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Review Article

Effect of culture environement on mesenchymal stem cell immunomodulatory ability

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Abstract

Mesenchymal Stem cells (MSCs) has fascinating immunomodulatory effect in vitro and in vivo. This effect has been documented by interesting researches worldwide. However the protocols of MSCs culture are different. This difference is translated on different results regarding the mediators as well as on potency of immunomodulatory effect in both vitro and in vivo. In this article we will analyze and discussing the effect of culture environment on MSC immunomodulatory effect.

Introduction

Allogeneic and autologous Mesenchymal Stem Cells (MSC) did not elicit immunological response and has immunomodulatory effect in vitro and in vivo. This effect has been documented by interesting researches worldwide. Previous studies showed that inhibitory mechanisms of MSCs depends on nature of stimulus [1-5]. However the protocols of MSCs culture are different. This difference could be translated on different results regarding the mediators as well as on potency of immunomodulatory effect in both vitro and in vivo.

In this article we will examine and address the impact of the culture environment on immunomodulatory effect taking in account the different utilized serum and other components of cultures, duration, special condition of cultures and inhibitory mediators as well as the magnitude of immunomodulatory effect.

Effect of origins and type of MSC on magnitude of inhibitory effect

Absence of significant stimulation of allogeneic lymphocytes by different type of MSCs has been documented [6]. MSC from different sources; Bone Marrow (BM) [7], Placenta (PL-MSC) [8], Umbilical Cord (UC-MSC) [6], Wharton's Jelly (WJ-MSC) [9], Umbilical Cord Lining (CL-MSCs) and Cord Blood (CB-MSCs) [10], Amniotic Membrane (AM-MSC) [6,11], tonsil [12], cornea [13] and Liver [14], Adipose Tissue (AT-MSC) [15], exert their immunomodulatory effect on immune cells. This could confirm the universal inhibitory effect of MSCs despite their origins or culture environment.

Studies showed that MSC derived from different origins have no difference in the immunomodulatory effect. One comparative study showed that BM-MSC had fewer inhibitory effects than other used MSC on T cell proliferation, while WJ-MSC had most prominent inhibition [15]. Others found no significant differences in ability to inhibit allo-activated immune cells proliferation by MSCs derived from different sources: AM and UC- and AT-MSC [6]. This finding supported by finding that MSCs from different sources had similar partial immunomodulation on Mixed Lymphocyte Reaction (MLR) [16].

In other hand, placenta and umbilical cord from the same donor, showed a significant difference in their immunosuppressive properties as assessed in MLR. The PL-MSCs and their Conditioned Medium (CM) affected the antigen presenting ability of Mononuclear Cells (MNC) and

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Dendritic Cells (DC) significantly as compared to Cord MSCs and their CM resulting in a reduced T-cell proliferation. Furthermore, the CD3(+) CD4(+) CD25(+) T regulatory cells were enriched in case of PL-MSCs [17]. Autologous MSC increased significantly long-term engraftment and tolerance to donor antigen, and allogeneic MSC increased significantly rejection of allogeneic BM cells and induce a memory T-cell response under appropriate conditions resulting in rejection of an allogeneic stem cell graft [18].

Fetal MSC cells made from second trimester amnion, amniotic fluid, and decidua demonstrated a significantly higher inhibition compared with maternal MSC. Fetal MSC mediated inhibition of MLR response mainly by IL-10, while other soluble factors are involved in maternal MSC [11]. Expression of HLA antigens, co-stimulatory factors and immune tolerance molecules are varied among different population of MSC. BM-MSC had the highest MHCII molecules and immune-related genes expression, and WJ-MSCs had the lowest expression [15].

In accordance, BM-MSC decreased significantly Natural Killer Cell (NK) cytotoxic activity and Interferon-γ (IFN-γ) secretion as compared to AT-MSC, despite equal inhibition of NK cell proliferation by both types of MSC. This had a negative impact on Graft Versus Host Disease (GVHD) inhibition and graft versus leukemia effect [19] and could indicate that the underlying mechanisms of MSC inhibitory effect is different according to its origin. This finding could differentiate for the first time between the inhibition of proliferation (quantitative inhibitory effect of MSCs) and the inhibition of underlying mediators (Qualitative effect of MSCs). It's interesting subject for research.

Careful analysis of results is needed. We should specify what we are looking for. Are looking for magnitude or for the underlying actors for this inhibitory effect.

Theoretically, inhibitory effect of MSCs originating from different sources (BM, AT, UC, PL, etc) of one donor should be tested in simultaneous experiments using same immune cells for same duration under same culture conditions.

Practically speaking, we can compare only between BM and UC MSC from ladies giving birth of child. However, these ladies will have difficulty in welcoming a procedure of BM aspiration at that special events especially in case of normal vaginal delivery.

Several published studies were done on human BM and UC MSC. This makes these MSC the most suitable target for future analytical studies.

Du Rocher B, et al. performed MLR for different duration (3,7 days), but they used each for different purposes rather than for comparing the magnitude of inhibitory effect in different time setting [20].

The suppressive effect of MSC derived from severe aplastic anemia patients either at diagnosis or after immunosuppressive therapy on T-cell activation is weaker than MSC derived from normal individuals [21]. Of note, most of cases have been subjected to immunosuppressive therapy insult and subsequent change of MSC environment.

