

Gulhane Military Medical Academy

Haydarpaşa training Hospital

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. Immunosuppressive solutions**
- 2. T cells isolation(rat)**
- 3. MSCs isolation(rat)**
- 4. MSCs cocultured with Immunosuppressive agent solutions(cyclosporin, evoralimus, tacrolimus, mikofenolat) to get modified stem cells (mMSCs)**

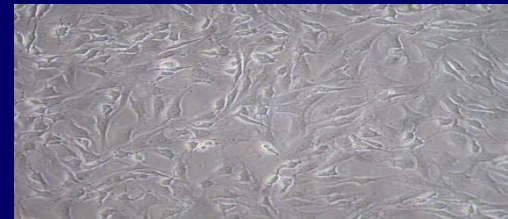
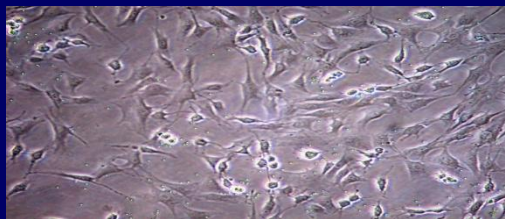
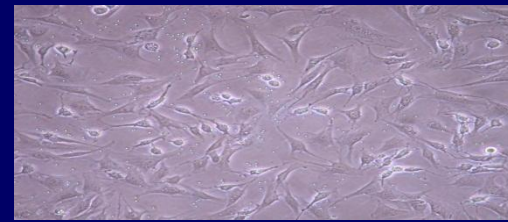
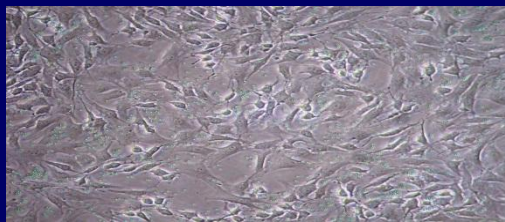
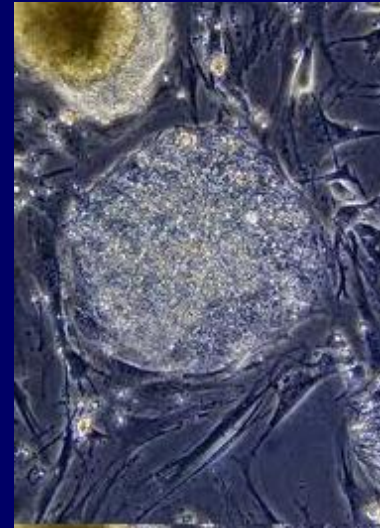
Materials and methods

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
- Kruskal-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 ($p < 0.05$).

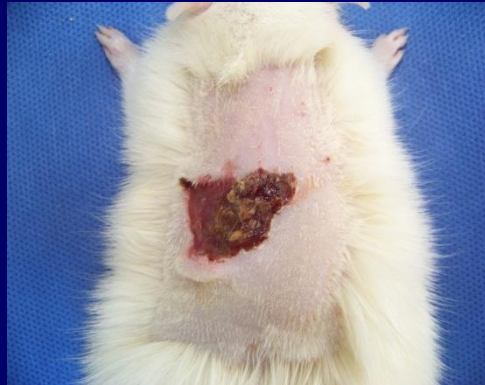
Results

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 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

Conclusion

Better understanding of interaction between MSC and different immunosuppressive drugs is thought to allow more successful skin xenotransplantation.