MicroRNA metabolism in tumors

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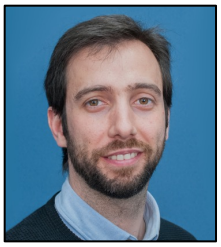


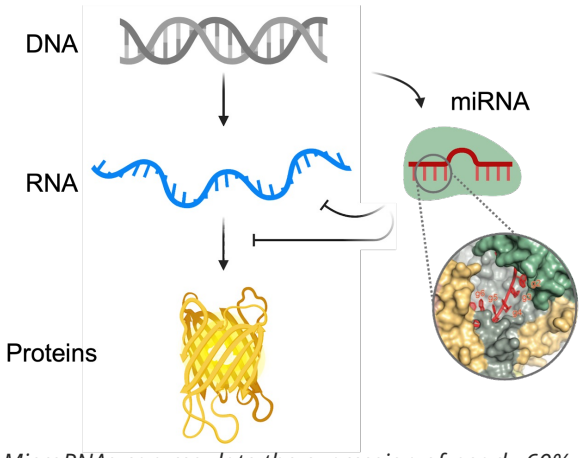
MicroRNAs (miRNAs) are a class of small non-coding RNAs with essential roles in gene expression. Their maturation requires the adequate RNA folding and the precise endonucleolytic cleavage of DROSHA and DICER1. The resulting products are mature miRNAs that provide specificity to Argonautes, a key component in RNA silencing. Thus, the malfunction of components of the biogenesis pathway can result in various molecular phenotypes such as aberrant products, localization, or stability.

Project 1. Defects during miRNA biogenesis

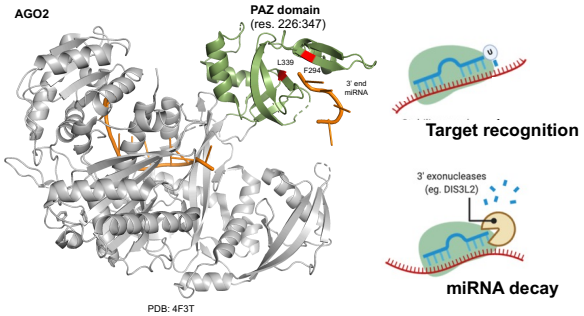
Mutations on key amino acid residues in DROSHA or DICER1 can promote misprocessing of miRNAs. These biogenesis defects lead to the production of aberrant miRNAs with altered target specificity. Comparison of miRNA processing between normal and tumoral samples shows increased levels of aberrant miRNAs. ***Here we will study the underlying mechanisms and downstream effects.***

Project 2: Regulators of miRNA decay

Half-lives of miRNAs range between hours and days. For example, miR-208 has a half-life of 2 weeks, while miR-16 can decay within minutes in response to cell cycle phases. Despite these disparities in their stability, little is known about the mechanisms that regulate miRNA decay and how they impact on miRNA levels and therefore activity in cancer cells. ***Here we will study the interplay between the PAZ domain and cellular factors.***



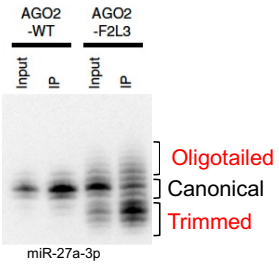
MicroRNAs can regulate the expression of nearly 60% of cellular transcripts through partial base-pair complementarity. Defects on their processing can have a profound impact on their target specificity.

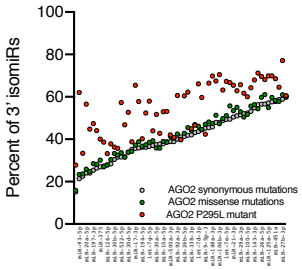


Argonaute PAZ domain protects the 3' end of miRNAs. Regulation of the 3' accessibility have important functions in miRNA target recognition and miRNA stability

Techniques

- Molecular cloning (Gibson cloning and mutagenesis)
- Western blot // Northern blot
- *In vitro* and *In cell* assays
- Next Generation Sequencing
- Bioinformatics and data analysis (R programming)
- Reporter assays (luciferase and fluorescent)





(Left) Northern blot illustrating the effects in miRNA trimming and tailing triggered by mutations on the PAZ domain. (Right) Bioinformatic analysis of a tumour biopsy with enhanced miRNA decay due to P295L mutation on AGO2.

Lab site and publications list:
https://sites.google.com/view/bofill-de-ros-lab/publications

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