

The genomics of small RNAs in insects

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Introduction

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Introduction

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

	Discovered	First described in insects
microRNAs (miRNAs)	1993	2001
endogenous small interfering RNAs (siRNAs)	2003	2008
Piwi-interacting RNAs (piRNAs)	2006	2006

Introduction

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

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Interact with members of the Argonaute protein family.

Introduction

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

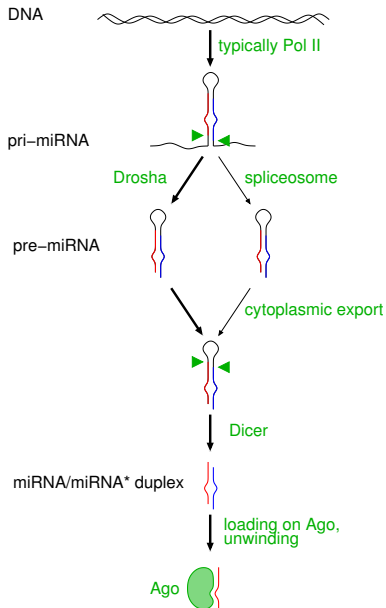
	Discovered	First described in insects
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Interact with members of the Argonaute protein family.

Three subfamilies:

- ▶ Ago (miRNAs and siRNAs);
- ▶ Piwi (piRNAs);
- ▶ Wago (some siRNAs in nematodes).

microRNA biogenesis



Introduction

miRNAs

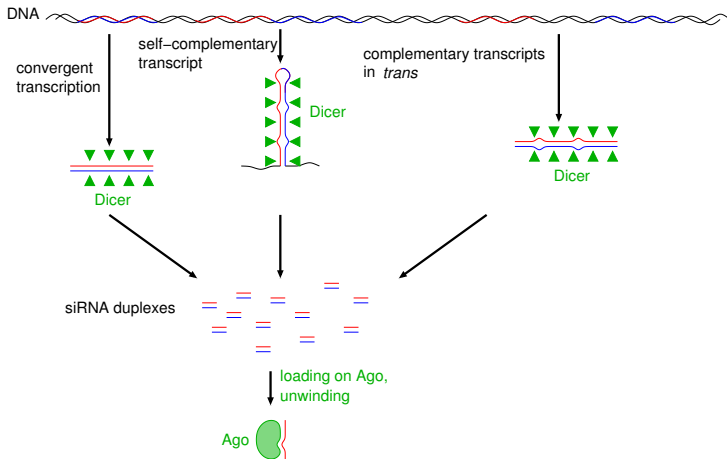
piRNAs

siRNAs

Associated proteins

Conclusion

siRNA biogenesis



Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

piRNA biogenesis

2006:

Does not involve Dicer.

Derive (apparently) from single-stranded precursors.

Expressed mostly in the germ line.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

microRNA genes in insects

Low diversity: < 500 known miRNA genes per species.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

microRNA genes in insects

Low diversity: < 500 known miRNA genes per species.

	Number of miRNA genes	Relative to coding genes		
		intergenic	sense	antisense
<i>D. melanogaster</i>	238	38%	53%	9%
<i>D. pseudoobscura</i>	208	100%	0%	0%
<i>A. gambiae</i>	67	100%	0%	0%
<i>A. mellifera</i>	174	100%	0%	0%
<i>B. mori</i>	483	100%	0%	0%

(data from miRBase, version 17: April 2011)

Introduction

miRNAs

piRNAs

siRNAs

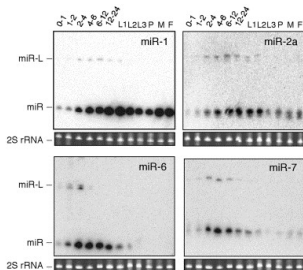
Associated proteins

Conclusion

microRNA genes in insects

Low diversity: < 500 known miRNA genes per species.

Very high abundance (for some miRNAs).



