Immune profile of equine mesenchymal stem/stromal cells (MSCs): induced vs primary cells

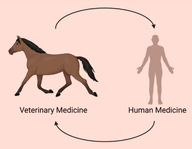
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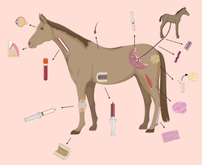
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INTRODUCTION

The horse is highly relevant both as patient and as translational model due to its physiological and pathological similarities to humans





Primary mesenchymal stromal/stem cells (MSCs) → **Interesting therapy in horses**

But:
- Senescence
- Repeat tissue harvestings
- Heterogeneic product

Induced pluripotent stem cells (iPSCs) → **Induced MSCs (iMSCs)**

But:
- Derived from reprogrammed cells
- May exhibit altered gene expression
- Function differs from primary MSCs?

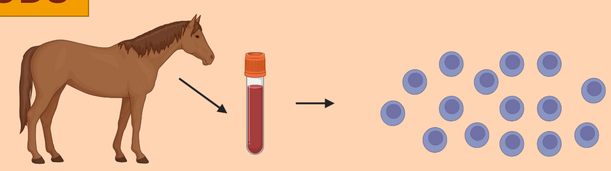
Promising alternative

The immunomodulatory profile of equine iMSCs is not yet well defined

OBJECTIVE

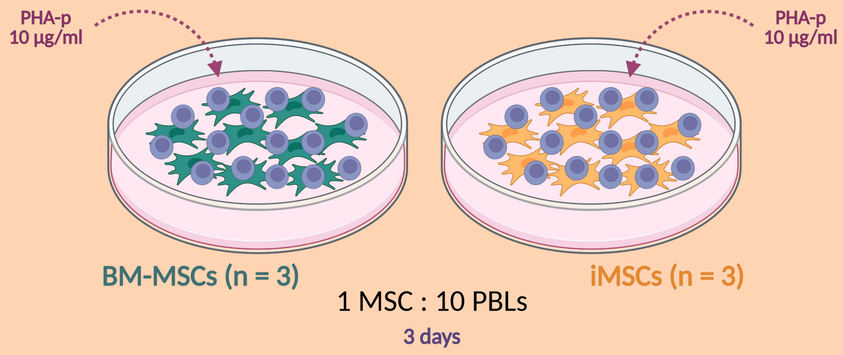
To compare the **immune profile** of **equine iMSCs** and **primary bone marrow-derived MSCs** (BM-MSCs) before and after exposing them to **equine activated allogeneic lymphocytes**.

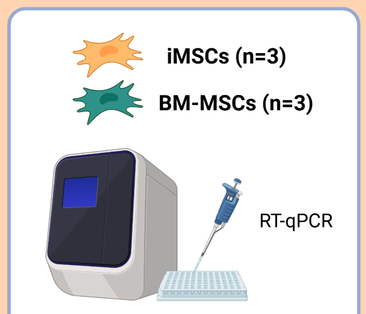
METHODS



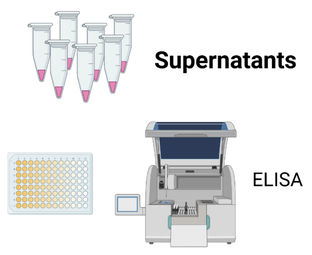
Co-culture activated PBLs with MSCs

IMMUNOSUPPRESSIVE ASSAY





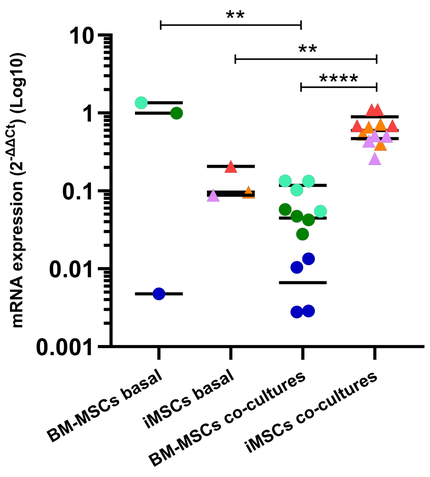
- Immunomodulatory genes: ***VCAM1***, ***iNOS2***, ***IDO1***, ***COX2*** and ***IL6***
- Immunogenic genes: ***MHC-I***, ***MHC-II***, ***CD40*** and ***CD80***



