Torello et al., Med Aromat Plants (Los Angel) 2016, 5:6
DOI: 10.4172/2167-0412.1000275

Medicinal & Aromatic Plants

Research Article Open Access

Extramedular Hematopoiesis in the Spleen of Obese Mice Modulation by the Alga *Chlorella*

Cristiane O Torello[1], Edgar J Paredes-Gamero[2], Fernanda Martins[1], Tamara C Lopes de Castro[1], Mario JA Saad[3], Sara TO Saad[3], Claudia Bincoletto[2] and Mary LS Queiroz[1]*

[1]*Department of Pharmacology/Hemocenter, University of Campinas, Campinas, SP, Brazil*
[2]*Department of Biochemistry, University of São Paulo, São Paulo, SP, Brazil*
[3]*Department of Internal Medicine, University of Campinas, Campinas, SP, Brazil*

Abstract

In this study, Balb/C mice received standard or high-fat diet (HFD) and were treated with Chlorella for 5 days prior and 4 weeks after the onset of HFD. We demonstrate here, for the first time in the literature, that in HFD-induced obesity, the rapid decline in the number of granulocyte and macrophage progenitors (CFU-GM) in the bone marrow is associated with a continuous migration/increase of these cells into the spleen, a process characterized as extramedullary hematopoiesis (EMH). No changes in the size of the primitive (LSK), and reduction in the size of the granulocyte/macrophage (GMP) hematopoietic populations in the bone marrow were observed. We also found that increased expression of C-C chemokine receptor type 2 (CCR2) on GMP in the spleen might be a mechanism related to the migration of CFU-GM to this organ. Increased serum colony-stimulating activity (CSA) was also found in obese mice. IL-6 serum levels, measured at the end of the treatment (12 weeks), when impaired glucose tolerance was already established (22), was increased. Treatment with Chlorella restored to normal values the numbers of CFU-GM in the marrow and spleen, the percentage of GMP in the marrow, the expression of CCR2 on spleen GMP, the increased serum levels of IL-6, and further increased CSA compared to obese mice. These findings suggest the ability of Chlorella to modulate the shift in hematopoietic topographical hierarchy, probably due its anti-inflammatory properties.

Keywords: *Chlorella*; Obesity; Splenic hematopoiesis; CCR2 expression; IL-6 serum levels

Abbreviations: BM: Bone marrow; CFU-GM: Number of colony-forming units of granulocytes and macrophages; CSA: Colony-stimulating activity; LSK: Primitive hematopoietic cells ($Lin^-Sca\text{-}1^+c\text{-}Kit^+$); GLUT4: Glucose transporter type-4; GMP: Granulocyte and macrophage progenitor; CCR2: C-C chemokine receptor type 2; IL: Interleukin; FFA: Free fatty acid levels; LDL: Low density lipoproteins.

Introduction

Obesity is a worldwide epidemic that results in enormous costs to health-care systems [1,2]. Data from the World Health Organization (WHO) have shown that the incidence of obesity worldwide has doubled since the 1980s [3]. Obesity-associated inflammation is widely regarded as one of the major factors driving insulin resistance (IR) and the onset of type-2 diabetes (T2D). A hallmark of inflammation in obesity is the accumulation and expansion of visceral adipose tissue (VAT) macrophages with an inflammatory phenotype, which, along with the decrease in anti-inflammatory T-regulatory cells in the VAT, results in an imbalanced environment and is thought to drive IR and the progression to T2D in obese subjects [4]. In spite of the relevance of the effects of inflammatory states on the hematopoietic system, leading to cytokine dysregulation, disturbances in cell proliferation, self-renewal rates, metabolism and cell cycle, little is known regarding the changes in the hematopoietic system induced by the inflammatory state carried by obesity [5].

An important aspect observed during chronic inflammatory states is the appearance of extramedullary hematopoiesis (EMH), which consists in the ability of marrow cells to home, proliferate, and mature in extramedullary organs of adult animals. This involves pathophysiologic alterations in the stem cells and their microenvironment, enveloping extracellular matrix and stromal cells, in addition to local and systemic chemokine production [6]. Of importance here are our previous studies showing the relevance of the restoration of both the myelosuppression and the increased splenic EMH for recovering the homeostatic balance in the immunocompromised host, as observed during chronic inflammatory states such as infection and tumors [7-16].

The search for natural agents able to minimize the undesirable effects of the available pharmacological treatment for obesity [17,18] is receiving increasing attention [19,20]. In this context, *Chlorella*, a microscopic single-celled freshwater alga containing all the ingredients necessary to promote human health [21] has emerged as an alternative agent against obesity-related complications [22,23]. *Chlorella* is called an adaptogen, meaning it helps protect the body against various stresses, including physical and psychogenic [7,24-32].

Of relevance, the stimulation of the pool of hematopoietic stem cells and the activation of mature leukocytes consisted of important aspects of *Chlorella* effects on the hematopoietic system. Our previous studies demonstrate a significant recovery in the reduced number of myeloid progenitor cells (CFU-GM) in the bone marrow of immunosuppressed host, in consequence of biologically active cytokine release, which was observed in several experimental models of psychogenical and physical stress [7,11,26,28-30,32-36]. These results demonstrated that *Chlorella* up-regulates the production of colony-stimulating factors in the same manner as for CFU-GM, leading to appropriate production

***Corresponding author:** Mary LS Queiroz, Department of Pharmacology and Hemocenter, Faculty of Medical Sciences, University of Campinas - UNICAMP, Rua Carlos Chagas 480, CEP 13083-878, Campinas, SP, Brazil, Phone: +551935218751; Fax: +551932892968; E-mail: queiroz.mary@gmail.com

Received November 08, 2016; **Accepted** November 15, 2016; **Published** November 22, 2016

Citation: Torello CO, Paredes-Gamer EJ, Martins F, de Castro TCL, Saad JAM, et al. (2016) Extramedular Hematopoiesis in the Spleen of Obese Mice Modulation by the *Alga Chlorella*. Med Aromat Plants (Los Angel) 5: 275. doi: 10.4172/2167-0412.1000275