ARCH – ESR 14 project (Diagenode)

Epigenetics refers to the heritable changes in gene expression that do not involve alteration in the underlying DNA sequence. The key processes that are responsible for epigenetic regulation are DNA methylation, modifications in chromatin (covalent modification of core histones) and posttranscriptional gene regulation by non-coding RNA (micro-RNAs). Epigenetic mechanisms are essential for normal development and maintenance of tissue-specific gene expression patterns in mammals. However, a number of well characterized epigenetic modifications are linked to aberrant gene functions and altered patterns of gene expression that play critical roles in different pathalogies, including cancers. Recently, it has become clear that disruption of epigenetic processes contributes to leukemic transformation. Notably, genome-wide DNA methylation studies have highlighted an important role of dysregulated methylation signature in AML from biological and clinical standpoint. However, the precise understanding of how epigenetic alterations contribute to myeloid leukemogenesis remains to be fully elucidated. This can be partially explained by the lack of adequate technology available to study clinical samples. Formalin-fixed paraffin-embedded (FFPE) samples are the most standard biological materials in pathology laboratories as it allows samples to be archived for long-term without specialized storage equipment. However, this fixation process results in severe degradation of nucleic acids rendering FFPE samples a challenging source material to get enough high-quality DNA or RNA. Another technical challenge is the amount of material available to perform the analysis. In most cases, early detection of cancers is very important to ensure high efficiency of the treatment. However this is associated with small amount of material available as it corresponds to early stage of the disease.

The ESR14 will focus his work on the developpment of methods allowing the analysis of the methylation for such a challenging samples. Moreover, innovative tools to study the hydroxymethation will also be developped as limited procedures are available to study this specific DNA modification especially for low cell input samples. These tools will later be used to identify variable regions that could account for MLL-rearranged-AML specificity and evaluate the impact of epigenomic variations on disease characteristics by confronting epigenomics and clinical data.

The ESR14 will be enrolled in the PhD Program in Translational and Molecular Medicine - DIMET at the University of Milano-Bicocca http://www.dimet.org/