**Differential Expression of Long Noncoding RNAs In Age-Related Macular Degeneration**

**ABSTRACT.**

It is now widely recognized that Long Noncoding RNAs (lncRNAs) play important roles in regulating gene expression and epigenetic state, and there is increasing recognition of the importance of lncRNAs in disease. Here we compare the expression of lncRNAs in normal human eyes, and eyes afflicted with Age-Related Macular Degeneration (AMD), by quantitating gene expression using the RNA-Seq high-throughput sequencing technique. Transcriptomes were evaluated for both normal and disease states, by tissue, and by disease phenotype. Our results suggest that lncRNAs that have demonstrated importance in regulating pathways important for the progression of AMD show significant differential expression as a function of disease state, tissue, and disease stage.

**INTRODUCTION.**

While protein coding genes and structural RNAs form a small fraction of the mammalian genome, it has become widely recognized that most of the genome is nonetheless actively transcribed, at least in a particular tissue or developmental stage [Quinn & Chang, 2016; Rinn & Chang, 2012]. While the proportion of these transcripts that have biological function is open to question [Ulitsky & Bartel, 2014], it has become evident that many non-protein coding RNA transcripts do in fact play critical roles in regulating gene expression and modulating biomolecular activities, and disregulation and mutation of noncoding RNAs have been strongly implicated in disease.

An important class of noncoding transcripts are the long noncoding RNAs or lncRNAs. lncRNAs are distinguished as longer than other categories of functional RNAs (such as microRNAs), and often have features in common with coding mRNAs, such polyadenylation and alternate splicing. However they are distinct from coding transcripts in that they do not feature conserved open reading frames, and behave differently in regard to cellular localization and degradation.

The roles of lncRNAs in regulation appear to be extraordinarily diverse, and include both *cis* and *trans* mechanisms. lncRNAs are believed to act as *cis* regulators in the case of enhancer RNAs such as HOTAIR, which are believed to stabilize complexes involving protein-expressing loci in their chromosomal neighborhood, triggering epigenetic changes at those targets [ref]. Another *cis* mechanism is transcriptional interference, a suggested mechanism of the Air lncRNA in silencing the paternal copy of the insulin-like growth factor 2 receptor [ref].