(from Aravin *et al.*, 2003)

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

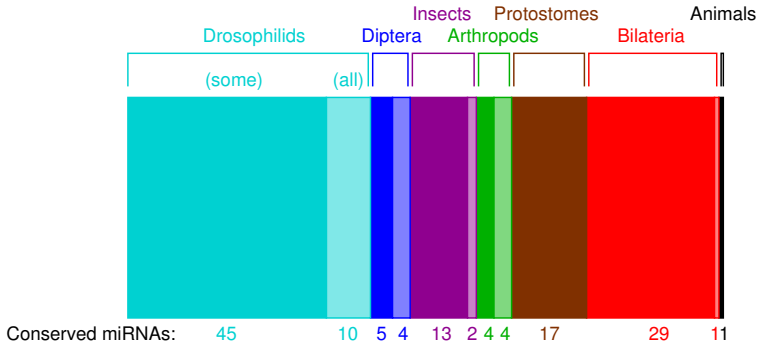
Conclusion

microRNA genes in insects

Low diversity: < 500 known miRNA genes per species.

Very high abundance (for some miRNAs).

miRNAs can be very well conserved in animals.



Introduction

miRNAs

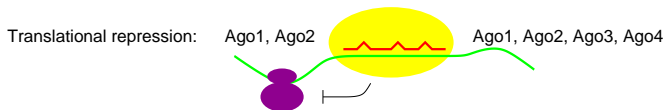
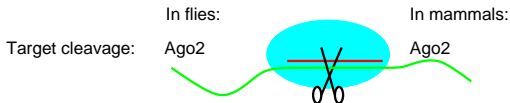
piRNAs

siRNAs

Associated proteins

Conclusion

miRNA mode of action



Introduction

miRNAs

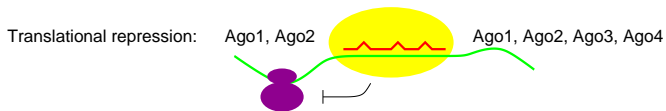
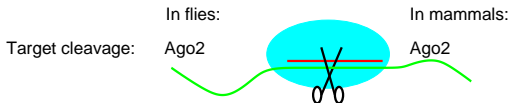
piRNAs

siRNAs

Associated proteins

Conclusion

miRNA mode of action



Definition of a functional imperfect complementarity?

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

miRNA mode of action

Introduction

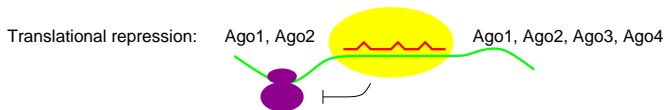
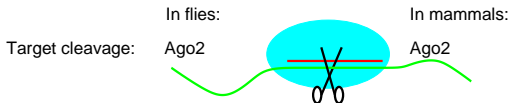
miRNAs

piRNAs

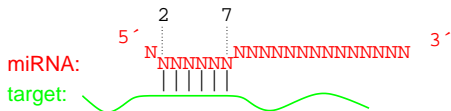
siRNAs

Associated proteins

Conclusion



Definition of a functional imperfect complementarity?



→ the “seed”

miRNA mode of action

Target prediction algorithms: find evolutionarily conserved seed matches in 3' UTRs.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

miRNA mode of action

Target prediction algorithms: find evolutionarily conserved seed matches in 3' UTRs.

Such short complementarities are very frequent (60 % of human genes are targeted by miRNAs: Friedman *et al.*, 2009). Similar proportions in other animals.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

miRNA mode of action

Target prediction algorithms: find evolutionarily conserved seed matches in 3' UTRs.

Such short complementarities are very frequent (60 % of human genes are targeted by miRNAs: Friedman *et al.*, 2009). Similar proportions in other animals.

⇒ miRNAs are implicated in every biological process in animals.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

miRNA mode of action

Target prediction algorithms: find evolutionarily conserved seed matches in 3' UTRs.

Such short complementarities are very frequent (60 % of human genes are targeted by miRNAs: Friedman *et al.*, 2009). Similar proportions in other animals.

⇒ miRNAs are implicated in every biological process in animals.