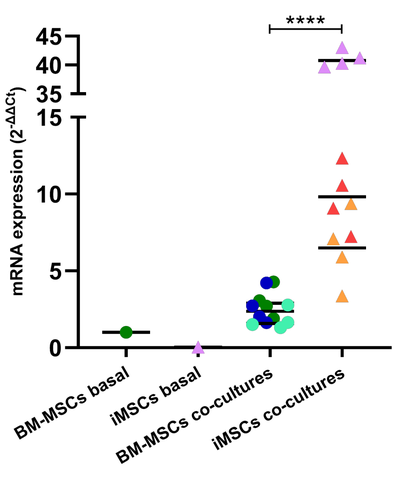
RESULTS

IMMUNOMODULATORY PROFILE

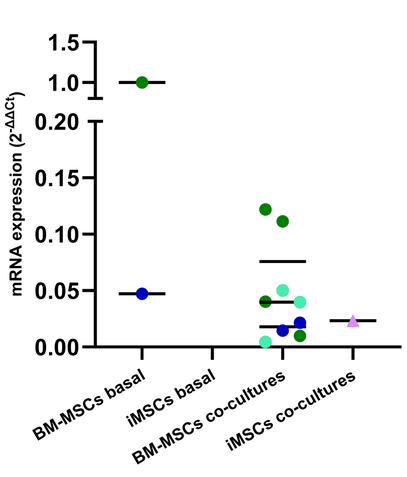
***VCAM1* expression**



***IDO1* expression**

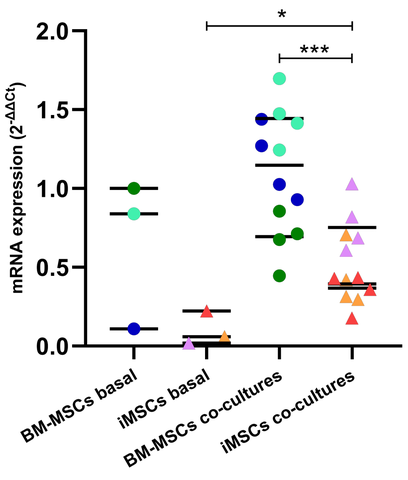


***iNOS2* expression**

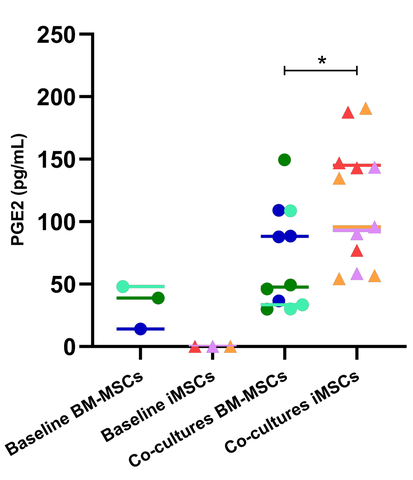


- **Slight induction** of ***VCAM1*** after exposure to activated lymphocytes in **iMSCs**
- **Induction** of ***IDO1*** after exposure to activated lymphocytes in both co-cultures
- Overall **low levels** of ***iNOS2*** expression

