MicroRNAs in normal mammary gland development

Fabienne Le Provost

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MicroRNAs in Normal Mammary Gland Development

Fabienne LE PROVOST
Institut National de la Recherche Agronomique, Jouy-en-Josas, France

microRNA

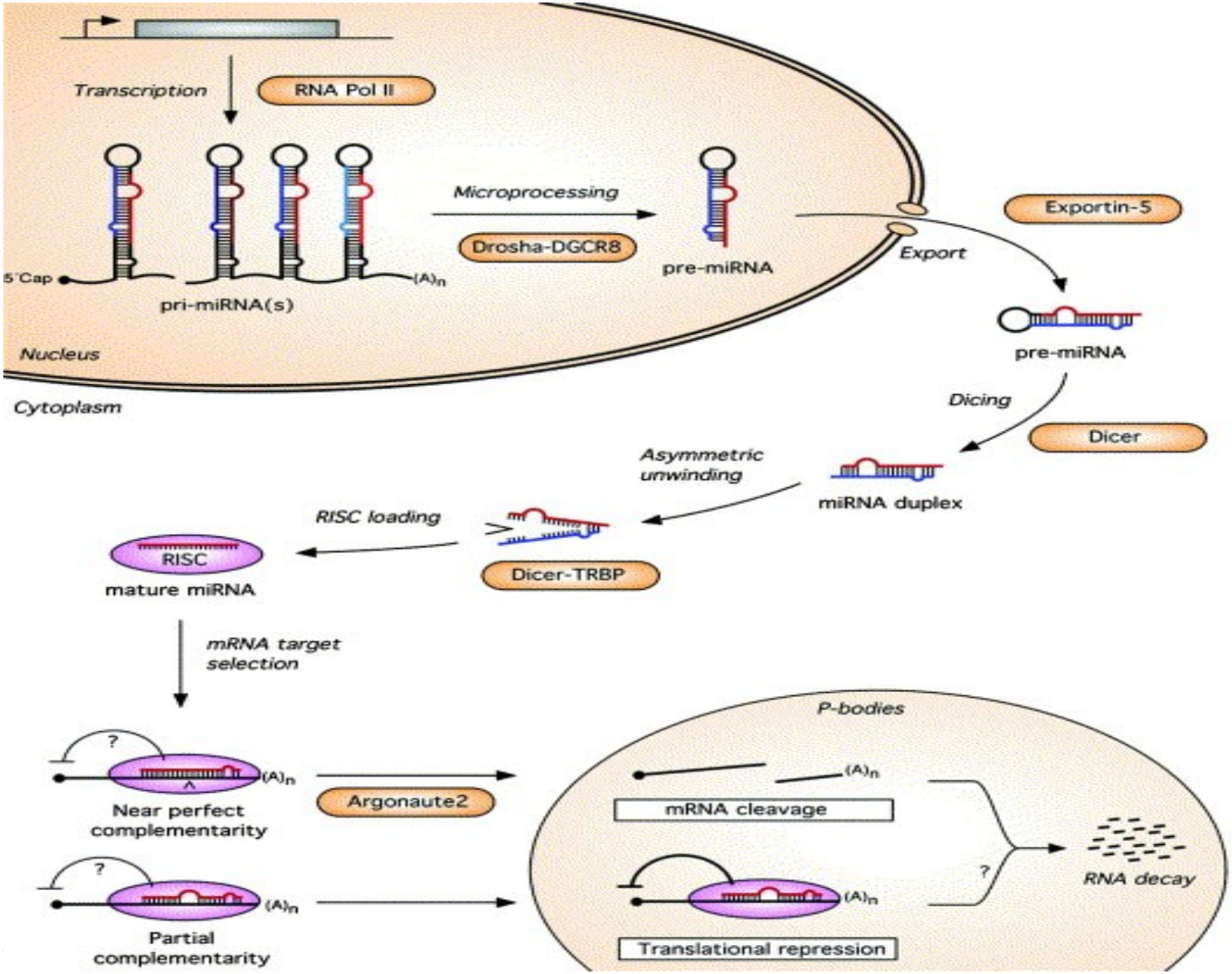
- Small non-coding RNA, 18-22 nt
- Endogenous
- Conserved during evolution
- Expression : ubiquist, tissue-specifics
- Fonctions : post-transcriptionnally regulate gene expression

  potentially regulate 30% of protein-encoding genes
- Biological processes : developmental changes, tissue morphogenesis, cell growth, differentiation, apoptosis,

  metabolism,

  also in diseases as diabetes, cancer, viral infection

microRNA biosynthesis



Wienholds and Plasterk, FEBS Letters, 2005

Cloning of new miRNA from normal mouse mammary gland

BMC Genomics

BioMed Central

Research article

Open Access

From 455 sequences obtained from mammary gland (V8w, Gd2, Gd6, Gd18, Ld4, ld1),
24 new miRNAs have been identified.

Tissue expression profiles :
No miRNA mammary gland specific.

This article is available from: http://www.biomedcentral.com/1471-2164/10/149

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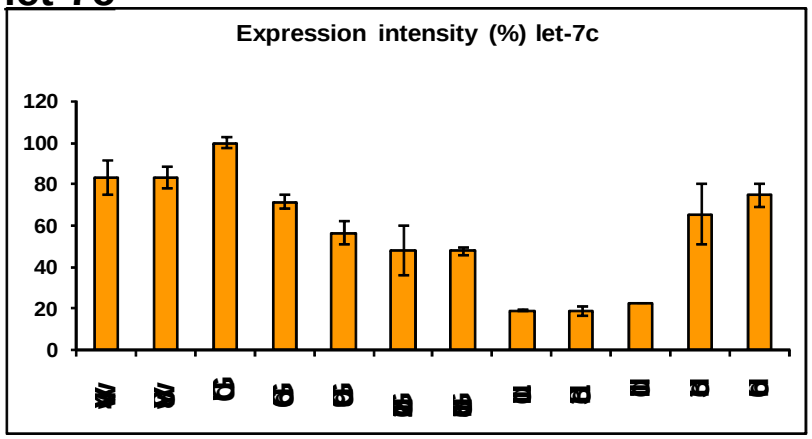
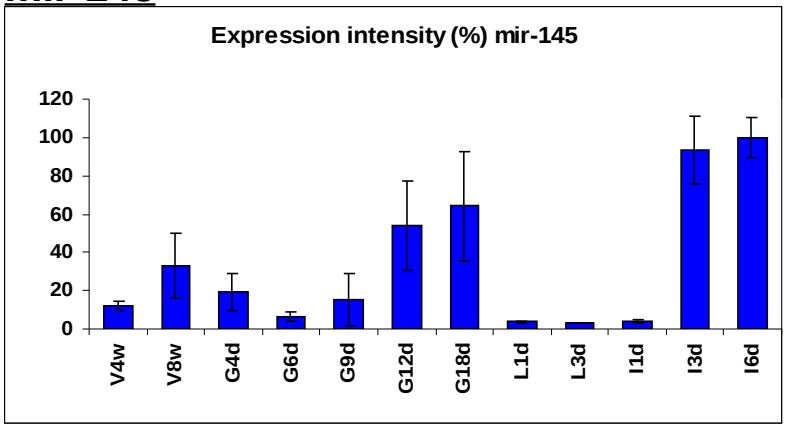
miR expression profils in mammary gland

