

SIROCCO

Silencing RNAs: organizers and coordinators of complexity in eukaryotic organisms

JUNE 2007 Newsletter 5

WMD 2—Web MicroRNA Designer

SIROCCO MONTH 6 of 48

WMD—a web tool for the automated design of artificial microRNAs

WMD version 2 has now been officially released by Partner 6 Detlef Weigel. More than 30 plants are available for amiRNA design using released transcripts or EST databases. Other new features include amiRNAs against non-annotated transcripts, "acceptable off-targets" and a blast against the transcripts in the plant databases to identify redundant entries and thus determine acceptable off-targets. AmiRNAs and WMD have been first described by Schwab et al., 2006. Please cite this paper if you are using WMD- designed amiRNAs in your own publication. [Link to PubMed](#)



Applications for new sequencing technologies

The latest sequencing technologies are proving to be useful in finding sites where a protein binds to the genome. The process of "tag sequencing" combines immunoprecipitation with sequencing in order to map protein-DNA interactions. Alternatively, DNase I hypersensitive sites where regulatory proteins dock onto DNA can be detected

<http://www.sciencemag.org/cgi/content/full/316/5828/1120>

Neurological Diseases Treated with siRNA

A report from the Harvard Medical School has shown that siRNA can reach the brain if delivered with a rabies virus glycoprotein. Treatment of brain diseases with siRNA has been difficult because the molecules were not able to cross the blood-brain barrier. In this study, the rabies virus glycoprotein (RVG) was used to pseudotype lentivirus in order to infect neuronal cells. The RVG-pseudotyped lentivirus encoding a short hairpin RNA targeting Japanese encephalitis virus was shown to protect against fatal viral encephalitis in mice. Intravenous administration would be the ideal means of delivery of siRNA because the brain is highly vascularised.

Kumar P, Wu H, McBride JL, Jung K-E, Kim MH, Davidson B, Lee SK, Shankar P and Manjunath N. Transvascular delivery of small interfering RNA to the central nervous system. *Nature* 2007 June 17. [PubMed](#)



RESEARCH

SPOTLIGHT

miRNAs in *Chlamydomonas*

Coordinator David Baulcombe and his lab have determined that miRNAs are found in the unicellular alga *Chlamydomonas reinhardtii*. miRNAs were thought to have been associated with multicellularity but it is now established that complex RNA-silencing systems evolved before this development. "*Chlamydomonas* can now be used to analyse complex systems involving positive and negative feedback mechanisms that are a frequent feature of regulation by siRNAs and miRNAs."

Molnar A, Schwach F, Studholme DJ, Thuene-mann EC, and Baulcombe DC. miRNAs control gene expression in the single-cell alga *Chlamydomonas reinhardtii*. *Nature* 2007 May 30.

Piwi proteins and piRNA in Zebrafish

Partner 5 René Ketting and his colleagues have shown that Zebrafish piRNAs are present in both ovary and testis, that many are derived from transposons, that they are Dicer-independent, and carry 2'O-methyl modifications. Piwi proteins, an animal-specific subclass of the Argonaute family, associate with piRNAs and are expressed in the germ cells.

Houwing S, Kamminga LM, Berezikov E, Cronembold D, Girard A, van den Elst H, Filipov DV, Blaser H, Raz E, Moens CB, Plasterk RHA, Hannon G, Draper BW, Ketting RF. A Role for Piwi and piRNAs in Germ Cell Maintenance and Transposon Silencing in Zebrafish. *Cell* 2007 Apr 6;129(1):69-82.

Argonaute Proteins

Partner 6 Gunter Meister, with co-author Lasse Peters, has published a comprehensive review which focuses on the cellular functions of mammalian Argonautes.

Peters L and Meister G. Argonaute Proteins: Mediators of RNA Silencing. *Molecular Cell* 2007 Jun 8;26(5):611-23.

Partner 4 Witold Filipowicz and co-author Suwendra Bhattacharyya, comment in a recent issue of *Cell* on a paper by Vasudevan and Steitz. Argonaute proteins are involved in repressing gene expression by mRNA degradation or translational arrest, but they also activate translation by binding to the 3'-UTR of TNF α mRNA. "... transcriptional factors frequently act as either activators or repressors depending on the promoter context. Clearly, RNA-binding proteins can serve as versatile regulators, too"

Bhattacharyya SN and Filipowicz W. Argonautes and Company: Sailing against the Wind. *Cell* 2007 Mar 23;128(6):1027-8.

Vasudevan S and Steitz JA. AU-rich-element-mediated upregulation of translation by FXR1 and Argonaute 2. *Cell* 2007 Mar 23;128(6):1105-18.

PARTNER MESSAGE BOARD



◆ SIROCCO 6-monthly reports are due by 30 June- only scientific reports required at this time www.sirocco-project.eu

◆ SIROCCO Annual Meeting at Harnack-Haus in Berlin 20-21 November 2007— rooms are booked for the nights of the 19th and 20th November

For visitor information: <http://www.berlin.de/>

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