Indoleamine 2,3-Dioxygenase (IDO) implicated on T cell suppression by allogeneic UC-MSCs in lupus patients. This effect induced through IFNγ produced predominantly by lupus CD8+ T cells. In contrast BM MSCs from patients with active lupus demonstrated defective IDO production in response to IFNγ and allogeneic CD8+ T cell stimulation [22]. A comparison between inhibitory effect with only single variable (autologous and allogeneic UC-MSCs versus autologous and allogeneic BM MSC) setting is needed.

In murine model, both allogenic and autologous MSC have similar inhibitory effect [1] in vitro. In contrary, origin of MSC could play a role. MSC from different origin of the same donor have different immunosuppressive effect. Where PL MSCs reduced T cell proliferation, affected the antigen presenting ability, enriched CD3(+) CD4(+) CD25(+) T regulatory cells and increased mRNA expression of FoxP3 as compared to UC MSCs [17].

Liver MSCs showed a higher expression of programmed death-ligand 1 (PD-L1) than BM MSCs, which associated with inhibition of T-cell in vitro [14].

A study showed that MSC from myelodysplastic syndromes (MDS) patients inhibit T-cell proliferation significantly lower than that of normal MSC, and had different mediators expression[23]. This finding could be attributed to MDS effect on BM environment.

MSC generated from BM positive CD271 cells had significantly suppressed the MNC [24]. T lymphocyte proliferation was significantly more inhibited by expanded Stro-1$^+$ [25]. MSC inhibitory mechanisms differ depending on nature of stimulus alloantigens or mitogen [26], where MSC exert inhibitory effect only on PHA activated T lymphocytes through Prostaglandins. This could signify the effect of culture environments on MSC immunomodulatory effect and the role of bidirectional interaction. This is supported by enhancement of MSC inhibitory effect following addition of third party monocytes [27] and expression of IDO by MSC after activation by allogeneic lymphocytes [28,29]. All these reports indicate that immune cells could be responsible for the first stimulating signals in MLR, or at least they are responsible for their modification. This could document the importance of interaction between MSC and culture environment on MSC inhibitory effect, and supported by a study showing that cell contact is required for MSC immunosuppression through upregulation of PD-L1 [30].

3-Effect of MSC thawing on magnitude of inhibitory effect

Most of published works reported post thaw cultured MSC immunosuppressive effect [7,31,32]. No difference in the suppression of lymphocyte proliferation by non-cultured post-thaw CB-MSC and that undergone post-thaw culture [33]. Viability did not differ significantly in MSC before freeze or after thaw, but cell health as measured by population doublings

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decreased with increased number of pre freeze passage. Donors variability, sample quality, method and freezing rate, cryopreservation solution and viability of post thaw MSC affect MSC outcome and culture environment with time[34,35].

Good manufacturing process was used to standardize the conditions of harvest and replication of cultured MSC. No changes after cryopreservation were noted in viability, surface antigens, ability of differentiation, malignant transformation, immunosuppressive effect and karyotypes as opposed to fresh MSCs [36]. This finding supported by finding that third party cryopreserved CB MSC can be used directly post thaw without culture [33].

Freshly thawed cryopreserved MSC are compromised in suppressing CD3/CD28-driven T cell proliferation. This is fully restored after 24 hours Post thawing MSC culture [37] and mitigated by use of IFNγ prelicensed thawed MSCs [38]. This could indicate that MSC are subjected to environment cryoinjuries and could explain the cause for inefficacy of MSC-based immunotherapy reported in clinical trials using cryopreserved MSC thawed immediately prior to infusion,.

Thawed AT-MSC had significant increase in pro-coagulant activity, and microenvironment encountered by MSC after administration may impact their modulation of inflammatory responses, as exposure to the lung microenvironment affected immunological pathways [39].

Cells harvested from continuous cultures have better immunomodulatory effect as compared to freeze-thawed MSCs. Improved clinical outcome with 100% response rate was obtained from fresh and low passage cells, twice the response rate observed in patients treated with freeze-thawed cells at higher passage [40]. This finding indicate need for further studies on effect of MSC environment in clinical setting. Paired comparison between fresh and freeze-thawed cells at low and higher passage are needed.

Effect of culture duration on magnitude of inhibitory effect

Immunomodulatory effect of MSCs on MLR has been reported on different duration; 3, 4, 5, 6 and 7 days. Significant inhibitory effect of MSCs on allogeneic MLR of 3 days duration has been reported [7,20, 31,41]. This inhibitory effect has been reported also by others on day 4 [42], day 5 [28,43], day 6 [44] and in culture of 7 days duration [20]. The origins of inhibited cells are different. Some of cells are autologous and some are allogeneic. In addition the nature of the cells are different; few are selected CD2 or CD3 lymphocytes [32], Dendritic Cells (DC) [45], Monocytes [20], B cells [46,47] and polymorphic mononuclear cells PMN [2], NK cells [19], CD4 and CD8 subsets of T lymphocytes [48]. These findings showed universal immune-modulatory capacity of MSCs despite diversity of culture environment responsive immunogenic cells and culture duration.

Difference in inhibitory mediators according to ratio of MSCs

MSC elicit more important immunomodulatory function on higher ratios [3,32]. There is a variable immunomodulatory function based on MSC ratios, where low numbers of MSC increasing T-cell proliferation [41]. This indicates the need to optimize the dose of injected MSC in order to have a favorable inhibitory effect in vivo. It seems to be that higher dose of MSC create a favorable environment for enhanced immunomodulatory effect.

