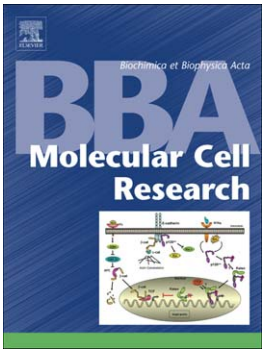

The Role of Microenvironment and Immunity in Drug Response in Leukemia

Emyr Bakker, Malak Qattan, Luciano Mutti, Constantinos Demonacos, Marija Krstic-Demonacos

PII: S0167-4889(15)00265-7
DOI: doi: 10.1016/j.bbamcr.2015.08.003
Reference: BBAMCR 17641

To appear in: *BBA - Molecular Cell Research*

Received date: 15 May 2015
Revised date: 13 July 2015
Accepted date: 1 August 2015

Please cite this article as: Emyr Bakker, Malak Qattan, Luciano Mutti, Constantinos Demonacos, Marija Krstic-Demonacos, The Role of Microenvironment and Immunity in Drug Response in Leukemia, *BBA - Molecular Cell Research* (2015), doi: 10.1016/j.bbamcr.2015.08.003

The Role of Microenvironment and Immunity in Drug Response in Leukemia

Emyr Bakker[1], Malak Qattan[2], Luciano Mutti[1], Constantinos Demonacos[3*] and Marija Krstic-Demonacos[1*#]

[1]School of Environment and Life Sciences, University of Salford, [2] King Saud University, [3] School of Pharmacy, University of Manchester

*Authors contributed equally
#Corresponding author

School of Environment & Life Sciences
College of Science & Technology
Cockcroft building room 305
University of Salford, Salford M5 4WT
Phone: +44 (0)161 295 5736
E-mail: M.Krstic-Demonacos@salford.ac.uk

Abstract

Leukemia is a cancer of the white blood cells, with over 54,000 new cases per year diagnosed worldwide and a 5-year survival rate below 60%. This highlights a need for research into the mechanisms behind its aetiology and causes of therapy failure. The bone marrow microenvironment, in which adult stem cells are maintained in healthy individuals, has been implicated as a source of chemoresistance and disease relapse. Here the various ways that the microenvironment can contribute to the resistance and persistence of leukemia are discussed. The targeting of the microenvironment by leukemia cells to create an environment more suitable for cancer progression is described. The role of soluble factors and microvesicles, as well as the importance of direct cell-cell contact, in addition to the effects of inflammation and immune surveillance in microenvironment-mediated drug resistance are discussed. An overview of the clinical potential of translating research findings to patients is also provided. Understanding of and further research into the role of the bone marrow microenvironment in leukemia progression and relapse is crucial towards developing more effective treatments and reduction in patient morbidity.

Keywords

Leukemia Microenvironment Inflammation Immune Surveillance Novel Therapeutics

Introduction

Recent advances in understanding the role of the tumour microenvironment (TME) in cancer and the central role of the stromal cells have uncovered new potential therapeutic opportunities to target cancer development and progression. Of particular interest is the effect of the microenvironment on haematological malignancies, usually referring to several levels of crosstalk between leukemia cells and the bone marrow microenvironment. This process is mediated in several different ways, for example by soluble factors and cell-cell contact and is suggested to affect chemotherapeutic response, potentially contributing to leukemia relapse. Different pathways play a role in the interaction between leukemia and the microenvironment depending on the type of leukemia. For example B cell receptor (BCR) associated kinases are important for chronic lymphocytic leukemia (CLL) expansion and maintenance. Adhesion molecules, cytokines and other signalling molecules all