BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Hu, Guang	Principle Investigator, Epigenetics and Stem Cell Biology Laboratory, National Institute of Environmental Health and Sciences
eRA COMMONS USER NAME (credential, e.g., agency login) GUANGH	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Fudan University, Shanghai, China	B.S.	07/98	Biochemistry
Baylor College of Medicine, Houston, TX	Ph.D.	10/03	Biochemistry

A. Personal Statement

Pluripotent stem cells can self-renewal and differentiate into all cell types in the adult body, and are thereby important for both basic and translational research. I am interested in understanding the molecular mechanisms that regulate the pluripotent state, and my group is actively pursuing this goal with the following research directions: 1) We have previously carried out a RNAi screen in embryonic stem cells (ESCs) and identified many novel regulators of pluripotency. We have since focused on several protein complexes and will continue to investigate their roles in controlling the pluripotent state in ESCs. 2) We are interested in the regulation of different pluripotent states, in particular the naïve and primed state. We are using both candidate and unbiased approaches to understand the maintenance of and transition between these states. 3) Pluripotent stem cells and germ cells are known to have intimate connections. We are studying our favorite pluripotency factors in germ cells, with the aim to better delineate their molecular functions in different biological contexts. Further, we are studying the transition between ESCs and GSCs as a new perspective to understand the establishment and resolution of the pluripotent state. Together, we aim to build a more comprehensive view of the molecular landscape that defines pluripotency, and to provide new insights to mammalian development.

B. Positions and Honors

Positions and Employment

09/2016-present Senior Investigator, Stem Cell Biology Group, Epigenetics and Stem Cell Biology Laboratory, National Institute of Environmental Health Sciences, RTP, NC

09/2016-present Director, Epigenomics and DNA Sequencing Core Facility, National Institute of Environmental Health Sciences, RTP, NC

10/2009-08/2016 Tenure-track Investigator, Stem Cell Biology Group, Epigenetics and Stem Cell Biology Laboratory, National Institute of Environmental Health Sciences, RTP, NC.

10/2003-09/2009 Post-doctoral fellow, Department of Medicine, Division of Genetics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

Other Experience and Professional Memberships

09/2016-present Director, Epigenomics Core Facility, Epigenetics and Stem Cell Biology Laboratory, National Institute of Enviromental Health Sciences, RTP, NC

2004-present Member, International Society Stem Cell Research

2003-2004 Member, American Society for Cell Biology

2001-2003 Member, Federation of American Societies for Experimental Biology

2000-2003 Member, Association for Research in Vision and Ophthalmology

Honors

2017-2018: NIH DDIR Innovation Award
2004-2007: Helen Hey Whitney Foundation postdoctoral research fellowship.
2002: ARVO/Retina Research Foundation/Joseph M. and Eula C. Lawrence Travel Fellowship
2002: Baylor College of Medicine Graduate School of Biomedical Sciences Annual Symposium platform presentation speaker.
2001, 2002: Baylor College of Medicine Department of Biochemistry and Molecular Biology V. C. Joshi Memorial Award for outstanding platform presentation.
2001: FASEB Summer Conference poster award
1999-2003: The Welch Foundation Fellowship

C. Contribution to Science

1. Biochemistry and Signal Transduction:

In my earlier research, I studied the regulation of G-protein coupled signal transduction in vision by a GTPase-accelerating protein (GAP), RGS9-1, with an emphasis on its role in the sensitivity and temporal resolution in vision. Using biochemical approaches, I found that RGS9-1 is phosphorylated in vivo and its phosphorylation may be a potential mechanism for feedback control of phototransduction. In addition, I identified and cloned R9AP, an RGS9-1 anchoring protein in vertebrates that recruits RGS9-1 to the photoreceptor disk membranes. I also showed that R9AP increases RGS9-1 GAP activity on reconstituted lipid vesicles, and thereby uncovered its critical function in the recovery kinetics of photo-response.

