Concorso pubblico, per titoli ed esami, per la copertura di n. 1 posto di Tecnologo di II livello - posizione economica D5 - a tempo determinato, con regime di impegno a tempo pieno presso il Dipartimento di Medicina di Precisione e Rigenerativa e Area Jonica DiMePRe-J, Sezione di Ematologia con Trapianto dell'Università degli Studi di Bari Aldo Moro, nell'ambito del Piano Nazionale di Ripresa e Resilienza, Missione 6 "Salute" – Componente 2 Investimento 2.1 "Valorizzazione e potenziamento della ricerca biomedica del SSN" finanziato dall'Unione Europea – NextGenerationEU, per il Progetto "Leukemic cell and microenvironment interactions as the culprit of chronicity in CLL" (codice progetto PNRR-MAD-2022-12376441_H93C22000800007), indetto con DDG n. 465 del giorno 19/04/2024

Domande elaborate dalla commissione esaminatrice per l'espletamento della prova orale.

TRACCIA 1

1- Nuove metodiche per l'identificazione e la quantificazione di target molecolari nelle neoplasie ematologiche.

2- Strumenti di ricerca in banche dati.

3- The formation of B-cell receptor immunoglobulin (BcR IG) is the result of a multi-step process that starts at the pro-B cell stage with the VDJ gene recombination of IG genes of the heavy chain, followed by VJ recombination of the light chain genes at the pre-B II cell stage. As a result, a fully functional BcR IG is expressed on the surface of any given naive B cell. After antigen encounter, somatic hypermutation (SHM) and class-switch recombination (CSR) act on the rearranged IG genes within the context of affinity maturation, leading to the expression of a BcR IG with unique immunogenetic and functional characteristics. Since B-cell neoplasms arise from the transformation of a single B cell, this renders IG gene rearrangements ideal clonal markers as they will be identical in all neoplastic cells of each individual clone. Furthermore, the rearranged IG sequence can also serve as a cell development/maturation marker, given that its configuration is tightly linked to specific B-cell developmental stages. Finally, in certain instances, as in the case of chronic lymphocytic leukemia (CLL), the clonotypic IG sequence and, more specifically, the load of somatic hypermutations within the rearranged IG heavy variable (IGHV) gene, holds prognostic and potentially predictive value. However, in order to take full advantage of the information provided from the analysis of the clonotypic IG gene rearrangement sequences, robust methods and tools need to be applied. Here, we provide details regarding the methodologies necessary to ensure reliable IG sequence analysis based on the recognized expertise of the European Research initiative on CLL (ERIC). All methodological and analytical steps are described below, starting from the isolation of blood mononuclear cells (PBMC), moving to the identification of the clonotypic IG rearrangement and ending with the accurate interpretation of the SHM status.

(Agathangelidis A, Rosenquist R, Davi F, Ghia P, Belessi C, Hadzidimitriou A, Stamatopoulos K. Immunoglobulin Gene Analysis in Chronic Lymphocytic Leukemia. Methods Mol Biol. 2019;1881:51-62. doi: 10.1007/978-1-4939-8876-1_5. PMID: 30350197.)

TRACCIA 2

1- Il sequenziamento del DNA in oncoematologia, dal Sanger agli approcci di nuova generazione.

2- La navigazione web come supporto informatico all'attività di ricerca scientifica.

3- RUNX1 is a DNA-binding transcription factor that binds to the DNA consensus sequence TGTGGT as a heterodimer with its cofactor core-binding factor subunit b (CBFb) (Figure 1). CBFb does not contact DNA directly, but it is required for efficient binding of RUNX1 [1,2]. The RUNX family of RUNT homology domain (RHD) transcription factors also includes RUNX2 and RUNX3, and all three RUNX proteins play multiple roles contributing both to normal development and to cancer in various tissues [3,4]. RUNX1 was originally termed AML1 because it was identified as a fusion protein with altered function in acute myeloid leukemia (AML) cells carrying the t(8;21) translocation (RUNX1/RUNX1T1). This fusion replaced the transactivation domain (TAD) of RUNX1 with the repressive domain of the ETO protein [4]. Dysregulated or mutated RUNX1 is able to contribute to leukemia in many ways whereby either too much [5] or too little RUNX1, or altered function of RUNX1, can promote AML [6] or myelodysplastic syndromes (MDS) [7]. Deregulation of RUNX1 or other RUNX proteins is also not just a feature of myeloid malignancy. In one study of T acute lymphoblastic leukemia (T-ALL), mutations of the RUNX1 RHD or TAD were also encountered in 18% of cases [8]. Furthermore, ectopic expression of RUNX2 can promote T-cell lymphoma and other cancers [3,4], while either loss of RUNX3 or reduced RUNX3 expression is a feature of gastric cancer [9]. Mutations or translocations of the RUNX1 and CBFb genes are now widely seen as major drivers of AML and MDS, and myeloid disorders carrying RUNX1 mutations frequently progress to AML. This review focuses on the molecular impact of different classes of RUNX1 mutations found either in AML as somatic mutations or in familial platelet disorder (FPD) as inherited germline mutations.

(Kellaway SG, Coleman DJL, Cockerill PN, Raghavan M, Bonifer C. Molecular Basis of Hematological Disease Caused by Inherited or Acquired RUNX1 Mutations. Exp Hematol. 2022 Jul;111:1-12. doi: 10.1016/j.exphem.2022.03.009. Epub 2022 Mar 24. PMID: 35341804.)

Il Segretario della Commissione
Sig. Fabio CORPOSANTO