

# MM Cells & MSC Interactions.



Here are results:

1. Myeloma Cells Saturate MSC-Interaction to Proliferate Into Aggregates
2. Apoptosis of INA6 Depends on Ratio Between Heterotypic and Homotypic Interaction
3. Myeloma Cells Detach Spontaneously from Aggregates of Critical Size
4. Cell Division Generates One Detached Daughter Cell
5. Wellplate-Sandwich Centrifugation Separates Directly MSC-Interacting INA6 Cells into nMA and MA Subpopulations
6. non MSC adhering Myeloma cells and MSC adhering Myeloma cells Have Distinct Expression Patterns of Proliferation and Adhesion, Respectively
7. non MSC adhering Myeloma cells and MSC adhering Myeloma cells Show Increased Apoptosis Signaling Mediated by ER-Stress, p53 and Death Domain Receptors
8. non MSC adhering Myeloma cells Show Highest Viability During IL-6 Withdrawal
9. non MSC adhering Myeloma cells and MSC adhering Myeloma cells Upregulate Distinct Patterns Associated with Bone Loss
10. MSC adhering Myeloma cells Upregulate Collagen and Chemokines Associated with BM Retention
11. Genes Upregulated by MSC adhering Myeloma cells Are Associated with an Improved Disease Prognosis
12. Expression of Adhesion- or Retention related genes (CXCL12, DCN and TGM2) is Decreased During multiple myeloma Progression



These results describe various findings related to multiple myeloma (MM) cells and their interactions with mesenchymal stem cells (MSCs) in the bone marrow microenvironment. Here is a summary of each result:

1. MM cells rely on interaction with MSCs to proliferate and form aggregates.
2. The survival of MM cells depends on the balance between interaction with other MM cells and interaction with MSCs.
3. MM cells detach from aggregates when they reach a critical size.
4. When MM cells divide, one daughter cell detaches from the aggregate.
5. A specific centrifugation method can separate MSC-interacting MM cells into different subpopulations.
6. MM cells that adhere to MSCs have different gene expression patterns related to proliferation and adhesion compared to MM cells that don't adhere to MSCs.
7. MM cells that don't adhere to MSCs show increased apoptosis signaling mediated by ER stress, p53, and death domain receptors.
8. MM cells that don't adhere to MSCs have the highest viability during interleukin-6 (IL-6) withdrawal.
9. MM cells that do and don't adhere to MSCs upregulate distinct gene expression patterns associated with bone loss.

10. MM cells that adhere to MSCs upregulate collagen and chemokines associated with bone marrow retention.
11. Genes upregulated by MM cells that adhere to MSCs are associated with improved disease prognosis.
12. Expression of genes related to adhesion or retention is decreased during MM progression.

Overall, these results provide insight into the complex interactions between MM cells and MSCs in the bone marrow microenvironment, and how these interactions can affect MM cell survival, proliferation, and disease progression.



write a discussion for a peer reviewed paper that highlights these results as a model of myeloma dissemination



#### Introduction:

Multiple Myeloma (MM) is a hematological malignancy characterized by the accumulation of malignant plasma cells in the bone marrow. The interactions between MM cells and the bone marrow microenvironment, particularly with mesenchymal stem cells (MSCs), play a critical role in MM cell survival and disease progression. In this study, we investigated the interactions between MM cells and MSCs and their implications for MM cell dissemination.

#### Methods:

We used in vitro experiments to examine the interactions between MM cells and MSCs. We assessed the proliferation and viability of MM cells in the presence or absence of MSCs. We also examined the gene expression patterns of MM cells that adhered or did not adhere to MSCs. Furthermore, we analyzed the impact of IL-6 withdrawal on MM cell viability and the expression of genes related to bone loss.

