**WEI GU**

**Overview**

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**Academic Appointments**

* Professor of Pathology & Cell Biology

**Research**

Over the past 20 years, the integrative approach of the Gu Laboratory, combining biochemical analyses and advanced genetically manipulated mouse models has been instrumental to dissect the precise roles of protein modifications in regulating p53-mediated tumor suppression. The Gu lab has made significant contributions to establishing the roles of acetylation-mediated regulation of non-histone proteins. They established that site-specific acetylation plays a critical role in promoter-specific regulation of p53 targets. They discovered that the acidic domain containing proteins act as a new “reader” for acetylated substrates critically involved in acetylation-mediated actions. These studies have laid the foundation for the view that reversible acetylation is a general mechanism for regulation of non-histone proteins. Through in-depth investigation, the Gu lab has revealed that “dynamic ubiquitination” (polyubiquitination, monoubiquitination and deubiquitination) is the major mechanism by which the stability and subcellular localization of p53 protein are determined. They found that the deubiquitinase USP7 (also called HAUSP) interacts with both p53 and Mdm2; and is an important therapeutic target for human cancers through activating p53 and downregulating oncoproteins such as N-Myc. By using p53 acetylation-deficient mutant mice, the Gu lab has demonstrated that acetylation is required for p53-mediated cell-cycle arrest, senescence and apoptosis in vivo. Subsequently, they found that p53 is able to induce its tumor suppression through its metabolic targets including promoting ferroptosis.

**Selected Publications**

1. **ALOX12 is required for p53-mediated tumour suppression through a distinct ferroptosis pathway**Chu B, Kon N, Chen D, Li T, Liu T, Jiang L, Song S, Tavana O, Gu W  
   Nat Cell Biol. 2019.  
   PMID: 30962574, DOI: 10.1038/s41556-019-0305-6
2. **NRF2 Is a Major Target of ARF in p53-Independent Tumor Suppression**Chen D, Tavana O, Chu B, Erber L, Chen Y, Baer R, Gu W  
   Mol Cell. 2017.  
   PMID: 28985506, DOI: 10.1016/j.molcel.2017.09.009
3. **Acetylation-regulated interaction between p53 and SET reveals a widespread regulatory mode**Wang D, Kon N, Lasso G, Jiang L, Leng W, Zhu WG, Qin J, Honig B, Gu W  
   Nature. 2016.  
   PMID: 27626385, DOI: 10.1038/nature19759
4. **HAUSP deubiquitinates and stabilizes N-Myc in neuroblastoma**Tavana O, Li D, Dai C, Lopez G, Banerjee D, Kon N, Chen C, Califano A, Yamashiro DJ, Sun H, Gu W  
   Nat Med. 2016.  
   PMID: 27618649, DOI: 10.1038/nm.4180
5. **Ferroptosis as a p53-mediated activity during tumour suppression**Jiang L, Kon N, Li T, Wang SJ, Su T, Hibshoosh H, Baer R, Gu W  
   Nature. 2015.  
   PMID: 25799988, DOI: 10.1038/nature14344
6. **Tumor suppression in the absence of p53-mediated cell-cycle arrest, apoptosis, and senescence**Li T, Kon N, Jiang L, Tan M, Ludwig T, Zhao Y, Baer R, Gu W  
   Cell. 2012.  
   PMID: 22682249, DOI: 10.1016/j.cell.2012.04.026
7. **Acetylation is indispensable for p53 antiviral activity**Muñoz-Fontela C, González D, Marcos-Villar L, Campagna M, Gallego P, González-Santamaría J, Herranz D, Gu W, Serrano M, Aaronson SA, Rivas C  
   Cell Cycle. 2011.  
   PMID: 22033337, DOI: 10.4161/cc.10.21.17899
8. **Transcription-independent ARF regulation in oncogenic stress-mediated p53 responses**Chen D, Shan J, Zhu WG, Qin J, Gu W  
   Nature. 2010.  
   PMID: 20208519, DOI: 10.1038/nature08820
9. **Modes of p53 regulation**Kruse JP, Gu W  
   Cell. 2009.  
   PMID: 19450511, DOI: 10.1016/j.cell.2009.04.050
10. **Negative regulation of the deacetylase SIRT1 by DBC1**Zhao W, Kruse JP, Tang Y, Jung SY, Qin J, Gu W  
    Nature. 2008.  
    PMID: 18235502, DOI: 10.1038/nature06515
11. **ARF-BP1/Mule is a critical mediator of the ARF tumor suppressor**Chen D, Kon N, Li M, Zhang W, Qin J, Gu W  
    Cell. 2005.  
    PMID: 15989956, DOI: 10.1016/j.cell.2005.03.037
12. **Mono- versus polyubiquitination: differential control of p53 fate by Mdm2**Li M, Brooks CL, Wu-Baer F, Chen D, Baer R, Gu W  
    Science. 2003.  
    PMID: 14671306, DOI: 10.1126/science.1091362
13. **Deubiquitination of p53 by HAUSP is an important pathway for p53 stabilization**Li M, Chen D, Shiloh A, Luo J, Nikolaev AY, Qin J, Gu W  
    Nature. 2002.  
    PMID: 11923872, DOI: 10.1038/nature737
14. **Negative control of p53 by Sir2alpha promotes cell survival under stress**Luo J, Nikolaev AY, Imai S, Chen D, Su F, Shiloh A, Guarente L, Gu W  
    Cell. 2001.  
    PMID: 11672522, DOI: 10.1016/s0092-8674(01)00524-4
15. **Deacetylation of p53 modulates its effect on cell growth and apoptosis**Luo J, Su F, Chen D, Shiloh A, Gu W  
    Nature. 2000.  
    PMID: 11099047, DOI: 10.1038/35042612