Involvement of CD206+ macrophages in altered metabolic profile of CD34+ CML cells via secretory cytokines

A. DAS[1], P. GUPTA[2], N. CHATTERJEE[1]*

[1]Chittaranjan National Cancer Institute, Kolkata, India

[2]Chittaranjan National Cancer Hospital, Kolkata, India

Corresponding author: Dr. Nabanita Chatterjee, Chittaranjan National Cancer Institute

E mail: nabanita.chatterje@yahoo.com

Introduction

Chronic myeloid leukemia (CML) is a hematological malignancy that is a form of myeloproliferative neoplasm caused by a reciprocal translocation and the formation of the oncogenic BCR-ABL fusion protein (1). Although tyrosine kinase inhibitors improved the prognosis of the disease, the limitations of resistance and recurrence still exist. Therefore, in-depth analysis of the microenvironment is needed for developing alternative novel therapies. Macrophages play a pivotal role in disease progression of CML (2). CD206+ M2 macrophages exert an immunosuppressive influence in the tumor microenvironment and it critically is involved in CML disease progression. Therefore, analysis of the role of CD163+CD206+ M2 macrophages is crucial in CML.

Aim and objective

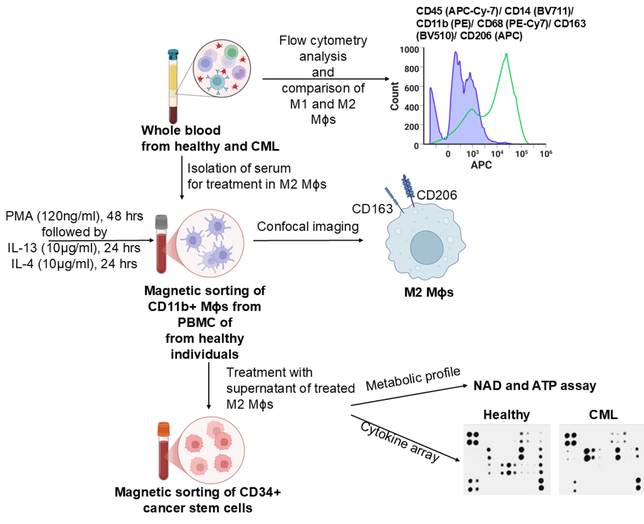
Despite the advancement in therapeutic approaches, limitations lie in disease recurrence and their drug resistance. Therefore, the development of alternative therapeutic approaches is crucial to deal with the poor prognosis of CML. The study aims to analyse the immuno-metabolic profile of the macrophage population to identify novel targets and develop alternative therapeutic approaches in CML.

Objective 1: To evaluate the macrophage subtype ratio in CML

Objective 2: To evaluate the role of CD163+CD206+ M2 macrophages in CML

Objective 3: To identify the metabolic changes in CD34+ cancer stem cells under the influence of CD163+CD206+ M2 macrophages.

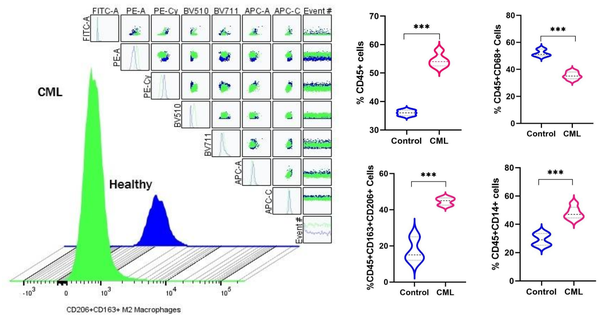
Methods



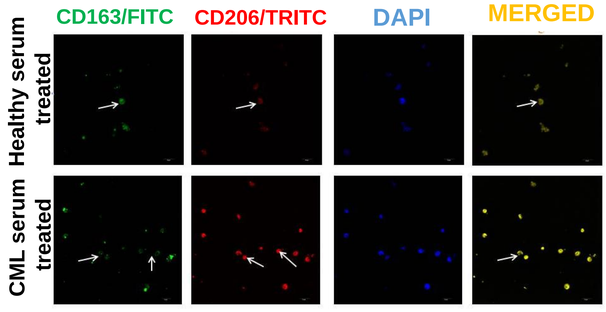
Future perspective

Analysis of Underlying signalling mechanism and metabolic profile of CD163+CD206+ M2 Macrophages need to be further investigated for developing M2 targeted therapeutic approach in resistant and recurrent CML

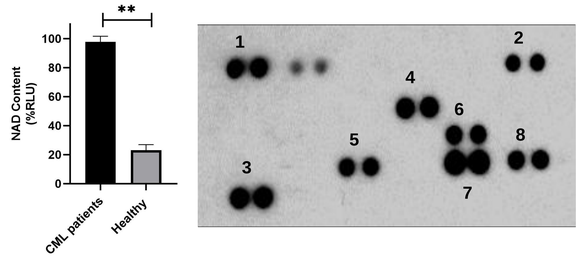
Results



Flow cytometry analysis showing ***higher percentage of CD163+CD206+ M2 Mϕs*** and lower percentage of CD45+CD68+ as represented M1 Mϕs with significance changes in CD45 and CD14 level in CML.



Confocal microscopy showed that CML serum induced ***higher co-expression of CD163-CD206*** in M2 Mϕs sorted from healthy PBMC, compared with healthy serum.



A numbered cytokines and associated chemokines increased in CML patients versus healthy age matched controls. A numbers mentioned in the blot were the representative expression of cytokines like 1: C5/5a, 2: CXCL1, 3:CD54(iCAM1), 4: IL-1ra, 5: IL-6, 6: IL-8, 7:IL-16, 8: CXCL10, along with the upregulated NAD level in CML.

conclusion

In a nutshell our study showed

- Higher percentage of CD163+CD206+ M2 macrophages in CML patients
- Increased proliferation of CD163+CD206+ macrophages correlated with CML disease progression
- M2 macrophages induce the proliferation of CD34+ cancer stem cells in CML

References

1.Wong, S. & Witte, O. N. The BCR-ABL story: Bench to bedside and back. Annu. Rev. Immunol. 22, 247–306.

2. Chiossone L, Conte R, Spaggiari GM, et al. Mesenchymal Stromal Cells Induce Peculiar Alternatively Activated Macrophages Capable of Dampening Both Innate and Adaptive Immune Responses. Stem Cells. 2016;34(7):1909-1921.

Acknowledgement

I am grateful to Director, CNCI and the Ministry of Health & Family Welfare for providing research facility and support, encouragement. I am also thankful to the intramural funding F'.No- N/1 96lDir-Miscl2022/358 for this research I am thankful Council of Scientific & Industrial Research for providing the fellowship. The volunteers participated in the study are highly appreciated and thankful. All the clinical samples, included in the study, were abided by the ethical guidelines.