Maybe just a small subset of predicted targets are really, functionally targeted.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

piRNAs are made from genomic clusters

Introduction

miRNAs

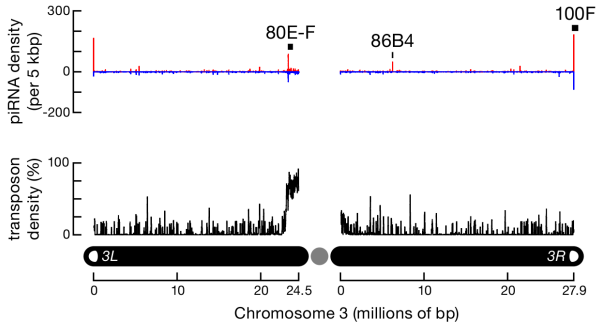
piRNAs

siRNAs

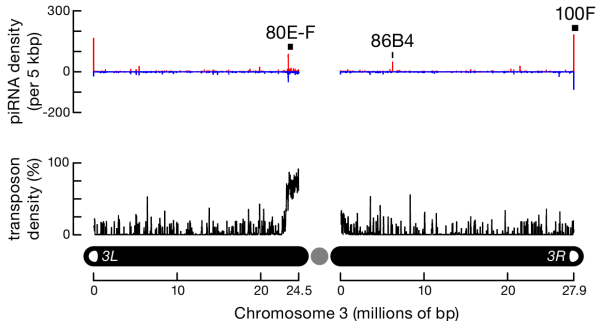
Associated proteins

Conclusion

piRNAs are made from genomic clusters



piRNAs are made from genomic clusters



Large diversity in sequence (millions of different piRNAs),
each of them being poorly abundant.

Introduction

miRNAs

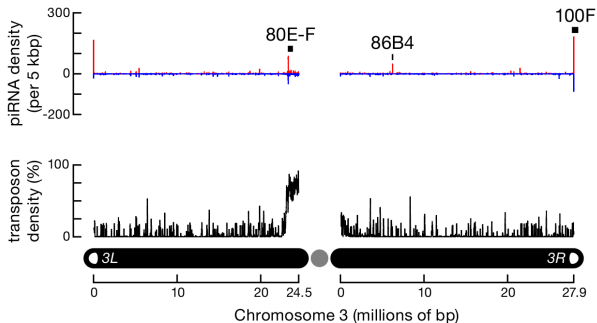
piRNAs

siRNAs

Associated proteins

Conclusion

piRNAs are made from genomic clusters



Large diversity in sequence (millions of different piRNAs),
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Poorly conserved, but piRNA cluster locations are conserved.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

piRNA biogenesis: a reactive “immune” system

Introduction

miRNAs

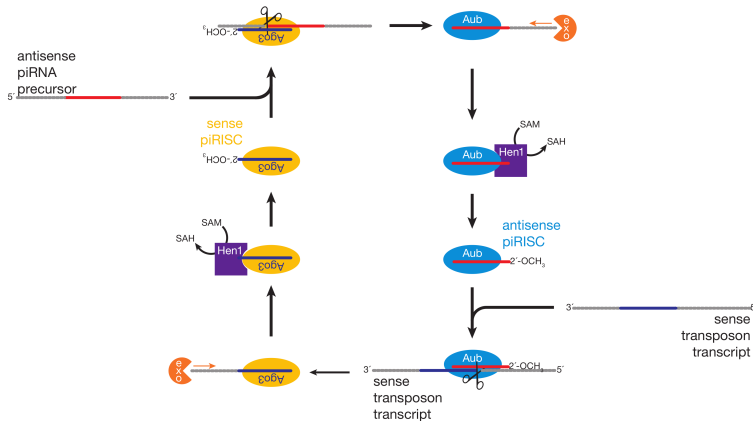
piRNAs

siRNAs

Associated proteins

Conclusion

piRNA biogenesis: a reactive “immune” system



Endogenous siRNAs

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Endogenous siRNAs

In the animal reign, endogenous siRNAs had only been found in worms (possess an RNA-dependent RNA polymerase, RdRP, that amplifies the RNAi response).

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Endogenous siRNAs

In the animal reign, endogenous siRNAs had only been found in worms (possess an RNA-dependent RNA polymerase, RdRP, that amplifies the RNAi response).

Detection of endogenous siRNAs in *Drosophila* by deep-sequencing.