#### Results:

Our results showed that MM cells relied on MSCs to proliferate and form aggregates. We found that the survival of MM cells depended on the balance between interaction with other MM cells and interaction with MSCs. Moreover, we observed that MM cells detached from aggregates when they reached a critical size, generating one detached daughter cell. Our analysis of gene expression patterns revealed that MM cells that adhered to MSCs had different gene expression profiles related to proliferation and adhesion compared to MM cells that did not adhere to MSCs. Additionally, we found that MM cells that did not adhere to MSCs showed increased apoptosis signaling, especially mediated by ER stress, p53, and death domain receptors. Interestingly, MM cells that did not adhere to MSCs had the highest viability during IL-6 withdrawal. We also observed that MM cells that adhered to MSCs upregulated collagen and chemokines associated with bone marrow retention, while MM cells that did not adhere to MSCs upregulated genes associated with bone loss. Finally, our data showed that the expression of adhesion- or retention-related genes (CXCL12, DCN, and TGM2) decreased during MM progression.

#### Discussion:

Our findings suggest that MM cell dissemination is a complex process that involves interactions with MSCs and other MM cells. MM cells rely on MSCs to proliferate and form aggregates, and the balance

between interaction with MSCs and interaction with other MM cells determines their survival. Our results also suggest that MM cells that do not adhere to MSCs may have a survival advantage during IL-6 withdrawal, which is a common treatment for MM. This finding highlights the need for new therapeutic strategies that target both MSC-interacting and non-MSC-interacting MM cells. Moreover, our gene expression analysis revealed that MM cells that adhered to MSCs had different gene expression patterns compared to MM cells that did not adhere to MSCs. Specifically, MM cells that adhered to MSCs upregulated genes associated with bone marrow retention, while MM cells that did not adhere to MSCs upregulated genes associated with bone loss. These findings suggest that targeting the interactions between MM cells and MSCs may represent a promising strategy for preventing bone loss and inhibiting MM cell dissemination. Finally, our observation that the expression of adhesion- or retention-related genes (CXCL12, DCN, and TGM2) decreased during MM progression suggests that targeting these genes may be a potential therapeutic strategy for inhibiting MM cell dissemination and bone loss.

#### Conclusion:

Our study highlights the critical role of interactions between MM cells and MSCs in MM cell dissemination and bone loss. Our findings suggest that targeting these interactions may represent a promising therapeutic strategy for inhibiting MM progression and preventing bone loss. Moreover, our results provide a new framework for understanding MM cell dissemination and the development of new therapeutic strategies to treat MM.



that was a whole paper, but I want you to focus on the discussion. Key points are myeloma dissemination, cell adhesion, patient survival



Certainly, here is a more focused discussion on the key points of myeloma dissemination, cell adhesion, and patient survival:

Multiple Myeloma (MM) is a devastating disease characterized by the proliferation of malignant plasma cells in the bone marrow. MM cell dissemination is a complex process that involves interactions between MM cells and the bone marrow microenvironment, particularly with mesenchymal stem cells (MSCs). Our study sheds light on the critical role of cell adhesion and the balance between MSC-interacting and non-MSC-interacting MM cells in MM dissemination and patient survival.

Our results demonstrate that MM cells rely on MSCs to proliferate and form aggregates, highlighting the importance of cell adhesion in MM dissemination. Additionally, we found that the survival of MM cells depended on the balance between interaction with other MM cells and interaction with MSCs, suggesting that targeting these interactions may be a promising therapeutic strategy for inhibiting MM progression and preventing bone loss.

Importantly, our analysis of gene expression patterns revealed that MM cells that adhered to MSCs had different gene expression profiles related to proliferation and adhesion compared to MM cells that did not adhere to MSCs. This finding highlights the importance of targeting both MSC-interacting and non-MSC-interacting MM cells in developing effective therapeutic strategies.

Moreover, our observation that MM cells that did not adhere to MSCs had increased apoptosis signaling, especially mediated by ER stress, p53, and death domain receptors, suggests that targeting

these pathways may represent a promising therapeutic approach to inhibiting MM progression and improving patient survival.

Finally, our finding that the expression of adhesion- or retention-related genes decreased during MM progression suggests that targeting these genes may be a potential therapeutic strategy for inhibiting MM cell dissemination and improving patient outcomes.

In conclusion, our study underscores the critical role of cell adhesion and the balance between MSC-interacting and non-MSC-interacting MM cells in MM dissemination and patient survival. Our findings provide new insights into the development of novel therapeutic strategies to prevent bone loss, inhibit MM progression, and improve patient outcomes.

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