Effect of Application of Mesenchymal Stem Cells Cultured With Different Immunosuppressive Agents On Rejection of Discordant Skin Xenograft

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Nothing to disclose
Objective

We investigated the effect of Mesenchymal Stem cells (MSCs) modified with different immunosuppressant agents on CD8+ T cell dependent cellular rejection of skin xenografts.
Materials and methods

Protocol

In-vitro

1. Immunsuppressive solutions
2. T cells isolation (rat)
3. MSCs isolation (rat)
4. MSCs cocultured with Immunsuppressive agent solutions (cyclosporin, evoralimus, tacrolimus, mikofenolat) to get modified stem cells (mMSCs)
Materials and methods

Protocol

In-vivo

1. Getting skin xenografts (Abdominoplasty material)
2. Creating Rat dorsal skin defect (2x2 cm)
3. Skin grafting
4. Injection of modified stem cells (mMSCs) on graft bed
Materials and methods (Invitro)
Materials and methods (Invivo)
Materials and methods

- SPSS 17.00
- Univariate ANOVA
- Kruskall-Vallis
- Mann-Whitney U
- Kaplan-Meier
- p < 0.05
Results

Decreased inhibitor effect of MSCs' on CD8+ T cell activation in the groups of cyclosporine A, tacrolimus and everolimus modified MSCs compared with naive MSCs and the mycophenolate modified MSCs (p<0.05)
Results

Proinflammatory cytokines, IL-2, IL-6 and IFN gamma, levels were high in the groups of cyclosporine A, tacrolimus and everolimus modified MSCs compared with naive MSCs and the mycophenolate modified MSCs (p<0.05).
The mean skin xenograft survival was 7.3 days in the control group.

The mean skin xenograft survival (11.7 days) was similar in the naive MSCs group and the modified groups (p>0.05).
Results

Skin xenograft survival time (day)

- Xenograft: 7.3 days
- MSCs: 11.8 days
- mMSCs(cyc-a): 11.7 days
- mMSCs(evo): 11.1 days
- mMSCs(Tac): 11.4 days
- mMSCs(MMF): 11.6 days
Conclusion

MSC modified with Cs A, tacrolimus, everolimus was found to have decreased immunosuppressive effects on CD8+ T cells and increased proinflammatory cytokines with contrast to modified with MMF.
Better understanding of interaction between MSC and different immunosuppressive drugs is thought to allow more successful skin xenotransplantation.