Proteomic analysis of bone marrow plasma from patients with Acute Myeloid Leukemia

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BACKGROUND

Acute Myeloid Leukemia (AML) is a hematological malignancy characterized by abnormal proliferation of myeloid cells, a decrease in apoptosis level and a blockage of cells differentiation. AML is largely heterogeneous and so many studies have accumulated on leukemogenic processes. The maintenance of the hematopoietic Stem Cell (SC) and the regulation of its self-renewal and differentiation *in vivo* depend on the *"indutive microenviroment of hematopoiesis"*, representative for signaling between SC and stroma through cytokines, chemokines and growth factors that interact with hematopoietic cells in the Bone Marrow (BM). In this context, the BM plasma may present a range of proteins that may be involved in this process.

OBJECTIVES

The aim of this study was to evaluate the protein expression profile from BM plasma samples of AML patients and compare with BM plasma from healthy donors.

METHODOLOGY

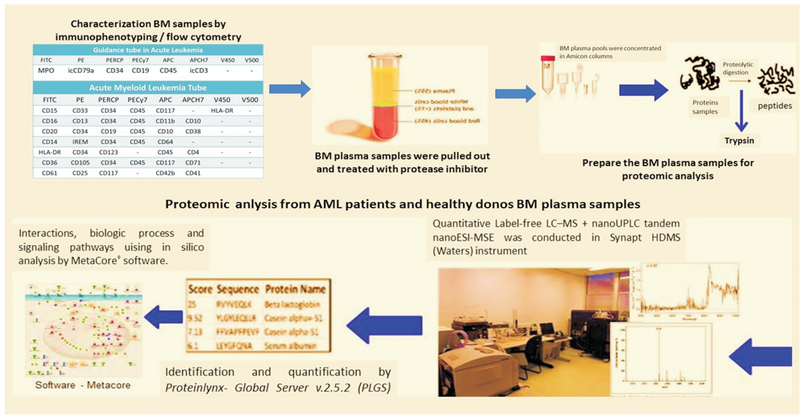


Figure 1: Immunophenotyping and proteomic analysis of BM plasma samples

RESULTS

BM samples characterized by immunophenotyping

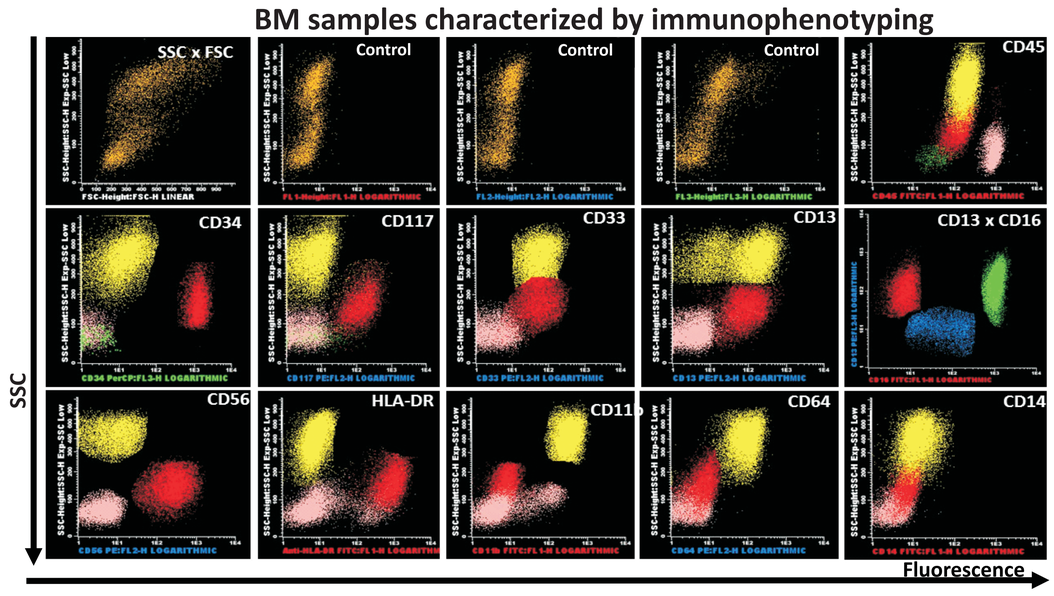
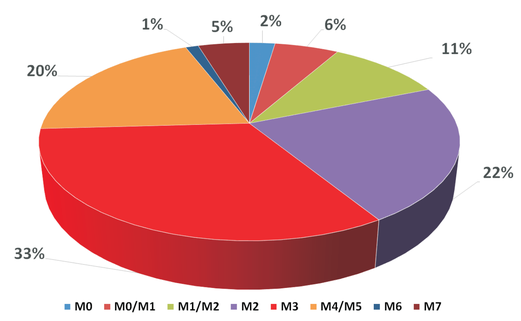


