

Explore gene regulation at the DNA level

Axiom® miRNA Target Site Genotyping Arrays

Genetic variants affecting miRNA pathways have been implicated in diseases such as cancer, neurological disorders, muscular hypertrophy, gastric mucosal atrophy, cardiovascular disease, and type 2 diabetes¹⁻³



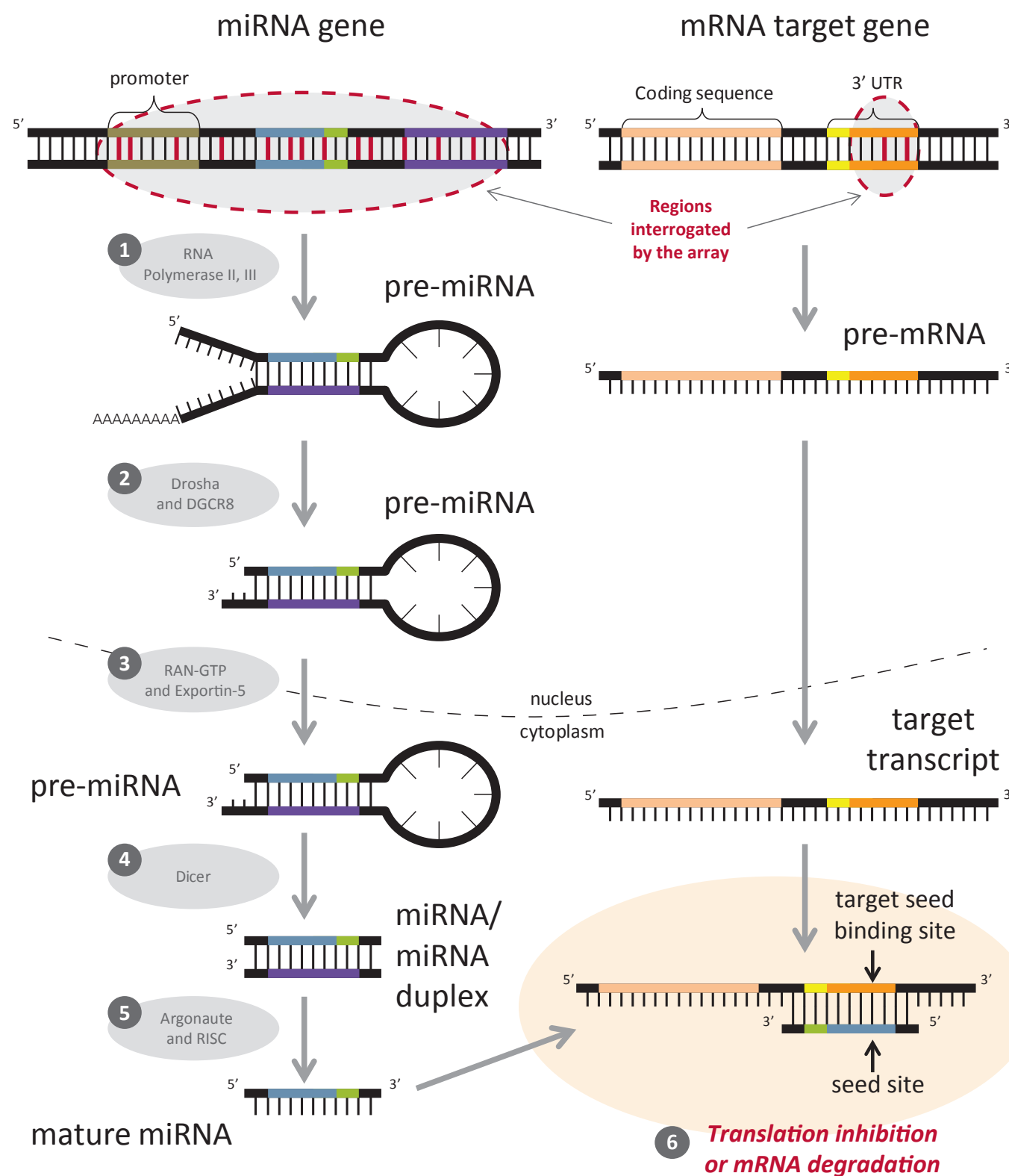
- Axiom® miRNA Target Site Array offers the only comprehensive tool for genome-wide evaluation of miRNA target sites that influence translation
- This array is easily customized to include other relevant content of your choosing, including long non-coding RNAs, for disease association studies
- This robust meta-analysis captures variation of non-coding regulatory regions of the genome and provides biological insights and generates new ideas for diagnosis and treatment of complex diseases for research purposes
- Over 80% of the 238,000 SNPs and indels on the array are not available on any other commercially available genotyping array

miRNA gene regulation

miRNA processing in humans

1. The miRNA gene is transcribed with RNA polymerase II and III, resulting in a pri-miRNA hairpin.
2. Proteins Drosha and DGCR8 liberate the hairpins by cleaving the excess RNA from the base, leaving a pre-miRNA.
3. The protein Exportin-5 exports the pre-miRNA from the nucleus to the cytoplasm.
4. The enzyme Dicer cleaves the loop from the hairpin, leaving an miRNA/miRNA duplex.
5. The miRNA/miRNA duplex is disassembled, becoming a mature miRNA, which couples with a group of proteins to form the RNA-induced silencing complex (RISC).
6. The mature miRNA and RISC complex bind to the 3' UTR of the target transcript.

If binding at the seed site is a perfect match, then translation will be inhibited or the mRNA will be degraded.



Genetic marker location or type	No. of markers*
mRNA target seed binding site	210,000
miRNA gene regulatory regions	15,000
miRNA hairpin ▪ includes 60 mature miRNA markers	160
Processing proteins	220
GWAS and ancestry informative	12,620
Total	238,000

*Values are rounded

Known or predicted disease category	No. of markers
Sanger cancer census genes ▪ with known germline mutations	8,488
ADME genes	3,746
Cardiovascular and type 2 diabetes associated genes	53,788
HLA genes	276
Immune response and inflammation genes	6,494

There are several control elements in the miRNA cascade that affect gene regulation. Affymetrix' Axiom® miRNA Target Site Genotyping Array **interrogates SNPs and indels in gDNA (shown in red)** that affect all known downstream miRNA-related gene regulation elements.

miRNAs are known to regulate gene expression by binding to a specific region of the 3' untranslated region (UTR) of mRNA genes. This target binding region is a 7 bp sequence that is complementary to the miRNA seed site. If the miRNA seed site is a perfect complement to the target binding site, then regulation takes place – translation is inhibited or the mRNA is degraded.

Can you afford NOT to understand gene regulation at the DNA level?

References

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2. Mishra P. J., Bertino J. R. MicroRNA polymorphisms: the future of pharmacogenomics, molecular epidemiology and individualized medicine. *Pharmacogenomics* **10**:399–416 (2009).
3. Hoffman A. E., *et al.* microRNA miR-196a-2 and Breast Cancer: A Genetic and Epigenetic Association Study and Functional Analysis. *Cancer Research* **69**:5970–5977 (2009).

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