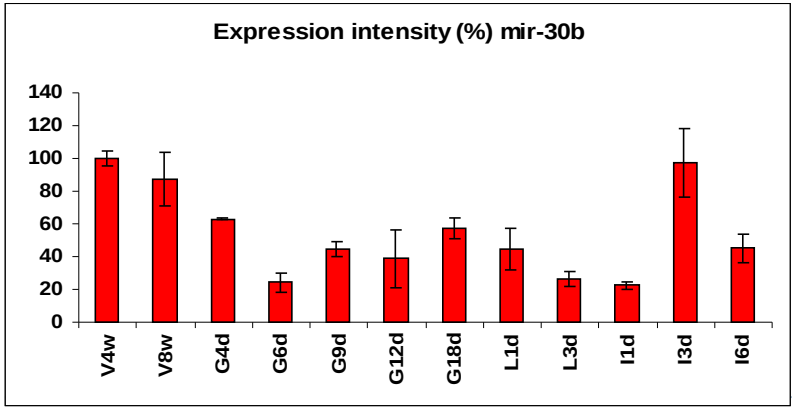
let-7c



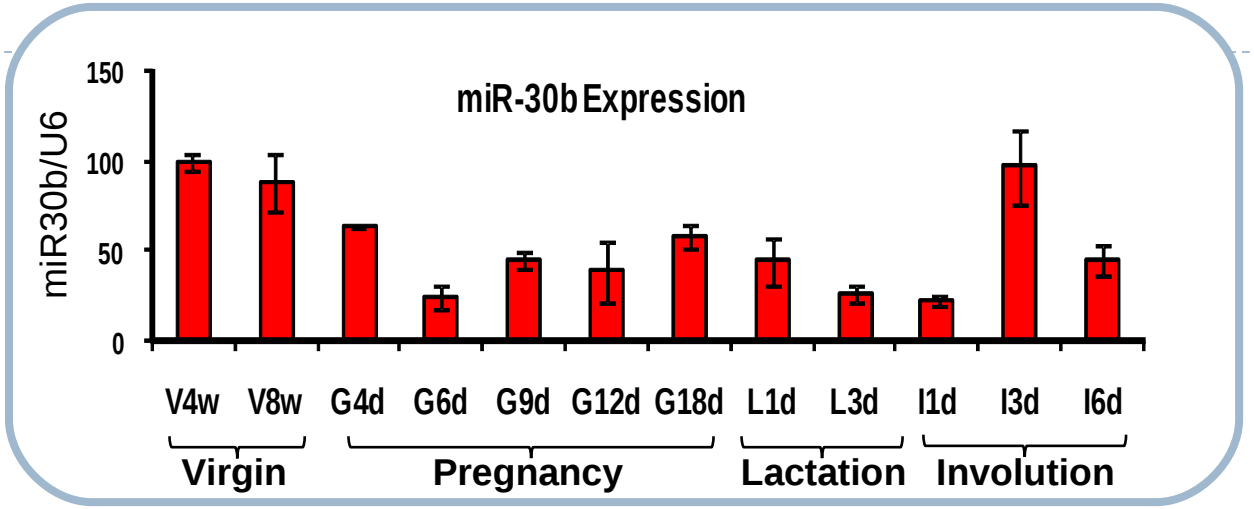
mir-145



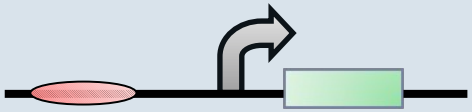
mir-30b



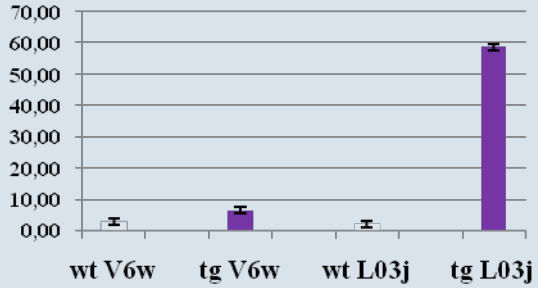
Role of miR-30b : over-expression



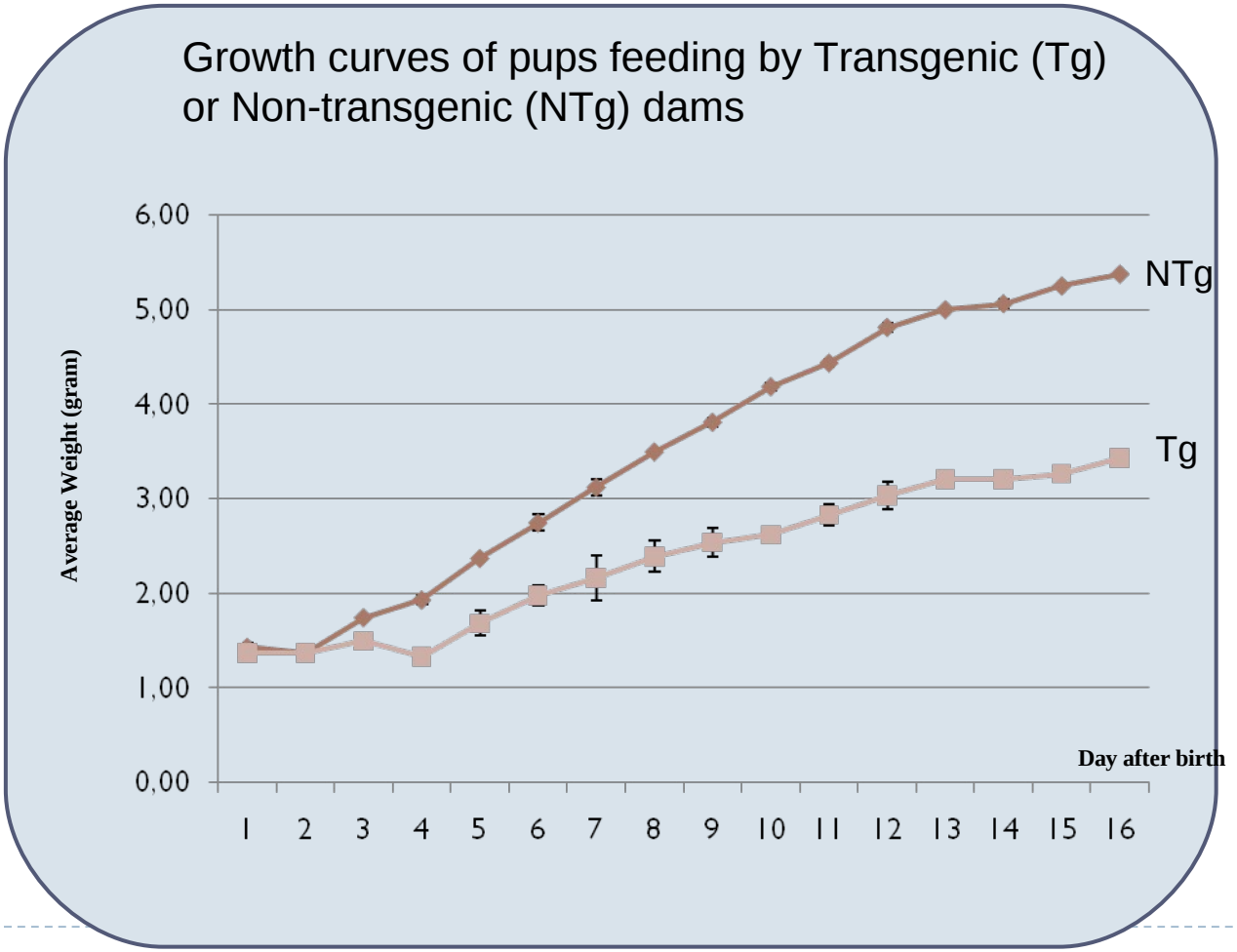
