

Micro RNAs: Regulators Regulating Regulators

Andrea Tanzer

Institute for Theoretical Chemistry and Structural Biology,
Univ.Vienna, Austria
at@tbi.univie.ac.at

The TBI Seminar, Bled 2005

Outline

Introduction

- Features of miRNAs

- HOX Genes

MicroRNAs within the HOX Gene Clusters

- mir-196 Downregulates Central HOX Genes

- mir-10 and The Anterior HOX Genes

Summary

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What Are MicroRNAs?

- ▶ **small non-coding RNAs (ncRNAs)**
- ▶ not translated into Protein
- ▶ function as RNA
like tRNA, rRNA, snoRNA
- ▶ target DNA and mRNA
- ▶ incorporated in protein complexes

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Where Can They Be Found?

- ▶ in eukaryotes: plants, fungi, animals
- ▶ intergenic regions,
upstream regions and
introns of protein coding genes
- ▶ single RNA genes or gene clusters

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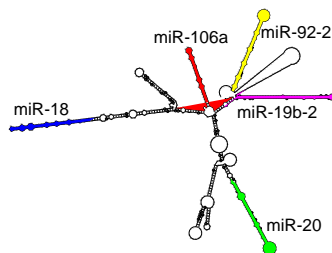
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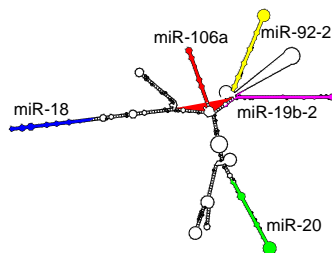
Maturation of miRNAs

- ▶ primary-precursor micro RNA (pri-miRNA)
- ▶ Cleavage I: Drosha
- ▶ precursor miRNA (pre-miRNAs)
- ▶ export to cytoplasm (exportin-5)
- ▶ Cleavage II: Dicer
- ▶ mature miRNA (miRNAs)
- ▶ miRNA-protein complex



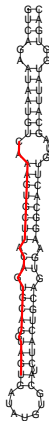
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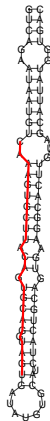
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Function of miRNAs

Cytoplasm:

- ▶ post-transcriptional gene silencing (PTGS)
mRNA degradation
translational repression

Nucleus:

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DNA methylation
Chromatin remodelling
Histone methylation

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- ▶ embryonic development
- ▶ antero-posterior axis
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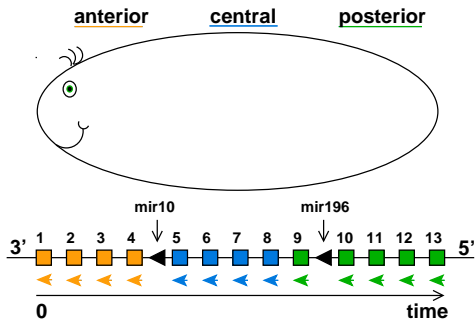
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Genomic Organisation of HOX Genes



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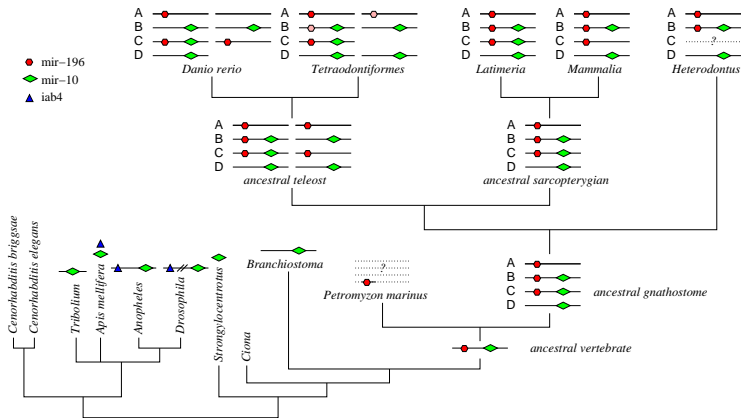
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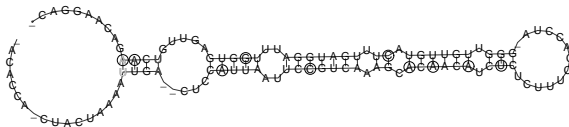
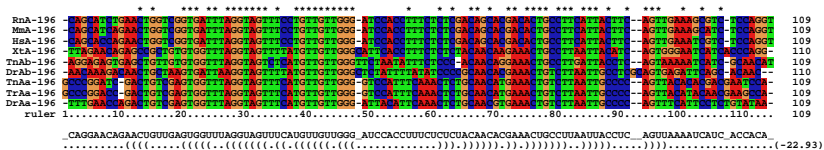
mir-10 and The Anterior HOX Genes