Difference in inhibitory effect mediators according to culture duration (assessment day)

There is a contradictory results regarding detected inhibitory mediators expressed by MSCs in MLR. Future studies comparing between MSC from different origins and inhibitory mediators (molecular, protein and regulatory cells) expressed by MSCs cultured for different durations; 3, 4,5, 6 and 7 days is mandatory.

Molecular inhibitory mediators

We reported the molecular expression by human MSC of TGF-B, Interleukin-10 (IL-10), Human Leukocyte Antigen-G (HLA-G), IDO and Leukemia Inhibitory Factor (LIF) in cultures with or without direct contact. However TGF-B and Il-10 were markedly increased in culture with direct contact. Expression of different genes by MSC in MLR has been reported despite using MSC from variable origins and species in different culture protocols [17,30,32,49].

Soluble inhibitory mediators and regulatory cells induction

Soluble factors and regulatory cells are implicated on MSC inhibitory effect despite difference in MSC origins and source, culture media, responding immune cells [7,10-15,17,28,30-32,43,50-59].

Effect of inflammatory environment

MSC immunomodulatory effect could be altered by local pro-inflammatory environment. BM-MSC and AT-MSC cultured with pro-inflammatory cytokines interleukin-1B (IL-1b), IL-6 and interleukin-23 (IL-23) showed suppressive ability of MSC on allogeneic T cell with significant increase of TGF-β and lower level of interleukin-4 (IL-4). This result is promising in cell-based therapy of degenerative, inflammatory and autoimmune disorders [60]. Treatment of corneal stroma derived MSC by pro-inflammatory cytokines and toll-like receptor ligands significantly increased cell surface adhesion and secretion of IL-6, interleukin-8 (IL-8) and C-X-C motif chemokine 10 (CXCL-10) levels [13].

MSC supernatant has an inhibitory effect in secondary MLR, but less important than primary MLR [3]. The immunosuppression of human MSCs is higher in cultures with direct contact than in cultures with indirect contact [9,14,32,61].

The contradictory result regarding the suppressive effect of MSC in culture without direct contact [3,62], could be explained partly by the need of higher MSC: lymphocyte ratio [29]. IDO gene expression was induced in WJ MSCs by

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inflammatory cytokine IFN-γ. Stimulation of WJ-MSCs by a relatively low concentration of IFN-γ does not lead to Human leukocyte antigen (HLA-DR) expression. WJ-MSCs exert their inhibitory effects by cell-cell contact with activated T cells and in part through IDO rather than soluble factors to achieve immunomodualation in severe cases of GVHD [9].

All these results could indicate that culture environment; presence of direct contact, availability of high concentration of different inflammatory cytokine, as well as MSC origin play a role in MSC immunomodulatory effect.

HLA-G expression is maintained after osteo-differentiation and can be boosted in inflammatory conditions mimicked by the addition of IFN-γ and TNF-α [63]. This stress on effect of surrounding culture environment in MSC immunomodulation.

MSC as a component of the hematopoietic microenvironment, could be targeted by alloreactivity of effector cells and inflammatory milieu induced by GVHD. Result showed three fold decrease of colony-forming unit (CFU) macrophage [64]. This finding supported by published results showing the non-beneficial effect of MSC infused for GVHD management. However, further researches are needed for definitive conclusion.

Others reported that immunomodulatory functions of MSC could be altered by pro-inflammatory cytokines such as IL-1b, IL-6 and IL-23. However, suppressive ability and efficacy of MSC in cell-based therapy was preserved through pro-inflammatory cytokine modulation [60].

Effect of nature and treatment of responding immunological cells on MSC response to inhibitory effect

Expression of IDO [10,28,65,66], HLA-G [7,63,67,68], LIF [31,69], PGE2 [70] , IL-10 [11,17,30,32], TGF-B [8,17, 32] and other mediators were reported by many researchers despite use of variable culture conditions with different density, ratio, treatment protocol, nature and method of selection of immune cells.

MSC act as secretome with universal constitutive secretion of immunomediators as evidenced by several reports worldwide. However, intervention of all parameters on MSC culture environment, and alternation of immunosuppressive effect needs future structured studies.

Effect of radiation on MSCs inhibitory effect

Both irradiated and non-irradiated BM-MSC from healthy donors and Autoimmune Disease (AD) patients had a suppressive effect on autologous and allogeneic PBMCs. [71]. Surprisingly, MSC from AD are not compromised in their immune response. However, others found that MSC surviving irradiation changed their cytokine secretion profile and became prematurely senescent. [72]. Effect of irradiation on MSC needs further exploration.

Effect of donor age on MSCs growth

Growth of MSC obtained from younger rats is faster and has more prominent inhibitory effect as compared with old animals. Aged AT MSC failed to induce any CD3(+)CD4(+) T cell suppression. Young MSC induced suppression was more prominent than seniors [73].

Studies are needed to study the difference in inhibitory effect between human MSC obtained from old and young individuals. Of note, MSCs obtained from bone marrow during total hip replacement is not an optimal source. As usually large number of these patients are old and many have concomitant or co-existing health problems.

Discussion and recommendation

Effect of culture environment on MSC should be studied on profound back ground

A closer look to the immunosuppressive effect of MSC should be studied on one way and 2 ways culture, as bidirectional interaction could imply several additional mediators and it's representative of real in vivo situation.

Efficient MSC transplantation needs standardized harvesting and cryopreservation procedures. Advanced standardized clinical studies adhering to GMP and quality assurance system for safe clinical grade production should be conducted.