Mice over-expressing miR-30b precursor



miR-30b expression in Tg mice



Role of miR-30b : over-expression



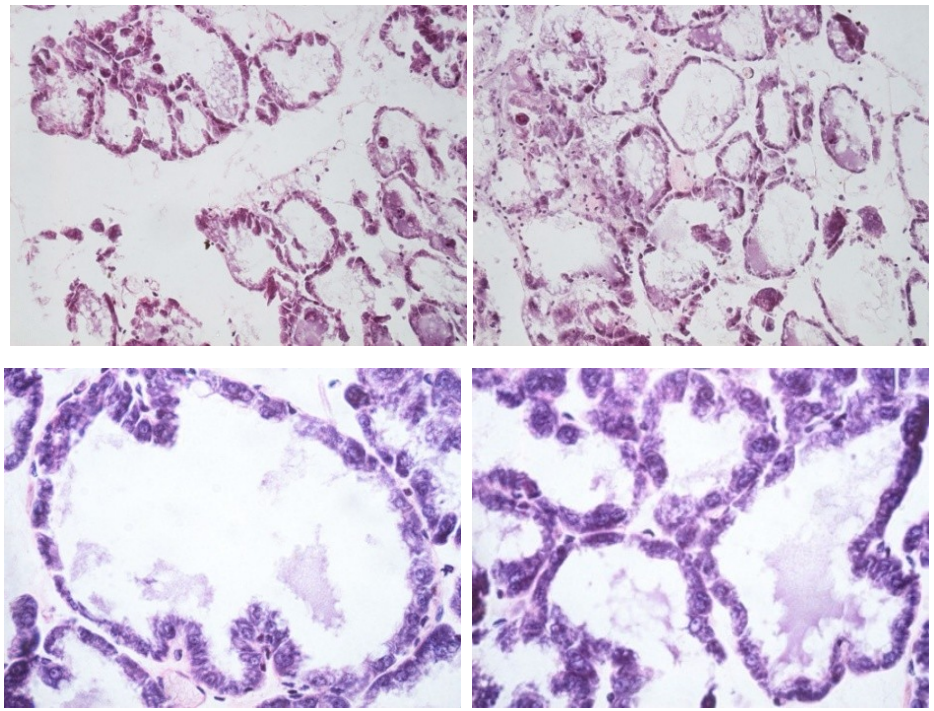
Role of miR-30b : over-expression

- Stages collected:
  - Virgin 6w, 13w
  - Pregnancy 6d, 14d, 18d
  - Lactation 3d, 12d
  - Involution 1d, 3d, 6d, 11d

