Study of degree of conservation in regulatory sequences of human intronic and intergenic miRNA genes in comparison to 16 vertebrate species.

Ankur Agarwal BBSI @ Pitt 2007

Mentor: Dr Takis Benos

Names of genome assemblies of 17 vertebrates

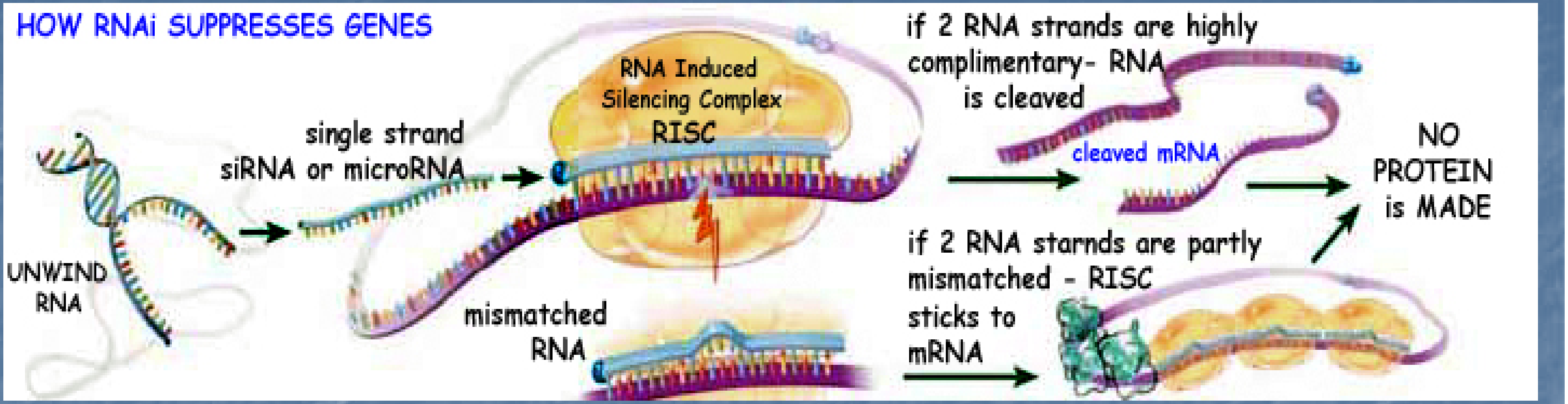
1. oryCun1-- Rabbit
2. danRer3-- Zebra fish
3. tetNig1-- Tetra Odon
4. monDom4-- Opossum
5. fr1-- Fugu
6. galGal2-- Chicken
7. rn4-- Rat
8. Mm8-- Mouse
9. echTel1-- Tenrec
10. loxAfr1-- Elephant
11. bosTau2-- Cow
12. canFam2-- Dog
13. panTro1-- Chimpanzee
14. dasNov1-- Armadillo
15. xenTro1-- Frog
16. rheMac2-- Macaque
17. Hg18-- Humans

miRNAs or microRNAs

- Single stranded RNA molecules.
- Encoded by genes transcribed from DNA but not translated into protein(non coding RNA).
- Partially complementary to mRNA molecules (coding RNA).
- Prevent protein translation through a mechanism similar to RNAi.

http://en.wikipedia.org/wiki/MicroRNA

miRNA action

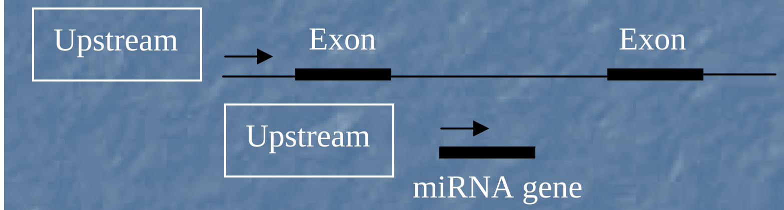


- The miRNA sequence combines with proteins to form a complex called RISC [RNA-Induced Silencing Complex].
- The RISC then captures a native mRNA molecule that complements the short miRNA sequence.
- If the pairing is essentially perfect, the native mRNA is cut into useless RNA fragments that aren't translated.
- If however, the pairing is less than perfect then the RISC complex binds to the mRNA and blocks ribosome movement along the native mRNA also halting translation.
- Net effect NO PROTEIN IS MADE.

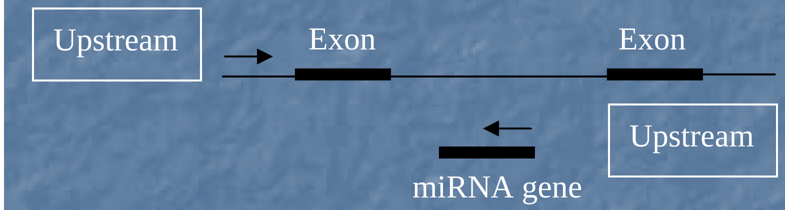
http://fig.cox.miami.edu/~cmallery/150/gene/how_siRNA_works.htm

Orientation of miRNA genes on the genome

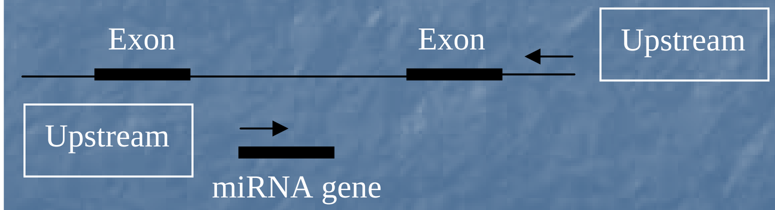
Positive and Positive


Upstream
Exon
Exon
Upstream
miRNA gene

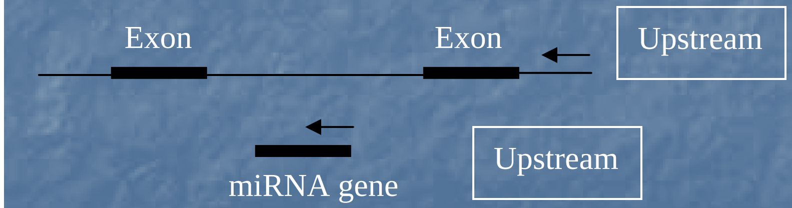
Positive and Negative


Upstream
Exon
Exon
Upstream
miRNA gene

Negative and Positive


Exon
Exon
Upstream
Upstream
miRNA gene

Negative and Negative


Exon
Exon
Upstream
Upstream
miRNA gene

The diagram depicts orientation of intronic miRNA genes only

A few notes

- Based on work done in Regulatory conservation of protein coding and miRNA genes in vertebrates : lessons from the opossum genome by Benos et al.
- Covers the analysis for only the intergenic genes. I replicated that work and did similar analysis for intronic same strand genes and intronic opposite strand genes.

References

- For the dataset containing all the discovered and classified human miRNAs: http://www.diana.pcbi.upenn.edu/cgi-bin/miRGen/v3/Genomics.cgi
- UCSC genome browser for a listing of all the discovered human genes.

Acknowledgements

- Dr Takis Benos – for the idea and hypothesis on intronic miRNA genes. For support and guidance.
- Dr Shaun Mahony and David Corcoran – for answering my queries and extending great help during the course of the project.
- Dr Judy Wieber for directing me to Dr Benos for a project and accepting me as a participant in the BBSI 2007 program that made all this work possible.
- UPitt, NIH, NSF