

Molecular and biological functions of imprinted miR-379/miR-410 cluster

BIOLOGIE & SANTÉ 2011



Labialle Stéphane, Marty Virginie, Hoareau Magali and Jérôme Cavaille

Université de Toulouse; UPS; Laboratoire de Biologie Moléculaire Eucaryote; F-31000 Toulouse; France
 CNRS; LBME; F-31000 Toulouse; France

ABSTRACT

Our current research interests focus on hundreds of mammalian-specific small regulatory RNAs that belong to the C/D RNA and microRNA families and whose genes map to four distinct chromosomal loci: the DLK1-DIO3 domain at human 14q32 (mouse distal 12), the SNURF-SNRPN at human 15q11q13 (mouse Chr.7), the primate-specific C19MC at human 19q13 and the rodent specific Sfmt2 cluster (mouse Chr.2). These small RNA genes are expressed in a tissue-specific manner, with strongest expression in the placenta and in the adult brain. More importantly, they are regulated by **genomic imprinting**, a developmentally regulated **epigenetic mechanism** that leads to mono-allelic expression in a parent-of-origin-specific manner, e.g. for a given gene, the paternal allele is turned on while the maternal allele is turned off (the converse can also be true for another gene locus).

Our current research is designed to explore the physiological roles of the **maternally-expressed miR-379/410 cluster** at the *Dlk1-Dio3* locus through the use a **KO mouse model** harboring an ~ 60 kb long, Cre-Lox mediated deletion encompassing the entire cluster.

The miR-379/miR-410 cluster

...~38 pre-miRNAs = 54 microRNAs; ~ 8% of mouse microRNAs
 ... Expressed from the maternally-inherited allele
 ... Biology of ES/iPS cells ? Neuronal plasticity? RNA target(s) ?

Genetic ablation of miR-379/miR-410 cluster

Genetically ablated miR-379/miR-410 cluster

Genetic ablation of miR-379/miR-410 alters Mendelian ratios upon maternal inheritance

(mixed BL/6 x 129 background)
 - 50% of (*ΔmiR*/+) genotypes are missing

Genetic ablation of miR-379/miR-410 leads to perinatal lethality upon maternal inheritance

- 50% of (*ΔmiR*/+) newborn mice die several hours after birth
 Physiological cause(s) ???

Genetic ablation of miR-379/miR-410 causes abnormal post-weaning growth upon maternal inheritance

(*ΔmiR*/+) are growth-retarded after weaning (recovery at >2-3 months)

Ongoing work...Ongoing work...

I_Behavior analysis

(-/*Δpat*) (Δ*miR*/+)

II_Transcriptome analysis

III_Histological analysis

(-/*Δpat*) (Δ*miR*/+)

CONTACT :

cavaille@ibcg.biotoul.fr



ICS