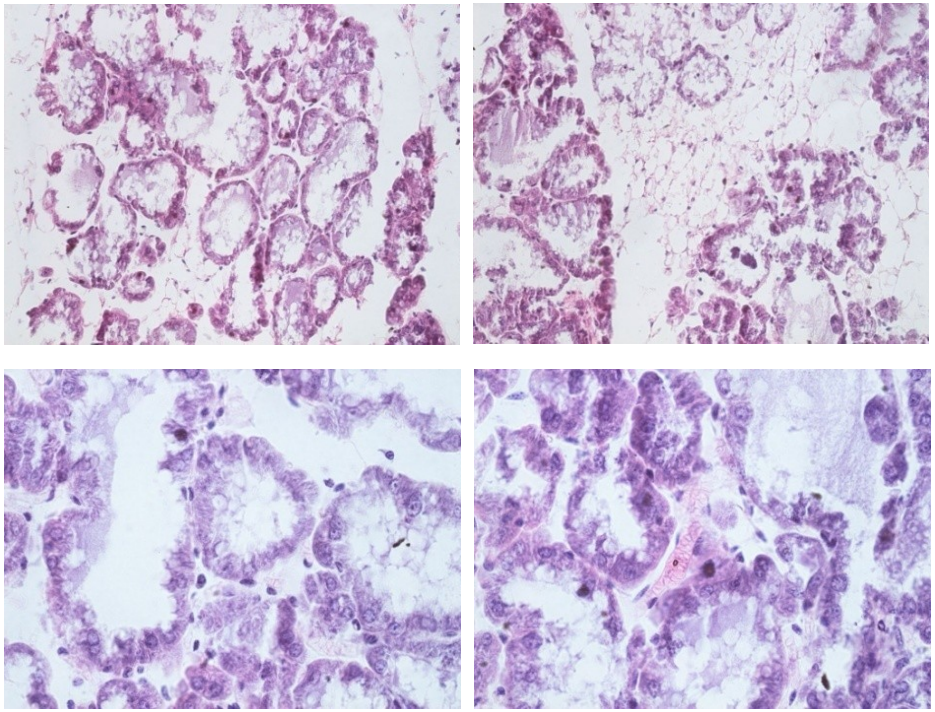
Role of miR-30b : over-expression

Lactation day-12

Non Tg



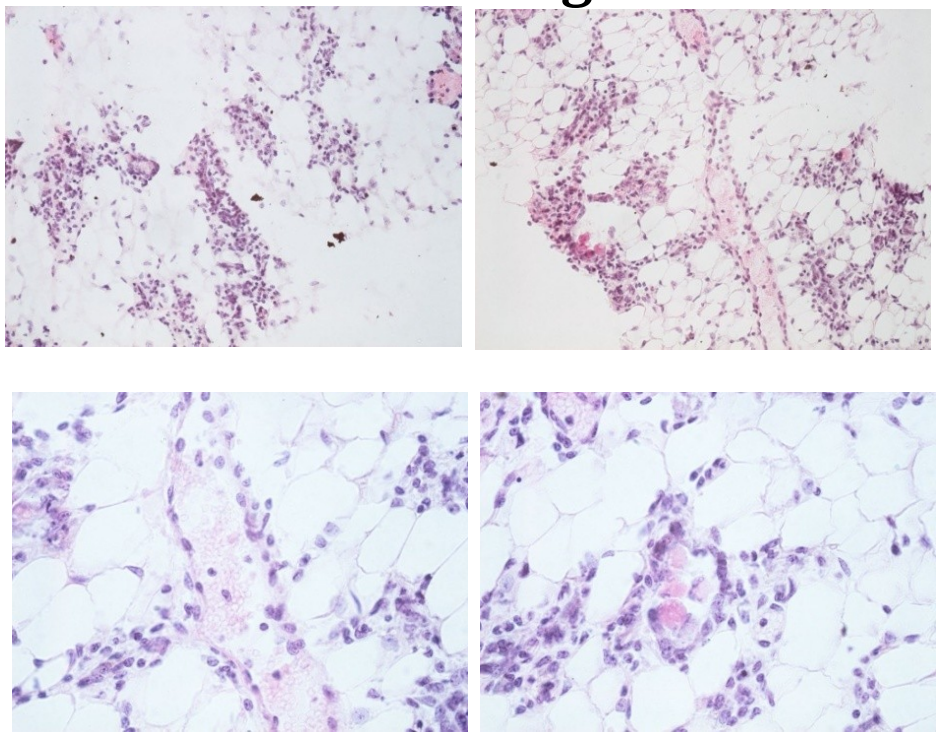
Tg



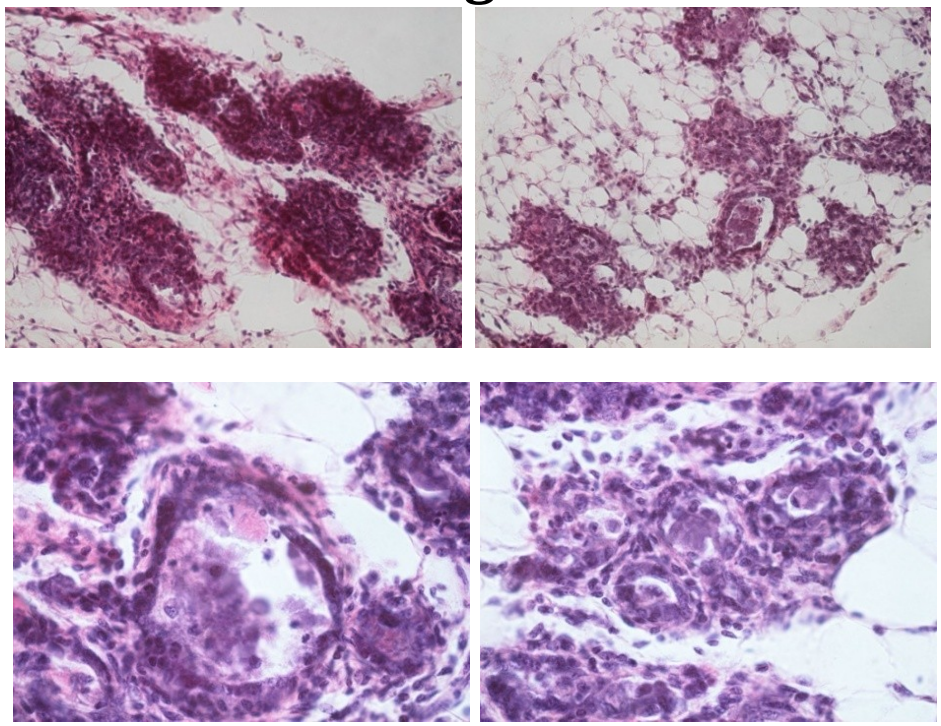
Role of miR-30b : over-expression

Involution day-6

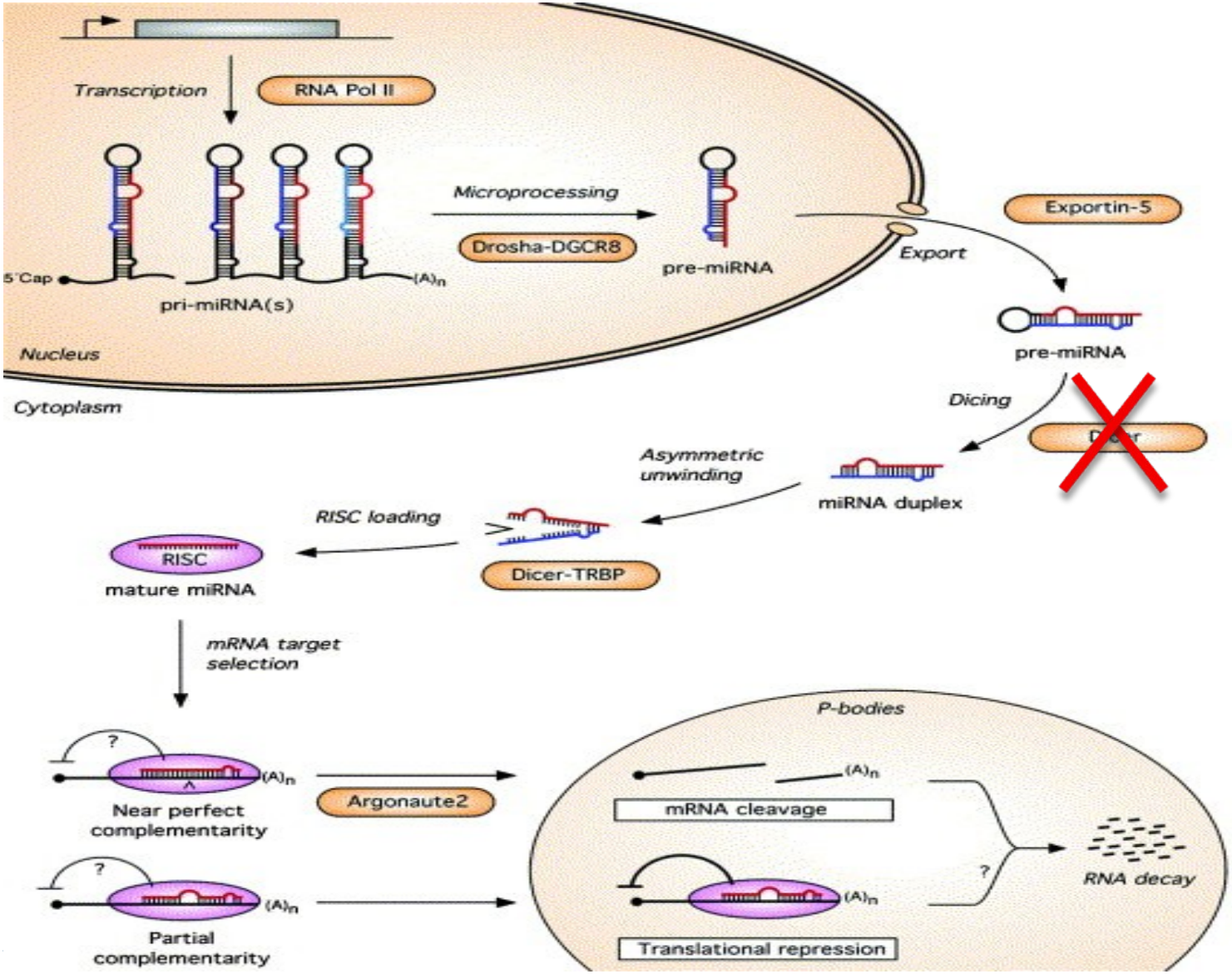
Non Tg



Tg



Down regulation of miRNAs biosynthesis



