

## **Memorandum**

To: Professor Shonnard  
From: Erik Lomas  
Date: 9/6/03  
Re: RNA Inhibition

As assigned, I have read an article dealing with the biochemical industry and will give you an overview of the article in the following paragraphs. The article I've read is "Censors of the Genome" by Nelson C. Lau and David P. Bartel, published in the August 2003 issue of Scientific American.

DNA bases are transcribed to mRNA when particular protein arrangements are docked onto the regulatory genes controlling gene expression. Years ago, a process called the interferon response was discovered. This process disables mRNA transcription when a cell is attacked by a virus, thus preventing any gene expression.

Within recent years more gene specific RNA interference has been discovered, whereby specific mRNA strings are destroyed. This process has been labeled RNAi. This discovery excited the scientific community because it offers hope for targeting specific genes involved with cancer and other genetic diseases. Also, researchers working with simpler organisms have learned how to use RNAi to suppress nearly any gene they can label. This could be extremely useful in determining the functionality of any given gene.

Researchers use RNAi by introducing sense or anti-sense RNA into an organism. Sense and antisense RNA are the complementary and duplicate RNA sequence of a gene respectively. These RNA sequences either bind to the mRNA or DNA to inhibit creation of the targeted protein. It was later discovered that sense and anti-sense RNA only play a small role in the inhibition of gene expression. The presence of double stranded RNA and interferons within mammalian cells promote the production of PKR enzyme and RNase L. PKR indiscriminately blocks translation of mRNA while RNase L destroys particular mRNA sequences.

The process by which cells target specific RNA strings involves a few enzymes and double stranded RNA. When an enzyme dubbed "Dicer" encounters double stranded RNA, it latches on and cleaves the double stranded RNA into segments around 22 nucleotides long, which are called siRNA. Some siRNA encounter another protein called RNA induced silencing complex (RISC). As other mRNA encoded with the same gene encounter RISC, a third enzyme called "Slicer" cleaves the mRNA.

These new discoveries offer a lot of promise. HIV, polio, and hepatitis C have already been temporarily stopped in human cell cultures. The main difficulty lies in delivery of treatment. Ingestion of RNA sequences is not feasible, but viruses carrying sense, antisense, or siRNA offer hopeful avenues for gene therapy.