Name

- Yung-Luen Yu

Title

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Contact

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Resume

- Degree:
  M.S., Graduate Institute of Life Sciences, National Tsing Hua University (1993-1995)
  Ph.D., Graduate Institute of Life Sciences, National Defense Medical Center (1996-2002)

- Professional Experiences:
  Postdoctoral fellow: Institute of Biomedical Sciences, Academia Sinica (2002-2004)
  Postdoctoral fellow: Department of Molecular and Cellular Oncology , University Texas M. D. Anderson Cancer Center (2005-2007)
  Assistant Professor: Graduate Institute of Cancer Biology, China Medical University (2007-2011)
  Associate Professor: Graduate Institute of Cancer Biology, China Medical University (2011-2015)
  Research Fellow, Center for Molecular Medicine, China Medical University Hospital (2011-)
  Professor: Graduate Institute of Cancer Biology, China Medical University (2015-)
  Director: Graduate Institute of Cancer Biology, China Medical University (2011-2016)
  Professor: Graduate Institute of Biomedical Sciences, China Medical

University (2016-)

- Honors and awards:
  Distinguished Teaching Professor, College of Medicine, China Medical University (2007)
  Distinguished Teaching Professor, College of Medicine, China Medical University (2009)

- Society memberships
  Phi Tau Phi Scholastic Honor Society (1993-present)
  American Association for Cancer Research (2010-present)

Fields of Specialty

- Epigenome,
- Cancer and Stem
- Cell Signaling

Research

My research achievements has contributed greatly to the understanding of the cell signaling and epigenome regulation involved in tumor progression and stem cells differentiation along with relevant clinical implications, using biochemical approach on *in vivo* disease model. Currently, my holds two grants from Ministry of Science and Technology and one grant from Ministry of Health and Welfare separately.

In recent five years, my lab with a number of significant contributions. For instances, resistance in EGFR target therapy remains a major clinical problem in treating EGFR-overexpressing triple-negative breast cancer (TNBC). By taking both the biochemistry and molecular biology approaches, my lab investigated the roles of non-canonical EGFR in TNBC. My lab identified a tyrosine phosphorylation site at Y72 of histone H4, which facilitates recruitment of histone methyltransferases (HMTases), SET8 and SUV4-20H, to enhance its K20 methylation, thereby promoting DNA synthesis and repair. These findings uncover a mechanism by which non-canonical EGFR transduces signal to chromatin for regulating DNA synthesis and repair. My lab study reveals a potent drug candidate for future development of a safe and effective therapeutic for EGFR-resistance target therapy in TNBC. This part of my research was published

in *Developmental Cell* as the co-corresponding author (***Developmental Cell***, **2014 July 30(2):224-237).**

In addition, my lab shows great interests on the molecular mechanisms associated with the ability of mesenchymal stem cells (MSCs) to directly differentiate or indirectly improve regeneration and repair injured brain. In this particular research, my lab identified a novel signal pathway critical for the differentiation of neuron, in which repression of Smurf2 on EZH2 leads to subsequent suppression on PPARγ, causing neuron differentiation. Knocking down EZH2 in human MSCs significantly improved behavioral measures of stroke-induced neurological deficit in animal models. This modification of MSCs to stimulate neuron differentiation has important clinical implication in the regeneration of neurodegenerative diseases. This part of my research was published in *EMBO Molecular Medicine* as the co-corresponding author (***EMBO Molecular Medicine***, **2013 5(4):531-47)**. Previously, stress-inducible protein-1 (STI-1) is the proposed ligand for the cellular prion protein (PrP^C), which is thought to facilitate recovery following stroke. STI-1 was upregulated in the ischemic brains from humans and rodents. The increase in STI-1 expression *in vivo* was not cell-type specific, as it was found in neurons, glia, and endothelial cells. Likewise, this increase in STI-1 expression can be mimicked by sublethal hypoxia in primary cortical cultures *in vitro*, and appear to have resulted from the direct binding of the hypoxia-inducible factor-1α (HIF-1α) to the STI-1 promoter. Importantly, this STI-1 signaling promoted MSCs proliferation and migration *in vitro* and recruitment to the ischemic brain *in vivo*, and augmenting its signaling facilitated neurological recovery in part by recruiting MSCs to the ischemic brain. Our results thus identified a novel mechanism by which ischemic insults can trigger a self-protective mechanism to facilitate recovery. **(*EMBO Molecular Medicine*, 2013 5(8):1227-46).**

My lab also actively cooperated with other academic institutes, in particular Dr. Shih-Hwa Chiou from National Yang-Ming University, for research on Glioblastoma multiforme (GBM). GBM is the most aggressive primary brain tumor with a poor prognosis. Our team collectively discovered an IL-6/miR142-3p-dependent feedback-loop which epigenetically regulates the progression and cancerous stem-like property of GBM for the development of a potential therapeutic target (***Molecular Cell*, 2013 52(5): 679-692**).