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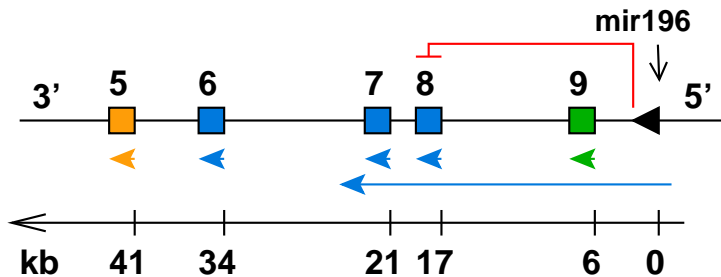
Phylogeny of mir-196



Sequence Conservation of mir-196 Homologs



Expression of Central HOX Genes



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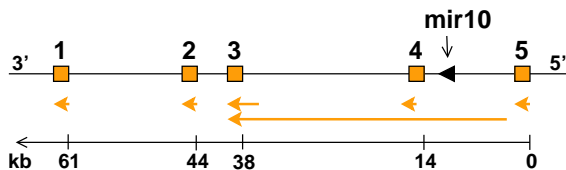
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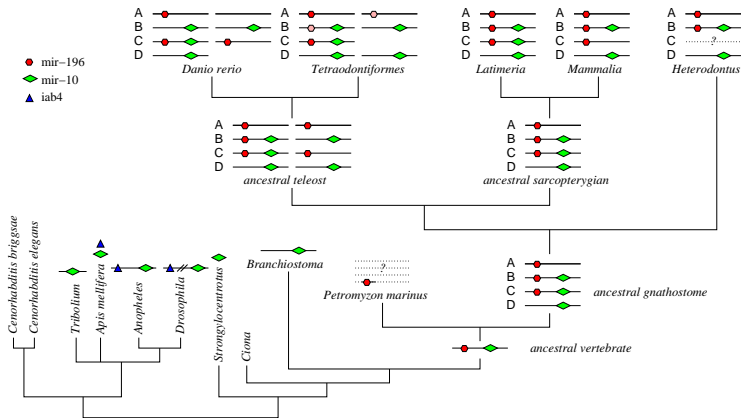
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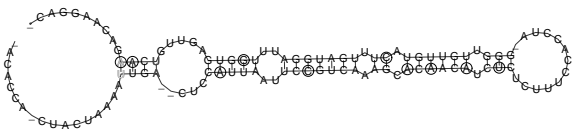
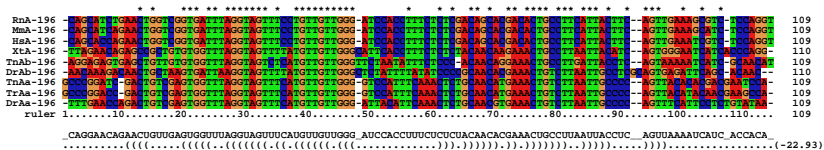
Expression of Anterior HOX Genes



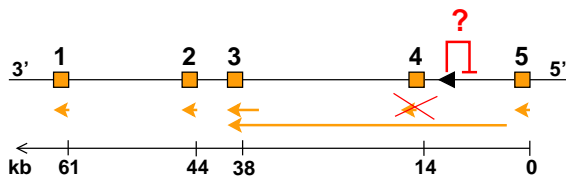
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Mir-10 - a *cis* acting microRNA?



Possible Function(s) of mir-10

- ▶ PTGS - target ?
- ▶ silencing of hox4?
- ▶ DNA methylation - mir-10?
- ▶ chromatin condensation?

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mir-196	mir-10
posterior	anterior
<i>trans</i>	<i>cis?</i>
HOXB8	mir-10?

How to measure coevolution of miRNA and target?

thanks.