BIOGRAPHICAL SKETCH

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NAME: Wenwei Hu

eRA COMMONS USER NAME: wenweihu

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Zhejiang University School of Medicine, Hangzhou, China	M.D.	07/1994	Clinical Medicine
Zhejiang University School of Medicine, Hangzhou, China	Ph.D.	12/1999	Molecular Cancer Biology
New York University School of Medicine, NY	Postdoc	09/2003	Molecular Cancer Biology
University of Medicine and Dentistry of New Jersey, NJ	Postdoc	06/2008	Molecular Cancer Biology

A. Personal Statement

The research interest of my laboratory is to understand the alteration of important cancer-related signaling pathway, including the p53 pathway, in tumorigenesis. My main expertise and research interest are to study genetic and environmental factors that modulate the function of tumor suppressor p53, which in turn impact upon tumorigenesis. p53 is the most frequently mutated gene in human tumors. Tumor-associated mutant p53 proteins often accumulate to very high levels in human tumors and gain new oncogenic functions. The recent research direction in my lab include: **1)** the gain of oncogenic function of mutant p53 in cancers and its regulation; **2)** the effect of chronic stress on tumor initiation and development and its underlying mechanism; **3)** the function of a multi-function cytokine LIF in cancer.

I believe that teaching future generations to become scientists is a fundamental responsibility of every academic faculty member. I have been actively participating in the teaching and mentoring. I serve as a course co-director to develop and teach two core courses for the Rutgers PhD program, including the mini-course “p53” and Cancer Pharmacology Course. These courses are very well-received by students. In addition to course teaching, I have mentored the lab research training for postdoctoral fellows, PhD students, master students, undergraduates and high school students. In addition to mentoring their research, I find it is also very important to encourage and inspire them to develop their careers in biomedical sciences. Several of my previous postdoctoral fellows are independent faculties in different universities and Medical schools. I have mentored several high school and undergraduates students from underrepresented backgrounds in the CURE program.

Ongoing and recently completed projects that I would like to highlight include:

NIH/NCI 1R01CA260837 Hu/Feng (MPI) 4/2021-3/2026
NIH/NCI
Gain-of-function mutant p53 and metabolic reprogramming in colorectal cancer
Role: PI
Goal: To determine the mechanism of gain-of-function mutant p53 in colorectal cancer (CRC) to provide effective targets and strategies for CRC therapy.
OVERLAP: NONE

NIH/NCI 1R01CA260838 Hu (PI) 2/2022-1/2027
NIH/NCI
Leukemia inhibitory factor in colorectal cancer

Role: PI
Goal: To determine the role and mechanism of LIF in colorectal cancer.
OVERLAP: NONE

Ludwig Institute for Cancer Research Princeton University Branch Grant Hu (PI) 1/2023-12/2023
Ludwig Institute for Cancer Research Princeton University Branch
Determine the role of leukemia inhibitory factor in cancer cachexia
Role: PI
Goal: A pilot grant to study the potential role and mechanism of LIF in cancer cachexia
OVERLAP: NONE

Citations:

a. Yu H., Yue X., Zhao Y., Li X., Wu L., Zhang C., Liu Z., Lin K., Xu-Monette Z., Young K., Liu J., Shen Z., Feng Z., **Hu W.** (2014) LIF negatively regulates tumor suppressor p53 through Stat3/ID1/MDM2 in colorectal cancers. ***Nature Communications****,* **5:**5218. (PMC4203416)
b. Chang C., Wang J., Zhao Y., Liu J., Yang X., Yue X., Wang H., Zhou F., Inclan-Rico J., Ponessa J., Xie P., Zhang L., Siracusa M., Feng Z., **Hu W.** (2021) Tumor suppressor p53 regulates intestinal type 2 immunity. ***Nature Communications****,* **12:**3371.
c. Wang J., Chang C., Yang X, Zhou F., Liu J., Zhu S., Yu X. Liu C., O'Sullivan T., Xie P., Feng Z., **Hu W**. (2022) Leukemia inhibitory factor protects against graft-versus-host disease while preserving graft-versus-leukemia activity. ***Blood***, 140(19):2076-2090.
d. Liu J, Zhang C, Zhang T, Chang CY, Wang J, Bazile L, Zhang L, Haffty BG, **Hu W (co-corresponding),** Feng Z. (2022) Metabolic enzyme LDHA activates Rac1 GTPase as a noncanonical mechanism to promote cancer. ***Nature Metabolism***. 4(12):1830-1846. PMID: 36536137