These studies have to compare between same players on different experiments. Definition of all items (origin and enrichment procedures of human MSC (BM, UC and PL MSC), use of PMNC in two ways MLR, ratio of MSC: PMNC, culture medium (calf or human serum) and culture duration are highly recommended.

PL-MSCs could represent an amazing splendid life giving source from young ladies for promising future therapeutic tool in regenerative medicine, as they act on qualitative and quantitative aspect of immune cell inhibition.

International Society for Cellular Therapy (ISCT) identified three preferred analytic methods: quantitative RNA analysis of selected gene products; flow cytometry analysis of functionally relevant surface markers and protein-based assay of secretome [74].

The contradiction on magnitude of MSC inhibitory effect, and the involvement of soluble mediators and regulatory cells in MSC suppressive activity could be affected by the culture environment. Use of non-irradiated MSC, and non-treated or selected PMNC cells will simulate in vivo conditions and will permit the interaction between all immune mediators.

Use of freshly retrieved MSC from continuous culture [40] for intravenous injection without freezing should be assessed along with others factors.

Despite different culture media and culture duration as well as different nature and treatment of responding immunological cells on MLR, most researchers showed implication of several soluble inhibitory mediators and increase of regulatory cells.

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However we cannot withdraw a conclusion from these variable experiments and clinical trials for the time being. We noticed that HLA-G was expressed significantly only on day 3 of co-culture but not on day 6 (unpublished observation).

In addition, study of galectins 1, 9, 11 and 13 expression by BM-MSC with or without differentiation, and cultivated in three culture mediums (standard medium: alpha-MEM+FGF2, the medium (with 5% Human Platelets Lysate (HPL)), the medium (10% HPL), showed that expression of different galectins are depend on the composition of the culture medium and type of galectin [75]. This finding should be taken in account in future studies, as it confirm implication of culture media in MSC changes. Recently, Sierra Parraga JM, et al. found that thawing of MSC affect adherence, viability, increased oxidative stress, and reduced mitochondrial activity, which implies reduced metabolism and survival of MSC [76].

Conclusion and future perspective

There is great need for consensus aiming at optimization of MSC-based therapeutic approaches in immunological diseases and GVHD.

Researches in agreement with consensus criteria of MSCs [77], with selection of MSC origin, specification of culture conditions and duration, knowing of MSC peak inhibitory effect, elucidation of core inhibitory mediators, and their implication in different time of expansion and MSC-MLR co-culture by using a matrix assay approach [78], could help in future definition of most appropriate MSC origin, culture condition, MSC retrieval time and therapeutic injection for management of immunological diseases and GVHD.

References

1. Sudres M, Norol F, Trenado A, Gregoire S, Charlotte F, et al. (2006) Bone marrow mesenchymal stem cells suppress lymphocyte proliferation in vitro but fail to prevent graft-versus-host disease in mice. J Immunol 176: 7761-7767. Link: https://bit.ly/2xc1j9L

2. Bartholomew A, Sturgeon C, Siatskas M, Ferrer K, McIntosh K, et al. (2002) Mesenchymal stem cells suppress lymphocyte proliferation in vitro and prolong skin graft survival in vivo. Exp Hematol 30: 42-48. Link: https://bit.ly/2xc1emt

3. Djouad F, Plence P, Bony C, Tropel P, Apparailly F, et al. (2003) Immunosuppressive effect of mesenchymal stem cells favors tumor growth in allogeneic animals. Blood 102: 3837-3844. Link: https://bit.ly/3aTs95c

4. Maitra B, Szekely E, Gjini K, Laughlin MJ, Dennis J, et al. (2004) Human mesenchymal stem cells support unrelated donor hematopoietic stem cells and suppress T-cell activation. Bone Marrow Transplant 33: 597-604. Link: https://go.nature.com/2Xinoy1

5. Yanez R, Lamana ML, Castro JG, Colmenero I, Ramírez M, et al. (2006) Adipose tissue-derived mesenchymal stem cells have in vivo immunosuppressive properties applicable for the control of the graft-versus-host disease. Stem Cells 24: 2582-2591. Link: https://bit.ly/2RmcnYO

6. Dabrowski FA, Burdzinska A, Kulesza A, Chlebus M, Kaleta B, et al. (2017) Mesenchymal Stem Cells from Human Amniotic Membrane and Umbilical Cord Can Diminish Immunological Response in an in vitro Allograft Model. Gynecol Obstet Invest 82: 267-275. Link: https://bit.ly/2RkLzId

7. Nasef A, Mathieu N, Chapel A, Frick J, François S, et al. (2007) Immunosuppressive effects of mesenchymal stem cells: involvement of HLA-G. Transplantation 84: 231-237. Link: https://bit.ly/2URP23h

8. Kim SH, Jung J, Cho KJ, Choi JH, Lee Hs, et al. (2018) Immunomodulatory Effects of Placenta-derived Mesenchymal Stem Cells on T Cells by Regulation of FoxP3 Expression. Int J Stem Cells 11: 196-204. Link: https://bit.ly/3b4rxtH

9. He H, Nagamura-Inoue T, Takahashi A, Mori Y, Yamamoto Y, et al. (2015) Immunosuppressive properties of Wharton's jelly-derived mesenchymal stromal cells in vitro. Int J Hematol 102: 368-378. Link: https://bit.ly/3c1v1wQ

