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Argonaute 2 as novel molecular determinant for myeloid differentiation

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microRNAs (miRNAs) are emerging as crucial factors for the establishment of complex regulatory circuitries involved in the regulation of hematopoietic cell fate determination. These small non-coding RNAs to exert their functional activity are assembled in RNA-induced silencing complexes (RISCs), where a member of Argonaute (Ago) family of proteins plays a central role in miRNA-mRNA target interaction and gene silencing. In human cells the miRNAs-Ago complex can also localize in the nucleus where Ago proteins can associate with promoter gene sequences to impact heterochromatin genomic structure and transcriptional silencing (Janowski BA et al., 2006; Meister G., 2013).

By using human myeloid cell lines and acute myeloid leukemia (AML) primary blasts we highlight Ago2 as a new player in myeloid cell fate determination. We observed that: *i)* Ago2 protein levels are strongly increased during 1,25-dihydroxyvitamin D3 (D3)-induced monocyte differentiation, whereas are down-regulated during Retinoic Acid (RA)-induced granulocyte differentiation; *ii)* Ago2 depletion by shRNA or small chemical compounds disrupting both miRNA-Ago2 complex interaction and Ago2 chromatin localization, results in a strong improvement of the RA-dependent myeloid differentiation.

These results are bringing out that the down-regulation of Ago2 expression/functional activity is required during RA-dependent myeloid differentiation and may represent a molecular determinant for the improvement of RA-treatment response in leukemic myeloid progenitors cells.

References

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Keywords

Argonaute 2, microRNA, myeloid differentiation.