Chromatin regulation: a basic research group moving into the MDS field

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Epigenetic information is written in chromatin. But how exactly do epigenetic mechanisms operate on the molecular level? How do chromatin alterations contribute to normal cell differentiation and disease? How does the environment influence these processes? And how does the metabolic state impact on chromatin structure and epigenetic memory?

These are questions addressed in the lab of Dr. Marcus Buschbeck that is located at the Josep Carreras Leukaemia Research Institute (IJC) in Badalona, Barcelona (Spain). We focus on molecular aspects of epigenetic regulation and on the question whether we can translate this knowledge into diagnostic and therapeutic tools for the management of diseases such as leukemias and myelodysplastic syndromes (MDS).

An ongoing study aims at the identification of response-predicting biomarkers of azacitidine treatment of high risk MDS patients and drug targets that could be used for an improved combinatorial therapy. The demethylating agent azacytidine (AZA) and its analogues are the major treatments given to high-risk MDS patients, but only 40% to 50% of treated patients show hematological improvements and a complete response is limited to as few as 10% to 15% *(Fenaux et al., Leuk Res, 2009)*. Both response-predicting biomarkers and new treatment options are needed to improve the clinical management of these patients. To identify such biomarkers and drug targets we have now started a project in collaboration with our colleagues Dr. Francesc Solé, Dr. Blanca Xicoy and Dr. Lurdes Zamora at the IJC Campus ICO-GTIP and its neighboring hospital ICO-Germans Trias i Pujol (GTIP). We are combining cell culture based experimentation with a longitudinal study of MDS patients undergoing azacitidine therapy. We have invested a sustantial amount of time to characterize AML cell lines from patients that had progressed from MDS to identify those that are most suitable models for experimentation. This now allows us to use powerful screening methods to preselect candidates worth to be tested in patient samples. If the approach is successful, in 2018 we will require the help from the MDS community to validate RNA biomarkers in independent patient cohorts. Thus, if you are handling bone marrow samples from MDS patients undergoing azacitidine treatment, please consider if you would be interested to participate and let us know. The sample requirement is a pellet of 1-2 million mononucleated bone marrow cells stored in Trizol for later RNA purification.

In a second more basic research project the Buschbeck group collaborates with the team of Prof. Dr. Katharina Goetze at the Technical University Munich (Germany). Funded through a project of the German Jose Carreras Leukaemia Foundation both teams aim to gain a better understanding about the involvement of chromatin regulators belonging to the group of Polycomb repressive complexes in the pathogenesis of MDS.

Campus Can Ruti in Badalona (close to Barcelona) and the new building of the Josep Carreras Leukaemia Research Institute, currently under construction.