10. Stubbendorff M, Deuse T, Hua X, Phan TT, Bieback K, et al. (2013) Immunological properties of extraembryonic human mesenchymal stromal cells derived from gestational tissue. Stem Cells Dev 22: 2619-2629. Link: https://bit.ly/2RfNkGP

11. Roelen DL, van der Mast BJ, in't Anker PS, Kleijburg C, Eikmans M, et al. (2009) Differential immunomodulatory effects of fetal versus maternal multipotent stromal cells. Hum Immunol 70: 16-23. Link: https://bit.ly/2UVcPQ1

12. Ding G, Wei L, Sun W, Zhang L (2015) The immunological characteristics of tonsil mesenchymal stem cells. Zhonghua Zheng Xing Wai Ke Za Zhi 31: 43-48. Link: https://bit.ly/3c1TvX2

13. Vereb Z, Póliska S, Albert R, Kristoffer Olstad O, Boratkó A, et al. (2016) Role of Human Corneal Stroma-Derived Mesenchymal-Like Stem Cells in Corneal Immunity and Wound Healing. Sci Rep 6: 26227. Link: https://bit.ly/2K0GqRT

14. de Mare-Bredemeijer EL, Mancham S, Verstegen MM, de Ruiter PE, van Gent R, et al. (2015) Human graft-derived mesenchymal stromal cells potently suppress alloreactive T-cell responses. Stem Cells Dev 24: 1436-1447. Link: https://bit.ly/2UQZUyd

15. Li X, Bai J, Ji X, Li R, Xuan Y, et al. (2014) Comprehensive characterization of four different populations of human mesenchymal stem cells as regards their immune properties, proliferation and differentiation. Int J Mol Med 34: 695-704. Link: https://bit.ly/2Vgo4Bg

16. Ock SA, Baregundi Subbarao R, Lee YM, Lee JH, Jeon RH, et al. (2016) Comparison of Immunomodulation Properties of Porcine Mesenchymal Stromal/Stem Cells Derived from the Bone Marrow, Adipose Tissue, and Dermal Skin Tissue. Stem Cells Int 9581350. Link: https://bit.ly/3bZ9IBr

17. Talwadekar MD, Kale VP, Limaye LS (2015) Placenta-derived mesenchymal stem cells possess better immunoregulatory properties compared to their cord-derived counterparts-a paired sample study. Sci Rep 5: 15784. Link: https://bit.ly/34l1ZWp

18. Nauta AJ, Westerhuis G, Kruisselbrink AB, Lurvink EG, Willemze R, et al. (2006) Donor-derived mesenchymal stem cells are immunogenic in an allogeneic host and stimulate donor graft rejection in a nonmyeloablative setting. Blood 108: 2114-21120. Link: https://bit.ly/3c1U1UY

19. Blanco B, Herrero-Sánchez MD, Rodríguez-Serrano C, García-Martínez ML, Blanco JF, et al. (2016) Immunomodulatory effects of bone marrow versus adipose tissue-derived mesenchymal stromal cells on NK cells: implications in the transplantation setting. Eur J Haematol 97: 528-537. Link: https://bit.ly/2VfAZDy

20. Du Rocher B, Mencalha AL, Gomes BE, Abdelhay E (2012) Mesenchymal stromal cells impair the differentiation of CD14(++) CD16(-) CD64(+) classical monocytes into CD14(++) CD16(+) CD64(++) activate monocytes. Cytotherapy 14: 12-25. Link: https://bit.ly/2xWxM3R

21. Bacigalupo A, Valle M, Podestà M, Pitto A, Zocchi E, et al. (2005) T-cell suppression mediated by mesenchymal stem cells is deficient in patients with severe aplastic anemia. Exp Hematol 33: 819-827. Link: https://bit.ly/2UQcRIQ

22. Wang D, Feng X, Lu L, Konkel JE, Zhang H, et al. (2014) A CD8 T cell/indoleamine 2,3-dioxygenase axis is required for mesenchymal stem cell suppression of human systemic lupus erythematosus. Arthritis Rheumatol 66: 2234-2245. Link: https://bit.ly/2V97fbD

Citation: Nasef A, Chapel A, Fouillard L (2020) Effect of culture environement on mesenchymal stem cell immunomodulatory ability. Stud Stem Cells Res Ther 6(1): 009-0015. DOI: https://dx.doi.org/10.17352/sscrt.000015

23. Liu LH, Chen H, Chen B, Sun Z, Ye LP, et al. (2008) Immuno-suppressive effects on T cells mediated by mesenchymal stem cells from patients with myelodysplastic syndrome. Zhongguo Shi Yan Xue Ye Xue Za Zhi 16: 299-304. Link: https://bit.ly/34oIOLA

24. Kuçi Z, Kuçi S, Zircher S, Koller S, Schubert R, et al. (2011) Mesenchymal stromal cells derived from CD271(+) bone marrow mononuclear cells exert potent allosuppressive properties. Cytotherapy 13: 1193-1204. Link: https://bit.ly/2wkyoQi

25. Nasef A, Zhang YZ, Mazurier C, Bouchet S, Bensidhoum M, et al. (2009) Selected Stro-1-enriched bone marrow stromal cells display a major suppressive effect on lymphocyte proliferation. Int J Lab Hematol 31: 9-19. Link: https://bit.ly/2XicCb2