1.1 **Hu G** and Wensel TG. Characterization of R9AP, a membrane anchor for the photoreceptor GAP, RGS9-1. **Methods Enzymol.** 2004;390:178-96.
1.2 **Hu G**, Zhang Z, and Wensel TG. Activation of RGS9-1 GTPase acceleration by its membrane anchor, R9AP. **J Biol. Chem.** 2003 Apr 18;278(16):14550-4.
1.3 Sokal I, **Hu G**, Liang Y, Mao M, Wensel TG, Palczewski K. Identification of protein kinase C isozymes responsible for the phosphorylation of photoreceptor-specific RGS9-1 at SER475. **J Biol. Chem.** 2003 Mar 7;278(10):8316-25.
1.4 **Hu G** and Wensel TG. R9AP, a membrane anchor for the photoreceptor GTPase accelerating protein, RGS9-1. **Proc. Natl. Acad. Sci.** 2002 Jul 23;99(15):9755-60.
1.5 **Hu G**, Jang GF, Cowan CW, Wensel TG, Palczewski K.. Phosphorylation of RGS9-1 by an endogenous protein kinase in Rod Outer Segments. **J Biol. Chem.** 2001 Jun 22;276(25):22287-95.

2. Functional RNAi screens:

To complement my trainings in biochemistry, I next pursued genetic approaches to investigate gene functions. I collaborated with others and generated novel RNAi vectors and whole-genome RNAi libraries for gene silencing in mammalian cells. We also developed a multiplex screening method to efficiently identify and test gene functions in cell culture and animal models.

2.1 Sun T, Aceto N, Meerbrey KL, Kessler JD, Zhou C, Migliaccio I, Nguyen DX, Pavlova NN, Botero M, Huang J, Bernardi RJ, Schmitt E, **Hu G**, Li MZ, Dephoure N, Gygi SP, Rao M, Creighton CJ, Hilsenbeck SG, Shaw CA, Muzny D, Gibbs RA, Wheeler DA, Osborne CK, Schiff R, Bentires-Alj M, Elledge SJ, Westbrook TF. Activation of multiple proto-oncogenic tyrosine kinases in breast cancer via loss of the PTPN12 phosphatase. **Cell.** 2011 Mar 4;144(5):703-18.
2.2 Meerbrey KL#, **Hu G#***, Kessler JD, Roarty K, Li M, Fang JE, Herschkowitz JI, Burrows AE, Ciccia A, Sun T, Schmitt EM, Bernardi RJ, Bland CS, Cooper TA, Rosen JM, Westbrook TF*, Elledge SJ*. The pInducer Toolkit for Inducible RNA Interference in Vitro and in Vivo. **Proc Natl Acad Sci.** 2011 Mar 1;108(9):3665-70. **#: Equal contribution. *: Co-corresponding authors.**
2.3 **Hu G**, Kim J, Xu Q, Leng Y, Orkin SH, Elledge SJ. A Genome-wide RNAi screen identifies a new transcriptional module required for self renewal. **Genes Dev.** 2009 Apr 1;23(7):837-48.
2.4 Ali N, Karlsson C, Aspling N, **Hu G**, Hacohen N, Scadden DT, Larsson J. Forward RNAi screens in primary human hematopoietic stem/progenitor cells. **Blood.** 2009 Apr 16;113(16):3690-5.

2.5 Westbrook TF, **Hu G**, Ang XL, Mulligan P, Pavlova NN, Liang A, Leng Y, Maehr R, Shi Y, Harper JW, Elledge SJ. SCFbeta-TRCP controls oncogenic transformation and neural differentiation through REST degradation. **Nature.** 2008 Mar 20;452(7185):370-4.

