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Epigenetic Regulation of Nuclear PI-PLCbeta1 Signalling Pathway in Low-Risk MDS Patients During Azacitidine Treatment

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Myelodysplastic syndromes (MDS) are a heterogeneous group of hematological malignancies characterized by epigenetic abnormalities and therefore treated with demethylating agents [1]. PI-PLCbeta1 has been reported to be a specific target for demethylating therapy in high-risk MDS patients, since azacitidine treatment can be associated with a PI-PLCbeta1 specific promoter demethylation and induction of both PI-PLCbeta1 gene and protein expression [1]. In the present study we investigated the role of epigenetic regulation of PI-PLCbeta1, mainly focusing on the functional role of azacitidine on the structure of the PI-PLCbeta1 promoter. We firstly examined the effect of azacitidine on PI-PLCbeta1 promoter methylation and gene expression in low-risk MDS. Moreover, we studied the expression of key molecules involved in the nuclear inositide signalling pathway, such as Cyclin D3. We also studied the correlation between the demethylating effect of azacitidine and the degree of recruitment to PI-PLCbeta1 promoter of some transcription factors implicated in hematopoietic stem cell proliferation and differentiation, as well as of the Methyl-CpG binding domain proteins (MBDs), which specifically interact with methylated DNA. Taken together, our results hint at a specific involvement of PI-PLCbeta1 in epigenetic mechanisms, and are particularly consistent with the hypothesis of a role for PI-PLCbeta1 in azacitidine-induced myeloid differentiation.

References

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