26. Rasmusson I, Ringdén O, Sundberg B, Le Blanc K (2005) Mesenchymal stem cells inhibit lymphocyte proliferation by mitogens and alloantigens by different mechanisms. Exp Cell Res 305: 33-41. Link: https://bit.ly/2xezyNP

27. Groh ME, Maitra B, Szekely E, Koç ON (2005) Human mesenchymal stem cells require monocyte-mediated activation to suppress alloreactive T cells Exp Hematol 33: 928-934. Link: https://bit.ly/34iOPcF

28. Meisel R, Zibert A, Laryea M, Göbel U, Däubener W, et al. (2004) Human bone marrow stromal cells inhibit allogeneic T-cell responses by indoleamine 2,3-dioxygenase-mediated tryptophan degradation. Blood 103: 4619-4621. Link: https://bit.ly/2xaFp6E

29. Nasef A, Ashammakhi N, Fouillard L (2008) Immunomodulatory effect of mesenchymal stromal cells: possible mechanisms. Regen Med 3: 531-546. Link: https://bit.ly/3c5l2H3

30. Luz-Crawford P1 Noël D, Fernandez X, Khoury M, Figueroa F, et al. (2012) Mesenchymal stem cells repress Th17 molecular program through the PD-1 pathway. PLoS 7: e45272. Link: https://bit.ly/39SX7Jk

31. Nasef A, Mazurier C, Bouchet S, François S, Chapel A, et al. (2008) Leukemia inhibitory factor: Role in human mesenchymal stem cells mediated immunosuppression. Cell Immunol 253: 16-22. Link: https://bit.ly/3aTdd75

32. Nasef A, Chapel A, Mazurier C, Bouchet S, Lopez M, et al. (2007) Identification of IL-10 and TGF-beta transcripts involved in the inhibition of T-lymphocyte proliferation during cell contact with human mesenchymal stem cells. Gene Expr 13: 217-226. Link: https://bit.ly/3aTdeHX

33. Williams LB, Tessier L, Koenig JB, Koch TG (2014) Post-thaw non-cultured and post-thaw cultured equine cord blood mesenchymal stromal cells equally suppress lymphocyte proliferation in vitro. PLoS One 9: e113615. Link: https://bit.ly/3e4vIaF

34. Pollock K, Sumstad D, Kadidlo D, McKenna DH, Hubel A (2015) Clinical mesenchymal stromal cell products undergo functional changes in response to freezing. Cytotherapy 17: 38-45. Link: https://bit.ly/2Xl3K4j

35. Naaldijk Y, Staude M, Fedorova V, Stolzing A (2012) Effect of different freezing rates during cryopreservation of rat mesenchymal stem cells using combinations of hydroxyethyl starch and dimethylsulfoxide. BMC Biotechnol 12: 49. Link: https://bit.ly/3c6TuBb

36. Luetzkendorf J, Nerger K, Hering J, Moegel A, Hoffmann K, et al. (2015) Cryopreservation does not alter main characteristics of Good Manufacturing Process-grade human multipotent mesenchymal stromal cells including immunomodulating potential and lack of malignant transformation. Cytotherapy 17: 186-198. Link: https://bit.ly/2xcEUsW

37. Francois M, Copland IB, Yuan S, Romieu-Mourez R, Waller EK, et al. (2012) Cryopreserved mesenchymal stromal cells display impaired immunosuppressive properties as a result of heat-shock response and impaired interferon-gamma licensing. Cytotherapy 14: 147-152. Link: https://bit.ly/2JQ6kaQ

38. Chinnadurai R, Copland IB, Garcia MA, Petersen CT, Lewis CN, et al. (2016) Cryopreserved Mesenchymal Stromal Cells Are Susceptible to T-Cell Mediated Apoptosis Which Is Partly Rescued by IFNgamma Licensing. Stem Cells 34: 2429-2442. Link: https://bit.ly/3c1Vr1K

39. Hoogduijn MJ, de Witte SF, Luk F, van den Hout-van Vroonhoven MC, Ignatowicz L, et al. (2016) Effects of Freeze-Thawing and Intravenous Infusion on Mesenchymal Stromal Cell Gene Expression. Stem Cells Dev 25: 586-597. Link: https://bit.ly/2wmnuJR

40. Moll G, Alm JJ, Davies LC, von Bahr L, Heldring N, et al. (2014) Do cryopreserved mesenchymal stromal cells display impaired immunomodulatory and therapeutic properties? Stem Cells 32: 2430-2442. Link: https://bit.ly/2XeqX8u

41. Zhou Y, Day A, Haykal S, Keating A, Waddell TK (2013) Mesenchymal stromal cells augment CD4+ and CD8+ T-cell proliferation through a CCL2 pathway. Cytotherapy 15: 1195-1207. Link: https://bit.ly/3aSzpOP

42. Potian JA, Aviv H, Ponzio NM, Harrison JS, Rameshwar P (2003) Veto-like activity of mesenchymal stem cells: functional discrimination between cellular responses to alloantigens and recall antigens. J Immunol 171: 3426-3434. Link: https://bit.ly/2Vax0s2

43. Mougiakakos D, Jitschin R, Johansson CC, Okita R, Kiessling R, et al. (2011) The impact of inflammatory licensing on heme oxygenase-1-mediated induction of regulatory T cells by human mesenchymal stem cells. Blood 117: 4826-4835. Link: https://bit.ly/34jP72R

