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Departmental Affiliations

Environmental Health and Engineering (Primar)

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Education

PhD, The Ohio State University, 2006

MS, Chinese Academy of Agricultural Sciences, 1998

BS, Qingdao Agricultural University, 1992

Overview

The long-term goal of the Wang laboratory is to determine how epigenetic codes, including patterns of DNA methylation and combinatorial patterns of simultaneously occurring histone modifications, are established and how this establishment goes awry upon environmental stimuli, thereby contributing to human diseases (such as cancers and autoimmune diseases).

Toward our goal, we have strived to develop both high throughput epigenomic profiling techniques, including ChIP-seq (Cell 2007) and novel computational algorithms (ACE-mapping (Genome Biology 2015), NORED and MethylMosaic (under review)). The ChIP-seq method opens a new Epigenomic era (Baylin and Schuebel, Nature 2007, 448,548-). Subsequently, we have characterized the human histone methylome (20 histone methylations; Baski et al., Cell, 2007 (as co-first author)) and histone acetylome (18 histone acetylations; Wang et al., Nature Genet, 2008). It is the data sets of this stripe that allows us to decode the "histone code" that different histone modifications, including histone acetylations and methylations, may modulate gene activity in a combinatorial way, potentially acting as different "codes." We identified numerous combinatorial patterns that are associated with different genes and a "backbone" composed of 17 active marks to regulate the expression of more than 3000 genes (Wang et al., Nature Genetics, 2008), reviewed in (Wang et al., Curr Genet and Dev, 2009; Dai and Wang, Current Environmental Health Reports, 2013). These combinatorial patterns and the backbone provide the first glimpse of what kind of "histone code" in the human genome. Also see debates in (Campos and Reinberg Annu. Rev. Genet. 2009 43, 559-; and Rando and Chang Annu. Rev. Biochem 2009 78, 245).

To further understand how these combinatorial patterns are established, we focused on combinatorial acetylation patterns that are regulated by two groups of enzymes, histone acetyltransferases (HATs) and deacetylases (HDACs), with antagonizing functions. We used ChIP-seq to examine the distribution patterns of HATs and HDACs in the human genome. Surprisingly, we found that corepressor HDACs bind to active genes with histone acetylations but not silent genes (Wang et al., Cell, 2009), changing the long-held OLD dogma with "corepressor HDACs for silent genes and coactivator HATs for active genes." The significance of related novel discoveries was recently reviewed in (Perissi et al., Nat Rev Genet 2010, 11, 109-). Currently, we are working on how acetylation patterns being regulated/established and how they engaging in transcription initiation/elongation. Eventually we want to establish a new model that we called "dancing with the enemy" to understand how the association of both HATs and HDACs with active genes regulates gene expression. The insights of aforementioned processes in normal cells will help to understand how abnormal acetylation patterns reprogram gene expression, thus contributing to the pathogenesis of environmental diseases/cancers. Lastly but significantly, our insights of the crosstalk between acetylation patterns and methylation patterns from (Wang et al., Cell 2009) have prompted Lee et al., (Cell 2010, 142, 682-) to proposed "the language of histone crosstalk" as an alternative of "histone code."

To understand the patterns of DNA methylation, in collaboration with Yi Zhang's group we recently characterized the DNA 5mc-5hmc methylome (Genes Dev, 2011). Our further ChIP-seq analyses of Tet1 suggest that Tet1 plays a role in the establishment of dynamic DNA methylation patterns (Nature, 2011). By understanding the establishment mechanism of DNA methylation patterns in normal cells, we aim to elucidate the processes that lead to abnormal DNA methylation patterns in human diseases. For example, cancer cells are characterized by promoter-region specific hypermethylation and global hypomethylation. Autoimmune diseases also have the problems of global hypomethylation.

In the Wang laboratory, we take advantage of our developed high throughput methods including ChIP-seq, RNA-seq, and BS-seq (bisulfite sequencing). Recently, we began to work on single-cell RNA-seq to tackle some really interesting questions. These global strategies allow us to make a final conclusion based on the genome-wide analysis data.

Honors and honors

2016 Catalyst Award, Johns Hopkins University

2012 Prestigious Kimmel Scholar, The Sidney Kimmel Foundation for Cancer Research;

2011 Ho-Ching Yang Memorial Faculty Award, JHU SPH;

2009 The No.3 most-cited biology papers of 2009 by TheScientist;

2009 Prestigious Lenfant Scholar, National Heart, Lung, and Blood Institute, NIH;

2009 Fellows Award for Research Excellence (FARE) 2010, NIH;

2008 Fellows Award for Research Excellence (FARE) 2009, NIH;

2006-10 NIH Postdoctoral Fellowship;

2006 SDB Travel Grant Award, Society for Developmental Biology (SDB);

2006 ASPB Travel Grant Award, American Society of Plant Biologists (ASPB);

Research Interests

Human Epigenome
 Histone Codes
 Histone Acetylation
 HATs and HDACs
 ChIP-seq
 DNA Methylation
 NORED
 MethylMosaic
 Autosomal chromosome Inactivation (ACI)
 Parkinson's disease, Asthma
 Cancer
 Autoimmune Diseases
 Bisphenol A
 Arsenic Exposure
 Next-generation Sequencing

Publications

5 representative publicati

*Wang, Z., *Barski, A., *Cuddapah, S., *Cui, K., *Roh, T-y, *Schones, D.E., *Wei, G., Chepelev, I., Zhao, K. (2007) High-resolution profiling of histone methylations in the human genome. *Cell* 129, 823-837 (*Contribute equally and are listed alphabetically) (5040 google citations) PMID:17512414

Wang, Z., Zang, C., Rosenfeld, J.A., Schones, D.E., Barski, A., Cuddapah, S., Cui, K., Roh, T-y, Peng, W., Zhang, M., Zhao, K. (2008). Combinatorial patterns of histone acetylations and methylations in the human genome. *Nature Genetics* 40, 897-903 PMID:18552846 (1636 citations)

Wang, Z., Zang, C., Cui, K., Schones, D.E., Barski, A., Peng, W., Zhao, K. (2009) Genome-wide mapping of HATs and HDACs reveals distinct functions in active and inactive genes. *Cell* 138,1019-1031 PMID:19698979 (867 citations)

*Li, Z, *Dai, H, Martos, S.N, Xu, B., Gao, Y, Zhu, G, Li, T, Schones, D.E., and Wang, Z†. (2015) Distinct roles of DNMT1-dependent and DNMT1-independent methylation patterns in the genome of mouse embryonic stem cells. *Genome Biology* 16:115 DOI: 10.1186/s13059-015-0685-2 (25 citations)

*Martos SN, *Li T, *Bossardi R, Lou D, Dai H, Xu J, Gao G, Wang Q, An C, Zhang X, Jia Y, Dawson V, Dawson TM, Ji HK, and Wang Z. (2017) Two approaches revealed a new paradigm of 'switchable or genetics-influenced allele-specific DNA methylation (ASM)' with potential in human disease. *Cell Discovery* 3, 17038: doi:10.1038/celldisc.2017.38