

Short Interfering RNA (That's "SIR" to you)

BMS 265
Todd Logan
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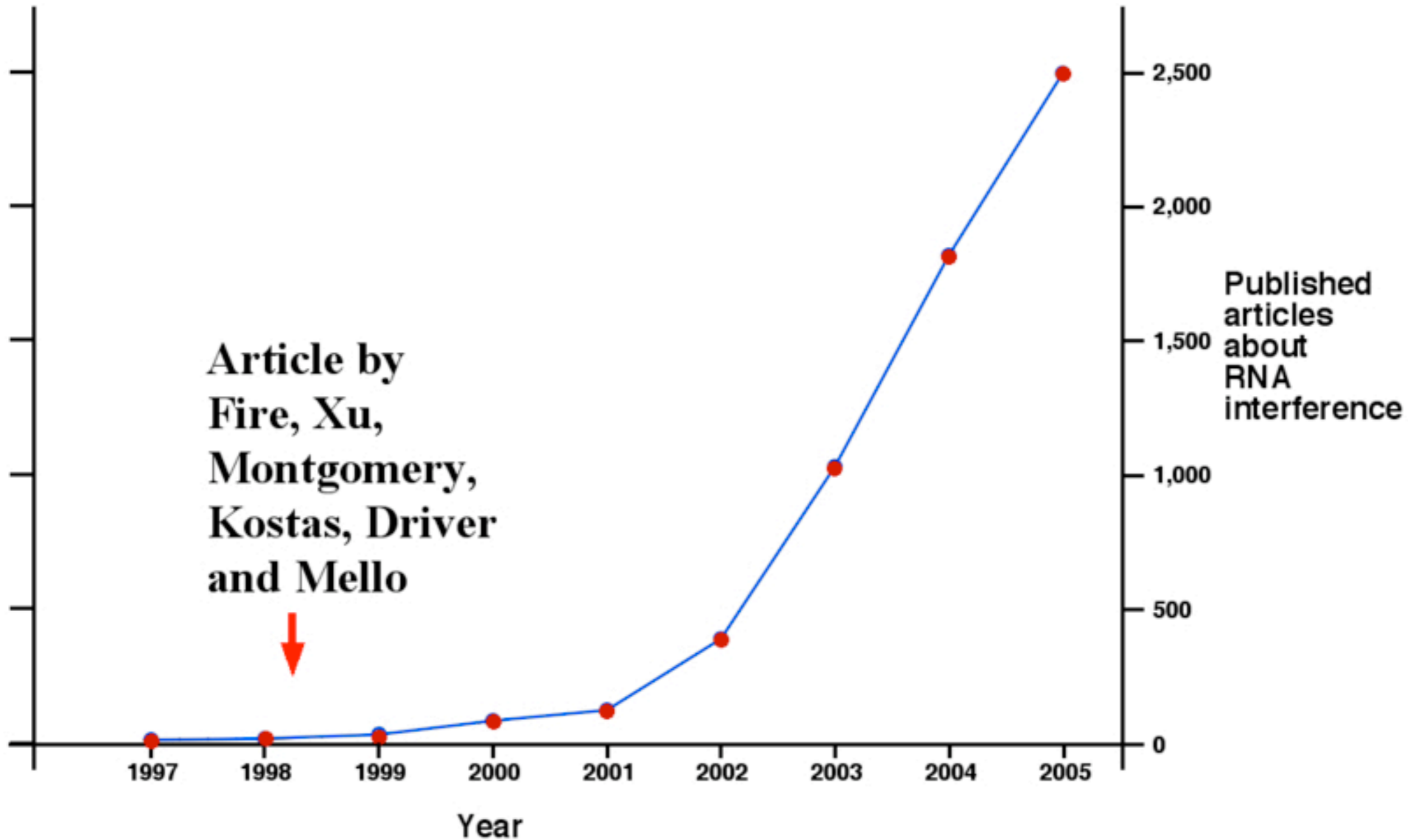
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- And then.....

siRNA's rise to fame



The Exemplary Members

- trans-acting small interfering RNAs (tasiRNAs)
- repeat-associated small interfering RNAs (rasiRNAs)
- scan RNAs (scnRNAs)
- long small interfering RNAs (lsiRNAs)