2.6 Schlabach MR#, Luo J#, Solimini NL#, **Hu G#**, Xu Q, Li M, Zhao Zh, Smogorzewska A, Sowa ME, Ang XL, Westbrook TF, Liang A, Chang K, Hackett JA, Harper JW, Hannon GJ, Elledge SJ. Cancer Proliferation Gene Discovery Through Functional Genomics. **Science.** 2008 Feb 1;319(5863):620-4. **#: Equal contribution.**

2.7 Silva JM, Li MZ, Chang K, Ge W, Golding MC, Rickles RJ, Siolas D, **Hu G**, Paddison PJ, Schlabach MR, Sheth N, Bradshaw J, Burchard J, Kulkarni A, Cavet G, Sachidanandam R, McCombie WR, Cleary MA, Elledge SJ, Hannon GJ. Second-generation shRNA libraries covering the mouse and human genomes. **Nat Genet.** 2005 Nov;37(11):1281-8.

2.8 Stegmeier F, **Hu G**, Rickles RJ, Hannon GJ, Elledge SJ. A lentiviral microRNA-based system for single-copy polymerase II-regulated RNA interference in mammalian cells. **Proc Natl Acad Sci.** 2005 Sep 13;102(37):13212-7.

3. Regulation of the pluripotent stem cell state:

The main focus of my research is on the regulation of the pluripotent stem cell state. I have carried out a genome-wide RNAi screen in mouse embryonic stem cells (ESCs) and identified a list of novel regulators of the pluripotent state. My group have further characterized several of the identified factors, including Ccr4-Not, INO80, THO, and Fip1, for their roles in ESC maintenance, somatic cell reprogramming, and mouse early development. We found that they regulate different steps in gene expression to support the pluripotent state. We are continuing to investigate the function of Ccr4-Not and INO80, and we are also carrying out additional screens to look for genes and pathways that are involved in other aspects of pluripotent stem cell biology.

3.1 Hirose K, Payumo AY, Cutie S, Hoang A, Zhang H, Guyot R, Lunn D, Bigley RB, Yu H, Wang J, Smith M, Gillett E, Muroy SE, Schmid T, Wilson E, Field KA, Reeder DM, Maden M, Yartsev MM, Wolfgang MJ, Grützner F, Scanlan TS, Szweda LI, Buffenstein R, **Hu G**, Flamant F, Olgin JE, Huang GN. Evidence for hormonal control of heart regenerative capacity during endothermy acquisition. **Science**. 2019 Apr 12;364(6436):184-188.

3.2 Fu H, Wang L, Wang J, Bennett BD, Li JL, Zhao B, **Hu G**. Dioxin and AHR impairs mesoderm gene expression and cardiac differentiation in human embryonic stem cells. **Sci Total Environ.** 2019 Feb 15;651(Pt 1):1038-1046.

3.3 Xu Y, Luo X, Fang Z, Zheng X, Zeng Y, Zhu C, Gu J, Tang F, Hu Y, **Hu G**, Jin Y, Li H. Transcription coactivator Cited1 acts as an inducer of trophoblast-like state from mouse embryonic stem cells through the activation of BMP signaling. **Cell Death Dis.** 2018 Sep 11;9(9):924.

3.4 Brumbaugh J, Di Stefano B, Wang X, Borkent M, Forouzmand E, Clowers KJ, Ji F, Schwarz BA, Kalocsay M, Elledge SJ, Chen Y, Sadreyev RI, Gygi SP, **Hu G**, Shi Y, Hochedlinger K. Nudt21 Controls Cell Fate by Connecting Alternative Polyadenylation to Chromatin Signaling. **Cell.** 2018 Jan 11;172(1-2):106-120.

3.5 Li P, Wang L, Bennett BD, Wang J, Li J, Qin Y, Takaku M, Wade PA, Wong J, **Hu G**. Rif1 promotes a repressive chromatin state to safeguard against endogenous retrovirus activation. **Nucleic Acids Res.** 2017 Dec 15;45(22):12723-12738.

3.6 Chen Q, **Hu G**. Post-transcriptional regulation of the pluripotent state. **Curr Opin Genet Dev.** 2017 Oct;46:15-23. Epub 2017 Jun 24.

