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Assistant Professor

Education: Ph.D. Institute of Basic Medical Sciences, National Cheng Kung University

Specialty: Cell Biology, Molecular Biology and Tumor Virology

Research experiences:

6/01'– 9/01'	Research Scientist Department of Pathology, University of Washington, Seattle, Washington, USA
7/04'-5/06'	Postdoc Division of Clinical Research, National Health Research Institutes, Tainan, Taiwan
6/06'-8/09'	Postdoc Department of Cell Biology, Max-Planck Institute of Biochemistry, Martinsried (Munich), Germany
8/09'-7/10'	Project Leader Biozentrum, University of Basel, Basel, Switzerland
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Research Interests

I. Regulation of centromere dynamics during mitosis

Faithful chromosome segregation is essential for the maintenance of genome stability. During mitosis, the eukaryotic cell constructs a bipolar array of microtubules that serves as the machinery to segregate duplicated chromosomes. The centromere, with its unique chromatin composition, specifies the assembly of kinetochores that provide the connection between chromosomes and spindle microtubules. The stability of this kinetochore-microtubule connection is monitored by an evolutionarily conserved mechanism termed the spindle assembly checkpoint (SAC), which halts mitotic progression until all chromosomes are properly aligned at the metaphase plate. The silencing of the SAC in order to initiate anaphase onset depends primarily on the distance between inner centromeres and outer kinetochores, which is determined by stretching centromeres under the pulling force exerted by spindle microtubules. It has long been inexplicable how SAC components sense signals emitted from centromeres/kinetochores. Interestingly, two centromere-associated proteins (Sgo1 and Sgo2) have shown tension-dependent translocation toward kinetochores, providing a plausible connection between centromere dynamics and the SAC. However, the underlying mechanism regulating centromere-associated proteins that is driven by the structural changes of the centromere remains unexplored and thus is the major research topic in our lab.

2. Virus-mediated hepatocarcinogenesis and aneuploidy

During evolution, polyploidy is thought to be an important mechanism that contributes to speciation. The onset of cellular polyploidy is recognized in all differentiated mammalian tissues and is often associated with terminal differentiation or cellular senescence. Particularly, polyploidy has been noted frequently in the normal liver, as well as in pathophysiological states of the liver. Increasing evidence suggests that genomic

instability in polyploid cells might provide a route to aneuploidy and thereby contributes to malignant cell transformation. Using hepatitis B virus infection as a model system, we are interested to investigate whether hepatocytes polyploidy plays a role in virus-mediated hepatocarcinogenesis.

Publication (2005~2010)

Virus-related:

1. Wang HC, Chang WT, Chang WW, Wu HC, Huang W, Lei HY, Lai MD, Fausto N, Su IJ: Hepatitis B virus pre-S2 mutant upregulates cyclin A expression and induces nodular proliferation of hepatocytes. *Hepatology* 2005, 41:761-770
2. Chuang HC, Lay JD, Hsieh WC, Wang HC, Chang Y, Chuang SE, Su IJ. Epstein-Barr virus LMP1 inhibits the expression of SAP gene and Upregulates Th1 cytokines in the pathogenesis of hemophagocytic syndrome. *Blood* 2005, 106:3090-3096
3. Wang HC, Lai MD, Huang W, Su IJ. Hepatitis B Virus Pre-S Mutants, ER stress and Hepatocarcinogenesis. Review Article. *Cancer Science* 2006, 97:683-688
4. Hsieh YH, Su IJ, Wang HC, Tsai JH, Huang YJ, Chang WW, Lai MD, Lei HY, Huang W. Hepatitis B virus pre-S2 mutant surface antigen induces degradation of cyclin-dependent kinase inhibitor p27Kip1 through c-Jun activation domain-binding protein 1. *Molecular Cancer Research* 2007 10: 2063-72
5. Su IJ, Wang HC, Wu HC, Huang WY. Ground glass hepatocytes contain pre-S mutants and represent preneoplastic lesions in chronic hepatitis B virus infection. Review Article. *J Gastroenterol Hepatol*. 2008 23(8 Pt 1):1169-74

Cell cycle related:

1. Wang L HC, Schwarzbraun T, Speicher MR, Nigg EA. Persistence of DNA threads in human anaphase cells suggests late completion of sister chromatid decatenation. *Chromosoma* 2008, 117(2):123-35
2. Hubner NC, Wang L HC, Kaulich M, Descombes M, Poser I, Nigg EA. Re-examination of siRNA specificity questions role of PICH and Tao1 in the spindle checkpoint and identifies Mad2 as a sensitive target for small RNAs. *Chromosoma* 2010, 119(2): 149-65
3. Wang L HC*, Mayer B, Stemmann O, and Nigg EA. Centromere DNA decatenation depends on separase activation and is required for mammalian cell division. *Journal of Cell Science* 2010, 123:806-813. *Corresponding author.