BCL7A in Acute Promyelocytic Leukemia

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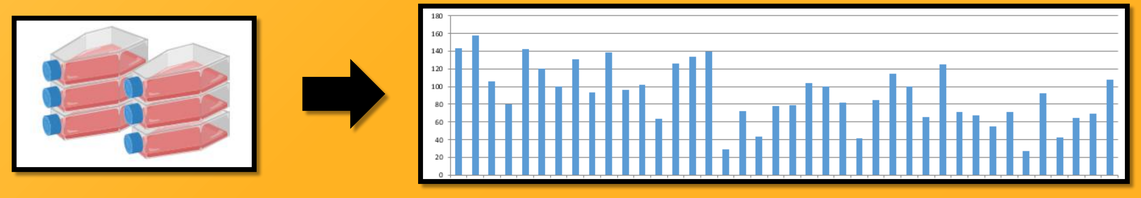
Introduction

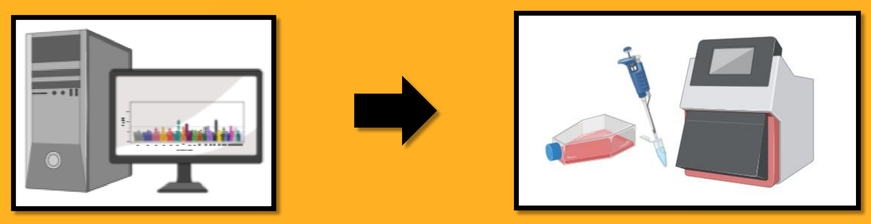
Modification of the gene expression profiles of the genome due to alterations in epigenetic mechanisms has been related to the development of several diseases including cancer[1,2]. One of the epigenetic factors are the chromatin remodeling complexes, among which is SWI/SNF, and mutations in several of its subunits have been found to be clearly related to tumor development[3–5]. The *BCL7A* subunit has been less studied than other subunits of the complex, but recently our research group has described a tumor suppressor role of *BCL7A* in diffuse large B-cell lymphoma (DLBCL)[6]. Furthermore, we have preliminary results obtained with an acute promyelocytic leukemia (APL) cell line (NB4) that show that perhaps *BCL7A* also has an important role in tumoral development in this type of leukemia. This cell line has silenced the expression of *BCL7A* because its promoter is hypermethylated and, in general, this type of phenomenon could render differences in cell proliferation. An in-depth study of the mechanisms on which this phenomenon is based could provide information that may be useful to improve methods of diagnosis and prognosis. Furthermore, this project is in an initial stage, but the understanding of the biochemical pathways that relate the hypermethylation of a promoter with a tumor phenotype could allow us to extrapolate this knowledge to similar situations in order to understand them in more detail and thus be more precise in designing possible therapeutic approaches not only for APL.

Objectives

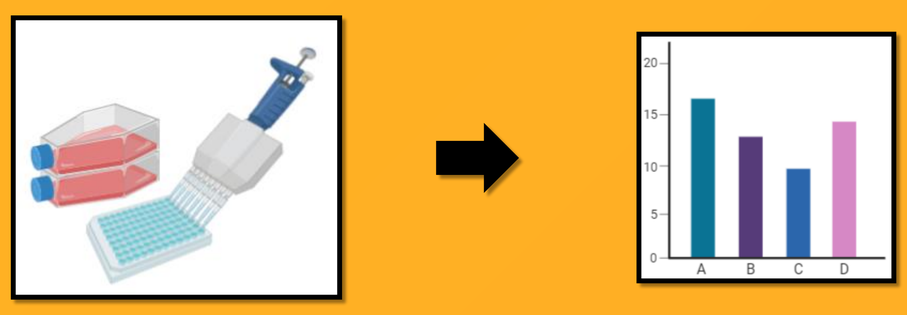
- Cell lines screening by studying the *BCL7A* expression level at mRNA level by quantitative PCR (qPCR).



- Experimental determination of the methylation level of the *BCL7A* promoter in NB4 cell line, to corroborate the information displayed in databases.