Paper & Project

(*Correspondence; †Co-first author)

1. Chen W†, **Yu YL†**, Lee SF, Chiang YJ, Chao JR, Huang JH, Chiong JH, Huang CJ, Lai MZ, Yang-Yen HF, and Yen JJY*. CREB is one component of the binding complex of the Ces-2/E2A-HLF binding element and is an integral part of the interleukin-3 survival signal. ***Mol Cell Biol.*** **2001** 21: 4636-46.

2. **Yu YL**, Chiang YJ, and Yen JJY. GATA *factors are essential for transcription of the survival gene *E4bp4* and the viability response of interleukin-3 in Ba/F3 hematopoietic cells. ***J Biol Chem.*** **2002** 277: 27144-53.

3. **Yu YL**, Chiang YJ, Chen YC, Papetti M, Juo CG, Skoultchi AI, and Yen JJY*. MAP kinase-mediated phosphorylation of GATA-1 promotes *Bcl-X_L* expression and cell survival. ***J Biol Chem.*** **2005** 280: 29533-42**.**

4. Wang SC†, Nakajima Y†, **Yu YL†**, Xia W, Chen CT, Yang CC, McIntush EW, Li LY, Hawke DH, Kobayashi R, and Hung MC*. Tyrosine phosphorylation controls PCNA function through protein stability. ***Nat Cell Bio.*** **2006** 8(12): 1359-1368.

5. Huo L, Wang YN, Xia W, Hsu SC, Lai CC, Li LY, Chang WC, Wang Y, Hsu MC, **Yu YL**, Huang TH, Ding Q, Chen CH, Tsai CH, and Hung MC*. RNA helicase A is a DNA-binding partner for EGFR mediated transcriptional activation in the nucleus. ***Proc Natl Acad Sci U S A.*** **2010** 107(37), 16125-16130.

6. Chang TH, Tsai MF, Su KY, Wu SG, Huang CP, Yu SL, **Yu YL**, Lan CC, Yang CH, Lin SB, Wu CP, Shih JY, Yang PC***.*** Slug Confers Resistance to the Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor. ***Am J Respir Crit Care Med.*** 15;183(8):1071-1079, **2011**.

7. **Yu YL*†**, Chou RH†, Chen LT, Shyu WC, Hsieh SC, Wu CS, Zeng HJ, Yeh SP, Yang DM, Hung SC, Hung MC*. EZH2 Regulates Neuronal Differentiation of Mesenchymal Stem Cells through PIP5K1C-dependent Calcium Signaling. ***J Biol Chem.*** **2011** 286(11):9657-9667.

8. Chou RH, **Yu YL***, Hung MC*. The roles of EZH2 in cell lineage commitment. ***Am J Transl Res.*** **2011** 3(3):243-250**.**

9. Wu CS, Yen CJ, Chou RH, Li ST, Huang WC, Ren CT, Wu CY*, **Yu YL***. Cancer-associated carbohydrate antigens as potential biomarkers for hepatocellular carcinoma. ***PLoS One.*** **2012** 7(7):e39466. Epub Jul 13.

10. **Yu YL*†**, Chou RH†, Wu CH, Wang YN, Chang WJ, Tseng YJ, Chang WC, Lai CC, Lee HJ, Huo L, Chen CH, Hung MC*. Nuclear EGFR Suppresses Ribonuclease Activity of Polynucleotide Phosphorylase through DNAPK-mediated Phosphorylation at Serine 776. ***J Biol Chem.*** **2012** 287(37):31015-31026.

