Composition of bone marrow mesenchymal stem cells' extracellular matrix as a therapeutic target in multiple myeloma

MEIR MEDICAL CENTER

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INTRODUCTION

Malignant multiple myeloma (MM) cells accumulate in the bone marrow (BM) where their interactions with the microenvironment promote disease progression and drug resistance. Previously, we have shown that extracellular matrix (ECM) from BM-MSCs (MM and normal donors- ND) affected MM cell lines differentially with a pro-MM effect attributed to MM-MSCs' ECM. Here we addressed the variance in composition of BM-MSC's extracellular matrix (ECM).

OBJECTIVES

Identifying ECM components produced by MM-MSCs that promote MM and assessing their potential as therapeutic targets.

METHODS

- Proteomic analysis (mass spectrometry) for ND/MM-MSCs ECMs.
- Validation by immunoblotting.
- Bioinformatics analyses (Webgestalt, ToppGene, STRING).

RESULTS

We identified 401 proteins in the BM-MSCs ECM of which 6 and 4 were unique to ND and MM-MSCs ECM, respectively (fig 1). Of the commonly expressed 391 proteins distinct differences in expression levels were registered in 44 *($p<0.05$).* The top elevated ECM proteins of the two sources are presented in fig. 2. Bioinformatics analyses of the unique and elevated proteins (FC 1.5, $p<0.05$) depicted fundamental differences in the biological role according to source (fig 3). Importantly, MM-MSCs ECM was enriched with protein involved in metabolism and traslation whereas ND-MSCs ECM displayed augmented ECM and adhesion.

A remarkable decrease was observed in MM-MSCs ECM Elastin (ELN) compared to ND-MSCs' ECM (FC= 49.1)(fig3).

Fig 1

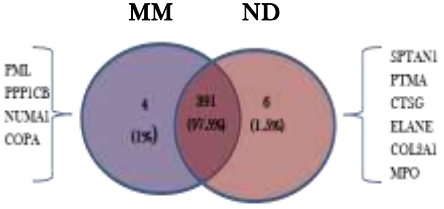


Fig 2

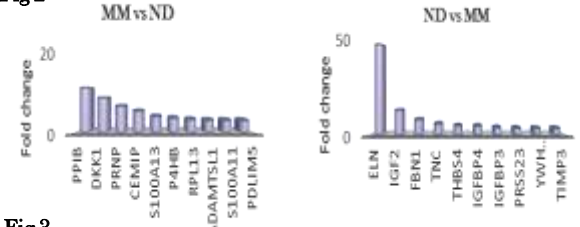


Fig 3

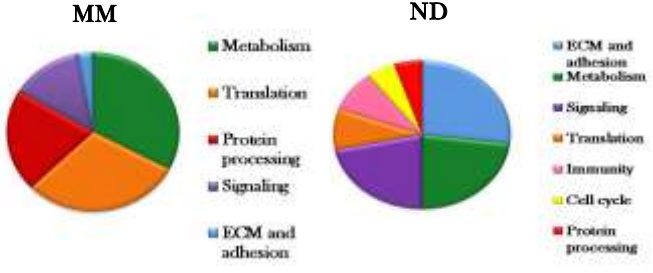
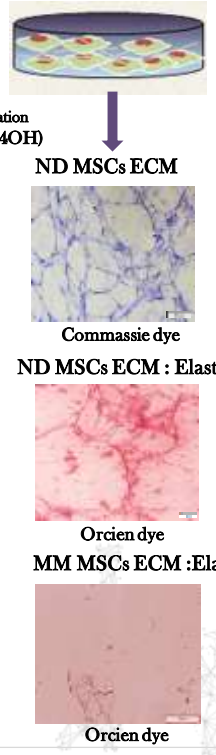


Fig 4



CONCLUSIONS

There exist distinct differences in the composition and expression levels of ECM components between ND-MSCs and MM-MSCs. Continued research will examine the significance of reduced ELN to MM promotion/progression and design of therapeutic exploitation.