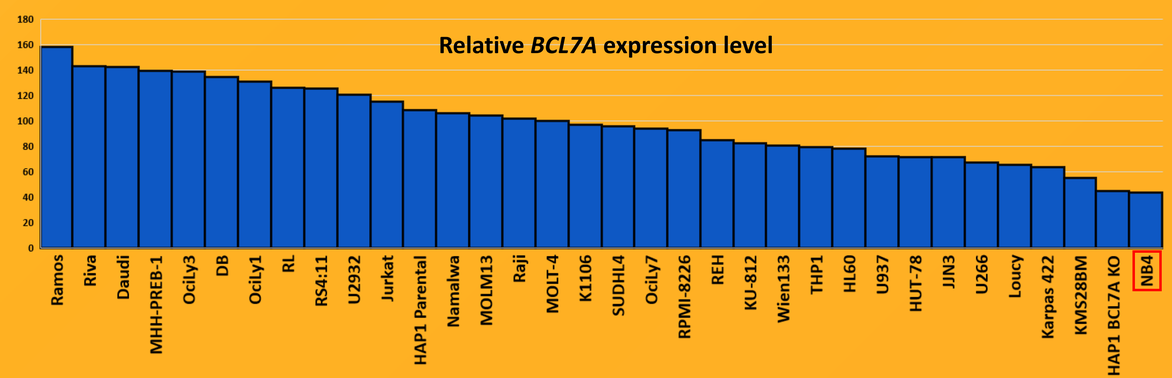


- To treat NB4 cells with and without *BCL7A* WT expression with the drug (ATRA: All-Trans Retinoic Acid) which is standardized to treat APL patients and see if *BCL7A* expression renders differences.

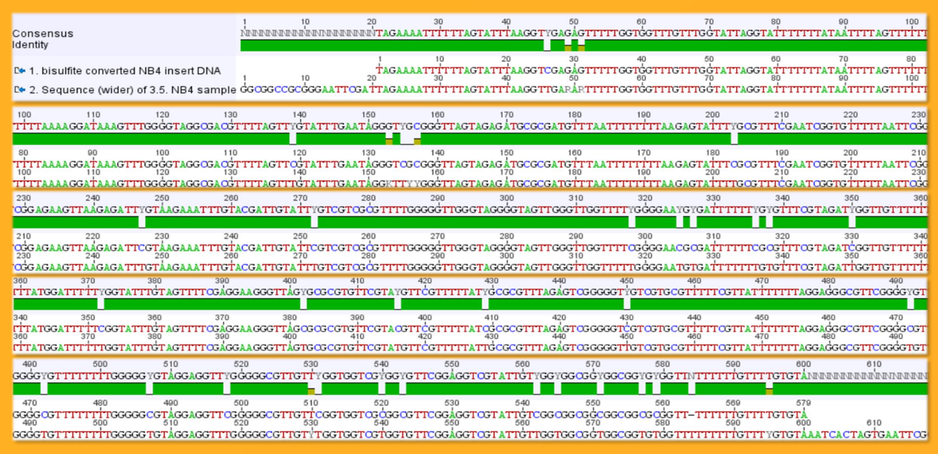


Preliminary Results

- Hematologic cell lines screening by qPCR

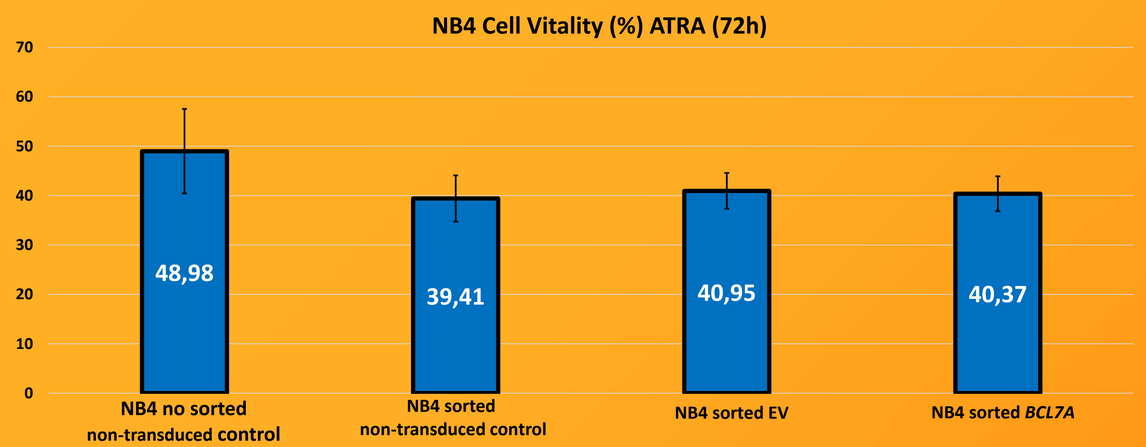


- *BCL7A* promoter hypermethylation experimental validation in NB4 by bisulfite conversion and DNA sequencing



More than the 50% of the CpG sites are methylated

- Relative viability 24 hours after treatment with ATRA of NB4 transduced with empty vector (EV) and *BCL7A* WT expression vector and controls



Conclusions

- ✓ Among our 34 hematological cell lines NB4 has the lowest *BCL7A* genetic expression at mRNA level.
- ✓ We got the experimental valitdation of the *BCL7A* promoter hypermethylation in NB4.
- ✓ On this first attempt treating NB4 cells with ATRA we did not see differences due to *BCL7A* expression. On the other hand, we are going to try other drugs with this cell model because it could give interesting results.

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References

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