B. Positions and Honors

Positions and Employment

7/2021- Present	Professor, Departments of Radiation Oncology, Pharmacology, Rutgers Cancer Institute of New Jersey, Rutgers State University of New Jersey
2/2015- 6/2021	Associate Professor, Departments of Radiation Oncology, Pharmacology, Rutgers Cancer Institute of New Jersey, Rutgers State University of New Jersey
7/2009-1/2015	Assistant Professor (tenure-track), Departments of Radiation Oncology, Pharmacology, Rutgers Cancer Institute of New Jersey, Rutgers State University of New Jersey
7/2008-6/2009	Instructor, Department of Pediatrics, University of Medicine and Dentistry of New Jersey

Other Experience and Professional Memberships

2020-2026	Standing member, NIH Cancer Cell Biology study section (CCB)
2019-Present	Member of Editorial Boards, eLife
2019-2020	Ad hoc reviewer, NIH Fellowships: Oncological Sciences study section (F09B)
2018-2020	Ad hoc reviewer, NIH Cancer Drug Development & Therapeutics study section (CDDT)
2017-2018	Ad hoc reviewer, NIH Tumor Cell Biology study section (TCB)
2015-Present	Reviewer, DOD Breast Cancer Research Program; Prostate Cancer Research Program
2014-Present	Reviewer, National Science Foundation (NSF) Graduate Research Fellowship Program,
2014-2016	Scientific Reviewer, Member of Busch Biomedical Research Advisory Committee (BRAC), Rutgers University
2012	Scientific Reviewer, Parkinson's UK Foundation, UK
2011, 2015	Scientific Reviewer, Research Foundation Flanders (FWO) Odysseus application Brussel, Belgium
2011	Scientific Reviewer, DOD Peer Reviewed Cancer Research Program (PRCRP)
2009-Present	Ad hoc reviewer for scientific journals, including Genes & Development, Cancer Cell, PNAS, Nature Communications, Oncogene, Cancer Research, FASEB Journal, etc. Genetic Mechanisms

Honors

2017	Rutgers University Board of Trustees Research Fellowship for Scholarly Excellence
2014	National Cancer Institute Network on Biobehavioral Pathways in Cancer (Network) affiliated investigator
2012	American Cancer Society Research Scholar
2011	New Investigate Award of the Ellison Medical Foundation
2010	DOD New Investigator Award for Genetic Cancer Research
2010	New Investigate Award of the Cancer Institute of New Jersey
2008	14th International p53 workshop travel award, Shanghai, China
1999	AACR-ITO EN, Ltd, Young Investigator Award, from AACR

