

SIROCCO

Silencing RNAs: organizers and coordinators of complexity in eukaryotic organisms

JULY 2009 Newsletter 30

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MiR-96 implicated in progressive hearing loss

SIROCCO Partner Tamas Dalmay - in collaboration with researchers in Spain, Germany and the UK - has discovered that miR-96 is associated with progressive hearing loss. The new mouse line *diminuendo* was analysed because the mice show progressive hearing loss from an early age. The researchers demonstrated that if the mice carried one copy of a miR-96 mutation they suffered progressive hearing loss, but if they carried two copies they were profoundly deaf. This is the first demonstration of a disease-causing mutation in the mature sequence of a microRNA and the first microRNA associated with hearing impairment. The single base mutation from A to T in the seed region of the murine miR-96 gene disrupts development of intricate sensory hair cells in the mutant mice. Human subjects suffering progressive hearing loss were also shown to have mutations in the miR-96 gene. In the human studies, two families showed mutations in miR-96 but each carried the mutation at different locations in the miR-96 gene. Neither mutation in humans is the same base as in the mouse, but all three are close to one another in the seed region of the miR-96 sequence.

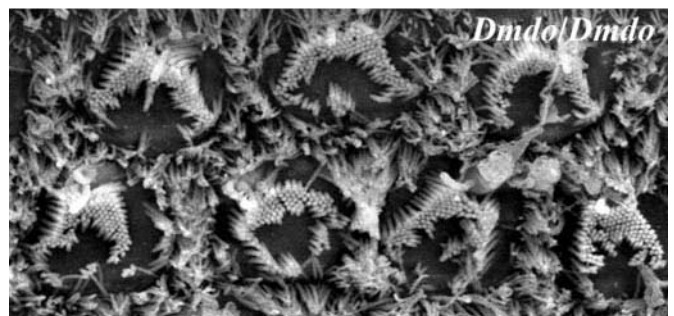
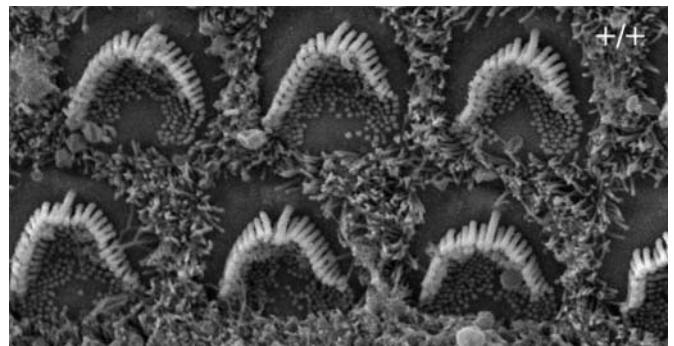
Hearing loss is a major problem in Europe with more than 70 million people affected - by the age of ten, one in 500 children has suffered significant hearing impairment and the majority of over-70s have some hearing loss.

This work was funded in part by SIROCCO and by the FP6 Integrated Project EuroHear.

Mutations in the seed region of human miR-96 are responsible for nonsyndromic progressive hearing loss. Mencía A, Modamio-Høybjør S, Redshaw N, Morín M, Mayo-Merino F, Olavarrieta L, Aguirre LA, del Castillo I, Steel KP, Dalmay T, Moreno F, Moreno-Pelayo MA. *Nature Genetics* 2009 May; 41(5):609-13.

An ENU-induced mutation of miR-96 associated with progressive hearing loss in mice.

Lewis MA, Quint E, Glazier AM, Fuchs H, De Angelis MH, Langford C, van Dongen S, Abreu-Goodger C, Piipari M, Redshaw N, Dalmay T, Moreno-Pelayo MA, Enright AJ, Steel KP. *Nature Genetics* 2009 May; 41(5):614-8.



Scanning electron micrographs of inner ear from five-day-old mice. Top: wild type mouse; bottom: mouse carrying two copies of the mutated miR-96 gene



RESEARCH SPOTLIGHT



[RNAi-mediated resistance to Potato spindle tuber viroid in transgenic tomato expressing a viroid hairpin RNA construct.](#)

Schwind N, Zwiebel M, Itaya A, Ding B, Wang MB, Krczal G, Wassenegger M.

Mol Plant Pathol. 2009 Jul; 10(4): 459-69.

[Recombinase-Mediated Cassette Exchange Provides a Versatile Platform for Gene Targeting: Knockout of miR-31b.](#)

Weng R, Chen YW, Bushati N, Cliffe A, Cohen SM. Genetics. 2009 Jun 29.

[Epub ahead of print]

[Structure of the HIV-1 Rev response element alone and in complex with regulator of virion \(Rev\) studied by atomic force microscopy.](#)

Pallesen J, Dong M, Besenbacher F, Kjems J.

FEBS J. 2009 Jul 3. [Epub ahead of print]

[A Brain-Derived Neurotrophic Factor Haplotype Is Associated with Therapeutic Response in Obsessive-Compulsive Disorder.](#)

Real E, Gratacòs M, Soria V, Escaramís G, Alonso P, Segalàs C, Bayés M, Cid RD, Menchón JM, Estivill X.

Biol Psychiatry. 2009 Jul 7.

[Epub ahead of print]

[Temporal resolution of two tracked NF-kappaB activation by Legionella pneumophila.](#)

Bartfeld S, Engels C, Bauer B, Aurass P, Flieger A, Brüggemann H, Meyer TF.

Cell Microbiol. 2009 Jul 2.

[Epub ahead of print]

Reporting Update

The evaluation of the updated Detailed Implementation Plan Month 25-42 has been received from external evaluator Aris Economides:

"this version is indeed much better organized than its predecessor. SIROCCO's partners have made a good effort to improve the structure of the report and to make sure that all of the deliverables are clearly listed and updated. They have also taken good care to clarify which aspects of the work have already been completed, which deliverables have been discontinued and the reasons for that, which deliverables have been extended and why, and which deliverables have been added as their new findings have opened up new avenues of investigation."

EC Project Officer Christina Kyriakopoulou adds: "Your updated plan is then accepted and will be included as an addendum to the SIROCCO contract by our administrative unit."

Many thanks to all the consortium for their efforts on the updated version of the DIP. The full contents of the evaluation letter from the external reviewer Aris Economides can be found on the project website www.sirocco-project.eu on the partner pages password: smallrna

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NEXT CONSORTIUM MEETING:
16-18 NOVEMBER 2009
HINXTON UK