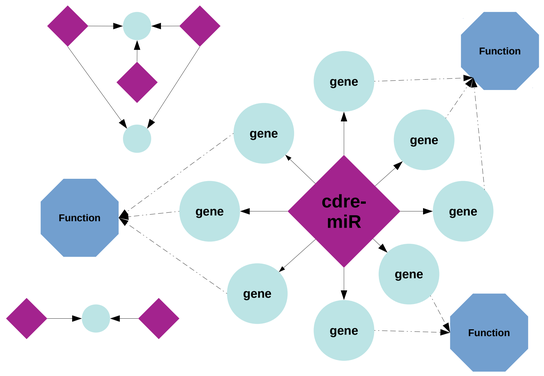
Commodore micro-RNAs in breast cancer molecular subtypes: functional regulation by highly connected, non-redundant micro-RNAs.

Guillermo de Anda-Jáuregui[1,2], Jesus Espinal-Enriquez[1,3] and Enrique Hernandez-Lemus[1,3]

1 Instituto Nacional de Medicina Genómica, México 2 Cátedras CONACYT, México 3 Centro de Ciencias de la Complejidad, UNAM, México

What is a commodore miR?



A commodore micro-RNA **(cdre-miR)** is a miR that can regulate the expression of a large gene set by itself, and through this regulation, control biological functions. In a miR-gene co-expression network, these nodes have **high degree and low redundancy coefficient [1]**.

What are breast cancer molecular subtypes?

Breast cancer is a heterogeneous disease. Based on gene expression patterns, there are four ***molecular subtypes*** with different clinical behaviors: **luminal A and B, Basal, and HER2-enriched**. Their co-expression networks have different structures [2].

References:
1 https://doi.org/10.1155/2018/9585383
2 https://doi.org/10.3389/fphys.2016.00568
3 https://doi.org/10.1016/j.cell.2011.02.013.

Contact me:
gdeanda@inmegen.edu.mx
Twitter: @gdeandajauregui

Questions:
•Are there cdre-miRs for each breast cancer molecular subtype?
•Are they the same?
•Do they control the same functions?

How to find them?

Get expression data from the Cancer Genome Atlas

Network: Calculate MI for all miR – gene pairs

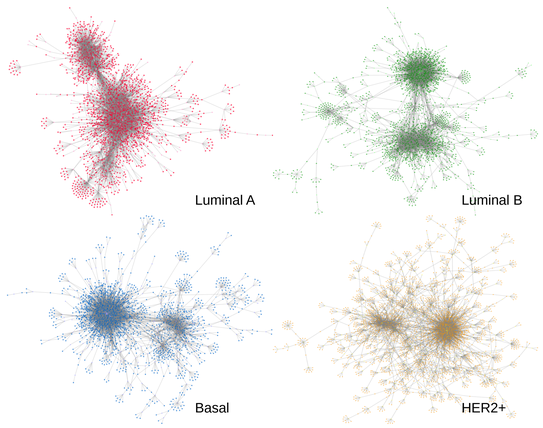
Filter links, keep those with highest MI (0.9999 quantile)

Select miRs with degree >= 100 & Redundancy =< 0.5

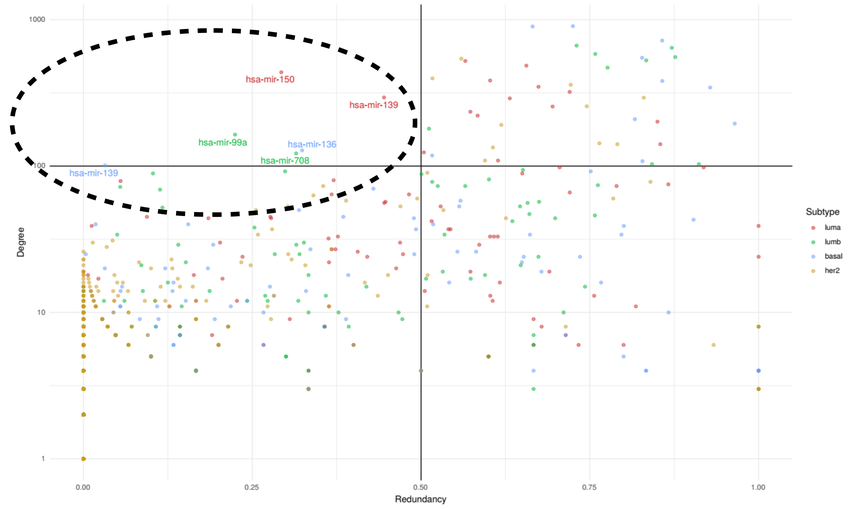
Enrichment analysis of cdre-miR neighborhoods

Validate miR – function association with literature

miR – gene coexpression networks



Do we have cdre-miRs?



We found 5 miRs that act like commodores in at the four subtypes:

mir-150 & mir-139 in LumA
mir-99a & mir-708 in LumB
Mir-136 & mir-139 in Basal

We found no cdre-miR in the **HER2+ subtype**

Only mir-139 acted as a cdre-miR in two subtypes: **LumA** and **Basal**

What functions do they control?

subtype	miR	GO representative term	Pubmed mentions	miR mentions
luma	hsa-mir-139	angiogenesis	3	112
basal	hsa-mir-139	angiogenesis	3	112
lumb	hsa-mir-708	cell adhesion	1	37
basal	hsa-mir-136	cell adhesion	5	39
basal	hsa-mir-139	cell adhesion	2	112
luma	hsa-mir-139	negative regulation of apoptotic process	2	112
luma	hsa-mir-139	positive regulation of gene expression	7	112
basal	hsa-mir-136	regulation of signaling receptor activity	1	39
luma	hsa-mir-150	signal transduction	30	240

We found several biological functions annotated in the Gene Ontology database associated to these cdre-miRs.

All of the functions that we were able to validate using an automatic analysis of Pubmed are well-known **hallmarks of cancer [3].**

What comes next?

The next step for this research is to **experimentally evaluate** the effect of the **perturbation of cdre-miRs** in the **activity of the identified functions,** using an *in vitro model.*

Want to know more?

Check our preprint

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