44. Chen JF, Gao J, Zhang D, Wang ZH, Zhu JY, et al. (2010) CD4+Foxp3+ regulatory T cells converted by rapamycin from peripheral CD4+CD25(-) naive T cells display more potent regulatory ability in vitro. Chin Med J 123: 942-948. Link: https://bit.ly/2JQLbxb

45. Sadeghi L, Kamali-Sarvestani E, Azarpira N, Shariati M, Karimi MH (2014) Immunomodulatory effects of mice mesenchymal stem cells on maturation and activation of dendritic cells. Iran J Immunol 11: 177-188. Link: https://bit.ly/3aWawBy

46. Cho KA, Lee JK, Kim YH, Park M, Woo SY, et al. (2017) Mesenchymal stem cells ameliorate B-cell-mediated immune responses and increase IL-10-expressing regulatory B cells in an EBI3-dependent manner. Cell Mol Immunol. Link: https://bit.ly/3c3BCqu

47. Shin TH, Lee BC, Choi SW, Shin JH, Kang I, et al. (2017) Human adipose tissue-derived mesenchymal stem cells alleviate atopic dermatitis via regulation of B lymphocyte maturation. Oncotarget 8: 512-522. Link: https://bit.ly/2UR21SF

48. Crop MJ, Baan CC, Korevaar SS, Ijzermans JN, Alwayn IP, et al. (2009) Donor-derived mesenchymal stem cells suppress alloreactivity of kidney transplant patients. Transplantation 87: 896-906. Link: https://bit.ly/3bXPt1N

49. Kwon MS, Noh MY, Oh KW, Cho KA, Kang BY, et al. (2014) The immunomodulatory effects of human mesenchymal stem cells on peripheral blood mononuclear cells in ALS patients. J Neurochem 131: 206-218. Link: https://bit.ly/34kQWwl

50. Engela AU, Baan CC, Litjens NH, Franquesa M, Betjes MG, et al. (2013) Mesenchymal stem cells control alloreactive CD8(+) CD28(-) T cells. Clin Exp Immunol 174: 449-458. Link: https://bit.ly/39Pfjn3

51. Yang SH, Park MJ, Yoon IH, Kim SY, Hong SH, et al. (2009) Soluble mediators from mesenchymal stem cells suppress T cell proliferation by inducing IL-10. Exp Mol Med 41: 315-324. Link: https://bit.ly/2xc82R3

52. Djouad F, Charbonnier LM, Bouffi C, Louis-Plence P, Bony C, et al. (2007) Mesenchymal stem cells inhibit the differentiation of dendritic cells through an interleukin-6-dependent mechanism. Stem Cells 25: 2025-2032. Link: https://bit.ly/3aRdoja

53. Pianta S, Bonassi Signoroni P, Muradore I, Rodrigues MF, Rossi D, et al. (2015) Amniotic membrane mesenchymal cells-derived factors skew T cell polarization toward Treg and downregulate Th1 and Th17 cells subsets. Stem Cell Rev 11: 394-407. Link: https://bit.ly/2V6oj1S

54. Cahill EF, Tobin LM, Carty F, Mahon BP, English K (2015) Jagged-1 is required for the expansion of CD4+ CD25+ FoxP3+ regulatory T cells and tolerogenic dendritic cells by murine mesenchymal stromal cells. Stem Cell Res Ther 6: 19. Link: https://bit.ly/2JPmBNi

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55. Prevosto C, Zancolli M, Canevali P, Zocchi MR, Poggi A (2007) Generation of CD4+ or CD8+ regulatory T cells upon mesenchymal stem cell-lymphocyte interaction. Haematologica 92: 881-888. Link: https://bit.ly/2Xq7L7A

56. Maccario R, Podestà M, Moretta A, Cometa A, Comoli P, et al. (2005) Interaction of human mesenchymal stem cells with cells involved in alloantigen-specific immune response favors the differentiation of CD4+ T-cell subsets expressing a regulatory/suppressive phenotype. Haematologica 90: 516-525. Link: https://bit.ly/2yJbG5m

57. Aggarwal S, Pittenger MF (2005) Human mesenchymal stem cells modulate allogeneic immune cell responses. Blood 105: 1815-1822. Link: https://bit.ly/3aUEZQr

58. Beyth S, Borovsky Z, Mevorach D, Liebergall M, Gazit Z, et al. (2005) Human mesenchymal stem cells alter antigen-presenting cell maturation and induce T-cell unresponsiveness. Blood 105: 2214-2219. Link: https://bit.ly/34iQSNT

59. English K, Barry FP, Mahon BP (2008) Murine mesenchymal stem cells suppress dendritic cell migration, maturation and antigen presentation. Immunol Lett 115: 50-58. Link: https://bit.ly/2y03EV8

60. Pourgholaminejad A, Aghdami N, Baharvand H, Moazzeni SM (2016) The effect of pro-inflammatory cytokines on immunophenotype, differentiation capacity and immunomodulatory functions of human mesenchymal stem cells. Cytokine 85: 51-60. Link: https://bit.ly/2wndyjk

61. Di Nicola M, Carlo-Stella C, Magni M, Milanesi M, Longoni PD, et al. (2002) Human bone marrow stromal cells suppress T-lymphocyte proliferation induced by cellular or nonspecific mitogenic stimuli. Blood 99: 3838-3843. Link: https://bit.ly/2JPO5lO

62. Krampera M, Glennie S, Dyson J, Scott D, Laylor R, et al. (2003) Bone marrow mesenchymal stem cells inhibit the response of naive and memory antigen-specific T cells to their cognate peptide. Blood 101: 3722-37229. Link: https://bit.ly/39RzlNT