Figure 2: Characterization by immunophenotyping and flow cytometry using monoclonal antibodies following FAB criteria. The dot-plot's graphics exemplify AML M2 subtype BM samples' characterization.

AML BM samples



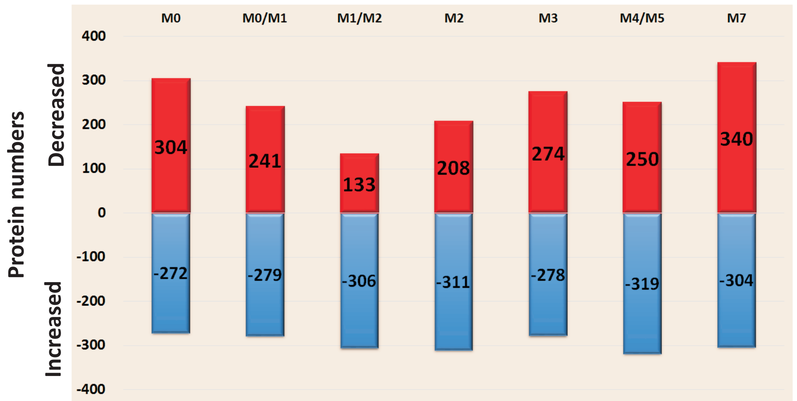
Graphic 1: 60 AML BM patients characterized by immunophenotyping

Proteomic analysis

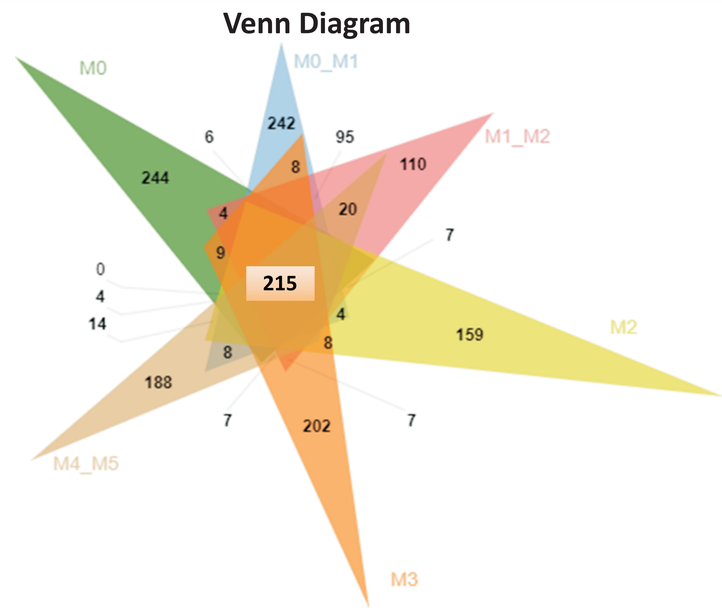
For proteomic analysis, we selected 17 BM plasma from AML patients which corresponds to following subtypes: AML M0 (n=1), AML M0/M1 (n=2), AML M1/M2 (n=2), AML M2 (n=3), AML M3 (n=4), AML M4/M5 (n=3), AML M7 (n=2) and 5 BM plasma from healthy donors.