The Wannabes

- micro RNAs (miRNAs)
- piwi-interacting RNAs (piRNAs)
- 21U-RNAs

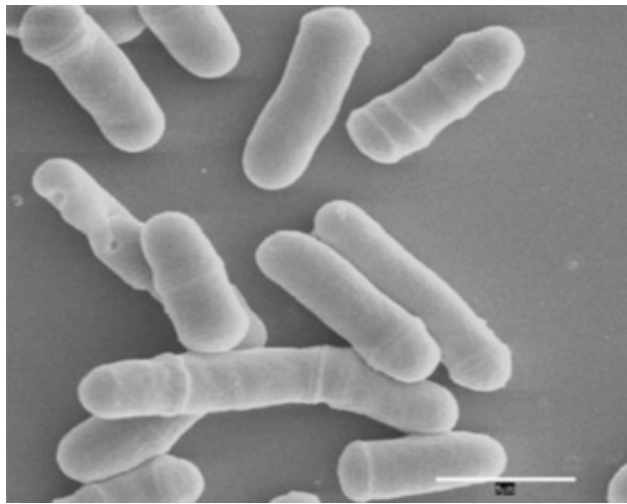
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S. pombe



A. thaliana



D. melanogaster



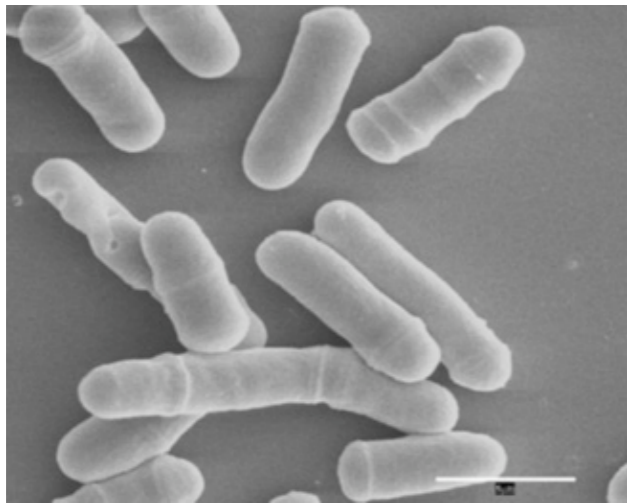
M. musculus



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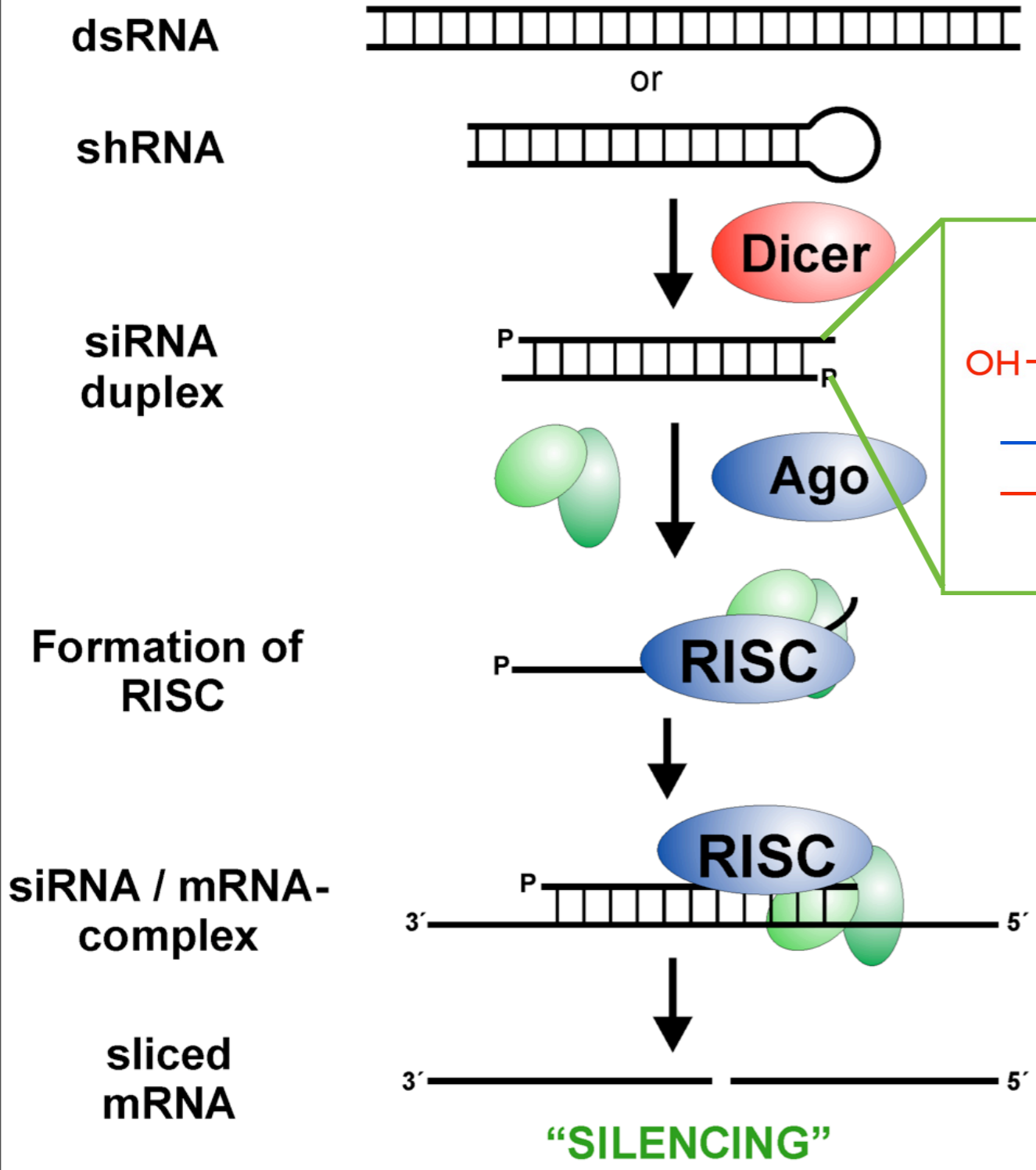
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siRNAs (or analogous small RNAs)
highly conserved

Biogenesis



OH

P

OH

P

— Guide

— Passenger

Schematic diagram of a duplex siRNA molecule with 2 nucleotide overhangs and a core 19 nucleotide base-paired region. Upon Dicer recruitment of Argonaute, this dsRNA will be unwound, yielding the guide strand, which will integrate with the RISC and the passenger strand, which will be subsequently degraded by exonucleases.

Diagram illustrating the major steps in siRNA biogenesis and subsequent siRNA-mediated gene silencing.

Cellular functions

- translational inhibition
- pathogen resistance
- chromatin remodeling
- genome stability
- DNA elimination

Partners in crime

- messenger RNA (mRNA)
- RNA dependent RNA polymerase (RdRP)
- Dicer
- Argonaute
- RNA-induced silencing complex (RISC)
- ADAR
- Armitage
- R2D2
- HEN1

Po'tential

- synthetic siRNAs, siRNA plasmids, siRNA viral vectors
- Transient or stable knockdown of target gene
- Exquisite specificity (disease relevant point mutations)
- Study of hypomorphic alleles
- Elucidation of roles of genes, causal pathways
- Genome-wide siRNA screens: novel gene discovery

Roles in disease

- Endogenous siRNAs in human disease?
- Induction of siRNA by *Pseudomonas syringae* in plants
- conserved role in immune response
- Synthetic siRNAs as novel therapeutics to treat asthma, diabetes, cancer and neurological disease
- siRNA therapy mediates improvement of ALS symptoms



The Revolution Starts Here

San Francisco, CA

Links

- <http://web.mit.edu/sirna/> - Database of tested siRNAs and shRNAs
- http://www.proteinlounge.com/sirna_database.asp - Comprehensive database of siRNA against all known mRNA sequences in a variety of organisms
- siRNA at Whitehead - A web-based siRNA Selection Program
- siSearch - a siRNA design tool using a number of popular design methods
- HuSiDa - Human siRNA Database