Wienholds and Plasterk, FEBS Letters, 2005

Down regulation of miRNAs biosynthesis

MMTV-cre

Lothar Hennighausen , LGP, NIH, Bethesda, USA

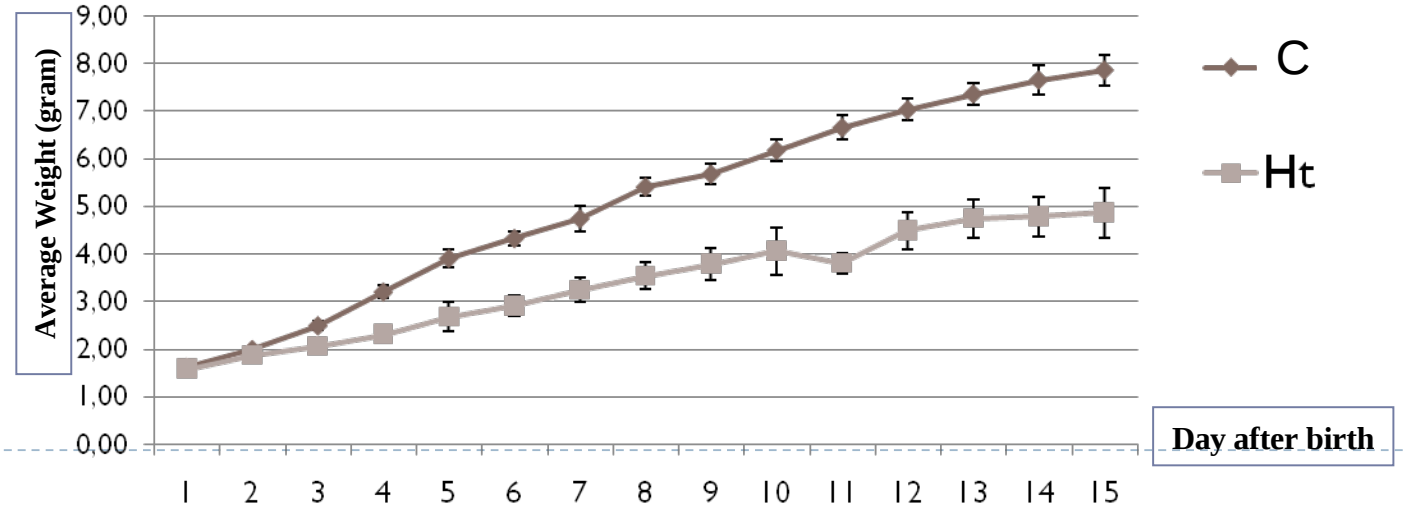
Dicer fl/fl

Brian D. Harfe et al., PNAS, 2005

Control (C) : Dicer fl/fl

Heterozygote (Ht) : MMTV-cre ; Dicer fl/+

Growth curves of pups feeding by Heterozygote (Ht) or Control (C) dams.