Identified and quantified proteins from BM plasma samples

Graphic 2: Differentially expressed proteins in BM plasma samples



Venn Diagram



Graphic 3. Venn Diagram showed 215 proteins commonly expressed in all AML BM plasmas subtypes when compared with healthy donors BM plasma.

In silico analysis

Biologic processes

Table 1. The most relevant biologic processes in AML BM plasma samples compared healthy donors BM plasma

The most relevant biologic processes altered commonly for all AML subtypes	Proteins involved
Cellular adhesion	Rabbconnectin, Rabb 3, INADL, Plakoglobin, Cadherin 11, Tubulin alpha, MUPP1, Axin 1, Axin 2.
Cytoskeleton	Dynein, axoneme, SHANK, tubulin alpha, SHANK1, AMPK gamma
Apoptosis	Tubulin alpha, APEX, clusterin, ALOX12
Signal Transduction	AMPK gamma, PDK e clusterin, PP2C alpha, PDK
Telomere length	TEP1, PDK
Immune Complement System	FHR-3, clusterin
Cell Cycle	GAPCENA, Tubulin alpha, PMF1

Signaling pathways

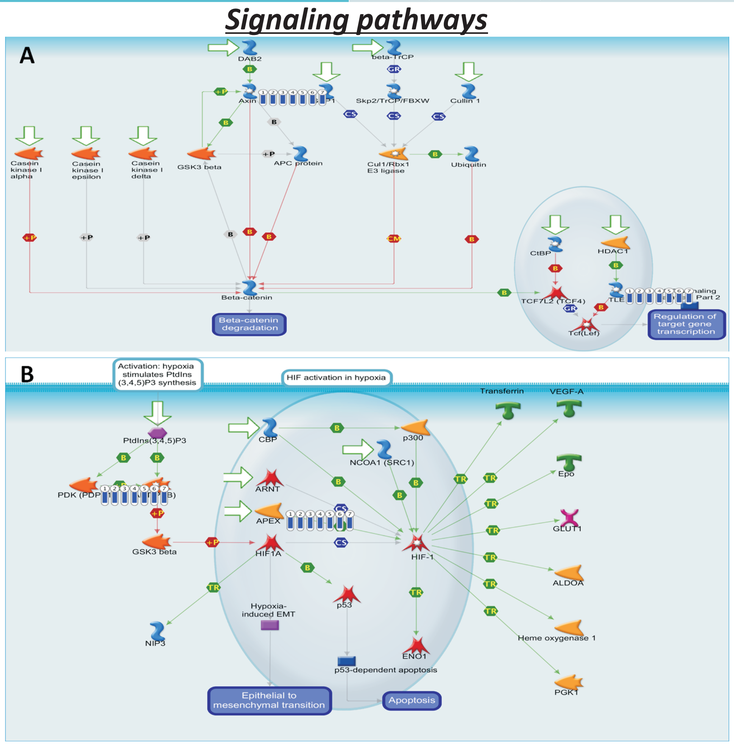


Figure 3: Metacore® analysis using these differently expressed proteins showed relevant signaling pathways that were altered in this context were: WNT signaling pathway **(A)** and Akt in hypoxia induced HIF-1α activation **(B)**.

CONCLUSION

These results showed 215 differently expressed proteins in all AML BM plasma instead of subtypes and this proteins could be involved in leukemogenic process. In this moment, we are analyzing and validating the common differentially expressed proteins using Western Blot analysis with individual BM plasma samples used in proteomic approach and other samples from AML and Healthy donors BM plasma. Supported by: CNPq, MS, FAPERJ.

Projeto Gráfico: Setor de Edição e Informação Técnico-Científica / INCA