11. Chiou SH, Jiang BH††, **Yu YL††**, Chou SJ, Tsai PH, Chang WC, Chen LK, Chen LH, Chien Y, Chiou GY. Poly(ADP-ribose) polymerase 1 regulates nuclear

reprogramming and promotes iPSC generation without c-Myc. ***J Exp Med.*** **2013** Jan 14; 210(1):85-98. (††co-second author)

12. **Yu YL*†**, Chou RH†, Shyu WC†, Hsieh SC, Wu CS, Chiang SY, Chang WJ, Chen JN, Tseng YJ, Lin YH, Lee W, Yeh SP, Hsu JL, Yang CC, Hung SC, Hung MC*. Smurf2-mediated degradation of EZH2 enhances neuron differentiation and improves functional recovery after ischaemic stroke. ***EMBO Mol Med.*** **2013** Apr; 5(4):531-47.

13. **Yu YL***, Chou RH, Liang JH, Chang WJ, Su KJ, Tseng YJ, Huang WC, Wang SC, Hung MC*. Targeting the EGFR/PCNA Signaling Suppresses Tumor Growth of Triple-Negative Breast Cancer Cells with Cell-Penetrating PCNA Peptides. ***PLoS One***. **2013** Apr 8; 8(4):e61362.

14. Lee SD, Lai TW, Lin SZ, Lin CH, Hsu YH, Li CY, Wang HJ, Lee W, Su CY, **Yu YL***, Shyu WC*. Role of stress-inducible protein-1 in recruitment of bone marrow derived cells into the ischemic brains. ***EMBO Mol Med.*** **2013** Aug; 5(8): 1227-46.

15. **Yu YL†**, Su KJ†, Hsieh YH, Lee HL, Chen TY, Hsiao PC, Yang SF*. Effects of EZH2 Polymorphisms on Susceptibility to and Pathological Development of Hepatocellular Carcinoma. ***PLoS One.*** **2013** Sep 10;8(9):e74870. doi: 10.1371/journal.pone.0074870.

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21. Chou RH, Lu CY; Wei-Lee, Fan JR, **Yu YL***, Shyu WC*. The potential therapeutic applications of olfactory ensheathing cells in regenerative medicine. ***Cell Transplant.*** **2014**;23(4-5):567-71.

22. Wu CS, Lee TY, Chou RH, Yen CJ, Huang WC, Wu CY, **Yu YL***. Development of a Highly Sensitive Glycan Microarray for Quantifying AFP-L3 for Early Prediction of Hepatitis B Virus-Related Hepatocellular Carcinoma. ***PLoS One.*** **2014** Jun 13;9(6):e99959.

23. Chou RH, Wang YN, Hsieh YH, Li LY, Xia W, Chang WC, Chang LC, Cheng CC, Lai CC, Hsu J L, Chang WJ, Chiang SY, Lee HJ, Liao HW, Chuang PH, Chen HY, Kuo SC, Chen CH, **Yu YL*** and Hung MC*. EGFR modulates DNA synthesis and repairs through Tyr phosphorylation of Histone H4. ***Dev Cell*** **2014** Jul 28;30(2):224-237.

24. Chou RH, Chiu L, **Yu YL***, Shyu WC*. The Potential Roles of EZH2 in Regenerative Medicine. ***Cell Transplant.*** **2015** Feb 2. [Epub ahead of print]

25. Chang LC, **Yu YL †**, Liu CY, Cheng YY, Chou RH, Hsieh MT, Lin HY, Hung HY, Huang LJ, Wu YC, Kuo SC. The newly synthesized 2-arylnaphthyridin-4-one, CSC-3436, induces apoptosis of non-small cell lung cancer cells by inhibiting tubulin dynamics and activating CDK1. ***Cancer Chemother Pharmacol.*** **2015 Jun**;75(6):1303-15. doi: 10.1007/s00280-015-2765-0. Epub 2015 May

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27. Su KJ, Lin CW, Chen MK, Yang SF, **Yu YL*,** Effects of EZH2 promoter polymorphisms and methylation status on oral squamous cell carcinoma susceptibility and pathology. ***Am J Cancer Res.*** **2015** Oct 15;5(11):3475-84. eCollection 2015.

28. Chang LC, **Yu YL †**, Hsieh MT, Wang SH, Chou RH, Huang WC, Lin HY, Hung HY, Huang LJ, Kuo SC. A novel microtubule inhibitor, MT3-037, causes cancer cell apoptosis by inducing mitotic arrest and interfering with microtubule dynamics. ***Am J Cancer Res.*** **2016** Mar 15;6(4):747-63. eCollection 2016.