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Acute myeloid leukemia stem cells (lscs): the key for prognosis and the route for potential targeted therapy

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IIn acute leukemia, among all prognostic factors, the most important is response to therapy. Response to therapy is classically evaluated by measuring minimal/measurable residual disease (MRD), at specified time points. However, in spite of its great value, MRD is not an absolute indicator of treatment outcome; some cases with negative MRD still experience relapse. This is more evident in AML compared to ALL which jeopardizes the value of MRD in AML follow up. Recently, it has been appreciated that relapse is mainly attributed to the persistence of the leukemia initiating cells, what is known as leukemia stem cells (LSC). It has been suggested that detection of LSCs would reduce false negative MRD results. Also targeting LSCs may be a potentially curative therapeutic approach. LSCs arise from a pool of mutated CD34+ stem cells. However, the exact immunophenotype of these cells is still controversial. LSCs share many markers with normal hematopoietic stem cells (HSC). In order to specifically target the malignant clone, it is essential to characterize the specific immunophenotype of the LSCs that would discriminate it from its normal counterpart. It has to be taken in consideration that marker expression differs between and within patients and therefore different immunophenotypically defined LSC compartments may be associated with specific subpopulations showing different sensitivity for therapy. Leukemia is now considered to be a stem cell disease with its characteristic refractory nature being blamed on a rare population of CD34+/CD38- LSCs. However, CD34-ve and CD38+ve LSC have been reported. Several other markers were claimed to characterize LSCs including CD33, CD45RA, CLL-1, TIM-3, CD47, CD96, IL-1 receptor accessory protein (IL1RAP), CD25, CD93, CD70/CD27, CD200, GPR56, JAM-C, CD9, IL1RAP and/or CD32. Targeting some of these surface antigens as a therapeutic approach is currently applied in clinical trials.

Biography

Azza Mahmoud Kamel is Professor of Clinical Pathology, NCI, Cairo University (since 1986), Doctorate Degree (MD) in Clinical Pathology, Faculty of Medicine, Cairo University (July 1976). Trained at and visited and collaborating with many international centers In Germany, France and USA; participated in 13 research projects. Thesis Supervision: 81MD and 12 MSc. Publications: Total Number: 182; First: 1976 Last: 2020; 34 in international Journals (Scopus), 45 International conference presentation and posters Reviewer for 15 International Publishers: Editor in chief of one, Associate Editor of two and Editorial Board Member of one Journal. Society membership: Seven Egyptian, One Arab and Four international. Awards:1- State Award in Medicine:1989 and 1996; 2- Cairo University Award of Appreciation, 2007. Established the BMT laboratory unit, NCI, Cairo University; including Immunogenetics, Flow cytometry, Molecular Genetics and pharmacogenomics: these are the main areas of expertise and research activities. The lab has obtained ISO 15189 accreditation.

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