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**Education**

- 1996-2000 B.S., Life Science, National Yang-Ming University, Taiwan
- 2000-2002 M.S., Biochemistry, National Yang-Ming University, Taiwan
- 2004-2009 Ph.D., Pharmacology/Biomedical Sciences, Rutgers University, USA

**Research and Professional Positions Held in Chronological Sequence**

- 2002-2003 Research assistant, Institute of Molecular Biology, Academia Sinica, Taiwan
- 2010-2017 Postdoctoral fellow, Department of Genetics, Harvard Medical School/ Mass General Hospital, Boston, MA, USA

**Research Interests**

Our lab is interested in the functions of non-coding RNAs. More than 90% of the human genome is transcribed into non-coding RNAs (ncRNAs), including microRNAs (miRNAs) and long noncoding RNAs (lncRNAs). lncRNAs play important roles in regulating a wide range of cellular functions and developmental processes via function critically in the cis- and trans-regulation of gene expression, epigenetic modulation in the nucleus and post-transcriptional control in the cytoplasm. We use an RNA-centric approach to reveal the network of ncRNA-protein-genome. We developed the methods to study the interactomes of non-coding RNAs using iDRiP-MS (*Nature Protocols*, 2021). The long-term goal is to develop a therapeutic technology for human diseases by targeting ncRNAs.

We study the roles of TERRA (Telomeric Repeat containing RNA) in epigenetic regulation, telomere maintenance, ageing and human diseases. TERRA is a long non-coding RNA, which is transcribed from the subtelomeric regions toward telomeres in most eukaryotic cells. We demonstrated that TERRA regulates the genomic occupancy of histone modifier ATRX and DNA G-quadruplex structures (*Nucleic Acids Research*, 2022). ATRX is a chromatin remodeler that is required for silencing retrotransposons and telomere maintenance. The mutations in the ATRX gene cause ATRX syndrome displaying severe defects in neuronal development. Given that TERRA antagonizes ATRX for gene expression, we are working on how modulating TERRA could attenuate the defects in patients carrying ATRX mutations.

TERRA is also highly expressed in ALT (Alternative Lengthening of Telomeres) cancer cells, which do not rely on telomerases activity to extend telomeres. The factors driving ALT remain elusive. We recently reported that TERRA invades double-stranded telomeric DNA to form R-loop structures and contributes the telomere clustering to promote homologous recombination between telomeres in ALT cells. One of TERRA interacting proteins, XPF, is recruited by R-loops and is required for DNA breaks at telomeres to drive telomere synthesis in ALT cancer cells. Our work uncovers the mechanism in which TERRA cooperates with DNA damage proteins to lengthen

telomeres in ALT cancer cells (*Nature Communications*, 2022). We are interested in therapeutic approaches that can overcome the drug resistance in ALT cancers. We would like to develop a friendly method for the medical diagnosis of ALT cancers in clinics.

In addition, we are interested in the functions of TERRA during human ageing and cellular senescence. We found that TERRA is upregulated in monocytes during human ageing (unpublished). The telomere damage is usually associated with increased TERRA levels. We hypothesize that TERRA forms R-loops at telomeres and triggers DNA damage response to induce cellular senescence. We are going to test if modulating TERRA levels or TERRA R-loops can suppress replicative senescence and delay ageing.

### **Major Honors and Awards**

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| 2002 | Young Student Travel Award from International Congress on Hormonal Steroids and Hormones and Cancer |
| 2005 | Young Investigator Award, Dept. Pharmacology, UMDNJ   |
| 2006 | Young Investigator Award, Dept. Pharmacology, UMDNJ   |
| 2007 | Student Travel Award, Graduate School of Biochemical Sciences, UMDNJ                                |
| 2020 | Outstanding Teaching Award, National Taiwan University  |