3.7 Zhou B, Liu J, Ren Z, Yao F, Ma J, Song J, Bennett B, Zhen Y, Wang L, **Hu G***, Hu S*. Cnot3 enhances human embryonic cardiomyocyte proliferation by promoting cell cycle inhibitor mRNA degradation. **Sci Rep.** 2017 May 4;7(1):1500. ***: Co-corresponding authors.**

3.8 Zheng X, Yang P, Lackford B, Bennett BD, Wang L, Li H, Wang Y, Miao Y, Foley JF, Fargo DC, Jin Y, Williams CJ, Jothi R, **Hu G**. CNOT3-Dependent mRNA Deadenylation Safeguards the Pluripotent State. **Stem Cell Reports.** 2016 Oct 8. pii: S2213-6711(16)30213-2.

3.9 Zhang S, Zhou B, Wang L, Li P, Bennett BD, Snyder R, Garantziotis S, Fargo DC, Cox AD, Chen L, **Hu G**. INO80 is required for oncogenic transcription and tumor growth in non-small cell lung cancer. **Oncogene.** 2016 Sep 19.

3.10 Zhou B, Wang L, Zhang S, Bennett B, He F, Zhang Y, Xiong C, Han L, Diao L, Li P, Fargo D, Cox A, **Hu G**. INO80 governs super-enhancer-mediated oncogenic transcription and tumor growth in melanoma. **Genes Dev.** 2016 Jun 15;30(12):1440-53.
3.11 Borkent M, Bennett BD, Lackford B, Bar-Nur O, Brumbaugh J, Wang L, Du Y, Fargo DC, Apostolou E, Cheloufi S, Maherali N, Elledge SJ, **Hu G***, Hochedlinger K*. A Serial shRNA Screen for Roadblocks to Reprogramming Identifies the Protein Modifier SUMO2. **Stem Cell Reports.** 2016 Mar 1. pii: S2213-6711(16)00055-2. ***: **Co-corresponding authors**.
3.12 Yang P, Zheng X, Jayaswal V, **Hu G**, Yang JY, Jothi R. Knowledge-Based Analysis for Detecting Key Signaling Events from Time-Series Phosphoproteomics Data. **PLoS Comput Biol.** 2015 Aug 7;11(8):e1004403.
3.13 Williams LH, Fromm G, Gokey NG, Henriques T, Muse GW, Burkholder A, Fargo DC, **Hu G**, Adelman K. Pausing of RNA Polymerase II Regulates Mammalian Developmental Potential through Control of Signaling Networks. **Mol Cell**. 2015 Mar 11.
3.14 Seo M, Lee S, Kim JH, Lee WH, **Hu G**, Elledge SJ, Suk K. RNAi-based functional selection identifies novel cell migration determinants dependent on PI3K and AKT pathways. **Nat Commun**. 2014 Oct 28;5:5217.
3.15 Bunch H, Zheng X, Burkholder A, Dillon ST, Motola S, Birrane G, Ebmeier CC, Levine S, Fargo D, **Hu G**, Taatjes DJ, Calderwood SK. TRIM28 regulates RNA polymerase II promoter-proximal pausing and pause release. **Nat Struct Mol Biol**. 2014 Oct;21(10):876-83.
3.16 Tang S, Huang G, Fan W, Chen Y, Ward JM, Xu X, Xu Q, Kang A, McBurney MW, Fargo DC, **Hu G**, Baumgart-Vogt E, Zhao Y, Li X. SIRT1-Mediated Deacetylation of CRABPII Regulates Cellular Retinoic Acid Signaling and Modulates Embryonic Stem Cell Differentiation. **Mol Cell**. 2014 Sep 18;55(6):843-55.
3.17 Wang L, Du Y, Ward JM, Shimbo T, Lackford B, Zheng X, Miao YL, Zhou B, Han L, Fargo DC, Jothi R, Williams CJ, Wade PA, **Hu G**. INO80 facilitates pluripotency gene activation in embryonic stem cell self-renewal, reprogramming, and blastocyst development. **Cell Stem Cell**. 2014 May 1;14(5):575-91.