C. Contribution to Science

1. **LIF in reproduction, tissue stem cell function and graft-versus-host disease (GVHD)**. I identified LIF as a novel p53 target gene that mediates the important function of p53 in maternal reproduction in addition to the well-known function of p53 as a tumor suppressor; p53 plays a critical role in embryonic implantation and maternal reproduction in mice and humans through its direct transcriptional regulation of LIF. This set of work for the first time demonstrates the important physiological role of p53 and its pathway in reproduction in vertebrates. This important function of the p53 family in reproduction may explain why p53 is conserved from invertebrates to vertebrates, and provides a plausible explanation of the evolutionary positive selection on some alleles in the genes in the p53 pathway. Further, we found that LIF regulates the function of the intestinal stem cells (ISCs) to maintain intestinal homeostasis and protect ISCs against radiation. Most recently, we found that LIF protects against GVHD without compromising the graft-versus-tumor (GVT) activity.
    a. **Hu W.**, Feng Z., Teresky A., Levine A.J. (2007) p53 regulates maternal reproduction through LIF. (with commentary) ***Nature*****, 450**:721-724.
    b. Kang H., Feng Z., Sun Y., Atwal G., Murphy M., Rebbeck T., Rosenwaks Z., Levine A.J., **Hu W.** (2009) Single-nucleotide polymorphisms in the p53 pathway regulate fertility in humans. ***Proc Natl Acad Sci U S A,*** **106**:9761-9766. (PMC2700980)
    c. Wang H, Wang J, Zhao Y, Zhang X, Liu J, Zhang C, Haffty B, Verzi M, Zhang L, Gao N, Feng Z, **Hu W.** (2020) LIF is essential for ISC function and protects against radiation-induced gastrointestinal syndrome. ***Cell Death Dis.*** **11:**588
    d. Wang J., Chang C., Yang X., Zhou F., Liu J., Zhu S., Yu X-Z., Liu C., O'Sullivan T.E., Xie P., Feng Z., **Hu W.** (2022) Leukemia inhibitory factor protects against graft-versus-host disease while preserving graft-versus-leukemia activity. (with commentary) ***Blood*** **140:**2076-2090.

2. **The role and mechanism of LIF in cancer.** While LIF was reported to play a tumor suppressive function in leukemia, the research in my lab has revealed an oncogenic role of LIF in solid cancer, which is under-studied. We found that **1)** LIF negatively regulates tumor suppressor p53 and activates the AKT-mTOR signaling, both of which contribute to the oncogenic function of LIF in breast and colorectal cancers. **2)** LIF promotes tumor metastasis through the induction of microRNAs to promote Epithelial-mesenchymal transition (EMT). **3)** Hypoxia induces LIF expression through HIF-2α, which is an important mechanism for the frequent LIF overexpression in solid tumors. **4)** LIF increases glucose uptake and drives glycolysis, contributing to tumorigenesis in breast cancers. **5)** We screened and identified a small-molecule inhibitor targeting the LIF signaling, which has the potential to be developed for LIF-based cancer therapy.
    a. Yu H., Yue X., Zhao Y., Li X., Wu L., Zhang C., Liu Z., Lin K., Xu-Monette Z., Young K., Liu J., Shen Z., Feng Z., **Hu W.** (2014) LIF negatively regulates tumor suppressor p53 through Stat3/ID1/MDM2 in colorectal cancers. ***Nature Communications,*** **5:**5218 doi:10.1038/ncomms6218. (PMC4203416)
    b. Yue X., Wu F., Wang J., Kim K., Santhamma B., Dileep KV., Zhang K., Viswanadhapalli S., Vadlamudi R., Ahmend G., Feng Z., Nickisch K., **Hu W.** (2020) EC330, a small molecule compound, is a potential novel inhibitor of LIF signaling. ***J Mol Cell Biol.*** **12:**477-480. (PMC7333478)
    c. Yue X., Wang J., Chang C.Y., Liu J., Yang X., Zhou F., Qiu X., Bhatt V., Guo J.Y., Su X., Zhang L., Feng Z., **Hu W.** (2022) Leukemia inhibitory facto drives glucose metabolic reprogramming to promote breast tumorigenesis. ***Cell Death Dis.*** **13:**370 (PMC9018736)

d. Wang J., Chang C.Y., Yang X., Zhou F., Liu J., Feng Z. **Hu W.** (2022) Leukemia inhibitory factor, a double-edged sword with therapeutic implications in human diseases. ***Mol Ther.*** doi: 10.1016/j.ymthe.2022.12.016.

