**ZHIGUO ZHANG**

**Overview**

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**Academic Appointments**

* Professor of Pediatrics, Genetics & Development

**Administrative Titles**

**Research**

Zhiguo Zhang’s laboratory studies epigenetic inheritance and cancer epigenetics. How epigenetic states are transmitted into daughter cells is a challenging, but yet poorly understood, question in the chromatin and epigenetic fields. Recently, it became clear that epigenetic alterations contribute to tumorigenesis and as well as the development of resistance to a variety of cancer therapy. However, how alterations in epigenetic landscape contribute to tumorigenesis and drug resistance is largely unexplored. The laboratory focuses on three major directions to study epigenetic inheritance and cancer epigenetics. First, how parental histones, the primary carrier of epigenetic information, are reassembled into nucleosomes following DNA replication in yeast and mammalian cells. Second, how onco-histone mutations found in pediatric gliomas reprogram cancer epigenomes. Third, how epigenetic changes drive drug resistance in brain tumors. The overall goal is to elucidate the molecular mechanisms of epigenetic inheritance and drug resistance and discover novel therapeutics for cancer treatment in the future.

**Selected Publications**

**1. DNA polymerase α interacts with H3-H4 and facilitates the transfer of parental histones to lagging strands**

Li Z, Hua X, Serra-Cardona A, Xu X, GanS, Zhou Z, Yang WS, ChenC, Xu R and Zhang Z**.**

**Sci. Adv.** 6: eabb5820**.**

**PMID:** 32923642DOI: 10.1126/sciadv.abb5820

**2. The Mcm2-Ctf4-Polα Axis Facilitates Parental Histone H3-H4 Transfer to Lagging Strands**Gan H, Serra-Cardona A, Hua X, Zhou H, Labib K, Yu C, Zhang Z  
Mol Cell. 2018.  
PMID: 30244834, DOI: 10.1016/j.molcel.2018.09.001

**3. A mechanism for preventing asymmetric histone segregation onto replicating DNA strands**Yu C, Gan H, Serra-Cardona A, Zhang L, Gan S, Sharma S, Johansson E, Chabes A, Xu RM, Zhang Z  
Science. 2018.  
PMID: 30115745, DOI: 10.1126/science.aat8849

**4. Multisite Substrate Recognition in Asf1-Dependent Acetylation of Histone H3 K56 by Rtt109**Zhang L, Serra-Cardona A, Zhou H, Wang M, Yang N, Zhang Z, Xu RM  
Cell. 2018.  
PMID: 30057113, DOI: 10.1016/j.cell.2018.07.005

**5. A novel enhancer regulates MGMT expression and promotes temozolomide resistance in glioblastoma**Chen X, Zhang M, Gan H, Wang H, Lee JH, Fang D, Kitange GJ, He L, Hu Z, Parney IF, Meyer FB, Giannini C, Sarkaria JN, Zhang Z  
Nat Commun. 2018.  
PMID: 30054476, DOI: 10.1038/s41467-018-05373-4

**6. Checkpoint Kinase Rad53 Couples Leading- and Lagging-Strand DNA Synthesis under Replication Stress**Gan H, Yu C, Devbhandari S, Sharma S, Han J, Chabes A, Remus D, Zhang Z  
Mol Cell. 2017.  
PMID: 29033319, DOI: 10.1016/j.molcel.2017.09.018

**7. RPA Interacts with HIRA and Regulates H3.3 Deposition at Gene Regulatory Elements in Mammalian Cells**Zhang H, Gan H, Wang Z, Lee JH, Zhou H, Ordog T, Wold MS, Ljungman M, Zhang Z  
Mol Cell. 2017.  
PMID: 28107649, DOI: 10.1016/j.molcel.2016.11.030

**8. The histone H3.3K36M mutation reprograms the epigenome of chondroblastomas**Fang D, Gan H, Lee JH, Han J, Wang Z, Riester SM, Jin L, Chen J, Zhou H, Wang J, Zhang H, Yang N, Bradley EW, Ho TH, Rubin BP, Bridge JA, Thibodeau SN, Ordog T, Chen Y, van Wijnen AJ, Oliveira AM, Xu RM, Westendorf JJ, Zhang Z  
Science. 2016.  
PMID: 27229140, DOI: 10.1126/science.aae0065

**9**. **Strand-specific analysis shows protein binding at replication forks and PCNA unloading from lagging strands when forks stall.**

Yu C, Gan H, Han J, Zhou ZX, Jia S, Chabes A, Farrugia G, Ordog T, Zhang Z.

*Mol Cell*. 2014

PMID: **25449133,** DOI: [10.1016/j.molcel.2014.09.017](https://doi.org/10.1016/j.molcel.2014.09.017)

**10. A Cul4 E3 ubiquitin ligase regulates histone hand-off during nucleosome assembly**Han J, Zhang H, Zhang H, Wang Z, Zhou H, Zhang Z  
Cell. 2013.  
PMID: 24209620, DOI: 10.1016/j.cell.2013.10.014

**11. The histone H3.3K27M mutation in pediatric glioma reprograms H3K27 methylation and gene expression**Chan KM, Fang D, Gan H, Hashizume R, Yu C, Schroeder M, Gupta N, Mueller S, James CD, Jenkins R, Sarkaria J, Zhang Z  
Genes Dev. 2013.  
PMID: 23603901, DOI: 10.1101/gad.217778.113

**12. Structural basis for recognition of H3K56-acetylated histone H3-H4 by the chaperone Rtt106**Su D, Hu Q, Li Q, Thompson JR, Cui G, Fazly A, Davies BA, Botuyan MV, Zhang Z, Mer G  
Nature. 2012.  
PMID: 22307274, DOI: 10.1038/nature10861

**13. Acetylation of histone H3 lysine 56 regulates replication-coupled nucleosome assembly**Li Q, Zhou H, Wurtele H, Davies B, Horazdovsky B, Verreault A, Zhang Z  
Cell. 2008.  
PMID: 18662540, DOI: 10.1016/j.cell.2008.06.018

**14. Rtt109 acetylates histone H3 lysine 56 and functions in DNA replication**Han J, Zhou H, Horazdovsky B, Zhang K, Xu RM, Zhang Z  
Science. 2007.  
PMID: 17272723, DOI: 10.1126/science.1133234