Task 1

Answer the following questions

a. What is the medically relevant insight from the article?

The study shows that long noncoding RNAs (lncRNAs), which make up most of the human transcriptome, are not just "noise" but play important roles in cell growth, morphology, and gene regulation. By knocking down 285 lncRNAs in human dermal fibroblasts, the authors found that about 30% influenced either proliferation or cell shape. For example, ZNF213-AS1 affected cell growth and migration and was linked to worse outcomes in some cancers, while RP11-398K22.12 regulated nearby brain-related genes in a cis manner. This suggests that lncRNAs could be potential biomarkers or even therapeutic targets in diseases like cancer, fibrosis, or neuro disorders.

b. Which genomics technology/ technologies were used?

1. Antisense oligonucleotides (ASOs, GapmeRs) – to knock down specific lncRNAs.

2. Cap Analysis of Gene Expression (CAGE) – to capture transcription start sites and measure transcriptomic responses.

3. RNA-seq of fractionated RNA – to determine lncRNA localization (chromatin, nuclear soluble, cytoplasmic).

4. Hi-C (chromosome conformation capture) – to study spatial DNA interactions for cis regulation.

5. Single-molecule RNA FISH – to confirm subcellular localization and cis effects.

6. These were combined with imaging (cell morphology, growth assays) for "molecular phenotyping"

Task 1

Further related research questions

a. List and explain at least three questions/ hypotheses you can think of that extend the analysis presented in the paper.

1. Cell-type specificity: Do the same lncRNAs (like ZNF213-AS1 or RP11-398K22.12) show similar growth or regulatory effects in other primary cell types (immune cells, epithelial cells), or are their roles fibroblast-specific?

2. Disease relevance: Since some lncRNAs were linked to pathways in cancer or brain function, can their expression or knockdown effects be validated in patient samples (e.g., tumors, neurodegenerative tissues)?

3. Therapeutic angle: If ASO-mediated knockdown alters key pathways, could targeted lncRNA inhibition serve as a therapeutic strategy in conditions like fibrosis or cancer? And importantly, what are the risks of off-target or cell-type-dependent effects?

b. [Optional] Devise a computational analysis strategy for (some of) the listed questions under 3a.