63. Montespan F, Deschaseaux F, Sensébé L, Carosella ED, Rouas-Freiss N (2014) Osteodifferentiated mesenchymal stem cells from bone marrow and adipose tissue express HLA-G and display immunomodulatory properties in HLA-mismatched settings: implications in bone repair therapy. J Immunol Res 2014: 230346. Link: https://bit.ly/34kS96R

64. Fasslrinner F, Wobus M, Duryagina R, Müller K, Stopp S, et al. (2012) Differential effects of mixed lymphocyte reaction supernatant on human mesenchymal stromal cells. Exp Hematol 40: 934-944. Link: https://bit.ly/2y2joa8

65. Hong J, Hueckelhoven A, Wang L, Schmitt A, Wuchter P, et al. (2016) Indoleamine 2,3-dioxygenase mediates inhibition of virus-specific CD8(+) T cell proliferation by human mesenchymal stromal cells. Cytotherapy 18: 621-629. Link: https://bit.ly/2Rm2LNy

66. Ciccocioppo R, Cangemi GC, Kruzliak P, Gallia A, Betti E, et al. (2015) Ex vivo immunosuppressive effects of mesenchymal stem cells on Crohn's disease mucosal T cells are largely dependent on indoleamine 2,3-dioxygenase activity and cell-cell contact. Stem Cell Res Ther 6: 137. Link: https://bit.ly/2JLAID6

67. Wang JP, Ou-Yang GF (2014) Mechanism of HLA-G participation in inhibiting lymphocyte proliferation by amniotic mesenchymal stem cells. Zhongguo Shi Yan Xue Ye Xue Za Zhi 22: 187-191. Link: https://bit.ly/3e466dQ

68. Selmani Z, Naji A, Zidi I, Favier B, Gaiffe E, et al. (2008) Human leukocyte antigen-G5 secretion by human mesenchymal stem cells is required to suppress T lymphocyte and natural killer function and to induce CD4+CD25highFOXP3+ regulatory T cells. Stem Cells 26: 212-222. Link: https://bit.ly/2RmEgjj

69. Najar M, Raicevic G, Boufker HI, Fayyad-Kazan H, De Bruyn C, et al. (2010) Adipose-tissue-derived and Wharton's jelly-derived mesenchymal stromal cells suppress lymphocyte responses by secreting leukemia inhibitory factor. Tissue Eng Part A 16: 3537-3346. Link: https://bit.ly/3cczVHJ

70. van den Berk LC, Jansen BJ, Snowden S, Siebers-Vermeulen KG, Gilissen C, et al. (2014) Cord blood mesenchymal stem cells suppress DC-T Cell proliferation via prostaglandin B2. Stem Cells Dev 23: 1582-1593. Link: https://bit.ly/2VgrRhY

71. Bocelli-Tyndall C, Bracci L, Spagnoli G, Braccini A, Bouchenaki M, et al. (2007) Bone marrow mesenchymal stromal cells (BM-MSCs) from healthy donors and auto-immune disease patients reduce the proliferation of autologous- and allogeneic-stimulated lymphocytes in vitro. Rheumatolog 46: 403-408. Link: https://bit.ly/3c2q3QE

72. Fekete N, Erle A, Amann EM, Fürst D, Rojewski MT, et al. (2015) Effect of high-dose irradiation on human bone-marrow-derived mesenchymal stromal cells. Tissue Eng Part C Methods 21: 112-122. Link: https://bit.ly/39LVeOA

73. Wu LW, Wang YL, Christensen JM, Khalifian S, Schneeberger S, et al. (2014) Donor age negatively affects the immunoregulatory properties of both adipose and bone marrow derived mesenchymal stem cells. Transpl Immunol 30: 122-127. Link: https://bit.ly/2UR0pZ9

74. Galipeau J, Krampera M, Barrett J, Dazzi F, Deans RJ, et al. (2016) International Society for Cellular Therapy perspective on immune functional assays for mesenchymal stromal cells as potency release criterion for advanced phase clinical trials. Cytotherapy 18: 151-159. Link: https://bit.ly/3e0YZDf

75. Jenhani F (2013) Expression Profile of Galectins (Gal-1, Gal-9, Gal-11 and Gal-13) in Human Bone Marrow Derived Mesenchymal Stem Cells in Different Culture Mediums. Stem Cell Biology in Normal Life and Diseases, Kamran Alimoghaddam, Intech Open. Link: https://bit.ly/2JLLM2X

76. Sierra Parraga JM, Rozenberg K, Eijken M, Leuvenink HG, Hunter J, et al. (2019) Effects of Normothermic Machine Perfusion Conditions on Mesenchymal Stromal Cells. Front Immunol 10: 765. Link: https://bit.ly/39U3Q5Q

77. Krampera M, Galipeau J, Shi Y, Tarte K, Sensebe L, et al. (2013) Immunological characterization of multipotent mesenchymal stromal cells–The International Society for Cellular Therapy (ISCT) working proposal. Cytotherapy 15: 1054-1061. Link: https://bit.ly/3c2qsTa

78. Chinnadurai R, Rajan D, Qayed M, Arafat D, Garcia M, et al. (2018) Potency Analysis of Mesenchymal Stromal Cells Using a Combinatorial Assay Matrix Approach. Cell Reports 2504-2517. Link: https://bit.ly/34l6sbD

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