3. **Tumor suppressor p53 regulation in cancer.** p53 protein levels and activity are under the tight regulation in cells to ensure the proper function of p53. My research contributes to the understanding of the regulation of p53 and its signaling pathway. ***1)*** I discovered a novel connection between chronic psychological stress and wild type p53 function; chronic stress inhibits p53 tumor suppressive function and in turn promotes tumorigenesis. ***2)*** I identified a functional single nucleotide polymorphism (SNP) in MDM2, SNP309, which increases the risk of cancer in humans. This study increases our understanding of the molecular, cellular and clinical impact of SNPs in the p53 pathway. Since the publication of this work, over 1000 papers have been published on SNP309, which makes it one of the most extensively studied SNPs in the p53 pathway. ***3)*** We demonstrated that p53 codon 72 SNP, a common functional SNP in p53, affects aging and longevity using genetic approaches in p53 codon 72 SNP transgenic mice. ***4)*** My very recent study revealed a previously unidentified p53 function in regulation of type 2 immunity in the gut in response to parasitic infections.
    a. Bond G.L., **Hu W. (co-first author)**, Bond E.E., Robins H., Lutzker S.G., Arva N.C., Bargonetti J., Bartel F., Taubert H., Wuerl P., Onel K., Yip L., Hwang S.J., Strong L.C., Lozano G., Levine A.J. (2004) A single nucleotide polymorphism in the MDM2 promoter attenuates the p53 tumor suppressor pathway and accelerates tumor formation in humans. (with commentary) ***Cell,*** **119**:591-602.
    b. Feng Z., Liu L., Zhang C., Zheng T., Wang J., Lin M., Zhao Y., Wang X, Levine A. **Hu W.** (2012) Chronic restraint stress attenuates p53 function and promotes tumorigenesis. ***Proc Natl Acad Sci U S A***, **109**:7013-7018. (PMC3345015)
    c. Zhao Y., Wu L., Yue X., Zhang C., Wang J., Li J., Sun X., Zhu Y., Feng Z., **Hu W.** (2018) A polymorphism in the tumor suppressor p53 affects aging and longevity in mouse models. ***eLife*** **7**: e34701. doi: 10.7554/eLife.34701(PMC5906094)
    d. Chang C., Wang J., Zhao Y., Liu J., Yang X., Yue X., Wang H., Zhou F., Inclan-Rico J., Ponessa J., Xie P., Zhang L., Siracusa M., Feng Z., **Hu W.** (2021) Tumor suppressor p53 regulates intestinal type 2 immunity. ***Nature Communications,*** **12:**3371.

4. **Gain-of-function mutant p53 regulation in cancer.** p53 is frequently mutated in cancer. Mutant p53 proteins often gain oncogenic functions (gain-of-function, GOF) to promote tumor development. Mutant p53 is frequently accumulated to very high levels in tumor cells, which is critical for mutant p53 GOF. The mechanisms for mutant p53 accumulation and GOF are poorly understood. The following studies from my lab contribute to the understanding of mechanism of mutant p53 accumulation and GOF in tumorigenesis: ***1)*** we identified following novel mechanisms for mutant p53 accumulation in tumor cells: **i)** the overexpression of BAG family proteins in tumors inhibits MDM2-mediated mutant p53 degradation; **ii)** the overexpression of tumor-associated MDM2 isoforms in tumors inhibits MDM2-mediated mutant p53 degradation; ***2)*** we identified a novel mutant p53 binding partner, Pontin, that promotes mutant p53 GOF through regulating its transcriptional activity; ***3)*** we revealed that mutant p53 activates small GTPase Rac1 *via* SUMOylation as a novel mechanism contributing to mutant p53 GOF.
    a. Zheng T., Wang J., Zhao Y., Zhang C., Lin M., Wang X., Yu H., Liu L., Feng Z., **Hu W.** (2013) Spliced MDM2 isoforms promote mutant p53 accumulation and gain-of-function in tumorigenesis. ***Nature Communications,*** **4**:2996 doi: 10.1038/ncomms3996.(PMC3960723)
    b. Yue X., Zhao Y., Liu J., Zhang C., Yu H., Wang J., Zheng T., Liu L., Li J., Feng Z., **Hu W.** (2015) BAG2 promotes tumorigenesis through enhancing mutant p53 protein levels and function. ***eLIFE***, 10.7554/eLife.08401. (PMC4561369)
    c. Yue X., Zhang C., Zhao Y., Liu J., Lin A, Tan V., Drake J., Liu L., Boateng M., Li J., Feng Z., **Hu W.** (2017) Gain-of-function mutant p53 activates small GTPase Rac1 through SUMOylation to promote tumor progression. ***Genes Dev.,*** **31**: 1641-1654. doi:10.1101/gad.301564.117
    d. Chan C., Sun Y., Ke H., Zhao Y., Belete M., Zhang C., Feng Z., Levine AJ, **Hu W.** (2021) Genetic and stochastic influences upon tumor formation and tumor types in Li-Fraumeni mouse models. ***Life Sci Alliance***., **4**: e202000952 (PMC7772779)

