

Drugging the Primate-Specific Long Non-Coding RNA World of Common Human Diseases

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Abstract

The RNA World Hypothesis posits that RNA, traditionally viewed as a messenger molecule, pre-dated DNA-based life forms. The Human Genome Project and subsequent work by the FANTOM and ENCODE Consortia revealed that a significant portion of the human genome comprises non-coding RNA, particularly long non-coding RNA (lncRNA). Our research has demonstrated that many lncRNA genes are primate-specific and have potential roles in human diseases such as type 2 diabetes, breast cancer, and epilepsy.

Over 95% of disease-associated variants identified in Genome-Wide Association Studies are non-coding, leading to a shift from viewing these variants as markers to seeing them as direct contributors. Our analyses identified the primate-specific lncRNA LOC157273 as a risk factor for multiple metabolic disorders. We have developed RNAi-based therapeutics targeting LOC157273, which show promise in controlling type 2 diabetes and normalizing fasting glucose levels.

In the context of cancer, we have characterized the role of lncRNAs in estrogen receptor alpha positive breast cancer. Our work in lncRNA proteogenomics has revealed the translation of short Open Reading Frames in specific lncRNAs, suggesting a potential source of antigens and signaling molecules in both immunity and cancer.

Our research also extends to the role of primate-specific lncRNAs in the human brain, particularly in relation to epilepsy. We have identified and validated several candidate epileptogenic transcripts, including the BDNF-AS1 lncRNA. Our findings suggest potential new therapeutic approaches for epilepsy patients refractory to existing treatments. Overall, our work underscores the importance of lncRNAs in human disease and their potential as therapeutic targets.

Biography:

Prof. Leonard Lipovich earned his B.A. cum laude in Biological Sciences (with a focus on Genetics and Development) from Cornell University in 1998. He obtained his PhD in Molecular Biotechnology from the University of Washington in 2003. Between 2003 and 2006, he did his postdoctoral training at the Genome Institute of Singapore, A*STAR in Singapore. In 2007, he got a tenure track position at the Centre for Molecular Medicine and Genetics (CMMG), Wayne State University. He was later promoted to full professor in 2019. In 2020, he moved to Mohammed Bin Rashid University of Medicine and Health Sciences in Dubai, and now he is a founder and CEO of Plasar (FZE), C.T.O., Joint Laboratory of Shenzhen Institutes of Advanced Technology (SIAT) of the Chinese Academy of Sciences (CAS) and Shenzhen Huayuan Biotechnology Co., Ltd. His research focuses on primate long-coding RNAs, and he has 87 peer-reviewed publications.

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All are welcome!