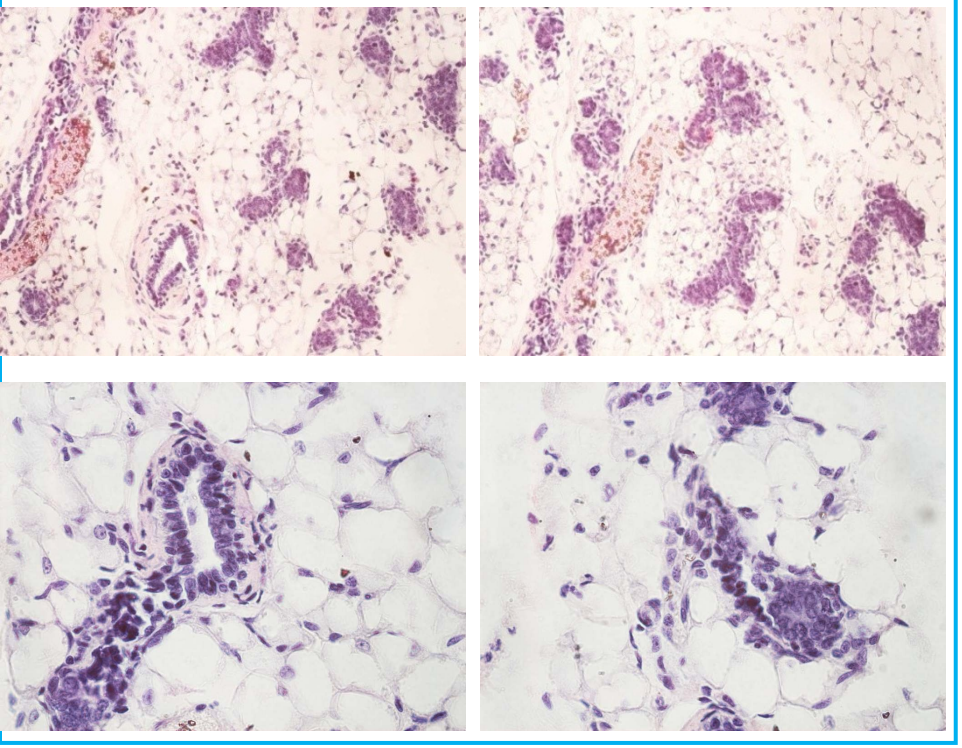
Down regulation of miRNAs biosynthesis

- Stages collected:
  - Virgin 6w
  - Pregnancy 6d, 12d, 16d
  - Lactation 3d, 7d
  - Involution 3d, 6d