Introduction

miRNAs

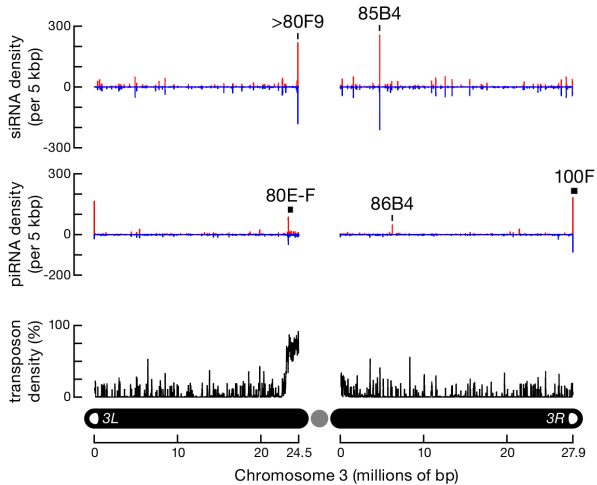
piRNAs

siRNAs

Associated proteins

Conclusion

Endogenous siRNAs



Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Associated proteins: variations on common themes

- ▶ Specialized effectors for siRNAs and miRNAs in insects.
- ▶ An alternative piRNA biogenesis pathway in flies.
- ▶ An RdRP in an arthropod.

Introduction

miRNAs

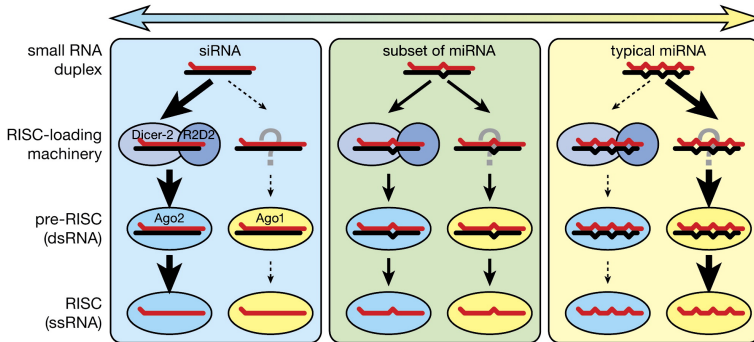
piRNAs

siRNAs

Associated proteins

Conclusion

miRNA sorting: an insect-specific feature



(from Tomari *et al.*, 2007)

Conclusion

- ▶ Regulators with specific targets (recognized by sequence complementarity).

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Conclusion

- ▶ Regulators with specific targets (recognized by sequence complementarity).
- ▶ An ancient evolutionary origin.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Conclusion

- ▶ Regulators with specific targets (recognized by sequence complementarity).
- ▶ An ancient evolutionary origin.
- ▶ A peculiar genomic organization for piRNAs and siRNAs.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Conclusion

- ▶ Regulators with specific targets (recognized by sequence complementarity).
- ▶ An ancient evolutionary origin.
- ▶ A peculiar genomic organization for piRNAs and siRNAs.
- ▶ Biological functions under investigation.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Conclusion

- ▶ Regulators with specific targets (recognized by sequence complementarity).
- ▶ An ancient evolutionary origin.
- ▶ A peculiar genomic organization for piRNAs and siRNAs.
- ▶ Biological functions under investigation.
- ▶ Insect-specific features for miRNA and piRNA biogenesis: uncoupling biological functions.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion

Acknowledgements

LBME du CNRS, Toulouse, France

Anna Sergeeva and Katia Chiron

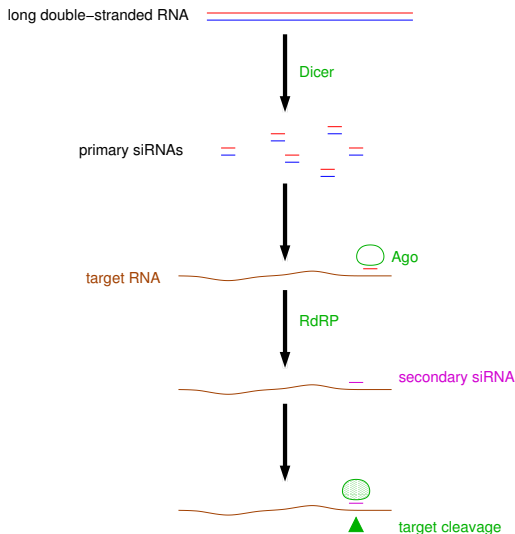
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UMass Medical School, Worcester, MA, USA

Phil Zamore, Megha Ghildiyal, Zamore lab



siRNA biogenesis: how widespread are RdRP's?



siRNA biogenesis: how widespread are RdRP's?

Ixodes scapularis has four RdRP genes.

Introduction

miRNAs

piRNAs

siRNAs

Associated proteins

Conclusion