Ribosomal proteins as distinct "passengers" of microvesicles: new semantics in myeloma and mesenchymal stem cells' communication

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Fig 1

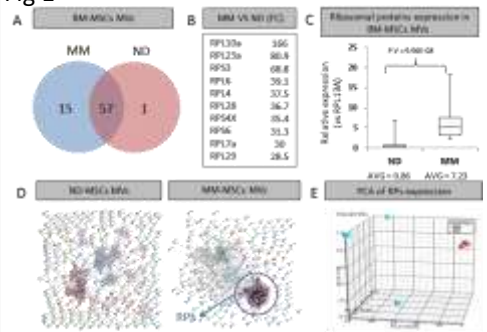


Fig 2

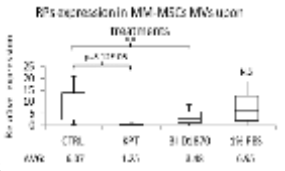


Fig 3

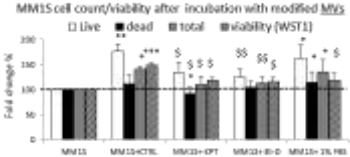


Fig 4

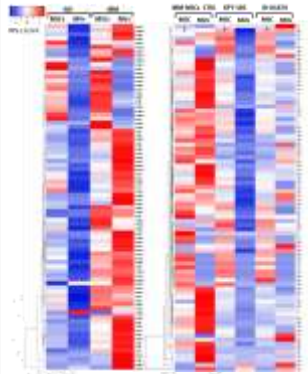
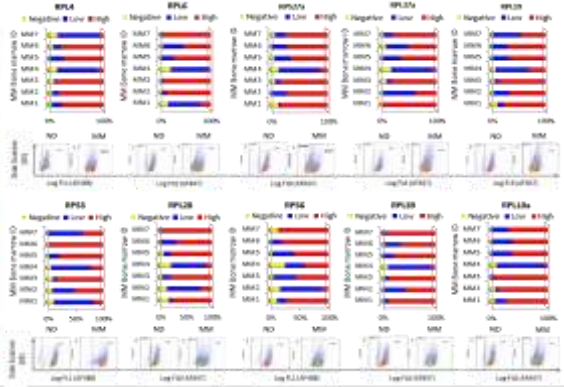


Fig 5



Aims

To assay the protein cargo transported from MM-MSCs to MM cells via MVs with focus on ribosomal proteins (RPs) and their role in MM translation and phenotype design.

Results (figures 1-3)

Proteomics analysis demonstrated increased levels and repertoire of RPs in MM-MSCs MVs compared to normal donors (ND) counterparts (n=3-8; *p= 9.96E-08*) (fig 1). We limited the RPs load in MM-MSCs MVs (fig 2), reapplied the modified MVs to MM cell lines and demonstrated that the RPs are essential to the proliferative effect of MM-MSCs MVs on MM cells (n=3; *p<0.05*)(fig 3). We also observed that inhibition with KPT-185 displayed the most extensive effect on RPs delivery into the MVs (↓80%; *p=3.12E-05)*.

Background

Aberrant mesenchymal stem cells (MSCs) in multiple myeloma (MM) bone marrows (BM) promote disease progression and drug resistance. Previously, we have demonstrated that microvesicles (MVs) from MM-MSCs promote MM

Methods

- *Proteomic analysis* (mass spectrometry)
- *Inhibitors of RPs* (starvation-1% FBS; RSK-Bi-D1870; XPO1-KPT-185)
- *BM-MSCs' RPs expression* : flow cytometry

Results (figure 4)

We assayed the expression of select RPs (n=10) in BM-MSCs cell populations (ND and MM; n≥6 each) and observed that each patient had several subgroups of BM-MSCs whereas the NDs were homogeneous and of lower expression.

Discussion

These findings bring to light a new mechanism in which the tumor microenvironment participates in cancer promotion. MVs-mediated horizontal transfer of RPs between niche MSCs and myeloma cells is a systemic way to bestow pro-cancer advantages. This capacity also differentiates normal MSCs from the MM-modified MSCs and may mark their reprogramming. Future studies will be aimed at assessing the clinical and therapeutic potential of the increased RPs levels in MM-MSCs MVs.