LincRNAs identified in human fat tissue

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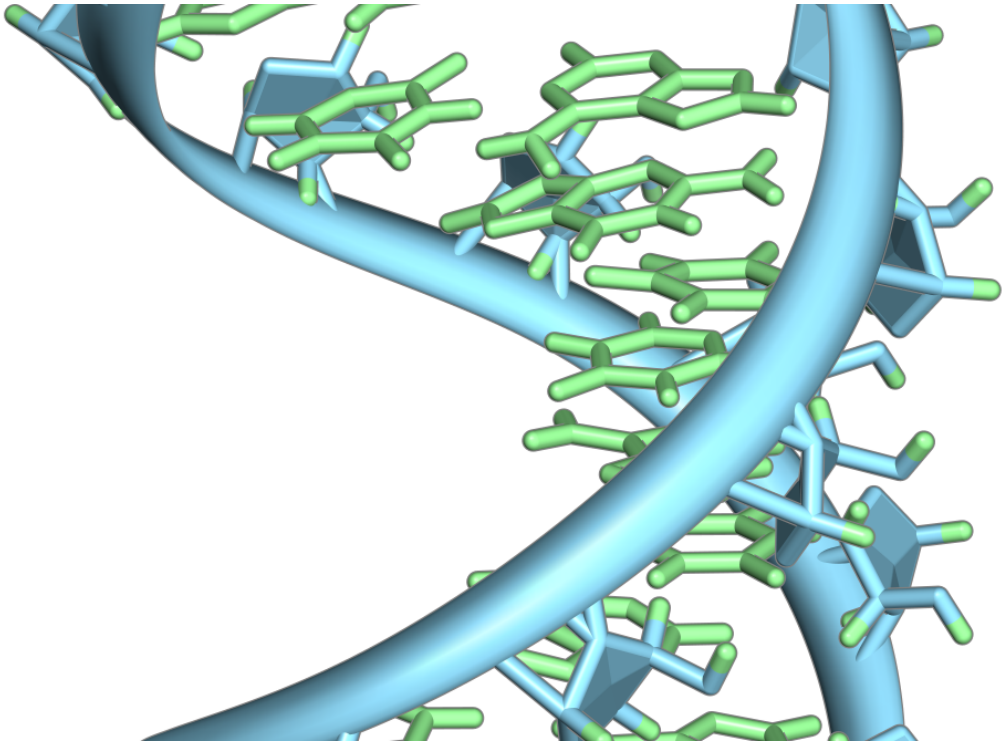

A hairpin loop from a pre-mRNA. Highlighted are the nucleobases (green) and the ribose-phosphate backbone (blue). Note that this is a single strand of RNA that folds back upon itself. Credit: Vossman/ Wikipedia

A large team of researchers from the U.S. and China has succeeded in identifying a number of RNA fragments found in human fat tissue. In their paper published in the journal *Science Translational Medicine* the group describes their study of the fragments they found and their possible links with obesity.

Prior research has reported RNA fragments in the human body known as long intergenic noncoding RNA (lincRNA). But as the researchers note, their role has not been very well understood. Some researchers in the past have even suggested that they were nonfunctional, but more recent research has suggested they play a role in regulating gene expression and thus protein function. In this new effort, the researchers took a close look at subcutaneous fat taken from the buttocks of 25 human volunteers to learn more about lincRNA in fat tissue.

In sequencing the RNA in the samples, the researchers found that they contained 1001 distinct lincRNAs. They also found that those lincRNAs were not the same as those in mouse fat tissue, suggesting the line is unique to humans. They also noted that one line called linc-ADAL appeared more often than any other in the fat tissue—and further testing of the line showed that it interacted with other cell elements involved in regulating fat cells and fat stores. This, of course, suggested a possible link between lincRNA in fat tissue and obesity. After excluding lines with more than a single exon, those with protein-coding functions or those with aberrant expressions, the team narrowed down the number of lincRNAs that had been annotated to 857. Further analysis reduced the number to 144 new lincRNA candidates expressed in human fat tissue.

The researchers also collected fat tissue from 22 people who had undergone bariatric surgery for treatment of obesity. Comparing tissue samples from before the surgery and from three months afterward, they found expression shifts in 53 of the lines they had identified in the first part of the study, further implicating lincRNA as a role player in obesity. They also noted there were differences in shifts in expression between male and female volunteers for 49 of the lincRNAs.

The researchers suggest that because of the uniqueness of the lines they found, it appears likely that the lincRNAs evolved rather quickly in the fat tissue. They suggest also that much more research will need to be

done to determine if there might be a way to manipulate lincRNA to reduce obesity in patients.

More information: Xuan Zhang et al. Interrogation of nonconserved human adipose lincRNAs identifies a regulatory role of linc-ADAL in adipocyte metabolism, *Science Translational Medicine* (2018). DOI: 10.1126/scitranslmed.aar5987

Abstract

Long intergenic noncoding RNAs (lincRNAs) have emerged as important modulators of cellular functions. Most lincRNAs are not conserved among mammals, raising the fundamental question of whether nonconserved adipose-expressed lincRNAs are functional. To address this, we performed deep RNA sequencing of gluteal subcutaneous adipose tissue from 25 healthy humans. We identified 1001 putative lincRNAs expressed in all samples through de novo reconstruction of noncoding transcriptomes and integration with existing lincRNA annotations. One hundred twenty lincRNAs had adipose-enriched expression, and 54 of these exhibited peroxisome proliferator–activated receptor γ (PPARγ) or CCAAT/enhancer binding protein α (C/EBPα) binding at their loci. Most of these adipose-enriched lincRNAs (~85%) were not conserved in mice, yet on average, they showed degrees of expression and binding of PPARγ and C/EBPα similar to those displayed by conserved lincRNAs. Most adipose lincRNAs differentially expressed (n = 53) in patients after bariatric surgery were nonconserved. The most abundant adipose-enriched lincRNA in our subcutaneous adipose data set, linc-ADAL, was nonconserved, up-regulated in adipose depots of obese individuals, and markedly induced during in vitro human adipocyte differentiation. We demonstrated that linc-ADAL interacts with heterogeneous nuclear ribonucleoprotein U (hnRNPU) and insulin-like growth factor 2 mRNA binding protein 2 (IGF2BP2) at distinct subcellular locations to regulate adipocyte differentiation and lipogenesis.