3.18 Cinghu S, Yellaboina S, Freudenberg JM, Ghosh S, Zheng X, Oldfield AJ, Lackford BL, Zaykin DV, **Hu G***, Jothi R*. Integrative framework for identification of key cell identity genes uncovers determinants of ES cell identity and homeostasis. **Proc Natl Acad Sci U S A**. 2014 Apr 22;111(16):E1581-90. ***: Co-corresponding authors.**
3.19 Lackford B1, Yao C, Charles GM, Weng L, Zheng X, Choi EA, Xie X, Wan J, Xing Y, Freudenberg JM, Yang P, Jothi R, **Hu G***, Shi Y*. Fip1 regulates mRNA alternative polyadenylation to promote stem cell self-renewal. **EMBO J**. 2014 Apr 16;33(8):878-89. ***: Co-corresponding authors.**
3.20 Zheng X, **Hu G**. Use of genome-wide RNAi screens to identify regulators of embryonic stem cell pluripotency and self-renewal. **Methods Mol Biol**. 2014;1150:163-73.
3.21 Wang L, Miao Y, Zheng X, Lackford B, Zhou B, Han L, Yao C, Ward J, Burkholder A, Lipchina I, Fargo DC, Hochedlinger K, Shi Y, Williams CJ, **Hu G**. The THO Complex Regulates Pluripotency Gene mRNA Export and Controls Embryonic Stem Cell Self-renewal and Somatic Cell Reprogramming. **Cell Stem Cell**. 2013 Dec 5;13(6):676-90.
3.22 Tajonar A, Maehr R, **Hu G**, Sneddon JB, Rivera-Feliciano J, Cohen DE, Elledge SJ, Melton DA.VGLL4 is a Novel Regulator of Survival in Human Embryonic Stem Cells. **Stem Cells**. 2013 Jun 14.
3.23 Plank M, **Hu G**, Silva AS, Wood SH, Hesketh EE, Janssens G, Macedo A, de Magalhães JP, Church GM. An analysis and validation pipeline for large-scale RNAi-based screens. **Sci Rep**. 2013;3:1076.
3.24 Zheng X, **Hu G**. Oct4GiP reporter assay to study genes that regulate mouse embryonic stem cell maintenance and self-renewal. **J Vis Exp**. 2012 May 30;(63). pii: 3987. doi: 10.3791/3987.
3.25 **Hu G**, Wade P. NuRD and Pluripotency: A Complex Balancing Act. **Cell Stem Cell**. 2012 May 4;10(5):497-503.
3.26 **Hu G**, Luo J. A primer on using pooled shRNA libraries for functional genomic screens. **Acta Biochimica et Biophysica Sinica**. 2012 Feb;44(2):103-12.
3.27 Zheng X, Dumitru R, Lackford B, Freudenberg JM, Singh AP, Archer TK, Jothi R, **Hu G**. Cnot1, Cnot2, and Cnot3 maintain mouse and human ES cell identity and inhibit extraembryonic differentiation. **Stem Cells**. 2012 May;30(5):910-22.
3.28 Aceto N, Sausgruber N, Brinkhaus H, Gaidatzis D, Martiny-Baron G, Mazzarol G, Confalonieri S, Quarto M, **Hu G**, Balwierz PJ, Pachkov M, Elledge SJ, van Nimwegen E, Stadler MB, Bentires-Alj M.

Tyrosine phosphatase SHP2 promotes breast cancer progression and maintains tumor-initiating cells via activation of key transcription factors and a positive feedback signaling loop. **Nat Med**. 2012 Mar 4;18(4):529-37.

3.29 Freudenberg JM, Ghosh S, Lackford B, Yellaboina S, Zheng X, Li R, Cuddapah S, Wade P, **Hu G***, Jothi R*. Acute depletion of Tet1-dependent 5-hydroxymethylcytosine levels impairs LIF/Stat3 signaling and results in loss of embryonic stem cell identity. **Nucleic Acids Res**. 2012 Apr;40(8):3364-77. ***: Co-corresponding authors**.

D. Additional Information: Ongoing Research Support

Nov, 2009 - present: 1Z01ES102745, Guang Hu (PI), Pluripotency regulators in development and disease