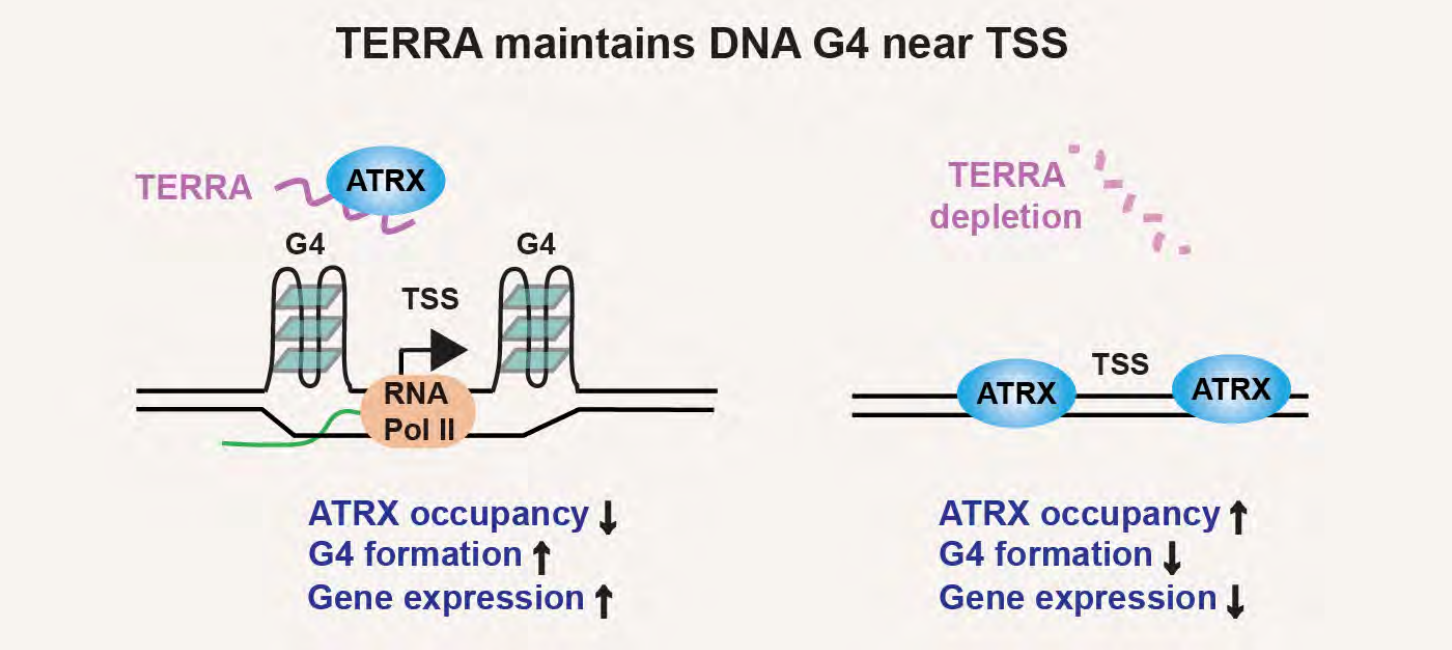
ACHIEVEMENTS

Novel Mechanism of Long Non-Coding RNA in Epigenetic Regulation Found



TERRA maintains DNA G4 near TSS.

Epigenetic regulation is a crucial mechanism for the regulation of gene activity; the process includes changes in DNA modification, DNA structure, histone modification, and association of non-coding RNAs. The majority of the human genome is transcribed into long non-coding RNAs (lncRNA). Certain lncRNAs have been found to be implicated in a wide range of developmental processes and human diseases. Dr. Hsueh-Ping Chu and her team at the Institute of Molecular and Cellular Biology discovered a new mechanism of long non-coding RNA in epigenetic regulation.

The genome consists of non-B form DNA structures, such as G-quadruplexes (G4), which are stacked guanine tetrads involved in regulation of transcription activity by recruiting transcription factors. TERRA, a long non-coding RNA with telomeric repeat sequences, can fold into an RNA G-quadruplex and interact with chromatin remodeler ATRX. Several graduate students, including Ru-Xuan Tsai, Kuo-Chen Fang, Po-Cheng Yang, Yu-Hung Hsieh, and I-Tien Chiang, discovered that TERRA regulates the DNA G4 structures and ATRX occupancy near transcription start sites to regulate gene expression. This is the first study to disclose that a long non-coding RNA is capable of regulating DNA G4 structures across the genome.

ATRX, a chromatin modifier with DNA G4 binding ability, has been identified as one of the genes most commonly associated with human intellectual disability. ATRX mutations lead to ATRX syndrome associated with clinical features such as mental retardation, facial, skeletal, and urogenital abnormalities, as well as mild thalassaemia. In particular, Dr. Chu's group found that TERRA prevents ATRX from binding to chromatin and thus maintains DNA G4 structures. The property of G-rich sequences in TERRA RNA is responsible for sequestering G4 binding proteins, which prevent DNA G4 from unwinding. These findings suggest potential applications for RNA therapy to control genomic structures, which in turn can regulate gene expression for the treatment of human diseases.

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