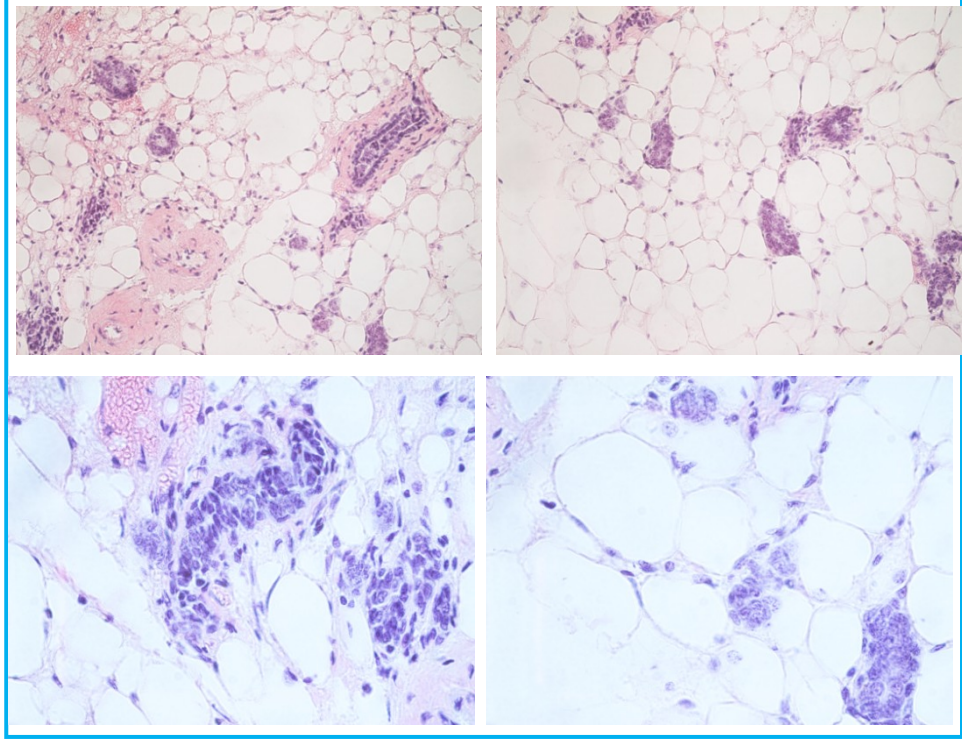
Down regulation of miRNAs biosynthesis

Gestation day-6

Control



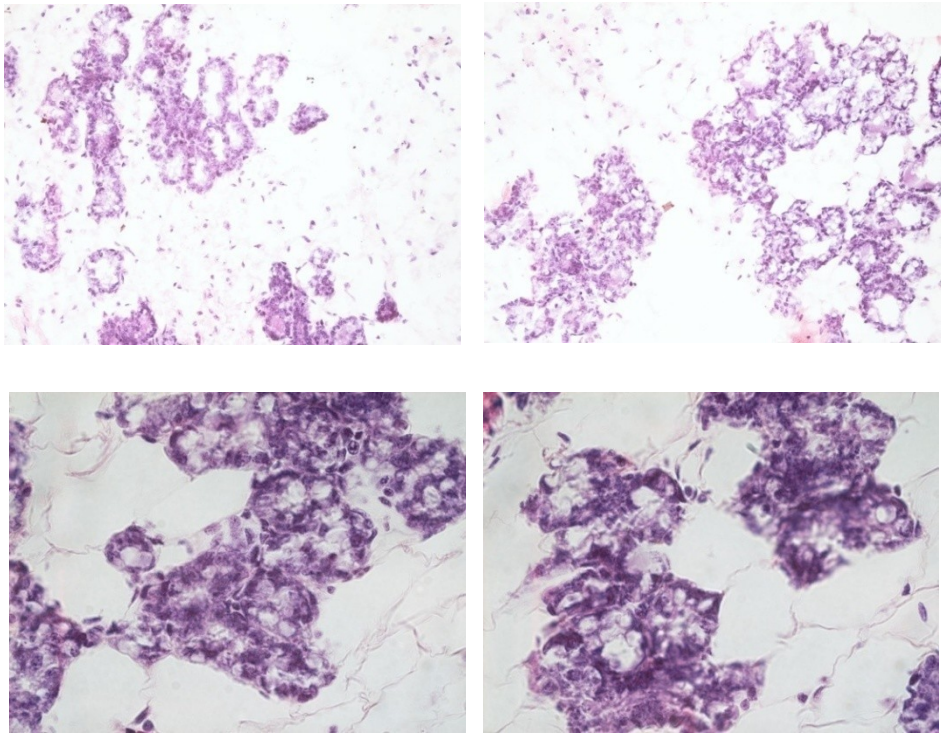
MD Heterozygote



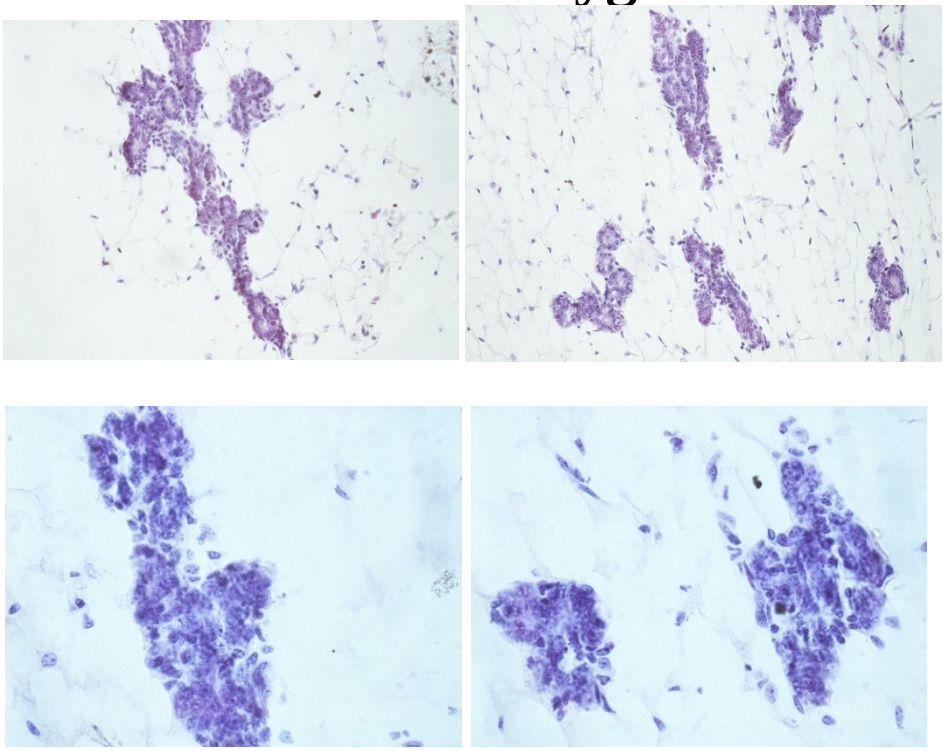
Down regulation of miRNAs biosynthesis

Gestation day-16

Control



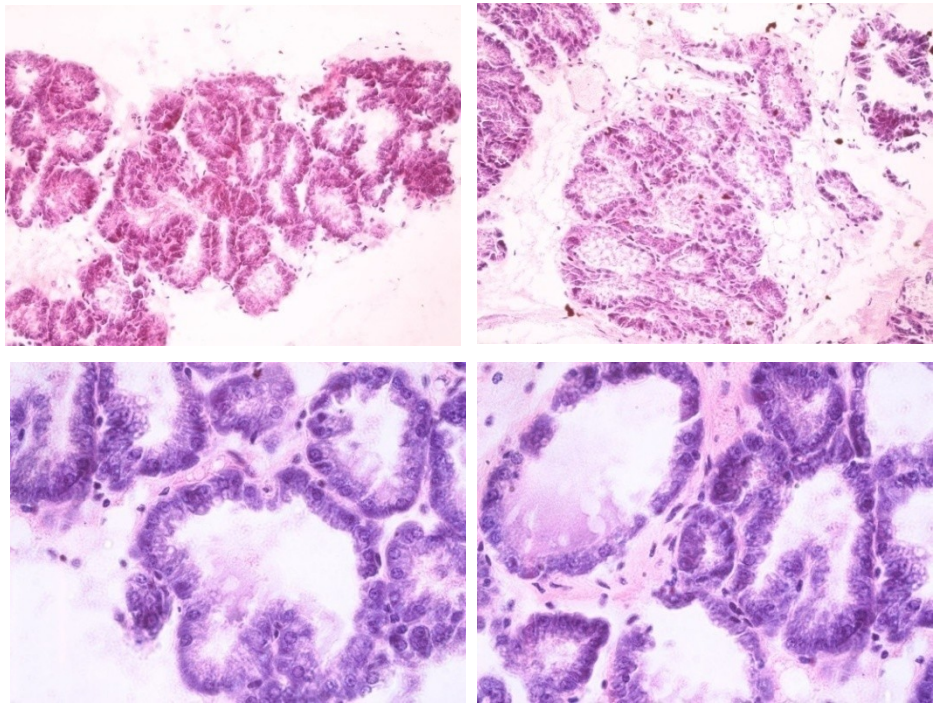
MD Heterozygote



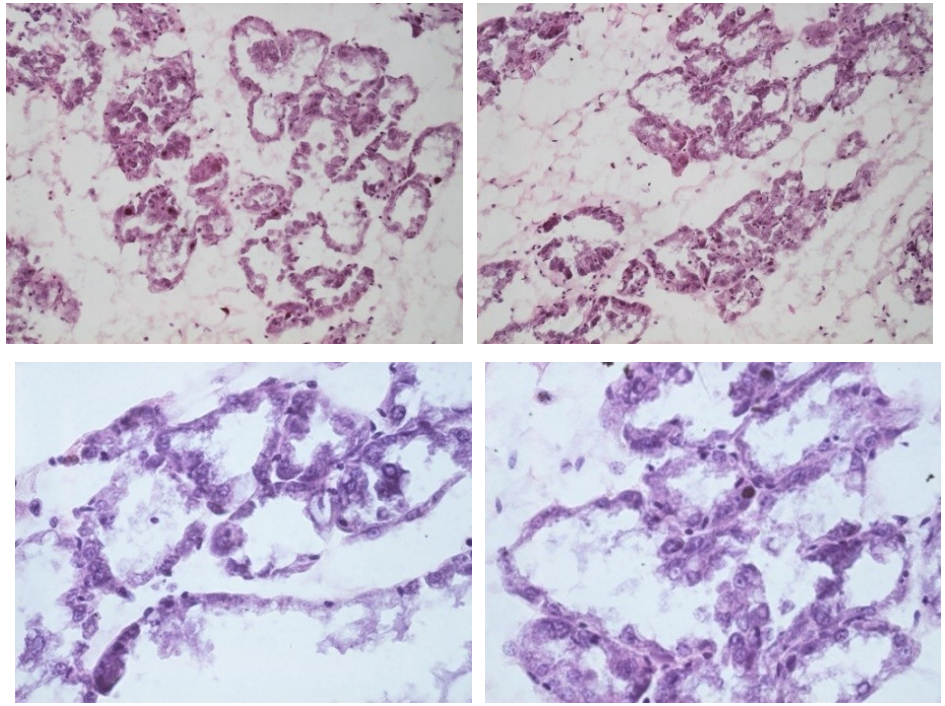
Down regulation of miRNAs biosynthesis

Lactation day-7

Control



MD Heterozygote

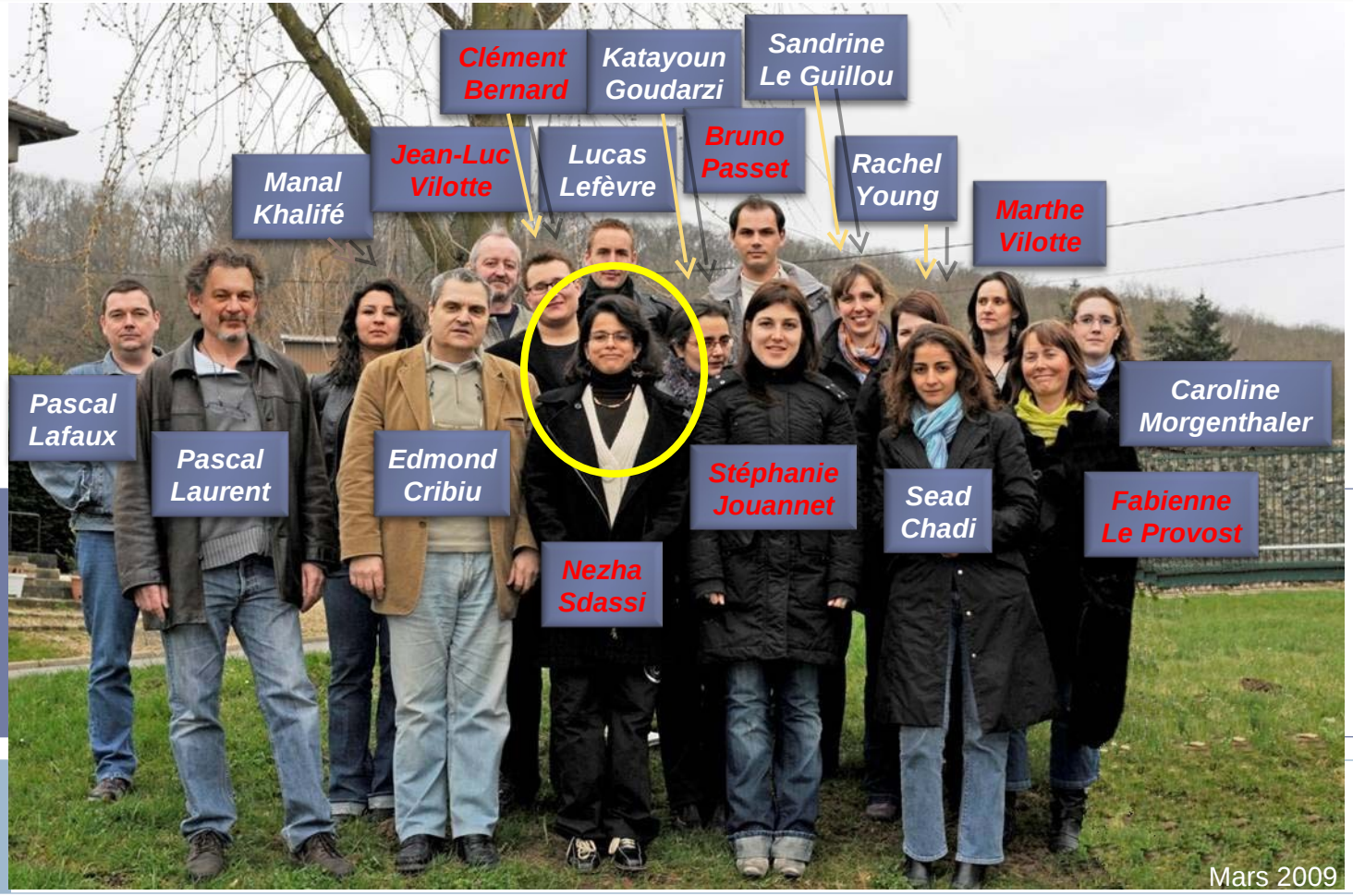


Conclusions

miRNAS are important to normal mammary gland development and differentiation

- Currently
  - Phenotype characterization :
    - Tissue structure by electronic microscopy
    - Specific cell markers by immunostaining
    - Epithelial cell populations analyses by FACS
  - Transcriptomic studies to characterize the signaling pathways involved
  - miR-30b targets

Team : DIfferentiation and Specialisation of Cells (DISC)
Lab : Génétique Animale et Biologie Intégrative (GABI), INRA, Jouy-en-Josas, France



Licia Silveri, Johann Laubier, Gaëlle Tilly, José Costa

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Poster # 81

MicroRNAs involvement in the development of the mouse mammary gland

Nezha SDASSI, Licia SILVERI, Johann LAUBIER, Bruno PASSET, Stéphanie JOUANNET, Clément BERNARD, José COSTA, Marthe VILOTTE, Jean-Luc VILOTTE, Fabienne LE PROVOST.

UMR 1313, Génétique Animale et Biologie Intégrative, Institut National de la Recherche Agronomique, 78 350 Jouy-en-Josas, France

miR librairy