5. **Metabolic reprogramming in cancer.** Collaborating with Dr. Zhaohui Feng's laboratory at Rutgers University, we identified several novel p53 target genes, including GLS2 and Parkin, which play important

roles in mediating the function of p53 in metabolic regulation. Parkin ubiquitinates and degrades HIF-1α and phosphoglycerate dehydrogenase (PHGDH) to suppress glycolysis and serine synthesis and inhibit tumor progression. We also found a novel function of E3 ubiquitin ligase CUL3 in regulation of lipid synthesis through degradation of lipogenic enzyme ACLY, which contributes to the function of CUL3 in tumor suppression. Recently, we found that metabolic enzyme LDHA activates Rac1 GTPase independently of LDHA enzyme activity as a noncanonical mechanism to promote cancer

a. Zhang C, Liu J, Huang G, Zhao Y, Yue X, Wu H, Li J, Zhu J, Haffty BG, **Hu W (co-corresponding),** Feng Z. (2016) Cullin3-KLHL25 ubiquitin ligase targets ACLY for degradation to inhibit lipid synthesis and tumor progression. ***Genes Dev***. 30(17):1956-70.
b. Liu J, Zhang C, Zhao Y, Yue X, Wu H, Huang S, Chen J, Tomsky K, Xie H, Khella K, Gatza M, Xia D, Gao J, White E, Haffty BG, **Hu W (co-corresponding),** Feng Z. (2017) Parkin targets HIF-1α for ubiquitination and degradation to inhibit breast tumor progression. ***Nature Communications***. 8(1):1823. doi: 10.1038/s41467-017-01947-w. PMID:29180628.
c. Liu J, Zhang C, Wu H, Sun X, Li X, Huang S, Yue X, Lu Z, Shen Z, Su X, White E, Haffty BG, **Hu W (co-corresponding),** Feng Z. (2020) Parkin ubiquitinates phosphoglycerate dehydrogenase to suppress serine synthesis and tumor progression. ***J Clin Invest*, 130:**3253-3269.
d. Liu J, Zhang C, Zhang T, Chang CY, Wang J, Bazile L, Zhang L, Haffty BG, **Hu W (co-corresponding),** Feng Z. (2022) Metabolic enzyme LDHA activates Rac1 GTPase as a noncanonical mechanism to promote cancer. ***Nature Metabolism***. 4(12):1830-1846. PMID: 36536137

Complete List of Published Work in MyBibliography (a total of 113 publications)**:**

http://www.ncbi.nlm.nih.gov/sites/myncbi/16U2iVIkGQOkG/bibliography/45876546/public/?sort=date&direction=descending