Exosomal Vesicles as a Promising Strategy for Severe COVID-19 in Multiple Myeloma Patients

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INTRODUCTION

- During the early phase of the pandemic, COVID-19 patients with multiple myeloma (MM) exhibited a 56% hospitalization rate, with 20% requiring critical care, and an 18% increased risk of death.
- MM patients with symptomatic COVID-19 infections undergoing anticancer therapy showed a 55% higher risk of mortality.
- Even in the post-pandemic world, MM patients remain at heightened risk for severe SARS-CoV-2 infections due to their immunocompromised status.
- In this study, we (1) developed a model to explain the pathogenesis and interplay between MM and severe SARS-CoV-2, and (2) explained the efficacy and therapeutic potential of exosomal vesicles as a therapeutic intervention against severe SARS-CoV-2 supported by clinical evidence.

HYPOXIA & MULTIPLE MYELOMA

- Hypoxia increases the expression of adhesions factors and promotes cytokine release.
- Upregulation of CXCR4 and VAL4 results in an increase of osteoblast adhesion.
- Increase of TGF-β and IL-6 promotes bone lesion formation.
- In MM, IL-6 acts as a survival factor for myeloma cells and reshapes the tumor microenvironment in the bone marrow, driving disease progression.
- IL-6 also stimulates upregulates pro-inflammatory pathways, inhibits apoptosis and alters the tumor microenvironment within the bone marrow.

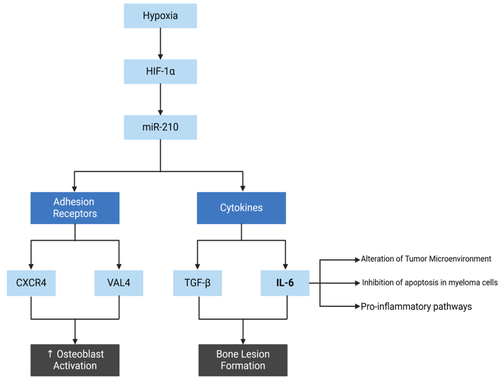


Figure 1- Hypoxia in Multiple Myeloma Cells.

MULTIPLE MYELOMA & SARS-COV-2 MODEL

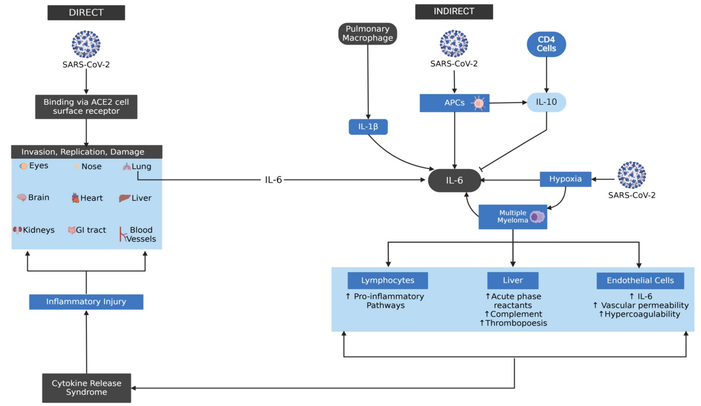


Figure 2- SARS-CoV-2 Infection in Multiple Myeloma Patients

- Severe SARS-CoV-2 infection causes multiple organ damage through IL-6-mediated inflammation and hypoxia-induced cellular metabolic alterations leading to cell death.
- Hypoxia is also induced by malignancy due to alterations in metabolism, resulting in greater IL-6 secretion.
- In MM, hypoxia induces increase secretion of IL-6 from multiple myeloma cells.
- IL-6 production leads to enhanced upregulation of downstream proinflammatory pathways resulting complement activation, acute phase reactant production, and vascular permeability resulting in increased cytokine release and systemic injury. This synergy results in enhanced systemic injury as compared to either alone.

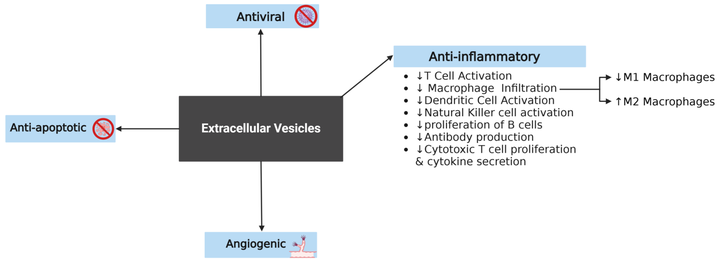


Figure 3- Functions of Exosomal Vesicles

EXOSOMAL VESICLES AS A THERAPY FOR SARS-COV-2 IN MULTIPLE MYELOMA PATIENTS

- In multiple myeloma mouse models, exosomal vesicles have induced apoptosis of multiple myeloma cells via apoEV-FASL and membrane trafficking Fas into MM cells.
- In clinical trials, exosomal vesicles has demonstrated over a 90% overall survival in critically ill non-myeloma patients with severe COVID-19 with results holding steady for several months.
- Given the safety, tolerability, and strong efficacy of this therapy, exosomal vesicles warrant consideration as a potential therapeutic agent against severe SARS-CoV-2 in multiple myeloma patients.

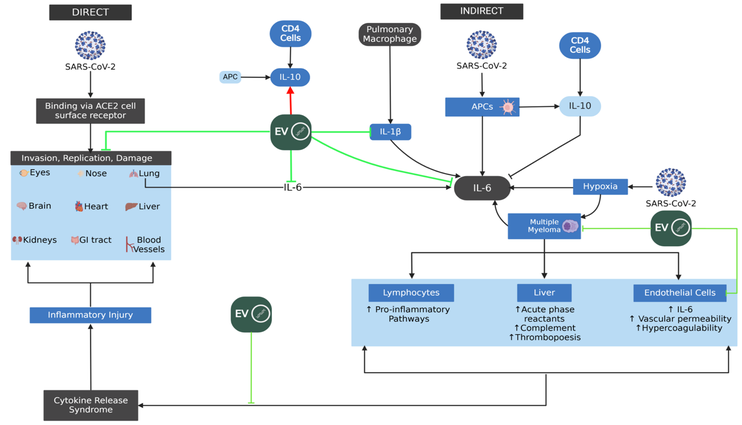


Figure 4- Exosomal vesicles (EVs) are a potential therapeutic agent against SARS-CoV-2 in patients with multiple myeloma.

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