Next-generation sequencing - a new era in hematological malignancies

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In order to determinate an accurate order of nucleotides in our chromosomes and in our genome a new era of DNA exploration has been developed, and this is DNA sequencing. The knowledge of DNA sequences has accelerated medical researches and is applied in a large number of fields. In the early 1970 DNA sequencing has been done using two dimensional chromatography but now, several new methods of DNA sequencing is been developed. Next-generation sequencing (NGS), the massively parallel sequencing technology enables the medical researchers to perform explorations at a level never achieved before. NGS is a revolution in the study of hematological malignancies and is filling the gap of unknown pathways and to uncover specific ways of treatment. There are a lot of studies and publications based on this "new era" technology bringing the need of this technology to be part of the clinical routine. The aim of NGS is the discovery of the genetic mutations in the hematological neoplasms, and to be able to create the best individualized target therapy for the hematological patients. NGS incudes different methods that make possible the exploration of the whole human genome but Whole Genome Sequencing (WGS), the sequencing of all exons with Whole Exome Sequencing (WES) and Sequencing of messaging RNA are the most important methods used.

Whole Genome Sequencing: uses two methods of preparation of the DNA libraries, one is called "paired-end sequencing" where are sequenced about 100 bp starting from the 400 bp endings of the DNA fragments. Using this method we can identify unique nucleotide variants (SNV), the insertions and deletions, but also the copy numbered changes. This method uses small quantities of DNA for the generation of the libraries and this is a big advantage when used in the hematological malignancies where the quantity of DNA is low or sometimes very low. The second method is the preparation of the DNA libraries using "mate -pair sequencing". This method is based on the generation of big fragmentations of DNA from 1 to 10 kb of length and this can be used for simultaneous detection of the mutations, structural abnormalities and also of the copy-numerical changes. But this method has an enormous disadvantage related to the big quantity of DNA needed to create the libraries being so limited od use for only a little number of tumors.

Whole-Exome-Sequencing (WES): is largely used for the study of the exons, called also the codifying genomes, and for the study of untranslated areas (regions). This method is based on the enrichment of exons areas and after that is passed in the next step, of the target sequencing. The Exome represents only 1,4% of the whole genome, so samples can be weld and sequenced together during one procedure of the machine. The weak point of WES is related with the incapacity of the enriched kits used for the whole exome. According to all this has been performed a lot of cohort studies for the hematological neoplasms. As expected the genes *TP53, ATM* and *RAS* has been confirmed as mutated in a variety of hematological malignancies. Also a whole new group of mutated genes and defective pathways has been discovered as a cause of hematological malignancies using NGS. Some of them were only mutated genes and some othes represented defective pathways leading to the hematological neoplasms. This discoveris are the start of creation of new effective and individualized target therapies for the hematological diseases.

***Keywords**: Next genome sequencing, DNA sequencing, Exome , Genome , Mutations*

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