 regulates cell growth through translational control of cyclin E1. ***Mol. Cell. Biol.*** (2010) 30: 5444-5453
7. **M. -C. Lai**, T. -Y. Peng and W. -Y. Tarn. Functional interplay between viral and cellular SR proteins in control of post-transcriptional gene regulation. ***FEBS J.*** (2009) 276: 1517-1526
8. **M. -C. Lai**, Y. -H. Wu Lee and W. -Y. Tarn. The DEAD-box RNA helicase DDX3 associates with export messenger ribonucleoproteins as well as tip-associated protein and participates in translational control. ***Mol. Biol. Cell*** (2008) 19: 3847-3858
9. **M. -C. Lai** and W. -Y. Tarn. Hypophosphorylated ASF/SF2 binds TAP and Is present in messenger ribonucleoproteins. ***J. Biol. Chem.*** (2004) 279: 31745- 31749
10. **M. -C. Lai**, H. -W. Kuo, W. -C. Chang and W. -Y. Tarn. A novel splicing regulator shares a nuclear import pathway with SR proteins. ***EMBO J.*** (2003) 22: 1359-1369
11. C. Li, R. -I. Lin, **M. -C. Lai**, P. Ouyang and W. -Y. Tarn. Nuclear Pnn/DRS protein binds to spliced mRNPs and participates in mRNA processing and export via interaction with RNPS1. ***Mol. Cell. Biol.*** (2003) 23: 7363-7376
12. **M. -C. Lai**, R. -I. Lin and W. -Y. Tarn. Differential effects of hyperphosphorylation on splicing factor SRp55. ***Biochem. J.*** (2003) 371: 937-945
13. **M. -C. Lai**, R. -I. Lin and W. -Y. Tarn. Transportin-SR2 mediates nuclear import of phosphorylated SR proteins. ***Proc. Natl. Acad. Sci. USA*** (2001) 98: 10154-10159
14. **M. -C. Lai**, R. -I. Lin, S. -Y. Huang, C. -W. Tsai and W. -Y. Tarn. A human importin- β

family protein, transportin-SR2, interacts with the phosphorylated RS domain of SR proteins. ***J. Biol. Chem.*** (2000) 257: 7950-7957

15. **M. -C. Lai**, B. -H. Teh and W. -Y. Tarn. The human papillomavirus type-5 E2 protein interacts with cellular splicing factors containing the RS domain. ***J. Biol. Chem.*** (1999) 274: 11832-11841
16. **M. -C. Lai**, Y. -C. Wang, F. -Y. Yang and L. -C. Au. Enhancement of transfection efficiency by using oligodeoxyribonucleotide as carrier. ***Anal. Biochem.*** (1997) 251: 292-294
17. W. -J. Peng, J. -T. Pan, **M. -C. Lai**, C. -F. Chiu and T. -H. Lin. The genome of moloney murine leukemia virus can be integrated by the Integrase of human Immunodeficiency virus type 1 expressed alone in vivo. ***Proc. Natl. Sci. Counc. ROC, Part B: Life Science*** (1997) 21: 144-160
18. C. -Y. Wang, C. -F. Yang, **M. -C. Lai**, Y. -H. Lee, T. -L. Lee and T. -H. Lin. Molecular dynamics simulation of a leucine zipper motif predicted for the integrase of human immunodeficiency virus type 1. ***Biopolymers*** (1994) 34: 1027-1036

Hypoxia induces autophagy through translational up-regulation of lysosomal proteins in human colon cancer cells

Ming-Chih Lai, Chiao-May Chang, and H. Sunny Sun

Hypoxia occurs in a wide variety of physiological and pathological conditions, including tumorigenesis. Tumor cells have to adapt to hypoxia by altering their gene expression and protein synthesis. Here, we showed that hypoxia inhibits translation through activation of PERK and inactivation of mTOR in human colon cancer HCT116 cells. Prolonged hypoxia (1% O2, 16 h) dramatically inhibits general translation in HCT116 cells, yet selected mRNAs remain efficiently translated under such a condition. Using microarray analysis of polysome- associated mRNAs, we identified a large number of hypoxia-regulated genes at the translational level. Efficiently translated mRNAs during hypoxia were validated by polysome profiling and quantitative real-time RT-PCR. Pathway enrichment analysis showed that many of the up-regulated genes are involved in lysosome, glycan and lipid metabolism, antigen presentation, cell adhesion, and remodeling of the extracellular matrix and cytoskeleton. The majority of down-regulated genes are involved in apoptosis, ubiquitin-mediated proteolysis, and oxidative phosphorylation. Further investigation showed that hypoxia induces lysosomal autophagy and mitochondrial dysfunction through translational regulation in HCT116 cells. The abundance of several translation factors and the mTOR kinase activity are involved in hypoxia-induced mitochondrial autophagy in HCT116 cells. Our studies highlight the importance of translational regulation for tumor cell adaptation to hypoxia.