miR-200 Family Regulation and its Role in Epithelial-Mesenchymal Transition

MicroRNAs (miRNAs) are non-coding RNAs, 18-25 nucleotides in length that regulate gene expression post-transcriptionally. miRNA action is performed through the inhibition in mRNA transcription into proteins. The participation of miRNA in cancer development has been discovered recently. It has been seen that miRNAs can prevent or enhance cancer depending on which genes are repressing.

miR-200 family is a group of microRNAs organized in two clusters involved in the maintenance of epithelial characteristics and in the inhibition of epithelial-mesenchymal transition (EMT). During EMT cells change their characteristics from epithelial to mesenchymal and this enables them to detach from the primary tumor and produce metastasis.

Hypothesis
Are microRNAs truly regulated as normal genes? Find cis-regulatory elements (promoter, transcription factor binding sites) and large regulatory elements (enhancers, repressors, insulators) for the two different clusters of miR-200 family, and compare them.

Materials & Methods

1. Luciferase reporter assay

2. Bioinformatics

Hypothetical chromatin marks used to identify active and repressed genomic regions.

3. ChIA-PET

Conclusions
I expect to identify different regulatory elements in the promoter regions of the two miR-200 clusters. Among the different transcription factors binding miR-200, I expect to find the ones already known (verifying results) and new ones (discoveries). Both clusters should be similarly regulated and any difference on them could mean that they have different functions, different targets and/or different signaling pathways involucrate.

Future approaches could be to identify and characterize every molecule involved in the regulation of miR-200. Once knowing its regulation, it could be possible to design drugs or techniques to enhance its expression and inhibit EMT in cancer. Repressing metastasis in cancer patients will highly decrease mortality rate.

References

Only relevant references are cited below:

- Antonio Díaz-López et al. (2014) Zeb1 and Snail engage miR-200 transcriptional and epigenetic regulation during EMT. Int. J. Cancer 135: 2582-2593
- ENTER Sanchez-Fueyo, Ningning Liu, Oriol de Barrio, et al. (2012) EMT-enabling transcription factors in cancer beyond EMT and tumor invasiveness. Springer