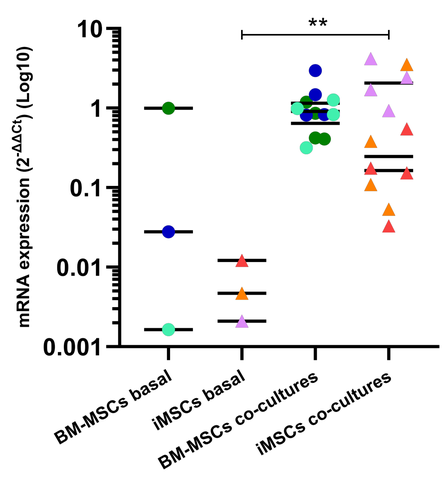
***COX2* expression**



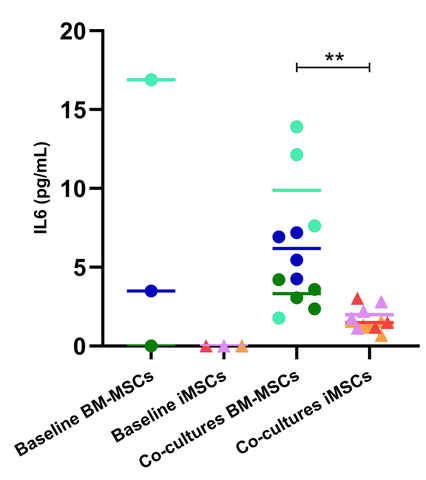
PGE2 secretion



***IL6* expression**



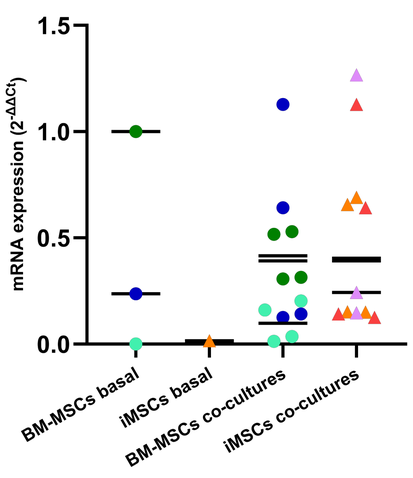
IL-6 secretion



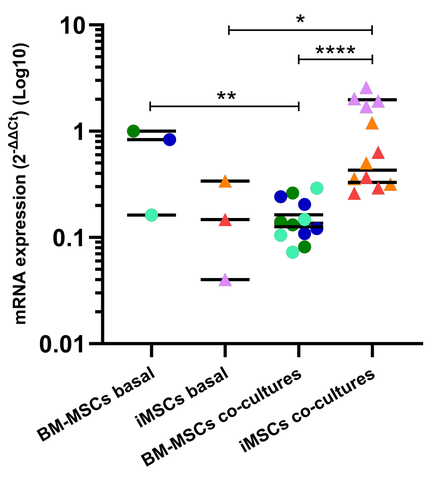
- ↑ ***COX2*** expression after the co-culture in **BM-MSCs** but ↑ **PGE2** secretion after the co-culture in **iMSCs**
- **Induction** of ***IL6*** expression after exposure to activated lymphocytes
- **Higher IL-6 secretion** in co-cultured **BM-MSCs** than in co-cultured **iMSCs**

IMMUNOGENIC PROFILE

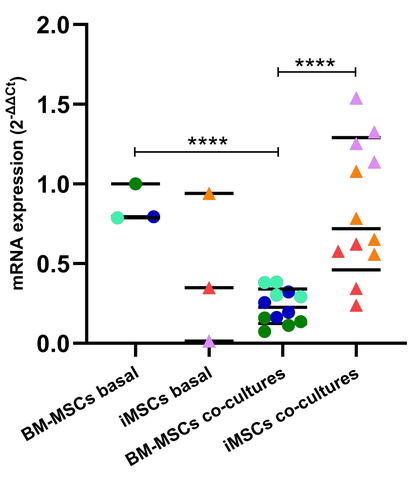
***MHC-I* expression**



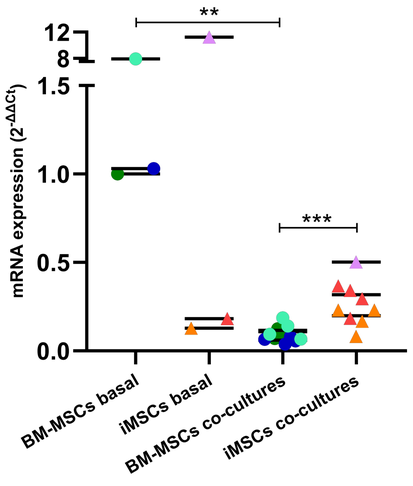
***MHC-II* expression**



***CD40* expression**



***CD80* expression**



- ↓ expression in **basal iMSCs** compared to **BM-MSCs**
- ↑ gene expression in **iMSCs co-cultures** than in **BM-MSCs co-cultures**

Donor 1 BM-MSCs · Donor 2 BM-MSCs · Donor 3 BM-MSCs · Line 1 iMSCs · Line 2 iMSCs · Line 3 iMSCs

Reference sample → BM-MSCs donor 1

* = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$; **** = $p < 0.0001$

CONCLUSIONS

- **Equine iMSCs** present a **lower immunomodulatory profile in basal conditions** but it is more **strongly induced** upon interaction with **activated allogeneic lymphocytes** → potential implications for their **therapeutic effectiveness**.
- Changes observed in **iMSCs' immunogenic profile** after their interaction with immune cells warrants **further investigation** to ensure that they could be **safely** administered.
- To conclude, additional investigation and ***in vivo* assays** are required to establish if iMSCs provide **superior clinical benefits** compared to traditional primary MSCs in equine subjects.

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